FACULTY OF PSYCHOLOGY
AND EDUCATIONAL SCIENCES

Depression prevention: Examining the causal role of cognitive control in depression vulnerability

Kristof Hoorelbeke

Supervisor: Prof. Dr. Ernst H. W. Koster

A dissertation submitted to Ghent University in partial fulfilment of the requirements for the degree of Doctor of Psychology

Academic year 2016–2017

GHENT
UNIVERSITY

FACULTY OF PSYCHOLOGY
AND EDUCATIONAL SCIENCES

Depression prevention:
Examining the causal role of cognitive control in depression vulnerability

Kristof Hoorelbeke

Supervisor: Prof. Dr. Ernst H.W. Koster

A dissertation submitted to Ghent University in partial fulfilment of the requirements for the degree of Doctor of Psychology

Academic year 2016-2017

GHENT
UNIVERSITY

Guidance Committee

Prof. Dr. Ernst H. W. Koster (promotor)

Department of Experimental-Clinical and Health Psychology, Ghent University.

Prof. Dr. Bart Soenens

Department of Developmental, Personality and Social Psychology, Ghent University.

Dr. Valentina Rossi

Department of Experimental-Clinical and Health Psychology, Ghent University.

Dr. Dimitri Van Ryckeghem

Department of Experimental-Clinical and Health Psychology, Ghent University.

Prof. Dr. Lesley Verhofstadt

Department of Experimental-Clinical and Health Psychology, Ghent University.

ACKNOWLEDGEMENTS

Life is a concept, like the "universe",
that expands as soon as we reach what we think is its edge. – Kamand Kojouri

Allow me to arouse our collective Amygdala before exposing you to a 300+ pages long exercise of prefrontal-brain-area-demolishing cognitive control. The process of writing a PhD is a long and sometimes lonely one. However, many people were present during this journey to compensate for this, as lights on the horizon guiding my way, as passengers, or even supporters alongside the road encouraging me to keep pursuing my goals. Some of you walked in and out of my life as our roads crossed, only to pop back up a couple of intersections later. Others were always present, supporting me unconditionally. This section goes out to all of you.

First, a special thanks to the Master Yoda of this story, Ernst, my supervisor. Thank you for all the opportunities you've given me which allowed me to further develop my skills and grow as a researcher, lecturer, and clinician / psychotherapist. Thank you for encouraging me to try to reach the seemingly impossible, to push my boundaries, to challenge my thoughts and perspectives, while granting me the freedom to pursue my interests in the field of experimental psychopathology. Thank you for your enthusiasm, support, feedback, and mentoring. I literally could not have done it without you! Whatever may come next, I believe we already accomplished some great things together during this journey and I hope this may continue for the future… Also thanks to the members of my guidance committee, Prof. dr. Lesley Verhofstadt, Prof. dr. Bart Soenens, dr. Valentina Rossi, and dr. Dimitri Van Ryckeghem, for the constructive feedback during our yearly meetings!

A second big 'thanks' goes out to all the interesting colleagues I met during my PhD, with a special thanks to some of my (former) close colleagues at the

Psychopathology and Affective Neuroscience (PAN) lab. Lynn, as my 'godmother' at UGent you introduced me to how things are done at the Faculty of Psychology and Educational Sciences during my early days here. Your kindness, patience (☺), sense of humour, in combination with your ability to always provide sober on the spot analyses of the situation didn't go unnoticed. I'm glad I also had the privilege to share the postgraduate CBT specialisation with you during the past three years. Thomas, you have the unique ability to surround yourself with positive energy and make everyone smile. It's almost magical. "What would Thomas do / think / say?", Laura and I often asked ourselves upon confrontation with difficult situations typical to conducting research. Of course both of us didn't act on it, as this probably would raise additional problems along the road. Ineke, for many of us you have been – and remain to be – a beacon of support and trust within the lab. Thank you for your support, your wisdom, and for always being available for your colleagues. It's people like you who blur the lines between the word "colleague" and "friend". I really enjoyed our research collaborations. Also "Thank you Laura!", with whom I've shared an office during the past four years. We started this chapter of our lives together and are now both approaching the end of it. It has been a real rollercoaster and I'm happy to have shared both the ups and downs of writing a PhD dissertation with you! Thank you Lin, who joined our battle against the clock in our office at the very last of these four years, and Selene and Jonathan, the ever happy PANlab couple. Thank you Jasmien, for your conscientious contributions to the PrevenD project. Elien, Jasmien, Nathan, and Lien, it has been an honour to get to know you better as your 'godfather' at UGent. I wish all of you the best for the future and am looking forward to continue our interesting collaborations! From here, we shift into a higher gear: thank you Rudi, Marie-Anne, Chris, Gilles, Sven, Anouk, Igor, Maud, Alvaro, Antonio, Jonas, Jasmina, Lien, Ivan, Katharina, Anna, Sara, Jozefien, Davide, Luyan, Mario, Priska, Sophie, Nele, Naomi, Romain, Berna, Jill, Wioleta, Kathryn, Lena, Malvika, ... Thank you for the talks, the smiles, the ideas, lunch meetings, collaborations, … Also thanks to my friends from the Family lab (Céline, Marieke, Joke, …), the Developmental Disorders lab (Rachida, Elke G., Elke B., Annabel, Sara, Valerie, Chloé, Ellen, …), Yolandi, and my colleagues from the Health Psychology and LIP lab. You make FPPW a nicer place!

During my PhD I also had the opportunity to go abroad for several conferences and courses (Miami, Amsterdam, Geneva, Vienna, Stockholm, Melbourne, …) where I met a lot of interesting people. Thank you to my friends from Leuven, Maddy, Isa, Marlies, … it's always nice to meet up with you abroad! Thank you Ulrike for the interesting Ghent – Berlin collaboration. Also thanks to Rebecca, Berenice, Samantha, and many other academic colleagues and international friends I've acquired along the way! I even went all the way Down Under for a research stay at the University of Western Australia, Perth. Thank you Colin, for kindly welcoming me to the CARE lab and sharing your interesting insights with me! Thank you Lies and Stijn, for making me feel at home in Australia right away. Thank you Henry, Ines, Bronwyn, Matthew, Georgina, Owen, Ben, Stephanie, Dan, Nigel, Patrick, Julian, … All of you contributed to this amazing experience!

Back to Ghent: thank you Sylvie, Annick, Wouter, Willem, and Linde for all the administrative help along the way. Thank you Chantal and colleagues, for brightening up the cafeteria. Thank you Roland, Jan, and Lemke, for your clinical insights and help at the University Hospital. Another word of gratitude goes to the subjects of my research, the participants – who sometimes aided me, sometimes sabotaged me, but had to endure a lot for the sake of science – and the thesis students I supervised during my PhD: Siebren, Lies, Jeffrey, Lien, Sylvie, Johanna, Alexis, Jana, Marlies, Bo, and Lazlo. I am proud to have witnessed you grow into excellent colleague clinicians / researchers!

Let's shift into an even higher gear. Thanks to my close friends, the 'dinner club' (Toon, Irma, & Jonas), Stefan, Stefanie and Sandro, Shaun and Dorien, Lien and Ben, my study buddies from BTP and Clinical Psychology, my school, musical, and philosophical friends, ... I have neglected all of you to some extent while pursuing my PhD. Thank you for your patience and support! Also thanks to all the friends whose name did not make the list but will always be in my heart, all of you are amazing!

Words simply cannot express how grateful I am to my family. Thank you mom and dad, the two of you made this possible for me! Thank you for your unconditional support, for stimulating me, being there for me to ventilate, loving me, … Both of you are fantastic, it's an honour to be your son and put to practice what you taught me

about life! Also a big 'thank you' to my dear twin sister, Manon – who has been stuck with me even before we were born –, my fantastic brother in law Ayrton, and the recent product of their love: Milo, our latest, smallest (yet also among the greatest) asset to the family. Also thanks to my grandparents, my extended family, and my future family (Kaatje, Danny, Fien & Niels, Philip, …). A final word of thanks goes out to my future wife: Roos. You have been there with me all the way, supporting me in times of need and distracting me in the most beautiful way. Priceless. THANK YOU! And for my future kids, let this book be proof that – no matter what your mom tells you or what you may come to believe while growing up – your dad hasn't been an idiot all the time. ;-)

It is a beautiful thing, writing a PhD. However, it comes at a terrible cost: someone will be tasked with reading *all* of this. For this, I wish my jury members the best of luck!

Kristof

April 2017

CONTENTS

CHAPTER 1

GENERAL INTRODUCTION

I haven't been able to read a book or watch a movie since the onset of my depression, it's as if I just can't focus and my memory isn't what it used to be – Tom, clinically depressed

Although most of my depressive complaints improved, I still can't cut loose from these negative thoughts that haunt me – Samantha, in (partial) remission of depression

I have difficulties falling asleep at night. It's as if my mind just can't shut off and keeps worrying about whatever happened that day, I just cannot control it – Student, at-risk for depression

At work, I just can't do it anymore, I'm constantly distracted by negative thoughts – Ana, clinically depressed

The statements above taken from clinical practice reflect some of the key challenges in treatment of depression today: current treatments show limited effects on cognitive symptoms and vulnerability factors for depression (e.g., cognitive control, rumination), which may contribute to the relatively poor treatment outcomes in terms of relapse prevention. In this dissertation we attempted to enhance our understanding of how information processing factors are causally involved in depression vulnerability and resilience in order to prevent depression.

According to the diagnostic criteria for mental disorders (American Psychiatric Association, 2013), 'depression' refers to a prolonged state of dysfunctioning which is mainly characterized by a negative mood and/or loss of interest or pleasure, in combination with at least three other cognitive, affective or somatic symptoms (e.g., psychomotor agitation/retardation, loss of appetite, feelings of worthlessness, indecisiveness). In order for patients to be diagnosed with 'major depressive disorder' (MDD), this combination of symptoms should cause clinically significant distress or impairment in daily life functioning (e.g., dysfunctioning in a professional context or other social relationships). Furthermore, this pattern of dysfunctioning should occur in absence of a history of (hypo)manic episodes and without being triggered by or being

directly attributable to substance abuse or other medical conditions (American Psychiatric Association, 2013).

As the leading cause of disability worldwide (World Health Organization, 2016), this highly prevalent mental disorder (Alonso et al., 2004; Kessler & Bromet, 2013) forms an important source of individual suffering, resulting in poor quality of life (IsHak et al., 2013) and impaired functioning. Importantly, these functional impairments often continue during remission (Endo, Haruyama, Muto, & Kato, 2012; de Vries, Koeter, Nieuwenhuijsen, & Schene, 2015). As a result, depression comes at a high societal cost: in 2004 the total annual cost of depression in Europe was estimated at €118 billion for 21 million patients, which corresponded to 1% of the total European economy (Sobocki, Jönsson, Angst, & Rehnberg, 2006; for a review on cost-of-illness studies, see Luppa, Heinrich, Angermeyer, Konig, & Riedel-Heller, 2007). Sobocki and colleagues (2006) estimated that €76 billion of this budget was due to indirect costs such as morbidity and increased mortality and another €42 billion due to direct treatment costs. In 2010 the annual cost per subject suffering from a mood disorder in Europe was estimated at €3406 (Gustavsson et al., 2011). Importantly, recent estimations of the World Health Organization suggest that currently 350 million people are affected by depression worldwide, reporting up to 800 000 suicides on a yearly basis (World Health Organization, 2016). These findings illustrate the enormous global burden of depression.

Although current treatments for depression often show promising short term effects (e.g., Cuijpers, Cristea, Karyotaki, Reijnders, & Huibers, 2016), existing pharmacological and psychotherapeutic interventions only show limited effects in terms of preventing recurrence of depressive episodes (Beshai, Dobson, Bockting, & Quigley, 2011; Bockting, Spinhoven, Wouters, Koeter, & Schene, 2009; Cox et al., 2012). That is, recurrence rates for depression have been reported up to 80%, increasing per previous episode, while interventions specifically focusing on prevention of the onset of future episodes still show room for improvement (Bockting et al., 2009; Burcusa & Iacono, 2007; Kessing, Hansen, & Andersen, 2004). For instance, over a five year period Bockting and colleagues (2009) observed a relapse rate of 79% for a combined group of patients receiving treatment as usual with or without an additional preventative

psychotherapeutic intervention. Relapse prevention seemed most effective for patients with a history of four or more depressive episodes. However, recurrence rates remained above 30% at one year follow-up and above 60% at five years follow-up for the group receiving the additional preventative psychotherapeutic intervention next to treatment as usual. Similar findings were reported by Teasdale and colleagues (2000), showing recurrence rates higher than 30% over a period of one year follow-up for patients receiving preventative mindfulness-based cognitive therapy next to treatment as usual. Overall, patients with a history of depression develop five to nine distinctive depressive episodes during their lifetime (Carr & McNulty, 2016).

Existing treatments also show limited effects in terms of reducing cognitive symptoms of depression (Gonda et al., 2015; Gualtieri, Johnson, & Benedict, 2006; Shilyansky et al., 2016), resulting in residual symptomatology during remission (e.g., Nierenberg et al., 2010). Importantly, prospective studies indicate that number of previous depressive episodes, residual symptomatology, and impaired emotion regulation processes form important predictors for recurrence of depression (Bockting, Spinhoven, Koeter, Wouters, & Schene, 2006; ten Doesschate, Bockting, Koeter, Schene, 2010). These findings suggest that current interventions fail in altering underlying vulnerability mechanisms for depression and demonstrate the importance of research aimed at improving our knowledge on depression vulnerability.

COGNITIVE VULNERABILITY TO DEPRESSION

Early cognitive approaches to depression suggest that information processing factors may represent more than just symptoms and may in fact be involved in the etiology of emotional disorders. For instance, Beck, Rush, Shaw, and Emery (1979) attribute a central role to schemata, cognitive structures developed based on early learning experiences. These structures influence information processing at the level of perceptions, interpretations, and (encoding and retrieval of) memories. In the context of depression, negative schemata regarding how a subject perceives oneself, the world and others, are expected to result in a perpetuating cycle of distorted information processing in which information contingent with one's schema is prioritized over

schema-incongruent information. Similarly, Bower's (1981, 1987) semantic network model suggests a positive feedback loop between mood-dependent encoding and retrieval of information, reinforcing depressogenic representations in memory. Although these early theoretical frameworks have dominantly been translated in clinical applications focusing on the content of information processing (e.g., changing dysfunctional cognitions via cognitive therapy), they have inspired researchers in the field of experimental psychopathology to focus on *cognitive and neurobiological processes* underlying vulnerability for emotional disorders. For instance, an early meta-analysis of Matt, Vázquez, and Campbell (1992) assessed evidence for biased recall of learned information in depression, showing differential patterns for healthy, subclinical, and clinically (or induced) depressed patients.

In the context of vulnerability for depression, an important question that currently remains to be further elucidated is how information processing factors contribute to the development of depressive symptomatology (rather than resilience) upon confrontation with adverse events (i.e., stressors). A common pathway that has been proposed here is cognitive *emotion regulation*: the process of influencing which emotions one has, when one experiences these emotions, and how these emotions are experienced and expressed (Gross, 1998). Different strategies to regulate emotions have been observed in healthy and patient samples, ranging from strategies such as positive reappraisal and putting into perspective to strategies such as self-blame and catastrophizing. Depending on the observed outcome(s) and efficiency of these strategies in adaptively coping with affective states, emotion regulation strategies have typically been categorized as 'adaptive' or 'maladaptive' (e.g., Garnefski, Kraaij, & Spinhoven, 2001), with maladaptive strategies being linked to more psychopathological processes and adaptive strategies predicting mental wellbeing (Gross & Jazaieri, 2014; Gross & John, 2003; Hu et al., 2014).[1]

[1] Although we will continue to use this categorization throughout the chapters of this dissertation, it is important to acknowledge that the extent to which engaging in a certain emotion regulation strategy is (mal)adaptive, depends on the flexible deployment of that emotion regulation strategy within a given context (e.g., Aldao, Sheppes, & Gross, 2015).

Among maladaptive emotion regulation strategies, rumination received most attention in depression research. In this context, rumination often refers to "behaviors and thoughts that focus one's attention on one's depressive symptoms and on the implications of these symptoms", as presented in the Response Styles Theory of Depression (p. 569, Nolen-Hoeksema, 1991; Nolen-Hoeksema & Morrow, 1991). Here, the emphasis is placed on the perseverative nature of this thinking style (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). Treynor, Gonzalez, and Nolen-Hoeksema (2003) identified two subtypes of rumination: brooding, often referred to as 'depressive rumination', and reflection, a more problem-solving focused type of rumination. This factor structure has been replicated in numerous studies and populations (e.g., Schoofs, Hermans, & Raes, 2010; Verstraeten, Vasey, Raes, & Bijttebier, 2010; Xavier, Cunha, & Pinto-Gouveia, 2016), in which brooding – a passive style of moody pondering – is typically linked to most detrimental outcomes (Schoofs et al., 2010; Treynor et al. 2003). Interestingly, elevated brooding levels have been observed in at-risk populations prior to the onset of a first depressive episode and following remission of depression. For instance, research indicates that children of a mother with a history of depression show elevated brooding scores (Gibb, Grassia, Stone, Uhrlass, and McGeary, 2012; Woody et al., 2016). Furthermore, individuals in remission of depression typically report higher brooding levels than subjects without a history of depression (Gibb et al., 2012; Woody, McGeary, & Gibb, 2014). Moreover, brooding levels are related to biomarkers of stress reactivity (e.g., Woody et al., 2014; for a meta-analysis see Ottaviani et al., 2016) and prospectively predict future depression while controlling for baseline depressive symptoms (Gibb et al., 2012; Schoofs et al., 2010; Treynor et al., 2003). These findings suggest that brooding may form a stable risk factor for the development of depressive episodes (for a review, see Nolen-Hoeksema et al., 2008; Olatunji, Naragon-Gainey, & Wolitzky-Taylor, 2013).

In contrast, adaptive emotion regulation strategies such as positive (re)appraisal – in which one reduces the emotion eliciting value of a stressful situation by attaching a positive meaning to the event (e.g., personal growth) – seem to act as protective factors for psychopathology (Garnesfki & Kraaij, 2006, 2016; Garnefski, Legerstee, Kraaij, Van Den Kommer, & Teerds, 2002; Martin & Dahlen, 2005). For instance, in a longitudinal

study Kraaij, Pruymboom, and Garnefski (2002) showed that positive (re)appraisal is related to lower depressive symptoms in the elderly while controlling for negative life events and prior depressive symptoms. Moreover, positive (re)appraisal has typically been related to indicators of wellbeing and resilience such as positive affect (Haga, Kraft, & Corby, 2009; Kraaij, Garnefski, & Schroevers, 2009; McRae, Jacobs, Ray, John, & Gross, 2012; Nowlan, Wuthrich, & Rapee, 2016), quality of life (Extremera & Rey, 2014; Li et al., 2015), and life satisfaction (Haga et al., 2009; McRae et al., 2012). As a result, several theoretical frameworks of resilience emphasize the importance of adaptive emotion regulation strategies such as positive (re)appraisal (e.g., Kalisch, Müller, & Tüscher, 2015; McRae & Mauss, 2016).

Cognitive control, emotion regulation, and depression

Interestingly, both rumination and reappraisal have been linked to *cognitive control* (Joormann & Gotlib, 2010), referring to executive processes – such as shifting, updating and monitoring of working memory representations, and inhibition of prepotent responses (Miyake et al., 2000) – that allow behavior to vary adaptively over time in line with one's goals. These executive processes are assumed to be imperative for flexible and efficient use of working memory, a limited-capacity system for the temporary storage of information (Baddeley & Hitch, 1974). Indeed, research suggests that cognitive emotion regulation draws on cognitive control. For instance, McRae and colleagues (2012) found the ability to reappraise during exposure to negative pictures to be positively related to set shifting and working memory task performance. Furthermore, studies looking into neural markers of reappraisal (e.g., Moser, Hartwig, Moran, Jendrusina, & Kross, 2014; Ochsner, Bunge, Gross, & Gabrieli, 2002) typically report activation of central cognitive control brain regions (e.g., prefrontal cortex; Miller & Cohen, 2001). In this context, recent meta-analytical findings suggest that activation of cognitive control regions attenuates amygdala activity while reappraising (Buhle et al., 2014).

Whereas cognitive control shows positive associations with adaptive emotion regulation strategies as indicators of resilience, *cognitive control deficits* may place one at risk for developing depressive symptomatology. That is, experiencing difficulties

disengaging from (task-irrelevant) negative information in working memory may result in repetitive negative thinking, making one more likely to ruminate in response to stressful events (De Raedt & Koster, 2010). Indeed, cross-sectional studies indicate that cognitive control is negatively related to rumination and depressive symptomatology (Beckwé, Deroost, Koster, De Lissnyder, & De Raedt, 2014; Joormann & Gotlib, 2010; Whitmer & Banich, 2007). Moreover, cognitive control deficits have been observed during different stages of depression vulnerability, with cognitive control deficits present in dysphoric (Joormann, 2004; Owens, Koster, & Derakshan, 2012), MDD (Joormann & Gotlib, 2010; Harvey et al., 2004; Levens & Gotlib, 2010), and formerly depressed patients (Levens & Gotlib, 2015; Paelecke-Habermann, Pohl, & Leplow, 2005). For instance, Beckwé and colleagues (2014) reported deficits in shifting from self-relevant negative information in high trait ruminators compared to low trait ruminators. Hilt, Leitzke, and Pollak (2014) observed an association between impaired cognitive control, assessed using an affective Go/No-go task, and rumination. Similarly, Levens and Gotlib (2015) tested the presence of updating deficits for emotional information using an affective 0-back and 2-back task. In line with previous findings in MDD samples (Levens & Gotlib, 2010), these researchers found evidence for impaired disengagement from negative information in working memory as well as reduced maintenance of positive information in RMD patients compared to never-depressed controls.

Importantly, prospective studies confirm the predictive value of cognitive control deficits in the context of depression vulnerability (e.g., Pe, Brose, Gotlib, & Kuppens, 2016; Pe, Raes, & Kuppens, 2013). For instance, in a six-month prospective study that examined interference resolution, Zetsche and Joormann (2011) showed that individual differences in interference control predict the maintenance and exacerbation of depressive symptoms and rumination six months later. Similarly, using observer ratings Kertz, Belden, Tillman, and Luby (2015) demonstrated that inhibition and shifting deficits in preschool aged children prospectively predict the onset and maintenance of depressive symptomatology, even after controlling for potential confounders such as IQ, baseline symptom severity, and parental factors.

Notably, emotion regulation processes are likely to mediate the association between cognitive control deficits and depressive symptomatology (e.g., Hsu et al., 2015). That is, Demeyer, De Lissnyder, Koster, and De Raedt (2012) found that cognitive control deficits in RMD patients predict depressive symptomatology at one year follow-up, where evidence suggested this relation to be fully mediated by rumination. Furthermore, several studies suggest a bidirectional association between cognitive control and depression vulnerability (e.g., Philippot & Brutoux, 2008). For instance, building on the idea that cognitive control deficits in MDD interact with rumination, Whitmer and Gotlib (2012) showed that deficits in switching ability in MDD patients are most apparent when in a ruminative state, demonstrating that rumination impairs cognitive control. Moreover, research indicates that early depressive symptomatology may hinder the development of cognitive control during adolescence (e.g., Vijayakumar et al., 2016), placing these individuals at increased risk to engage in maladaptive emotion regulation strategies. Similarly, in another prospective study assessing executive functioning, rumination, and depressive symptomatology over a fifteen-month period, Connolly and colleagues (2014) established that rumination predicts future decreases in cognitive control. This is in line with the observation that cognitive control deficits are inversely related to amount of previous depressive episodes (Vanderhasselt & De Raedt, 2009) and hospitalizations (Harvey et al., 2004).

Overall, these findings suggest that cognitive control deficits and rumination mutually reinforce one another, increasing depression vulnerability on both a cognitive and biological level (for reviews, see De Raedt & Koster, 2010; Joormann & D'Avanzato, 2010; Joormann & Vanderlind, 2014). However, cross-sectional and prospective findings do not allow to infer conclusions regarding the causal nature of these relations. For this purpose, experimental manipulation of cognitive control would be necessary, for instance, using modified cognitive control or working memory tasks specifically tailored to adaptively stimulate cognitive functioning (i.e., *cognitive control training*). In this context, numerous studies have focused on whether cognitive transfer effects can be obtained to closely related and more distal cognitive processes (e.g., Jaeggi, Buschkuehl, Jonides, & Perrig, 2008; Jaeggi, Buschkuehl, Jonides, & Shah, 2011; Klingberg et al., 2005; Klingberg, Forssberg, & Westerberg, 2002; Olesen, Westerberg, &

Klingberg, 2004; Westerberg et al., 2007). Although this has yielded inconsistent findings regarding the extent to which cognitive transfer effects may occur (e.g., performance on measures of intelligence; Harrison et al., 2013; for recent reviews, see Melby-Lervag, Redick, & Hulme, 2016; Shipstead, Redick, & Engle, 2010, 2012), evidence suggests that cognitive functions show plasticity, indicating that cognitive training may affect functioning on both a cognitive and neurobiological level (Klingberg, 2010).

This has encouraged researchers in the field of experimental psychopathology to use cognitive training procedures as a means to test the causal influence of information processing factors in depression vulnerability (for a review, see Mor & Daches, 2015). Here, a recent meta-analysis by Motter and colleagues (2016) suggests that cognitive training can exert beneficial effects on depression outcomes.

RESEARCH OBJECTIVES OF THE DISSERTATION

The main goal of this PhD was to test the causal influence of cognitive control in depression vulnerability. At the theoretical level this would enhance our understanding of how information processing factors are involved in emotion regulation, and how this may be related to vulnerability for or resilience against the development of depressive symptomatology. At the clinical level establishing causal involvement of cognitive control in (vulnerability for) depression offers the possibility to expand existing treatments with tailored interventions specifically targeting cognitive control impairments and rumination. In this context, cognitive control training holds the potential to become an add-on intervention for patients in a state of clinical depression as well as a preventative intervention for at-risk groups such as patients in the phase of remission or healthy subjects showing heightened levels of trait rumination or subclinical depressive symptoms. In this dissertation we subsequently present a review of current state-of-the-art findings regarding cognitive control training and (vulnerability for) depression, after which we present several experimental tests of the preventative potential of cognitive control training and a cross-sectional test of the

theoretical framework regarding the role of cognitive control following remission from depression.

In **Chapter 2**, we present a systematic review regarding effects of cognitive control training on vulnerability for depression. In total, 7633 records were screened from which 34 studies are included and discussed in the systematic review. After providing an overview of central constructs, several variations of cognitive control training are presented after which effects in at-risk, MDD, and remitted depressed patients are discussed. In addition to a detailed discussion of the state-of-the-art evidence for effects of cognitive control training on vulnerability for depression, special attention is paid to methodological limitations of existing studies. That is, an important amount of studies in this field have relied on suboptimal designs to test the causal influence of cognitive control on depression vulnerability (e.g., Siegle, Ghinassi, & Thase, 2007). Furthermore, special attention is being paid to establishing cognitive transfer, the role of potential moderators such as intensity of training and use of emotional information, as well as sequential pathways through which cognitive control training may alter depressive symptomatology. For each of these points, specific recommendations for future research are given.

Chapter 3 contains an experimental study in which we tested the causal influence of cognitive control on indicators of depression vulnerability using the adaptive PASAT training procedure (Hoorelbeke, Koster, Vanderhasselt, Callewaert, & Demeyer, 2015). Previous studies using the adaptive PASAT suggest that this type of training may have beneficial effects on rumination (e.g., Siegle et al., 2007, 2014) and depressive symptomatology (e.g., Segrave, Arnold, Hoy, & Fitzgerald, 2014; Siegle et al., 2007). However, these early studies show important design limitations, and – with the exception of Brunoni et al. (2014) – have typically combined the adaptive PASAT training with the Wells' attention training task (Wells, 2000). Although these findings may indicate causal involvement of information processing factors in depression vulnerability, this procedure does not allow to disentangle specific training effects related to cognitive control, nor to control for motivational effects of undergoing training. Furthermore, previous studies using the adaptive PASAT have typically focused on curative effects whereas the preventive potential of adaptive PASAT training

remains mainly untested (e.g., Brunoni et al., 2014; Siegle et al., 2007). Hence, we explored effects of a two week adaptive PASAT training (compared to an active control condition) in students showing elevated trait rumination scores, putting them at-risk to develop depressive complaints in response to stressors. We hypothesized to find beneficial effects on stress reactivity and depressive rumination in response to a lab stressor (stress induction procedure) and a naturalistic stressor (exam period at one month follow-up).

Following promising effects on stress reactivity and depressive symptomatology in at-risk students (Hoorelbeke et al., 2015), **Chapter 4** proceeded exploring the preventative potential of adaptive PASAT training in a healthy convenience sample, testing the influence of cognitive control on indicators of depression vulnerability *and* resilience. For this purpose, we extended our scope to adaptive emotion regulation strategies such as positive (re)appraisal. After providing a cross-sectional test of the association between cognitive control, adaptive and maladaptive emotion regulation strategies, Chapter 4 presents an experimental test of the role of cognitive control in (mal)adaptive emotion regulation. Effects were assessed in a highly controlled lab setting and in response to stressful events in daily life. For this purpose, a two week adaptive PASAT training procedure was followed by a lab assessment of positive reappraisal ability in response to recall of a negative autobiographical memory. Moreover, effects of cognitive control on the interplay of affect and (mal)adaptive emotion regulation in daily life were assessed during a seven day long follow-up procedure using experience sampling (Larson & Csikszentmihalyi, 1983). Here, effects of training were assessed on *deployment* of rumination and positive reappraisal in response to affective states, as well as *efficacy* of emotion regulation (i.e., the implications of responding to a given affective state with rumination or positive appraisal for future ratings of positive / negative affect). Effects of cognitive control training were compared with an active control group that completed a novel training task specifically constructed to closely match the training mechanisms of the adaptive PASAT task while putting a limited load on cognitive control processes. This allows to control for motivational effects of undergoing cognitive training as well as the influence of broader shared information processing factors (e.g., sustained attention). Hence,

effects resulting from comparison of both training conditions are likely to reflect the causal influence of cognitive control on (mal)adaptive emotion regulation.

Based on these early promising findings suggesting the preventative potential of cognitive control training (Hoorelbeke et al., 2015; Hoorelbeke, Koster, Demeyer, Loeys, & Vanderhasselt, 2016), we set-up a more stringent test of the causal influence of cognitive control on depression vulnerability and resilience. **Chapter 5** contains the protocol of a double-blind randomized controlled trial study on the preventative potential of cognitive control training for remitted depressed patients. The study was pre-registered in ClinicalTrials.Gov (identifier NCT02407652) and the protocol was made available via open access publication (Hoorelbeke, Faelens, Behiels, & Koster, 2015). Following an extensive prescreening procedure, eligible remitted depressed patients completed a baseline assessment including specific indicators of depression vulnerability (e.g., rumination, residual symptomatology, cognitive functioning) and resilience (e.g., self-reported resilience, adaptive emotion regulation), as well as broader indicators of functioning (e.g., quality of life, disability). Objective and subjective cognitive control were assessed prior to training, immediately following two weeks of training, and at three months follow-up, allowing to test the stability of cognitive transfer effects. Moreover, the three distinctive assessment points allow to test an influential theoretical assumption regarding effects of cognitive control training on depression vulnerability. That is, cognitive control training is hypothesized to show immediate effects on depressive rumination, which may then further impact depressive symptomatology (Siegle et al., 2007, 2014). Additional strengths of this design are the inclusion of a psycho-education session prior to training in order to stimulate training retention, assessment of blinding, credibility and expectancy, and daily monitoring of online effects of performing the training task (e.g., allowing to rule out the hypothesis that effects of training may be due to habituation to stress (stress inoculation)).

The results of this confirmatory, randomized controlled trial study are reported in **Chapter 6**, in which we tested effects of cognitive control training on primary outcome measures depressive rumination and depressive symptomatology in remitted depressed patients using both intention-to-treat and completers-only analysis. Second, we tested whether effects of cognitive control training can extend to indicators of

functioning and resilience. Third, we provide a direct test of the assumption that cognitive control influences depressive symptomatology via maladaptive emotion regulation. Specifically, we tested a mediation model in which increase in cognitive control from baseline to post-training assessment is used to predict depressive symptomatology at three months follow-up via post-training depressive rumination (while controlling for baseline depressive symptomatology and rumination).

Finally, **Chapter 7** presents the results of a cross-sectional exploratory study focusing on how cognitive vulnerability and protective factors are related to (residual) depressive symptomatology following remission from depression. Based on the literature, depressive rumination and indicators of objective and subjective cognitive control were selected as cognitive vulnerability factors. Positive reappraisal and resilience were selected as potential protective factors. We hypothesized that indicators of cognitive control would be related to residual depressive symptoms and resilience. However, we expected this association to occur via emotion regulation. In order to test this hypothesis without forcing the data into an a priori model, we used network analysis to explore the best fitting structure for the data, subsequently presenting an association network, adaptive LASSO concentration network, and a directed relative importance network.

We conclude this dissertation with an integrated discussion of these findings, focusing on the theoretical and clinical implications, important limitations, and providing recommendations for future cognitive control training studies in the context of prevention of depression.

REFERENCES

Aldao, A., Sheppes, G., & Gross, J. J. (2015). Emotion regulation flexibility. *Cognitive Therapy and Research*, *39*, 263–278. doi: 10.1007/s10608-014-9662-4

Alonso, J., Angermeyer, M. C., Bernert, S., Bruffaerts, R., Brugha, T. S.,Bryson, H., ... Vollebergh, W. A. (2004). Prevalence of mental disorders in Europe: Results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatrica Scandinavica, 109,* 21-27. doi: 10.1111/j.1600-0047.2004.00327.x

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: Author.

Baddeley, A. D., & Hitch, G. (1974). Working memory. In G. H. Bower (Ed.), *The psychology of learning and motivation: Advances in research and theory* (pp. 47–89). New York: Academic Press.

Beck, A. T., Rush, A. J., Shaw, B. F., & Gemery, G. (1979). *Cognitive therapy of depression.* New York: Guildford Press.

Beckwé, M., Deroost, N., Koster, E. H. W., De Lissnyder, E., & De Raedt, R. (2014). Worrying and rumination are both associated with reduced cognitive control. *Psychological Research*, *78*, 651–660. doi: 10.1007/s00426-013-0517-5

Beshai, S., Dobson, K. S., Bockting, C. L. H., & Quigley (2011). Relapse and recurrence prevention in depression: Current research and future prospects. *Clinical Psychology Review, 31*, 1349-1360. doi: 10.1016/j.cpr.2011.09.003

Bockting, C. L. H., Spinhoven, P., Koeter, M. W. J., Wouter, L. F., & Schene, A. H. (2006). Prediction of recurrence in recurrent depression and the influence of consecutive episodes on vulnerability for depression: A 2-year prospective study. *Journal of Clinical Psychiatry, 67*, 747-755.

Bockting, C. L. H., Spinhoven, P., Koeter, M. W. J., Wouter, L. F., & Schene, A. H. (2009). Long-term effects of preventive cognitive therapy in recurrent depression: A 5.5-year follow-up study. *Journal of Clinical Psychiatry, 70,* 1621-1628. doi: 10.4088/JCP.08m04784blu

Bower, G. H. (1981). Mood and memory. *American Psychologist, 36*, 129-148.

Bower, G. H. (1987). Commentary on mood and memory. *Behaviour Research and Therapy, 25,* 443-455.

Brunoni, A. R., Boggio, P. S., De Raedt, R., Bensenor, I. M., Lotufo, P. A., Namur, V., . . . Vanderhasselt, M. A. (2014). Cognitive control therapy and transcranial direct current stimulation for depression: A randomized, double-blinded, controlled trial. *Journal of Affective Disorders, 162*, 43-49. doi: 10.1016/j.jad.2014.03.026

Buhle, J. T., Silvers, J. A., Wager, T. D., Lopez, R., Onyemekwu, C., Kober, H., . . . Ochsner, K. N. (2014). Cognitive reappraisal of emotion: A meta-analysis of human neuroimaging studies. *Cerebral Cortex, 24*, 2981-2990. doi: 10.1093/cercor/bht154

Burcusa, S. L., & William, G. I. (2007). Risk for recurrence in depression. *Clinical Psychology Review, 27*, 959-985. doi: 10.1016/j.cpr.2007.02.005

Carr, A., & McNulty, M. (2016). Depression. In A. Carr & M. McNulty (Eds.), *The handbook of Adult Clinical Psychology: An evidence-based practice approach* (265-316) New York: Routlegde.

Connolly, S. L., Wagner, C. A., Shapero, B. G., Pendergast, L. L., Abramson, L. Y., & Alloy, L. B. (2014). Rumination prospectively predicts executive functioning impairments in adolescents. *Journal of Behavior Therapy and Experimental Psychiatry*, *45*, 46–56. doi: 10.1016/j.jbtep.2013.07.009

Cox, G. R., Fisher, C. A., De Silva, S., Phelan, M., Akinwale, O. P., Simmons, M. B., & Hetrick S. E.. (2012). Interventions for preventing relapse and recurrence of a depressive disorder in children and adolescents. *Cochrane Database of Systematic Reviews*, Issue 11. Art. No.: CD007504. DOI: 10.1002/14651858.CD007504.pub2

Cuijpers, P., Cristea, I. A., Karyotaki, E., Reijnders, M., & Huibers, M. J. H. (2016). How effective are cognitive behavior therapies for major depression and anxiety disorders? A meta-analytic update of the evidence. *World Psychiatry, 15,* 245-258. doi: 10.1002/wps.20346

De Raedt, R., & Koster, E. H. W. (2010). Understanding vulnerability for depression from a cognitive neuroscience perspective: A reappraisal of attentional factors and a new conceptual framework. *Cognitive Affective & Behavioral Neuroscience*, *10,* 50–70. doi: 10.3758/cabn.10.1.50

de Vries, G., Koeter, M., Nieuwenhuijsen, K., & Schene, A. H. (2015). Predictors of impaired work functioning in employees with major depression in remission. *Journal of Affective Disorders, 185*, 180- 187. doi: 10.1016/j.jad.2015.07.013

Demeyer, I., De Lissnyder, E., Koster, E. H. W., & De Raedt, R. (2012). Rumination mediates the relationship between impaired cognitive control for emotional information and depressive symptoms: A prospective study in remitted depressed adults. *Behaviour Research and Therapy*, *50*, 292–297. doi:10.1016/j.brat.2012.02.012

Endo, M., Haruyama, Y., Muto, T., & Kato, R. (2012). Recurrence of sickness absence due to depression after returning to work at a Japanese IT company. *Industrial Health, 51*, 165-171. doi: 10.2486/indhealth.2012-0063

Extremera, N., & Rey, L. (2014). Health-related quality of life and cognitive emotion regulation strategies in the unemployed: A cross-sectional survey. *Health and Quality of Life Outcomes, 12*:172. doi: 10.1186/s12955-014-0172-6

Garnefski, N., & Kraaij, V. (2006). Relationships between cognitive emotion regulation strategies and depressive symptoms: A comparative study of five specific samples. *Personality and Individual Differences, 40*, 1659-1669. doi: 10.1016/j.paid.2005.12.009

Garnefski, N., Kraaij, V., & Spinhoven, P. (2001). Negative life events, cognitive emotion regulation and emotional problems. *Personality and Individual Differences, 30*, 1311-1327.

Garnefski, N. & Kraaij, V. (2016). Specificity of relations between adolescents' cognitive emotion regulation strategies and symptoms of depression and anxiety. *Cognition & Emotion,*. doi: 10.1080/02699931.2016.1232698

Garnefski, N., Legerstee, J., Kraaij, V., Van Den Kommer, T., & Teerds, J. (2002). Cognitive coping strategies and symptoms of depression and anxiety: A comparison between adolescents and adults. *Journal of Adolescence, 25,* 603-611. doi: 10.1006/jado.0507

Gibb, B. E., Grassia, M. Stone, L. B., Uhrlass, D.J., & McGeary, J. E. (2012). Brooding rumination and risk for depressive disorders in children of depressed mothers. *Journal of Abnormal Child Psychology, 40*, 317-326. doi: 10.1007/s10802-011-9554-y

Gonda, X., Pompili, M., Serafini, G., Carvalho, A. F., Rihmer, Z., & Dome, P. (2015). The role of cognitive dysfunction in the symptoms and remission from depression. *Ann Gen Psychiatry, 14*:27. doi: 10.1186/s12991-015-0068-9

Gross, J. J. (1998). The emerging field of emotion regulation: An integrative review. *Review of General Psychology, 2*, 271 - 299. doi: 1089-2680/98/$3.00

Gross, J. J., & Jazaieri, H. (2014). Emotion, emotion regulation, and psychopathology: An affective science perspective. *Clinical Psychological Science, 2*, 387 - 401. doi: 10.1177/2167702614536164

Gross, J. J., & John, O. P. (2003). Individual differences in two emotion regulation processes: Implications for affect, relationships, and well-being. *Journal of Personality and Social Psychology, 85*, 348-362. doi: 10.1037/0022-3514.85.2.348

Gualtieri, C. T., Johnson, L. G., & Benedict, K. B. (2006). Neurocognition in Depression: Patients on and off medication versus healthy comparison subjects. *J Neuropsychiatry Clin Neurosci, 18,* 217 – 225.

Gustavsson, A., Svensson, M., Jacobi, F., Allgulander, C., Alonso, J., Beghi, E., . . . Olesen, J. (2011). Cost of disorders of the brain in Europe in 2010. *European Neuropsychopharmacology, 21,* 718-779. doi: 10.1016/j.euroneuro.2011.08.008

Haga, S. M., Kraft, P., & Corby, E. K. (2009). Emotion regulation: Antecedents and well-being outcomes of cognitive reappraisal and expressive suppression in cross-cultural samples. *Journal of Happiness Studies, 10*, 271-291. doi: 10.1007/s10902-007-9080-3

Harrison, T. L., Shipstead, Z., Hicks, K. L., Hambrick, D. Z., Redick, T. S., & Engle, R. W. (2013). Working memory training may increase working memory capacity but not fluid intelligence. *Psychological Science*, *24*, 2409–2419. doi: 10.1177/0956797613492984

Harvey, P. O., Le Bastard, G., Pochon, J. B., Levy, R., Allilaire, J. F., Dubois, B., & Fossti, P. (2004). Executive functions and updating of the contents of working memory in unipolar depression. *Journal of Psychiatric Research*, *38*, 567–576. doi: 10.1016/j.jpsychires.2004.03.003

Hilt, L., Leitzke, B., & Pollak, S. (2014). Cognitive Control and Rumination in Youth: The Importance of Emotion. *Journal of Experimental Psychopathology*, *5*, 302–313.

doi:10.5127/jep.038113

Hoorelbeke, K., Faelens, L., Behiels, J., & Koster, E. H. W. (2015). Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Protocol for a randomized controlled trial. *Bmc Psychiatry, 15.* doi: 10.1186/s12888-015-0511-0

Hoorelbeke, K., Koster, E. H. W., Demeyer, I., Loeys, T., & Vanderhasselt, M. A. (2016). Effects of cognitive control training on the dynamics of (mal)adaptive emotion regulation in daily life. *Emotion*, *16*, 945-956. doi: 10.1037/emo0000169

Hoorelbeke, K., Koster, E. H. W., Vanderhasselt, M. A., Callewaert, S., & Demeyer, I. (2015). The influence of cognitive control training on stress reactivity and rumination in response to a lab stressor and naturalistic stress. *Behaviour Research and Therapy*, *69*, 1–10.

Hsu, K. J., Beard, C., Rifkin, L., Dillon, D. G., Pizzagalli, D. A., & Björgvinsson, T. (2015). Transdiagnostic mechanisms in depression and anxiety: The role of rumination and attentional control. *Journal of Affective Disorders*, *188*, 22–27. doi: 10.1016/j.jad.2015.08.008

Hu, T. Q., Zhang, D. J., Wang, J. L., Mistry, R., Ran, G. M., & Wang, X. Q. (2014). Relation between emotion regulation and mental health: A meta-analysis review. *Psychological Reports, 114*(2), 341-362. doi: 10.2466/03.20.PR0.114k22w4

IsHak, W. W., Balayan, K., Bresee, C., Greenberg, J. M., Fakhry, H., Christensen, S., & Rapaport, M. H. (2013). A descriptive analysis of quality of life using patient-reported measures in major depressive disorder in a naturalistic outpatient setting. *Quality of Life Research, 22*(3), 585-596. doi: 10.1007/s11136-012-0187-6

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Perrig, W. J. (2008). Improving fluid intelligence with training on working memory. *Proceedings of the National Academy of Sciences of the United States of America*, *105*, 6829–6833. doi: 10.1073/pnas.0801268105

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Shah, P. (2011). Short- and long-term benefits of cognitive training. *Proceedings of the National Academy of Sciences of the United States of America*, *108*, 10081–10086. doi: 10.1073/pnas.1103228108

Joormann, J. (2004). Attentional bias in dysphoria: The role of inhibitory processes.

Cognition & Emotion, *18*, 125–147. doi: 10.1080/02699930244000480

Joormann, J., & D'Avanzato, C. (2010). Emotion regulation in depression: Examining the role of cognitive processes. *Cognition & Emotion*, *24*, 913–939. doi: 10.1080/02699931003784939

Joormann, J., & Gotlib, I. H. (2010). Emotion regulation in depression: Relation to cognitive inhibition. *Cognition & Emotion, 24*, 281-298. doi: 10.1080/02699930903407948

Joormann, J., & Vanderlind, M. W. (2014). Emotion regulation in depression: The role of biased cognition and reduced cognitive control. *Clinical Psychological Science*, *2*, 402–421. doi: 10.1177/2167702614536163

Kalisch, R., Müller, M. B., & Tüscher, O. (2015). A conceptual framework for the neurobiological study of resilience. *Behavioral and Brain Sciences, 38*, 1 - 79. doi: 10.1017/S0140525X1400082X, e0

Kertz, S. J., Belden, A. C., Tillman, R., & Luby, J. (2015). Cognitive Control Deficits in Shifting and Inhibition in Preschool Age Children are Associated with Increased Depression and Anxiety Over 7.5 Years of Development. *Journal of Abnormal Child Psychology*, 1–12. doi:10.1007/s10802-015-0101-0

Kessing, L. V., Hansen, M. G., & Andersen, P. K. (2004). Course of illness in depressive and bipolar disorders: Naturalistic study, 1994 – 1999. *British Journal of Psychiatry, 185*, 372-377.

Kessler, R. C., & Bromet, E. J. (2013). The epidemiology of depression. *Annu Rev Public Health, 34*, 119-138. doi: 10.1146/annurev-publhealth-031912-114409

Klingberg, T. (2010). Training and plasticity of working memory. *Trends in Cognitive Sciences*, *14*, 317–324.

Klingberg, T., Fernell, E., Olesen, P. J., Johnson, M., Gustafsson, P., Dahlström, K., … Westerberg, H. (2005). Computerized training of working memory in children with ADHD--a randomized, controlled trial. *Journal of the American Academy of Child and Adolescent Psychiatry*, *44*, 177–86. doi: 10.1097/00004583-200502000-00010

Klingberg, T., Forssberg, H., & Westerberg, H. (2002). Training of working memory in children with ADHD. *Journal of Clinical and Experimental Neuropsychology*, *24*, 781–791. doi: 10.1076/jcen.24.6.781.8395

Kraaij, V., Garnefski, N., & Schroevers, M. J. (2009). Coping, goal adjustment, and

positive and negative affect in definitive infertility. *Journal of Health Psychology, 14,* 18. doi: 10.1177/1359105308097939

Larson, R., & Csikszentmihalyi, M. (1983). The experience sampling method. *New Directions for Methodology of Social and Behavioral Science, 15*, 41-56.

Levens, S. M., & Gotlib, I. H. (2010). Updating positive and negative stimuli in working memory in depression. *Journal of Experimental Psychology. General*, *139*, 654–664. doi: 10.1037/a0020283

Levens, S. M., & Gotlib, I. H. (2015). Updating emotional content in recovered depressed individuals: Evaluating deficits in emotion processing following a depressive episode. *Journal of Behavior Therapy and Experimental Psychiatry*, *48*, 156–163. doi: 10.1016/j.jbtep.2015.03.009

Li, L., Zhu, X., Yang, Y. He, J., Yi., J., Wang, Y., & Zhang, J. (2015). Cognitive emotion regulation: Characteristics and effect on quality of life in women with breast cancer. *Health and Quality of Life Outcomes, 13*:51. doi: 10.1186/s12955-015-0242-4

Luppa, M., Heinrich, S., Angermeyer, M. C., Konig, H. H., & Riedel-Heller, S. G. (2007). Cost-of-illness studies of depression: A systematic review. *Journal of Affective Disorders, 98*, 29-43. doi: 10.1016/j.jad.2006.07.017

Matt, G. E., Vázquez, C., & Campbell, W. K. (1992). Mood-congruent recall of affectively toned stimuli: A meta-analytic review. *Clinical Psychology Review, 12,* 227-255.

Martin, R. C., & Dahlen, E. R. (2005). Cognitive emotion regulation in the prediction of depression, anxiety, stress, and anger. *Personality and Individual Differences, 39*, 1249-1260. doi: 10.1016/j.paid.2005.06.004

McRae, K., Jacobs, S. E., Ray, R. D., John, O. P., & Gross, J. J. (2012). Individual differences in reappraisal ability: Links to reappraisal frequency, well-being, and cognitive control. *Journal of Research in Personality, 46,* 2-7. doi: 10.1016/j.jrp.2011.10.003

McRae, K., & Mauss, I. B. (2016). Increasing positive emotion in negative contexts: Emotional consequences, neural correlates, and implications for resilience. In J. D. Greene, I. Morrison & M. E. P. Seligman (Eds.), Positive Neuroscience (1-37). New York: Oxford University Press.

Melby-Lervag, M., Redick, T., & Hulme, C. (2016).Working memory training does not

improve performance on measures of intelligence or other measures of "far transfer": Evidence form a meta-analytic review. *Perspectives on Psychological Science, 11,* 512-534. doi: 10.1177/1745691616635612

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24*, 167-202.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive Psychology*, *41*, 49–100. doi: 10.1006/cogp.1999.0734

Mor, N., & Daches, S. (2015). Ruminative Thinking: Lessons Learned From Cognitive Training. *Clinical Psychological Science*, *3*, 574–592. doi: 10.1177/2167702615578130

Moser, J. S., Hartwig, R., Moran, T. P., Jendrusina, A. A., & Kross, E. (2014). Neural markers of positive reappraisal and their associations with trait reappraisal and worry. *Journal of Abnormal Psychology, 123*(1), 91-105. doi: 10.1037/a0035817

Motter, J. N., Pimontel, M. A., Rindskopf, D., Devanand, D. P., Doraiswamy, M. P., & Sneed, J. R. (2016). Computerized cognitive training and functional recovery in major depressive disorder: A meta-analysis. *Journal of Affective Disorders*, *189*, 184–191. doi: 10.1016/j.ad.2015.09.022

Nierenberg, A. A., Husain, M. M., Trivedi, M. H., Fava, M., Warden, D., Wisniewski, S. R., . . . Rush A. J. (2010). Residual symptoms after remission of major depressive disorder with citalopram and risk of relapse: A STAR*D report. *Psychological Medicine, 40*, 41-50. doi: 10.1017/S0033291709006011

Nolen-Hoeksema, S. (1991). Responses to depression and their effects on the duration of depressive episodes. *Journal of Abnormal Psychology, 100,* 569-582.

Nolen-Hoeksema, S., & Morrow, J. (1991). A prospective study of depression and posttraumatic stress symptoms after a natural disaster - The 1989 Loma-Prieta earthquake. *Journal of Personality and Social Psychology, 61*(1), 115–121. doi: 10.1037/0022-3514.61.1.115

Nolen-Hoeksema, S., Wisco, B. E., & Lyubomirsky, S. (2008). Rethinking rumination. *Perspectives on Psychological Science, 3*, 400–424. doi: 10.1111/j.1745-6924.2008.00088.x

Nowlan, J. S., Wuthrich, V. M., & Rapee, R. M. (2016). The impact of positive reappraisal on positive (and negative) emotion among older adults. *International Psychogeriatrics, 28*, 681-693. doi: 10.1017/S1041610215002057

Ochsner, K. N., Bunge, S. A., Gross, J. J., & Gabrieli, J. D. E. (2002). Rethinking feelings: An fMRI study of the cognitive regulation of emotion. *Journal of Cognitive Neuroscience, 14*, 1215-1229. doi: 10.1162/089892902760807212

Olatunji, B. O., Naragon-Gainey, K., & Wolitzky-Taylor, K. B. (2013). Specificity of rumination in anxiety and depression: A multimodal meta-analysis. *Clinical Psychology Science and Practice, 20*, 225-257. doi: 10.1111/cpsp.12037

Olesen, P. J., Westerberg, H., & Klingberg, T. (2004). Increased prefrontal and parietal activity after training of working memory. *Nature Neuroscience*, *7*, 75–79. doi:10.1038/nn1165

Ottaviani, C., Thayer, J. F., Verkuil, B., Lonigro, A., Medea, B., Couyoumdjian, A., & Brosschot, J. F. (2016). Physiological concomitants of perseverative cognition: A systematic review and meta-analysis. *Psychological Bulletin, 142*, 231-259. doi: 10.1037/bul0000036

Owens, M., Koster, E. H. W., & Derakshan, N. (2012). Impaired filtering of irrelevant information in dysphoria: An ERP study. *Social Cognitive and Affective Neuroscience*, *7*, 752–763. doi: 10.1093/scan/nsr050

Paelecke-Habermann, Y., Pohl, J., & Leplow, B. (2005). Attention and executive functions in remitted major depression patients. *Journal of Affective Disorders*, *89*, 125–135. doi: 10.1016/j.jad.2005.09.006

Pe, M. L., Brose, A., Gotlib, I. H., & Kuppens, P. (2016). Affective updating ability and stressful events interact to prospectively predict increases in depressive symptoms over time. *Emotion*, *16*, 73–82. doi:10.1037/emo0000097

Pe, M. L., Raes, F., & Kuppens, P. (2013). The cognitive building blocks of emotion regulation: Ability to update working memory moderates the efficacy of rumination and reappraisal on emotion. *Plos One*, *8*, 12. doi:10.1371/journal.pone.0069071

Philippot, P., & Brutoux, F. (2008). Induced rumination dampens executive processes in dysphoric young adults. *Journal of Behavior Therapy and Experimental Psychiatry*, *39*, 219–227. doi:10.1016/j.jbtep.2007.07.001

Schoofs, H., Hermans, D., & Raes, F. (2010). Brooding and reflection as subtypes of rumination: Evidence from confirmatory factor analysis in nonclinical samples using the Dutch Ruminative Response Scale. *Journal of psychopathology and Behavioral Assessment, 32*, 609-617. doi: 10.1007/s10862-010-9182-9

Segrave, R. A., Arnold, S., Hoy, K., & Fitzgerald, P. B. (2014). Concurrent cognitive control training augments the antidepressant efficacy of tDCS: A pilot study. *Brain Stimulation, 7*(2), 325-331. doi: 10.1016/j.brs.2013.12.008

Shilyansky, C., Williams, L. M., Gyurak, A., Harris, A., Usherwood, T., & Etkin, A. (2016). Effect of antidepressant treatment on cognitive impairments associated with depression: A randomised longitudinal study. *The Lancet Psychiatry*. doi: 10K1016+S2215-0366(16)00012-2

Shipstead, Z., Redick, T. S., & Engle, R. (2010). Does working memory training generalize? *Psychologica Belgica*, *17*, 245–276. doi: 10.3758/PBR.17.2.193

Shipstead, Z., Redick, T. S., & Engle, R. W. (2012). Is working memory training effective? *Psychological Bulletin*, *138*, 628–654. doi: 10.1037/a0027473

Siegle, G. J., Ghinassi, F., & Thase, M. E. (2007). Neurobehavioral therapies in the 21st century: Summary of an emerging field and an extended example of cognitive control training for depression. *Cognitive Therapy and Research, 31*(2), 235-262. doi: 10.1007/s10608-006-9118-6

Siegle, G. J., Price, R. B., Jones, N. P., Ghinassi, F., Painter, T., & Thase, M. E. (2014). You gotta work at it: Pupillary indices of task focus are prognostic for response to a neurocognitive intervention for rumination in depression. *Clinical Psychological Science, 2*, 455-471. doi: 10.1177/2167702614536160

Sobocki, P., Jönsson, B., Angst, J., & Rehnberg, C. (2006). Cost of depression in Europe. *Journal of Mental Health Policy and Economy, 9*, 87-98.

Teasdale, J. D., Segal, Z. V., Williams, J. M. G., Ridgeway, V. A., Soulsby, J. M., & Lau, M. A. (2000). Prevention of relapse/recurrence in major depression by mindfulness-based cognitive therapy. *Journal of Consulting and Clinical Psychology, 68*, 615-623. doi: 10.1037//0022-006X.68.4.615

ten Doesschate, M. C., Bockting, C. L. H., Koeter, M. W. J., & Schene, A. H. (2010). Prediction of recurrence in recurrent depression: A 5.5-year prospective study. *Journal of Clinical Psychiatry, 71,* 984-991. doi: 10.4088/JCP.08m04858blu

Treynor, W., Gonzalez, R., & Nolen-Hoeksema, S. (2003). Rumination reconsidered: A psychometric analysis. *Cognitive Therapy and Research, 27,* 247–259.

Vanderhasselt, M.-A., & De Raedt, R. (2009). Impairments in cognitive control persist during remission from depression and are related to the number of past episodes: An event related potentials study. *Biological Psychology*, *81*, 169–176.

Verstraeten, K., Vasey, M. W., Raes, F., & Bijttebier, P. (2010). Brooding and reflection as components of rumination in late childhood. *Personality and Individual Differences, 48,* 367-372. doi: 10.1016/j.paid.2009.11.001

Vijayakumar, N., Whittle, S., Yücel, M., Byrne, M. L., Schwartz, O., Simmons, J. G., & Allen, N. B. (2016). Impaired maturation of cognitive control in adolescents who develop major depressive disorder. *Journal of Clinical Child & Adolescent Psychology*, *45*, 31–43. doi: 10.1080/15374416.2014.987381

Wells, A. (2000). *Emotional disorders and metacognition innovative Cognitive Therapy*. New York: Wiley.

Westerberg, H., Jacobaeus, H., Hirvikoski, T., Clevberger, P., Ostensson, M., Bartfai, A., & Klingberg, T. (2007). Computerized working memory training after stroke - A pilot study. *Brain Injury*, *21*, 21–29. doi: 10.1080/02699050601148726

Whitmer, A. J., & Banich, M. T. (2007). Inhibition versus switching deficits in different forms of rumination. *Psychological Science*, *18*(6), 546–553.

Whitmer, A. J., & Gotlib, I. H. (2012). Switching and backward inhibition in major depressive disorder: The role of rumination. *Journal of Abnormal Psychology*, *121*, 570–578. doi: 10.1037/a0027474

Woody, M. L., Kudinova, A. Y., McGeary, J. E., Knopik, V. S., Palmer, R. H. C., & Gibb, B. E. (2016). Influence of maternal depression on children's brooding rumination: Moderation by CRHR1 TAT haplotype. *Cognition & Emotion, 30*, 302-314. doi: 10.1080/02699931.2014.998631

Woody, M. L., McGeary, J. E., & Gibb, B. E. (2014). Brooding rumination and heart rate variability in women at high and low risk for depression: Group differences and moderation by COMT genotype. *Journal of Abnormal Psychology, 123*, 61-67. doi: 10.1037/a0035450

World Health Organization (2016). Depression: World Health Organization Fact sheet no 369. Accessed on 13-01-2017 from

http://www.who.int/mediacentre/factsheets/fs369/en/ [Web Page].

Xavier, A., Cunha, M., & Pinto-Gouveia, J. (2016). Rumination in adolescence: The distinctive impact of brooding and reflection on psychopathology. *Spanish Journal of Psychology, 19*, e37. doi: 10.1017/sjp.2016.41

Zetsche, U., & Joormann, J. (2011). Components of interference control predict depressive symptoms and rumination cross-sectionally and at six months follow-up. *Journal of Behavior Therapy and Experimental Psychiatry, 42*, 65–73. doi: 10.1016/j.jbtep.2010.06.001

CHAPTER 2

COGNITIVE CONTROL INTERVENTIONS FOR DEPRESSION: A SYSTEMATIC REVIEW OF FINDINGS FROM TRAINING STUDIES[1]

ABSTRACT

There is a strong interest in cognitive control training as a new intervention for depression. Given the recent promising meta-analytical findings regarding the effects of cognitive training on cognitive functioning and depressive symptomatology, the current review provides an in-depth discussion of the involvement of cognitive control in depression. We consider the state-of-the-art research on how manipulation of cognitive control may influence cognitive and depression-related outcomes. Evidence for the effectiveness of cognitive control training procedures are discussed in relation to three stages of depression (at-risk, clinically depressed, remission) and the training approach that was deployed, after which the putative theoretical mechanisms are discussed. Finally, we provide ways in which cognitive control training can be utilized in future research.

[1] Based on Koster*, E. H. W., Hoorelbeke*, K., Onraedt, T., Owens, M., & Derakshan, N. (2017) Cognitive control interventions for depression: A systematic review of findings from training studies. *Clinical Psychology Review, 53,* 79-92. doi: 10.1016/j.cpr.2017.02.002

Note: Ernst H. W. Koster and Kristof Hoorelbeke contributed equally to the manuscript and share first authorship. Ernst H. W. Koster explicitly agreed for the inclusion of the paper in this PhD dissertation.

Depression is the leading cause of disability worldwide, and is a major contributor to the global burden of disease (World Health Organization, 2012). Moreover, depression is one of the most common and debilitating psychiatric disorders with an estimated 8 to 20% of the population experiencing at least one depressive episode during their lifetime. Despite the availability of well-established psychological and pharmacological treatment options for depression, that have acceptable short-term effectiveness, various challenges in the treatment of depression remain. Major challenges are that relapse or recurrence rates after remission or recovery remain very high and tend to increase (up to 80%) with the number of episodes (Beshai, Dobson, Bockting, & Quigley, 2011). Moreover, there is a substantial proportion of patients who fail to respond to treatment (Thomas et al., 2013). Treatment-resistant and recurrent depressive episodes are strongly associated with poor psychosocial outcomes due to increasing social problems (e.g., elevated divorce rates) and financial problems (e.g., multiple sick leaves, unemployment).

A crucial idea is that current treatments insufficiently target key underlying vulnerability factors of depression, causing depression to remit insufficiently or, when remitted, to still act as a risk factor for new depressive episodes. Although cognitive impairments such as concentration, memory, and attentional problems were initially considered side effects of the affective problems, recent neurobiological as well as cognitive research indicates that diminished cognitive control over information in working memory may be a key psychological vulnerability factor (Joormann, Yoon, & Zetsche, 2007; Millan et al., 2012; Siegle, Ghinassi, & Thase, 2007). These information processing factors are thought to have proximal links with rumination, a key maladaptive emotion regulation strategy, that can in turn influence depressive symptoms (Joormann & D'Avanzato, 2010; Joormann & Vanderlind, 2014). Importantly, recent findings suggest that existing antidepressant treatments do not impact cognitive impairments in depression (Shilyansky et al., 2016).

Cognitive control refers to the executive processes that allow information processing and behavior to vary adaptively over time depending on current goals, rather than remain rigid and inflexible. These cognitive control processes include a broad class of mental operations including goal or context representation and

maintenance, and strategic processes such as attention allocation and stimulus-response mapping. Miyake et al. (2000) have suggested that executive functions mapping cognitive control can be operationalized into three major, interrelated yet separable functions: mental set shifting (shifting), information updating and monitoring of working memory representations (updating), and inhibition of prepotent responses (inhibition). Joormann and colleagues (2007) have argued, based on the work of Hasher and Zacks (1979), that cognitive control processes play a crucial role in determining the content of working memory, conceptualized as a limited-capacity system for the temporary storage of information (Baddeley & Hitch, 1974; Jonides et al., 2008). Difficulties in exerting cognitive control over negative information operations could explain the proliferation of negative information in working memory (Joormann et al., 2007), directly linking cognitive control impairments to perseverative negative thinking (depressive rumination), a well-supported vulnerability factor for depression (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008).

There is converging evidence from psychopathology and neurobiological research to indicate that depression is associated with broad impairments on cognitive control tasks (for a recent meta-analysis, see Snyder, 2013). Moreover, across a variety of different tasks individuals at-risk for depression have also been found to display reduced cognitive control. For instance, cognitive control deficits have been observed in participants showing heightened trait rumination (e.g., Beckwé, Deroost, Koster, De Lissnyder, & De Raedt, 2014) and subclinical levels of depressive symptomatology (dysphorics; e.g., Derakshan, Salt, & Koster, 2009; Joormann, 2004; Owens, Koster, & Derakshan, 2012). Similarly, cognitive control impairments have been observed in a vast amount of studies exploring cognitive functioning in depressive patients (e.g., Deveney & Deldin, 2006; Goeleven, De Raedt, Baert, & Koster, 2006; Harvey et al., 2004; Levens & Gotlib, 2010; Merriam, Thase, Haas, Keshavan, & Sweeney, 1999; Murphy et al., 1999), and remain evident following remission from depression (e.g., Demeyer, De Lissnyder, Koster, & De Raedt, 2012; Levens & Gotlib, 2015; Paelecke-Habermann, Pohl, & Leplow, 2005; Vanderhasselt & De Raedt, 2009). Importantly, impaired cognitive control is mainly observed in at-risk samples when individuals are processing emotionally negative information (e.g., angry faces or negative self-referring words),

whereas the impairments appear to be more broadly present in individuals that meet clinical levels of depression (Snyder, 2013). Furthermore, several studies suggest that cognitive control deficits are most apparent when engaging in rumination (e.g., Philippot & Brutoux, 2008; Whitmer & Gotlib, 2012). Research indicates that these impairments are not merely correlates of depression, but predict future rumination and the development of new depressive symptoms in prospective studies in healthy (e.g., Pe, Brose, Gotlib, & Kuppens, 2016; Zetsche & Joormann, 2011) and at-risk samples (e.g., Demeyer et al., 2012).

At the neuropsychological level, fronto-limbic disruptions are thought to play a crucial role in cognitive impairments involved in emotion regulation (for reviews, see Pizzagalli, 2011; Roiser, Elliott, & Sahakian, 2012). Key findings from neuroimaging studies have shown that depression is associated with disrupted brain activity in the dorsolateral prefrontal cortex (DLPFC) and anterior cingulate cortex (ACC) (Davidson, Pizzagalli, Nitschke, & Putman, 2002; Etkin, Gyurak, & O'Hara, 2013; Pizzagalli, 2011), with decreased activation in these prefrontal areas being related to reduced cognitive control (Collette & Van der Linden, 2002; Smith & Jonides, 1999). Depression-related increased and sustained amygdala activity in response to negative information (Surguladze et al., 2005; Taylor & Fragopanagos, 2005) has also been related to impaired recruitment of frontal areas (Siegle, Thompson, Carter, Steinhauer, & Thase, 2007). These findings suggest that disrupted connectivity in the limbic-frontal circuitry could play a major role in explaining the hallmark features of depression such as problems in regulating mood and sustained negative affect (De Raedt & Koster, 2010; Joormann et al., 2007). Collectively, it is fair to conclude that improving cognitive control can have profound implications for ensuring better treatment outcomes in depression (Roiser et al., 2012; Siegle, Ghinassi, et al., 2007).

Building on the evidence implicating cognitive control in depression vulnerability (for excellent reviews providing in depth discussions of how cognitive control is related to maladaptive emotion regulation strategies, see Joormann & D'Avanzato, 2010; Joormann & Vanderlind, 2014; Mor & Daches, 2015), the current paper reviews the state-of-the-art research on the efficacy of cognitive control training targeting impaired emotion regulation and depressive symptomatology. Although in its infancy, this

research domain is rapidly expanding with recent meta-analytic evidence suggesting beneficial effects of cognitive training on depression outcomes (Motter et al., 2016). However, existing studies strongly differ in training procedures deployed, intensity of training, comparison groups, outcomes, and quality of the research designs in general. Importantly, including studies with suboptimal designs in meta-analyses holds the risk of accumulating bias (Higgins & Green, 2011). This would only allow a very limited selection of the existing studies to be included in a meta-analysis, not fully representing the cognitive control training literature. Furthermore, including such heterogeneous studies in one meta-analysis – in absence of a sufficient amount of studies to conduct moderator analysis for type of intervention, intensity of training, phase of illness, etc. – is itself suboptimal as it may obscure genuine differences in training effects (Higgins & Green, 2011). As a result, based on the Cochrane recommendations for systematic reviews / meta-analyses (Higgins & Green, 2011), the cognitive control training literature would benefit from a systematic review specifically focusing on current findings and challenges regarding the application of cognitive control training as a potential novel intervention tool throughout the different stages of depression. Hence, we provide an overview of methods used in training cognitive control as well as effects of cognitive control training on impaired emotion regulation and depressive complaints in at-risk, clinically depressed, and remitted depressed patient samples. Given that these studies often use a broad conceptual operationalization of cognitive control and show considerable overlap between executive functions, we will consistently refer to 'cognitive control training' while acknowledging where studies may differ in the specific components of cognitive control of interest.

EXPERIMENTAL MANIPULATION OF COGNITIVE CONTROL

Given the accumulating evidence that points towards the involvement of processes of cognitive control in different stages of depression, it is imperative that research addresses the question of causality. For this purpose, existing cognitive paradigms can be modified to manipulate cognitive processes. An example of this is seen in the Cognitive Bias Modification technique used to manipulate allocation of

attention (CBM; Koster, Fox, & MacLeod, 2009; MacLeod, Rutherford, Campbell, Ebsworthy, & Holker, 2002; for a recent review, see Koster & Hoorelbeke, 2015). In a similar vein, in the context of cognitive control, a number of 'cognitive control training' (CCT) tasks have been developed with this purpose in mind.

Siegle, Ghinassi, et al. (2007) have adjusted the Paced Auditory Serial Addition Task (PASAT; Gronwall, 1977; for a review, see Tombaugh, 2006). During the adaptive PASAT, a series of digits is presented and participants continuously add the currently presented digit to the previously presented digit. They need to provide a response to the sum of the last two presented digits which generates interference with updating the last heard digits in working memory. Task difficulty is tailored to participant's performance by changing the inter-stimulus interval between each digit, causing the digits to follow faster or slower. Doing so, it is assumed that cognitive control is being trained in a challenging task context. A second frequently used cognitive task to manipulate cognitive control is the dual n-back task. In the adaptive dual n-back task (Jaeggi, Buschkuehl, Jonides, & Perrig, 2008) combinations of visual (e.g., square position) and auditory (e.g., spoken letter) stimuli are presented simultaneously on each trial. On every presentation, participants have to respond if one or both of the currently presented stimuli matches a stimulus presented *n* steps before by pressing the respective response buttons. The difficulty of the task is adapted at the block-level, where based on participant's performance the level of *n* of the subsequent block is changed according to the number of errors per session (Jaeggi et al., 2008). Another example is the modified Negative Affective Priming task. In the Negative Affective Priming (NAP) task (Joormann, 2006), a complete trial is comprised of two sequential trials: a prime trial and a probe trial. Both trials consist of a simultaneously presented distractor and target stimulus. In all trials, participants are required to respond to the target by categorizing it as negative or positive, while ignoring (inhibiting) the distractor. In order to train cognitive control, researchers have manipulated the ratio of negative and positive distractors and targets, training participants to either attend to negative words or to inhibit them (e.g., Daches & Mor, 2014). Other examples include modifications of the Flanker task in which participants train inhibition of irrelevant non-

emotional information (distractor arrows flanking the target arrow) throughout a series of incongruent trials (e.g., Cohen et al., 2016).

Although the above presented training tasks represent widely adopted CCT approaches in the context of depression (cf. infra), several variations have been used in the broader field of cognitive transfer. That is, there is a long history of studies trying to establish transfer effects on cognitive tasks in non-clinical research with healthy populations. This has turned out to be a challenging endeavor (for a review, see Shipstead, Redick, & Engle, 2012). In this context, the distinction between (1) improvements on the specific training task, (2) *near transfer*, being improvements on tasks that are similar to the training tasks, and (3) *far transfer*, being improvements on tasks or other measures that are not of the same nature or appearance as the training task, is crucial (Shipstead, Redick, & Engle, 2010). Observing improvement on training and near transfer tasks is necessary to demonstrate the mechanism by which far transfer can occur. Critical to far transfer is the assumption that the training task and the outcome share a more general underlying processing component, and that training-induced plasticity will lead to benefits in daily life performance (Shipstead et al., 2010).

Establishing Cognitive Transfer

Experimental studies, manipulating cognitive control while keeping other variables constant, have provided evidence for the efficacy of cognitive training tasks in increasing cognitive functioning in healthy populations (e.g., Harrison et al., 2013; Jaeggi, Buschkuehl, Shah, & Jonides, 2014). However, cognitive transfer effects have often been limited to near transfer, whereas demonstrating far transfer effects on unrelated tasks has been more troublesome (e.g., Harrison et al., 2013; Redick et al., 2013; for critical reviews, see Buschkuehl, Jaeggi, & Jonides, 2012; Jaeggi, Buschkuehl, Jonides, & Shah, 2012; Klingberg, 2010; Morrison & Chein, 2011; Shipstead et al., 2012).

Some far transfer effects have been demonstrated using (parts of) the commercialized Cogmed training battery (Klingberg et al., 2005; Klingberg, Forssberg, & Westerberg, 2002; Westerberg et al., 2007), a multifaceted training approach using a combination of varying tasks and stimulus types. Most transfer effects of the Cogmed

training battery were found in children with ADHD on cognitive control, fluid intelligence (Klingberg et al., 2005) and symptom severity ratings (Klingberg et al., 2002). However, effects were not always tested against an active control condition, permitting placebo effects to play an important role (Shipstead et al., 2012). Large-scale studies in children with low WMC found no lasting effects of intensive cognitive training (Roberts et al., 2016). Moreover, meta-analytic examination of CCT in ADHD indicated little transfer to symptomatology (Cortese et al., 2015). Transfer on cognitive control and fluid intelligence was also replicated in a healthy young adult sample (Olesen, Westerberg, & Klingberg, 2004). Using a different battery of cognitive control tasks, including working memory, perceptual speed and episodic memory training tasks, Schmiedek, Lövdén, and Lindenberger (2010) found positive transfer effects on cognitive abilities. However, these effects cannot be simply attributed to CCT because of the combination with the other training tasks.

In contrast to the multifaceted approach, Jaeggi et al. (2008) used a single, but adaptive task. Their study, indicating that the adaptive dual n-back task could lead to an increase in fluid intelligence, has been one of the most influential and cited CCT studies. Every participant performed the dual n-back task for approximately 25 minutes per day, for a period of 8 to 19 days. Compared to a no-training control group and controlling for baseline scores, participants in the training group showed a significant increase in fluid intelligence scores. Further analyses indicated that the gain was responsive to the dosage of training. In a follow-up study Jaeggi et al. (2010) demonstrated that a single n-back task can have the same training potential related to fluid intelligence as the dual n-back task. Also Chein and Morrison (2010) found transfer effects of an adaptive complex working memory span task on cognitive control and reading comprehension. Using a variant of the single n-back task that was made more appealing to children, Jaeggi, Buschkuehl, Jonides, and Shah (2011) showed that transfer to fluid intelligence was dependent of improvements during training, and this effect remained at follow-up, three months later. Reviewing the literature, Klingberg (2010, p. 322) concludes that “the observed training effects suggest that working memory training could be used as a remediating intervention for individuals for whom low working memory capacity is a limiting factor for academic performance or everyday life”. However, as Shipstead et al.

(2012) state, several concerns over the utility of working memory training remain, leading the authors to conclude that the current literature provides insufficient evidence of the efficacy of working memory training (p. 647; but see Au et al., 2015). An extensive recent review of the literature echoed this conclusion and argues that better practices need to be adopted in the literature on cognitive training (Simons et al., 2016).

Despite the criticism on whether cognitive training can change working memory capacity or fluid intelligence, several other findings indicate that extensive practice or training can have sustained influences on cognitive processing speed and efficiency (e.g., Colzato, van den Wildenberg, Zmigrod, & Hommel, 2012; Green & Bavelier, 2003; Lundqvist, Grundström, Samuelsson, & Rönnberg, 2010; Nouchi et al., 2013). Furthermore, research into the effects of training on the neural correlates of working memory functions has shown training induced associations with prefrontal mechanisms of control (Westerberg & Klingberg, 2007). Evidence for functional changes in fronto-parietal brain areas after different types of cognitive training has also been reported in the literature (for a review, see Klingberg, 2010), suggesting cognitive training induces changes in both the central executive component of working memory and maintenance processes. Importantly, when comparing brain changes between a control and a video gaming training group, trained for 2 months for at least 30 minutes per day with a platform game, significant gray matter increase can be observed in left dorsolateral prefrontal cortex (DLPFC) after training (Kühn, Gleich, Lorenz, Lindenberger, & Gallinat, 2013). Given the key role of the DLPFC in cognitive control, and depression-related reduced brain activity in the DLPFC, this finding indicates the potential of using CCT to counteract depression (see Siegle, Ghinassi, et al., 2007).

In sum, despite ongoing controversy about the claim that cognitive control or working memory processes can be trained in healthy individuals to transfer to general cognitive performance, there is extensive research indicating that sustained practice of specific cognitive operations can have reliable effects on cognitive performance on related tasks (near transfer) at behavioural and neural levels. Furthermore, when exploring effects of cognitive control manipulations on outcome measures other than cognitive functioning (e.g., indicators of emotional well-being), lack of far cognitive

transfer effects may warrant careful interpretation of experimental findings. However, this does not necessarily rule out transfer to emotional processes. Indeed, the above mentioned inconsistencies in establishing cognitive transfer effects have not withheld researchers from exploring the clinical potential of CCT. In the following section we discuss how the systematic literature search was conducted, after which we review existing evidence for the clinical potential of CCT throughout the different stages of depression.

METHOD

Literature Search

The search was conducted in accordance with the guidelines for transparent reporting of systematic reviews and meta-analyses (Moher, Liberati, Tetzlaff, Altman, & Prisma Group, 2009). During the first phase, Web of Science and PubMed – two central databases in the field of clinical psychology / psychiatry – were searched to identify CCT studies for potential inclusion in the systematic review. The last search was conducted on August 16, 2016. Given the diversity in applications of CCT in the context of (vulnerability for) depression (e.g., at-risk groups or outcomes, MDD and RMD samples), the search included key words specifying the type of intervention only. For this purpose, we used a broad range of terms that have often been used in the context of CCT for depression: *cognitive control therapy* OR *cognitive control training* OR *cognitive control task* OR *neurocognitive training* OR *cognitive training* OR *executive control training* OR *working memory training* OR *cognitive emotional training* OR *cognitive remediation* OR *neurobehavioral therapy* (all fields were entered at the level of record title).

Second, for each of the selected CCT manuscripts during the previous phase, Google Scholar profiles of the first authors were screened for additional CCT studies. Furthermore, we conducted an extra search for papers reporting results of protocols that were identified during the previous phase, and screened reference lists of identified theoretical papers, reviews, or meta-analyses regarding CCT for depression.

Inclusion Criteria

Studies were selected if they met the following inclusion criteria: (a) The study was a published manuscript written in English (to avoid file drawers, PhD theses were also considered); (b) Studies included an experimental manipulation of cognitive control using cognitive training methodology. The training procedure should be targeting executive processes regulating working memory functioning (e.g., updating, inhibition, shifting; Miyake et al., 2000). For this purpose, studies strictly reporting effects of cognitive bias modification training or mere attention training were excluded. (c) Effects of CCT were evaluated in at-risk (e.g., showing subclinical levels of depressive symptomatology, elevated trait rumination scores, children of parents with MDD, etc.; excluding anxiety and/or psychotic disorders), clinically depressed (MDD, excluding bipolar disorder), or remitted depressed (RMD) samples. Additionally, convenience samples with a specific focus on factors associated with depression risk (e.g., maladaptive emotion regulation, depressive symptomatology, stress/emotional reactivity, affect, etc.) were also included as 'at-risk studies'.

Study Selection

During the first phase of the search 5547 records were identified via Web of Science and PubMed (see Figure 1). A first screening took place based on title, after which the abstracts of the remaining 1160 records were screened. Prior to evaluation of the full-text articles, duplicates were removed. Full copies of 116 articles were read which resulted in the inclusion of 28 manuscripts reporting effects of CCT in the context of (vulnerability for) depression. Additionally, two records were identified as relevant protocols, along with 18 theoretical papers / reviews / meta-analyses. In a second phase, snowballing took place based on the Google Scholar profiles of the first authors of the selected CCT manuscripts (636 records). Moreover, reference lists of the theoretical papers / reviews / meta-analyses were screened for additional CCT studies (1448 records), and results of protocols were searched for online (two records). These records were again screened based on title and/or abstract, after which duplicates were removed prior to conducting a full-text screening. Fifteen additional unique CCT full-text manuscripts were evaluated, resulting in the inclusion of five manuscripts reporting

effects of CCT in the context of (vulnerability for) depression. After both phases 33 manuscripts were included in the systematic review, reporting findings of a total of 34 CCT experiments (cfr. Figure 1).

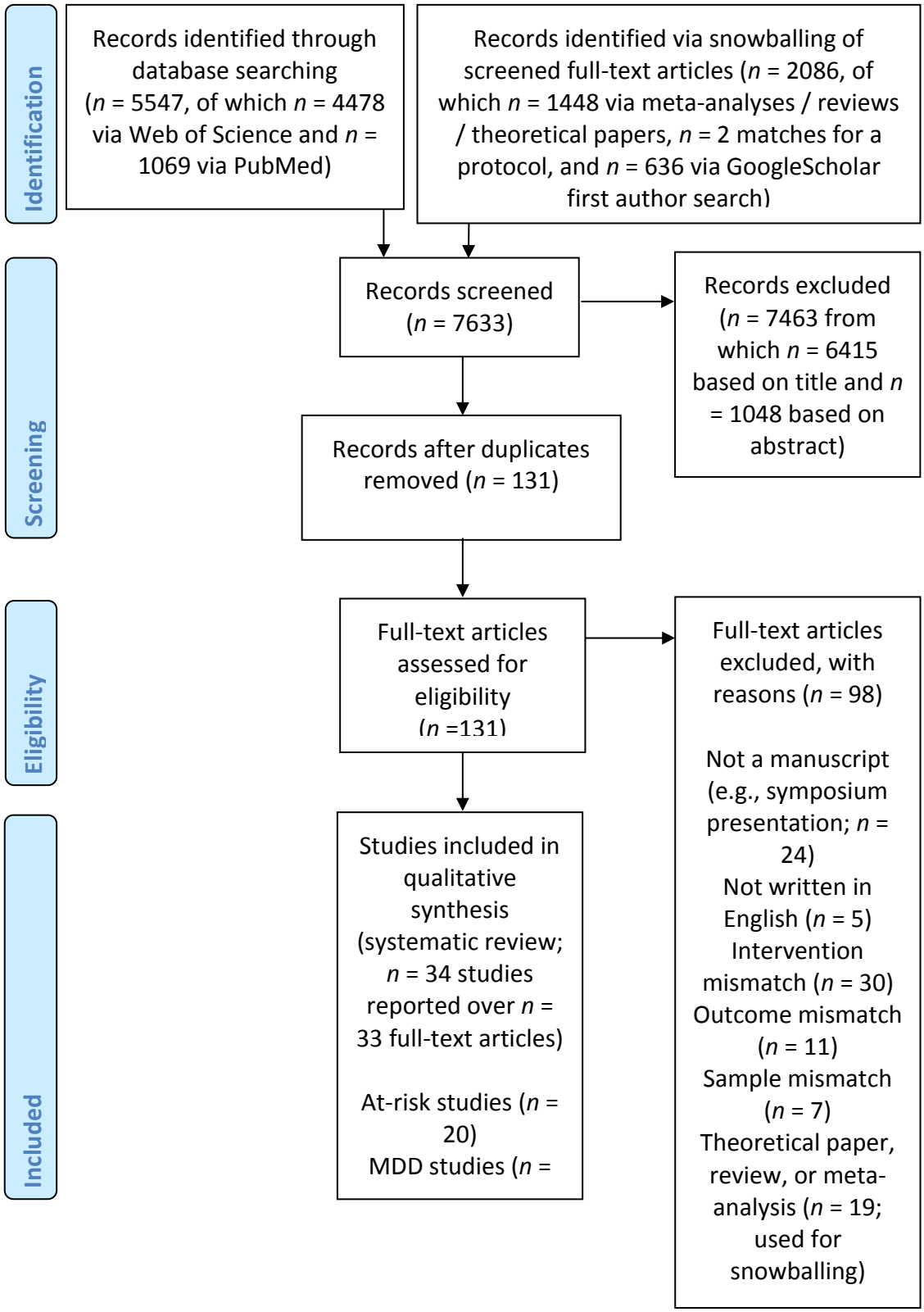


Figure 1. PRISMA flow chart

Coding Procedure

Each screening phase was conducted by two independent coders using a predefined strategy. Discrepancies between both coders were discussed with one of the first authors of this manuscript. During the full-text screening phase, both coders operated independently based on predefined coding strategies for exclusion and inclusion. Both coders were trained using a selection of the identified records. If coders opted for inclusion of the article, the article was categorized as 'at-risk', 'MDD' or 'RMD'. Quality of the rating procedure was assessed using indicators of inter rater agreement. This yielded $\kappa = .87$ and $\kappa = .83$ for inter rater agreement on inclusion / exclusion and categorization of the to-be-included manuscripts respectively, suggesting excellent agreement (Orwin, 1994).

RESULTS

Cognitive Control Training for At-risk Samples

Single-session manipulations or extensive training procedures? We identified 20 studies reporting effects of CCT on cognitive risk factors for depression (e.g., rumination, mood, depressive symptoms; see Figure 1; for a more detailed description of the research designs deployed in each at-risk study, see Appendix Table 1) in healthy or at-risk samples, from which six studies explored effects of a single-session manipulation. Critical review of these studies suggests that single-session manipulations are nonsufficient to yield reliable effects on (neurological indicators of) cognitive functioning (Calkins, Deveney, Weitzman, Hearon, & Siegle, 2011; Cohen et al., 2016; Daches, Mor, & Hertel, 2015), state rumination, or mood (Calkins et al., 2011; Daches et al., 2015; de Putter, Vanderhasselt, Baeken, De Raedt, & Koster, 2015). Interestingly, in absence of immediate effects on self-report measures for mood and state rumination, de Putter et al. (2015) observed beneficial effects of CCT on heart rate variability as a physiological indicator of stress reactivity during a rumination induction procedure. Furthermore, Cohen, Mor, and Henik (2015) found beneficial effects of a single-session cognitive control manipulation on susceptibility to a rumination induction procedure.

Moreover, CCT seemed to buffer negative effects of trait brooding on mood during this induction procedure. In this context, it is interesting to note that Quinn, Keil, Utke, and Joormann (2014) found that individual differences in trait rumination predicted response to cognitive control manipulations in healthy participants. That is, only participants high in trait rumination showed beneficial effects of a single-session manipulation of cognitive control on cortisol response to a stress induction procedure. These findings suggest that given more extensive training, exerting cognitive control over (emotional) information may act to reduce cognitive vulnerability for depression.

Indeed, following-up on their initial promising effects (Cohen et al., 2015), Cohen et al. (2016) reported beneficial effects of an 18-session modified Flanker task training on amygdala activity and behavioral interference of aversive pictures in healthy participants. Moreover, Cohen and colleagues (2016) reported a tendency towards increased connectivity between the amygdala and prefrontal regions, two key structures in the context of vulnerability for depression. Importantly, change in amygdala activity was associated with reduced interference of aversive stimuli. Linking cognitive and emotional transfer measures to neurophysiological parameters, this innovative study provides insights in the mechanisms that may underlie beneficial effects of CCT. Furthermore, in contrast to the promising effects following 18 sessions of training, Cohen et al. (2016) found no beneficial effects following the first session, demonstrating the need for repeated practice. Moreover, extending findings of de Putter and colleagues (2015), Xiu, Zhou and Jiang (2016) reported beneficial effects of 20 days of adaptive Running memory task training on high-frequency heart rate variability during an emotion regulation task. Additionally, Gavelin, Boraxbekk, Stenlund, Järvholm, and Neely (2015) explored effects of a multi-session and multi-training task approach on a wide variety of cognitive transfer measures in patients suffering from exhaustion disorder, showing beneficial effects on several near and far cognitive transfer tasks. Interestingly, patients in the combined CCT + TAU condition also reported less subjective cognitive complaints and showed a stronger decrease in burnout symptoms compared to a TAU control group. These findings demonstrate the need for repeated exposure to CCT tasks in order to accomplish cognitive and emotional transfer.

Evidence from adaptive PASAT training studies. Among multi-session CCT studies, the most widely adopted training approach is the adaptive PASAT. That is, from all studies identified as 'cognitive control training' studies using multiple sessions in this review, 12 manuscripts report effects of an adaptive PASAT manipulation. Here it is noteworthy that some studies combine the PASAT with an attention training developed by Wells (Wells, 2000). This is a selective attention training consisting of counting sounds accompanied by naturalistic sounds. Five of these have explored effects of this training approach on cognitive risk factors for depression in healthy or at-risk populations. In line with the above mentioned multi-session CCT studies of Cohen et al. (2016) and Gavelin et al. (2015), the adaptive PASAT trains cognitive control using non-emotional stimuli, which are believed to be presented in a stressful task context (Siegle, Ghinassi, et al., 2007). Initial studies have found mixed evidence for beneficial effects of this training on cognitive vulnerability for depression and depressive symptomatology. For instance, in a community sample with elevated depressive symptoms, Calkins, McMorran, Siegle, and Otto (2015) reported promising effects of a brief combined training procedure (three sessions of adaptive PASAT and Wells' attention training over two weeks) on self-reported mood and depressive symptomatology compared to an active control condition. Calkins and Otto (2013) also explored effects of a brief CCT procedure on mood and depressive symptomatology in a community sample characterized by heightened obsessive compulsive symptoms and low depressive symptomatology. Again, beneficial effects on mood were found. However, no differential effects on depressive symptomatology and a trend towards worsening of obsessive compulsive symptoms was reported. It is possible that the lack of effects on depressive symptoms in this study can be attributed to low levels of depressive symptomatology at baseline and the distinctive pattern of cognitive impairments that may underlie obsessive compulsive processes (e.g., Remijnse et al., 2013). Interestingly, using the same brief three-session training procedure, Moshier, Molokotos, Stein, and Otto (2015) could not replicate beneficial effects on depressive symptomatology in students or community adults with either euthymic or depressed mood.

Using a more extensive adaptive PASAT training procedure (10 sessions over two weeks), Hoorelbeke, Koster, Vanderhasselt, Callewaert, and Demeyer (2015) found

beneficial effects on stress reactivity and brooding in a sample of high trait ruminators. That is, compared to an active control condition, the CCT group was less susceptible to a stress induction procedure in lab context in terms of momentary rumination and self-reported mood. Interestingly, participants from the CCT group also reported a decrease in brooding from baseline to four-week follow-up assessment, which took place during the examination period, a naturalistic stressor for students. Again, these findings suggest that at-risk groups may benefit from extensive training. Additionally, in line with previous findings suggesting that cognitive control impairments become more apparent when engaging in rumination (Philippot & Brutoux, 2008; Whitmer & Gotlib, 2012), these findings suggest that effects of CCT in at-risk groups should be assessed in a challenging context. In following up on these initial promising results, Hoorelbeke, Koster, Demeyer, Loeys, and Vanderhasselt (2016) explored effects of CCT on the interplay between affect and emotion regulation in daily life using experience sampling. In a convenience sample of undergraduate students, they found that one of the mechanisms underlying the effects of adaptive PASAT on stress reactivity and trait rumination is that it allows individuals to engage less in ruminative thought processes when confronted with decreases in positive affect. However, next to demonstrating cognitive transfer on a dual n-back task, overall transfer effects on emotion regulation processes were limited in this healthy population.

Evidence from n-back training approaches using neutral stimuli. Dual n-back training forms a second widely adopted training approach. Following the initial promising findings of Jaeggi et al. (2008, 2010), Owens, Koster, and Derakshan (2013) explored whether eight sessions of adaptive dual n-back training could improve reduced working memory capacity and impaired filtering of irrelevant information in dysphoric participants, where filtering efficiency was measured by electroencephalographic recording of an event-related potential sensitive to the ratio of relevant to irrelevant information maintained in working memory. Dysphoric participants in the adaptive training group showed training-related gains in cognitive control that were accompanied by gains in working memory capacity and filtering efficiency compared to the non-adaptive control group. These results were among the first to provide promising findings in support of (adaptive) cognitive control training in

improving cognitive as well as neural efficiency in dysphoric individuals. However, adopting a similar training approach using six sessions of dual n-back training over a period of one week in trait ruminators yielded no beneficial effects on working memory task performance in two CCT studies (Onraedt & Koster, 2014). Furthermore, no differential effects of training were found on self-reported rumination or depressive symptomatology over time (Onraedt & Koster, 2014). Similarly, Owens and colleagues (2013) did not find beneficial effects on depressive symptomatology. Importantly, in one of both training studies conducted by Onraedt and Koster (2014), there was a tendency that improvement in CCT task performance predicted a decrease in depressive symptomatology over time, suggesting that more extensive training may be warranted.

In this context, it is interesting to note that Takeuchi et al. (2013, 2014) adopted a training procedure in which a sample of healthy students had to complete 27 sessions of a multi-task training approach including the dual n-back task over a period of four weeks. Takeuchi et al. (2013) reported beneficial cognitive transfer effects on untrained verbal and visual working memory tasks. Interestingly, the CCT group also experienced beneficial effects on self-reported negative mood. Furthermore, during an implicit face-matching task intended to evoke negative affect, participants from the CCT group demonstrated reduced brain activity related to negative emotions in the left posterior insula and left frontoparietal area (Takeuchi et al., 2014). As suggested by Takeuchi and colleagues (2014, p. 11), this may reflect increased cognitive capacity allowing better management of emotional information. However, an important disadvantage of this study is that effects of CCT were compared to a no-training control condition.

Training cognitive control over emotional information. In contrast to the dual n-back training studies that have tried to reduce cognitive vulnerability for depression by manipulating cognitive control over neutral information in at-risk populations, studies using affective modifications of this training paradigm have been more successful in demonstrating cognitive and emotional transfer. Note however that studies exploring effects of affective modifications of the dual n-back have also typically relied on more intensive training procedures. Schweizer, Hampshire, and Dalgleish (2011) were the first to extend the dual n-back training procedure to target the

processing of emotional information in working memory. They modified the dual n-back task by changing the squares and spoken letters by pictures of faces and spoken words respectively. Schweizer et al. (2011) compared effects of the affective modification of the dual n-back with a neutral dual n-back training group, and an active control group over a training period of 20 days. Compared to the active control group, digit span and fluid intelligence scores improved significantly after dual n-back training for both the emotional and neutral training group. Furthermore, Schweizer et al. (2011) found that the emotional dual n-back training group showed greater transfer effects to emotional Stroop compared to the neutral training group, suggesting that affective modifications of CCT tasks may promote transfer to emotional outcome measures. Indeed, in a follow-up study, Schweizer, Grahn, Hampshire, Mobbs, and Dalgleish (2013) found that improved emotional dual n-back task performance over a 20-days training period was related to increased efficiency of the frontoparietal brain regions. Moreover, emotional CCT was associated with decreased reports of emotional distress after viewing distressing movie clips when instructed to regulate emotions, relative to movie clips during which participants did not have to regulate emotions. These findings indicate that emotional CCT improves emotion regulation. Finally, improvements in emotion regulation were associated with increased activation of the same frontoparietal regions involved in emotional dual n-back task progress.

Further elucidating the relation between cognitive control over emotional information and rumination, Daches and Mor (2014) found beneficial effects of a training to inhibit negative information (compared to a training to attend to negative information and a sham training). The inhibition training group was characterized by a non-significant trend towards increase in inhibition of irrelevant negative information on the NAP following training, whereas training participants to attend to negative information decreased inhibition to emotional stimuli over time. Moreover, only the inhibition training group showed a reduction in brooding over time. However, no beneficial effects were observed for depressive symptomatology.

Interim conclusion. Taken together, these findings suggest that, given extensive repeated training, CCT holds potential as a preventive intervention for depression (see Appendix Table 1). That is, several studies have reported beneficial effects on

behavioral and self-report measures of cognitive functioning, neurophysiological indicators of (affective) information processing and emotion regulation, and self-reported mood and emotion regulation. However, demonstrating both cognitive and emotional transfer has proven to be challenging with absence of effects often being reported in studies utilizing a limited amount of training sessions (independent of the CCT approach that was utilized; cfr. Appendix Table 1). Furthermore, limited effects on depressive symptomatology in healthy populations are to be expected given the nature of the population and the premise that CCT is only useful when there are cognitive control *deficits*, which may simply not be the case in healthy samples. Finally, there is a positive evolution in CCT-studies towards adoption of active control conditions (see Appendix Table 1). However, many studies have relied on relatively small samples, which may have yielded insufficient power to consistently detect training effects when analyzing between-group interactions. Nonetheless, given these mixed findings more research is necessary exploring the mechanisms underlying effects (or absence of effects) of CCT in at-risk populations.

Cognitive Control Training in MDD Samples

Evidence from adaptive PASAT training studies. In the context of CCT for depression, one of the most influential studies was carried out by Siegle, Ghinassi, et al. (2007). Siegle, Ghinassi, et al. (2007; see Appendix Table 2 for a more detailed description of the research designs deployed in each MDD study) investigated the added benefit of CCT in clinically depressed patients receiving TAU (outpatient day-treatment in combination with psychotropic medication) compared to a control group only receiving TAU. They were the first to explore the clinical potential of CCT using a training protocol that was composed of two components known to activate the prefrontal cortex, being Wells' attention training and the adaptive PASAT. After two weeks of treatment, participants who received CCT showed significant improvements in non-adaptive PASAT performance compared to the control group. Furthermore, self-reported rumination and depressive symptomatology significantly decreased relative to the control group. Interestingly, a subset of the participants from the CCT condition also completed fMRI assessment, suggesting that disruptions in the amygdala and DLPFC related to depression normalized after CCT (Siegle, Ghinassi, et al., 2007).

In a follow-up report, Siegle and colleagues (2014) extended the data obtained in the previous study (Siegle, Ghinassi, et al., 2007). Beneficial effects of CCT on rumination remained and a general improvement in depressive symptomatology was observed. However, in contrast to rumination scores, no differential group effects were found for depressive symptomatology. Furthermore, pupil dilation indices during pre- and post PASAT administration were used as a physiological measure of cognitive load during task performance (see Beatty, 1982). Higher pupil dilation during pre-training PASAT performance and lower pupil reaction in rest were associated with a greater decrease in rumination scores after CCT, indicating training was most beneficial for those strongly engaging with training. Importantly, during a one year follow-up, Siegle et al. (2014) observed less intensive outpatient day-treatment visits in participants who performed at least one session of CCT compared to a group of service control patients. These findings indicate that changes in rumination following CCT precede changes in depressive symptoms (Siegle et al., 2014), suggesting that CCT is capable to contribute to stable changes in the underlying pathogenic mechanisms of depression.

Following-up on the initial findings of Siegle, Ghinassi, et al. (2007; Siegle et al., 2014) with TAU, researchers have explored whether combining CCT with alternative therapeutic interventions (other than antidepressants) may yield additional treatment effects. For instance, Moshier (2015) explored whether CCT consisting of the adaptive PASAT training and Wells' attention task may add to the effects of a brief behavior activation intervention for MDD. However, no additional effects of CCT were found compared to an active control condition undergoing the behavior activation intervention in combination with a sham training.

Interestingly, several studies have combined CCT with other forms of neurostimulation, such as transcranial Direct Current Stimulation (tDCS). For instance, Segrave et al. (2014) explored the antidepressant effects of simultaneous CCT (similar to the training reported by Siegle, Ghinassi, et al., 2007) and tDCS. Participants undergoing concurrent CCT and tDCS were characterized by heightened cognitive control over negative stimuli at follow-up. Interestingly, improved cognitive control over negative stimuli was associated with lower ratings of depression severity at follow-up. Furthermore, Segrave et al. (2014) reported a decrease in depression severity

directly following five sessions of CCT (CCT and sham tDCS) or tDCS (sham training and tDCS). However, only the combination of CCT and tDCS provided sustained treatment effects at three weeks follow-up (Segrave et al., 2014). This indicates that stimulating cognitive control, using neurostimulation techniques or computerized training tasks, has a beneficial effect on depressive symptomatology directly following training, and that in the long term patients might even benefit from a combined approach.

Also exploring combined effects of CCT and tDCS, Brunoni and colleagues (2014) used the adaptive PASAT in absence of the Wells' attention training. Depressed participants were randomly assigned to either 10 sessions of combined CCT and tDCS, or CCT and sham tDCS. Both training groups showed a significant decrease in depressive symptomatology directly following training, as well as at two weeks follow-up. Furthermore, increase in performance on the cognitive training task was associated with a greater reduction in depressive symptomatology. Interestingly, exploratory analyses seem to indicate that whereas both CCT groups showed a reduction in depressive symptomatology, older populations in particular might benefit from the combined administration of CCT and tDCS. Vanderhasselt et al. (2015) explored whether combined CCT and tDCS can be implemented to reduce depressive rumination. Results revealed a significant reduction in brooding in both CCT groups (i.e., CCT + tDCS, and CCT + sham tDCS). Moreover, increase in cognitive control during training was related to decrease in brooding over time. These findings confirm that CCT not only targets depressive symptomatology, but also important cognitive risk factors for depression, such as rumination. However, an additional sham training group would be necessary to check for placebo effects of undergoing a computerized training.

Alternative training approaches using neutral stimuli. Around the same time of the Siegle, Ghinassi, et al. (2007) report, Elgamal, McKinnon, Ramakrishnan, Joffe, and MacQueen (2007) reported effects of a cognitive remediation program containing multiple training tasks among which a training targeting executive functioning. Compared to a no-training MDD control condition and healthy control group, beneficial effects were reported for a multitude of cognitive transfer measures. However, no beneficial effects were found on depressive mood. Similar findings were reported by Trapp, Engel, Hajak, Lautenbacher, and Gallhofer (2016), where beneficial effects on

neuropsychological indicators of working memory, memory, and executive functioning were reported in absence of significant differences between both conditions on change in depressive symptomatology. However, it should be noted that the latter finding may have been an artifact of modest sample size, since Trapp et al. (2016) reported moderate yet non-significant effects of CCT in favor of the training condition on depressive symptomatology (Cohen's *d* = .67).

Interestingly, Alvarez, Sotres, León, Estrella, and Sosa (2008) explored effects of a multi-task non-emotional CCT and its interaction with antidepressant medication in students diagnosed with MDD. In addition to cognitive transfer effects, long-term beneficial effects on depressive symptomatology only remained in participants receiving CCT (independent of antidepressant intake). There was also a tendency for reduced self-reported trait anxiety in the CCT conditions. Furthermore, results suggested that effects of CCT in MDD may extend to self-reported attention problems and externalizing problems. However, early training studies typically lacked adequate control conditions, so the degree to which motivational effects influenced CCT was unclear. Moreover, intervention intensity in Alvarez et al. (2008) was dependent on CCT task performance, which is likely to induce bias when exploring treatment effects.

In contrast to its more frequent application in healthy and at-risk samples, only one study has evaluated the effects of a non-emotional adaptive n-back training approach in clinically depressed patients. Using a double-blind randomized controlled trial (RCT) design, Wanmaker, Geraerts, and Franken (2015) explored effects of 24 sessions of a combined non-emotional CCT in patients suffering from clinical depression and/or anxiety. However, with the exception of increased Reading span task performance following CCT, no beneficial effects were found for other cognitive transfer measures, self-reported rumination, depressive symptomatology, or anxiety (Wanmaker et al., 2015).

Training cognitive control over emotional information. Although findings are mixed, in general the presented studies point to the potential of CCT for remediating cognitive impairments and (cognitive risk for) depression. However, an important question that remains unaddressed is whether CCT interventions for depression should

focus on increasing general cognitive control, or directly target cognitive control in the context of emotional information processing. In a recent double-blind RCT study, Iacoviello et al. (2014) tested the superiority of an emotional CCT over a non-emotional CCT. At the end of four weeks of training, both training groups showed a similar increase in cognitive control, but only the emotional CCT group was characterized by a reduced memory bias for negative self-referent information. Concerning the clinical outcomes, both training groups showed a significant reduction in depression severity over time, but participants of the emotional CCT group reported marginally significant lower levels of depression severity following four weeks of training compared to participants of the non-emotional CCT group. However, in contrast to previous studies, Iacoviello et al. (2014) did not find significant effects of CCT on self-reported levels of rumination. Given the limited sample size (see Appendix Table 2), the lack of training effects on rumination might be due to limited power. For instance, the authors reported a medium-sized (d = 0.66) yet non-significant reduction in rumination in the emotional CCT group, whereas in the non-emotional training group a small effect-size was reported (d = 0.39). These preliminary findings indicate that using emotional stimuli may increase the efficacy of existing CCT methods in treating affective and cognitive characteristics of depression. However, sufficiently powered follow-up studies are necessary.

Cognitive control training for treatment resistant depression. In a sample of treatment resistant MDD patients, Bowie and colleagues (2013) explored effects of cognitive remediation therapy – including intensive online cognitive training – on cognitive functioning. This revealed beneficial effects on a broad range of neuropsychological measures, among which indicators of attention / processing speed, verbal learning and memory. No significant effects were found for executive functioning and broader indicators of interpersonal competence and functioning. However, cognitive improvements were related to amount of completed training sessions, while cognitive training targeting executive functioning was only scheduled during the last two weeks of the ten week intervention. Furthermore, cognitive improvements were related to improvements in measures of interpersonal competence. Interestingly, Morimoto et al. (2014) explored the potential of CCT in an older clinical population

suffering from treatment resistant geriatric depression which was due to non-response to antidepressant medication. Following four weeks of cognitive training, participants in the CCT condition showed *similar* treatment effects of 12 weeks of antidepressant treatment in a control group that was not selected to be treatment resistant. Furthermore, participants from the cognitive training group showed a greater increase in executive control, which was related to a reduction in depressive symptomatology. Importantly, the effects of four weeks of CCT remained stable at 12 weeks follow-up (Morimoto et al., 2014). This study illustrates that specific (treatment resistant) depressive subpopulations can benefit from CCT.

Interim conclusion. In sum, although some studies have failed to find effects of CCT on rumination and depressive symptomatology in MDD samples, most CCT studies have yielded promising effects in MDD samples in terms of reducing cognitive vulnerability for depression (see Appendix Table 2). This is in line with recent meta-analytical findings confirming the beneficial effects of cognitive training on working memory functioning, symptom severity, and daily functioning in depression (Motter et al., 2016), with effects on these outcome measures ranging from small to moderate. Although such results suggest that effects of CCT may complement effects of antidepressant treatments and TAU, no additional effects were found when combining CCT with a brief behavior activation protocol. This may indicate that the mechanisms targeted via behavior activation do not rely on cognitive control. Interestingly, first findings seem to indicate that effects of CCT can be increased by specifically targeting emotional information processing. However, given that only one study has compared effects of an affective CCT with a training fostering general cognitive control, replication of these findings is warranted. Preliminary evidence suggests there are specific predictors of response to CCT (e.g., pupil dilation, task performance). Furthermore, recent studies suggest that specific subgroups of MDD patients may benefit from combining CCT with additional neurostimulation techniques. However, caution is warranted given that many of the above presented findings are based on potentially underpowered analyses that were mostly not preregistered. Furthermore, in contrast to CCT studies in healthy and at-risk populations, CCT studies using MDD samples are

typically based on less stringent designs, often lacking an adequate control condition for the cognitive training condition.

Cognitive Control Training for RMD Samples

As to our knowledge, only one study has directly addressed the question whether CCT can have beneficial effects on cognitive vulnerability for depression in RMD patients (see Appendix Table 3). In a double-blind RCT study, Hoorelbeke and Koster (2017; Hoorelbeke, Faelens, Behiels, & Koster, 2015) explored the effects of a two-week multi-session CCT. Effects were assessed immediately following training and at three months follow-up. After having established near cognitive transfer, using intention-to-treat analysis, Hoorelbeke and Koster (2017) found immediate and stable effects on brooding and (residual) depressive symptomatology. Moreover, similar effects were found when using alternative measures of maladaptive emotion regulation and residual symptomatology. Furthermore, effects were not limited to reducing maladaptive processes, but also transferred to resilience and completers reported reduced cognitive complaints and increased functioning at three-months follow-up. Interestingly, mediation analysis provided evidence for the proposed mechanism underlying CCT for depression (Siegle et al., 2014; Siegle, Ghinassi, et al., 2007). That is, beneficial effects of increased cognitive control during training on depressive symptomatology at three-months follow-up, were partially mediated by immediate training effects on brooding (Hoorelbeke & Koster, 2017).

In sum, this study provided first evidence for the effectiveness of CCT in reducing cognitive vulnerability for recurrent depression in a RMD sample. Although these first findings are encouraging and in line with previous findings in MDD samples, these effects clearly need replication.

CRITICAL APPRAISAL OF THE EVIDENCE

CCT is considered a promising intervention since it targets specific risk factors for depression. Despite a decade of research our review cannot unambiguously answer the question whether CCT is an effective intervention for depressive complaints given the

mixed findings and the strong variability in research quality. After initial promising findings in studies using more intensive CCT procedures (e.g., Alvarez et al., 2008; Siegle et al., 2014; Siegle, Ghinassi, et al., 2007), a number of studies have tried to extend training effects (a) using a more limited amount of training sessions (e.g., Calkins et al., 2015; Calkins & Otto, 2013; Moshier, 2015; Moshier et al., 2015), and (b) in a wide variety of populations ranging from healthy to clinical samples, a combination which has yielded inconsistent findings. Furthermore, with the exception of some studies that have shown to be adequately powered for the presented analyses, a substantial amount of CCT studies have relied on limited sample sizes, which has resulted in not being able to consistently detect moderate effects of CCT on rumination (e.g., d = 0.66; Iacoviello et al., 2014) and depressive symptomatology (e.g., d = 0.67; Trapp et al., 2016). These factors may have led to an underestimation of training effects in the latter studies. However, it is also important to note that early training studies have typically relied on suboptimal designs (e.g., lack of active control conditions), which do not control for the motivational effects of undergoing CCT. This, in its turn, may have led to an initial overestimation of training effects, although more recent studies comparing training procedures of similar intensity with adequate control conditions have observed similar effect-sizes in at-risk and patient samples (e.g., Hoorelbeke & Koster, 2017; Hoorelbeke, Koster, Vanderhasselt, Callewaert, & Demeyer, 2015). Importantly, this is in line with recent meta-analytical findings regarding effects of general cognitive training in depression (Motter et al., 2016). Another factor that seems to be important in observing transfer is task engagement / motivation (e.g., Siegle et al., 2014), where studies may benefit from explicitly framing training procedures (and active control trainings) as interventions (e.g., using psycho-education).

Overall, a number of studies obtained promising findings but it is clear that strides need to be made before CCT can be considered an evidence-based intervention. Progress in CCT research will require a detailed understanding of the precise cognitive mechanisms that are altered through training and identification of sequential pathways through which CCT alters depressive symptoms, identifying the mediating mechanism(s). A fine-grained analysis of moderating factors as detailed in our paper is crucial to advance answering these main questions. Therefore, we will now discuss the

state-of-the-art with regard to these questions and provide a number of recommendations for future research in this area.

Transfer Effects of CCT

As stated, in healthy individuals there has been quite extensive research using training paradigms that have been modified for clinical purposes. For instance, Olesen et al. (2004) reported increased prefrontal and parietal activity following five weeks of CCT, suggesting training related plasticity in the neural systems that underlie working memory functioning. One of the paradigms that has generated extensive research on near and far transfer is the dual n-back task where initially research has indicated that extensive training on the dual n-back but also the single n-back can show far transfer to key cognitive variables such as fluid intelligence (e.g., Jaeggi et al., 2008, 2010, 2011). Yet, a recent well-controlled dual n-back training study could not replicate these findings (Redick et al., 2013). Furthermore, other studies using a broad battery of tasks targeting working memory capacity and executive functions (e.g., multiple adaptive single- and complex working memory span tasks) failed to observe transfer to fluid intelligence after demonstrating near transfer (e.g., Harrison et al., 2013). However, recent meta-analytical findings confirm that dual n-back training can improve fluid intelligence (Au et al., 2015). These mixed findings indicate the need for multiple measures of both near and far transfer (for reviews see Klingberg, 2010; Shipstead et al., 2012; Simons et al., 2016).

It is clear from our review of the current data that there are also mixed findings as well as important limitations to the current literature of clinical CCT studies. That is, in more clinical studies it is typically feasible to only administer a small number of transfer tasks where in most research only close cognitive transfer is assessed with tasks highly similar to the training procedures. As a result, there is a likelihood that strategy learning can explain training-related improvements without broader improvement of executive functions. Furthermore, with the exception of a few studies included in this systematic review that have explored effects of CCT on a wide variety of neuropsychological / cognitive measures in MDD patients (e.g., Bowie et al., 2013; Trapp et al., 2016), the majority of studies consider examining cognitive transfer a

manipulation check without trying to precisely identify the cognitive effects of training in a comprehensive way.

Here, it is crucial that in order to determine causal effects of cognitive control on depressive symptoms, which is possible using CCT, establishing that there is change in cognitive control which is (a) due to training (compared with placebo) and (b) related to the magnitude of change in depressive symptoms is required for strong *causal* conclusions. Thus based on the pattern of findings, researchers need to be careful in their interpretations. That is, some studies obtained effects on depressive symptoms without measuring or observing cognitive change which, because of the experimental manipulation of CCT, may be interpreted as evidence that cognitive control is causally involved. Yet, such conclusions need to be tempered because other variables cannot be fully excluded and the key mechanisms influencing depressive symptoms do not necessarily have to be cognitive control. Alternatively, other CCT studies where cognitive control changed in function of training but depressive outcomes did not change could be taken as evidence for the absence of a causal relationship between cognitive control and depression. Indeed, such studies should be given equal weight as studies where significant changes in depressive outcomes are obtained as they may help to quantify the causal relationship. Obviously, such studies do need to be carefully examined taking into account statistical power and methodological qualities. For instance, with regard to the latter notion, if depressive outcomes are measured directly after one week of training, absence of any effects on depressive outcomes could be due to insufficient training or too limited time for CCT to have an influence on depressive symptoms that are typically assessed in relation to the past two weeks (for instance in the BDI-II). Furthermore, extending the analytical procedures used in CCT studies may also further enhance our understanding of training effects, where (especially) studies presenting null-findings would benefit from statistical analyses that allow to accumulate evidence in favor of the null-hypothesis of no training effect (e.g., Bayes factor).

In relation to the issue of inconsistent transfer effects in clinical CCT studies we think the following desiderata are useful for future research: CCT studies should (a) contain multiple training sessions; That is, the current literature indicates that single-session manipulations and low intensity training procedures fail in altering cognitive

functions underlying depression vulnerability. However, the current literature does not allow for clear-cut indications of the amount of training sessions necessary to establish stable transfer effects. For instance, training approaches such as the adaptive PASAT have shown relatively long-term beneficial effects following 10 sessions of CCT or in some cases even less in at-risk and clinical populations, whereas in other cases no effects were found using other intensive training procedures targeting cognitive control (e.g., following 24 sessions). To answer this question requires adjusted designs and analyses taking into account variability in the degree of training session adherence. Furthermore, previous studies suggest that cognitive deficits are most apparent in an affective context or in the context of depressive rumination. As such, (b) cognitive control training should be targeting cognitive functioning in a task context that may elicit cognitive processes directly involved in repetitive negative thinking. One possibility could be using emotional stimuli or training cognitive control using neutral stimuli in a stressful / frustrating task context. Currently, it is unclear to what extent training approaches differ in this. Directly related to this, (c) (cognitive) transfer effects would ideally be assessed in a similar emotional task context, rather than exploring effects on more general indicators of cognitive functioning and far transfer measures. In this context, recent training studies exploring effects on underlying neurological mechanisms have yielded promising findings (e.g., Cohen et al., 2016). Furthermore CCT studies should ideally: (d) contain multiple measures of cognitive transfer (e.g., Schwarb, Nail, & Schumacher, 2016) *or* should use training paradigms where such transfer has already been demonstrated convincingly; (e) whenever feasible explore the relationship between cognitive and emotional transfer (but see Moreau, Kirk, & Waldie, 2016), integrating indicators of neurophysiological mechanisms of depression vulnerability on multiple levels (e.g., HPA axis activation, neural filtering, functional connectivity). For instance, future research may benefit from exploring associations between changed brain connectivity (e.g., Cohen et al., 2016) and changes in behavioral outcomes as a function of training; (f) extensively report analyses examining change in cognitive control as well as associations between change in cognitive control and change in depressive symptoms, even when not significant. Furthermore, in order to allow effects of CCT on emotional outcomes to occur, designs should ideally (g) contain follow-up assessments and (h) samples that allow sufficient improvement in and

heterogeneity regarding the emotional outcomes (e.g., clinical populations). These simple desiderate will reduce file drawer problems in future (meta-)analyses of causal effects of CCT where the criteria of Hill (1965) with regard to determining causal effects could provide a useful tool to systematically analyze the literature on cognitive control and depression in a systematic way (see for instance Van Bockstaele et al., 2014).

Sequential Pathways Through Which CCT Alters Depressive Symptoms

How does CCT alter depressive outcomes? At the moment there are different ideas why CCT influences depressive outcomes. Most views provide pathways that include various mediating factors in their explanation (e.g., stress-reactivity, rumination, cognitive biases), indicating the need to carefully map the sequence of effects obtained with CCT. One influential theory proposed by Siegle, Ghinassi, et al. (2007) suggests that CCT specifically targets the neurocircuitry that has been identified in relation to depression. This theory builds on observations of reduced frontal activity (predominantly at the level of the DLPFC) and sustained amygdala activity (e.g., Sheline et al., 2001; Siegle, Thompson, et al., 2007) which has been related to cognitive risk factors such as rumination and sustained negative affect. The key notion here is that in depressed individuals in emotionally challenging situations, the DLPFC – which is a central region involved in the application of cognitive control (Cohen, 2001; Miller & Cohen, 2001; Ridderinkhof, Van Den Wildenberg, Segalowitz, & Carter, 2004) – is less actively recruited to dampen activity of the amygdala. In empirical studies this has been related to reduced functional connectivity between the anterior cingulate cortex (signaling cognitive conflict) and frontal regions (Holmes & Pizzagalli, 2007). In relation to CCT, it is thought that in order to successfully perform the PASAT one needs to recruit the DLPFC (e.g., Lazeron, Rombouts, deSonneville, Barkhof, & Scheltens, 2003) while downplaying interference from limbic pathways which become activated since the adaptive PASAT is highly challenging and by design evokes frequent errors (Siegle, Ghinassi, et al., 2007; Tombaugh, 2006). Similarly, meta-analytical findings suggest n-back task performance heavily relies on DLPFC activity (Owen, McMillan, Laird, & Bullmore, 2005).

There are some initial data supporting this view. For instance, Siegle, Ghinassi, et al. (2007) explored effects of CCT on DLPFC and amygdala activity in a subsample of MDD patients. Following treatment, these patients demonstrated decreased disruptions in DLPFC and amygdala activity while performing a cognitive and emotional task. Moreover, other pieces of evidence stem from CCT research where pupil dilation was measured. Pupil dilation is considered a psychophysiological marker of cognitive effort linked to DLPFC activity. In recent CCT studies, beneficial effects of CCT on rumination were mostly obtained in participants with higher levels of pupil dilation suggesting that beneficial effects of CCT are limited to individuals who are able to recruit sufficient DLPFC activity while training (Siegle et al., 2014). Finally, an important recent study provided 18 sessions of a modified Flanker training to healthy participants, which resulted in reduced amygdala activity and behavioral interference of aversive stimuli (Cohen et al., 2016). Furthermore, Cohen and colleagues (2016) observed increased amygdala – prefrontal region connectivity following CCT. Additionally, researchers have also reported associations between neural indicators of increased cognitive task performance and observed improvements in emotion regulation following CCT (e.g., Schweizer et al., 2013). However, despite these encouraging data, the neural underpinnings of CCT remain to be investigated further.

Based on our review of the CCT studies many of the studies consider emotion regulation as an important mediating factor of CCT. This is in line with theoretical models of emotion regulation in depression (Joormann & Vanderlind, 2014). However, to our knowledge only one study has directly examined the sequential effect of CCT on rumination and subsequent depressive symptoms. In a sample of RMD patients, Hoorelbeke and Koster (2017) have tested whether cognitive transfer effects of a two-week cognitive control manipulation predicts depressive symptomatology at three months follow-up via depressive rumination (brooding) immediately following training. While controlling for baseline depressive symptomatology and brooding, increase in cognitive control task performance predicted lower depressive rumination immediately following training, which partially mediated effects on depressive symptomatology at three months follow-up. It is noteworthy that these effects were small and suggest partial mediation, indicating that effects of CCT may be due to other, to be identified

cognitive mechanisms. Interestingly, one could think that CCT could augment adaptive emotion regulation strategies. However, this idea was not supported in multiple studies (Hoorelbeke & Koster, 2017; Hoorelbeke et al., 2016).

Another complementary option is that CCT influences cognitive vulnerability for depression by targeting different cognitive biases. There is extensive research showing that multiple cognitive biases at the level of attention, interpretation and memory influence depressive symptoms through their influence on stress reactivity (for reviews, see Everaert, Koster, & Derakshan, 2012; Farb, Irving, Anderson, & Segal, 2015; Gotlib & Joormann, 2010). Interestingly, recent work has shown that cognitive control over emotional information is linked to a host of these information-processing biases (Everaert, Grahek, & Koster, 2016), where the specific interplay between such biases has also been linked to rumination and depressive symptoms (Everaert, Grahek, Van den Bergh, et al., 2016). Unfortunately, currently there are no studies using more extensive training procedures mapping such influences of CCT.

It is clear that there are a number of interesting proposals on the pathways through which CCT influences depressive symptoms. This area of research is in its infancy but nevertheless of key relevance for progressing our understanding and improving the efficacy of CCT for depression. In order to be able to map sequential effects related to CCT we make the following recommendations, CCT studies should: (a) include measures of potential mediating variables; (b) include multiple time points in order to examine mediation; and (c) compare CCT with active control conditions to ensure that mechanisms can be linked to cognitive control. One promising way forward is to combine CCT with experience sampling methodology (ESM; see for instance Hoorelbeke et al., 2016) in order to be able to measure changes in relevant variables before, during, as well as following CCT to obtain a clear picture on the temporal effects elicited through CCT. Moreover, an ESM approach allows to map changes in the dynamic between affect and emotion regulation processes, which could be more informative than merely focusing on mean levels of mood and emotion regulation. Here, it is important that studies on CCT move away from simplistic notions of considering some emotion regulation strategies as adaptive and others as maladaptive. Emotion research suggests that the effects of different emotion regulation strategies

depend on their context and the flexibility of their application (Aldao, 2013; Aldao, Sheppes, & Gross, 2015; Bonanno, Papa, Lalande, Westphal, & Coifman, 2004), where ESM allows to do justice to more fine-grained approaches to emotion regulation.

Analysis of Moderating Factors

Depression is a highly heterogeneous construct where there is large variability in the symptoms expressed by patients. Moreover, when considering the practical application of CCT for prevention and/or treatment of depression, there are many variables that could have an impact on the efficacy of CCT. Examples of such variables are the timing of the CCT intervention, the length of the intervention, the use of other therapies or interventions, etc. Examining for whom CCT is efficacious is an important endeavor for clinical purposes and could simultaneously provide useful insights into the working mechanisms of CCT. It is therefore not surprising that the question of moderating factors has already received some attention in the literature. For instance, Quinn and colleagues (2014) successfully tested the assumption that trait rumination moderates training effects in healthy participants.

In several studies it has been shown that there is individual variability in the engagement with CCT and improvement throughout the training sessions (e.g., Bowie et al., 2013). As described earlier, Siegle et al. (2014) found that higher levels of engagement on a cognitive transfer measure (non-adaptive PASAT) through pupil dilation forms a predictor of stronger benefits of training with regard to improvements in rumination. Importantly, whether this variable was associated with effects of CCT on other depressive outcomes is not reported. In other studies, progress during training has been associated with the efficacy of training. For instance, the slope of training progress has been associated with lower post-training brooding levels in a MDD sample (Vanderhasselt et al., 2015). Furthermore, several studies have reported associations between increased CCT or cognitive transfer task performance and depressive outcomes or broader indicators of functioning in at-risk (e.g., Hoorelbeke, Koster, et al., 2015) and clinically depressed samples (e.g., Bowie et al., 2013; Brunoni et al., 2014; Segrave et al., 2014). However, it is noteworthy that engagement with and progress in training or on cognitive transfer measures are not consistently linked to the depressive

outcomes of CCT since some studies failed to find such associations (e.g., Calkins et al., 2015; Daches & Mor, 2014; Onraedt & Koster, 2014; Takeuchi et al., 2014) and many studies do not report such analyses.

Other moderating variables that have occasionally been reported in studies are age (e.g., Brunoni et al., 2014). However, the recent meta-analysis by Motter et al. (2016) indicated decreased effects of CCT with increasing age. Furthermore, Motter et al. (2016) found no moderating effects of gender or medication status. Clearly, the latter finding that cognitive training is equally effective regardless of medication use is promising since this suggests that CCT can be combined with other evidence-based treatments.

Interestingly, one plausible candidate moderator has received very scarce support so far. That is, one might expect that the level of cognitive impairments at the start of training is a moderator of treatment effects. Yet, this variable is not consistently associated with outcome in current reports (e.g., Moshier, 2015) or is not reported. Since this is a null finding, several explanations are possible. It could be that there is a restriction of range phenomenon in depressed samples or there might be a non-linear relation between cognitive control impairments and CCT related improvements. Alternatively, it could also be that CCT is effective only in the group that has some but not too extensive impairments in cognitive control. Especially in the population of severely depressed patients CCT might not be sufficient to improve cognitive control (potentially through limited task engagement). Future research should investigate the usefulness of sequential treatment strategies to remediate cognitive impairments in severe populations where for instance neuromodulation techniques (e.g., repetitive transcranial magnetic stimulation) could precede CCT (see De Raedt, Vanderhasselt, & Baeken, 2015).

Identifying moderators of the efficacy of CCT on depressive symptoms is an area of large clinical and theoretical interest. To date, current research has identified a number of moderators related to training as well as client characteristics that influence the efficacy of CCT. In order to improve upon the current state-of-the-art we propose the following recommendations: there is a strong need for (a) confirmatory research to

replicate the moderators that have been observed; (b) CCT studies containing larger sample sizes, which would allow researchers to identify potential moderators; and (c) targeted research on specific clinical moderators that have a high likelihood of influencing CCT efficacy (e.g., severity, etc.). Basic research on the presence of cognitive control impairments has shown cognitive control impairments mainly at group levels (Snyder, 2013). However, there is quite substantial heterogeneity in the presence of cognitive control impairments. Here it is important that the basic research needs to get a better handle on the role of cognitive control impairments at the individual level which will likely be highly informative on generating more specific hypotheses on potential moderating roles of such variables in the efficacy of CCT.

DISCUSSION

The current review aimed to provide a state-of-the-art on cognitive control training in depression. One of the clear benefits of this intervention is that it targets a specific, well-established cognitive risk factor that is associated with maladaptive emotion regulation and depression risk. Moreover, there is research showing that traditional interventions such as antidepressant medication do not remediate this risk factor (Shilyansky et al., 2016). Importantly, an initial meta-analysis recently indicated that training cognitive functioning yields moderate to large effects on near and far cognitive transfer measures in MDD samples (e.g., attention, working memory, intelligence). Furthermore, Hedges' *g* effect-sizes of .43 and .72 were reported for symptom severity and daily life functioning respectively, suggesting that effects of cognitive training on depression-related outcomes are in the range of small to moderate (Motter et al., 2016). Therefore, we sought to describe this emerging research area with regard to the current empirical research, the theoretical underpinnings, and the potential clinical application of cognitive control training in relation to the prevention and treatment of depression.

In our systematic review it is clear that there is quite substantial heterogeneity between different studies. Beneficial effects of CCT are mainly observed in populations with clear impairments at the onset of training when training is rather extensive. Within

training it seems key that individuals are engaged with training that demands activating frontal areas such as the DLPFC which are implicated in attentional control, while ignoring task-unrelated stressful thoughts. As such it seems plausible that CCT firstly impacts repetitive negative thinking (rumination) to subsequently reduce depression levels. However, at the same time our review clearly shows that research will need to further establish the working mechanism in a more detailed manner since empirical evidence on this is only in its infancy.

CCT has several features that make it attractive clinically. It can be easily disseminated online, is low cost intensive, and may target mechanisms that are otherwise not changed through traditional interventions. Interestingly, the research shows that the engagement with training is key to obtain transfer effects in interaction with the levels of cognitive impairment at the onset of training. This suggests that not everyone with depression risk or complaints will benefit from training because (a) their working memory functioning is not impaired (for instance, Owens et al., 2012 showed individuals with high depression levels frequently have intact working memory capacity); and (b) they are insufficiently able to engage in training because of several reasons (e.g., lack of motivation). Clinically, we may need to apply CCT in a more tailored intervention based on participant status and working memory baseline measures. Moreover, monitoring training progress can provide an indication of task engagement to show the increments in training are met with increments in behavioral change. Looking at the learning curve of depressed participants across training is key to understanding how and when we can expect transfer and benefits from training.

In sum, research on CCT is an exciting area where there are promising clinical benefits to training. There is a clear need for larger scale, confirmatory research as well as innovative ways to tailor this treatment, track changes within training, and optimize effect sizes.

ACKNOWLEDGEMENTS

This research was supported by Grant BOF16/GOA/017 for a Concerted Research Action of Ghent University (awarded to Ernst Koster). Kristof Hoorelbeke is funded by Ghent University (Special Research Fund, BOFDOC2015002801) and Thomas Onraedt is funded by the Fund for Scientific Research Flanders (FWO). Research assistant Jill van Put and student Lena Hofbauer provided practical assistance during the systematic literature search phase.

REFERENCES

Aldao, A. (2013). The Future of Emotion Regulation Research: Capturing Context. *Perspectives on Psychological Science*, *8*, 155–172. doi: 10.1177/1745691612459518

Aldao, A., Sheppes, G., & Gross, J. J. (2015). Emotion regulation flexibility. *Cognitive Therapy and Research*, *39*, 263–278. doi: 10.1007/s10608-014-9662-4

Alvarez, L. M., Sotres, C. J. F., León, S. O., Estrella, J., & Sosa, S. J. J. (2008). Computer program in the treatment for major depression and cognitive impairment in university students. *Computers in Human Behavior*, *24*, 816–826. doi: 10.1016/j.chb.2007.02.013

Au, J., Sheehan, E., Tsai, N., Duncan, G. J., Buschkuehl, M., & Jaeggi, S. M. (2015). Improving fluid intelligence with training on working memory: a meta-analysis. *Psychonomic Bulletin & Review*, *22*, 366–377. doi: 10.3758/s13423-014-0699-x

Baddeley, A. D., & Hitch, G. (1974). Working memory. In G. H. Bower (Ed.), *The psychology of learning and motivation: Advances in research and theory* (pp. 47–89). New York: Academic Press.

Beatty, J. (1982). Phasic not tonic pupillary responses vary with auditory vigilance performance. *Psychophysiology*, *19*, 167–172. doi: 10.1037/0033-2909.91.2.276

Beckwé, M., Deroost, N., Koster, E. H. W., De Lissnyder, E., & De Raedt, R. (2014). Worrying and rumination are both associated with reduced cognitive control. *Psychological Research*, *78*, 651–660. doi: 10.1007/s00426-013-0517-5

Beshai, S., Dobson, K. S., Bockting, C. L., & Quigley, L. (2011). Relapse and recurrence prevention in depression: current research and future prospects. *Clinical Psychology Review*, *31*, 1349–1360.

Bonanno, G. A., Papa, A., Lalande, K., Westphal, M., & Coifman, K. (2004). The importance of being flexible: The ability to both enhance and suppress emotional expression predicts long-term adjustment. *Psychological Science*, *15*, 482–487. doi: 10.1111/j.0956-7976.2004.00705.x

Bowie, C. R., Gupta, M., Holshausen, K., Jokic, R., Best, M., & Milev, R. (2013). Cognitive remediation for treatment-resistant depression: effects on cognition and functioning and the role of online homework. *The Journal of Nervous and Mental*

Disease, *201*, 680–5. doi: 10.1097/NMD.0b013e31829c5030

Brunoni, A. R., Boggio, P. S., De Raedt, R., Bensenor, I. M., Lotufo, P. A., Namur, V., … Vanderhasselt, M. A. (2014). Cognitive control therapy and transcranial direct current stimulation for depression: A randomized, double-blinded, controlled trial. *Journal of Affective Disorders*, *162*, 43–49. doi: 10.1016/j.jad.2014.03.026

Buschkuehl, M., Jaeggi, S. M., & Jonides, J. (2012). Neuronal effects following working memory training. *Developmental Cognitive Neuroscience*. doi: 10.1016/j.dcn.2011.10.001

Calkins, A. W., Deveney, C. M., Weitzman, M. L., Hearon, B. A., & Siegle, G. J. (2011). The effects of prior cognitive control task exposure on responses to emotional tasks in healthy participants. *Behavioural and Cognitive Psychotherapy*, *39*, 205–220. doi: 10.1017/s1352465810000652

Calkins, A. W., McMorran, K. E., Siegle, G. J., & Otto, M. W. (2015). The effects of computerized cognitive control training on community adults with depressed mood. *Behavioural and Cognitive Psychotherapy*, *43*, 578–589. doi: 10.1017/S1352465814000046

Calkins, A. W., & Otto, M. W. (2013). Testing the Boundaries of Computerized Cognitive Control Training on Symptoms of Obsessive Compulsive Disorder. *Cognitive Therapy and Research*, *37*, 587–594. doi: 10.1007/s10608-012-9496-x

Chein, J. M., & Morrison, A. B. (2010). Expanding the mind's workspace: training and transfer effects with a complex working memory span task. *Psychonomic Bulletin & Review*, *17*, 193–199. doi: 10.3758/PBR.17.2.193

Cohen, J. D. (2001). Cognitive Control (Executive Functions): Role of Prefrontal Cortex. In *International Encyclopedia of the Social & Behavioral Sciences* (pp. 2089–2094). doi: 10.1016/B0-08-043076-7/03505-1

Cohen, N., Margulies, D. S., Ashkenazi, S., Schaefer, A., Taubert, M., Henik, A., … Okon-Singer, H. (2016). Using executive control training to suppress amygdala reactivity to aversive information. *NeuroImage*, *125*, 1022–31. doi: 10.1016/j.neuroimage.2015.10.069

Cohen, N., Mor, N., & Henik, A. (2015). Linking executive control and emotional response: A training procedure to reduce rumination. *Clinical Psychological Science*, *3*, 15–25. doi: 10.1177/2167702614530114

Collette, F., & Van der Linden, M. (2002). Brain imaging of the central executive component of working memory. *Neuroscience and Biobehavioral Reviews*, *26*, 105–125.

Colzato, L. S., van den Wildenberg, W. P., Zmigrod, S., & Hommel, B. (2012). Action video gaming and cognitive control: playing first person shooter games is associated with improvement in working memory but not action inhibition. *Psychological Research*, *77*, 234–239. doi: 10.1007/s00426-012-0415-2

Cortese, S., Ferrin, M., Brandeis, D., Buitelaar, J., Daley, D., Dittmann, R. W., … European ADHD Guidelines Group (EAGG) (2015). Cognitive training for attention-deficit/hyperactivity disorder: meta-analysis of clinical and neuropsychological outcomes from randomized controlled trials. *Journal of the American Academy of Child and Adolescent Psychiatry*, *54*, 164–74. doi: 10.1016/j.jaac.2014.12.010

Daches, S., & Mor, N. (2014). Training ruminators to inhibit negative information: A preliminary report. *Cognitive Therapy and Research*, *38*, 160–171. doi: 10.1007/s10608-013-9585-5

Daches, S., Mor, N., & Hertel, P. (2015). Rumination: Cognitive consequences of training to inhibit the negative. *Journal of Behavior Therapy and Experimental Psychiatry*, *49*, 76–83. doi: 10.1016/j.jbtep.2015.01.010

Davidson, R. J., Pizzagalli, D., Nitschke, J. B., & Putman, K. (2002). Depression: Perspectives from affective neuroscience. *Annual Review of Psychology*, *53*, 545–574.

de Putter, L. M. S., Vanderhasselt, M. A., Baeken, C., De Raedt, R., & Koster, E. H. W. (2015). Combining tDCS and Working Memory Training to Down Regulate State Rumination: A Single-Session Double Blind Sham-Controlled Trial. *Cognitive Therapy and Research*, *39*, 754–765. doi: 10.1007/s10608-015-9710-8

De Raedt, R., & Koster, E. H. W. (2010). Understanding vulnerability for depression from a cognitive neuroscience perspective: A reappraisal of attentional factors and a new conceptual framework. *Cognitive Affective & Behavioral Neuroscience*, *10*, 50–70. doi: 10.3758/cabn.10.1.50

De Raedt, R., Vanderhasselt, M.-A., & Baeken, C. (2015). Neurostimulation as an intervention for treatment resistant depression: From research on mechanisms towards targeted neurocognitive strategies. *Clinical Psychology Review*. doi:

10.1016/j.cpr.2014.10.006

Demeyer, I., De Lissnyder, E., Koster, E. H. W., & De Raedt, R. (2012). Rumination mediates the relationship between impaired cognitive control for emotional information and depressive symptoms: A prospective study in remitted depressed adults. *Behaviour Research and Therapy*, *50*, 292–297. doi: 10.1016/j.brat.2012.02.012

Derakshan, N., Salt, M., & Koster, E. H. W. (2009). Attentional control in dysphoria: An investigation using the antisaccade task. *Biological Psychology*, *80*, 251–255. doi: 10.1016/j.biopsycho.2008.09.005

Deveney, C. M., & Deldin, P. J. (2006). A preliminary investigation of cognitive flexibility for emotional information in major depressive disorder and non-psychiatric controls. *Emotion*, *6*, 429–37. doi: 10.1037/1528-3542.6.3.429

Elgamal, S., McKinnon, M. C., Ramakrishnan, K., Joffe, R. T., & MacQueen, G. (2007). Successful computer-assisted cognitive remediation therapy in patients with unipolar depression: a proof of principle study. *Psychological Medicine*, *37*, 1229–38. doi: 10.1017/S0033291707001110

Etkin, A., Gyurak, A., & O'Hara, R. (2013). A neurobiological approach to the cognitive deficits of psychiatric disorders. *Dialogues in Clinical Neuroscience*, *15*, 419–29.

Everaert, J., Grahek, I., & Koster, E. H. W. (2016). Individual differences in cognitive control modulate cognitive biases linked to depressive symptoms. *Cognition & Emotion*.

Everaert, J., Grahek, I., Van den Bergh, N., Buelens, J., Duyck, W., & Koster, E. H. W. (2016). Mapping the interplay among cognitive biases, emotion regulation, and depressive symptoms. *Cognition & Emotion*.

Everaert, J., Koster, E. H. W., & Derakshan, N. (2012). The combined cognitive bias hypothesis in depression. *Clinical Psychology Review*, *32*, 413–424.

Farb, N. A. S., Irving, J. A., Anderson, A. K., & Segal, Z. V. (2015). A two-factor model of relapse/recurrence vulnerability in unipolar depression. *Journal of Abnormal Psychology*, *124*, 38–53. doi: 10.1037/abn0000031

Gavelin, H. M., Boraxbekk, C.-J., Stenlund, T., Järvholm, L. S., & Neely, A. S. (2015). Effects of a process-based cognitive training intervention for patients with stress-related exhaustion. *Stress*, 1–11.

Goeleven, E., De Raedt, R., Baert, S., & Koster, E. H. W. (2006). Deficient inhibition of emotional information in depression. *Journal of Affective Disorders*, *93*, 149–157. doi: 10.1016/j.jad.2006.03.007

Gotlib, I. H., & Joormann, J. (2010). Cognition and Depression: Current Status and Future Directions. In S. NolenHoeksema, T. D. Cannon, & T. Widiger (Eds.), *Annual Review of Clinical Psychology, Vol 6* (pp. 285–312). Palo Alto: Annual Reviews. doi: 10.1146/annurev.clinpsy.121208.131305

Green, C. S., & Bavelier, D. (2003). Action video game modifies visual selective attention. *Nature*, *423*, 534–7. doi: 10.1038/nature01647

Gronwall, D. M. A. (1977). Paced Auditory Serial Addition Task - Measure of recovery from concussion. *Perceptual and Motor Skills*, *44*, 367–373.

Harrison, T. L., Shipstead, Z., Hicks, K. L., Hambrick, D. Z., Redick, T. S., & Engle, R. W. (2013). Working memory training may increase working memory capacity but not fluid intelligence. *Psychological Science*, *24*, 2409–2419. doi: 10.1177/0956797613492984

Harvey, P. O., Le Bastard, G., Pochon, J. B., Levy, R., Allilaire, J. F., Dubois, B., & Fossti, P. (2004). Executive functions and updating of the contents of working memory in unipolar depression. *Journal of Psychiatric Research*, *38*, 567–576. doi: 10.1016/j.jpsychires.2004.03.003

Hasher, L., & Zacks, R. T. (1979). Automatic and effortful processes in memory. *Journal of Experimental Psychology-General*, *108*, 356–388. doi: 10.1037//0096-3445.108.3.356

Higgins, J. P. T., & Green, S. (Eds.). (2011). *Cochrance Handbook for Systematic Reviews of Interventions* (Version 5.1.0). Available from www.handbook.cochrane.org

Hill, A. B. (1965). The environment and disease: Association or causation? *Proceedings of the Royal Society of Medicine*, *58*, 295–300.

Holmes, A. J., & Pizzagalli, D. A. (2007). Task feedback effects on conflict monitoring and executive control: Relationship to subclinical measures of depression. *Emotion*, *7*, 68–76.

Hoorelbeke, K., Faelens, L., Behiels, J., & Koster, E. H. W. (2015). Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Protocol for a randomized controlled trial. *Bmc Psychiatry*, *15*, 125.

Hoorelbeke, K., & Koster, E. H. W. (2017). Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Evidence from a double-blind randomized controlled trial study. *Journal of Consulting and Clinical Psychology, 85,* 135–146. doi: 10.1037/ccp0000128

Hoorelbeke, K., Koster, E. H. W., Demeyer, I., Loeys, T., & Vanderhasselt, M. A. (2016). Effects of cognitive control training on the dynamics of (mal)adaptive emotion regulation in daily life. *Emotion*, *16*, 945-956. doi: 10.1037/emo0000169

Hoorelbeke, K., Koster, E. H. W., Vanderhasselt, M. A., Callewaert, S., & Demeyer, I. (2015). The influence of cognitive control training on stress reactivity and rumination in response to a lab stressor and naturalistic stress. *Behaviour Research and Therapy*, *69*, 1–10.

Iacoviello, B., Huryk, K., Alvarez, E., Collins, K., Murrough, J., Iosifescu, D., & Charney, D. (2014). Cognitive-Emotional Training as an Intervention for Major Depressive Disorder. *Biological Psychiatry*, *75*, 119S–119S.

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Perrig, W. J. (2008). Improving fluid intelligence with training on working memory. *Proceedings of the National Academy of Sciences of the United States of America*, *105*, 6829–6833. doi: 10.1073/pnas.0801268105

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Shah, P. (2011). Short- and long-term benefits of cognitive training. *Proceedings of the National Academy of Sciences of the United States of America*, *108*, 10081–10086. doi: 10.1073/pnas.1103228108

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Shah, P. (2012). Cogmed and working memory training—Current challenges and the search for underlying mechanisms. *Journal of Applied Research in Memory and Cognition*. doi: 10.1016/j.jarmac.2012.07.002

Jaeggi, S. M., Buschkuehl, M., Shah, P., & Jonides, J. (2014). The role of individual differences in cognitive training and transfer. *Memory & Cognition*, *42*, 464–480. doi: 10.3758/s13421-013-0364-z

Jaeggi, S. M., Studer-Luethi, B., Buschkuehl, M., Su, Y. F., Jonides, J., & Perrig, W. J. (2010). The relationship between n-back performance and matrix reasoning - implications for training and transfer. *Intelligence*, *38*, 625–635. doi: 10.1016/j.intell.2010.09.001

Jones, N. P., Siegle, G. J., Muelly, E. R., Haggerty, A., & Ghinassi, F. (2010). Poor performance on cognitive tasks in depression: Doing too much or not enough? *Cognitive Affective, and Behavioral Neuroscience*, *10*, 129–140. doi: 10.3758/CABN.10.1.129

Jonides, J., Lewis, R. L., Nee, D. E., Lustig, C. A., Berman, M. G., & Moore, K. S. (2008). The mind and brain of short-term memory. *Annual Review of Psychology*, *59*, 193–224. doi: 10.1146/annurev.psych.59.103006.093615

Joormann, J. (2004). Attentional bias in dysphoria: The role of inhibitory processes. *Cognition & Emotion*, *18*, 125–147. doi: 10.1080/02699930244000480

Joormann, J. (2006). Differential effects of rumination and dysphoria on the inhibition of irrelevant emotional material: Evidence from a Negative Priming Task. *Cognitive Therapy and Research*, *30*, 149–160. doi: 10.1007/s10608-006-9035-8

Joormann, J., & D'Avanzato, C. (2010). Emotion regulation in depression: Examining the role of cognitive processes. *Cognition & Emotion*, *24*, 913–939. doi: 10.1080/02699931003784939

Joormann, J., & Vanderlind, M. W. (2014). Emotion regulation in depression: The role of biased cognition and reduced cognitive control. *Clinical Psychological Science*, *2*, 402–421. doi: 10.1177/2167702614536163

Joormann, J., Yoon, K. L., & Zetsche, U. (2007). Cognitive inhibition in depression. *Applied & Preventive Psychology*, *12*, 128–139. doi: 10.1016/j.appsy.2007.09.002

Klingberg, T. (2010). Training and plasticity of working memory. *Trends in Cognitive Sciences*, *14*, 317–324.

Klingberg, T., Fernell, E., Olesen, P. J., Johnson, M., Gustafsson, P., Dahlström, K., … Westerberg, H. (2005). Computerized training of working memory in children with ADHD--a randomized, controlled trial. *Journal of the American Academy of Child and Adolescent Psychiatry*, *44*, 177–86. doi: 10.1097/00004583-200502000-00010

Klingberg, T., Forssberg, H., & Westerberg, H. (2002). Training of working memory in children with ADHD. *Journal of Clinical and Experimental Neuropsychology*, *24*, 781–791. doi: 10.1076/jcen.24.6.781.8395

Koster, E. H. W., Fox, E., & MacLeod, C. (2009). Introduction to the Special Section on Cognitive Bias Modification in Emotional Disorders. *Journal of Abnormal Psychology*, *118*, 1–4. doi: 10.1037/a0014379

Koster, E. H. W., & Hoorelbeke, K. (2015). Cognitive bias modification for depression. *Current Opinion in Psychology*, *4*, 119–123. doi: 10.1016/j.copsyc.2014.11.012

Kühn, S., Gleich, T., Lorenz, R. C., Lindenberger, U., & Gallinat, J. (2013). Playing Super Mario induces structural brain plasticity: Gray matter changes resulting from training with a commercial video game. *Molecular Psychiatry*, *19*, 265–271. doi: 10.1038/mp.2013.120

Lazeron, R. H., Rombouts, S. A., deSonneville, L., Barkhof, F., & Scheltens, P. (2003). A paced visual serial addition test for fMRI. *Journal of Neurological Science*, *213*, 29–34.

Levens, S. M., & Gotlib, I. H. (2010). Updating positive and negative stimuli in working memory in depression. *Journal of Experimental Psychology. General*, *139*, 654–664. doi: 10.1037/a0020283

Levens, S. M., & Gotlib, I. H. (2015). Updating emotional content in recovered depressed individuals: Evaluating deficits in emotion processing following a depressive episode. *Journal of Behavior Therapy and Experimental Psychiatry*, *48*, 156–163. doi: 10.1016/j.jbtep.2015.03.009

Lundqvist, A., Grundström, K., Samuelsson, K., & Rönnberg, J. (2010). Computerized training of working memory in a group of patients suffering from acquired brain injury. *Brain Injury*, *24*, 1173–1183.

MacLeod, C., Rutherford, E., Campbell, L., Ebsworthy, G., & Holker, L. (2002). Selective attention and emotional vulnerability: assessing the causal basis of their association through the experimental manipulation of attentional bias. *Journal of Abnormal Psychology*, *111*, 107–123.

Merriam, E. P., Thase, M. E., Haas, G. L., Keshavan, M. S., & Sweeney, J. a. (1999). Prefrontal cortical dysfunction in depression determined by Wisconsin Card Sorting Test performance. *The American Journal of Psychiatry*, *156*, 780–782.

Millan, M. J., Agid, Y., Brüne, M., Bullmore, E. T., Carter, C. S., Clayton, N. S., … Young, L. J. (2012). Cognitive dysfunction in psychiatric disorders: characteristics, causes and the quest for improved therapy. *Nature Reviews*, *11*, 141–168. doi: 10.1038/nrd3628

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience*, *24*, 167–202. doi:

10.1146/annurev.neuro.24.1.167

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive Psychology*, *41*, 49–100. doi: 10.1006/cogp.1999.0734

Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & Prisma Group. (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *Annals of Internal Medicine*, *151*, 264-W64.

Mor, N., & Daches, S. (2015). Ruminative Thinking: Lessons Learned From Cognitive Training. *Clinical Psychological Science*, *3*, 574–592. doi: 10.1177/2167702615578130

Morimoto, S. S., Wexler, B. E., Liu, J., Hu, W., Seirup, J., & Alexopoulos, G. S. (2014). Neuroplasticity-based computerized cognitive remediation for treatment-resistant geriatric depression. *Nature Communications*, *5:4579*. doi: 10.1038/ncomms5579

Morrison, A. B., & Chein, J. M. (2011). Does working memory training work? The promise and challenges of enhancing cognition by training working memory. *Psychonomic Bulletin & Review*, *18*(1), 46–60. doi: 10.3758/s13423-010-0034-0

Moshier, S. J. (2015). *Cognitive control training as an adjunct to behavioral activation therapy in the treatment of depression*. Boston University.

Moshier, S. J., Molokotos, E. K., Stein, A. T., & Otto, M. W. (2015). Assessing the effects of depressed mood and cognitive control training on memory confidence and accuracy following repeated checking. *International Journal of Cognitive Therapy*, *8*, 206–221. doi: 10.1521/ijct_2015_8_02

Motter, J. N., Pimontel, M. A., Rindskopf, D., Devanand, D. P., Doraiswamy, M. P., & Sneed, J. R. (2016). Computerized cognitive training and functional recovery in major depressive disorder: A meta-analysis. *Journal of Affective Disorders*, *189*, 184–191. doi: 10.1016/j.ad.2015.09.022

Murphy, F. C., Sahakian, B. J., Rubinsztein, J. S., Michael, A., Rogers, R. D., Robbins, T. W., & Paykel, E. S. (1999). Emotional bias and inhibitory control processes in mania and depression. *Psychological Medicine*, *29*, 1307–1321. doi: 10.1017/S0033291799001233

Nolen-Hoeksema, S., Wisco, B. E., & Lyubomirsky, S. (2008). Rethinking rumination.

Perspectives on Psychological Science, *3*, 400–424. doi: 10.1111/j.1745-6924.2008.00088.x

Nouchi, R., Taki, Y., Takeuchi, H., Hashizume, H., Nozawa, T., Kambara, T., … Kawashima, R. (2013). Brain training game boosts executive functions, working memory and processing speed in the young adults: a randomized controlled trial. *Plos One*. doi: 10.1371/journal.pone.0055518

Olesen, P. J., Westerberg, H., & Klingberg, T. (2004). Increased prefrontal and parietal activity after training of working memory. *Nature Neuroscience*, *7*, 75–79. doi: 10.1038/nn1165

Onraedt, T., & Koster, E. H. W. (2014). Training Working Memory to Reduce Rumination. *Plos One*, *9*, 12. doi: 10.1371/journal.pone.0090632

Orwin, R. G. (1994). Evaluating coding decisions. In H. Cooper & L. V Hedges (Eds.), *The handbook of research synthesis*. New York: Russell Sage Foundation.

Owen, A. M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. In *Human Brain Mapping* (pp. 46–59). doi: 10.1002/hbm.20131

Owens, M., Koster, E. H. W., & Derakshan, N. (2012). Impaired filtering of irrelevant information in dysphoria: An ERP study. *Social Cognitive and Affective Neuroscience*, *7*, 752–763. doi: 10.1093/scan/nsr050

Owens, M., Koster, E. H. W., & Derakshan, N. (2013). Improving attention control in dysphoria through cognitive training: Transfer effects on working memory capacity and filtering efficiency. *Psychophysiology*, *50*, 297–307. doi: 10.1111/psyp.12010

Paelecke-Habermann, Y., Pohl, J., & Leplow, B. (2005). Attention and executive functions in remitted major depression patients. *J Affect Disord*, *89*, 125–135. doi: 10.1016/j.jad.2005.09.006

Pe, M. L., Brose, A., Gotlib, I. H., & Kuppens, P. (2016). Affective updating ability and stressful events interact to prospectively predict increases in depressive symptoms over time. *Emotion*, *16*, 73–82. doi: 10.1037/emo0000097

Philippot, P., & Brutoux, F. (2008). Induced rumination dampens executive processes in dysphoric young adults. *Journal of Behavior Therapy and Experimental Psychiatry*, *39*, 219–227. doi: 10.1016/j.jbtep.2007.07.001

Pizzagalli, D. A. (2011). Frontocingulate dysfunction in depression: Towards biomarkers

of treatment response. *Neuropsychopharmacology Review*, *36*, 183–206.

Quinn, M. E., Keil, D. C., Utke, S., & Joormann, J. (2014). Trait rumination moderates the effect of executive control training. *Journal of Experimental Psychopathology*, *5*, 289–301. doi: 10.5127/jep.0038713

Redick, T. S., Shipstead, Z., Harrison, T. L., Hicks, K. L., Fried, D. E., Hambrick, D. Z., … Engle, R. W. (2013). No evidence of intelligence improvement after working memory training: A randomized, placebo-controlled study. *Journal of Experimental Psychology-General*, *142*, 359–379. doi: 10.1037/a0029082

Remijnse, P. L., van den Heuvel, O. A., Nielen, M. M. A., Vriend, C., Hendriks, G.-J., Hoogendijk, W. J. G., … Chelminski, I. (2013). Cognitive Inflexibility in Obsessive-Compulsive Disorder and Major Depression Is Associated with Distinct Neural Correlates. *PLoS ONE*, *8*, e59600. doi: 10.1371/journal.pone.0059600

Ridderinkhof, K. R., Van Den Wildenberg, W. P. M., Segalowitz, S. J., & Carter, C. S. (2004). Neurocognitive mechanisms of cognitive control: The role of prefrontal cortex in action selection, response inhibition, performance monitoring, and reward-based learning. *Brain and Cognition*. doi: 10.1016/j.bandc.2004.09.016

Roberts, G., Quach, J., Spencer-Smith, M., Anderson, P. J., Gathercole, S., Gold, L., … Wake, M. (2016). Academic Outcomes 2 Years After Working Memory Training for Children With Low Working Memory: A Randomized Clinical Trial. *JAMA Pediatrics*. doi: 10.1001/jamapediatrics.2015.4568

Roiser, J. P., Elliott, R., & Sahakian, B. J. (2012). Cognitive mechanisms of treatment in depression. *Neuropsychopharmacology : Official Publication of the American College of Neuropsychopharmacology*, *37*, 117–36. doi: 10.1038/npp.2011.183

Schmiedek, F., Lövdén, M., & Lindenberger, U. (2010). Hundred Days of Cognitive Training Enhance Broad Cognitive Abilities in Adulthood: Findings from the COGITO Study. *Frontiers in Aging Neuroscience*, *2*. doi: 10.3389/fnagi.2010.00027

Schwarb, H., Nail, J., & Schumacher, E. H. (2016). Working memory training improves visual short-term memory capacity. *Psychological Research*, *80*, 128–48. doi: 10.1007/s00426-015-0648-y

Schweizer, S., Grahn, J., Hampshire, A., Mobbs, D., & Dalgleish, T. (2013). Training the Emotional Brain: Improving Affective Control through Emotional Working Memory Training. *Journal of Neuroscience*, *33*, 5301–5311. doi: 10.1523/jneurosci.2593-

12.2013

Schweizer, S., Hampshire, A., & Dalgleish, T. (2011). Extending Brain-Training to the Affective Domain: Increasing Cognitive and Affective Executive Control through Emotional Working Memory Training. *Plos One*, *6*, 7. doi: 10.1371/journal.pone.0024372

Segrave, R. A., Arnold, S., Hoy, K., & Fitzgerald, P. B. (2014). Concurrent cognitive control training augments the antidepressant efficacy of tDCS: A pilot study. *Brain Stimulation*, *7*, 325–331. doi: 10.1016/j.brs.2013.12.008

Sheline, Y. I., Barch, D. M., Donnelly, J. M., Ollinger, J. M., Snyder, A. Z., & Mintun, M. A. (2001). Increased amygdala response to masked emotional faces in depressed subjects resolves with antidepressant treatment: An fMRI study. *Biological Psychiatry*, *50*, 651–658. doi: 10.1016/S0006-3223(01)01263-X

Shilyansky, C., Williams, L. M., Gyurak, A., Harris, A., Usherwood, T., & Etkin, A. (2016). Effect of antidepressant treatment on cognitive impairments associated with depression: A randomised longitudinal study. *The Lancet Psychiatry*. doi: 10K1016+S2215-0366(16)00012-2

Shipstead, Z., Redick, T. S., & Engle, R. (2010). Does working memory training generalize? *Psychologica Belgica*, *17*, 245–276. doi: 10.3758/PBR.17.2.193

Shipstead, Z., Redick, T. S., & Engle, R. W. (2012). Is working memory training effective? *Psychological Bulletin*, *138*, 628–654. doi: 10.1037/a0027473

Siegle, G. J., Ghinassi, F., & Thase, M. E. (2007). Neurobehavioral therapies in the 21st century: Summary of an emerging field and an extended example of cognitive control training for depression. *Cognitive Therapy and Research*, *31*, 235–262. doi: 10.1007/s10608-006-9118-6

Siegle, G. J., Price, R. B., Jones, N. P., Ghinassi, F., Painter, T., & Thase, M. E. (2014). You gotta work at it: Pupillary indices of task focus are prognostic for response to a neurocognitive intervention for rumination in depression. *Clinical Psychological Science*, *2*, 455–471. doi: 10.1177/2167702614536160

Siegle, G. J., Thompson, W. S., Carter, C. S., Steinhauer, S. R., & Thase, M. E. (2007). Increased amygdala and decreased dorsolateral prefrontal BOLD responses in unipolar depression: Related and independent features. *Biological Psychiatry*, *61*, 198–209.

Simons, D. J., Boot, W. R., Charness, N., Gathercole, S. E., Chabris, C. F., Hambrick, D. Z., & Stine-Morrow, E. A. L. (2016). Do "Brain-Training" Programs Work? *Psychological Science in the Public Interest, 17*, 103-186. doi: 10.1177/1529100616661983

Smith, E. E., & Jonides, J. (1999). Storage and executive processes in the frontal lobes. *Science*, *283*, 1657–1661.

Snyder, H. R. (2013). Major Depressive Disorder is associated with broad impairments on neuropsychological measures of executive function: A meta-analysis and review. *Psychological Bulletin*, *139*, 81–132.

Surguladze, S., Brammer, M. J., Keedwell, P., Giampietro, V., Young, A. W., Travis, M. J., … Phillips, M. L. (2005). A differential pattern of neural response toward sad versus happy facial expressions in major depressive disorder. *Biological Psychiatry*, *57*, 201–209.

Takeuchi, H., Taki, Y., Nouchi, R., Hashizume, H., Sekiguchi, A., Kotozaki, Y., … Kawashima, R. (2013). Effects of working memory training on functional connectivity and cerebral blood flow during rest. *Cortex*, *49*, 2106–2125. doi: 10.1016/j.cortex.2012.09.007

Takeuchi, H., Taki, Y., Nouchi, R., Hashizume, H., Sekiguchi, A., Kotozaki, Y., … Kawashima, R. (2014). Working memory training improves emotional states of healthy individuals. *Frontiers in Systems Neuroscience*, *8*, 1–14. doi: 10.3389/fnsys.2014.00200

Taylor, J. G., & Fragopanagos, N. (2005). The interaction of attention and emotion. *Neural Networks*, *18*, 353–369.

Thomas, L., Kessler, D., Campbell, J., Morrison, J., Peters, T. J., Williams, C., … Wiles, N. (2013). Prevalence of treatment-resistant depression in primary care: Cross-sectional data. *British Journal of General Practice*, *63*, E852–E858. doi: 10.3399/bjgp13X6675430

Tombaugh, T. N. (2006). A comprehensive review of the Paced Auditory Serial Addition Test (PASAT). *Archives of Clinical Neuropsychology*, *21*, 53–76.

Trapp, W., Engel, S., Hajak, G., Lautenbacher, S., & Gallhofer, B. (2016). Cognitive remediation for depressed inpatients: Results of a pilot randomized controlled trial. *The Australian and New Zealand Journal of Psychiatry*, *50*, 46–55. doi: 10.1177/0004867415622271

Van Bockstaele, B., Verschuere, B., Tibboel, H., De Houwer, J., Crombez, G., & Koster, E. H. W. (2014). A review of current evidence for the causal impact of attentional bias on fear and anxiety. *Psychological Bulletin*, *140*, 682–721. doi: 10.1037/a0034834

Vanderhasselt, M.-A., & De Raedt, R. (2009). Impairments in cognitive control persist during remission from depression and are related to the number of past episodes: An event related potentials study. *Biological Psychology*, *81*, 169–176.

Vanderhasselt, M.-A., De Raedt, R., Namur, V., Lotufo, P. A., Bensenor, I. M., Boggio, P. S., & Brunoni, A. R. (2015). Transcranial electric stimulation and neurocognitive training in clinically depressed patients: A pilot study of the effects on rumination. *Prog Neuropsychopharmacol Biol Psychiatry*, *57*, 93–99. doi: 10.1016/j.pnpbp.2014.09.015

Wanmaker, S., Geraerts, E., & Franken, I. H. A. (2015). A working memory training to decrease rumination in depressed and anxious individuals: A double-blind randomized controlled trial. *Journal of Affective Disorders*, *175*, 310–319. doi: 10.1016/j.jad.2014.12.027

Wells, A. (2000). *Emotional disorders and metacognition innovative Cognitive Therapy*. New York: Wiley.

Westerberg, H., Jacobaeus, H., Hirvikoski, T., Clevberger, P., Ostensson, M., Bartfai, A., & Klingberg, T. (2007). Computerized working memory training after stroke - A pilot study. *Brain Injury*, *21*, 21–29. doi: 10.1080/02699050601148726

Westerberg, H., & Klingberg, T. (2007). Changes in cortical activity after training of working memory - A single-subject analysis. *Physiology & Behavior*, *92*, 186–192.

Whitmer, A. J., & Gotlib, I. H. (2012). Switching and backward inhibition in major depressive disorder: The role of rumination. *Journal of Abnormal Psychology*, *121*, 570–578. doi: 10.1037/a0027474

WHO. (2012). Depression: World Health Organization Fact sheet no 369. Accessed on 29-05-2014 from http://www.who.int/mediacentre/factsheets/fs369/en/

Xiu, L., Zhou, R., & Jiang, Y. (2016). Working memory training improves emotion regulation ability: Evidence from HRV. *Physiology and Behavior*, *155*, 25–29. doi: 10.1016/j.physbeh.2015.12.004

Zetsche, U., & Joormann, J. (2011). Components of interference control predict depressive symptoms and rumination cross-sectionally and at six months follow-

up. *Journal of Behavior Therapy and Experimental Psychiatry*, *42*, 65–73. doi: 10.1016/j.jbtep.2010.06.001

APPENDIX

-Table 1: provides an overview of CCT studies focusing on cognitive vulnerability factors for depression in healthy or at-risk samples

-Table 2: provides an overview of CCT studies in MDD samples

-Table 3: provides an overview of CCT studies in RMD samples

Supplemental Table 1. Overview of effects of CCT on cognitive and depressive vulnerability outcomes in healthy- or at-risk samples

Study	**Sample**	**Stimulus material**	**Training conditions [amount of training sessions, training period]**	**Training effects**	**Within-group effects (CCT condition)**
Calkins, Deveney, Weitzman, Hearon, & Siegle (2011)	Healthy community sample (*n* = 59)	Neutral (numbers, tones)	Adaptive PASAT and Wells' attention training (CCT, *n* = 27) vs. peripheral vision task (*n* = 31) [Single-session manipulation]	Effects of a mood induction were stronger following exposure to the CCT tasks compared to the peripheral vision task (significant: PANAS state positive affect; trend level: PANAS state negative affect) No differential effects were found on emotional reactivity towards images (ERRT) or attentional bias towards threatening stimuli (dot probe task)	-Adaptive PASAT performance was unrelated to self-reported affect throughout the mood induction procedure and bias towards threatening stimuli -Adaptive PASAT performance was related to increased positive experience of pleasant images and reduced negative experience of unpleasant images (ERRT)
Calkins, McMorran, Siegle, & Otto (2015)	Community sample with elevated depressive symptoms (*n* = 48)	Neutral (numbers, tones)	Adaptive PASAT and Wells' attention training (CCT, *n* = 24) vs. adaptive peripheral vision task (*n* = 24) [3 sessions, 2 weeks]	Beneficial effects on depressive symptomatology (BDI-II) Trend towards lower negative affect post-training (PANAS state)	-Increased adaptive PASAT performance was related to increased positive affect (PANAS state, VAS relaxed/tense) -This was unrelated to negative affect (PANAS state, VAS) or depressive symptomatology (BDI-II)
Calkins & Otto (2013)	Community sample	Neutral (numbers,	Adaptive PASAT and Wells' attention	Cognitive transfer: -No differential effects on goal	-Increased adaptive PASAT performance was related to

	showing elevated obsessive compulsive symptoms and low depressive symptoms (*n* = 48)	tones)	training (CCT, *n* = 24) vs. adaptive peripheral vision task (*n* = 24) [3 sessions, 2 weeks]	disengagement (Anagram task) Beneficial effects of CCT on trait negative affect and marginal effects on trait positive affect (PANAS trait) Trend towards worsening of obsessive compulsive symptoms (OCI-R) compared to the active control condition No differential effects on depressive symptomatology (BDI-II)	reduced obsessive compulsive symptoms (OCI-R) and increased positive affect (PANAS) -This was unrelated to negative affect (PANAS). -Higher mean adaptive PASAT performance was (marginally) related to more time spent on (un)solvable anagrams
Cohen et al. (2016)	Healthy participants (*n* = 26)	Neutral (orientation of arrows)	High-frequent Executive Control training (Modified Flanker task with 80% incongruent trials, CCT; *n* = 13) vs. Low-frequent Executive Control training (20% incongruent trials; *n* = 13) [(1) Single-session manipulation, (2) followed by 18 sessions of training over 6 days]	Cognitive transfer effects: -Increased task performance on incongruent trials compared to the control group -Reduced amygdala activity and behavioral interference of aversive pictures following multiple-session CCT, but not following the single-session manipulation -Tendency towards increased amygdala – prefrontal region connectivity	-Change in amygdala activity was associated with reduced interference of aversive stimuli -Increased amygdala – prefrontal region connectivity

Cohen, Mor, & Henik (2015)	Convenience sample (*n* = 68)	Paired neutral training stimuli (orientation of arrows) with emotional information (pictures)	Modified Flanker task (pairing of incongruent trials and negative emotional stimuli; CCT, *n* = 37) vs. sham training (pairing of congruent trials and negative emotional information; *n* = 31) [Single-session manipulation]	Increased resilience to state rumination (VAS) following a rumination induction procedure No immediate effects of training on change in mood (VAS) throughout a rumination induction procedure However, compared to the sham training, CCT buffered negative effects of trait brooding (RRS) on sad mood (VAS) during a rumination induction procedure	-The CCT group was characterized by a reduction of emotional interference of negative pictures on a discrimination task
Daches & Mor (2014)	Trait ruminators (brooders; *n* = 85)	Emotional (words)	Inhibition of negative content (modified NAP task, CCT; *n* = 31) vs. Attend to negative (modified NAP task; *n* = 25) vs. sham training (*n* = 29) [4 sessions, 2 weeks]	Cognitive transfer: -Following training the CCT group showed higher levels of inhibition bias compared to the attend to negative information control group Although a Time x Group interaction for brooding (RRS) was significant, follow-up between group comparisons indicated that groups did not significantly differ in brooding following training No beneficial effects on depressive symptomatology (BDI-II) were found	-Change in inhibition in the CCT group was non-significant -The CCT group reported a decrease in brooding levels from baseline to post-training -Change in inhibition bias was unrelated to the reduction in brooding
Daches, Mor, & Hertel (2015)	Convenience sample	Emotional (words)	Inhibition of negative content (modified	Cognitive transfer: -High ruminators show training	-Rumination moderated effects of CCT on inhibition

	(compares high and low trait ruminators based on median split; *n* = 140)		NAP task, CCT; *n* = 68) vs. Attend to negative (modified NAP task; *n* = 72) [Single-session manipulation]	incongruent effects on inhibition -No interaction of training on inhibition over time in low ruminators -No differential effects of training on interpretation bias in high ruminators, and a tendency in low ruminators No beneficial effects on state rumination (MRSI) or mood (VAS)	and interpretation bias -High ruminators show negative effects of training on inhibition, no beneficial effects on inhibition were found in low ruminators -High ruminators demonstrated a stronger interpretation bias than low ruminators following training
de Putter, Vanderhasselt, Baeken, De Raedt, & Koster (2015)	Healthy participants (*n* = 57)	Neutral (letters & locations)	tDCS + Dual n-back (*n* = 19) vs. tDCS + Single 1-back (*n* = 19) vs. sham tDCS + Dual n-back (*n* = 19) [Single-session manipulation]	Cognitive transfer: -There were no differential effects on working memory task performance (R-Span task) -The sham tDCS + Dual n-back condition showed slower task switching than the groups including tDCS (IST) No differential effects on mood were found (POMS) throughout the experiment Groups did not differ in their ruminative response to a rumination induction procedure (MRSI) However, conditions including the dual n-back training component	

				responded to the rumination induction procedure with increased heart rate variability, suggesting beneficial effects of CCT on emotion regulation processes
Gavelin, Boraxbekk, Stenlund, Järvholm, & Neely (2015)	Exhaustion disorder (*n* = 59)	Neutral (letters, words, numbers, geometric shapes)	6 cognitive tasks + TAU (Updating: Letter memory running span task, Keep track task; Shifting: Alternating runs with digits, Unpredictable task cueing paradigm; Visuospatial short-term memory: Visuospatial span task; Episodic memory: Three-word-associates task; TAU: stress rehabilitation program; *n* = 27) vs. TAU (*n* = 32) [36 sessions, 12 weeks]	Cognitive transfer: -Beneficial effects on Letter memory running span task performance -Overall beneficial effects of training on cognitive functioning (driven by near transfer effects on 3-back task performance and Recall of concrete nouns; far transfer effects: Raven's matrices) -No differential effects were found for Inhibition cost, Shift cost, Digit span forwards, Digit span backwards, Letter-number sequencing (near transfer), and Digit symbol task (far transfer) Beneficial effects on self-reported cognitive complaints (6-QEMP; but no differential effects on PRMQ Prospective and Retrospective) Beneficial effects on self-reported burnout complaints (SMBQ)
Hoorelbeke, Koster, Demeyer,	Convenience sample (*n* =	Neutral (numbers)	Adaptive PASAT (CCT, *n* = 29)	Cognitive transfer effects: -Marginal beneficial effects on

Loeys, & Vanderhasselt (2016)	61)		vs. low cognitive load / attention training (*n* = 32) [10 sessions, 2 weeks]	cognitive control task performance (dual n-back) No differential effects on reappraisal ability in lab context CCT condition showed a tendency to respond with less rumination to reductions of positive affect in daily life (ESM) No differential effects on deployment of positive appraisal and efficacy of emotion regulation in daily life (ESM)	
Hoorelbeke, Koster, Vanderhasselt, Callewaert, & Demeyer (2015)	Trait ruminators (*n* = 47)	Neutral (numbers)	Adaptive PASAT (CCT, *n* = 25) vs. adaptive Visual Search task (*n* = 22) [10 sessions, 2 weeks] *Analyses of training effects on rumination in response to a naturalistic stressor are based on *n* = 37 (CCT: *n* = 20, control: *n* = 17)	Cognitive transfer effects: -No differential effects on working memory task performance (O-Span) Beneficial effects of CCT on stress reactivity in lab context (VAS negative affect; thought intrusions – breathing focus task) Beneficial effects of CCT on brooding (RRS) in response to a naturalistic stressor (examinations) at 4 weeks follow-up No additional beneficial effects on	-Increased performance on cognitive transfer measure (O-Span) following CCT predicted a reduction in brooding and increased self-reported resilience (this was not the case for the active control condition) -Effects of CCT on stress reactivity (VAS) and thought intrusions (breathing focus task) immediately following two weeks of training marginally predicted effects on brooding in response to

				depressive symptomatology (BDI-II, MASQ-D30), anxiety (MASQ-30), worrying (PSWQ), resilience (RS), attentional control (ACS), and affect (PANAS)	the naturalistic stressor at 4 weeks follow-up
Moshier, Molokotos, Stein, & Otto (2015)	Student- and community sample with euthymic (*n* = 37) or depressed mood (*n* = 32)	Neutral (numbers, tones)	Euthymic mood / Adaptive PASAT and Wells' Attention Training (CCT, *n* = 16) vs. Depressive mood / Adaptive PASAT and Wells' Attention Training (CCT, *n* = 20) vs. Euthymic mood / Peripheral Vision Task (*n* = 16) vs. Depressive mood / Peripheral Vision Task (*n* = 17) [3 sessions, 2 weeks]	Comparison of training effects on depressive symptomatology (BDI-II) in the depressed mood group yielded no significant effects No differential effects of depressive mood group and cognitive training condition on meta-memory and memory accuracy (in the context of a repeated knob-checking task, cfr. OCD induction)	
Onraedt & Koster (2014) – Study 1	Trait ruminators (*n* = 72)	Neutral (letters & locations)	Adaptive dual n-back (CCT, *n* = 21) vs. single 1-back (*n* = 25) vs. no training (*n* = 26) [6 sessions, 1 week]	Cognitive transfer effects: -No differential effects on working memory capacity (R-Span task) -No differential effects on emotional and non-emotional shift cost (IST-task) No differential effects on rumination, brooding (RRS), or	-Improved performance on CCT task, which was marginal significantly related to a decrease in depressive symptomatology over time -Improved CCT task performance was unrelated to difference scores for cognitive transfer tasks and

				depressive symptomatology (BDI-II) following training and at 2-weeks follow-up	rumination
Onraedt & Koster (2014) – Study 2	Trait ruminators (*n* = 45)	Neutral (letters & locations)	Dual n-back (CCT, *n* = 21) vs. Single 1-back (*n* = 24) [6 sessions, 1 week]	Cognitive transfer effects: -No differential effects on cognitive transfer tasks (R-Span task, O-Span task, emotional 2-back task) No differential effects on rumination, brooding, reflection (RRS), or depressive symptomatology (BDI-II) following training and at 2-weeks follow-up No moderation of metacognitions regarding rumination (NBRS, PBRS)	-Improved performance on CCT task, which was marginal significantly related to increased working memory capacity (O-Span) -Improved CCT task performance was unrelated to difference scores for other cognitive transfer tasks, depressive symptomatology and rumination
Owens, Koster, & Derakshan (2013)	Dysphorics (*n* = 22)	Neutral (letters & locations)	Adaptive dual n-back (CCT, *n* = 11) vs. dual 1-back (*n* = 11) [8 sessions, 2 weeks]	Cognitive transfer effects: -Improved working memory capacity scores (change detection task performance) -Improved filtering efficiency (ERP component for Contralateral Delay Activity) No differential immediate effects of training on depressive symptomatology (BDI-II)	
Quinn, Keil, Utke, & Joormann (2014)	Students (*n* = 69)	Neutral (words) & emotional	Affective n-back (affective CCT; *n* = 23) vs. Neutral n-back	No differential effects of training condition on self-reported anxiety (VAS) or cortisol response to a stress	

		(words)	(neutral CCT; *n* = 23;) vs. Control condition (affective control task; *n* = 23) [Single-session manipulation]	induction procedure No moderating effect of trait rumination to self-reported anxiety following a stress induction procedure Trait rumination moderates the relation between training condition and effect of stress induction on cortisol: no differential cortisol response in low trait ruminators, whereas high trait ruminators benefited from CCT compared to the control group. Affective and neutral n-back conditions did not differ.	
Schweizer, Hampshire, & Dalgleish (2011)	Convenience sample (*n* = 45)	Emotional (words & faces) and neutral (letters & locations)	Affective dual n-back (affective CCT, *n* = 15) vs. Neutral dual n-back (neutral CCT, *n* = 14) vs. Feature match task (active control, *n* = 16) [20 sessions, 4 weeks]	Cognitive transfer: -The neutral and affective CCTs showed beneficial effects on working memory functioning (Digit span) and G*f* (Raven's Progressive Matrices) The affective CCT provided additional beneficial effects on an affective transfer measure (Emotional Stroop)	-Trend for increased training task performance to be related with G*f*
Schweizer, Grahn, Hampshire,	Convenience sample (*n* = 32)	Emotional (words & faces)	Affective dual n-back (affective CCT; *n* = 17) vs. Feature match task	Cognitive transfer: -Beneficial effects of CCT on behavioral and neurological	-Cognitive task improvements were associated with increased

Mobbs, & Dalgleish (2013)			(active control, *n* = 15) [20 sessions, 4 weeks]	indicators of cognitive functioning (non-adaptive affective dual n-back task performance; frontoparietal demand network) -Beneficial effects of CCT on emotion regulation (regulate vs. attend to induction procedure)	efficiency of the frontoparietal brain regions -Improvements in emotion regulation were associated with increased activation of the same frontoparietal regions involved in emotional dual n-back task progress
Takeuchi et al. (2014)	Convenience sample (*n* = 61)	Neutral	4 cognitive tasks (visuospatial WM task, auditory backward operation span task, dual WM task, dual n-back task; CCT; *n* = 41) vs. no training (*n* = 20) [27 sessions, 4 weeks]	Cognitive transfer: -Beneficial effects of CCT on untrained verbal and visual working memory tasks [reported in Takeuchi et al. (2013)] Beneficial effects on self-reported negative mood: anger/hostility, depression/dejection, fatigue/inertia (POMS) and state anger (STAXI) (But no beneficial effects on self-reported tension/anxiety, vigor/activity, and confusion/bewilderment; POMS) Beneficial effects on negative emotion-related activity (left posterior insula, left frontoparietal area) during tasks evoking negative emotions	-Improved performance on CCT task was unrelated to emotional state change and change in functional activity parameters
Xiu, Zhou, & Jiang	Healthy	Neutral	CCT (3 variants of the	Cognitive transfer effects:	

(2016)	students (*n* = 40)	(letters, animals, or locations)	Running Working Memory task: Letter Running Working Memory task + Animal Running Working Memory task + Location Running Working Memory task; *n* = 20) vs. no training (*n* = 20) [20 sessions, 3 weeks]	-Beneficial effects on RT-indices of working memory ability (2-back task), but no differential effects on accuracy scores. No differential effects of training condition on subjective emotion ratings during an emotion regulation task Beneficial effects of training on high-frequency heart rate variability (HF-HRV) during an emotion regulation task (cognitive down-regulation of negative film clips) as an indicator of emotion regulation ability

Note: All studies have been selected based on (a) inclusion of a CCT procedure, in combination with (b) the sample characteristics (at-risk for depression; e.g., rumination, dysphoria), *or* (c) inclusion of outcome measures which allow evaluation of effects of CCT on cognitive vulnerability for depression (e.g., mood, rumination, depressive symptomatology). Additional within-group effects are only reported in case of absence of reported between group analyses or when they provide additional information relating to effects of CCT on cognitive vulnerability for depression.

Supplemental Table 2. Overview of effects of CCT in MDD samples

Study	**Sample**	**Stimulus material**	**Training conditions [amount of training sessions, training period]**	**Training effects**	**Within-group effects (CCT condition)**
Alvarez, Sotres, León, Estrella, & Sosa (2008)	MDD students (*n* = 31)	Neutral (numbers & letters)	Alcor ('Series game' and 'Goose game', CCT; *n* = 10) vs. Alcor + antidepressant medication (combined CCT treatment, *n* = 10) vs. antidepressant medication (*n* = 11) [2 times per week, length of treatment was depending on task performance, until participants reached level 60 for 'Series Game' and level 70 for 'Goose game']	Cognitive transfer: -beneficial effects on Intelligence Quotient (WAIS) Beneficial effects on depressive symptomatology (BDI) and trait anxiety (tendency, STAI) at conclusion of CCT No significant Time x Group interaction for state anxiety (STAI) Beneficial effects on externalized problems (EPA) and attention problems (APAS)	
Bowie et al. (2013)	Treatment resistant MDD (*n* = 33)	Unspecified	Online cognitive training (Scientific Brain Training Pro package, containing	Cognitive transfer: -beneficial effects on attention and processing speed (compound of Symbol Coding Task, Continuous	-Cognitive improvements were related to perceived competence with computerized cognitive

			processing speed and attention training as well as working memory, delayed memory and executive functions training) + cognitive remediation group therapy (computer-based exercises, strategic self-monitoring and discussing applications of learned techniques in daily life) (*n* = 17) vs. waiting list condition (*n* = 16) [online training: 2 sessions of 20 minutes daily; group session: 90 minutes per week; 10 weeks] *Completers only analysis is based on *n* = 11 (CCT) and *n* = 10 (waiting list)	Performance Test-Identical Pairs Version, Controlled Oral Word Association Test and Animal Naming tests, Trail Making Test part A) -beneficial effects on verbal learning and memory (Hopkins Verbal Learning Test) -no differential effects on executive functioning (Letter Number Sequencing Test, Trail Making Test part B, Stroop color-word test). *Note: these cognitive functions were only targeted during the last two weeks of online training* No differential effects on functioning and competence (Social Skills Performance interpersonal competence Assessment and Advanced Finances task) nor on the Interview-based assessment of Real-world functioning (Longitudinal Interval Follow-up Evaluation Range of Impaired Functioning Tool)	remediation and amount of online training sessions completed -Cognitive improvements were related to improvements on ratings for impaired real-world behavior, but not significantly related to improvements in objective measures of interpersonal or adaptive competence. -Severity of depression was related to higher completion rates for the online training. Such associations were not found for perceived competence, intrinsic motivation, or anxiety severity
Brunoni et al.	MDD	Neutral	Active tDCS + CCT		-Decrease in depressive

(2014)	patients (*n* = 37)	(numbers)	(adaptive PASAT; *n* = 20) vs. sham tDCS + CCT (adaptive PASAT; *n* = 17) [10 sessions, 2 weeks]		symptomatology throughout CCT (HAMD-21, BDI-II) -Older age predicted greater enhancement of tDCS on CCT -Greater PASAT improvement predicted increased beneficial effects on depressive symptomatology
Elgamal, McKinnon, Ramakrishnan, Joffe, & MacQueen (2007)	Non-acute recurrent MDD patients (*n* = 24) and healthy controls (*n* = 22)	Neutral (see Chen et al., 1997)	PSSCogReHab cognitive remediation software program (training of attention, verbal memory, psychomotor speed and executive functions; CCT, *n* = 12) vs. no training MDD controls (*n* = 12) vs. no training healthy controls (*n* = 22) [On average 2 weekly sessions, 10 weeks]	Cognitive transfer: -Beneficial effects of CCT on general episodic verbal learning and memory compared to both control conditions (Total CVLT performance; beneficial effects on Short-delay free recall, Short-delay cued recall, and Long-delay free recall, but no differential effects on interference List B Learning or recognition hits) -Beneficial effects of CCT on total speed on the measure for visual selective attention (Ruff's 2 & 7 Selective Attention test) -Beneficial effects on Digit Span Forwards task performance, but no differential effects on Digit Span Backwards task performance -Beneficial effects on Trail Making Test A performance, but no	

				differential effects on Trail Making B performance -No differential effects on abstract verbal reasoning (WAIS-R Similarities subtest) or verbal association fluency (COWAT) No differential effects on depressive mood (HAMD)	
Iacoviello et al. (2014)	MDD patients (*n* = 21)	Emotional (faces) vs. neutral (geometric shapes)	Adaptive emotional Faces Memory task (adaptive emotional n-back, emotional CCT; *n* = 11) vs. Adaptive neutral n-back task (neutral CCT; *n* = 10) [8 sessions, 4 weeks]	Cognitive transfer: No differential effects of neutral and emotional CCT on cognitive task performance (composite score for attention span and working memory: Digit Span Forward, Digit Span Backward, Letter Number Sequencing) Differential effects of training on depressive symptomatology (HAM-D). The emotional CCT group showed a tendency for lower depressive symptomatology immediately following training compared to the neutral CCT. 6:11participants in the emotional CCT group showed a reduction in HAM-D of ≥ 50% vs. 1:10 in the neutral CCT group	-Small to medium sized though non-significant reduction in rumination (RRS) -The emotional CCT group showed a significant reduction in short-term memory for negative self-referential information (SRIP task) -Tendency for increased cognitive functioning (composite score attention span and working memory: Digit Span Forwards, Digit Span Backwards, Letter Number Sequencing). No significant increase in the neutral CCT group.

Morimoto et al. (2014)	Treatment resistant geriatric depressed patients (failed at least one adequate antidepressant trial; *n* = 43)	Neutral (among others: geometric shapes, colors, words)	3 bottom-up training tasks (auditory tone sweep, phonemic discrimination, visual discrimination) + 2 top-down training tasks (Catch the ball, Semantic Strategy) + continuation of intake of antidepressants to which participants previously demonstrated no response (CCT, *n* = 10) vs. TAU (escitalopram, *n* = 33)* [30 hours, 4 weeks; vs. escitalopram, 12 weeks] *Participants in the CCT condition were preselected treatment resistant patients, whereas this was not the case in the TAU control group	Cognitive transfer: -Beneficial effects on executive functioning (Trails B + tendency for Stroop Color-Word) Beneficial effects on depressive symptomatology (MADRS) Cognitive training was equally effective in treatment resistant patients as escitalopram treatment in patients *unselected* on being treatment resistant Furthermore, training effects emerged faster in the cognitive training group (following 4 weeks compared to 12 weeks)	-Improved cognitive control: Stroop Color-Word task performance, Trails B performance, design fluency switching (D-KEFS) -Trend for improved semantic clustering (DRS I/P) -No improvement in working memory (WAIS-IV digits backwards) or verbal memory (CVLT-ii long delay recall) functioning -Increased Trails B task performance was related to a reduction in depressive symptomatology -Beneficial treatment effects were sustained at 3-months follow-up -9 CCT patients met criteria for response to treatment at the end of the 4-week training (8 met criteria for remission), 6 CCT patients met criteria for response to treatment at 3-month follow-up (all 6 met criteria for remission)
Moshier (dissertation,	MDD patients (*n* =	Neutral (numbers,	Adaptive PASAT + Wells' attention	Cognitive transfer: -No beneficial effects on inhibition	-Stronger initial cognitive control (adaptive PASAT ISI)

2015)	34)	tones)	training + brief behavior activation intervention (CCT, *n* = 21) vs. peripheral vision task + brief behavior activation intervention (active control, *n* = 13) [4 sessions, 4 weeks] *Analyses of cognitive transfer effects relied on *n* = 26 (CCT: *n* = 14, active control: *n* = 12)	of emotional processing (NAP) or attentional shifting (IST) CCT had no added effects to behavior activation therapy concerning depressive symptomatology (BDI-II, MADRS), rumination, brooding (RRS), environmental reward (RPI), and anxiety (BAI)	was related to better improvement in depressive symptoms and less improvement in brooding (*Note:* *r* = -.51; MADRS, *r* = -.36, BDI-II; *r* = .32, RRS; n.s. due to *n* = 12). Not replicated in hierarchical regression model after controlling for baseline symptom level -High levels of baseline inhibitory control of negative emotional material predicted lower depressive symptomatology (MADRS, tendency) at follow-up
Segrave, Arnold, Hoy, & Fitzgerald (2014)	MDD patients (*n* = 26)	Neutral (numbers, tones/bird sounds)	tDCS + CCT (Adaptive PASAT and Wells' attention training; *n* = 8) vs. sham tDCS + CCT (Adaptive PASAT and Wells' attention training; *n* = 9) vs. tDCS + sham training (adaptive Peripheral Vision Task; *n* = 9)	Cognitive transfer: -tDCS + CCT group showed the strongest increase in negative 2-back functioning -No differential effects on positive and neutral 2-back task accuracy. No differential effects on positive, negative, and neutral 2-back RT data Beneficial effects of tDCS and CCT on depressive symptomatology (MADRS) immediately following training. Depressive	-Increased negative 2-back task accuracy was associated with lower depression severity at 3-week follow-up

			[5 sessions, 5 days]	symptomatology only further decreased at 3-week follow-up in the tDCS + CCT condition Trend for difference in response rates immediately following training: only responders in the two CCT groups (33 – 44%) vs. no responders in the tDCS + sham training condition Differential effects on response rate at 3-week follow-up: beneficial effect of added tDCS to CCT Immediate effects of CCT and tDCS on alternative outcome measure for depressive symptomatology (BDI-II). Only effects at 3-week follow-up in CCT + tDCS and sham training + tDCS condition	
Siegle, Ghinassi, & Thase (2007)	MDD patients (*n* = 23)	Neutral (numbers, tones/bird sounds)	Adaptive PASAT and Wells' attention training (CCT) + TAU (*n* = 15) vs. TAU (*n* = 8) [6 sessions, 2 weeks]	Cognitive transfer effects -Beneficial effects on cognitive control (non-adaptive PASAT) -No transfer on the Digit Sorting task (ceiling effect prior to training) Beneficial effects on depressive symptomatology (BDI-II) and rumination (RSQ)	-fMRI data on a subsample (*n* = 6) suggests decreased disruptions in DLPFC and amygdala activity during a cognitive (digit sorting task) and emotional (personal relevance rating) task respectively following CCT

				No differential effects on pupil dilation in response to emotional information	
Siegle et al. (2014) [extended sample from Siegle et al., 2007]	MDD patients (*n* = 43)	Neutral (numbers, tones/bird sounds)	Adaptive PASAT and Wells' attention training (CCT) + TAU (*n* = 23) vs. TAU (*n* = 20)* [6 sessions, 2 weeks] *For service utilization analyses Siegle et al. (2014) compared participants of the CCT condition and participants of the TAU group who after completing the training also performed at least one session of CCT (*n* = 43) with a group of service control patients (*n* = 57) *Non-adaptive PASAT performance was compared with a	Cognitive transfer: -Increased non-adaptive PASAT performance compared to healthy controls -Increased task-related processing (on-task power) compared to TAU -No differential effects on non-task-related processing (off-task power) Beneficial effects of CCT on rumination and brooding (RSQ), no effects on reflection No differential effects on depressive symptomatology (BDI-II) Participants who performed at least one CCT session had fewer intensive outpatient day-treatment visits in the year following treatment than a control group No such effects were found for medication management visits or regular outpatient therapy	-Less increased task-related processing (on-task power) was related to more decreased rumination -Change in rumination (RSQ) and depression (BDI-II) levels were unrelated -Decreased rumination was predicted by higher initial task-related processing (on-task power, non-adaptive PASAT) and lower non-task-related processing (off-task power), and the related unfocus index -Decreased pupil dilation following the intervention -Decrease in pre- versus post-CCT intensive outpatient day-treatment visits -Amount of completed CCT sessions was unrelated to post year service utilization

			healthy control sample from Jones, Siegle, Muelly, Haggerty, & Ghinassi (2010; *n* = 19)	
Trapp, Engel, Hajak, Lautenbacher, & Gallhofer (2016)	MDD patients (*n* = 46)	Unspecified	Cognitive remediation + TAU (10 cognitive training tasks targeting executive functioning, visuomotor functioning, and memory functioning; CCT condition, *n* = 23) vs. TAU (control group, *n* = 23) [12 sessions, 4 weeks]	Cognitive transfer: -beneficial effects after four weeks of training on working memory functioning (Wechsler Memory Scale: significant effects for spatial span backward and logical memory immediate recall; a tendency for digit span backward and visual reproduction immediate recall; no effects for digit span forward and spatial span forward) -beneficial effects on memory (Wechsler Memory Scale: significant effects on visual reproduction delayed recall and logical memory delayed recall) -beneficial effects on executive functioning (significant effects on the Trail Making Test part B and delta score Trail Making Test part B minus part A; a tendency for performance on the Wisconsin Card Sorting Test) -no differential effects on attention (degraded Continuous Performance

				Test & Trail Making Test part A) No immediate beneficial effects on depressive symptomatology (BDI and HAMD). *Note: possibly due to limited power as Cohen's d = .67 in favor of the CCT condition*	
Vanderhasselt et al. (2015) [additional analyses for Brunoni et al., 2014]	MDD patients (*n* = 33)	Neutral (numbers)	Active tDCS + CCT (adaptive PASAT; *n* = 19) vs. sham tDCS + CCT (adaptive PASAT; *n* = 14) [10 sessions, 2 weeks]		-Increased performance on the CCT task with no differential effect of tDCS (absence of an interaction effect) -However, the slope of improvement in CCT task performance (adaptive PASAT ISI slope) tended to be steeper in the sham tDCS + CCT condition compared to the active tDCS + CCT group -CCT reduced brooding (no differential effects of tDCS) -The greater the improvement in working memory functioning throughout training, the larger the decrease in brooding
Wanmaker, Geraerts, & Franken (2015)	Patients with clinical anxiety	Neutral (letters & locations,	Adaptive Dual n-back task + Symmetry span (CCT, *n* = 36)	Cognitive transfer: -Beneficial effects of CCT on inhibition (Reading Span)	

	and/or MDD (*n* = 75)	geometrical shapes)	vs. 0-back task + Non-adaptive Symmetry span (*n* = 39)* [24 sessions, 4 weeks] *91% of patients have been in therapy and/or are currently in another form of therapy	-No differential effects on shifting (IST) and training incongruent effects on updating (backwards Digit Span) No differential effects on rumination or its subtypes brooding and reflection (RRS), trait and state anxiety (STAI), or depressive symptomatology (BDI-II) No effects at 2-months follow-up

Note: Studies have been selected based on (a) inclusion of a CCT procedure, and (b) the sample characteristics (MDD patients). Additional within-group effects are only reported in case of absence of reported between-group analyses, when they provide additional information relating to effects of CCT on depressive outcomes. In case all comparison groups contain the same CCT procedure (e.g., when the between-group manipulation is tDCS), effects are reported in this table on within-CCT group level instead of at between-group level.

Supplemental Table 3. Overview of effects of CCT in RMD samples

Study	**Sample**	**Stimulus material**	**Training conditions [amount of training sessions, training period]**	**Training effects**	**Within-group effects**
Hoorelbeke & Koster (2017) [Protocol: Hoorelbeke, Faelens, Behiels, & Koster, 2015]	Remitted depressed patients (*n* = 68)	Neutral (numbers)	Adaptive PASAT (CCT, *n* = 34) vs. low cognitive load / attention training (*n* = 34) [10 sessions, 2 weeks] *Completers-only analysis at 3-months follow-up is based on *n* = 57 (CCT: *n* = 28, control: *n* = 29)	Cognitive transfer: -Beneficial effects on cognitive task performance (non-adaptive PASAT) immediately following training and at 3-months follow-up -Completers show a tendency to report reduced cognitive complaints Beneficial effects on brooding (RRS) and depressive symptomatology (BDI-II) immediately following training and at 3-months follow-up Beneficial effects on general maladaptive emotion regulation (CERQ), residual symptomatology (RDQ). Completers reported increased functioning in daily life at 3-months follow-up (WHODAS 2.0) No beneficial effects were found for adaptive emotion regulation (CERQ) and quality of life (QLDS)	-Over all participants, the effect of gains in cognitive control on depressive symptomatology (BDI-II) at follow-up, were partially mediated by immediate training effects on brooding (post-training; RRS), while controlling for baseline depressive symptomatology and brooding

Note: Studies have been selected based on (a) inclusion of a CCT procedure, and (b) the sample characteristics (RMD patients).

CHAPTER 3

THE INFLUENCE OF COGNITIVE CONTROL TRAINING ON STRESS REACTIVITY AND RUMINATION IN RESPONSE TO A LAB STRESSOR AND NATURALISTIC STRESS[1]

ABSTRACT

Cognitive control impairments have been identified as an underlying mechanism for rumination, a key predictor of depression. Literature suggests that cognitive control training (CCT) targeting working memory functioning can increase effectiveness of existing antidepressant treatments to reduce rumination. However, it remains unclear whether CCT can also be implemented as a preventive intervention for depression, increasing resilience. For this purpose, at-risk undergraduate students (high trait ruminators) were allocated to a CCT or active control condition, consisting of 10 online training sessions. Working memory functioning was assessed preceding and following the training and reactivity to a lab stressor was assessed directly following training. Finally, at four weeks follow-up, brooding – the maladaptive form of rumination – was re-assessed in response to a naturalistic stressor (examination period). Although we did not find direct transfer effects of CCT on working memory functioning, increase in working memory functioning following CCT was related to post-training brooding and resilience levels. Moreover, participants receiving CCT demonstrated lower stress reactivity in the lab and a decrease in brooding following a naturalistic stressor at follow-up, indicating temporal stability of our findings. These findings suggest that CCT can be considered a promising preventive intervention to reduce stress reactivity and rumination.

[1] Based on Hoorelbeke, K., Koster, E.H.W., Vanderhasselt, M-A., Callewaert, S., & Demeyer, I. (2015). The influence of cognitive control training on stress reactivity and rumination in response to a lab stressor and naturalistic stress. *Behaviour Research and Therapy, 69*, 1-10. doi: 10.1016/j.brat.2015.03.010

Depression is an important mental health problem (Kessler & Wang, 2009; WHO, 2012), associated with major individual suffering and high societal costs (IsHak et al., 2013; Luppa, Heinrich, Angermeyer, Konig, & Riedel-Heller, 2007). Current treatments of depression show rather limited success concerning effect size and long-term outcome (for a review, see Cuijpers, Andersson, Donker, & van Straten, 2011). This suggests that these interventions fail to influence key depressogenic mechanisms. Hence, identifying and changing such mechanisms is a major challenge for depression research.

Rumination – a maladaptive emotion regulation strategy that is characterized by the tendency to respond to a stressful event with repetitive, perseverative, and negative thinking – has been identified as an important risk factor for depression, influencing the course of a current episode as well as predicting future depressive episodes (Nolen-Hoeksema & Morrow, 1991; Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). Moreover, rumination shows relative stability when taking into account changes in depressive symptomatology (Nolen-Hoeksema et al., 2008). In particular brooding – the depressive subtype of rumination that is characterized by a passive style of moody pondering, self-blame and criticism (Treynor, Gonzalez, & Nolen-Hoeksema, 2003) – has been linked to negative information processing biases (Joormann, Dkane, & Gotlib, 2006) and future depressive symptomatology (Treynor et al., 2003). Furthermore, brooding has shown to moderate the relation between stress and depressive symptomatology (Cox, Funasaki, Smith, & Mezulis, 2012).

Accordingly, several researchers have argued that targeting rumination and stress reactivity in therapy could be an important strategy to prevent the (re-)occurrence of depressive episodes as well as enhance treatment (e.g., van Vugt, Hitchcock, Shahar, & Britton, 2012; Watkins et al., 2011). In the current study, we sought to examine whether training cognitive control, a key mechanism implied in rumination, can be beneficial to reduce stress reactivity, rumination, and brooding in particular in an at-risk sample characterized by high rumination scores. We start by considering the relationship between cognitive control, rumination, and depression.

Cross-sectional (Davis & Nolen-Hoeksema, 2000; Joormann, 2006; Joormann & Gotlib, 2010) as well as prospective studies (Connolly et al., 2014; Demeyer, De Lissnyder, Koster, & De Raedt, 2012; Zetsche & Joormann, 2011) have consistently linked rumination to impaired cognitive control (for a review, see Joormann & D'Avanzato, 2010).[2] Importantly, cognitive control impairments have been identified in at-risk (Owens, Koster, & Derakshan, 2012), currently depressed (De Lissnyder, Koster, Everaert, et al., 2012), and remitted depressed populations (Vanderhasselt & De Raedt, 2009), and predict higher levels of rumination and depressive symptoms in response to stress (De Lissnyder, Koster, Goubert, et al., 2012; Zetsche & Joormann, 2011). Moreover, it has been suggested that cognitive control impairments reflect increased biological vulnerability to depression (i.e., hypofrontality), which through rumination and its detrimental effects (e.g., sustained negative mood) is thought to further increase cognitive *and* biological vulnerability for recurrent depression (for a conceptual framework on the relation between cognitive control impairments and increasing biological and cognitive vulnerability in recurrent depression, see De Raedt & Koster, 2010).

To examine whether cognitive control plays a causal role in depression vulnerability, experimental designs manipulating cognitive control and examining subsequent effects on stress reactivity and rumination are of crucial importance. In recent years, important progress has been made in this area, using modified working memory training tasks such as the adaptive Paced Auditory Serial Addition Task (PASAT; e.g., Siegle, Ghinassi, & Thase, 2007) to train cognitive control. During the adaptive PASAT, participants are presented with a stream of auditory presented digits and are instructed to indicate the sum of the last two digits, which relies on continuously updating working memory. Depending on the accuracy of the responses, the inter

[2] 'Cognitive control' refers to the broad definition of the concept under which different executive functions are situated, including shifting, inhibition, and information updating in working memory (Collette et al., 2005; Miyake et al., 2000). Several researchers (Joormann & Quinn, 2014; Siegle et al., 2007) have argued that training cognitive control to improve working memory (CCT) could be of interest for treating the neurobiological and cognitive impairments underlying depression. Therefore, we focus on modified working memory training tasks.

stimulus interval (ISI) would decrease or increase, modifying task difficulty. Siegle et al. (2007) demonstrated the added value of combining cognitive control training (CCT) with treatment as usual (TAU), which led to a greater reduction in rumination and depressive symptomatology compared to a TAU control group. These findings have recently been replicated and extended, showing a reduced need for outpatient services one year following the combined intervention (Siegle et al., 2014). Importantly, Siegle et al. (2014) argue that changes in depressive symptomatology are secondary to changes in rumination.

These findings suggest a causal role of cognitive control in depressive rumination and demonstrate an added value of combining CCT with regular treatment (e.g., Siegle et al., 2014). However, until now it remains unclear whether working memory based CCT can also be implemented for *preventive purposes*. Rumination forms an important predictor for depression, and at-risk populations – characterized by heightened levels of rumination – might benefit from CCT given that cognitive control impairments predict higher levels of rumination in response to stress (De Lissnyder, Koster, Goubert, et al., 2012; Zetsche & Joormann, 2011). Moreover, rumination is known to mediate the relation between stressful events and depressive symptomatology (Michl, McLaughlin, Shepherd, & Nolen-Hoeksema, 2013). Training cognitive control thus holds the potential to improve emotion regulation in the wake of stress as increased cognitive control might reduce the extent to which subjects respond to a stressful event with rumination, increasing resilience to depression. This would fit the recent plea to invest in preventive programs and innovative treatment delivery methods to increase the quality of mental health care in order to reduce the burden of mental illness (Kazdin & Blase, 2011). Hence, a main goal of this study is to explore whether CCT can be used to increase stress resilience in an at-risk population.

Furthermore, there are still a number of remaining questions about clinically oriented CCT studies using the adaptive PASAT. First, in above mentioned studies (Siegle et al., 2007; Siegle et al., 2014), CCT consisted of the adaptive PASAT *as well as* the Wells' attention training, during which participants are instructed to focus on auditory stimuli (Wells, 2000). Therefore, it was not clear to what extent observed improvements in cognitive control are due to the PASAT training. However, since

performance on the PASAT has been related to DLPFC activity (Lazeron, Rombouts, de Sonneville, Barkhof, & Scheltens, 2003) and pilot work indicates that stimulating the left DLPFC can increase therapeutic effects of CCT (Segrave, Arnold, Hoy, & Fitzgerald, 2014; but see Brunoni et al., 2014), it is plausible that an important part of the therapeutic effects reported in previous CCT studies can be attributed to the adaptive PASAT component. Moreover, Brunoni et al. (2014) have recently provided evidence for the effectiveness of the adaptive PASAT in absence of the Wells' attention training in reducing depressive symptomatology in a clinical sample. Given these findings, we will only use the adaptive PASAT as CCT.

Second, while previous CCT studies have compared training effects with a passive control group, the lack of an active control group with regard to the computerized training does not allow to rule out placebo effects. Related to the latter point, Calkins, McMorran, Siegle, and Otto (2015) demonstrated the potential of the combined CCT in reducing depressive symptomatology compared to an adaptive version of the Peripheral Vision task. Other researchers have proposed to use the adaptive Visual Search task as an active control group in working memory training studies (Harrison et al., 2013; Redick et al., 2013). During this visual search training (VST), participants respond to the orientation of a target letter in the presence of distractors. Task difficulty is modified based on individual performance levels. The adaptive component allows researchers to control for effects of performing a computerized training (Shipstead, Redick, & Engle, 2012) without the task being related to working memory functioning (Kane, Poole, Tuholski, & Engle, 2006; Redick et al., 2013). Furthermore, in contrast to tasks used in previous CCT studies (Calkins, Deveney, Weitzman, Hearon, & Siegle, 2011; Calkins et al., 2015), the VST allows researchers to check whether training progress was made in both conditions leaving only the specific content (i.e., whether or not targeting working memory) as the experimental manipulation. Given that this approach allows a more clear interpretation of training effects (Harrison et al., 2013; Redick et al., 2013; Shipstead et al., 2012), we used the VST as an active control group.

Current Study

Cognitive training focusing on remediating cognitive control impairments shows potential as an intervention for depression given that previous studies have demonstrated that impaired cognitive control increases the chance of deploying rumination in response to stressful events. This is important, as rumination – and more specifically, brooding – have shown to predict the occurrence of future depressive symptomatology. The current study examined whether working memory based CCT can heighten resilience to stress and reduce rumination in the wake of stress. Undergraduate students showing a tendency to ruminate were followed over time as they approached their examination period. Participants were randomly allocated to a CCT or VST condition, the latter being the active control group (Time 1). To determine the effectiveness of CCT in increasing resilience towards depression, we measured stress reactivity in the lab (i.e., positive and negative affect, and state rumination) directly following two weeks of training (Time 2), as well as brooding levels in confrontation with a naturalistic stressor (examinations) four weeks following training (Time 3).

As a manipulation check, we hypothesize that – although both groups will show progress throughout the training sessions – transfer effects of training on working memory will only occur in the CCT group (Hypothesis 1). Related to the increase in cognitive control, as operationalized by working memory performance, we expected participants from the CCT group to be more resilient when confronted with a stressful event in a highly controlled lab context. Specifically, we expected to find smaller effects of the stress-induction procedure on ratings of mood and on a behavioral measure of state rumination (content and intensity of momentary thought intrusions) in the CCT group (Hypothesis 2). Furthermore, we expected to find the CCT to increase resilience when confronted with a naturalistic stressor: we expected participants from the CCT condition to report lower levels of brooding compared to the active control group while participants are confronted with an ecological valid stressor (examinations; Hypothesis 3).

METHOD

Participants

Based on an online pre-screening of undergraduate-students of Ghent University, participants showing heightened trait rumination levels (above percentile 70) were invited. This was operationalized by a Ruminative Response Scale-score ≥ 43 (RRS; Nolen-Hoeksema & Morrow, 1991). 53 participants responded to the invitation (27%), completed the baseline assessment and were randomly assigned to a CCT or VST. Due to individual technological problems (e.g., using incompatible operating systems, experiencing problems with unpacking, installing or running the program) four participants dropped out during the training period. 49 participants completed the post-training assessment session, from which one participant was excluded from data-analysis due to not having performed the training sessions as instructed (as shown by an accuracy rate < 10% on the last two sessions; see Table 1 for mean accuracy rates), and one participant due to not having delivered the training data. Results concerning effects of CCT on working memory functioning and emotional reactivity to the lab stressor are based on the remaining 47 participants (CCT group: *n* = 25; VST group: *n* = 22). Finally, another 4 participants were excluded due to not responding to the follow-up assessment call within the time limit and 6 due to not having started the examination period at follow-up. This brings us to a sample size of 37 for the follow-up results (CCT group: *n* = 20; VST group: *n* = 17). Participants were reimbursed for participating (€40). This study was approved by the local ethical committee of Ghent University and all participants provided written informed consent.

Table 1

Training session accuracy rates as a function of training condition

	Training condition			
	Cognitive control (*n* = 25)		Visual search (*n* = 22)	
	M % correct	*SD*	*M % correct*	*SD*
Session 1	54.51	2.66	71.97	6.52
Session 2	56.47	2.09	72.73	5.66
Session 3	56.72	2.22	70.93	6.37
Session 4	56.98	2.53	72.97	5.68
Session 5	57.35	2.25	73.39	5.41
Session 6	57.91	2.88	74.04	4.84
Session 7	58.18	1.99	74.01	5.87
Session 8	57.93	2.21	74.50	4.31
Session 9	58.40	2.34	73.74	5.27
Session 10	58.41	2.74	73.30	6.29

Apparatus and Material

The Automated O-Span task (Turner & Engle, 1989; Unsworth, Heitz, Schrock, & Engle, 2005) and adaptive PASAT task were programmed and run using the INQUISIT Millisecond software package. The VST and Breathing Focus task (Borkovec, Robinson, Pruzinsky, & Depree, 1983) were run on E-Prime 2.0. Tasks were run on a Dell Dimension 4600 computer with a 72 Hz, 17-inch color monitor.

Questionnaires. *Depressive symptomatology* was assessed using the Beck Depression Inventory (BDI-II-NL; Beck, Steer, & Brown, 1996; Van der Does, 2002). This 21-item self-report measure has proven to have good psychometric properties. Second, a short version of the Mood and Anxiety Symptom Questionnaire (MASQ-D30; Clark & Watson, 1991; Wardenaar et al., 2010) was used as a transdiagnostic measure for *depressive and anxious symptomatology*. This validated questionnaire is based on the Tripartite model of anxiety and depression (Clark & Watson, 1991), containing three subscales: general distress, anhedonic depression, and anxious arousal.

The tendency to respond to a stressor with *rumination* was assessed using the Ruminative Response Scale (RRS-NL-EXT; Nolen-Hoeksema & Morrow, 1991; Treynor et al., 2003). In addition to a rumination total score, the RRS-NL-EXT provides a Brooding and a Reflection subscale, of which Brooding is viewed as the most maladaptive form of

rumination (Joormann et al., 2006; Treynor et al., 2003). The Penn State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990; van Rijsoort, Vervaeke, & Emmelkamp, 1997) was used to measure *worrying*. Both measures exhibit adequate psychometric properties (Treynor et al., 2003; van Rijsoort, Emmelkamp, & Vervaeke, 1999).

We used the Positive and Negative Affect Schedule (PANAS; Engelen, De Peuter, Victoir, Van Diest, & Van den Bergh, 2006; Watson, Clark, & Tellegen, 1988) to assess *positive and negative affective states*, comprising 10 items each. Self-reported *attentional control* was measured using the 20-item Attentional Control Scale (ACS-NL; Derryberry & Reed, 2002; Verwoerd, Cieraad, & de Jong, 2007). The ACS shows adequate psychometric properties (Judah, Grant, Mills, & Lechner, 2014). Finally, the 25-item Dutch Resilience Scale (RS-NL; Portzky, 2008; Wagnild & Young, 1993) was used to take into account self-reported levels of *resilience*. All questionnaires were administered at Time 1 and Time 2. For the follow-up assessment (Time 3), all questionnaires but the BDI-II-NL were presented online.

Training tasks.

Cognitive control training (CCT) task. We used a modified version of the PASAT (Gronwall, 1977; Siegle et al., 2007) to train cognitive control. Participants were presented with series of auditory digits and were asked to continuously respond to the sum of the last two digits by clicking on the corresponding number. All possible responses (1 – 18) were continuously presented on the screen throughout the course of the training task. Task difficulty was modified within the task depending on the participants' performance. Each session of the adaptive PASAT started with an inter stimulus interval (ISI) of 3000 ms. Every four consecutive accurate responses, the ISI decreased with 100 ms, increasing task difficulty. Vice versa, four consecutive inaccurate responses were followed by an increase in the ISI of 100 ms. Each session participants completed 400 trials of this task uninterrupted, after having completed 5 practice trials during which feedback was presented. This corresponds to 20 min of training on an average ISI of 3000 ms. Median ISI per session will be used as an indicator of task performance and the altering ISI was visible for the participant during the

training. Moreover, participants are provided with an online representation of the current amount of consecutive (in)correct responses.

Visual search training (VST) task. The VST (Harrison et al., 2013; Redick et al., 2013) was used as an active control group. During the VST task, participants were presented with an array of letters, existing of one target letter (letter "F", presented as a standard "F" or mirror-reversed "F") and a variable amount of distractors depending on the array size (letters "E", mirror-reversed "E", and/or inverted "T"). Following a fixation dot in the center of the screen, the array was presented for 500 ms, followed by presentation of a mask during 2500 ms (a 16 x 16 array of black squares). Participants had to indicate the orientation of the target letter by pressing "w" or ";" (on an AZERTY keyboard) using their left or right index finger respectively. Each training session started from difficulty level one with a 2 x 2 array (1 target and 3 distractors). Task difficulty was modified based on performance of the participant at block level. Each block consisted out of 24 trials, participants were subjected to 10 blocks (20 min) per training session. Following each block, participants received feedback on their performance. They were aware that a within-block accuracy rate of ≥ 87.5% led to an increase in the amount of distractors for the following block, while an accuracy rate of ≤ 75% was followed by a decrease. Depending on task difficulty level, distractors were homogeneous (odd-numbered levels) or heterogeneous (even-numbered levels). In line with previous studies, mean difficulty levels were used.

In both conditions, participants were not informed about the purpose of the cognitive training.

Transfer Tasks.

Operation-span task (O-Span). Cognitive control was operationalized as 'working memory functioning', which was assessed using the Automated O-Span task (Turner & Engle, 1989; Unsworth et al., 2005) preceding and following training. The Automated O-Span task is a complex working memory span task. During this task, participants are sequentially presented with mathematical problems and letters (F, H, J, K, L, N, P, Q, R, S, T, or Y). Each trial started with the presentation of a math problem that needed to be solved as fast and accurately as possible, after which participants

were presented with a possible solution and had to report whether this was correct. Each math problem was followed by the presentation of a letter that remained on screen for 800 ms. After a variable amount of sequentially presented math problems and letters (3 – 7), participants had to identify the recalled letters in correct order on a 4 x 3 matrix. The task started with a practice phase focusing on the recall of series of letters (two trials of two letters), followed by a practice phase during which 15 math problems were presented (e.g., "(7 x 3) – 3 = ?"). During the latter phase, participants' reaction times were administered. Based on performance during this phase, a time limit was calculated (mean RT math problems practice phase plus 2.5 SDs) which restricted future presentation duration of math problems. In a third practice phase, both tasks were combined in three series, each containing two math problems and two letters. During the test phase participants were presented with 75 math problems and letters, divided over 15 series. Participants were instructed to keep accuracy rates above 85% while solving the math problems as fast as possible in order to prevent participants from mentally rehearsing the letters. An O-Span score was generated, comprising the sum of recalled letters of accurate series.

Stress induction.

Induction task. We used a validated procedure to induce stress in the lab (Rossi & Pourtois, 2012) and modified the cover story so that it would fit the context of our study. Importantly, a written script was used to standardize the induction procedure. Participants were led to believe that the training sessions aimed to increase sustained attention and that they should be able to perform the following sustained attention task above average. Moreover, they were told that they participated in a replication study and that their performance would be compared to the performance of 42 undergraduate students from an American university. To increase social pressure, participants were led to believe that results would be presented at an important upcoming international conference and that they are expected to perform well in order to make such a presentation possible. Following instructions, participants were subjected to a visual oddball task in which tilted lines were presented during 250 ms each. The task started with a learning phase during which participants became familiar with the standard line (35°). Next, participants were instructed to mentally count the

amount of times a divergent line was presented (target). Participants completed three blocks of 100 stimuli, each containing 20 target lines. The difference between the standard line and the target lines increased over blocks, from 3° during the first block, to 5° during the second, and 10° during the third block. Stimuli were presented with an ISI ranging from 1150 ms to 1500 ms. On 50 of the 100 trials, horizontal peripheral distractors were presented during 250 ms. At the end of each block, participants had to enter the amount of targets that were presented, followed by false feedback on their performance. Feedback consisted out of a neutral face and a 'personalized' text balloon stating the participants' performance was poor, scoring beneath the average of the norm group. This was accompanied by a scatterplot, illustrating the poor performance compared to the norm group. As task difficulty decreased, their relative performance did not increase, inducing stress (Nummenmaa & Niemi, 2004).

Induction assessment. In line with Rossi and Pourtois (2012), seven visual analogue scales (VAS) were adopted from the Profile Of Mood States (McNair, Lorr, & Dropplemann, 1992) to assess effects of the stress induction on mood. Three scales provided a mean estimate of positive affect (Dutch equivalents of 'energetic', 'satisfied', and 'happy'), another three scales provided a mean estimate of negative affect (Dutch equivalents of 'angry', 'tense', and 'depressed'). One scale provided an estimate of fatigue. As a manipulation check, one item assessed the extent to which participants attributed task outcome internally, while another item assessed the extent to which performance was influenced by task difficulty. All VASs were presented horizontally, 10 cm long with scores ranging from 0 to 100.

A modified version of the Breathing Focus task (Borkovec et al., 1983; Hirsch, Hayes, & Mathews, 2009; Ruscio & Borkovec, 2004) was used as a behavioral measure to study the effects of the induction procedure on thought processes (positive and negative thought intrusions). During the Breathing Focus task, participants were asked to focus attention on their respiration during five minutes. Every 20 or 40 sec a tone was presented (10 times), after which participants had to indicate whether at the time of the tone they were (a) completely focused on their respiration, (b) distracted by positive thoughts, (c) distracted by negative thoughts, (d) distracted by neutral thoughts, or (e) their state did not fit the other options. In the latter case, participants

had to write down a brief description of the state before pressing the 'e'-key on the keyboard. In all other cases, participants responded with the corresponding letter ('a', 'b', 'c', or 'd'), after which they were asked to focus on their respiration again (presented during 2000 ms) and a new trial started. Both the VASs and the Breathing Focus task were administered twice: once preceding the induction procedure and once directly following the induction procedure.

Procedure

The study comprised of two assessment sessions in sound attenuated booths at the faculty of Psychology and Educational Sciences of Ghent University (Time 1, Time 2), 10 online homework sessions, and an online follow-up assessment during the examination period, four weeks following training (Time 3; see Figure 1).

At Time 1, participants filled out the questionnaires after having read and agreed to the informed consent. This was followed by the Automated O-Span task and an explanation on how to install and perform the training tasks at home. Participants were randomly assigned to the CCT or the VST condition. A written manual was provided, including the necessary software and their subject number. Participants were instructed to complete 10 training sessions over a period of 14 days, preferentially only performing one session a day. During the training period, participants could contact the researchers for technical support. Participants were asked to provide us with the data at least the evening before Time 2 and were reminded of their appointment by e-mail.

Fourteen days following Time 1, participants returned to the faculty where they filled out the questionnaires and were subjected to a post-training assessment of cognitive control, using the Automated O-Span task. Following this phase, participants entered the stress induction procedure, in which they were subjected to the pre-induction Breathing Focus task, followed by the VASs, the cover story and the stress induction task. This was followed by a post-induction assessment of mood, using the VASs, and the post-induction Breathing Focus task. The second lab session ended with giving a (partial) debriefing on the stress induction procedure, instructions concerning the follow-up assessment, and payment of €40.

At four weeks follow-up – during the first or second week of the examination period – participants were invited to fill out the online questionnaires within 48 h (Time 3). Simultaneously participants replied to whether they had already entered the examination period (i.e., had completed at least one exam) and provided us with the amount of days that had passed since their most recent exam by selecting the corresponding date. This indicator of elapsed time between naturalistic stressor and follow-up assessment will be taken into account when analyzing training effects on brooding. After having completed the online questionnaires, participants received a written debriefing and were provided the chance to discuss the study.

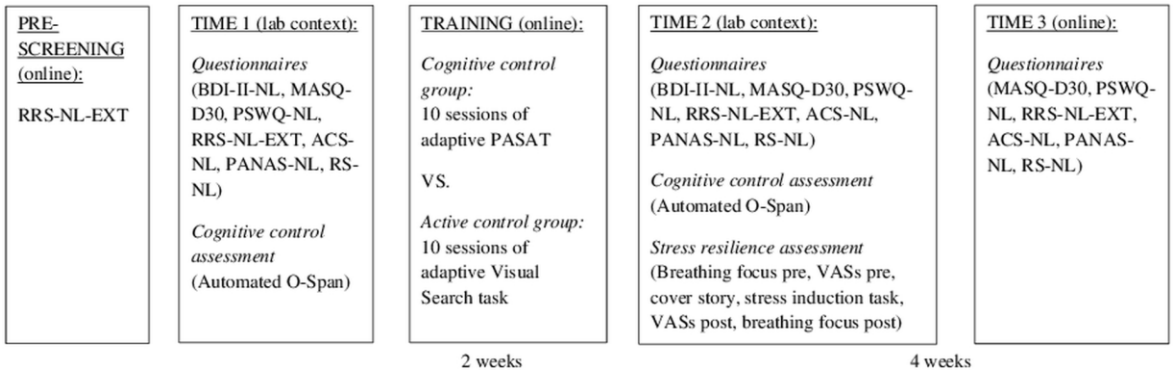


Figure 1. Procedure

RESULTS

Group Characteristics

Participants were randomly divided into a CCT (n = 25) or VST (n = 22) condition. Descriptive information for both groups can be found in Table 2. Both groups did not differ significantly at baseline concerning the self-report measures (all ts < 1.07).[3] An independent samples t-test revealed that the CCT group (M = 20.84; SD = 2.27) did not

[3] Excluding dysphoric participants based on their baseline BDI-scores (BDI ≥ 14) did not change the direction of any of the reported interaction effects. The beneficial effects of CCT on stress reactivity (in response to a lab stressor, using VAS mood ratings and a behavioral measure for state rumination) or brooding in response to a naturalistic stressor remained significant (except for the Time x Group interaction for amount of self-reported negative thoughts, that turned marginally significant given the smaller sample size).

Table 2

Group characteristics as a function of training condition

	Training condition			
	Cognitive control (*n* = 25)		Visual search (*n* = 22)	
	Time 1 *M (SD)*	Time 2 *M (SD)*	Time 1 *M (SD)*	Time 2 *M (SD)*
Depressive symptomatology	12.92 (9.73)	12.12 (11.33)	10.86 (7.75)	9.41 (7.84)
General distress	24.28 (10.13)	23.76 (9.84)	21.64 (7.38)	19.59 (6.36)
Anhedonic depression	33.16 (8.61)	33.68 (9.16)	32.09 (8.65)	31.23 (7.43)
Anxious arousal	16.24 (6.02)	16.60 (7.25)	16.36 (4.82)	13.86 (4.21)
Worrying	57.16 (13.18)	55.12 (14.36)	58.55 (8.85)	56.00 (7.88)
Trait rumination	51.84 (10.20)	48.88 (11.27)	53.32 (8.89)	50.95 (9.88)
Brooding	12.88 (3.77)	11.76 (3.90)	13.14 (2.88)	12.55 (2.87)
Reflection	11.60 (3.70)	10.96 (3.78)	10.55 (2.99)	9.73 (3.47)
Attentional control	47.52 (9.44)	47.36 (9.05)	47.27 (6.78)	46.64 (7.01)
Positive affect	28.64 (7.17)	28.24 (8.29)	28.64 (6.44)	27.27 (6.09)
Negative affect	16.60 (5.09)	17.48 (7.56)	15.68 (5.29)	13.95 (3.39)
Resilience	70.92 (9.60)	71.68 (9.83)	72.27 (7.54)	72.18 (7.71)

Note: Independent *t*-tests indicate that both groups did not significantly differ at T1 or T2, except for T2 momentary negative affect ($t(34.18) = 2.11$, $p < .05$).

differ from the VST group (*M* = 20.45; *SD* = 1.97) concerning age, *t*(45) = 0.62, *p* = .54. The training groups differed significantly concerning gender distribution: the VST group contained four male participants whereas there were no male participants in the CCT group, $\chi^2(1, n = 47) = 4.97$, $p < .05$.

Progress on Training Tasks

In line with previous studies, median ISI levels were used to check progress on the PASAT, while mean difficulty levels were used in the VST condition. While an increase in difficulty level is indicative for progress in the VST condition, a decrease in median ISI is indicative for progress in the CCT condition. We used two Repeated Measures ANOVA's to examine the effect of Time (10 sessions) on task performance. For the CCT group, we found a significant main effect of Time (10 sessions) on median ISI, $F(9, 16) = 81.54$, $p < .001$, $\eta_p^2 = .98$. The main effect of Time was also significant in the VST group, $F(9, 13) = 7.56$, $p < .01$, $\eta_p^2 = .84$. Both training groups improved with practice (see Figure 2A and B).

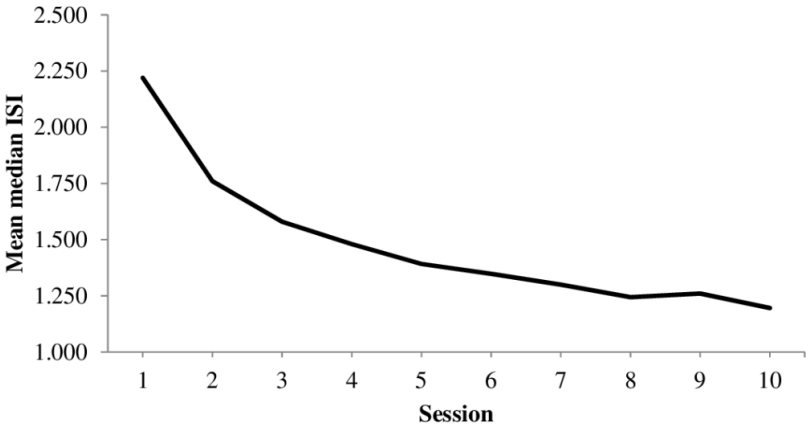


Figure 2A. Cognitive control training progress

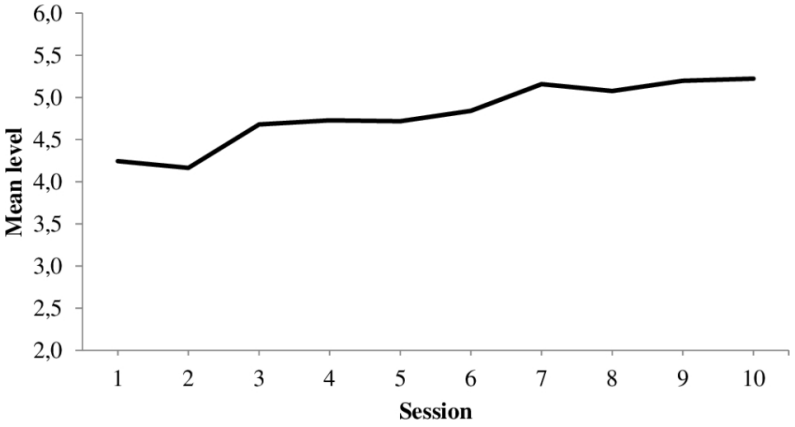


Figure 2B. Visual search training progress

Effects of Training

Working memory. A 2 (Time: Baseline vs. Post-training) x 2 (Group: CCT vs. VST) Mixed ANOVA was used to examine transfer effects of training to O-Span performance, an indicator for working memory functioning and cognitive control (Hypothesis 1). This revealed a significant main effect of Time, $F(1, 45) = 19.66$, $p < .001$, $\eta_p^2 = .30$. This is indicative for a general increase in working memory performance (Pre: $M = 44.66$, $SD = 15.40$; Post: $M = 53.43$, $SD = 15.29$). We did not find a significant Time x Group interaction, $F(1, 45) = 0.51$, $p = .48$, $\eta_p^2 = .01$, or a main effect of Group ($F < 0.33$).

In order to ensure whether any observed changes in stress reactivity and rumination were associated with changes in cognitive control, we have used regression analyses to assess effects of change in working memory functioning (Δ O-Span score = O-Span post – O-Span pre; a positive value is indicative for an increase in working memory functioning) on post-training emotional outcomes (self-report measures) while controlling for baseline scores. Interestingly, for participants of the CCT group, increase in working memory functioning was a significant predictor for post-training brooding ($\beta = -.23$, $t(22) = 2.41$, $p < .05$) while controlling for baseline levels of brooding ($\beta = .81$, $t(22) = 8.63$, $p < .001$). Similarly, while controlling for baseline resilience ($\beta = .88$, $t(22) = 11.81$, $p < .001$), increase in working memory functioning predicted increased resilience following training ($\beta = .21$, $t(22) = 2.77$, $p < .05$; all other ts < 1.22). Importantly, increase

in working memory performance was *not* related to any of the post-training self-report measures while controlling for baseline functioning in the VST group (all *t*s < 0.82).[4]

Stress resilience in lab context. To check for effects of CCT on stress resilience in a lab context (Hypothesis 2), we used 2 (Time: Pre- vs. Post stress induction) x 2 (Group: CCT vs. VST) Mixed ANOVA's with state rumination (Breathing Focus Task) or VAS mood ratings as dependent variables.

Breathing focus task. For the behavioral measure of state rumination / content of thought intrusions, a main effect of Time indicated that participants from both training groups reported being less focused on their respiration following the stress induction procedure, $F(1, 45) = 9.67$, $p < .01$, $\eta_p^2 = .18$ (Pre: $M = 5.17$, $SD = 2.19$; Post: $M = 4.47$, $SD = 2.46$; all other Fs < 1.80). Concerning the amount of positive thoughts that were reported, we found a significant Time x Group interaction ($F(1, 45) = 5.99$, $p < .05$, $\eta_p^2 = .12$; all other Fs < 2.15). Follow-up paired samples *t*-tests revealed a drop in positive thoughts following the stress induction for the VST group, $t(21) = 2.82$, $p < .05$, $d = .85$, while the mean amount of positive thoughts remained stable in the CCT group, $t(24) = 0.69$, $p = .50$, $d = .14$ (see Table 3 for descriptives). For negative thoughts, analysis revealed a significant main effect of Time ($F(1, 45) = 23.55$, $p < .001$, $\eta_p^2 = .34$) and a significant Time x Group interaction ($F(1, 45) = 4.74$, $p < .05$, $\eta_p^2 = .10$; main effect of Group: $F < 1.27$). The stress induction led to an increased amount of negative thoughts in the VST ($t(21) = 4.18$, $p < .001$, $d = .97$) and CCT condition ($t(24) = 2.32$, $p < .05$, $d = .42$). However, independent samples *t*-tests revealed that this increase was more pronounced in the VST group: whereas both groups did not differ in levels of reported negative thoughts before undergoing the stress induction procedure ($t(45) = 0.16$, $p = .87$), we found a trend towards significance following the stress induction ($t(45) = 1.73$, $p = .09$). Finally, the induction procedure did not affect the amount of reported neutral thoughts, however, overall participants of the CCT group reported

[4] Using an alternative approach, correlating Δ O-Span scores with Δ self-reported brooding- and resilience scores provided similar findings (resilience: $r = .47$, $p < .05$; brooding: $r = .37$, $p = .069$), although the effect of brooding became marginally significant.

experiencing more neutral thoughts (CCT: *M* = 2.42, *SD* = 1.57; VST: *M* = 1.52, *SD* = 1.43), main effect of Group, $F(1, 45) = 4.13$, $p < .05$, $\eta_p^2 = .08$ (all other *F*s < 0.39).

Table 3

Effects of stress induction as a function of time and training condition

	Cognitive control (*n* = 25)				Visual search (*n* = 22)			
	Pre		*Post*		*Pre*		*Post*	
	M	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
BFT								
Focused	4.76	1.92	4.08	2.47	5.64	2.42	4.91	2.43
Positive thoughts	1.44	1.39	1.68	1.99	1.59	1.22	.64	1.00
Negative thoughts	1.24	1.23	1.88	1.79	1.18	1.22	2.86	2.12
Neutral thoughts	2.52	1.66	2.32	1.75	1.50	1.50	1.55	1.68
Other reactions	0.04	0.20	0.04	0.20	0.09	0.29	0.05	0.21
VAS								
Positive affect	54.19	18.01	38.97	14.40	51.88	15.88	31.61	17.77
Negative affect	20.07	16.25	22.11	16.90	16.33	13.64	29.85	19.03

Note: BFT = Breathing Focus Task, VAS = Visual Analogue Scales.

Visual analogue scales. Using the VAS, participants reported experiencing a general decrease in positive affect following the induction procedure (Pre: *M* = 53.11, *SD* = 16.91; Post: *M* = 35.53, *SD* = 16.32), $F(1, 45) = 112.16$, $p < .001$, $\eta_p^2 = .71$ (all other *F*s < 2.29). For negative affect we also found a main effect of Time, $F(1, 45) = 13.69$, $p < .01$, $\eta_p^2 = .23$. Importantly, we found a significant Time x Group interaction, $F(1, 45) = 7.45$, $p < .01$, $\eta_p^2 = .14$ (main effect of Group: $F < 0.21$). Whereas the VST group was characterized by an increase in negative affect ($t(21) = 3.46$, $p < .01$, $d = .82$), we did not observe this change in the CCT group ($t(24) = 1.06$, $p = .30$, $d = .12$; see Table 3).

In general, an increase in experienced task difficulty was reported using VAS ($F(1, 45) = 10.55$, $p < .01$, $\eta_p^2 = .19$; Pre: *M* = 43.40, *SD* = 20.86; Post: *M* = 57.23, *SD* = 21.44; all other *F*s < 1.98). The induction procedure did not influence the extent to which participants experienced being in control of task outcome, which served as a manipulation check (all *F*s < 1.28; Pre: *M* = 65.21, *SD* = 21.77; Post: *M* = 60.43, *SD* = 25.37). Neither did the induction procedure influence reported feelings of being numb / tired (all *F*s < 1.41; Pre: *M* = 48.94, *SD* = 22.54; Post: *M* = 46.13, *SD* = 24.35).

Stress resilience in response to naturalistic stress. We used a 2 (Time: Pre-training vs. Follow-up) x 2 (Group: CCT vs. VST) Mixed ANOVA to examine effects of CCT

on stress resilience in a naturalistic context. Stress resilience was operationalized by brooding scores (RRS; dependent variable), the more depressive subtype of rumination (Cox et al., 2012). The following results are based on the subsample which completed the follow-up assessment during the first two weeks of their examination period (CCT group: *n* = 20; VST group: *n* = 17). The amount of days that have passed since the most recent exam, which forms an indicator of elapsed time between stressor and assessment, was added as covariate to control for individual differences in intensity of the stress induction (both groups did not differ in the amount of days that had elapsed since the most recent exam, $t(35) = 1.04$, $p = .306$; $M = 2.51$, $SD = 2.46$). This is important as rumination has proven to show a linear or quadratic decrease as days pass following an exam, with the strongest decrease in rumination occurring during the first two days (Grant & Beck, 2010).

This approach revealed a significant main effect of Time, $F(1, 34) = 12.45$, $p < .01$, $\eta_p^2 = .27$, and a significant Time x Group interaction, $F(1, 34) = 4.27$, $p < .05$, $\eta_p^2 = .11$ (all other Fs < 1.17).[5] Follow-up paired samples *t*-tests indicate that, whereas brooding remained stable in the VST group (based on estimated marginal means; pre: $M = 13.17$, $SE = 0.82$; follow-up: $M = 12.59$, $SE = 0.79$), $t(16) = 1.48$, $p = .16$, the CCT group was characterized by decreased brooding (pre: $M = 13.11$, $SE = 0.76$; post: $M = 11.20$, $SE = 0.73$), $t(19) = 4.12$, $p < .01$. This confirms our third hypothesis, indicating CCT shows potential in reducing brooding after confrontation with a stressor.[6]

When looking at the CCT group ($n = 20$), change in brooding over time (Time 1 – Time 3; positive scores indicate a decrease) was related to stress susceptibility during

[5] Excluding the covariate Time since previous exam – i.e., not taking into account individual differences in confrontation with the naturalistic stressor – reduces the strength of the presented effects of CCT on brooding in response to a naturalistic stressor, resulting in a marginally significant Time x Group interaction, $F(1, 35) = 3.62$, $p = .065$, $\eta_p^2 = .09$ (main effect of Time: $F(1, 35) = 15.62$, $p < .001$, $\eta_p^2 = .31$; main effect of Group: $F(1, 35) = 0.44$, $p = .512$, $\eta_p^2 = .01$).

[6] Other self-report measures than brooding were assessed at baseline to check for baseline group differences and were further added for exploratory reasons. They did not show to be influenced by CCT (interaction effects: all Fs < 1.45). These data are available upon request (see Table 4). However, these findings are beyond the scope of this article and will not be further discussed.

Table 4

Group characteristics as a function of training condition

	Training condition					
	Cognitive control (*n* = 20)			Visual search (*n* = 17)		
	Time 1 *M* (*SD)*	Time 2 *M* (*SD)*	Time 3 *M* (*SD)*	Time 1 *M* (*SD)*	Time 2 *M* (*SD)*	Time 3 *M* (*SD)*
Depressive sympt.	12.60 (9.95)	11.40 (11.34)	/	10.82 (7.73)	9.41 (7.55)	/
General distress	23.60 (9.97)	23.50 (9.74)	24.10 (6.23)	22.41 (6.81)	20.18 (6.42)	24.29 (7.28)
Anhedonic depr.	32.55 (8.05)	33.40 (8.78)	34.90 (6.64)	32.41 (6.84)	31.53 (6.76)	35.29 (5.82)
Anxiety arousal	16.30 (6.04)	16.65 (7.80)	18.45 (6.60)	17.24 (5.12)	14.41 (4.53)	18.00 (6.03)
Worrying	56.30 (14.12)	53.70 (15.35)	55.35 (13.78)	58.18 (9.72)	56.06 (8.66)	56.06 (10.46)
Trait rumination	52.30 (9.91)	48.85 (11.22)	50.05 (10.16)	53.00 (7.34)	52.06 (8.63)	51.24 (8.74)
Brooding	13.10 (3.65)	11.90 (3.88)	11.25 (3.34)	13.18 (2.83)	12.94 (2.75)	12.53 (3.00)
Reflection	12.20 (3.30)	11.10 (3.18)	11.20 (2.95)	10.29 (2.89)	9.76 (3.42)	10.18 (3.68)
Attentional control	47.25 (10.14)	47.55 (9.62)	48.00 (9.27)	48.24 (7.08)	47.41 (7.22)	48.88 (7.56)
Positive affect	28.95 (7.18)	28.40 (8.48)	26.15 (7.47)	28.12 (5.93)	26.35 (5.61)	23.88 (6.25)
Negative affect	16.40 (5.35)	17.30 (8.16)	20.20 (7.66)	16.00 (4.82)	14.12 (3.53)	17.18 (5.34)
Resilience	70.95 (9.84)	71.45 (9.92)	72.25 (8.88)	72.76 (7.45)	72.41 (7.53)	73.82 (7.75)

Note: Independent *t*-tests indicate that both groups did not significantly differ at T1, T2, or T3.

the stress induction procedure in lab context directly following training. Participants that were more susceptible to the stress induction procedure, as shown by reporting less positive thoughts and more neutral thoughts following the induction, showed the tendency to experience a smaller decrease in brooding scores over time (Positive thoughts: r = .41, p = .076; Neutral thoughts: r = -.46, p < .05; all other rs < .30). Moreover, participants reporting more general negative affect following the induction (as assessed by the VAS negative affect compound score), were characterized by the tendency to experience more brooding at follow-up (r = .42, p = .066). This seems to be due to the extent to which participants experienced depressive feelings following the induction procedure (VAS feeling depressed; r = .49, p < .05; all other rs < .29).

DISCUSSION

We set out to examine whether CCT targeting working memory functioning has beneficial effects on stress reactivity and rumination in individuals at-risk for depression. Compared to the active control group, we expected to find that CCT would exert direct effects on working memory functioning, and boost resilience, as operationalized by stress reactivity and rumination in response to a lab stressor directly following two weeks of training and brooding in response to naturalistic stress four weeks following training.

Although both training groups showed an increase in performance on the training task throughout the 10 training sessions, we did not find clear transfer effects of CCT on working memory performance as assessed by the Automated O-Span task. However, participants who showed a higher increase in working memory functioning – which was used as an indicator of increase in cognitive control – reported less ruminative brooding and higher self-reported resilience following training, while controlling for baseline levels of brooding or resilience. Importantly, increase in working memory functioning was *not* related to any of the self-report measures in the active control group. These findings suggest that an increase in working memory functioning in response to training may predict an adaptive response to stressful situations.

The absence of transfer of CCT on working memory functioning as assessed by the Automated O-Span task might be due to several causes. First, the general increase in O-Span scores might reflect a repetition learning effect. Second, since the sample consisted of undergraduate students, ceiling effects might have hampered us from finding bigger transfer effects on working memory functioning in the CCT group. Third, the Automated O-Span task might lack sensitivity in finding transfer effects caused by the CCT. Research using the adaptive PASAT has typically used the non-adaptive PASAT or Digit Sorting task to investigate transfer effects (Siegle et al., 2007; Siegle et al., 2014). Given that these tasks require participants to mentally manipulate the to be remembered content, they might have been a better indicator for close transfer. Perhaps if a more challenging and sensitive transfer task would have been used, a larger increase in working memory functioning would have been observed in the CCT group. Fourth, in combination with the methodological factors described above, the general increase in working memory task performance might also be due to another issue that is directly related to the use of an active control condition in training studies. That is, all cognitive training tasks will influence attentional processes to some extent. Although visual search has previously shown to be unrelated to performance on working memory capacity tasks (Kane et al., 2006), it is likely that daily practice with the VST task trains other cognitive factors (e.g., sustained attention) that can influence performance on cognitive transfer tasks. Accordingly, increased working memory task performance in the CCT and VST group might reflect two *distinctive processes* (e.g., VST: increased sustained attention rather than working memory functioning; CCT: both increased attention processes *and* working memory functioning), from which only actual increase in working memory functioning is related to stress reactivity and brooding. Indeed, the finding that increased working memory task performance only predicted decreased brooding and increased resilience in the CCT group whereas no such relation occurred in the VST group seems to confirm this interpretation. Nonetheless, the lack of clear transfer effects on working memory functioning requires some caution in drawing causal conclusions about the role of working memory in stress reactivity and rumination since we cannot fully exclude the possibility that task characteristics of CCT (unrelated to working memory) differentially influenced stress reactivity and brooding.

Importantly, results indicate that CCT was successful in increasing resilience: confrontation with a lab stressor did not lead to a decrease in positive thoughts in the CCT group in contrast to the active control group, which showed to be more reactive to stress as indicated by a decrease in positive thoughts and a trend towards a stronger increase in negative thoughts. Furthermore, in contrast to participants of the control group, participants of the CCT group did not respond to the induction procedure with an increase in self-reported negative affect. Interestingly, these positive effects of CCT on reactivity to stress in the lab were accompanied by – and predicted – a decrease in brooding at follow-up when confronted with a naturalistic stressor. This suggests that the demonstrated transfer effects of CCT on stress reactivity and emotion regulation reflect increased cognitive control when confronted with a stressful event. During the adaptive PASAT, the demand on working memory is high and even gradually increases, this increased task difficulty is associated with greater emotional reactivity (e.g., frustration, negative thoughts, small amount of negative affect). As a result, cognitive control is trained in an emotional task context (Siegle et al., 2007), which means that the frontolimbic circuits are triggered. Increased cognitive control then might allow subjects to employ more adaptive emotion regulation strategies when confronted with a stressful event, reducing brooding and increasing resilience to depression.

Although our findings confirm the hypothesized relationship between cognitive control, stress reactivity and brooding in response to lab and naturalistic stressors, there is a discrepancy between the immediate effects of CCT on stress reactivity and rumination in response to the lab stressor and self-reported brooding directly following training (Time 2; e.g., Table 2). We propose three factors that might have contributed to these findings. First, given that cognitive control was trained in an emotional / stressful task context (Siegle et al., 2007) we believe that this discrepancy reflects the need to assess ruminative processes in at-risk undergraduate students in the presence of stressors. Second, the relation between cognitive control and emotion regulation is reciprocal and CCT could induce a mutually reinforcing increase in both cognitive control and emotion regulation over time. Third, when analyzing rumination directly following training using retrospective self-report questionnaires, evaluation will be more strongly biased by situations occurring before the training took place or during

first days of training than when including a follow-up assessment or a behavioral measure of rumination.

The current study is the first to show the potential of CCT targeting working memory functioning in increasing resilience towards depression in an at-risk population. CCT showed transfer on emotion regulation in response to a lab stressor and a naturalistic stressor at follow-up. This adds to the ecological validity of our findings and provides evidence for the temporal stability of CCT effects in increasing resilience. Our findings are in line with emerging research focusing on increasing cognitive control over emotional stimuli using other training tasks (Cohen, Mor, & Henik, 2015; Daches & Mor, 2014). Moreover, the current study extends recent findings indicating that CCT forms a promising intervention to reduce brooding as it is the first to demonstrate the effectiveness of the adaptive PASAT in absence of the Wells' attention training, compared to an active control group. In general, our findings show the potential of CCT as a highly accessible preventive intervention for depression.

However, several limitations should be taken into account. The lack of a transparent relation between CCT and increase in working memory performance forms a first limitation of this study. Furthermore, we have only used one indicator of working memory capacity. Second, the single-blind design might have influenced assessment of stress reactivity in the lab. However, a detailed script was used for the induction procedure and our findings were further validated by the decrease in brooding scores when confronted with a naturalistic stressor. Third, we did not assess stress reactivity in the lab at baseline to safeguard credibility of the induction procedure following training. Fourth, experienced difficulty of both training tasks was not assessed, which does not allow to rule out effects of potential group differences in training task difficulty (e.g., habituation to stress) on responses to the stress induction procedure. However, during the stress induction procedure both groups did not differ in experienced task difficulty and experienced control over performance on this task. Fifth, although both groups mainly contained female participants, a gender difference occurred: the control group contained more men (n = 4) than the CCT group (n = 0). As women are more prone to brooding (Johnson & Whisman, 2013), this might have influenced chances of finding beneficial effects of computer training sessions on

brooding in the CCT group compared to the active control group. However, re-analyzing the data excluding the male participants did not alter our main findings. Sixth, due to nonresponse and differences in students having examinations at follow-up (individual differences in academic trajectories), follow-up results are based on a limited sample size (*n* = 37). Cautious interpretation of these findings is thus warranted. Finally, based on existing research (Grant & Beck, 2010) the current study has assessed a limited amount of characteristics concerning the naturalistic stressor (i.e., time since previous exam) whereas other factors might also have been of importance but were not taken into account in this study (e.g., perceptions concerning the examinations).

Future studies should focus on further elucidating the involvement of working memory functioning in brooding, stress reactivity, and resilience in general, using different indicators of working memory functioning. On top of the suggestions that have been made throughout the discussion, follow-up studies should use a double-blind design and target a sample with more variability in cognitive functioning. Furthermore, it would be important to get a clear view on potential individual differences predicting effectiveness of CCT in order to identify specific subgroups of vulnerable populations that might benefit from CCT.

Summary

The current experimental study provides evidence for the effectiveness of a working memory based cognitive control training (CCT) in increasing resilience to depression in an at-risk population. Compared to an active control group, CCT was associated with reduced stress reactivity in response to a lab stressor, as indicated by ratings of mood and a behavioral measure of rumination. Furthermore, CCT showed to reduce brooding four weeks following training as participants were confronted with a naturalistic stressor, providing evidence for the temporal stability and ecological validity of our findings. Implications and limitations were discussed, suggestions for future studies were made.

ACKNOWLEDGMENTS

We are grateful to Thomas Redick for providing the Visual Search Training paradigm and Greg Siegle for the Cognitive Control Training protocol. We are also grateful to Valentina Rossi and Thomas Onraedt for assistance with some of the tasks. This research was supported by a Special Research Fund (BOF) of Ghent University awarded to Kristof Hoorelbeke (B/13808/01). MAV is a postdoctoral research fellow of the Research Foundation Flanders (FWO).

REFERENCES

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for Beck Depression Inventory II*. San Antonio, Texas: Psychological Corporation.

Borkovec, T. D., Robinson, E., Pruzinsky, T., & Depree, J. A. (1983). Preliminary exploration of worry: Some characteristics and processes. *Behaviour Research and Therapy, 21*, 9-16. doi: 10.1016/0005-7967(83)90121-3

Brunoni, A. R., Boggio, P. S., De Raedt, R., Bensenor, I. M., Lotufo, P. A., Namur, V., . . . Vanderhasselt, M. A. (2014). Cognitive control therapy and transcranial direct current stimulation for depression: A randomized, double-blinded, controlled trial. *Journal of Affective Disorders, 162*, 43-49. doi: 10.1016/j.jad.2014.03.026

Calkins, A. W., Deveney, C. M., Weitzman, M. L., Hearon, B. A., & Siegle, G. J. (2011). The effects of prior cognitive control task exposure on responses to emotional tasks in healthy participants. *Behavioural and Cognitive Psychotherapy, 39*, 205-220. doi: 10.1017/s1352465810000652

Calkins, A. W., McMorran, K. E., Siegle, G. J., & Otto, M. W. (2015). The effects of computerized cognitive control training on community adults with depressed mood. *Behavioural and Cognitive Psychotherapy, 43*, 578-589. doi: 10.1017/S1352465814000046

Clark, L. A., & Watson, D. (1991). Tripartite model of anxiety and depression: Psychometric evidence and taxonomic implications. *Journal of Abnormal Psychology, 100*, 316-336.

Cohen, N., Mor, N., & Henik, A. (2015). Linking executive control and emotional response: A training procedure to reduce rumination. *Clinical Psychological Science, 3*, 15-25. doi: 10.1177/2167702614530114

Collette, F., Van der Linden, M., Laureys, S., Delfiore, G., Degueldre, C., Luxen, A., & Salmon, E. (2005). Exploring the unity and diversity of the neural substrates of executive functioning. *Human Brain Mapping, 25*, 409-423. doi: 10.1002/hbm.20118

Connolly, S. L., Wagner, C. A., Shapero, B. G., Pendergast, L. L., Abramson, L. Y., & Alloy, L. B. (2014). Rumination prospectively predicts executive functioning

impairments in adolescents. *Journal of Behavior Therapy and Experimental Psychiatry, 45*, 46-56. doi: 10.1016/j.jbtep.2013.07.009

Cox, S., Funasaki, K., Smith, L., & Mezulis, A. H. (2012). A prospective study of brooding and reflection as moderators of the relationship between stress and depressive symptoms in adolescence. *Cognitive Therapy and Research, 36*, 290-299. doi: 10.1007/s10608-011-9373-z

Cuijpers, P., Andersson, G., Donker, T., & van Straten, A. (2011). Psychological treatment of depression: Results of a series of meta-analyses. *Nordic Journal of Psychiatry, 65*, 354-364. doi: 10.3109/08039488.2011.596570

Daches, S., & Mor, N. (2014). Training ruminators to inhibit negative information: A preliminary report. *Cognitive Therapy and Research, 38*, 160-171. doi: 10.1007/s10608-013-9585-5

Davis, R. N., & Nolen-Hoeksema, S. (2000). Cognitive inflexibility among ruminators and nonruminators. *Cognitive Therapy and Research, 24*, 699-711. doi: 10.1023/A:1005591412406

De Lissnyder, E., Koster, E. H. W., Everaert, J., Schacht, R., Van den Abeele, D., & De Raedt, R. (2012). Internal cognitive control in clinical depression: General but no emotion-specific impairments. *Psychiatry Research, 199*, 124-130. doi: 10.1016/j.psychres.2012.04.019

De Lissnyder, E., Koster, E. H. W., Goubert, L., Onraedt, T., Vanderhasselt, M. A., & De Raedt, R. (2012). Cognitive control moderates the association between stress and rumination. *Journal of Behavior Therapy and Experimental Psychiatry, 43*, 519-525. doi: 10.1016/j.jbtep.2011.07.004

De Raedt, R., & Koster, E. H. W. (2010). Understanding vulnerability for depression from a cognitive neuroscience perspective: A reappraisal of attentional factors and a new conceptual framework. *Cognitive Affective & Behavioral Neuroscience, 10*, 50-70. doi: 10.3758/cabn.10.1.50

Demeyer, I., De Lissnyder, E., Koster, E. H. W., & De Raedt, R. (2012). Rumination mediates the relationship between impaired cognitive control for emotional information and depressive symptoms: A prospective study in remitted depressed adults. *Behaviour Research and Therapy, 50*, 292-297. doi: 10.1016/j.brat.2012.02.012

Derryberry, D., & Reed, M. A. (2002). Anxiety-related attentional biases and their regulation by attentional control. *Journal of Abnormal Psychology, 111*, 225-236. doi: 10.1037/0021-84X.111.2.225

Engelen, U., De Peuter, S., Victoir, A., Van Diest, I., & Van den Bergh, O. (2006). Verdere validering van de Positive and Negative Affect Schedule (PANAS) en vergelijking van twee Nederlandstalige versies. *Psychologie en Gezondheid, 34*, 89-102.

Grant, D. M., & Beck, J. G. (2010). What predicts the trajectory of rumination?: A prospective evaluation. *Journal of Anxiety Disorders, 24*, 480-486. doi: 10.1016/j.janxdis.2010.03.004

Gronwall, D. (1977). Paced Auditory Serial-Addition Task: A measure of recovery from concussion. *Perceptual and Motor Skills, 44*, 367-373.

Harrison, T. L., Shipstead, Z., Hicks, K. L., Hambrick, D. Z., Redick, T. S., & Engle, R. W. (2013). Working memory training may increase working memory capacity but not fluid intelligence. *Psychological Science, 24*, 2409-2419. doi: 10.1177/0956797613492984

Hirsch, C. R., Hayes, S., & Mathews, A. (2009). Looking on the bright side: Accessing benign meanings reduces worry. *Journal of Abnormal Psychology, 118*, 44-54. doi: 10.1037/a0013473

IsHak, W. W., Balayan, K., Bresee, C., Greenberg, J. M., Fakhry, H., Christensen, S., & Rapaport, M. H. (2013). A descriptive analysis of quality of life using patient-reported measures in major depressive disorder in a naturalistic outpatient setting. *Quality of Life Research, 22*, 585-596. doi: 10.1007/s11136-012-0187-6

Johnson, D. P., & Whisman, M. A. (2013). Gender differences in rumination: A meta-analysis. *Personality and Individual Differences, 55*, 367-374. doi: 10.1016/j.paid.2013.03.019

Joormann, J. (2006). Differential effects of rumination and dysphoria on the inhibition of irrelevant emotional material: Evidence from a Negative Priming Task. *Cognitive Therapy and Research, 30*, 149-160. doi: 10.1007/s10608-006-9035-8

Joormann, J., & D'Avanzato, C. (2010). Emotion regulation in depression: Examining the role of cognitive processes. *2010, 24*, 913-939. doi: 10.1080/02699931003784939

Joormann, J., Dkane, M., & Gotlib, I. H. (2006). Adaptive and maladaptive components of rumination? Diagnostic specificity and relation to depressive biases. *Behavior Therapy, 37*, 269-280.

Joormann, J., & Gotlib, I. H. (2010). Emotion regulation in depression: Relation to cognitive inhibition. *Cognition & Emotion, 24*, 281-298. doi: 10.1080/02699930903407948

Joormann, J., & Quinn, M. E. (2014). Cognitive processes and emotion regulation in depression. *Depression and Anxiety, 31*, 308-315. doi: 10.1002/da.22264

Judah, M. R., Grant, D. M., Mills, A. C., & Lechner, W. V. (2014). Factor structure and validation of the attentional control scale. *Cognition & Emotion, 28*, 433-451. doi: 10.1080/02699931.2013.835254

Kane, M. J., Poole, B. J., Tuholski, S. W., & Engle, R. W. (2006). Working memory capacity and the top-down control of visual search: Exploring the boundaries of "executive attention". *Journal of Experimental Psychology-Learning Memory and Cognition, 32*, 749-777. doi: 10.1037/0278-7393.32.4.749

Kazdin, A. E., & Blase, S. L. (2011). Rebooting psychotherapy research and practice to reduce the burden of mental illness. *Perspectives on Psychological Science, 6*, 21-37.

Kessler, R. C., & Wang, P. S. (2009). The epidemiology of depression. In I. H. Gotlib & C. L. Hammen (Eds.), *Handbook of depression: 2nd edition*. New York: Guilford.

Lazeron, R. H., Rombouts, S. A., de Sonneville, L., Barkhof, F., & Scheltens, P. (2003). A paced visual serial addition test for fMRI. *Journal of Neurological Science, 213*, 29-34.

Luppa, M., Heinrich, S., Angermeyer, M. C., Konig, H. H., & Riedel-Heller, S. G. (2007). Cost-of-illness studies of depression: A systematic review. *Journal of Affective Disorders, 98*, 29-43. doi: 10.1016/j.jad.2006.07.017

McNair, D. M., Lorr, M., & Dropplemann, L. F. (1992). *Manual: Profile of Mood States Revised*. San Diego, CA: Educational and Industrial Testing Service.

Meyer, T. J., Miller, M. L., Metzger, R. L., & Borkovec, T. D. (1990). Development and validation of the Penn State Worry Questionnaire. *Behaviour Research and Therapy, 28*, 487-495. doi: 10.1016/0005-7967(90)90135-6

Michl, L. C., McLaughlin, K. A., Shepherd, K., & Nolen-Hoeksema, S. (2013). Rumination as a mechanism linking stressful life events to symptoms of depression and anxiety: Longitudinal evidence in early adolescents and adults. *Journal of Abnormal Psychology, 122*, 339-352. doi: 10.1037/a0031994

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive Psychology, 41*, 49-100. doi: 10.1006/cogp.1999.0734

Nolen-Hoeksema, S., & Morrow, J. (1991). A prospective study of depression and posttraumatic stress symptoms after a natural disaster - The 1989 Loma-Prieta earthquake. *Journal of Personality and Social Psychology, 61*, 115-121. doi: 10.1037/0022-3514.61.1.115

Nolen-Hoeksema, S., Wisco, B. E., & Lyubomirsky, S. (2008). Rethinking rumination. *Perspectives on Psychological Science, 3*, 400-424. doi: 10.1111/j.1745-6924.2008.00088.x

Nummenmaa, L., & Niemi, P. (2004). Inducing affective states with success-failure manipulations: A meta-analysis. *Emotion, 4*, 207-214. doi: 10.1037/1528-3542.4.2.207

Owens, M., Koster, E. H. W., & Derakshan, N. (2012). Impaired filtering of irrelevant information in dysphoria: An ERP study. *Social Cognitive and Affective Neuroscience, 7*, 752-763. doi: 10.1093/scan/nsr050

Portzky, M. (2008). *RS-nl: Resilience Scale - Nederlandse versie*. Amsterdam: Harcourt Test Publishers.

Redick, T. S., Shipstead, Z., Harrison, T. L., Hicks, K. L., Fried, D. E., Hambrick, D. Z., . . . Engle, R. W. (2013). No evidence of intelligence improvement after working memory training: A randomized, placebo-controlled study. *Journal of Experimental Psychology-General, 142*, 359-379. doi: 10.1037/a0029082

Rossi, V., & Pourtois, G. (2012). State-dependent attention modulation of human primary visual cortex: A high density ERP study. *Neuroimage, 60*, 2365-2378. doi: 10.1016/j.neuroimage.2012.02.007

Ruscio, A. M., & Borkovec, T. D. (2004). Experience and appraisal of worry among high worriers with and without generalized anxiety disorder. *Behaviour Research and Therapy, 42*, 1469-1482. doi: 10.1016/j.brat.2003.10.007

Segrave, R. A., Arnold, S., Hoy, K., & Fitzgerald, P. B. (2014). Concurrent cognitive control training augments the antidepressant efficacy of tDCS: A pilot study. *Brain Stimulation, 7*, 325-331. doi: 10.1016/j.brs.2013.12.008

Shipstead, Z., Redick, T. S., & Engle, R. W. (2012). Is working memory training effective? *Psychological Bulletin, 138*, 628-654. doi: 10.1037/a0027473

Siegle, G. J., Ghinassi, F., & Thase, M. E. (2007). Neurobehavioral therapies in the 21st century: Summary of an emerging field and an extended example of cognitive control training for depression. *Cognitive Therapy and Research, 31*, 235-262. doi: 10.1007/s10608-006-9118-6

Siegle, G. J., Price, R. B., Jones, N. P., Ghinassi, F., Painter, T., & Thase, M. E. (2014). You gotta work at it: Pupillary indices of task focus are prognostic for response to a neurocognitive intervention for rumination in depression. *Clinical Psychological Science, 2*, 455-471. doi: 10.1177/2167702614536160

Treynor, W., Gonzalez, R., & Nolen-Hoeksema, S. (2003). Rumination reconsidered: A psychometric analysis. *Cognitive Therapy and Research, 27*, 247-259.

Turner, M. L., & Engle, R. W. (1989). Is working memory capacity task dependent? *Journal of Memory and Language, 28*, 127-154. doi: 10.1016/0749-596X(89)90040-5

Unsworth, N., Heitz, R., Schrock, J., & Engle, R. W. (2005). An automated version of the operation span task. *Behavior Research Methods, 37*, 498-505. doi: 10.3758/bf03192720

Van der Does, A. J. W. (2002). *BDI-II-NL. Handleiding: De Nederlandse versie van de Beck Depression Inventory - 2nd edition*. Lisse: Harcourt Test Publishers.

van Rijsoort, S., Emmelkamp, P., & Vervaeke, G. (1999). The Penn State Worry Questionnaire and the Worry Domains Questionnaire: Structure, reliability and validity. *Clinical Psychology & Psychotherapy, 6*, 297-307. doi: 10.1002/(SICI)1099-0879(199910)6:4<297::AID-CPP206>3.0.CO;2-E

van Rijsoort, S., Vervaeke, G., & Emmelkamp, P. (1997). The Penn Sate Worry Questionnaire and the Worry Domains Questionnaire: First results in a normal Dutch population. *Gedragstherapie, 30*, 121-128.

van Vugt, M. K., Hitchcock, P., Shahar, B., & Britton, W. (2012). The effects of mindfulness-based cognitive therapy on affective memory recall dynamics in despression: A mechanistic model of rumination. *Frontiers in Human Neuroscience, 6*, 13. doi: 10.3389/fnhum.2012.00257

Vanderhasselt, M.-A., & De Raedt, R. (2009). Impairments in cognitive control persist during remission from depression and are related to the number of past episodes: An event related potentials study. *Biological Psychology, 81*, 169-176. doi: 10.1016/j.biopsycho.2009.03.009

Verwoerd, J., Cieraad, R., & de Jong, P. J. (2007). ACS: Dutch translation of the Attentional Control Scale. Retrieved 08-03-2014 from http://www.ekgp.ugent.be/pages/nl/vragenlijsten/ACS-NL.pdf.

Wagnild, G. M., & Young, H. M. (1993). Development and psychometric evaluation of the resilience scale. *Journal of Nursing Measurement, 1*, 165-178.

Wardenaar, K. J., van Veen, T., Giltay, E. J., de Beurs, E., Penninx, B., & Zitman, F. G. (2010). Development and validation of a 30-item short adaptation of the Mood and Anxiety Symptoms Questionnaire (MASQ). *Psychiatry Research, 179*, 101-106. doi: 10.1016/j.psychres.2009.03.005

Watkins, E. R., Mullan, E., Wingrove, J., Rimes, K., Steiner, H., Bathurst, N., . . . Scott, J. (2011). Rumination-focused cognitive-behavioural therapy for residual depression: phase II randomised controlled trial. *British Journal of Psychiatry, 199*, 317-322. doi: 10.1192/bjp.bp.110.090282

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *Journal of Personality and Social Psychology, 54*, 1063-1070.

Wells, A. (2000). *Emotional disorders and metacognition innovative Cognitive Therapy*. New York: Wiley.

WHO. (2012). Depression: World Health Organization Fact sheet no 369. Accessed on 29-05-2014 from http://www.who.int/mediacentre/factsheets/fs369/en/.

Zetsche, U., & Joormann, J. (2011). Components of interference control predict depressive symptoms and rumination cross-sectionally and at six months follow-up. *Journal of Behavior Therapy and Experimental Psychiatry, 42*, 65-73. doi: 10.1016/j.jbtep.2010.06.001

CHAPTER 4

EFFECTS OF COGNITIVE CONTROL TRAINING ON THE DYNAMICS OF (MAL)ADAPTIVE EMOTION REGULATION IN DAILY LIFE[1]

ABSTRACT

Cognitive control plays a key role in both adaptive emotion regulation, such as positive reappraisal, and maladaptive emotion regulation, such as rumination, with both strategies playing a major role in resilience and well-being. As a result, cognitive control training targeting working memory functioning (CCT) may have the potential to reduce maladaptive emotion regulation and increase adaptive emotion regulation. The current study explored the effects of CCT on positive reappraisal ability in a lab context, and deployment and efficacy of positive appraisal and rumination in daily life. A sample of undergraduates (n = 83) was allocated to CCT or an active control condition, performing 10 online training sessions over a period of 14 days. Effects on regulation of affective states in daily life were assessed using experience sampling over a seven-day post-training period. Results revealed a positive association between baseline cognitive control and self-reported use of adaptive emotion regulation strategies, whereas maladaptive emotion regulation strategies showed a negative association. CCT showed transfer to working memory functioning on the dual n-back task. Overall, effects of CCT on emotion regulation were limited to reducing deployment of rumination in low positive affective states. However, we did not find beneficial effects on indicators of adaptive emotion regulation. These findings are in line with previous studies targeting maladaptive emotion regulation, but suggest limited use in enhancing adaptive emotion regulation in a healthy sample.

[1] Based on Hoorelbeke, K., Koster, E.H.W., Demeyer, I., Loeys, T., & Vanderhasselt, M-A. (2016). Effects of cognitive control training on the dynamics of (mal)adaptive emotion regulation in daily life. *Emotion, 16,* 945-956. doi: 10.1037/emo0000169

How people respond to stressful events and negative emotions has important consequences for their mental health. For instance, responding with negative and repetitive moody pondering (i.e., brooding, a subtype of rumination; Treynor, Gonzalez, & Nolen-Hoeksema, 2003) to negative affect following a stressful event such as loss of job is known to be an important risk factor for developing mood disorders (D'Avanzato, Joormann, Siemer, & Gotlib, 2013; Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). In contrast, applying a strategy such as cognitive (re-)appraisal in which the emotion-eliciting value of a stressful situation is reduced through cognitive strategies (Gross, 2002) is known to have beneficial effects on well-being and mental health (Gross & John, 2003; Haga, Kraft, & Corby, 2009; Hu et al., 2014). This process of influencing which emotions one has, when one experiences these emotions, and how these emotions are experienced and expressed is known as emotion regulation (p. 275; Gross, 1998) and plays an important role in maintaining and ameliorating mental health (Gross & Jazaieri, 2014). Given their differential effects on mental health, rumination (among strategies such as catastrophizing, self-blame, etc.) has been conceptualized as a maladaptive emotion regulation strategy, whereas cognitive reappraisal (among strategies such as putting into perspective, positive refocusing, etc.) has been categorized as an adaptive emotion regulation strategy (Garnefski, Kraaij, & Spinhoven, 2001). Furthermore, adaptive emotion regulation strategies form an important predictor for resilience, the phenomenon of maintaining one's mental health even when confronted with adversity (Kalisch, Müller, & Tüscher, 2015).

Importantly, research indicates that cognitive control processes, such as shifting, inhibition, and updating of representations in working memory (Miyake et al., 2000), form an important underlying mechanism for emotion regulation (for a review see Joormann & D'Avanzato, 2010). That is, these executive processes are key to efficient deployment of limited working memory capacity, which is central to goal-directed behavior. Malfunctioning of these top-down processes following confrontation with an external or internal stressor may underlie maladaptive responses such as perseverative negative thinking. Indeed, a vast amount of cross-sectional and prospective studies have provided evidence for an association between impaired cognitive control and deployment of maladaptive emotion regulation strategies, for instance brooding and

rumination (De Lissnyder et al., 2012; Demeyer, De Lissnyder, Koster, & De Raedt, 2012; Joormann, 2006; Joormann & Gotlib, 2008; Zetsche & Joormann, 2011). Given the role of cognitive control and maladaptive emotion regulation strategies in developing depressive symptomatology (e.g., Demeyer et al., 2012; Nolen-Hoeksema et al., 2008), this has led researchers to develop computerized training tasks to remediate cognitive control impairments.

Siegle, Ghinassi, and Thase (2007) have developed an adaptive version of the Paced Auditory Serial Addition Task (PASAT; Gronwall, 1977). This cognitive control training (CCT) targeting working memory functioning has shown to reduce emotional reactivity and brooding in undergraduate students at-risk for developing depressive symptomatology (Hoorelbeke, Koster, Vanderhasselt, Callewaert, & Demeyer, 2015). Moreover, administering CCT in depressive patients has shown not only to reduce rumination (Siegle et al., 2007; Siegle et al., 2014; Vanderhasselt et al., 2015), but also depressive symptomatology (Brunoni et al., 2014; Siegle et al., 2007). Importantly, it has been suggested that the effects of CCT on depressive symptomatology are secondary to changes in emotion regulation (Siegle et al., 2014). These findings highlight the potential of CCT targeting working memory functioning in reducing maladaptive emotion regulation (e.g., rumination), and in turn, depressive symptomatology.

However, Joormann and D'Avanzato (2010) have suggested that the role of cognitive control is not confined to maladaptive emotion regulation strategies, but that cognitive control impairments also “discourage the use of more effective emotion regulation strategies, such as reappraisal” (p. 928; p. 412; Joormann & Vanderlind, 2014). Indeed, research suggests that cognitive control plays an important role in the deployment of adaptive emotion regulation strategies (Buhle et al., 2014; Moser, Hartwig, Moran, Jendrusina, & Kross, 2014; Vanderhasselt et al., 2014). Moreover, it has been argued that these cognitive emotion regulation strategies rely on a network of neural activation involving structures implicated in cognitive control and reduced emotional processing (Hajcak, MacNamara, & Olvet, 2010). For instance, Ochsner, Bunge, Gross, and Gabrieli (2002) have provided evidence for the involvement of the prefrontal cortex in reappraisal, which forms a central region for cognitive control

(Miller & Cohen, 2001). Furthermore, meta-analytic findings suggest activation of cognitive control regions during reappraisal, which attenuates amygdala activity (Buhle et al., 2014). Yet, compared to research exploring the role of cognitive control in maladaptive emotion regulation, evidence for a causal relation between cognitive control underlying adaptive emotion regulation is more limited. Interestingly, despite the emerging evidence for the potential of CCT in reducing maladaptive emotion regulation, so far no study has addressed the potential of CCT targeting working memory functioning in facilitating the use of adaptive emotion regulation strategies (see Joormann & Vanderlind, 2014). This forms an important impetus, as deployment of adaptive emotion regulation strategies is considered an important resilience factor (Kalisch et al., 2015). Maintaining a unilateral focus on reducing maladaptive emotion regulation strategies and psychopathology thus limits the potential applications and benefits of CCT. For instance, next to reducing maladaptive processes, CCT might also be used to increase resilience and thus ameliorate well-being and mental health.

Another issue that might limit our understanding of the causal influence of cognitive control on adaptive and maladaptive emotion regulation is that CCT studies have typically relied on lab assessments and self-report questionnaires that were administered at limited time points to assess effects of training (e.g., Calkins, McMorran, Siegle, & Otto, 2015; Hoorelbeke, Koster, et al., 2015; Siegle et al., 2014). However, such an approach does not allow to directly test whether CCT impacts emotion regulation in a naturalistic context, nor does it allow to study its effects on the complex dynamics between affective state and emotion regulation.[2] Consequently, it would be beneficial to assess the interplay between affect and emotion regulation in daily life using experience sampling methodology (ESM; Larson & Csikszentmihalyi, 1983). This technique allows multiple assessments of affective state and emotion

[2] Emotions have been conceptualized to mainly differ from mood states concerning duration, the presence of a specific object that precedes the onset of an emotion, and related to these objects, the extent to which they give rise to a response tendency (Gross, 1998). However, the way emotion regulation has typically been studied using ESM does not allow to differentiate between emotion and mood as it provides no information concerning the object and duration of a certain affective state. As a result, when it pertains to ESM-measures, we refer to 'affective states' rather than 'emotions'.

regulation during the course of a day, where ratings are made related to that specific moment and situation (e.g., Moberly & Watkins, 2008; Pe, Raes, & Kuppens, 2013). Using this technique, Pe, Raes, Koval, et al. (2013) have found that cognitive control moderates the impact of regulation of affect in daily life: impaired cognitive control was related to increased negative affect following rumination, and reduced efficacy of reappraisal in regulating affective states. These findings illustrate the specific involvement of cognitive control in the deployment of adaptive and maladaptive emotion regulation strategies in relation to positive and negative affect. However, to date ESM has not been implemented to assess effects of CCT on regulation of affective states. Accordingly, we used this technique to explore whether CCT can be used to increase deployment and efficacy of an adaptive emotion regulation strategy, and to reduce the use and impact of maladaptive emotion regulation strategies.

Current Study

The current study examined the relation between cognitive control and emotion regulation by exploring the effects of a working memory based CCT on the ability of positive reappraisal in lab context and regulation of affective states in daily life. That is, training effects were explored on the deployment *and* efficacy of adaptive (positive appraisal) as well as maladaptive (depressive rumination) emotion regulation strategies in daily life using ESM, taking evaluation of CCT to the next level. This approach is useful in exploring the potential of CCT in increasing resilience and mental well-being, given that adaptive emotion regulation strategies such as positive (re-)appraisal have been put forward as an important resilience factor (Kalisch et al., 2015). This study specifically targeted an unselected undergraduate student sample in order to explore whether stimulating cognitive control in a population that is not specifically characterized by cognitive control deficits can be used to foster predictors of resilience and well-being. The combination of examining the effect of cognitive control on positive reappraisal in the lab and positive appraisal in daily life has key benefits. That is, positive reappraisal has been theorized as a component of the general process of positive appraisal (Kalisch et al., 2015). Exploring how participants perform on an instructed reappraisal exercise in the lab allows to test the involvement of cognitive control in this subcomponent of positive appraisal. For this purpose we rely on recall of

an autobiographical memory of a negative situation as autobiographical memories have previously been used to explore the involvement of cognitive processes in emotion regulation and the underlying neural correlates (e.g., Holland & Kensinger, 2013; Kross, Davidson, Weber, & Ochsner, 2009). Furthermore, the type of episodic autobiographic information recollected during such an exercise implies at least partially re-experiencing this negative event (Wheeler, Stuss, & Tulving, 1997). This allows to explore effects of cognitive control on emotion regulation ability in the context of a well-defined emotionally relevant situation. In contrast, the ESM measures provide information concerning the dynamics of positive appraisal in relation to daily life stressors. However, this information is unspecific concerning the type and content of stressor.

Participants were randomly allocated to either a working memory based CCT or an active control training condition after having completed a baseline assessment of emotion regulation (cfr. self-report questionnaires) and working memory functioning as an indicator of cognitive control (Time 1). Cognitive control was reassessed immediately after two weeks of online training (working memory based CCT or active control), followed by a lab assessment of the ability to positively reappraise a negative past event (Time 2). Following the post-training assessments, daily fluctuations in affect, positive appraisal, and rumination were registered over a period of seven days (eight assessments a day; ESM). In line with previous findings, we hypothesized that performance at baseline assessment of cognitive control (i.e., working memory functioning) would be positively related to adaptive emotion regulation strategies as assessed by self-report measures, whereas maladaptive emotion regulation strategies would show an inverse relation. Second, the CCT group would show a more distinct increase in cognitive control following training. Third, we expected to find beneficial effects of CCT on adaptive emotion regulation, as shown by (1) an increased ability of positive reappraisal of a negative autobiographical memory upon instruction in the lab, and (2) increased deployment and efficacy of positive appraisal in daily life, in contrast to the maladaptive emotion regulation strategy, rumination.

METHOD

Participants

Unselected undergraduate-students of Ghent University were recruited using an online system. Eighty-three participants completed the baseline assessment and were randomly assigned to a CCT or active control condition (sham training). Ten participants did not complete the training sessions due to individual technological problems (e.g., incompatible operating systems, unstable internet connection; *n* = 6) or reasons unrelated to technical aspects of the training (e.g., impossibility to return to the lab two weeks following baseline assessment, physical health reasons unrelated to the experiment; *n* = 4) and were excluded from data-analysis. Another 12 participants did not take into account the explicit instructions concerning dose regulation of training (i.e., did not complete training, performed multiple sessions a day in order to reach the deadline). 61 participants adequately completed training within the two week period (CCT: *n* = 29, sham: *n* = 32). During the experiment, three participants were tested sequentially in sound attenuated booths. Participants were reimbursed for participating (€60). The local ethical committee of Ghent University approved this study and all participants provided written informed consent.

Apparatus and Material

The dual n-back task (Jaeggi et al., 2010) and both training tasks were programmed and run using the INQUISIT Millisecond software package. The dual n-back task was run on Dell Dimension 4600 computers with 72 Hz, 17-inch color monitors. The training was performed online in-browser using the INQUISIT Web application. Participants' own smartphones were used to assess affect and emotion regulation during the ESM procedure, using a combination of SurveySignal software (Hofmann & Patel, 2015) and LimeSurvey. These questionnaires, experimental tasks, and training procedures will be explained in greater detail in the following sections.

Questionnaires. We used the Beck Depression Inventory (BDI-II-NL; Beck, Steer, & Brown, 1996; Van der Does, 2002) to assess *depressive symptomatology* at baseline and the Dutch Resilience Scale (RS-NL; Portzky, 2008; Wagnild & Young, 1993) to assess

baseline *resilience*. The Positive and Negative Affect Schedule (PANAS; Engelen, De Peuter, Victoir, Van Diest, & Van den Bergh, 2006; Watson, Clark, & Tellegen, 1988) was used to assess *positive and negative affective states* at baseline and following training.

Several questionnaires were used to assess *adaptive and maladaptive emotion regulation* at baseline. The Ruminative Response Scale (RRS-NL-EXT; Nolen-Hoeksema & Morrow, 1991; Treynor et al., 2003) assessed rumination, brooding and reflection. Furthermore, the Cognitive Emotion Regulation Questionnaire (CERQ; Garnefski et al., 2001) provided us with assessments of five adaptive (acceptance, positive refocusing, refocus on planning, positive reappraisal, and putting into perspective) and four less adaptive strategies (self-blame, rumination, catastrophizing, and blaming others). In line with Vanderhasselt et al. (2014), we have calculated a CERQ compound score for adaptive emotion regulation as well as maladaptive emotion regulation. Finally, the Response to Positive Affect Scale (RPA-NL; Feldman, Joormann, & Johnson, 2008; Raes, Daems, Feldman, Johnson, & Van Gucht, 2009) was used to explore how participants responded to positive affect, resulting in two adaptive strategies (self-focused and emotion focused positive rumination) and one less adaptive strategy (dampening of positive affect).

Training tasks.

Cognitive control training. We used a modified version of the Paced Auditory Serial Addition Task (PASAT; Gronwall, 1977; Siegle et al., 2007) to train participants' cognitive control (CCT condition). Task characteristics were identical to the CCT described in Hoorelbeke, Koster, et al. (2015). During this task, participants had to add serially presented numbers (1 – 9), responding to the sum of the last two presented stimuli (2 – 18). Based on their within-session performance, the InterStimulus Interval (ISI) was automatically adjusted (baseline: 3000 ms, +/- 100 ms every 4 consecutive correct or incorrect responses). Following each training session (400 trials), mood was assessed ('energetic', 'tense', 'frustrated', 'sad', 'happy') using visual analogue scales (VAS; 1 – 100), as well as the extent to which participants have experienced negative thoughts and stress throughout training, and experienced task competence ('During the task I felt as if I was doing great').

Active control training. In search for a suitable active control task for the sham condition, we have developed a low cognitive load version of the adaptive PASAT. During this attention training, participants from the sham condition were instructed to respond to the auditory presented stimuli (1 – 18) immediately by clicking on the corresponding number. As in the adaptive PASAT, ISI was adjusted every four (in-)correct consecutive responses. All other task characteristics were similar to the adaptive PASAT, allowing to control for motivational effects of undergoing CCT and specifically filtering out the working memory component whereas attentional processes are trained in both conditions (e.g., sustained attention).

Transfer tasks.

Cognitive control. The dual n-back task is a working memory task relying on several executive functions such as inhibition and updating (Jaeggi, Buschkuehl, Jonides, & Perrig, 2008; Jaeggi et al., 2010). Therefore, this task was used as an indicator of cognitive control. During this task, participants were confronted with a series of sequentially presented visual (squares) and auditory (letters) stimuli. Participants had to respond if at least one of the presented stimuli matched the stimuli presented n steps before (matching the visual stimulus: press "A"; matching the auditory stimulus: press "L"; matching both: press "A" and "L" simultaneously). Following 30 practice trials, cognitive control was assessed using 3 blocks of n = 2, n = 3, and n = 4, containing 20 trials each (total of 180 test trials). In line with Jaeggi et al. (2010), we used the proportion of hits minus false alarms averaged over the auditory and visual modality, averaged over all experimental blocks / n-back levels as our dependent variable.

Positive reappraisal ability. We assessed effects of CCT on the process of positive reappraisal using a pen and paper structured autobiographical memory recall procedure, followed by a structured reappraisal procedure. During each phase participants were provided with standardized verbal instructions and a written example illustrating the extent of details that should be provided and the direction of the exercise. In the first phase of this procedure, participants were asked to recall an autobiographic memory of a negative situation and imagine the related sensations, feelings, thoughts, and behaviors to stimulate integration of several types of information in order to promote re-experiencing the negative situation. Next, the

participants were to write down this negative situation in a detailed manner. After thoroughly reading this situation, participants had to rate the extent to which the situation was experienced as negative, positive, and arousing at that moment, as well as vividness of the memory using VAS (1 – 100). In the second phase of the reappraisal ability assessment procedure, participants were instructed to formulate an alternative appraisal that would allow them to reflect upon the previously reported situation in a positive manner. Participants were provided a couple of minutes for this assignment and were asked to write down the alternative appraisal of the situation and read it. This was again followed by situation ratings of negativity, positivity, and arousal using VAS. One additional VAS was used to assess the experienced difficulty of positively reappraising the situation. Throughout this procedure, affect was assessed three times (preceding recall of a negative memory, following recall, following reappraisal), using six VAS that were adopted from the Profile Of Mood States (McNair, Lorr, & Dropplemann, 1992) in line with Rossi and Pourtois (2012). Three scales provided a mean estimate of positive affect (Dutch equivalents of 'energetic', 'satisfied', and 'happy'; 1 = not at all; 100 = very much), another three scales provided a mean estimate of negative affect (Dutch equivalents of 'angry', 'tense', and 'depressed').

Deployment and efficacy of emotion regulation in daily life. We explored the influence of CCT on emotion regulation in daily life using ESM (Larson & Csikszentmihalyi, 1983). During a period of seven days following training, participants received eight signals a day between 09:00 AM and 09:00 PM. In line with Moberly and Watkins (2008) we used a time-stratified strategy: each day was divided into eight intervals of 90 min, signals were sent at random moments within each of the eight intervals. A reminder signal was sent if no response was given within 15 min following the previous signal. Two consecutive signals were separated by at least 30 min. Using SurveySignal software (see Hofmann & Patel, 2015), each signal was delivered as a text message on the participants' smartphone, containing a link that directed the participant to an online survey that was created using LimeSurvey. Every signal, current affective state was assessed using the six VAS that were also used to check for effects of affect during the positive reappraisal procedure in lab context (energetic, satisfied, happy, angry, tense, depressed). Participants rated their affective state as experienced just

before receiving the signal. Two different emotion regulation strategies were assessed ("Since the previous signal, to what extent were you …"), using two items to assess ruminative self-focus ("Focused on feelings", "Focused on problems"; Moberly & Watkins, 2008), and one item to assess positive appraisal ("Focused on a positive meaning"). The order of affect items and emotion regulation items was randomized per participant and signal. Participants responded by entering a score ranging from 1 (for affect items and emotion regulation items: not at all) to 100 (affect items: very much; emotion regulation items: almost all of the time). Ratings of emotion regulation always related to the period since the previous signal that was responded to, except for the very first signal of the ESM procedure, which related to the period since waking up.

Procedure

As illustrated in Figure 1, after giving informed consent participants completed self-report questionnaires (BDI-II-NL, RRS-NL-EXT, RPA-NL, CERQ, RS, PANAS), followed by a baseline assessment of cognitive control (dual n-back task; Time 1). Next, participants received instructions and a manual concerning the training procedure. Participants then performed 10 online training sessions over a period of 14 days, completing maximum one session a day. Depending on the subject number that was entered, participants either received the CCT or sham training. Participants then returned to the lab for a post-training assessment (Time 2) of mood (PANAS) and cognitive control (dual n-back task). Moreover, the ability of positive reappraisal of a previous negative event was examined during this session. Given that the assessment of ability to reappraise contains the recall of a negative autobiographical memory, participants were also instructed to recall a positive memory before ending the second lab session. Next, participants were registered in SurveySignal, received instructions concerning the ESM procedure, and a manual containing clear definitions of the items. One day following registration, daily fluctuations in affect and emotion regulation were assessed (eight signals a day between 09:00 AM and 09:00 PM) during a period of seven days. Upon completion of the experience sampling phase, participants were re-invited to the faculty for an oral and written debriefing as well as reimbursement.

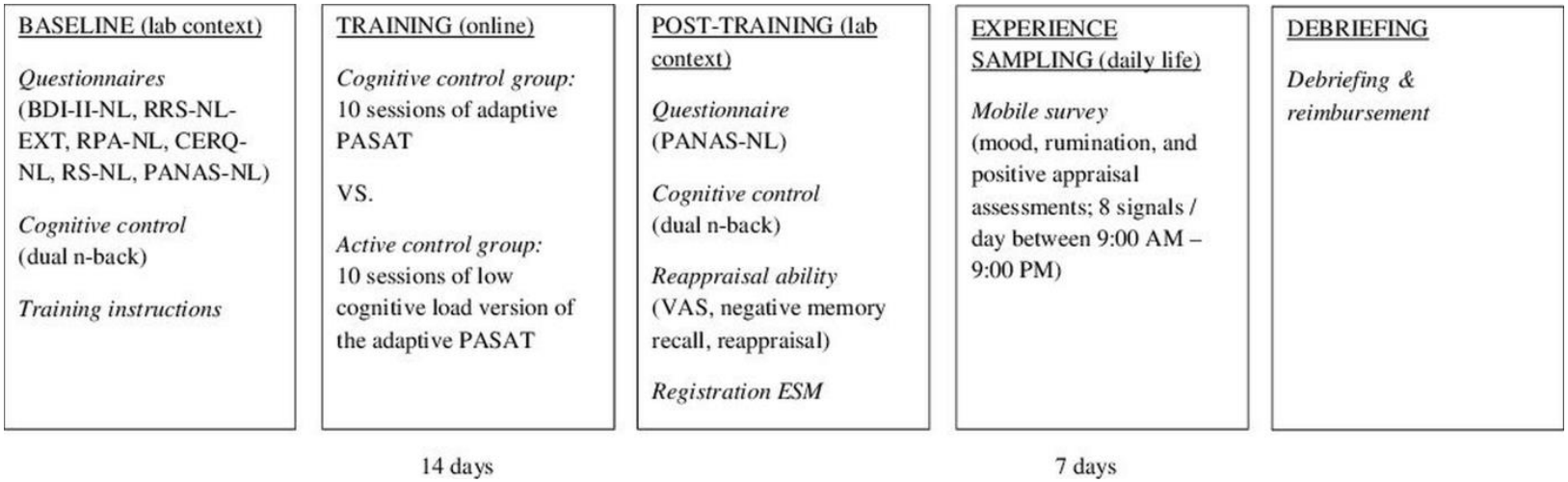


Figure 1. Procedure

Note: BDI = Beck Depression Inventory, RRS = Ruminative Response Scale, RPA = Response to Positive Affect Scale, CERQ = Cognitive Emotion Regulation Questionnaire, PANAS = Positive and Negative Affect Schedule, PASAT = Paced Auditory Serial Addition Task, VAS = visual analogue scale, ESM = Experience Sampling Method

RESULTS

Group Characteristics

Eighty-three subjects participated to the baseline assessment of this study of which 61 adequately completed training (CCT: n = 29; sham: n = 32).[3] Descriptive information for both training groups can be found in Table 1. Both groups did not differ significantly at baseline concerning age (CCT: M = 21.59, SD = 2.87; sham: M = 21.19, SD = 2.07; $t(59) = 0.63$, $p = .53$) or gender distribution (male/female; CCT: 4/25; sham: 5/27; $\chi^2(1, n = 61) = 0.04$, $p = .84$). However, there were marginally significant baseline group differences in self-reported resilience levels ($t(59) = 1.92$, $p = .06$) and negative mood state ($t(45.68) = 1.74$, $p = .09$), both in favor of the sham group (see Table 1). Importantly, both groups did not differ concerning the amount of depressive symptomatology or self-reported use of adaptive and maladaptive emotion regulation strategies (all ts < 1.37). At the post-training lab assessment mood was re-assessed, allowing us to check for the influence of group differences in mood state on performance on the cognitive control assessment task (dual n-back). However, both groups did not differ in self-reported levels of positive affect or negative affect following training (all ts < 1.09). Analyses of the effects of training (Hypothesis 2 and 3) were based on the subsample of 61 participants that successfully completed training. As individual differences play an important role in cognitive task performance and the

[3] Excluded participants did not differ from included participants concerning our variables of interest at baseline (cognitive control, depressive rumination / brooding, and positive reappraisal; ts < 1.36). However, excluded participants did report higher baseline levels of depressive symptomatology ($p < .05$; excluded participants: M = 11.45, SD = 5.88; included participants: M = 7.82, SD = 5.94), which was accompanied by increased catastrophizing ($p < .05$; excluded participants: M = 8.59, SD = 3.47; included participants: M = 6.82, SD = 2.77) and a tendency to report more dampening of positive affect ($p = .054$; excluded participants: M = 13.50, SD = 4.19; included participants: M = 11.61, SD = 3.78). Although the current study sought out to explore effects of CCT in healthy / unselected undergraduate students, this finding indicates that future studies targeting (sub)clinically depressed populations and other risk groups should take into account population specific threats for training retention in order to avoid sampling bias (e.g., adding a daily reminder signal and psycho-education; Hoorelbeke, Faelens, et al., 2015).

current study used unselected undergraduate students, we controlled for baseline levels of cognitive control when exploring transfer effects on the dual n-back task. Correlational analyses concerning baseline cognitive control and baseline self-reported emotion regulation (Hypothesis 1, n = 75) were based on the sample of 83 participants from which 8 outliers ($D > 4 / n$; Bollen & Jackman, 1990) were excluded based on Cook's D (calculated using the subscales of the emotion regulation self-report questionnaires).

Table 1

Group characteristics as a function of training condition

	Training condition			
	Cognitive control (n = 29)		Sham (n = 32)	
	M	*SD*	*M*	*SD*
Depressive symptomatology	8.28	5.79	7.41	6.14
RRS trait rumination	42.41	10.92	42.00	12.74
Brooding	10.17	2.99	9.75	3.45
Reflection	8.59	3.20	8.97	3.81
RPA Self-focus	8.48	2.50	9.37	2.60
RPA Dampening	12.10	4.25	11.16	3.30
RPA Emotion focus	13.62	2.14	13.56	2.50
CERQ Self-blame	10.90	2.99	10.25	2.90
CERQ Acceptance	12.45	3.88	12.84	3.06
CERQ Rumination	12.03	4.21	12.12	4.23
CERQ Positive refocusing	10.14	4.02	10.06	3.55
CERQ Refocus on planning	13.38	3.06	14.41	2.92
CERQ Positive reappraisal	11.86	3.65	12.59	3.31
CERQ Putting into perspective	13.00	4.46	12.66	3.48
CERQ Catastrophizing	6.86	2.77	6.78	2.81
CERQ Blaming others	6.66	2.07	7.06	2.35
Resilience	75.59	8.27	79.59	8.01
Positive affect (baseline)	32.38	5.98	32.38	6.49
Negative affect (baseline)	16.14	5.39	14.13	3.32
Positive affect (post-training)	31.14	5.57	30.06	5.16
Negative affect (post-training)	14.79	4.33	13.72	3.37

Note: RRS = Ruminative Response Scale, RPA = Response to Positive Affect Scale, CERQ = Cognitive Emotion Regulation Questionnaire

Cognitive Control and Emotion Regulation at Baseline: Cross-sectional Data

We explored the association between baseline levels of cognitive control and self-reported emotion regulation using Pearson's correlations (n = 75). As expected, this approach revealed significant associations and tendencies indicating that reduced cognitive control was related to the use of maladaptive emotion regulation strategies such as brooding (RRS Brooding: r = -.27, p < .05), rumination (CERQ Rumination: r = -.25, p < .05), self-blame (CERQ Self-Blame: r = -.32, p < .01), and catastrophizing (CERQ Catastrophizing: r = -.24, p < .05). Participants with reduced cognitive control also showed the tendency to respond to positive affect with dampening (RPA Dampening: r = -.23, p = .052). In contrast, better baseline cognitive control was positively related to – or showed a tendency towards – adaptive emotion regulation strategies such as acceptance (CERQ Acceptance: r = .24, p < .05), positive refocusing (CERQ Positive Refocusing: r = .24, p < .05), and putting into perspective (CERQ Putting Into Perspective: r = .22, p = .063; all other rs < .15). In sum, participants with higher levels of baseline cognitive control showed the tendency to report deploying more adaptive emotion regulation strategies in general (CERQ Compound Adaptive: r = .22, p = .064), whereas maladaptive emotion regulation in general was negatively related to cognitive control (CERQ Compound Maladaptive: r = -.35, p < .01).

Training Task Process Measures

In accordance with previous studies, median ISI scores per session were used to assess progress on the PASAT. The same approach was used for the sham training task. However, as both tasks differ, we performed two separate Repeated Measures ANOVA's to explore whether progress was made in both groups, as shown by a decrease in ISI over Time (10 sessions). As expected, both groups showed a significant increase in performance over time (CCT: $F(9, 20) = 38.49$, p < .001, η_p^2 = .95; sham: $F(9, 23) = 6.55$, p < .001, η_p^2 = .72; see Table 2 for mean ISI and accuracy rates).

Independent samples t-tests were used to explore group differences on process measures of training task experience (average VAS mood ratings and thought processes throughout and following training sessions; see Table 3). This approach revealed that

participants from the CCT group showed the tendency to report higher levels of frustration following completion of a training session compared with participants from the active control condition, $t(49.27) = 1.86$, $p = .07$, $d = .46$, 95% CI [-0.55, 13.79]. Both groups did not differ concerning the other mood ratings, nor did they differ concerning the amount of experienced negative thoughts throughout training or experienced task competence (all $ts < 1.26$).

Table 2

Training session mean median ISI and accuracy rates as a function of training condition

	Training condition					
	Cognitive control (*n* = 29)			Sham (*n* = 32)		
	M ISI (ms)	*SD ISI*	*M % correct*	*M ISI (ms)*	*SD ISI*	*M % correct*
Session 1	2034	321	55.03	653	154	62.25
Session 2	1631	269	56.83	594	129	61.84
Session 3	1428	299	57.38	563	136	62.47
Session 4	1310	232	58.38	534	123	62.75
Session 5	1207	227	58.62	522	118	63.19
Session 6	1162	241	59.14	508	140	62.75
Session 7	1100	258	59.28	515	137	62.75
Session 8	1048	242	59.28	513	152	62.56
Session 9	1010	244	59.52	516	137	62.97
Session 10	1000	245	60.24	494	122	62.50

Note: ISI = InterStimulus Interval

Table 3

Process measures of training task experience

	Training condition			
	Cognitive control (*n* = 29)		Sham (*n* = 32)	
	M	*SD*	*M*	*SD*
During a training session				
Negative thoughts	39.87	17.39	34.33	18.60
Stressed	60.03	9.83	56.55	15.26
Competence	40.77	10.84	44.41	14.20
Following a training session				
Tense	53.98	12.36	49.94	14.51
Energetic	37.62	12.74	40.22	11.38
Frustrated	57.21	9.66	50.59	17.45
Sad	29.98	18.46	24.56	15.36
Happy	47.29	14.99	49.60	9.73

Effects of Training

Cognitive control. In line with previous work indicating the importance of taking into account individual differences in cognitive functioning when exploring cognitive transfer (Jaeggi, Buschkuehl, Shah, & Jonides, 2014; Whitlock, McLaughlin, & Allaire, 2012), our data suggests that baseline cognitive control performance forms an important predictor of increase in cognitive control following CCT (β = -.54, p < .01; Δ dual n-back = n-back post-training – n-back pre-training; a positive score is indicative for an increase in cognitive control following training). This suggests that participants showing less cognitive control at baseline – as indicated by worse performance on the dual n-back task – benefit most from CCT. Accordingly, we explored effects of CCT on cognitive control levels using an univariate ANCOVA with post-training dual n-back score as dependent variable and Group (CCT vs. sham) as categorical independent variable, while controlling for baseline levels of cognitive control (covariate n-back pre-training). This approach revealed a significant effect of covariate baseline cognitive control (F(1, 58) = 27.51, p < .001, η_p^2 = .32) and a marginal significant effect of Group (F(1, 58) = 3.52, p = .066, η_p^2 = .06). Post-hoc paired samples t-tests indicate that both the CCT (Pre-training: M = 0.71, SD = 0.49; Post-training: M = 1.04, SD = 0.49; t(28) = 3.39, p < .01, d = .63, 95% CI [0.13, 0.54]) and sham group (Pre-training: M = 0.62, SD = 0.58; Post-training: M = 0.79, SD = 0.55; t(31) = 2.05, p = .05, d = .36, 95% CI [0.00, 0.33]) showed a significant increase in cognitive control over time. However, independent samples t-tests indicate that whereas both groups did not differ at baseline (t(59) = 0.66, p = .51, d = .17, 95% CI [-0.18, 0.37]), the CCT group showed a tendency to perform better following training (t(59) = 1.94, p = .057, d = .48, 95% CI [-0.01, 0.53]); see Figure 2).

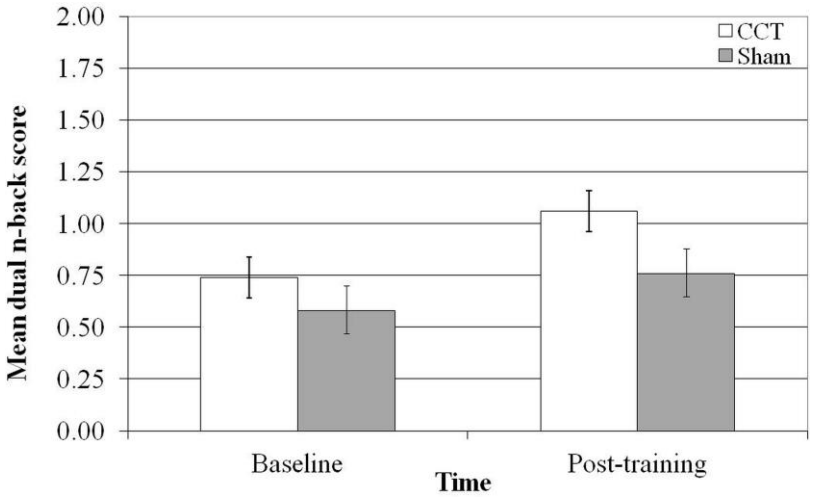


Figure 2. Increase in cognitive control (*M* & *SE*).

Positive reappraisal ability. Participants were instructed to recall a negative autobiographical memory[4], which was rated on vividness. An independent *t*-test indicates that both groups did not differ in vividness of recalled negative memory (CCT: *M* = 77.42, *SD* = 19.45; sham: *M* = 82.72, *SD* = 20.16), *t*(59) = 1.04, *p* = .30, *d* = .27, 95% CI [-4.87, 15.47]. Participants were then instructed to reappraise and rate the ease of this process. In contrast to our hypothesis, both groups did not differ concerning experienced ease of positive reappraisal (CCT: *M* = 57.10, *SD* = 23.90; sham: *M* = 53.49, *SD* = 27.26), *t*(59) = 0.55, *p* = .59, *d* = .14, 95% CI [-9.59, 16.81]. The recalled negative autobiographical memory was rated preceding and following instructed reappraisal on the extent to which it was experienced as being negative, positive, and arousal eliciting.

[4] Participants also rated mood preceding (VAS1) and following (VAS2) the recall of a negative autobiographical memory, as well as following positive reappraisal (VAS3; see Table 4 for descriptives). Effects of recalling a negative autobiographical memory on positive and negative affect were assessed using two 2 (Time: VAS1 vs. VAS2) x 2 (Group: CCT vs. sham) Mixed ANOVA's. Following the recall of a negative autobiographical memory, both groups showed a decrease in positive affect as shown by a main effect of Time ($F(1, 59) = 52.57$, $p < .001$, $\eta_p^2 = .47$; all other *F*s < 0.93). For ratings of negative affect, a Mixed ANOVA revealed a general increase in negative affect ($F(1, 59) = 43.58$, $p < .001$, $\eta_p^2 = .43$; all other *F*s < 0.11). Similarly, we used two 2 (Time: VAS2 vs. VAS3) x 2 (Group CCT vs. sham) Mixed ANOVA's to assess effects of positive reappraisal of a negative memory on positive and negative affect. This revealed a general increase in positive affect following reappraisal ($F(1, 59) = 63.64$, $p < .001$, $\eta_p^2 = .52$; all other *F*s < 2.34) as well as a general decrease in negative affect ($F(1, 59) = 41.50$, $p < .001$, $\eta_p^2 = .41$; all other *F*s < 0.58).

Three Mixed 2 (Time: pre-reappraisal vs. post-reappraisal) x 2 (Group: CCT vs. sham) ANOVA's revealed a main effect of Time for each of the three analyses, indicating that the negative autobiographical memory of the situation was rated as being less negative ($F(1, 59) = 92.44$, $p < .001$, $\eta_p^2 = .61$), more positive ($F(1, 59) = 86.70$, $p < .001$, $\eta_p^2 = .60$), and less arousal eliciting ($F(1, 59) = 75.01$, $p < .001$, $\eta_p^2 = .56$) following instructed positive reappraisal. However, in contrast to our expectations we did not find effects of Group or significant Time x Group interactions (all *F*s < 1.83; see Table 4 for descriptives).[5]

Table 4

Visual analogue scale ratings throughout the reappraisal procedure

	Training condition			
	Cognitive control (*n* = 29)		Sham (*n* = 32)	
	M	*SD*	*M*	*SD*
Mood ratings				
Positive affect 1	57.05	17.89	52.96	16.95
Negative affect 1	21.70	17.39	19.96	13.96
Positive affect 2	41.91	18.65	37.80	20.14
Negative affect 2	35.97	21.82	35.68	18.43
Positive affect 3	52.12	18.40	52.85	17.39
Negative affect 3	25.85	20.87	22.86	16.95
Situation ratings				
Negativity 1	77.02	18.88	77.49	15.08
Positivity 1	12.50	13.36	17.22	18.50
Arousal 1	75.33	22.33	66.89	27.44
Negativity 2	49.67	24.14	47.78	23.27
Positivity 2	44.10	24.71	44.53	24.68
Arousal 2	51.76	24.88	43.90	27.70

[5] Controlling for changes in positive (Δ positive affect during recall = positive affect VAS1 – positive affect VAS 2; Δ positive affect during reappraisal = positive affect VAS2 – positive affect VAS 3; a positive score is indicative for a decrease in positive affect) and negative affect (Δ negative affect during recall = negative affect VAS1 – negative affect VAS 2; Δ negative affect during reappraisal = negative affect VAS2 – negative affect VAS3; a negative score is indicative for an increase in negative affect) following recall of the negative memory did not influence these null-findings, neither did controlling for vividness of the negative autobiographical memory.

Deployment and efficacy of emotion regulation in daily life. Participants responded to 87.73% of the daily assessments of affect and emotion regulation, with an average latency of 4 min 58 sec.[6] To examine *deployment* of rumination and positive appraisal in daily life in response to positive and negative affective states, we used a multilevel regression modeling approach. At level 1, we modeled how affect at time t-1 in individual j, denoted below as $X_{t-1,j}$, predicted the emotion regulation strategy (i.e., the extent to which participants engaged in rumination or positive appraisal since the previous signal) at time t in individual j, denoted as Y_{tj}:

$$Y_{tj} = \beta_{0j} + \beta_{1j} X_{t-1,j} + e_{ij}$$

To disentangle the within-subject effect from the between-subject effect, subject-centered predictors were used (Bolger & Laurenceau, 2013). At level 2, we modeled how the subject-specific intercept and slope were a function of training (CCT or sham) that participant j received:

$$\beta_{0j} = \gamma_{00} + \gamma_{01} CCT_j + b_{0j}$$
$$\beta_{1j} = \gamma_{10} + \gamma_{11} CCT_j + b_{1j}$$

A bivariate normal distribution was assumed for the random effects b_{0j} and b_{1j}, with an unstructured covariance, and a multivariate normal distribution for the residuals e_{ij} with an autoregressive AR(1) structure to account for the temporal correlation within an individual. Such multilevel model was fitted separately for every combination of affect (positive/negative) and emotion regulation strategy (rumination/positive appraisal). The estimated parameters of interest γ_{10} and γ_{11} are

[6] Participants from the CCT group (*n* = 29) responded to 87% of the SurveySignal messages via their smartphones. In total, 86% of all sent signals were followed by completion of the questionnaire within the specified time-frame for the CCT condition. Participants of the active control condition (*n* = 32) showed similar response- and questionnaire completion rates: they responded to 88% of the signals, providing all necessary data in most of the cases (87%). On average, participants of the active control condition provided a response 4 min 51 sec (*SD* = 1 min 52 sec) after the text message was sent, whereas this was 5 min 14 sec (*SD* = 1 min 25 sec) for the CCT condition. Importantly, both groups did not significantly differ concerning mean response time as indicated by an independent samples *t*-test, $t(57.18) = 0.93$, $p = .35$.

presented in Table 5. We found a significant positive association between negative affect and rumination (γ_{10} = 0.18, *SE* = 0.06, *p* < .01). That is, higher levels of negative affect within a subject reported at time t-1 were associated with higher rumination reported at time t. Similarly, we found a negative association between positive affect and rumination (γ_{10} = -0.13, *SE* = 0.03, *p* = .001): higher levels of positive affect within a subject reported at time t-1 were associated with lower rumination reported at time t. There was a marginal significant effect of Group for the negative association between positive affect and rumination (γ11 = 0.09, *SE* = 0.05, *p* = .06). For the sham training group lower levels of positive affect were related to a stronger engagement in subsequent ruminative thinking (*β* = -.13), whereas levels of positive affect were less predictive for rumination in the CCT condition (*β* = -.04). None of the other associations were significantly different between both training groups (all *p*s > .73).

Table 5

Deployment of rumination and appraisal in response to positive and negative affect

	γ_{10} *[95% CI]*	*SE*	*t*	γ_{11} *[95% CI]*	*SE*	*t*
NA → Rumination	0.18 [0.07,0.29]	0.06	3.23**	-0.03 [-0.18,0.13]	0.09	-0.35
NA → Appraisal	0.05 [-0.07,0.17]	0.06	0.90	0.03 [-0.14,0.19]	0.09	0.30
PA → Rumination	-0.13 [-0.19,-0.06]	0.03	-3.97***	0.09 [-0.01,0.18]	0.05	1.86
PA → Appraisal	0.07 [-0.03,0.17]	0.05	1.40	-0.02 [-0.16,0.13]	0.07	-0.22

Note: NA = negative affect, PA = positive affect; * = *p* < .05, ** = *p* < .01, and *** = *p* < .001

Next, to examine the extent to which use of the emotion regulation strategy reported at time t-1 was associated with change in affect from time t-1 to time t (i.e., *efficacy*), we again used multilevel modeling. At level 1, we modeled how affect at time t (denoted as Y_{tj}) was predicted by using an emotion regulation strategy at time t-1 (denoted as $X_{t-1,j}$), while controlling for the affect at time t-1 (denoted as $Y_{t-1,j}$), i.e.:

$$Y_{tj} = \beta_{0j} + \beta_{1j} X_{t-1,j} + \beta_{2j} Y_{t-1,j} + e_{ij}$$

while at level 2 we again modeled those intercepts and slopes as a function of training:

$$\beta_{0j} = \gamma_{00} + \gamma_{01}\, CCT_j + b_{0j}$$

$$\beta_{1j} = \gamma_{10} + \gamma_{11}\, CCT_j + b_{1j}$$

$$\beta_{2j} = \gamma_{20} + \gamma_{21}\, CCT_j + b_{2j}$$

The estimated parameters of interest γ_{10} and γ_{11} are presented in Table 6. We found a significant positive association between rumination and negative affect (γ_{10} = 0.22, *SE* = 0.03, $p < .001$). That is, higher levels of rumination within a subject reported at time t-1 were associated with higher negative affect reported at time t, after controlling for negative affect at time t-1. Similarly, we found a negative association between positive appraisal and negative affect (γ_{10} = -0.09, *SE* = 0.03, $p < .01$), a negative association between rumination and positive affect (γ_{10} = -0.17, *SE* = 0.04, $p < .001$), and a positive association between positive appraisal and positive affect (γ_{10} = 0.21, *SE* = 0.03, $p < .001$); each time controlling for the affect reported at time t-1. None of these associations were significantly different between both training groups (all *p*s > .13).

Table 6
Efficacy of rumination and appraisal

	γ_{10} *[95% CI]*	*SE*	*T*	γ_{11} *[95% CI]*	*SE*	*t*
Rumination → NA	0.22 [0.15,0.28]	0.03	6.41***	0.07 [-0.02,0.17]	0.05	1.50
Appraisal → NA	-0.09 [-0.14,-0.03]	0.03	-3.03**	-0.05 [-0.13,0.03]	0.05	1.14
Rumination → PA	-0.17 [-0.24,-0.09]	0.04	-4.59***	-0.02 [-0.13,0.08]	0.05	-0.39
Appraisal → PA	0.21 [0.15,0.27]	0.03	6.88***	0.01 [-0.08,0.10]	0.04	0.82

Note: NA = negative affect, PA = positive affect; * = $p < .05$, ** = $p < .01$, and *** = $p < .001$

DISCUSSION

Previous studies indicate the importance of cognitive control for emotion regulation processes. The aims of the current study were twofold: (1) we examined the relationship between cognitive control and self-reported emotion regulation cross-

sectionally, and (2) we examined effects of CCT on reappraisal ability and emotion regulation processes in daily life (i.e., deployment and efficacy of rumination and positive appraisal) to further unravel the causal role of cognitive control in emotion regulation. Given the proposed role of adaptive emotion regulation in resilience and mental well-being, we set out to explore whether CCT holds potential in increasing resilience in a convenience sample.

First, the cross-sectional findings indicate a positive association between baseline cognitive control and adaptive emotion regulation strategies assessed using self-report questionnaires at baseline. Moreover, maladaptive emotion regulation strategies show a negative association with baseline cognitive control. These findings are in line with theoretical frameworks concerning the role of cognitive control in emotion regulation (Joormann & D'Avanzato, 2010; Joormann & Vanderlind, 2014), suggesting that impaired cognitive control does not merely increase the use of maladaptive emotion regulation strategies, but are also related to reduced resilience via decreased use of adaptive emotion regulation strategies. However, these cross-sectional findings do not allow to draw conclusions on the causal nature of this relation. Accordingly, a second aim of this study was to explore effects of a cognitive control manipulation – using CCT that has previously shown to be effective in reducing rumination and depressive symptomatology in at-risk undergraduates (e.g., Hoorelbeke, Koster, et al., 2015) and clinically depressed samples (e.g., Siegle et al., 2007) – on reappraisal ability in lab context and emotion regulation in daily life. For this purpose, effects of CCT were compared to an active control training.

Throughout 10 online training sessions both groups showed a significant increase in training task performance. Importantly, compared to the active control group, participants in the CCT group performed marginally significant better on the dual n-back task following training. This transfer effect indicates that CCT was successful in improving working memory functioning, but only when baseline characteristics in cognitive control ability were controlled for. It should be noted that specific sample characteristics in combination with the operationalization of our active control condition (an attention training) could have limited this transfer effect. That is, previous studies have typically explored effects of adaptive PASAT training in at-risk

undergraduate students or clinically depressed patient samples. In contrast, the current study explored effects of CCT in an *unselected* undergraduate student sample in order to explore the potential of CCT in increasing predictors of resilience and mental well-being in general (i.e., adaptive emotion regulation). However, at-risk samples and patient samples are known to show lower levels of cognitive control compared to healthy populations (e.g., Beckwé, Deroost, Koster, De Lissnyder, & De Raedt, 2014; Joormann, 2004), and ceiling effects could pose a problem when demonstrating transfer to cognitive tasks in undergraduate student samples (Hoorelbeke, Koster, et al., 2015; Onraedt & Koster, 2014). Indeed, our findings suggest that it is important to take into account individual differences in baseline cognitive control when exploring transfer effects of CCT on cognitive tasks in an unselected student population. That is, lower baseline cognitive control was related to a stronger increase in cognitive control throughout CCT.

Although our findings suggest that CCT can be used to increase cognitive control in unselected undergraduate students, this did not affect adaptive emotion regulation processes. After training, groups did not differ in self-reported experienced ease of reappraising a negative autobiographical memory in a lab context, nor did CCT influence the effects of this instructed reappraisal exercise on emotional ratings of the situation. This finding might be due to demand effects, given that both groups were explicitly instructed to positively reappraise the situation. However, both groups also did not report differential effects of the reappraisal exercise on affective state. Second, on our daily life measures, deployment of positive appraisal predicted a general increase in positive affect and a reduction in negative affect, indicating the importance of adaptive emotion regulation strategies for mental well-being. However, both training groups did not significantly differ in the deployment and efficacy of positive appraisal in daily life. Thus, CCT targeting working memory functioning – at least in its current operationalization and this specific population – did not increase resilience and mental well-being via stimulating the deployment, ability and efficacy of positive (re-)appraisal.

In contrast to the null-findings for adaptive emotion regulation, CCT did exert a small effect on maladaptive emotion regulation in this population, which was observed at the level of deployment of rumination in response to reduced positive affect. That is,

participants of the sham group showed a stronger tendency to respond with rumination to low levels of positive affect, whereas levels of positive affect were less predictive for future rumination in the CCT group. This seems to indicate that increasing cognitive control might serve to prevent further mood deterioration when experiencing lower levels of positive affect given that – in line with the Response Styles Theory of depression (Nolen-Hoeksema & Morrow, 1991) and previous ESM studies (e.g., Brans, Koval, Verduyn, Lim, & Kuppens, 2013) – our ESM efficacy measures indicate that rumination has detrimental effects on affect. That is, rumination predicts higher future levels of negative affect and reduced positive affect. This process might elucidate previous findings in at-risk undergraduate students showing a buffering effect of CCT compared to a sham training on positive and negative thought processes following a general decline in positive affect during a stress induction procedure (Hoorelbeke, Koster, et al., 2015). In this light, the latter could then have resulted in further increased negative affect in the sham condition compared to the CCT.

In line with the literature, the effects observed in this study thus demonstrate that: (1) Cognitive control shows a positive association with adaptive emotion regulation and a negative association with maladaptive emotion regulation strategies, linking cognitive control impairments to increased vulnerability for depression and reduced resilience; (2) Cognitive control can be trained by performing an adaptive and engaging computer task as indicated by transfer to another measure of working memory functioning; (3) Inducing cognitive control lowers participants' risk to respond with rumination when experiencing low levels of positive affect, which is in line with previous work in at-risk and MDD patient samples indicating that CCT shows potential as a preventive intervention for depression (Hoorelbeke, Koster, et al., 2015; Siegle et al., 2014); and (4) Overall effects were limited and did not show transfer to deployment, ability, or efficacy of adaptive emotion regulation.

The current findings of divergent effects of CCT on adaptive versus maladaptive emotion regulation could indicate that cognitive control plays a stronger role in maladaptive emotion regulation compared with adaptive emotion regulation. Cognitive control is crucial to efficient working memory functioning, where a lack of cognitive control places one at risk to persevere in habitual maladaptive strategies. However, it is

possible that in absence of these habitual maladaptive processes, cognitive control plays a less determining role in adaptive emotion regulation in daily life. As a result, where cognitive control impairments have shown to disrupt healthy emotion regulation, it could be that in healthy functioning individuals stimulating cognitive control does not improve emotion regulation. This is in line with findings suggesting that difficulties with reappraisal are only present in severely depressed patients (e.g., Dillon & Pizzagalli, 2013) and may imply that CCT does not increase resilience or well-being through adaptive emotion regulation in samples that are not characterized by cognitive control deficits. Furthermore, context specific features may also influence the extent to which certain adaptive emotion regulation strategies rely on cognitive control processes (e.g., stressful situations). An alternative explanation is that, although increased working memory functioning may contribute to adaptive emotion regulation, a brief training period may not be sufficient to demonstrate immediate effects on deployment and efficacy of adaptive emotion regulation strategies in daily life. That is, in order to overcome habitual use of emotion regulation strategies (i.e., following years of reinforcement of deployment of emotion regulation strategies), more extensive training might be necessary, possibly combined with additional interventions targeting emotion regulation to stimulate cognitive change. Given the impact of psychopathology on cognitive development (e.g., Vijayakumar et al., 2016), this might especially be the case in populations experiencing early onset of depressive symptoms.

Our study is the first to combine CCT with ESM, allowing to explore effects of CCT on emotion regulation processes in daily life, adding to the ecological validity of our findings. This combination offers an important advantage as it provides insights in the potential mechanisms underlying the relation between cognitive control, emotion regulation, and affect. Furthermore, to our knowledge this study is the first to explore effects of a multisession CCT targeting working memory functioning on adaptive as well as maladaptive emotion regulation strategies, extending previous findings. Related to adaptive emotion regulation processes, an important feature of this study is its aim to explore the effectiveness of CCT as an intervention to increase functioning and well-being in a general (student) population, whereas previous work has typically focused on

emotional dysfunctioning, either from a preventive (Hoorelbeke, Koster, et al., 2015) or a curative stance (e.g., Siegle et al., 2014).

However, several limitations should be noted. First, we experienced substantial drop-out. Although the excluded participants did not significantly differ from the included participants concerning our main variables of interest, small baseline group differences occurred for depressive symptomatology and catastrophizing, providing a potential source of sampling bias. Furthermore, given the importance of task engagement for training outcome (Siegle et al., 2014), future studies should invest in methods that might increase training retention (e.g., Hoorelbeke, Faelens, Behiels, & Koster, 2015). Second, positive reappraisal ability was assessed using a structured pen and paper procedure. This might have reduced the extent to which the reappraisal exercise placed demands on cognitive control processes. Furthermore, given that this study included healthy participants and the time to reappraise was not measured, we think the absence of a group difference could be attributed to a ceiling effect with all participants being able to reappraise. Third, we did not include a pre-training ESM period which does not allow to compare pre- and post-training differences in emotion regulation processes. Instead, we relied on emotion regulation questionnaires at baseline, indicating no significant group differences. Fourth, effects reported in this study are constricted to a seven-day period following training. Finally, sample size was limited and, given the exploratory nature of the paper, we did not consider any multiple testing corrections. This may have led to an increase in the number of false positives, but minimizes the risk of missing true effects. Nonetheless, careful interpretation of our findings is warranted, as this study represents a first step that should be replicated using larger samples.

Our study paves an interesting way forward. Future studies should go beyond exploring effects of experimental manipulations on self-report questionnaires or indicators of functioning in lab context. Moreover, future studies could extend the scope of the ESM protocol to other indicators of cognitive emotion regulation at item-level and rely on different outcome measures (other than efficacy and deployment) to assess effects of CCT on the process of emotion regulation. Furthermore, from both a positive psychological and preventive perspective, future studies should not limit their

scope to merely exploring effects of interventions on indicators of dysfunctioning given that fostering functioning could increase general well-being as well as show transdiagnostic preventive effects.

Summary

The current study explored the role of cognitive control in adaptive and maladaptive emotion regulation, testing the effectiveness of cognitive control training (CCT) in increasing resilience in a general student population. Using experience sampling method, effects of a multisession CCT on adaptive and maladaptive emotion regulation were compared with an active control condition. Baseline cognitive control showed a positive association with self-reported use of adaptive emotion regulation strategies and a negative association with maladaptive emotion regulation strategies. Although CCT showed transfer to working memory functioning, we did not find transfer effects to a lab assessment of positive reappraisal ability, nor to deployment or efficacy of positive appraisal in daily life. Therefore, in contrast to previous studies in at-risk or clinical populations, CCT did not increase resilience in an unselected student population. Concerning maladaptive emotion regulation, we found a buffering effect of training on deployment of rumination in response to low levels of positive affect.

ACKNOWLEDGMENTS

We are grateful to Jana Stassen for providing practical aid during the stage of data collection. We are also grateful to Reitske Meganck and Petra Warreyn for their input concerning analysis of qualitative data collected during the positive reappraisal exercise in the lab. This research was supported by a Special Research Fund (BOF) of Ghent University awarded to Kristof Hoorelbeke (B/13808/01).

REFERENCES

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for Beck Depression Inventory II*. San Antonio, Texas: Psychological Corporation.

Beckwé, M., Deroost, N., Koster, E. H. W., De Lissnyder, E., & De Raedt, R. (2014). Worrying and rumination are both associated with reduced cognitive control. *Psychological Research, 78*, 651-660. doi: 10.1007/s00426-013-0517-5

Bolger, N., & Laurenceau, J.-P. (2013). *Intensive longitudinal methods: An introduction to diary and experience sampling research*. New York: Guilford Press.

Bollen, K. A., & Jackman, R. W. (1990). Regression diagnostics: An expository treatment of outliers and influential cases. In J. Fox & J. S. Long (Eds.), *Modern methods of data analysis* (pp. 257-291). Newbury Park, CA: Sage.

Brans, K., Koval, P., Verduyn, P., Lim, Y. L., & Kuppens, P. (2013). The regulation of negative and positive affect in daily life. *Emotion, 13*, 926-939. doi: 10.1037/a0032400

Brunoni, A. R., Boggio, P. S., De Raedt, R., Bensenor, I. M., Lotufo, P. A., Namur, V., . . . Vanderhasselt, M. A. (2014). Cognitive control therapy and transcranial direct current stimulation for depression: A randomized, double-blinded, controlled trial. *Journal of Affective Disorders, 162*, 43-49. doi: 10.1016/j.jad.2014.03.026

Buhle, J. T., Silvers, J. A., Wager, T. D., Lopez, R., Onyemekwu, C., Kober, H., . . . Ochsner, K. N. (2014). Cognitive reappraisal of emotion: A meta-analysis of human neuroimaging studies. *Cerebral Cortex, 24*, 2981-2990. doi: 10.1093/cercor/bht154

Calkins, A. W., McMorran, K. E., Siegle, G. J., & Otto, M. W. (2015). The effects of computerized cognitive control training on community adults with depressed mood. *Behavioural and Cognitive Psychotherapy, 39*, 205-220. doi: 10.1017/S1352465814000046

D'Avanzato, C., Joormann, J., Siemer, M., & Gotlib, I. H. (2013). Emotion regulation in depression and anxiety: Examining diagnostic specificity and stability of strategy use. *Cognitive Therapy and Research, 37*, 968-980. doi: 10.1007/s10608-013-9537-0

De Lissnyder, E., Koster, E. H. W., Goubert, L., Onraedt, T., Vanderhasselt, M. A., & De Raedt, R. (2012). Cognitive control moderates the association between stress and rumination. *Journal of Behavior Therapy and Experimental Psychiatry, 43*, 519-525. doi: 10.1016/j.jbtep.2011.07.004

Demeyer, I., De Lissnyder, E., Koster, E. H. W., & De Raedt, R. (2012). Rumination mediates the relationship between impaired cognitive control for emotional information and depressive symptoms: A prospective study in remitted depressed adults. *Behaviour Research and Therapy, 50*, 292-297. doi: 10.1016/j.brat.2012.02.012

Dillon, D. G., & Pizzagalli, D. A. (2013). Evidence of successful modulation of brain activation and subjective experience during reappraisal of negative emotion in unmedicated depression. *Psychiatry Research, 212*, 99-107. doi: 10.1016/j.pscychresns.2013.01.001

Engelen, U., De Peuter, S., Victoir, A., Van Diest, I., & Van den Bergh, O. (2006). Verdere validering van de Positive and Negative Affect Schedule (PANAS) en vergelijking van twee Nederlandstalige versies. *Psychologie en Gezondheid, 34*, 89-102.

Feldman, G. C., Joormann, J., & Johnson, S. L. (2008). Responses to positive affect: A self-report measure of rumination and dampening. *Cognitive Therapy and Research, 32*, 507-525.

Garnefski, N., Kraaij, V., & Spinhoven, P. (2001). Negative life events, cognitive emotion regulation and emotional problems. *Personality and Individual Differences, 30*, 1311-1327.

Gronwall, D. (1977). Paced Auditory Serial-Addition Task: A measure of recovery from concussion. *Perceptual and Motor Skills, 44*, 367-373.

Gross, J. J. (1998). The emerging field of emotion regulation: An integrative review. *Review of General Psychology, 2*, 271 - 299. doi: 1089-2680/98/$3.00

Gross, J. J. (2002). Emotion regulation: Affective, cognitive, and social consequences. *Psychophysiology, 39*, 281-291. doi: 10.1017.S0048577201393198

Gross, J. J., & Jazaieri, H. (2014). Emotion, emotion regulation, and psychopathology: An affective science perspective. *Clinical Psychological Science, 2*, 387-401. doi: 10.1177/2167702614536164

Gross, J. J., & John, O. P. (2003). Individual differences in two emotion regulation processes: Implications for affect, relationships, and well-being. *Journal of Personality and Social Psychology, 85*, 348-362. doi: 10.1037/0022-3514.85.2.348

Haga, S. M., Kraft, P., & Corby, E. K. (2009). Emotion regulation: Antecedents and well-being outcomes of cognitive reappraisal and expressive suppression in cross-cultural samples. *Journal of Happiness Studies, 10*, 271-291. doi: 10.1007/s10902-007-9080-3

Hajcak, G., MacNamara, A., & Olvet, D. M. (2010). Event-Related Potentials, emotion, and emotion regulation: An integrative review. *Developmental Neuropsychology, 35*, 129-155. doi: 10.1080/87565640903526504

Hofmann, W., & Patel, P. V. (2015). SurveySignal: A convenient solution for experience sampling research using participants' own smartphones. *Social Science Computer Review, 33*, 235-253. doi: 10.1177/0894439314525117

Holland, A. C., & Kensinger, E. A. (2013). The neural correlates of cognitive reappraisal during emotional autobiographical memory recall. *Journal of Cognitive Neuroscience, 25*, 87-108.

Hoorelbeke, K., Faelens, L., Behiels, J., & Koster, E. H. W. (2015). Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Protocol for a randomized controlled trial. *Bmc Psychiatry, 15.* doi: 10.1186/s12888-015-0511-0

Hoorelbeke, K., Koster, E. H. W., Vanderhasselt, M. A., Callewaert, S., & Demeyer, I. (2015). The influence of cognitive control training on stress reactivity and rumination in response to a lab stressor and naturalistic stress. *Behaviour Research and Therapy, 69*, 1-10.

Hu, T. Q., Zhang, D. J., Wang, J. L., Mistry, R., Ran, G. M., & Wang, X. Q. (2014). Relation between emotion regulation and mental health: A meta-analysis review. *Psychological Reports, 114*, 341-362. doi: 10.2466/03.20.PR0.114k22w4

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Perrig, W. J. (2008). Improving fluid intelligence with training on working memory. *Proceedings of the National Academy of Sciences of the United States of America, 105*, 6829-6833. doi: 10.1073/pnas.0801268105

Jaeggi, S. M., Buschkuehl, M., Shah, P., & Jonides, J. (2014). The role of individual differences in cognitive training and transfer. *Memory & Cognition, 42*, 464-480. doi: 10.3758/s13421-013-0364-z

Jaeggi, S. M., Studer-Luethi, B., Buschkuehl, M., Su, Y. F., Jonides, J., & Perrig, W. J. (2010). The relationship between n-back performance and matrix reasoning - Implications for training and transfer. *Intelligence, 38*, 625-635. doi: 10.1016/j.intell.2010.09.001

Joormann, J. (2004). Attentional bias in dysphoria: The role of inhibitory processes. *Cognition & Emotion, 18*, 125-147. doi: 10.1080/02699930244000480

Joormann, J. (2006). Differential effects of rumination and dysphoria on the inhibition of irrelevant emotional material: Evidence from a Negative Priming Task. *Cognitive Therapy and Research, 30*, 149-160. doi: 10.1007/s10608-006-9035-8

Joormann, J., & D'Avanzato, C. (2010). Emotion regulation in depression: Examining the role of cognitive processes. *2010, 24*, 913-939. doi: 10.1080/02699931003784939

Joormann, J., & Gotlib, I. H. (2008). Updating the contents of working memory in depression: Interference from irrelevant negative material. *Journal of Abnormal Psychology, 117*, 182-192. doi: 10.1037/0021-843x.117.1.182

Joormann, J., & Vanderlind, M. W. (2014). Emotion regulation in depression: The role of biased cognition and reduced cognitive control. *Clinical Psychological Science, 2*, 402-421. doi: 10.1177/2167702614536163

Kalisch, R., Müller, M. B., & Tüscher, O. (2015). A conceptual framework for the neurobiological study of resilience. *Behavioral and Brain Sciences, 38*, 1-79. doi: 10.1017/S0140525X1400082X, e0

Kross, E., Davidson, M., Weber, J., & Ochsner, K. (2009). Coping with emotions past: The neural bases of regulating affect associated with negative autobiographical memories. *Biological Psychiatry, 65*, 361-366.

Larson, R., & Csikszentmihalyi, M. (1983). The experience sampling method. *New Directions for Methodology of Social and Behavioral Science, 15*, 41-56.

McNair, D. M., Lorr, M., & Droppleman, L. F. (1992). *Manual: Profile of Mood States Revised*. San Diego, CA: Educational and Industrial Testing Service.

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24*, 167-202.

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive Psychology, 41*, 49-100. doi: 10.1006/cogp.1999.0734

Moberly, N. J., & Watkins, E. R. (2008). Ruminative self-focus and negative affect: An experience sampling study. *Journal of Abnormal Psychology, 117*, 314-323. doi: 10.1037/0021-843X.117.2.314

Moser, J. S., Hartwig, R., Moran, T. P., Jendrusina, A. A., & Kross, E. (2014). Neural markers of positive reappraisal and their associations with trait reappraisal and worry. *Journal of Abnormal Psychology, 123*, 91-105. doi: 10.1037/a0035817

Nolen-Hoeksema, S., & Morrow, J. (1991). A prospective study of depression and posttraumatic stress symptoms after a natural disaster - The 1989 Loma-Prieta earthquake. *Journal of Personality and Social Psychology, 61*, 115-121. doi: 10.1037/0022-3514.61.1.115

Nolen-Hoeksema, S., Wisco, B. E., & Lyubomirsky, S. (2008). Rethinking rumination. *Perspectives on Psychological Science, 3*, 400-424. doi: 10.1111/j.1745-6924.2008.00088.x

Ochsner, K. N., Bunge, S. A., Gross, J. J., & Gabrieli, J. D. E. (2002). Rethinking feelings: An fMRI study of the cognitive regulation of emotion. *Journal of Cognitive Neuroscience, 14*, 1215-1229. doi: 10.1162/089892902760807212

Onraedt, T., & Koster, E. H. W. (2014). Training working memory to reduce rumination. *Plos One, 9*, 12. doi: 10.1371/journal.pone.0090632

Pe, M. L., Raes, F., Koval, P., Brans, K., Verduyn, P., & Kuppens, P. (2013). Interference resolution moderates the impact of rumination and reappraisal on affective experiences in daily life. *Cognition & Emotion, 27*, 492-501. doi: 10.1080/02699931.2012.719489

Pe, M. L., Raes, F., & Kuppens, P. (2013). The cognitive building blocks of emotion regulation: Ability to update working memory moderates the efficacy of rumination and reappraisal on emotion. *Plos One, 8*, 12. doi: 10.1371/journal.pone.0069071

Portzky, M. (2008). *RS-nl: Resilience Scale - Nederlandse versie*. Amsterdam: Harcourt Test Publishers.

Raes, F., Daems, K., Feldman, G. C., Johnson, S. L., & Van Gucht, D. (2009). A psychometric evaluation of the Dutch version of the Response to Positive Affect Questionnaire. *Psychologica Belgica, 49*, 293-310. doi: 10.5334/pb-49-4-293

Rossi, V., & Pourtois, G. (2012). State-dependent attention modulation of human primary visual cortex: A high density ERP study. *Neuroimage, 60*, 2365-2378. doi: 10.1016/j.neuroimage.2012.02.007

Siegle, G. J., Ghinassi, F., & Thase, M. E. (2007). Neurobehavioral therapies in the 21st century: Summary of an emerging field and an extended example of cognitive control training for depression. *Cognitive Therapy and Research, 31*, 235-262. doi: 10.1007/s10608-006-9118-6

Siegle, G. J., Price, R. B., Jones, N. P., Ghinassi, F., Painter, T., & Thase, M. E. (2014). You gotta work at it: Pupillary indices of task focus are prognostic for response to a neurocognitive intervention for rumination in depression. *Clinical Psychological Science, 2*, 455-471. doi: 10.1177/2167702614536160

Treynor, W., Gonzalez, R., & Nolen-Hoeksema, S. (2003). Rumination reconsidered: A psychometric analysis. *Cognitive Therapy and Research, 27*, 247-259.

Van der Does, A. J. W. (2002). *BDI-II-NL. Handleiding: De Nederlandse versie van de Beck Depression Inventory - 2nd edition*. Lisse: Harcourt Test Publishers.

Vanderhasselt, M.-A., De Raedt, R., Namur, V., Lotufo, P. A., Bensenor, I. M., Boggio, P. S., & Brunoni, A. R. (2015). Transcranial electric stimulation and neurocognitive training in clinically depressed patients: A pilot study of the effects on rumination. *Prog Neuropsychopharmacol Biol Psychiatry, 57*, 93-99. doi: 10.1016/j.pnpbp.2014.09.015

Vanderhasselt, M.-A., Koster, E. H. W., Onraedt, T., Bruyneel, L., Goubert, L., & De Raedt, R. (2014). Adaptive cognitive emotion regulation moderates the relationship between dysfunctional attitudes and depressive symptoms during a stressful life period: A prospective study. *Journal of Behavior Therapy and Experimental Psychiatry, 45*, 291-296. doi: 10.1016/j.jbtep.2014.01.003

Vijayakumar, N., Whittle, S., Yücel, M., Byrne, M. L., Schwartz, O., Simmons, J. G., & Allen, N. B. (2016). Impaired maturation of cognitive control in adolescents who

develop major depressive disorder. *Journal of Clinical Child & Adolescent Psychology*, *45*, 31–43. doi: 10.1080/15374416.2014.987381

Wagnild, G. M., & Young, H. M. (1993). Development and psychometric evaluation of the resilience scale. *Journal of Nursing Measurement, 1*, 165-178.

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *Journal of Personality and Social Psychology, 54*, 1063-1070.

Wheeler, M. A., Stuss, D. T., & Tulving, E. (1997). Toward a theory of episodic memory: The frontal lobes and autonoetic consciousness. *Psychological Bulletin, 121*, 331-354.

Whitlock, L. A., McLaughlin, A. C., & Allaire, J. C. (2012). Individual differences in response to cognitive training: Using a multi-modal, attentionally demanding game-based intervention for older adults. *Computers in Human Behavior, 28*, 1091-1096. doi: 10.1016/j.chb.2012.01.012

Zetsche, U., & Joormann, J. (2011). Components of interference control predict depressive symptoms and rumination cross-sectionally and at six months follow-up. *Journal of Behavior Therapy and Experimental Psychiatry, 42*, 65-73. doi: 10.1016/j.jbtep.2010.06.001

CHAPTER 5

INTERNET-DELIVERED COGNITIVE CONTROL TRAINING AS A PREVENTIVE INTERVENTION FOR REMITTED DEPRESSED PATIENTS: PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL[1]

ABSTRACT

This chapter presents the protocol of a pre-registered study that aims to test the effectiveness of cognitive control training as a preventive intervention in a remitted depressed sample. We present a double blind randomized controlled design. Remitted depressed adults will complete 10 online sessions of a cognitive control training targeting working memory functioning or a low cognitive load training (active control condition) over a period of 14 days. Effects of training on primary outcome measures of rumination and depressive symptomatology will be assessed pre-post training and at three months follow-up, along with secondary outcome measure adaptive emotion regulation. Long-term effects of cognitive control training on broader indicators of functioning will be assessed at three months follow-up (secondary outcome measures). This study will provide information about the effectiveness of cognitive control training for remitted depressed adults in reducing vulnerability for depression. Furthermore, this study will address key questions concerning the mechanisms underlying the effects of cognitive control training, will take into account the subjective experience of the patients (including a self-report measure for cognitive functioning), and explore whether these effects extend to broad measures of functioning such as Quality of Life and disability.

Trial registration: This study is registered with ClinicalTrials.Gov, number NCT02407652.

[1] Based on Hoorelbeke, K., Faelens, L., Behiels, J., & Koster, E.H.W. (2015). Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Protocol for a randomized controlled trial. *BMC Psychiatry, 9*, 15:125. doi: 10.1186/s12888-015-0511-0

Improving the effectiveness of psychotherapeutic interventions for depression forms an important challenge for depression research. That is, patients who initially respond successful to therapy, often show residual symptoms which increases the chance of recurrence of depressive episodes. Moreover, existing treatments are less effective for chronic depression (Cuijpers, Andersson, Donker, & van Straten, 2011) and not all depressive symptoms show an equal response to treatment (Millan et al., 2012). For instance, cognitive symptoms such as impaired executive- and working memory functioning and their biological substrates often remain present although the patient is considered to be in remission (e.g., Vanderhasselt & De Raedt, 2009; Xu et al., 2012). Importantly, it has been suggested that reduced cognitive functioning – i.e., impaired regulation of working memory, or 'cognitive control' – is not merely a byproduct of depression, but places remitted depressed (RMD) patients in a distinct vulnerable position for recurrence of depression (De Raedt & Koster, 2010; Gotlib & Joormann, 2010).

Indeed, the number of previous depressive episodes shows a negative correlation with behavioral indices of cognitive control (Harvey et al., 2004). Furthermore, prospective studies suggest that self-reported cognitive control impairments (Letkiewicz et al., 2014) and their behavioral indices (Zetsche & Joormann, 2011) predict the development of future depressive symptomatology. Interestingly, impaired cognitive control has typically been linked to maladaptive emotion regulation strategies such as rumination (De Lissnyder et al., 2012; Joormann & Gotlib, 2010; Zetsche & Joormann, 2011), an important cognitive vulnerability factor for depression (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). Especially brooding – a subtype of rumination that is characterized by a passive style of moody pondering – has shown to predict the occurrence of future depressive symptomatology (Treynor, Gonzalez, & Nolen-Hoeksema, 2003). Importantly, prospective studies indicate that the use of maladaptive emotion regulation strategies link impaired cognitive control to the development of future depressive symptomatology in RMD (Demeyer, De Lissnyder, Koster, & De Raedt, 2012). Thus, via maladaptive emotion regulation cognitive control impairments convey an important risk for recurrent depression (but see Aker, Harmer, & Landro, 2014). Moreover, this mechanism is believed to sustain and increase

biological and cognitive vulnerability for recurrent depression (for a review, see De Raedt & Koster, 2010).

In accordance with studies indicating plasticity of executive and working memory functioning (Klingberg, 2010), these findings have led researchers to try to remediate cognitive control impairments in depression using cognitive training tasks. In a pilot study, Siegle, Ghinassi, and Thase (2007) demonstrated that combining treatment as usual (TAU) with a cognitive control training (CCT) shows potential in reducing rumination as well as depressive symptomatology in a limited MDD sample. The CCT existed of the adaptive Paced Auditory Serial Addition Task (PASAT; Gronwall, 1977) and Well's Attention training (Wells, 2000). Furthermore, Siegle et al. (2014) have extended these findings, showing long term beneficial effects of CCT by demonstrating a reduced need for outpatient services at one year follow-up. Interestingly, whereas previous studies have demonstrated the potential of a combined CCT approach (Calkins, McMorran, Siegle, & Otto, 2015; Segrave, Arnold, Hoy, & Fitzgerald, 2014; Siegle et al., 2007, 2014), other authors have shown that the training component targeting working memory functioning (the adaptive PASAT) might suffice to reduce brooding (Vanderhasselt et al., 2015) and depressive symptomatology (Brunoni et al., 2014) in MDD patients.

These first experimental findings are in line with existing conceptual frameworks concerning the role of cognitive control and rumination in recurrent depression (De Raedt & Koster, 2010; Joormann & D'Avanzato, 2010), suggesting that by remediating cognitive control impairments, one might decrease cognitive vulnerability for future depression. Accordingly, Siegle et al. (2014) have suggested that effects of CCT on depressive symptomatology are preceded by changes in rumination. However, to date no experimental study has directly tested this mediation effect. Furthermore, previous studies have typically explored curative effects of CCT in MDD patients whereas only more recently the preventive potential of CCT has been explored in student populations. For instance, in a single session cognitive control manipulation, Cohen, Mor, and Henik (2015) have demonstrated that inducing cognitive control while processing negative information buffers against negative effects of a subsequent rumination induction procedure (i.e., state rumination, rumination-related sad mood).

Moreover, training inhibition of emotional information has shown to reduce rumination in at-risk students (Daches & Mor, 2014). Interestingly, researchers have found that the adaptive PASAT shows promise in reducing stress reactivity and rumination in response to a lab stressor directly following training and a naturalistic stressor at one month follow-up in an at-risk student sample (Hoorelbeke, Koster, Vanderhasselt, Callewaert, & Demeyer, 2015). Furthermore, decreased stress reactivity in confrontation with a lab stressor predicted lower brooding levels following confrontation with naturalistic stress (i.e., examination period). These findings suggest that CCT targeting working memory functioning shows potential as a preventive intervention for depression.

Rational for the Proposed Study

Previous studies indicate that the effects of CCT are not limited to the mere reduction of current depressive symptomatology in MDD patients, but might also extend to increasing resilience in at-risk populations. However, several theoretical gaps remain to be addressed.

First, in order to fully explore the potential of CCT targeting working memory functioning in reducing (cognitive) vulnerability for depression, a test of training effects in a RMD sample would be desirable. That is, RMD patients form a high-risk group for developing future depressive episodes (Burcusa & Iacono, 2007) and prospective studies indicate that impaired cognitive control forms an important vulnerability factor in RMD (Demeyer et al., 2012). Second, from a theoretical stance it would be interesting to explore the proposed mediational pathway from effects of CCT on rumination to reduced future depressive symptomatology. Third, with the exception of Siegle et al. (2014) who explored effects of CCT on outpatient service use, previous studies have limited their scope to exploring effects of CCT on rumination and depressive symptomatology. We aim at extending previous findings by also exploring effects of CCT on adaptive emotion regulation as well as broader indicators of (dis-)functioning such as experienced disability, experienced remission from depression, and Quality of Life. Furthermore, we are not only interested in change in behavior indices of cognitive control, but also in the clinical experience of RMD patients concerning these cognitive factors (e.g., self-report measures of executive- and working memory functioning).

Finally, in order to reduce sources of bias in exploring the potential of CCT as a preventive intervention, a rigid methodological approach – i.e., a double-blind randomized controlled trial (RCT) – is required.

METHOD

Design

We present a 2 (Condition) x 3 (Time) double blind, randomized controlled design. Adult RMD participants will be randomly allocated to either an online CCT intervention targeting working memory functioning or a low cognitive load training (active control condition). Both groups will perform 10 online training sessions over a period of 14 days, flanked by pre- and post-training lab assessments. Participants will return to the lab for a final assessment at three months follow-up (see Figure 1 for an overview of the design). This study has been approved by the local ethical committee of the Faculty of Psychology and Educational Sciences of Ghent University and was registered with ClinicalTrials.gov, number NCT02407652.

Participants

Inclusion and exclusion criteria. To be eligible for participation to this study, participants aged between 23 and 65 should report a history of depression (at least one prior depressive episode) and report stable (partial) remission (≥ 6 months). Consequently, participants should not meet criteria for a current depressive episode before starting training as assessed by the Mini-International Neuropsychiatric Interview (MINI; Sheehan et al., 1989). However, they should meet the criteria for a previous episode. The depressive episode should not have occurred in the context of a bipolar disorder. Neither should the participant report a history of psychosis, excessive substance abuse, or report experiencing cognitive impairments due to brain injury. A history of other comorbid disorders is allowed – yet these should not lead to current impairments – in order to increase the clinical relevance and validity of our study. Therapeutic maintenance contact (with a frequency less than once per three weeks) and use of antidepressant medication is allowed and will be registered. Importantly,

antidepressant medication should be kept at a constant level throughout the course of the study.

Recruitment. RMD participants will be recruited using advertisements in popular (online) magazines and newspapers as well as flyers that were placed in 106 local drugstores (Ghent area). Furthermore, drawing on an existing database, 23 potentially interested participants will be contacted based on their interest in a prior prospective study of our lab (at that point, all of these participants had given their permission to be re-contacted in case a related study was planned). After having expressed interest in this study (i.e., by phone or e-mail), participants will be contacted by phone to provide further information and to screen eligibility based on a selection of relevant questions of the MINI screening version. To screen whether participants show a history of depression, we will ask questions concerning current and previous depressive symptoms, and collect information concerning the amount of episodes and past as well as current treatment. Furthermore, we will check whether (professional or similar) activities were resumed following the last depressive episode. If the participant seems eligible and is interested in participating in the study, he or she will be invited to the lab for a structured clinical interview (MINI). In the lab, the MINI screening version will be used to check for indicators of currently present comorbid disorders and – if this proves to be necessary – will be followed by the corresponding parts of the MINI interview to allow to control for presence of comorbid disorders. The parts related to MDD will be fully assessed to assure that participants do not meet the criteria for MDD before entering the study. Meeting eligibility criteria will allow the participant to enroll in the study, starting immediately with randomization over one of both conditions and the baseline assessment.

Measures

Primary outcome measures. Rumination and depressive symptomatology form our primary outcome measures. *Rumination* will be assessed using the Ruminative Response Scale (RRS; Nolen-Hoeksema & Morrow, 1991; Treynor et al., 2003). This 22-item questionnaire provides a total rumination score (range: 22 – 88), as well as Brooding and Reflection subscale scores (range: 5 – 20). Brooding is characterized by a

passive style of moody pondering and is the most maladaptive form of depressive rumination (Joormann, Dkane, & Gotlib, 2006; Treynor et al., 2003). *Depressive symptomatology* will be assessed using the 21-item (range: 0 – 63) Beck Depression Inventory (BDI-II; Beck, Steer, & Brown, 1996; Van der Does, 2002). Both primary outcome measures exhibit adequate psychometric properties (Beck et al., 1996; Treynor et al., 2003; Van der Does, 2002).

Secondary outcome measures. Adaptive emotion regulation and indicators of RMD functioning will be our secondary outcome measures. *Adaptive emotion regulation* will be assessed using the five adaptive subscales of the Cognitive Emotion Regulation Questionnaire (CERQ; Garnefski, Kraaij, & Spinhoven, 2001). The four less adaptive strategies (self-blame, rumination, catastrophizing, and blaming others) can be used as a second, alternative measure for maladaptive emotion regulation (range: 4 – 20).

Functioning will be operationalized by indices of disability, quality of life, resilience, and remission from depression. *Disability* will be assessed using the self-report version of the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0; Üstün, Kostanjsek, Chatterji, & Rehm, 2010), consisting of 36 items. This measure is based on the conceptual framework of the International Classification of Functioning (ICF) and provides indicators of overall functioning and six specific domains of functioning (Cognition, Mobility, Self-care, Getting along, Life activities, and Participation). Furthermore, the questionnaire provides an estimate of the amount of days in the past month during which the difficulties (a) were present, (b) prevented the participant from performing his/her daily activities or work, or (c) formed a source of reduced functioning. *Quality of life* will be assessed using the depression-specific 34-item (range: 0 – 34) Quality of Life in Depression Scale (QLDS; Hunt & McKenna, 1992; Tuynman-Qua, de Jonghe, & McKenna, 1997). *Resilience* will be assessed using the Resilience Scale (RS; Portzky, 2008; Wagnild & Young, 1993). We will use the 25-item version of the RS using four point Likert-scales (range: 25 – 100). Finally, self-reported *remission from depression* will be assessed using the 41-item Remission of Depression Questionnaire (RDQ; Peeters, Nicolson, Wichers, & Hacker, 2013; Zimmerman et al., 2013) for which a high score is indicative for more psychopathology (range: 0 – 82).

Manipulation check, training process and cognitive transfer measures. As a manipulation check and process measure, *training task performance* will be assessed in both conditions using median inter stimulus interval (ISI) levels per training session. Furthermore, as a process measure of effects of completing an online training session, mood ('energetic', 'tense', 'frustrated', 'sad', 'happy') will be assessed using visual analogue scales (VAS; 1 – 100). The extent to which participants have experienced negative thoughts and stress throughout the training session will also be assessed using VAS, along with experienced task competence ('During the task I felt as if I was doing great'). It has been suggested that training cognitive control in a frustrating task-context – and thus, eliciting low levels of negative affect while training – contributes to the beneficial effects of CCT (Hoorelbeke et al., 2015). These process measures allow to explore the mechanism underlying CCT. Furthermore, we will use the Credibility/Expectancy Questionnaire (CEQ; Devilly & Borkovec, 2000; Godfrin, Goeleven, & Schoof, 2004) to check for baseline group differences in treatment credibility/expectancy and to check for successful blinding of participants (post-training). Moreover, we will monitor intake of antidepressants and other forms of therapy as well as stressful life events that might influence our findings. For the latter, we will use the List of Threatening Experiences (LTE; Brugha & Cragg, 1990; Rosmalen, Bos, & de Jonge, 2012).

Close transfer to *cognitive control* will be assessed using the non-adaptive PASAT (Gronwall, 1977). During this task, participants are presented with a practice phase consisting of 10 trials, followed by a test phase, consisting of three blocks with increasing difficulty (ISI block 1 = 3000 ms; ISI block 2 = 2000 ms; ISI block 3 = 1500 ms), each containing 60 trials. Furthermore, we will include the Behavior Rating Inventory of Executive Function Adult version (BRIEF-A; Roth, Lance, Isquith, Fischer, & Giancola, 2013) as a self-report measure to assess experienced cognitive control. This 75-item self-report questionnaire provides several estimates of executive and working memory functioning (e.g., inhibition, shifting, emotional control, working memory).

Interventions

Participants will either be subjected to an online CCT targeting working memory functioning (the adaptive PASAT) or a closely matched low cognitive load training. This allows to rule out motivational aspects of performing an adaptive computer task online. The tasks will be presented in-browser, using a Millisecond software Web license. Both training groups will be asked to perform 10 sessions of 400 trials (which takes 20 min per session at an average inter stimulus interval (ISI) of 3000 ms), providing similar learning experiences in both conditions. Prior to training, both groups will receive oral and written psycho-education concerning cognitive control training (based on the protocol of Siegle et al., 2007) in order to enhance task engagement. This is important as previous work indicates that task engagement forms an important predictor of response to CCT (Siegle et al., 2014). Importantly, no explicit information will be given about the to be expected results. Furthermore, participants will receive an automated text message on a daily basis to prevent attrition during the training period (using SurveySignal software; Hofmann & Patel, 2015).

Cognitive control training condition. We will use an adaptive version of the PASAT (Gronwall, 1977; Siegle et al., 2007) to train participants' cognitive control in the CCT condition. Participants will be presented with a continuous stream of auditory digits (1 – 9) and are instructed to immediately respond to the sum of the last two heard digits by clicking the corresponding response buttons (1 – 18). The speed of number presentation is adapted based on participants' performance in order to train cognitive control in a frustrating task context. Participants begin each session with a 3000 ms ISI, which is reduced by 100 ms following every four consecutive correct responses, increasing task difficulty. Following every four incorrect responses the ISI increases with 100 ms, reducing task difficulty. Throughout each session participants are presented with their current ISI and amount of consecutive correct and incorrect responses. Participants' responses and response times are being measured. In line with previous training studies the median ISI per session will be used as an indicator of ones performance during the training sessions.

Active control condition. In the active control condition, participants will be presented with a low cognitive load version of the adaptive PASAT. This training task shows high resemblance to the adaptive PASAT concerning stimuli, responses,

modification of task difficulty, and evaluation of session performance. However, in this low cognitive load version of the adaptive PASAT participants are instructed to immediately respond to the last heard digit instead of mentally manipulating the content in working memory (i.e., instead of responding to the sum of the last two heard digits as in the CCT condition). To better resemble the response options of the adaptive PASAT, participants in the active control condition are presented auditory stimuli ranging from 1 – 18.

Sample Size

We are the first to explore effects of CCT targeting working memory functioning in a RMD sample which makes it impossible to provide an exact estimate of effect size for the main outcome measure in this sample. However, previous work on MDD patients has yielded an effect size of $\eta_p^2 = .19$ for brooding (Siegle et al., 2014), whereas work with at-risk undergraduate students revealed an effect size of $\eta_p^2 = .11$ in confrontation with naturalistic stress (Hoorelbeke et al., 2015). Given that this study will use an at-risk sample (RMD), we will base estimations of sample size on the latter effect size. In order to be able to detect a similar effect over two time points with $\alpha = .05$ and $1-\beta = .80$, the total sample size should at least be 68 (*n* CCT = 34, *n* active control = 34). We will stop recruiting once 68 participants have entered the training phase.

Randomization

Upon entering the study, participants will receive a sealed envelope containing an exterior subject number that will be used for registration purposes during the assessment sessions in the lab (baseline, post-training, and follow-up). The envelope will contain a training manual, an URL that directs participants to the online training task, and a personal training task identification code that should be used while performing the ten online training sessions at home. Prior to the study, an independent researcher will randomly link the training task identification codes to the subject numbers that will be used in the lab using an automated randomization program (RandList; randomisation.eu). This researcher will prepare the envelopes and keep a list of the linked subject numbers and training session identification codes in a locked

closet at the office and a copy at home for safe keeping. Based on the training task identification codes, participants will either perform the CCT or low cognitive load training.

Blinding

We present a double blind RCT design. Prior to the randomization procedure, the independent researcher will reset the online training task so that even-numbered training task identification codes will redirect the participants to one condition (CCT or active control), whereas odd-numbered training task identification codes will redirect the participants to the other condition. The researchers of this study will not be aware of the training task identification codes (these are randomly generated and presented in a sealed envelope) or the link between even- or odd-numbered identification codes and training condition. Furthermore, participants will be instructed not to share details concerning the content of the training task or the personal training task identification code with the researchers.

During data-analysis, the researchers will remain blind of training task condition by separating (a) analysis of training task performance and process measures (based on even- or odd-numbered training task identification codes) from (b) analysis of training effects on the outcome measures. Concerning the latter, the independent researcher will provide the researchers with a list grouping the subject numbers – used during the lab sessions – in two non-informative conditions following completion of data-collection. Importantly, at this point (lab) subject numbers will not be linked to the personal training task identification codes. This allows blind evaluation of training effects. The blinding will only be broken for the more explorative analyses linking training task process measures with the outcome measures. Furthermore, we will use the CEQ-data to check for successful blinding of participants.

Analysis

In line with Consolidated Standards of Reporting Trials (CONSORT; Moher et al., 2010), we will use intention-to-treat (ITT) analysis to test effects of CCT on primary and secondary outcome measures post-training and at follow-up. Missing data will be

handled using the Last-Observation-Carried-Forward (LOCF) method. Effects of CCT will be tested using Repeated Measures, analysis of variance (ANOVA), or covariance (ANCOVA) with follow-up *t*-tests. Exploratory analysis will take into account potential moderators of training effects such as variability in baseline depressive symptomatology and cognitive control. ITT might not necessarily apply to the exploratory analyses such as analysis of process measures of training. As secondary analysis, we will also perform completers-only analyses. Explorative within-group mediation analysis will be performed using a stepwise regression approach (Baron & Kenny, 1986) and the Preacher and Hayes (Preacher & Hayes, 2004) bootstrapping method.

Procedure

Eligibility will be assessed by a clinical psychologist. Participants will first undergo a telephone screening to assess eligibility (see Figure 1). Second, potential participants will be invited to the lab where eligibility will be further assessed using the MINI. After giving informed consent, eligible participants will be randomized and the baseline assessment will take place (see Table 1). At baseline (Time 1), the behavior measure for cognitive control will be completed followed by the self-report measure for cognitive control (BRIEF-A). Next, participants will complete the other self-report questionnaires (primary outcome measures: BDI-II, RRS; secondary outcome measures: CERQ, QLDS, WHODAS 2.0, RS, RDQ) and will receive psycho-education concerning cognitive training for depression and practical information about the intervention. Participants will be instructed to complete 10 training sessions during a period of 14 days following the baseline assessment and will be asked to perform only one session a day. At the end of the baseline assessment session, the CEQ will be administered and participants' telephone number will be registered using SurveySignal software. During the 14-days period of online training, participants will receive a daily automated text message reminding them to complete the training. Each training session will consist of 400 trials of the adaptive PASAT or a low cognitive load training and will include assessments of affect and worrying throughout and following training. Upon completing training, participants will return to the lab for the post-training assessment (Time 2) during which direct effects of CCT on cognitive control and the primary outcome

measures and adaptive emotion regulation will be assessed. At the end of the post-training session the CEQ will be administered to rule out group differences in expectancy and credibility of the intervention. Finally, participants will return to the lab at three months follow-up (Time 3) during which long-term effects on cognitive control and the primary and secondary outcome measures (including indicators of functioning) will be assessed. At each time point we will assess stressful life events (LTE), intake of antidepressants and other forms of therapy. Upon completion of the follow-up assessment session, participants will receive reimbursement (€75) followed by a partial written and oral debriefing. Importantly, participants will only receive feedback concerning their condition following processing of the data of the total sample. If CCT shows to have beneficial effects in RMD, participants from the active control condition will be offered the chance to perform the CCT online.

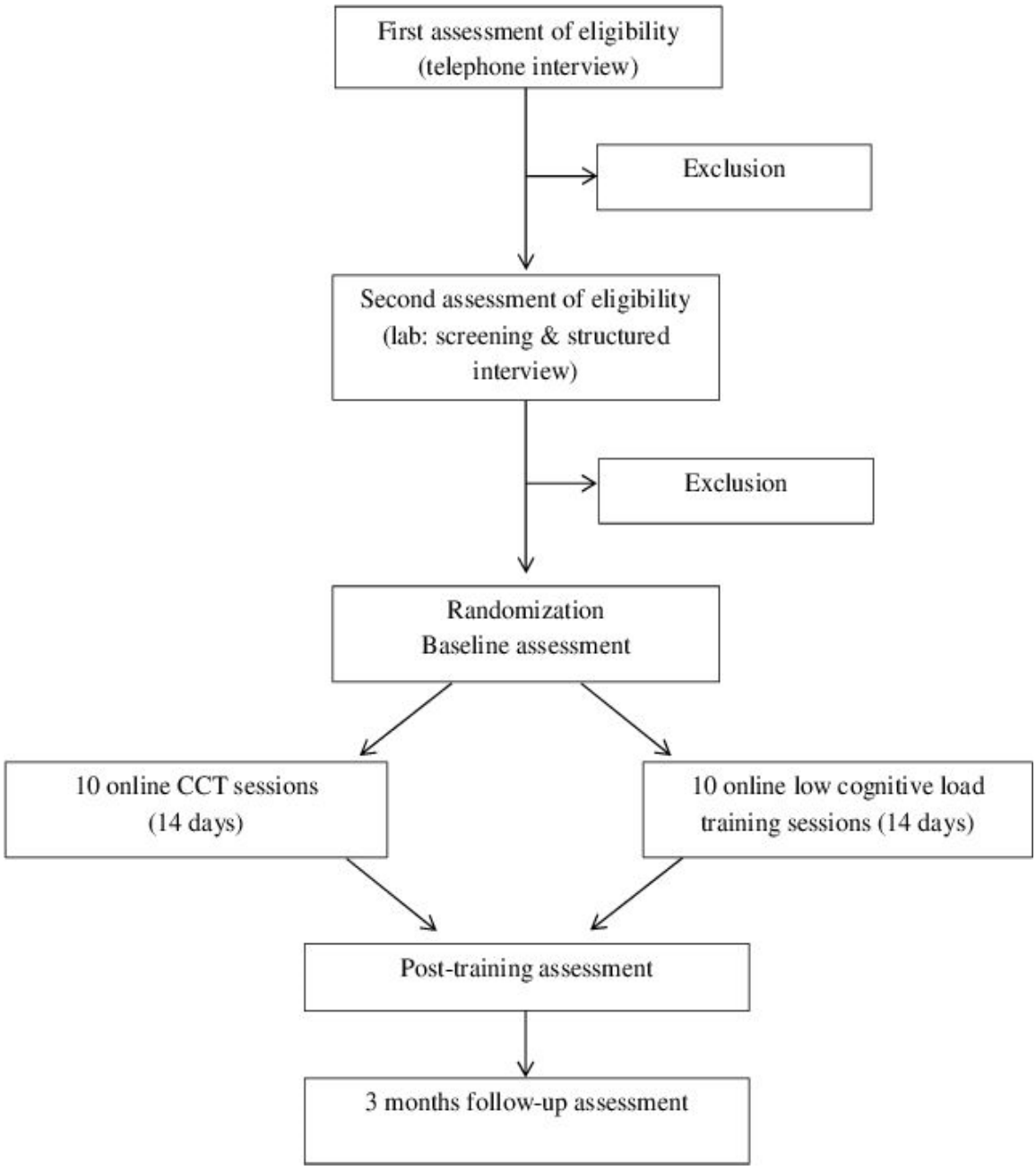


Figure 1. Study flowchart

Table 1

Schedule of measures

Instrument	Telephone screening	Baseline	Online training	Post-training (2 weeks)	Follow-up (3 months)
Inclusion criteria interview	X				
MINI Screen and structured interview		X			
Process measures of affect during training			X		
Process measures of training task performance (ISI)			X		
Credibility and expectancy of treatment (CEQ)		X		X	
Stressful life events (LTE)		X		X	X
Self-reported use of antidepressants and other forms of therapy		X		X	X
Cognitive control (non-adaptive PASAT / transfer task)		X		X	X
Self-reported cognitive control (BRIEF-A)		X		X	X
Depressive symptomatology (BDI-II)		X		X	X
Depressive rumination (RRS)		X		X	X
Cognitive emotion regulation (CERQ)		X		X	X
Quality of Life (QLDS)		X			X
Disability (WHODAS 2.0)		X			X
Resilience (RS)		X			X
Remission from depression (RDQ)		X			X

DISCUSSION

Prevention of recurrent depression is an important target for interventions. Previous findings indicate that CCT shows potential in reducing depressive symptomatology and rumination in MDD as well as cognitive vulnerability in at-risk undergraduate students. To test the potential of CCT as a preventive intervention for depression, the present study aims to test the effectiveness of CCT in a RMD sample. We will test whether CCT targeting working memory functioning – as compared to a low cognitive load training – can be used to reduce vulnerability for depression over a 3.5 months period. We hypothesize that CCT will have beneficial effects on primary outcome measures depressive rumination (i.e., brooding) and depressive symptomatology and hope to see these findings extend to adaptive emotion regulation and long-term functioning (secondary outcome measures).

This double blind RCT study forms a first test of the potential of CCT as a preventive intervention for depression in RMD. Furthermore, these findings will be informative to the literature as several exploratory questions will be addressed in order to further elucidate the role of cognitive control in vulnerability for depression. First, we will explore whether effects of CCT on depressive symptomatology are mediated by rumination. Second, we will explore whether effects of CCT extend to measures of adaptive emotion regulation and indices of functioning such as quality of life and disability. Third, in order to further elucidate the mechanisms involved during CCT, we could explore how process measures of CCT relate to effects of training.

Overall, this study will further enhance the knowledge on the role of cognitive control in emotion regulation and vulnerability for depression. This study forms a first step in testing the effectiveness of CCT targeting working memory functioning as a preventive intervention for (recurrent) depression. If these first results show to be promising, future work should focus on replicating the effects of CCT and exploring how this preventive intervention could best be implemented.

ACKNOWLEDGMENTS

This research will be supported by a Special Research Fund (BOF) of Ghent University awarded to Kristof Hoorelbeke (B/13808/01). A license to use the WHODAS 2.0 for the purpose of this study was achieved by the WHO (22-10-2014).

REFERENCES

Aker, M., Harmer, C., & Landro, N. I. (2014). More rumination and less effective emotion regulation in previously depressed women with preserved executive functions. *Bmc Psychiatry, 14*, 10. doi: 10.1186/s12888-014-0334-4

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research - Conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology, 51*, 1173-1182.

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for Beck Depression Inventory II*. San Antonio, Texas: Psychological Corporation.

Brugha, T. S., & Cragg, D. (1990). The List of Threatening Experiences: the reliability and validity of a brief life events questionnaire. *Acta Psychiatrica Scandinavica, 82*, 77-81.

Brunoni, A. R., Boggio, P. S., De Raedt, R., Bensenor, I. M., Lotufo, P. A., Namur, V., . . . Vanderhasselt, M. A. (2014). Cognitive control therapy and transcranial direct current stimulation for depression: A randomized, double-blinded, controlled trial. *Journal of Affective Disorders, 162*, 43-49. doi: 10.1016/j.jad.2014.03.026

Burcusa, S. L., & Iacono, W. G. (2007). Risk for recurrence in depression. *Clinical Psychology Review, 27*, 959-985.

Calkins, A. W., McMorran, K. E., Siegle, G. J., & Otto, M. W. (2015). The effects of computerized cognitive control training on community adults with depressed mood. *Behavioural and Cognitive Psychotherapy*, *39*, 205–220. doi: 10.1017/S1352465814000046

Cohen, N., Mor, N., & Henik, A. (2015). Linking executive control and emotional response: A training procedure to reduce rumination. *Clinical Psychological Science, 3*, 15-25. doi: 10.1177/2167702614530114

Cuijpers, P., Andersson, G., Donker, T., & van Straten, A. (2011). Psychological treatment of depression: Results of a series of meta-analyses. *Nordic Journal of Psychiatry, 65*, 354-364. doi: 10.3109/08039488.2011.596570

Daches, S., & Mor, N. (2014). Training ruminators to inhibit negative information: A preliminary report. *Cognitive Therapy and Research, 38*, 160-171. doi: 10.1007/s10608-013-9585-5

De Lissnyder, E., Koster, E. H. W., Goubert, L., Onraedt, T., Vanderhasselt, M. A., & De Raedt, R. (2012). Cognitive control moderates the association between stress and rumination. *Journal of Behavior Therapy and Experimental Psychiatry, 43*, 519-525. doi: 10.1016/j.jbtep.2011.07.004

De Raedt, R., & Koster, E. H. W. (2010). Understanding vulnerability for depression from a cognitive neuroscience perspective: A reappraisal of attentional factors and a new conceptual framework. *Cognitive Affective & Behavioral Neuroscience, 10*, 50-70. doi: 10.3758/cabn.10.1.50

Demeyer, I., De Lissnyder, E., Koster, E. H. W., & De Raedt, R. (2012). Rumination mediates the relationship between impaired cognitive control for emotional information and depressive symptoms: A prospective study in remitted depressed adults. *Behaviour Research and Therapy, 50*, 292-297. doi: 10.1016/j.brat.2012.02.012

Devilly, G. J., & Borkovec, T. D. (2000). Psychometric properties of the credibility/expectancy questionnaire. *Journal of Behavior Therapy and Experimental Psychiatry, 31*, 73-86.

Garnefski, N., Kraaij, V., & Spinhoven, P. (2001). Negative life events, cognitive emotion regulation and emotional problems. *Personality and Individual Differences, 30*, 1311-1327.

Godfrin, K., Goeleven, E., & Schoof, P. (2004). Dutch translation of the Credibility/Expectancy Questionnaire (CEQ-NL). Unpublished document.

Gotlib, I. H., & Joormann, J. (2010). Cognition and Depression: Current Status and Future Directions. In S. NolenHoeksema, T. D. Cannon, & T. Widiger (Eds.), *Annual Review of Clinical Psychology, Vol 6* (Vol. 6, pp. 285-312). Palo Alto: Annual Reviews.

Gronwall, D. (1977). Paced Auditory Serial-Addition Task: A measure of recovery from concussion. *Perceptual and Motor Skills, 44*, 367-373.

Harvey, P. O., Le Bastard, G., Pochon, J. B., Levy, R., Allilaire, J. F., Dubois, B., & Fossti, P. (2004). Executive functions and updating of the contents of working memory in

unipolar depression. *Journal of Psychiatric Research, 38*, 567-576. doi: 10.1016/j.jpsychires.2004.03.003

Hofmann, W., & Patel, P. V. (2015). SurveySignal: A convenient solution for experience sampling research using participants' own smartphones. *Social Science Computer Review*, *33*, 235-253. doi: 10.1177/0894439314525117

Hoorelbeke, K., Koster, E. H. W., Vanderhasselt, M. A., Callewaert, S., & Demeyer, I. (2015). The influence of cognitive control training on stress reactivity and rumination in response to a lab stressor and naturalistic stress. *Behaviour Research and Therapy, 69*, 1–10.

Hunt, S. M., & McKenna, S. P. (1992). The QLDS: A scale for the measurement of quality of life in depression. *Health Policy, 22*, 307-319.

Joormann, J., & D'Avanzato, C. (2010). Emotion regulation in depression: Examining the role of cognitive processes. *2010, 24*, 913-939. doi: 10.1080/02699931003784939

Joormann, J., Dkane, M., & Gotlib, I. H. (2006). Adaptive and maladaptive components of rumination? Diagnostic specificity and relation to depressive biases. *Behavior Therapy, 37*, 269-280.

Joormann, J., & Gotlib, I. H. (2010). Emotion regulation in depression: Relation to cognitive inhibition. *Cognition & Emotion, 24*, 281-298. doi: 10.1080/02699930903407948

Klingberg, T. (2010). Training and plasticity of working memory. *Trends in Cognitive Sciences, 14*, 317-324.

Letkiewicz, A. M., Miller, G. A., Crocker, L. D., Warren, S. L., Infantolino, Z. P., Mimnaugh, K. J., & Heller, W. (2014). Executive function deficits in daily life prospectively predict increases in depressive symptoms. *Cognitive Therapy and Research, 38*, 612-620. doi: 10.1007/s10608-014-9629-5

Millan, M. J., Agid, Y., Brüne, M., Bullmore, E. T., Carter, C. S., Clayton, N. S., . . . Young, L. J. (2012). Cognitive dysfunction in psychiatric disorders: characteristics, causes and the quest for improved therapy. *Nature Reviews, 11*, 141-168. doi: 10.1038/nrd3628

Moher, D., Hopewell, S., Schulz, K. F., Montori, V., Gotzsche, P. C., Devereaux, P. J., . . . Altman, D. G. (2010). CONSORT 2010 Explanation and elaboration: Updated

guidelines for reporting parallel group randomised trials. *British Medical Journal*, 340:328. doi: 10.1136/bmj.c869

Nolen-Hoeksema, S., & Morrow, J. (1991). A prospective study of depression and posttraumatic stress symptoms after a natural disaster - The 1989 Loma-Prieta earthquake. *Journal of Personality and Social Psychology, 61*, 115-121. doi: 10.1037/0022-3514.61.1.115

Nolen-Hoeksema, S., Wisco, B. E., & Lyubomirsky, S. (2008). Rethinking rumination. *Perspectives on Psychological Science, 3*, 400-424. doi: 10.1111/j.1745-6924.2008.00088.x

Peeters, F., Nicolson, N., Wichers, M., & Hacker, P. (2013). Remission of Depression Questionnaire - Dutch translation (RDQ-NL). Unpublished document.

Portzky, M. (2008). *RS-nl: Resilience Scale - Nederlandse versie*. Amsterdam: Harcourt Test Publishers.

Preacher, K. J., & Hayes, A. F. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behavior Research Methods, Instruments, and Computers, 36*, 717-731. doi: 10.3758/BF03206553

Rosmalen, J. G. M., Bos, E. H., & de Jonge, P. (2012). Validation of the Long-term Difficulties Inventory (LDI) and the List of Threatening Experiences (LTE) as measures of stress in epidemiological population-based cohort studies. *Psychological Medicine, 42*, 2599-2608. doi: 10.1017/S0033291712000608

Roth, R. M., Lance, C. E., Isquith, P. K., Fischer, A. S., & Giancola, P. R. (2013). Confirmatory factor analysis of the Behavior Rating Inventory of Executive Function-Adult version in healthy adults and application to attention-deficit/hyperactivity disorder. *Archives of Clinical Neuropsychology, 28*, 425-434. doi: 10.1093/arclin/act031

Segrave, R. A., Arnold, S., Hoy, K., & Fitzgerald, P. B. (2014). Concurrent cognitive control training augments the antidepressant efficacy of tDCS: A pilot study. *Brain Stimulation, 7*, 325-331. doi: 10.1016/j.brs.2013.12.008

Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., . . . Dunbar, G. C. (1989). The Mini-International Neuropsychiatric Interview (MINI): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry, 59*, 22-33.

Siegle, G. J., Ghinassi, F., & Thase, M. E. (2007). Neurobehavioral therapies in the 21st century: Summary of an emerging field and an extended example of cognitive control training for depression. *Cognitive Therapy and Research, 31*, 235-262. doi: 10.1007/s10608-006-9118-6

Siegle, G. J., Price, R. B., Jones, N. P., Ghinassi, F., Painter, T., & Thase, M. E. (2014). You gotta work at it: Pupillary indices of task focus are prognostic for response to a neurocognitive intervention for rumination in depression. *Clinical Psychological Science, 2*, 455-471. doi: 10.1177/2167702614536160

Treynor, W., Gonzalez, R., & Nolen-Hoeksema, S. (2003). Rumination reconsidered: A psychometric analysis. *Cognitive Therapy and Research, 27*, 247-259.

Tuynman-Qua, H., de Jonghe, F., & McKenna, S. P. (1997). Quality of Life in Depression Scale (QLDS). Development, reliability, validity, responsiveness and application. *Eur Psychiatry, 12*, 199-202.

Üstün, T., Kostanjsek, N., Chatterji, S., & Rehm, J. (2010). Measuring health and disability: Manual for WHO Disability Assessment Schedule (WHODAS 2.0). World Health Organization, Switzerland: Geneva.

Van der Does, A. J. W. (2002). *BDI-II-NL. Handleiding: De Nederlandse versie van de Beck Depression Inventory - 2nd edition*. Lisse: Harcourt Test Publishers.

Vanderhasselt, M.-A., & De Raedt, R. (2009). Impairments in cognitive control persist during remission from depression and are related to the number of past episodes: An event related potentials study. *Biological Psychology, 81*, 169-176. doi: 10.1016/j.biopsycho.2009.03.009

Vanderhasselt, M.-A., De Raedt, R., Namur, V., Lotufo, P. A., Bensenor, I. M., Boggio, P. S., & Brunoni, A. R. (2015). Transcranial electric stimulation and neurocognitive training in clinically depressed patients: A pilot study of the effects on rumination. *Prog Neuropsychopharmacol Biol Psychiatry, 57*, 93-99. doi: 10.1016/j.pnpbp.2014.09.015

Wagnild, G. M., & Young, H. M. (1993). Development and psychometric evaluation of the resilience scale. *Journal of Nursing Measurement, 1*, 165-178.

Wells, A. (2000). *Emotional disorders and metacognition innovative Cognitive Therapy*. New York: Wiley.

Xu, G. Y., Lin, K. G., Rao, D. P., Dang, Y. M., Ouyang, H. Y., Guo, Y. B., . . . Chen, J. C. (2012). Neuropsychological performance in bipolar I, bipolar II and unipolar depression patients: A longitudinal, naturalistic study. *Journal of Affective Disorders, 136*, 328-339. doi: 10.1016/j.jad.2011.11.029

Zetsche, U., & Joormann, J. (2011). Components of interference control predict depressive symptoms and rumination cross-sectionally and at six months follow-up. *Journal of Behavior Therapy and Experimental Psychiatry, 42*, 65-73. doi: 10.1016/j.jbtep.2010.06.001

Zimmerman, M., Martinez, J. H., Attiullah, N., Friedman, M., Toba, C., Boerescu, D. A., & Ragheb, M. (2013). A new type of scale for determining remission from depression: The Remission from Depression Questionnaire. *Journal of Psychiatric Research, 47*, 78-82. doi: 10.1016/j.jpsychires.2012.09.006

CHAPTER 6

INTERNET-DELIVERED COGNITIVE CONTROL TRAINING AS A PREVENTIVE INTERVENTION FOR REMITTED DEPRESSED PATIENTS: EVIDENCE FROM A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL STUDY[1]

ABSTRACT

Cognitive control impairments may place remitted depressed (RMD) patients at increased risk for developing future depressive symptomatology by disrupting emotion regulation processes. The current chapter presents the results of a double-blind randomized controlled trial study testing whether internet-delivered cognitive control training (CCT) can be used as an intervention to increase resilience to depression in RMD patients (for the protocol, please see Chapter 5). Compared to an active control condition, CCT demonstrated beneficial effects on a cognitive transfer task, brooding, depressive symptomatology, residual complaints, self-reported use of general maladaptive emotion regulation strategies, and resilience after controlling for intention-to-treat. Furthermore, completers of the CCT reported a reduction in experienced disability and cognitive complaints. However, no beneficial effects were found for self-reported use of adaptive emotion regulation strategies. These findings demonstrate the effectiveness of CCT as an intervention to reduce cognitive vulnerability, residual symptomatology, and foster resilience following recovery from depression. CCT thus holds potential as a preventive intervention for RMD patients.

Trial Registration: ClinicalTrials.gov identifier: NCT02407652

[1] Based on Hoorelbeke, K., & Koster, E.H.W. (2017). Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Effects of a randomized controlled trial. *Journal of Consulting and Clinical Psychology, 85,* 135-146. doi: 10.1037/ccp0000128

Achieving stable remission following major depressive disorder (MDD) remains an important challenge for current treatments of depression (Hardeveld, Spijker, De Graaf, Nolen, & Beekman, 2010). Given the high risk for new depressive episodes, studying causal mechanisms of depression vulnerability in remitted depressed individuals (RMD) is an important research priority. There is emerging evidence that RMD individuals are still characterized by impaired cognitive control as shown by behavioral (Lange et al., 2012; Levens & Gotlib, 2015) as well as neuroimaging data (Norbury, Godlewska, & Cowen, 2014; Vanderhasselt & De Raedt, 2009). The term cognitive control refers to executive processes such as shifting, inhibition and updating of information in working memory (Miyake et al., 2000).

Importantly, control over content in working memory may play a causal role in perseverative negative thinking concerning one's problems or feelings (i.e., depressive rumination or *brooding*) (Cohen, Mor, & Henik, 2015). Provided that engaging in maladaptive emotion regulation strategies such as depressive rumination has typically been linked to sustained negative affect and depressive symptomatology (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008; Treynor, Gonzalez, & Nolen-Hoeksema, 2003), cognitive control impairments place RMD patients at increased risk for recurrent depression (Demeyer, De Lissnyder, Koster, & De Raedt, 2012). As a result, it has been suggested that directly targeting these cognitive and neurobiological processes underlying vulnerability for depression may have beneficial effects (Segrave, Arnold, Hoy, & Fitzgerald, 2014; Siegle, Ghinassi, & Thase, 2007).

In this context, cognitive control training (CCT) has recently gained interest as a means to examine the causal influence of cognitive control on depressive symptoms as well as an adjunctive curative intervention for MDD. For instance, Siegle and colleagues (2007) introduced a variant of CCT combining an adaptive version of the Paced Auditory Serial Addition Task (PASAT; Gronwall, 1977) and a task training selective attention (Wells' Attention Training; Wells, 2000). The non-adaptive PASAT has previously been used as an assessment task for executive functioning in multiple clinical populations (e.g., traumatic brain injury, multiple sclerosis, depression), and as a stress induction procedure given the high rate of errors that typically occur during the non-adaptive PASAT (for a review on the non-adaptive PASAT, please see Tombaugh, 2006). That is,

during this task participants are presented with a continuous stream of digits and have to continuously respond to the sum of the last two heard digits, which has been proposed to activate the prefrontal cortex – a key cognitive control region (Cohen, 2001) – in a stressful context (Siegle et al., 2007, p. 245). Given the disturbed patterns of activation of frontal and limbic regions often reported in MDD (e.g., Davidson, Pizzagalli, Nitschke, & Putman, 2002; Pizzagalli, 2011), Siegle et al. (2007) developed an adaptive version of the PASAT during which task difficulty is modified based on the performance of the participant (i.e., every four consecutive correct responses are followed by a decrease in the inter-stimulus interval (ISI) of 100 ms, and vice versa). As a result, it has been suggested that during the adaptive PASAT participants have to recruit the dorsolateral prefrontal cortex (e.g., Lazeron, Rombouts, deSonneville, Barkhof, & Scheltens, 2003) while being exposed to interference from limbic pathways (Siegle et al., 2007). At the behavioral level, this may allow participants to gain control over thought processes upon confrontation with a stressor, potentially reducing perseverative negative thinking such as depressive rumination. Given that depressive rumination is a well-known cognitive risk factor for sustained and future depressive symptomatology (Nolen-Hoeksema et al., 2008; Treynor et al., 2003), this may then have beneficial effects on other depression-related outcomes (e.g., depressive symptomatology).

Indeed, combining six sessions of CCT with treatment as usual (TAU), Siegle and colleagues (2007) demonstrated beneficial effects on rumination (Siegle et al., 2007, 2014) and depressive symptomatology (Siegle et al., 2007) in a MDD sample compared to a TAU control group. Furthermore, in the year following the intervention, CCT showed beneficial effects on use of outpatient care services (Siegle et al., 2014), suggesting that CCT may have stable effects on depression-related outcomes and that these effects may be mediated by brooding. Confirming the suggested mechanisms underlying effects of CCT, Siegle et al. (2007) found that CCT may serve to reduce depression-related disruptions in amygdala and prefrontal activity.

Interestingly, recent work indicates that CCT specifically targeting working memory functioning (the adaptive PASAT component) shows potential in reducing rumination (Vanderhasselt et al., 2015) and depressive symptomatology (Brunoni et al.,

2014) in absence of Wells' Attention Training in MDD patients. However, initial studies in clinical populations often lack an adequate control group to control for motivational effects of undergoing CCT (e.g., Brunoni et al., 2014; Siegle et al., 2007) and findings in non-clinical samples have been mixed (e.g., Calkins, Deveney, Weitzman, Hearon, & Siegle, 2011; Calkins, McMorran, Siegle, & Otto, 2015; Hoorelbeke, Koster, Demeyer, Loeys, & Vanderhasselt, 2016; Hoorelbeke, Koster, Vanderhasselt, Callewaert, & Demeyer, 2015; Moshier, Molokotos, Stein, & Otto, 2015). Furthermore, previous studies are often characterized by a unilateral focus on indicators of dysfunctioning. As a result, it has not been tested whether effects of CCT may extend to broader indicators of functioning in clinical samples. Additionally, to our knowledge no previous study has explored effects of adaptive PASAT training in RMD patients, nor has the suggested mediation effect (i.e., increase in cognitive control affects depressive symptomatology via depressive rumination) been directly tested, which is crucial to advance our understanding of the preventive potential of CCT.

Current Study

Given that cognitive impairments and residual depressive symptoms often persist during remission from depression and form an important vulnerability factor, we tested whether CCT targeting working memory functioning can be used to reduce cognitive vulnerability for depression in a RMD sample, in order to prevent recurrence of depressive symptomatology. We conducted a double-blind randomized controlled trial (RCT) study comparing effects of CCT to an active control condition.

We hypothesized that: (a) CCT would have beneficial effects on primary outcome measures brooding and depressive symptomatology (Time 2 and 3); (b) It has been suggested that effects of cognitive control manipulation on depressive symptomatology (Time 3) may be mediated by depressive rumination (Time 2) (Siegle et al., 2014). We provided a test of this assumption; (c) We further extended previous work by broadening the scope of training effects to indicators of functioning, predicting beneficial effects on adaptive emotion regulation (Time 2 and 3), resilience, quality of life, disability, and a self-report measure for remission from depression (Time 3).

METHOD

Design and Power

The study was pre-registered on ClinicalTrials.Gov (identifier: NCT02407652) and the complete protocol of this 2 (Condition) x 3 (Time) double-blind RCT was submitted for open access publication prior to data-collection (Hoorelbeke, Faelens, Behiels, & Koster, 2015). The study was approved by the local ethics committee and written informed consent was obtained for all participants. Sixty eight RMD patients were recruited to detect effects of CCT approaching those reported in previous studies (Hoorelbeke, Koster, et al., 2015; Siegle et al., 2014, 2007) with 80% power on primary outcome measures depressive rumination and symptomatology. Following baseline assessment, RMD patients were randomly assigned to 10 sessions (two weeks) of CCT (*n* = 34) or a low cognitive load training (active control condition; *n* = 34). Effects were assessed post-training and at three months follow-up.

Randomization and Blinding

Randomization over training condition (simple randomization, CCT vs. low cognitive load training; allocation ratio = 1:1) took place using automated randomization software (RandList; randomisation.eu). To ensure blinding of researchers, using RandList an independent researcher linked subject numbers (used during the lab assessments by the researchers for the questionnaires and cognitive transfer task) with training identification codes (used at home by the participants to perform the training). Based on the training identification codes – which were presented in a sealed envelope containing a personalized training manual – participants performed the CCT or low cognitive load training. This prevented awareness of training condition allocation. Technical queries that could reveal training condition were also resolved by the independent researchers. Furthermore, during data-analysis the researchers remained blind to training task condition. Specifically, the independent researcher provided the researchers with a list grouping the subject numbers in two non-informative conditions and analysis of training-related process measures were separated from analysis of training effects on outcome measures. Successful blinding of

participants was evaluated at baseline and immediately following training using the Credibility/Expectancy Questionnaire (CEQ; Devilly & Borkovec, 2000). Furthermore, at three-months follow-up participants completed a one-item measure assessing whether participants experienced the intervention as being a 'placebo'.

Participants

Participants (adults aged 23 – 65) were recruited via advertisements and a lab database. The study was conducted at the Faculty of Psychology and Educational Sciences of Ghent University. Following a brief telephone screening to assess eligibility, participants were invited for a more extensive structured clinical interview (Mini-International Neuropsychiatric Interview, MINI; Sheehan et al., 1989). Participants with a history of depression showing stable remission (≥ 6 months) were deemed eligible if: (a) the episode did not occur in the context of a bipolar disorder, (b) there was no history of psychosis, extensive substance abuse, or brain injury, nor were there current comorbid disorders, and (c) use of antidepressant medication was kept stable and therapeutic contact was limited to maintenance contact (< 1 / 3 weeks).

Interventions

Following a psycho-education session at baseline to foster task engagement (Siegle et al., 2014), participants performed 10 online sessions of the adaptive PASAT (*CCT condition*) or a low cognitive load training (*active control condition*) over a period of two weeks. Each session was performed online in-browser on the personal computer of the participant using a Millisecond software Web license, allowing participants to receive the complete intervention at home (e.g., Hoorelbeke et al., 2016) rather than in a lab context (e.g., Calkins et al., 2015; Siegle et al., 2014). It is noteworthy that recent meta-analytic findings indicate that performing CCT at home (instead of in the lab) does not affect cognitive transfer (Au et al., 2015), while performing the intervention online provides a more ecological valid training context which may foster transfer on depression-related outcomes.

Importantly, participants were only allowed to perform 10 sessions of CCT during the two-week training period, which was monitored online. Breach of protocol

(performing less than 10 sessions over the two-week training period or continuing training following the post-training assessment) was seen as non-compliance to the intervention and taken into account for the intention-to-treat (ITT; cf. infra) and completers-only analysis. None of the participants continued training outside the training period. Due to technical difficulties two participants in the active control condition completed 11 sessions during the training period.[2] To increase compliance, participants received a training manual following the psycho-education session and automated daily reminders via text message during the two-week training period (using SurveySignal software; Hofmann & Patel, 2015).

In both conditions participants were confronted with a continuous stream of auditory digits. In the CCT condition participants were instructed to continuously respond to the sum of the last two heard digits (stimuli: 1 – 9) by clicking on the corresponding response button (ranging from 1 – 18), whereas participants performing the low cognitive load task (Hoorelbeke et al., 2016) had to immediately respond to the last heard digit. To train cognitive functioning, speed of number presentation was adapted based on participants' performance: each training session started with an ISI of 3000 ms, which decreased / increased with 100 ms following every four consecutive correct / incorrect responses. In each condition, participants performed 400 training trials per session, providing an equal amount of training opportunities per participant (independent of training task performance; e.g., Hoorelbeke et al., 2016). Overall, when taking into account increased task performance over the 10 training sessions in this sample, which – due to the adaptive nature of the task (see Appendix Table 1 for mean ISI per session per condition) – reduces the length of the training sessions over the two-week period, on average participants completed the CCT intervention in 142.82 minutes (not taking into account practice trials). In line with previous studies, individual progress on the training tasks over time was assessed using median ISI levels per session.

Outcome Measures

[2] Excluding these two participants from the primary analyses did not affect our main findings indicating beneficial effects of CCT.

Cognitive transfer. *Near transfer* (i.e., transfer of cognitive training on performance on tasks that are similar to the training task) was assessed at baseline, post-training, and follow-up using accuracy scores of a non-adaptive version of the PASAT (Gronwall, 1977) during which participants performed three blocks of increasing difficulty (ISI block 1 = 3000 ms; ISI block 2 = 2000 ms; ISI block 3 = 1500 ms). Participants performed a total of 180 test trials (60 trials per block) following a practice phase of 10 trials. Furthermore, *cognitive complaints* were assessed using the Global Executive scale of the Behavior Rating Inventory of Executive Function Adult Version (BRIEF-A; range: 70 – 210; Scholte & Noens, 2011). The Global Executive scale of this 75-item self-report questionnaire combines experienced difficulties for a broad range of cognitive functions in daily life, providing estimates of executive and working memory functioning (e.g., experienced difficulties in daily life situations with inhibition, shifting, emotional control, working memory).

Primary outcome measures. *Depressive rumination* (range: 5 – 20) was assessed using the Brooding subscale of the Ruminative Response Scale (RRS; Nolen-Hoeksema & Morrow, 1991; Treynor et al., 2003) and *depressive symptomatology* using the Beck Depression Inventory (BDI-II, range: 0 – 63; Beck, Steer, & Brown, 1996; Van der Does, 2002). Both primary outcome measures were assessed at baseline, post-training, and three months follow-up, with higher scores indicating more symptoms or maladaptive processes.

Secondary outcome measures. The Cognitive Emotion Regulation Questionnaire (CERQ; Garnefski, Kraaij, & Spinhoven, 2001) was used as an alternative measure for *maladaptive emotion regulation* (next to the RRS; compound score maladaptive emotion regulation, range: 16 – 80) and *adaptive emotion regulation* processes (compound score adaptive emotion regulation, range: 20 – 100) at baseline, post-training, and follow-up. Furthermore, as indicators of general functioning, we assessed *disability* (World Health Organization Disability Assessment Schedule 2.0, WHODAS 2.0; Üstün, Kostanjsek, Chatterji, & Rehm, 2010), *quality of life* (Quality of Life in Depression Scale, QLDS; range: 0 – 34; Hunt & McKenna, 1992; Tuynman-Qua, de Jonghe, & McKenna, 1997), *resilience* (Resilience Scale, RS; range: 25 – 100; Portzky, 2008; Wagnild & Young, 1993), and *remission from depression* (Remission of Depression

Questionnaire, RDQ; range: 0 – 82; Peeters, Nicolson, Wichers, & Hacker, 2013; Zimmerman et al., 2013) at baseline and follow-up. For all secondary outcome measures, except for resilience and adaptive emotion regulation, a higher score is indicative for more maladaptive processes.

Other measures. Potential confounders such as life events, treatment credibility and expectancy were assessed using the List of Threatening Experiences (LTE; Brugha & Cragg, 1990; Rosmalen, Bos, & de Jonghe, 2012) and the Credibility/Expectancy Questionnaire (CEQ; Devilly & Borkovec, 2000). An additional item assessed whether participants experienced the training as being a bogus training (placebo: yes / no) and intake of antidepressants and other forms of therapy was monitored.

Procedure

Following a telephone screening, potential participants were invited to the lab for a more extensive structured clinical interview. If all criteria were met, participants were randomized and entered the baseline assessment (Time 1) where they gave written informed consent, received psycho-education, and completed the baseline cognitive task and self-report questionnaires. After receiving training instructions, participants performed ten online sessions of CCT or a low cognitive load version over a two week period after which they returned to the lab for a post-training assessment (Time 2) of the primary outcome measures, (mal)adaptive emotion regulation, cognitive functioning, and treatment expectancy/credibility. At three months follow-up (Time 3), participants returned to the lab where the baseline measures were re-assessed. Please see Hoorelbeke, Faelens, et al. (2015) for a more thorough description of the protocol. No deviations from the pre-registered protocol were made throughout the study.

Statistical Analysis

In line with the Consolidated Standards of Reporting Trials (CONSORT; Moher et al., 2010), effects of CCT on primary and secondary outcome measures will be tested using intention-to-treat (ITT) analysis. This allows a more stringent test of effects of CCT, taking into account each participant that was randomized to CCT or low cognitive load training when evaluating training effects. Specifically, in line with the pre-

registered protocol (Hoorelbeke, Faelens, et al., 2015), missing data and/or non-compliance to the treatment protocol were handled using the Last-Observation-Carried-Forward (LOCF) method. Effects of CCT will be tested using Repeated Measures ANOVA's with follow-up independent and paired samples *t*-tests (two-sided, $\alpha = .05$) to further elucidate interaction effects. As secondary analysis, we will also perform completers-only analyses. Explorative within-group mediation analysis will be performed using the Preacher and Hayes bootstrapping method (Preacher & Hayes, 2004), testing whether increase in cognitive control predicts lower levels of depressive symptomatology at three-months follow-up via depressive rumination (brooding) immediately following two weeks of training.[3]

RESULTS

Group Characteristics

Participants were randomly allocated to a CCT (*n* = 34) or active control condition (*n* = 34; see Figure 1 for the CONSORT patient flow diagram). Both groups did not differ concerning demographic variables, variables specific to history of depression (e.g., age of onset, amount / duration of episodes), or amount of days between completion of each assessment phase (see Table 1). Importantly, independent samples *t*-tests indicate that both groups did not significantly differ at baseline concerning cognitive transfer- and outcome measures (all *t*s < 1.73; see Table 2).

[3] Effects of (potential) violations of test assumptions due to the distribution of variables were evaluated using transformation. However, the main analysis proved to be robust, adding to the validity of the reported findings.

Table 1

Demographic and study progress information by group

	Training condition				
	Cognitive control (n = 34)	Active control (n = 34)	Statistic	df	p
Age ($M \pm SD$)	46.12 ± 10.80	47.82 ± 12.20	t = 0.61	66	.544
Gender (male : female)	12 : 22	11 : 23	χ^2 = 0.07	1	.798
Age of onset ($M \pm SD$)	28.77 ± 11.63	25.82 ± 13.98	t = 0.94	66	.349
Amount of depressive episodes ($M \pm SD$)	2.79 ± 3.28	3.79 ± 5.05	t = 0.97	66	.337
Episode length in months ($M \pm SD$)	6.81 ± 4.06	7.19 ± 5.26	t = 0.34	66	.738
Time since previous episode in years ($M \pm SD$)	6.49 ± 7.05	5.91 ± 5.64	t = 0.37	66	.710
Received inpatient treatment (yes : no)	10 : 24	14 : 20	χ^2 = 1.03	1	.310
Current use of antidepressant medication (yes : no)	11 : 23	17 : 17	χ^2 = 2.19	1	.139
Therapeutic maintenance contact (yes : no)	4 : 30	9 : 25	χ^2 = 2.38	1	.123
Days from baseline to post-training assessment[a]	14.09 ± 0.98	13.97 ± 1.00	t = 0.50	65	.621
Days from post-training assessment to follow-up[b]	90.88 ± 8.32	88.82 ± 6.84	t = 1.10	64	.277

Note: [a] For these values, CCT (n = 33) and active control (n = 34), not taking into account exclusion due to change in antidepressants use; [b] For these values, CCT (n = 32) and active control (n = 34), not taking into account exclusion due to change in antidepressants use

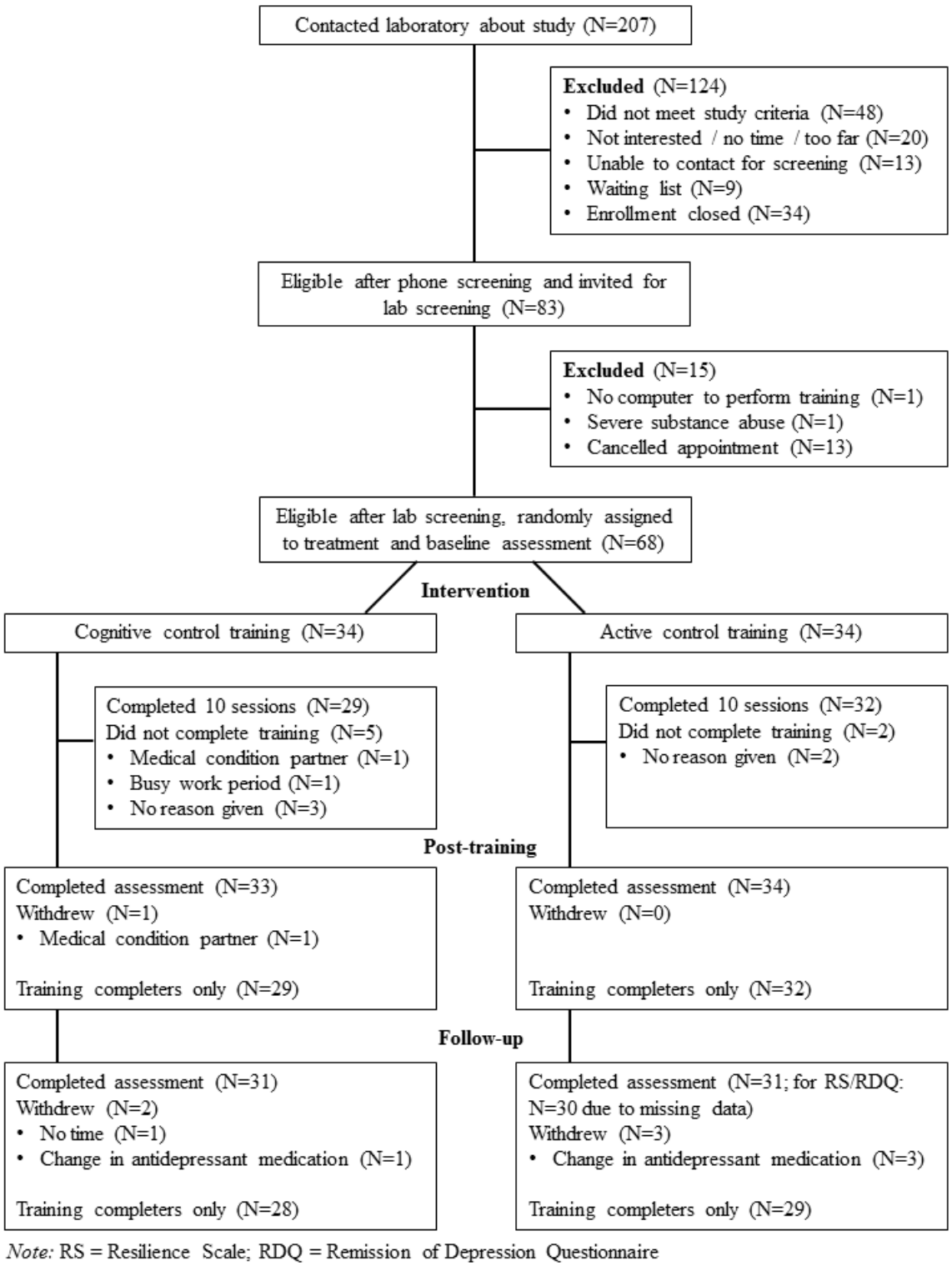


Figure 1. Consort diagram for flow of participants

Training Task Process Measures

Progress on training task. Training task progress was assessed using participants' median ISI scores per session (Hoorelbeke, Koster, et al., 2015). Due to the different nature of both training tasks, for each group we performed a Repeated Measures ANOVA to explore whether progress was made over the ten training sessions. In line with our expectations, both groups showed a significant increase in task performance throughout the two week training period, as shown by a decrease in ISI (CCT: $F(9, 20) = 18.95$, $p < .001$, $\eta_p^2 = 0.90$; active control: $F(9, 23) = 4.82$, $p = .001$, $\eta_p^2 = 0.65$; see Appendix Table 1).

Perception of the training as an intervention. As expected, results from 2 (Time: Pre- vs. Post-training) x 2 (Group: CCT vs. active control) Mixed ANOVA's indicate that both groups did not significantly differ concerning self-reported credibility of the intervention and expectancy (as shown by the absence of an interaction effect for both measures in Table 3; see Table 2 for descriptives). Furthermore, the proportion of participants that perceived the intervention as a placebo was limited (ratio "placebo" : "no-placebo"; CCT: 3:31; active control: 4:30) and did not differ between both groups ($\chi^2 = 0.16$, $p = .690$). This indicates that blinding of participants was successful.

Effects of Training

Effects of CCT on cognitive transfer measures (cognitive task performance and self-reported cognitive complaints), primary outcome measures (depressive rumination and depressive symptomatology) and secondary outcome measure (mal)adaptive emotion regulation (CERQ) were assessed using 3 (Time: Pre-training, Post-training, Follow-up) x 2 (Group: CCT vs. active control) Mixed ANOVA's. Given that some of the secondary outcome measures were only assessed at baseline and three months follow-up, effects on secondary outcome measures quality of life, resilience, disability and remission were explored using 2 (Time: Pre-training vs. Follow-up) x 2 (Group: CCT vs. active control) Mixed ANOVA's. Effects are reported in Table 3 taking into account ITT. Where the expected interaction effects were not found using ITT analysis, we then proceeded with a secondary completers-only analysis.

Table 2

Group characteristics as a function of training condition

	Training condition											
	Cognitive control (*n* = 34)						Active control (*n* = 34)					
	Time 1		Time 2		Time 3		Time 1		Time 2		Time 3	
Variables	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Cognitive transfer measures												
Cogn. task accur.	50.82	17.89	82.53	16.72	77.61	17.04	51.03	12.91	63.04	16.90	66.11	17.33
Cogn. complaints	117.15	24.84	112.62	25.47	107.97	24.10	119.65	22.47	118.03	23.77	117.32	25.99
Primary outcome measures												
Depressive sympt.	8.77	8.65	5.38	7.10	4.50	5.10	7.27	6.28	9.29	9.37	9.29	7.28
Trait rumination	43.00	11.88	34.71	10.01	30.06	6.72	43.29	12.27	44.29	12.58	40.35	14.06
Brooding	10.29	3.77	8.21	2.57	7.12	1.95	10.35	2.91	10.71	3.40	9.44	3.23
Reflection	9.59	3.46	8.12	3.07	7.00	2.32	9.85	3.56	9.79	3.49	9.21	3.84
Secondary outcome measures												
Adaptive ER	59.15	13.34	58.88	15.87	55.71	17.16	56.65	14.31	54.82	14.19	56.00	14.86
Maladaptive ER	36.21	9.41	30.62	9.69	26.56	7.88	36.24	10.86	35.94	10.51	32.91	9.47
Quality of Life	4.24	6.28	/	/	2.79	4.20	3.32	4.55	/	/	4.59	5.44
Disability	17.23	13.73	/	/	14.71	14.82	19.66	11.41	/	/	20.97	14.34
Resilience	76.41	10.37	/	/	82.94	11.98	75.50	11.32	/	/	75.53	11.52
Remission	19.44	15.61	/	/	13.94	11.96	19.24	14.87	/	/	24.77	16.46
Other variables												
Credibility	0.21	2.74	0.48	2.74	/	/	-0.21	2.32	-0.50	2.57	/	/
Expectancy	0.54	2.64	0.51	2.55	/	/	-0.54	2.52	-0.52	2.72	/	/
Stressful events	1.27	1.40	0.47	0.66	0.74	0.93	1.15	1.26	0.50	0.86	0.85	1.11

Note: ER = Emotion Regulation; These descriptives represent information on Group level at Baseline (Time 1), Post-training (Time 2), and Follow-up (Time 3) taking into account intention-to-treat. Independent samples *t*-tests indicate that both groups did not significantly differ at

Time 1 concerning the cognitive transfer and outcome measures (all *t*s < 1.73). Participants also did not differ in amount of experienced stressful / life events from one year prior to participation to the study until the follow-up assessment (all *t*s < 0.49)

Table 3

Evidence for training effects from Mixed ANOVA's

	Main effect of Time				Main effect of Group				Time x Group interaction			
Variables	*F*	*df*	*p*	η_p^2	*F*	*df*	*p*	η_p^2	*F*	*df*	*p*	η_p^2
Cognitive transfer measures												
Non-adaptive PASAT accuracy[a]	93.86	2, 65	< .001	0.74	7.87	1, 66	.007	0.11	18.52	2, 65	< .001	0.36
Cognitive complaints[a]	3.65	2, 65	.032	0.10	1.09	1, 66	.300	0.02	1.20	2, 65	.308	0.04
Primary outcome measures												
Brooding[a]	12.10	2, 65	< .001	0.27	7.85	1, 66	.007	0.11	4.70	2, 65	.012	0.13
Depressive symptomatology[a]	0.79	2, 65	.459	0.02	2.56	1, 66	.115	0.04	7.04	2, 65	.002	0.18
Secondary outcome measures												
Maladaptive emotion regulation[a]	17.39	2, 65	< .001	0.35	3.60	1, 66	.062	0.05	5.79	2, 65	.005	0.15
Adaptive emotion regulation[a]	0.66	2, 65	.519	0.02	0.45	1, 66	.505	0.01	0.87	2, 65	.425	0.03
Resilience[b]	12.30	1, 66	.001	0.16	2.60	1, 66	.111	0.04	12.08	1, 66	.001	0.16
Remission from depression[b]	0.00	1, 66	.993	0.00	2.76	1, 66	.101	0.04	11.21	1, 66	.001	0.15
Disability[b]	0.14	1, 66	.714	0.00	2.30	1, 66	.134	0.03	1.36	1, 66	.249	0.02
Quality of Life[b]	0.02	1, 66	.904	0.00	0.19	1, 66	.668	0.00	3.46	1, 66	.067	0.05
Other measures												
Credibility[b]	0.00	1, 66	.982	0.00	1.88	1, 66	.176	0.03	0.56	1, 66	.455	0.01
Expectancy[b]	0.00	1, 66	.984	0.00	3.58	1, 66	.063	0.05	0.01	1, 66	.927	0.00

Note: The presented statistics take into account intention-to-treat analysis; [a] Represents results of 3 (Time) x 2 (Group) Mixed ANOVA's; [b] Represents results of 2 (Time) x 2 (Group) Mixed ANOVA's

Cognitive transfer effects. Using ITT analysis, we found an effect of CCT on *cognitive task performance*, as indicated by the significant Time x Group interaction effect (see Table 3). Follow-up paired samples *t*-tests indicate that both groups continued to perform well at the three month follow-up compared to the baseline assessment of cognitive functioning (CCT: $t(33) = 10.80$, $p < .001$, $d = 1.85$, 95% CI [21.75, 31.85]; active control: $t(33) = 8.19$, $p < .001$, $d = 1.40$, 95% CI [11.33, 18.83]), with cognitive task performance at both the post-training assessment (independent samples *t*-test, $t(66) = 4.78$, $p < .001$, $d = 1.16$, 95% CI [11.35, 27.64]) and the follow-up assessment ($t(66) = 2.76$, $p = .007$, $d = 0.67$, 95% CI [3.18, 19.83]) significantly higher in the CCT group than in the active control condition (see Table 2). The results were similar when not taking into account ITT and including completers only (see Appendix Table 2).

We did not find differential effects of training on *self-reported cognitive complaints* when taking into account ITT: we only found a general decrease in cognitive complaints over time (Baseline: $M = 118.40$, $SD = 23.54$; Post-training: $M = 115.32$, $SD = 24.60$; Follow-up: $M = 112.65$, $SD = 25.32$; see Table 3). However, results for completers only do show a near significant effect of CCT on cognitive complaints (Time x Group interaction: $F(2, 54) = 2.70$, $p = .076$, $\eta_p^2 = 0.09$), with follow-up paired samples *t*-tests suggesting a marginal significant decrease in cognitive complaints from baseline to the post-training assessment in the CCT group ($t(28) = 2.03$, $p = .053$, $d = 0.38$, 95% CI [-0.05, 9.16]), and a significant decrease in cognitive complaints from the post-training assessment to three months follow-up ($t(27) = 2.72$, $p = .011$, $d = 0.51$, 95% CI [1.72, 12.28]), which was not the case in the active control condition (all *t*s < 0.96, see Appendix Table 2). However, this did not result in a significant group difference in self-reported cognitive complaints at three months follow-up, $t(55) = 1.71$, $p = .094$, $d = 0.45$, 95% CI [-1.92, 23.85].

Effects on primary outcome measures: brooding and depressive symptomatology. Taking into account ITT, we found beneficial effects of CCT on both *brooding* and *depressive symptomatology* as shown by the significant Time x Group interactions (see Table 3 and Figure 2A/B). Follow-up paired samples *t*-tests indicate that the immediate beneficial effects of CCT on depressive symptomatology (from

baseline to the post-training assessment; $t(33) = 2.83$, $p = .008$, $d = 0.49$, 95% CI [0.95, 5.82]) remained stable from post-training to the three month follow-up ($t(33) = 0.88$, $p = .385$, $d = 0.15$, 95% CI [-1.16, 2.92]). In contrast, no change in depressive symptomatology occurred in the active control condition (all ts < 1.58). Independent samples *t*-tests indicate that the CCT group reported significantly lower levels of depressive symptomatology than the active control condition at three months follow-up ($t(66) = 3.15$, $p = .002$, $d = 0.76$, 95% CI [1.75, 7.84]), whereas there was a tendency towards a group difference immediately following two weeks of training ($t(66) = 1.94$, $p = .057$, $d = 0.47$, 95% CI [-0.11, 7.94]). Similarly, only the CCT condition showed an immediate reduction in brooding (from baseline to the post-training assessment; CCT: $t(33) = 2.97$, $p = .006$, $d = 0.51$, 95% CI [0.66, 3.52]; active control: $t(33) = 0.91$, $p = .371$, $d = 0.16$, 95% CI [-0.44, 1.14]). Furthermore, although both groups reported a significant reduction in brooding from post-training to three months follow-up (CCT: $t(33) = 2.63$, $p = .013$, $d = 0.45$, 95% CI [0.25, 1.93]; active control: $t(33) = 2.62$, $p = .013$, $d = 0.45$, 95% CI [0.28, 2.25]), independent samples *t*-tests indicate that brooding levels were significantly lower in the CCT condition at post-training ($t(66) = 3.42$, $p = .001$, $d = 0.83$, 95% CI [1.04, 3.96]) and follow-up ($t(54.24) = 3.59$, $p = .001$, $d = 0.87$, 95% CI [1.03, 3.62]; see Table 2). These interaction effects were also found when performing completers-only analysis.[4]

Effects on secondary outcome measures.

(Mal)Adaptive emotion regulation. Results for ITT analysis on the alternative measure for *maladaptive emotion regulation* are in line with the above reported beneficial effects on brooding. That is, we found a significant Time x Group interaction effect for CERQ maladaptive emotion regulation (see Table 3 and Figure 2C), with follow-up paired samples *t*-tests indicating immediate beneficial effects of CCT (from baseline to post-training assessment; $t(33) = 3.72$, $p < .001$, $d = 0.64$, 95% CI [2.53,

[4] Effects of CCT on the primary outcome measures remained after controlling for change in process measures of training session experience (i.e., rated mood and thoughts during and immediately following completion of an online training session; for a complete description of the protocol, please see Hoorelbeke, Faelens, et al., 2015 or Chapter 5 of this thesis). This indicates that training effects may not be reduced to habituation to stress.

8.65]), and a further decrease in maladaptive emotion regulation from post-training to the three month follow-up ($t(33) = 2.56$, $p = .015$, $d = 0.44$, 95% CI [0.83, 7.29]). In line with the results for brooding, the active control condition only showed a decrease in maladaptive emotion regulation from post-training to follow-up (from baseline to post-training: $t(33) = 0.35$, $p = .728$, $d = 0.06$, 95% CI [-1.41, 2.00]; from post-training to follow-up: $t(33) = 2.65$, $p = .012$, $d = 0.45$, 95% CI [0.70, 5.36]). Importantly, in absence of baseline group differences, compared to the active control condition the CCT condition reported deploying less maladaptive emotion regulation strategies immediately following training ($t(66) = 2.17$, $p = .034$, $d = 0.53$, 95% CI [0.43, 10.22]) and at three months follow-up ($t(66) = 3.01$, $p = .004$, $d = 0.73$, 95% CI [2.14, 10.57]; see Table 2). In contrast to the beneficial effects on maladaptive emotion regulation processes, CCT did not affect self-reported use of *adaptive emotion regulation strategies* (see Table 2, Table 3). Similar interaction effects were found when deploying completers-only analysis.

Other indicators of functioning. CCT had beneficial effects on *resilience* and *remission from depression* (see Table 3). In contrast to the active control condition ($t(33) = 0.03$, $p = .979$, $d = 0.01$, 95% CI [-2.20, 2.26]), follow-up paired samples *t*-tests revealed that participants in the CCT condition showed a significant increase in resilience ($t(33) = 4.31$, $p < .001$, $d = 0.74$, 95% CI [3.44, 9.62]; see Table 2 and Figure 2D), resulting in a significant group difference in self-reported resilience levels at three months follow-up in favor of the CCT condition (independent samples *t*-test, $t(66) = 2.60$, $p = .011$, $d = 0.63$, 95% CI [1.72, 13.10]). Furthermore, the CCT group showed a significant reduction in residual symptomatology (RDQ; $t(33) = 2.31$, $p = .027$, $d = 0.40$, 95% CI [0.65, 10.35]) while participants from the active control condition reported an increase in residual symptoms at three months follow-up ($t(33) = 2.43$, $p = .021$, $d = 0.42$, 95% CI [0.91, 10.15]; see Table 2). In line with the findings for our primary outcome measure for depressive symptomatology (BDI-II), participants from the CCT condition reported significantly lower levels of residual symptomatology (RDQ) at three months follow-up (independent samples *t*-test, $t(66) = 3.10$, $p = .003$, $d = 0.75$, 95% CI [3.86, 17.79]).

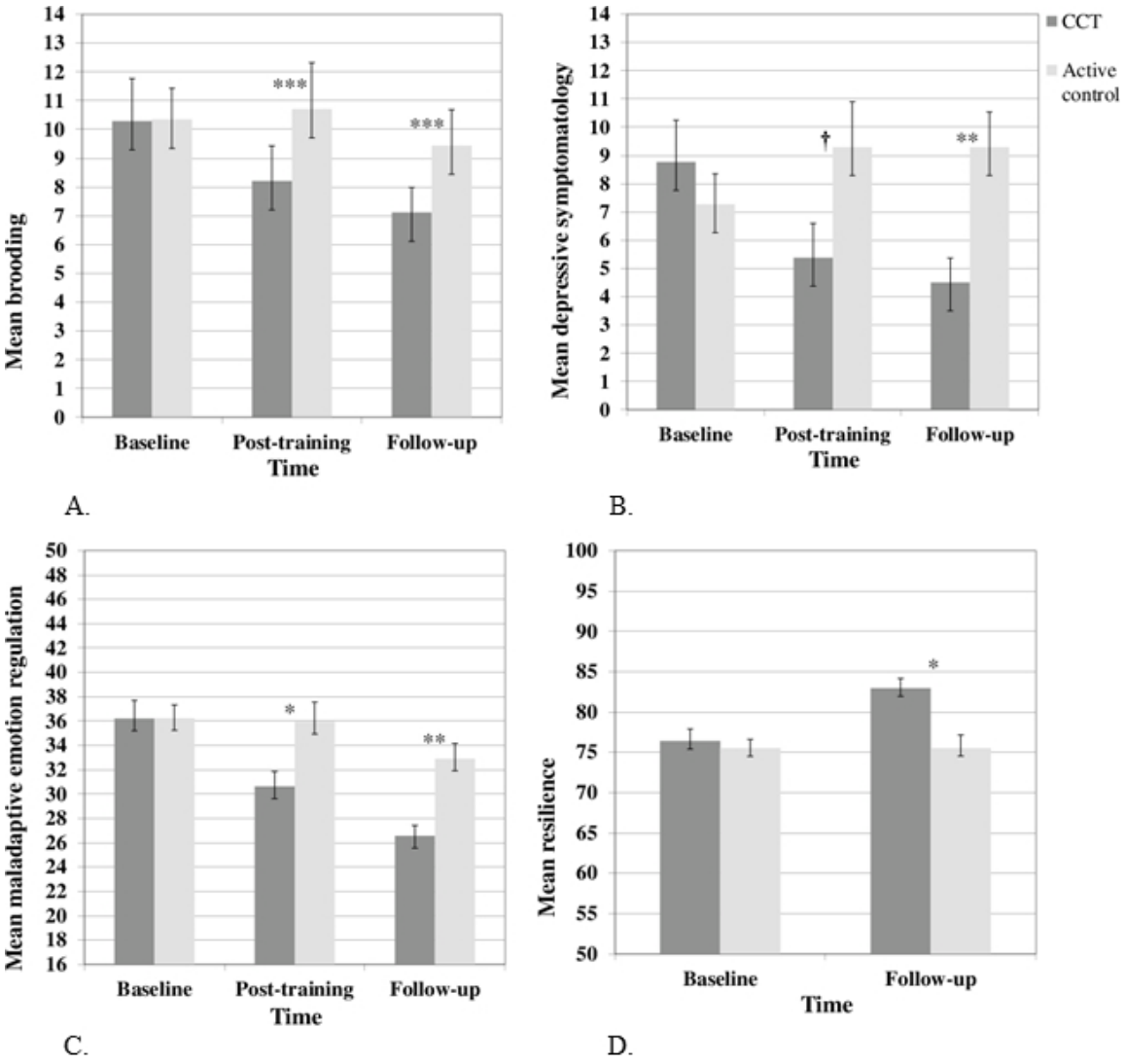


Figure 2. Effects of training on the primary outcome measures, maladaptive emotion regulation and resilience (M, SE)

Note: Independent samples t-tests, † = $p < 0.100$, * = $p < 0.050$, ** = $p < 0.010$, *** = $p \leq 0.001$; A. Time x Group effect on brooding; B. Time x Group effect on depressive symptomatology; C. Time x Group effect on maladaptive emotion regulation; D. Time x Group effect on resilience

We found a marginal significant interaction for *Quality of Life* (see Table 3), which turned significant when performing completers-only analyses (Time x Group interaction: $F(1, 55) = 4.63$, $p = .036$, $\eta_p^2 = 0.08$). However, follow-up paired samples *t*-tests suggest that Quality of Life remained stable in both groups (all *t*s < 1.66; see Appendix Table 2). Moreover, both groups did not significantly differ in self-reported Quality of Life at three months follow-up ($t(55) = 1.43$, $p = .158$, $d = 0.38$, 95% CI [-0.72, 4.32]). Completers-only analysis also yielded a significant Time x Group interaction effect for *WHODAS disability score* (Time x Group interaction: $F(1, 55) = 7.05$, $p = .010$, $\eta_p^2 = 0.11$), with follow-up paired samples *t*-tests suggesting a significant increase in functioning (a decrease in disability) in the CCT group only (CCT: $t(27) = 3.30$, $p = .003$, $d = 0.62$, 95% CI [2.34, 10.01]; active control: $t(28) = 0.61$, $p = .545$, $d = 0.11$, 95% CI [-2.99, 5.54]; see Appendix Table 2). As a result, in absence of baseline group differences, the CCT group reported significantly lower levels of experienced disability at three months follow-up (independent samples *t*-test, $t(55) = 2.58$, $p = .012$, $d = 0.69$, 95% CI [2.01, 15.87]).

Mediation Hypothesis

We conducted multiple regression analyses to test whether effects of cognitive control on depressive symptomatology were mediated by brooding. To ensure sufficient variability in change in cognitive control over time and to have the necessary power to detect mediation effects, we relied on the sample of participants used for the primary analyses ($n = 68$). Increase in cognitive control from baseline to post-training (Δ non-adaptive PASAT task performance) entered the model as the independent variable. Post-training brooding was selected as mediator and follow-up depressive symptomatology as dependent variable. Effects of baseline depressive symptomatology ($B = 0.29$, $t = 3.21$, $p = .002$) and baseline brooding ($B = -0.03$, $t = 0.15$, $p = .879$) on the dependent variable were controlled for by entering both variables as covariates in the model (see Figure 3).

Results indicate that initial increase in cognitive control (Δ non-adaptive PASAT task performance) predicted lower post-training brooding levels (A-path; $B = -0.05$, $t = 2.13$, $p = .037$) and less depressive symptomatology at three months follow-up (C-path;

B = -0.13, *t* = 3.11, *p* = .003). Furthermore, post-training brooding predicted more future depressive symptomatology (B-path; *B* = 0.94, *t* = 4.10, *p* < .001). Given that both A- and B-paths were significant, we continued the mediation analysis via the Preacher and Hayes bootstrapping method (Preacher & Hayes, 2004) with bias-corrected confidence estimates, using 5000 bootstrap resamples to obtain the 95% confidence interval (CI) of the indirect effect (Preacher & Hayes, 2008). Results confirmed the mediating role of brooding for the effect of cognitive control on depressive symptomatology (*B* = -0.04, 95% CI [-0.10, -0.01]). Given that the direct effect of cognitive control on depressive symptomatology remained significant when controlling for the mediator (C'-path; *B* = -0.09, *t* = 2.30, *p* = .025), these findings suggest partial mediation.

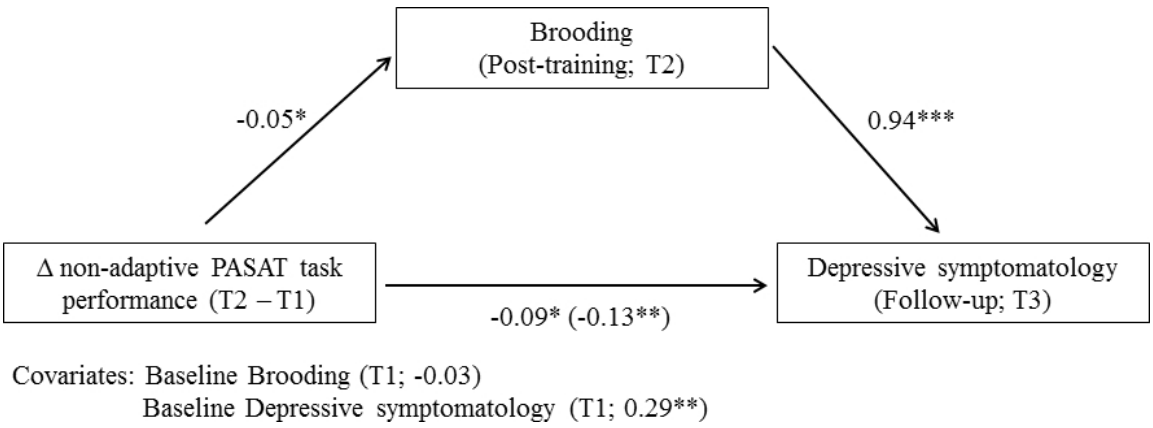


Figure 3. Mediation model

DISCUSSION

This RCT study demonstrates the preventive potential of CCT following recovery from depression. We found near transfer of training on a cognitive transfer task, suggesting successful manipulation of cognitive control. Moreover, participants completing the CCT intervention reported a reduction in cognitive complaints over time. In line with our first hypothesis, findings indicated immediate and lasting beneficial effects of CCT on primary outcome measures brooding and depressive symptomatology, even after controlling for ITT. The finding that similar effects were

obtained for alternative measures of maladaptive emotion regulation (CERQ) and residual depressive symptomatology (RDQ) adds to the validity of the reported effects. These moderate to strong effects are in line with previous studies exploring the preventive and curative potential of CCT in at-risk and MDD populations (Calkins et al., 2015; Hoorelbeke, Koster, et al., 2015; Siegle et al., 2014). Furthermore, in contrast to Siegle et al. (2014), participants in the CCT condition showed the tendency to report less depressive symptomatology immediately following training. This between-group difference in depressive symptomatology turned significant at three months follow-up. Interestingly, this is in line with previous findings suggesting that beneficial effects of CCT may gradually develop over time. Confirming our second hypothesis, effects of cognitive control on depressive symptomatology were partially mediated by brooding, suggesting both direct and indirect beneficial effects of CCT on depressive symptomatology. Importantly, CCT also showed transfer to indicators of functioning (e.g., resilience, disability), confirming our third hypothesis. However, in accordance with previous experimental studies (Hoorelbeke et al., 2016), CCT did not exert effects on adaptive emotion regulation strategies. Similarly, effects on quality of life were limited.

The lack of training effects on adaptive emotion regulation may indicate that cognitive control is less crucial to deployment of adaptive emotion regulation strategies once recovery from depression has occurred. Alternatively, it is possible that – while stimulating cognitive control may provide individuals with the necessary cognitive resources to disengage from perseverative negative thinking processes – in order to adopt more adaptive emotion regulation strategies in daily life, combining CCT with other therapeutic interventions may be warranted (e.g., emotion regulation skill training). Furthermore, a growing literature suggests that the extent to which engaging in a certain emotion regulation strategy is adaptive depends on the flexible deployment of that emotion regulation strategy within a given context (Aldao, Sheppes, & Gross, 2015; Aldao, 2013; Bonanno, Papa, Lalande, Westphal, & Coifman, 2004). Moreover, previous findings indicate the importance of taking into account the interaction between both adaptive and maladaptive emotion regulation strategies in relation to psychopathology (e.g., Aldao, Jazaieri, Goldin, & Gross, 2014; Aldao & Nolen-Hoeksema,

2012; Conklin et al., 2015), whereas we have explored the effects on adaptive and maladaptive emotion regulation separately.

On a theoretical level, these experimental findings confirm the causal role of cognitive control in maladaptive emotion regulation as a vulnerability factor for (residual) depressive symptomatology. Furthermore, these findings indicate that cognitive control may contribute to resilience and functioning. Although it has been proposed that cognitive control may play a role in resilience via adaptive emotion regulation strategies, the current findings indicate that other mechanisms may underlie the observed relation between cognitive control and resilience. These findings have significant clinical implications, suggesting that directly targeting cognitive control via cognitive training reduces residual symptomatology and holds the potential to contribute to the prevention of recurring depressive episodes.

Demonstrating the efficacy of CCT as a neurobehavioral intervention for RMD patients, this RCT is the first study to provide experimental evidence for the causal role of cognitive control in cognitive vulnerability for depression and resilience following recovery from a depressive episode. Other strengths of this study are the use of an active control condition that is closely matched to the intervention, extending the focus to a wide range of indicators of functioning (among which alternative measures for the primary outcome measures), and repeated assessment of cognitive transfer effects at three months follow-up. Although participants maintained their training-related improvements, we observed a subtle reduction. This could indicate that booster sessions may be warranted to increase long-term beneficial effects of CCT on stable remission.

Certain limitations should be taken into account. This study is the first to explore effects of CCT in a RMD population whereas previous studies have typically explored effects in healthy, at-risk (student) samples, or MDD patients (e.g., Brunoni et al., 2014; Calkins et al., 2015; Hoorelbeke, Koster, et al., 2015; Segrave et al., 2014; Siegle et al., 2014). Despite these promising results, replication is warranted. Furthermore, effects were assessed using self-report questionnaires until three months follow-up. Future studies should explore long-term effects using structured interviews to directly assess

the efficacy of CCT in reducing recurrence of depressive episodes. Additionally, to further enhance our understanding of the mechanisms underlying beneficial effects of CCT on depression vulnerability, future studies could combine CCT with experience sampling (e.g., Hoorelbeke et al., 2016) in clinical samples. Third, we relied on a cognitive task showing high resemblance to the training task to assess close cognitive transfer. As a result, strategy learning may have confounded the cognitive transfer effects. Future studies could deploy multiple transfer tasks. Importantly, there is increasing evidence for the neural underpinnings of effects of CCT (Cohen et al., 2016; Schweizer, Grahn, Hampshire, Mobbs, & Dalgleish, 2013; Siegle, Ghinassi, & Thase, 2007) and cognitive transfer effects of the training procedure used in this study have also been established using a dual n-back task (Hoorelbeke et al., 2016). In the current study we instead added a measure for the clinical experience of the patient (self-reported cognitive complaints). Finally, due to sample size restrictions, we did not explore potential moderators of training success (e.g., medication use). It is likely that beneficial effects of CCT may be increased using a stepped-care and individually tailored training approach. Overall, although this is an interesting initial test of the potential of CCT as a preventive intervention for recurrent depression, replication in a larger sample of RMD patients is desirable following-up participants over a clinically more meaningful timeframe in terms of exploring effects on recurrence of depression.

Summary

This double-blind RCT study provides evidence for the effectiveness of a working memory based CCT in reducing cognitive vulnerability for depression and increasing resilience in RMD patients. Compared to an active control condition, CCT demonstrated beneficial effects on cognitive functioning, brooding, and depressive symptomatology immediately following training and at three months follow-up. Similar findings were obtained using alternative measures of maladaptive emotion regulation and residual symptomatology. In line with existing theories, improvement in cognitive control predicted lower future levels of depressive symptomatology, which was partially mediated by brooding. Additional beneficial effects were found on resilience and disability. However, no effects were found on indicators of adaptive emotion

regulation. Overall, these findings demonstrate the potential of CCT as a preventive intervention following recovery from depression.

ACKNOWLEDGMENTS

This research was supported by a Special Research Fund (BOF) of Ghent University awarded to Kristof Hoorelbeke (B/13808/01) and by Grant BOF10/GOA/014 for a Concerted Research Action of Ghent University awarded to Ernst Koster. We thank Ineke Demeyer and Laura de Putter for overseeing the blinding procedure and Stephanie Stevens for proofreading the manuscript. Students Lien Faelens, Jeffrey Behiels, and Sylvie Van Paemele assisted during the phase of data collection.

REFERENCES

Aldao, A. (2013). The Future of Emotion Regulation Research: Capturing Context. *Perspectives on Psychological Science*, *8*, 155–172. doi: 10.1177/1745691612459518

Aldao, A., Jazaieri, H., Goldin, P. R., & Gross, J. J. (2014). Adaptive and maladaptive emotion regulation strategies: Interactive effects during CBT for social anxiety disorder. *Journal of Anxiety Disorders*, *28*, 382–389. doi: 10.1016/j.janxdis.2014.03.005

Aldao, A., & Nolen-Hoeksema, S. (2012). When are adaptive strategies most predictive of psychopathology? *Journal of Abnormal Psychology*, *121*, 276–281. doi: 10.1037/a0023598

Aldao, A., Sheppes, G., & Gross, J. J. (2015). Emotion regulation flexibility. *Cognitive Therapy and Research*, *39*, 263–278. doi: 10.1007/s10608-014-9662-4

Au, J., Sheehan, E., Tsai, N., Duncan, G. J., Buschkuehl, M., & Jaeggi, S. M. (2015). Improving fluid intelligence with training on working memory: a meta-analysis. *Psychonomic Bulletin & Review*, *22*, 366–377. doi: 10.3758/s13423-014-0699-x

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for Beck Depression Inventory II*. San Antonio, Texas: Psychological Corporation.

Bonanno, G. A., Papa, A., Lalande, K., Westphal, M., & Coifman, K. (2004). The importance of being flexible: The ability to both enhance and suppress emotional expression predicts long-term adjustment. *Psychological Science*, *15*, 482–487. doi: 10.1111/j.0956-7976.2004.00705.x

Brugha, T. S., & Cragg, D. (1990). The List of Threatening Experiences: the reliability and validity of a brief life events questionnaire. *Acta Psychiatrica Scandinavica*, *82*, 77–81.

Brunoni, A. R., Boggio, P. S., De Raedt, R., Bensenor, I. M., Lotufo, P. A., Namur, V., … Vanderhasselt, M. A. (2014). Cognitive control therapy and transcranial direct current stimulation for depression: A randomized, double-blinded, controlled trial. *Journal of Affective Disorders*, *162*, 43–49. doi: 10.1016/j.jad.2014.03.026

Calkins, A. W., Deveney, C. M., Weitzman, M. L., Hearon, B. A., & Siegle, G. J. (2011). The effects of prior cognitive control task exposure on responses to emotional tasks in

healthy participants. *Behavioural and Cognitive Psychotherapy*, *39*, 205–220. doi: 10.1017/s1352465810000652

Calkins, A. W., McMorran, K. E., Siegle, G. J., & Otto, M. W. (2015). The effects of computerized cognitive control training on community adults with depressed mood. *Behavioural and Cognitive Psychotherapy*, *43*, 578–589. doi: 10.1017/S1352465814000046

Cohen, J. D. (2001). Cognitive Control (Executive Functions): Role of Prefrontal Cortex. In *International Encyclopedia of the Social & Behavioral Sciences* (pp. 2089–2094). doi: 10.1016/B0-08-043076-7/03505-1

Cohen, N., Margulies, D. S., Ashkenazi, S., Schaefer, A., Taubert, M., Henik, A., … Okon-Singer, H. (2016). Using executive control training to suppress amygdala reactivity to aversive information. *NeuroImage*, *125*, 1022–31. doi: 10.1016/j.neuroimage.2015.10.069

Cohen, N., Mor, N., & Henik, A. (2015). Linking executive control and emotional response: A training procedure to reduce rumination. *Clinical Psychological Science*, *3*, 15–25. doi: 10.1177/2167702614530114

Conklin, L. R., Cassiello-Robbins, C., Brake, C. A., Sauer-Zavala, S., Farchione, T. J., Ciraulo, D. A., & Barlow, D. H. (2015). Relationships among adaptive and maladaptive emotion regulation strategies and psychopathology during the treatment of comorbid anxiety and alcohol use disorders. *Behaviour Research and Therapy*, *73*, 124–130. doi: 10.1016/j.brat.2015.08.001

Davidson, R. J., Pizzagalli, D., Nitschke, J. B., & Putman, K. (2002). Depression: Perspectives from affective neuroscience. . *Annual Review of Psychology*, *53*, 545–574.

Demeyer, I., De Lissnyder, E., Koster, E. H. W., & De Raedt, R. (2012). Rumination mediates the relationship between impaired cognitive control for emotional information and depressive symptoms: A prospective study in remitted depressed adults. *Behaviour Research and Therapy*, *50*, 292–297. doi: 10.1016/j.brat.2012.02.012

Devilly, G. J., & Borkovec, T. D. (2000). Psychometric properties of the credibility/expectancy questionnaire. *Journal of Behavior Therapy and Experimental Psychiatry*, *31*, 73–86.

Garnefski, N., Kraaij, V., & Spinhoven, P. (2001). Negative life events, cognitive emotion regulation and emotional problems. *Personality and Individual Differences*, *30*, 1311–1327. doi: 10.1016/s0191-8869(00)00113-6

Gronwall, D. M. A. (1977). Paced Auditory Serial Addition Task - Measure of recovery from concussion. *Perceptual and Motor Skills*, *44*, 367–373.

Hardeveld, F., Spijker, J., De Graaf, R., Nolen, W. A., & Beekman, A. T. F. (2010). Prevalence and predictors of recurrence of major depressive disorder in the adult population. *Acta Psychiatrica Scandinavica*, *122*, 184–191. doi: 10.1111/j.1600-0447.2009.01519.x

Hofmann, W., & Patel, P. V. (2015). SurveySignal: A convenient solution for experience sampling research using participants' own smartphones. *Social Science Computer Review*, *33*, 235–253. doi: 10.1177/0894439314525117

Hoorelbeke, K., Faelens, L., Behiels, J., & Koster, E. H. W. (2015). Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Protocol for a randomized controlled trial. *Bmc Psychiatry*, *15*, 125.

Hoorelbeke, K., Koster, E. H. W., Demeyer, I., Loeys, T., & Vanderhasselt, M. A. (2016). Effects of cognitive control training on the dynamics of (mal)adaptive emotion regulation in daily life. *Emotion*, *16*, 945-956. doi: 10.1037/emo0000169

Hoorelbeke, K., Koster, E. H. W., Vanderhasselt, M. A., Callewaert, S., & Demeyer, I. (2015). The influence of cognitive control training on stress reactivity and rumination in response to a lab stressor and naturalistic stress. *Behaviour Research and Therapy*, *69*, 1–10.

Hunt, S. M., & McKenna, S. P. (1992). The QLDS: A scale for the measurement of quality of life in depression. *Health Policy*, *22*, 307–319.

Lange, C., Adli, M., Zschucke, E., Beyer, R., Ising, M., Uhr, M., & Bermpohl, F. (2012). Affective set-shifting deficits in patients with major depression in remission. *Journal of Psychiatric Research*, *46*, 1623–1626. doi: 10.1016/j.jpsychires.2012.09.007

Lazeron, R. H., Rombouts, S. A., deSonneville, L., Barkhof, F., & Scheltens, P. (2003). A paced visual serial addition test for fMRI. *Journal of Neurological Science*, *213*, 29–34.

Levens, S. M., & Gotlib, I. H. (2015). Updating emotional content in recovered

depressed individuals: Evaluating deficits in emotion processing following a depressive episode. *Journal of Behavior Therapy and Experimental Psychiatry*, *48*, 156–163. doi: 10.1016/j.jbtep.2015.03.009

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive Psychology*, *41*, 49–100. doi: 10.1006/cogp.1999.0734

Moher, D., Hopewell, S., Schulz, K. F., Montori, V., Gotzsche, P. C., Devereaux, P. J., … Altman, D. G. (2010). CONSORT 2010 Explanation and elaboration: Updated guidelines for reporting parallel group randomised trials. *British Medical Journal*, 340:28. doi: 10.1136/bmj.c869

Moshier, S. J., Molokotos, E. K., Stein, A. T., & Otto, M. W. (2015). Assessing the effects of depressed mood and cognitive control training on memory confidence and accuracy following repeated checking. *International Journal of Cognitive Therapy*, *8*, 206–221. doi: 10.1521/ijct_2015_8_02

Nolen-Hoeksema, S., & Morrow, J. (1991). A prospective study of depression and posttraumatic stress symptoms after a natural disaster - The 1989 Loma-Prieta earthquake. *Journal of Personality and Social Psychology*, *61*, 115–121. doi: 10.1037/0022-3514.61.1.115

Nolen-Hoeksema, S., Wisco, B. E., & Lyubomirsky, S. (2008). Rethinking rumination. *Perspectives on Psychological Science*, *3*, 400–424. doi: 10.1111/j.1745-6924.2008.00088.x

Norbury, R., Godlewska, B., & Cowen, P. J. (2014). When less is more: A functional magnetic resonance imaging study of verbal working memory in remitted depressed patients. *Psychological Medicine*, *44*, 1197–1203. doi: 10.1017/S0033291713001682

Peeters, F., Nicolson, N., Wichers, M., & Hacker, P. (2013). *Remission of Depression Questionnaire - Dutch translation (RDQ-NL)*.

Pizzagalli, D. A. (2011). Frontocingulate dysfunction in depression: Towards biomarkers of treatment response. *Neuropsychopharmacology Review*, *36*, 183–206.

Portzky, M. (2008). *RS-nl: Resilience Scale - Nederlandse versie*. Amsterdam: Harcourt Test Publishers.

Preacher, K. J., & Hayes, A. F. (2004). SPSS and SAS procedures for estimating indirect effects in simple mediation models. *Behavior Research Methods, Instruments, and Computers*, *36*, 717–731. doi: 10.3758/BF03206553

Preacher, K. J., & Hayes, A. F. (2008). Asymptotic and resampling strategies for assessing and comparing indirect effects in multiple mediator models. *Behavior Research Methods*, *40*, 879–891. doi: 10.3758/BRM.40.3.879

Rosmalen, J. G. M., Bos, E. H., & de Jonge, P. (2012). Validation of the Long-term Difficulties Inventory (LDI) and the List of Threatening Experiences (LTE) as measures of stress in epidemiological population-based cohort studies. *Psychological Medicine*, *42*, 2599–2608. doi: 10.1017/S0033291712000608

Scholte, E., & Noens, I. (2011). *BRIEF-A Handleiding: Vragenlijst executieve functies voor volwassenen*. Amsterdam: Hogrefe.

Schweizer, S., Grahn, J., Hampshire, A., Mobbs, D., & Dalgleish, T. (2013). Training the Emotional Brain: Improving Affective Control through Emotional Working Memory Training. *Journal of Neuroscience*, *33*, 5301-5311. doi: 10.1523/jneurosci.2593-12.2013

Segrave, R. A., Arnold, S., Hoy, K., & Fitzgerald, P. B. (2014). Concurrent cognitive control training augments the antidepressant efficacy of tDCS: A pilot study. *Brain Stimulation*, *7*, 325–331. doi: 10.1016/j.brs.2013.12.008

Sheehan, D. V, Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., … Dunbar, G. C. (1989). The Mini-International Neuropsychiatric Interview (MINI): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *Journal of Clinical Psychiatry*, *59*, 22–33.

Siegle, G. J., Ghinassi, F., & Thase, M. E. (2007). Neurobehavioral therapies in the 21st century: Summary of an emerging field and an extended example of cognitive control training for depression. *Cognitive Therapy and Research*, *31*, 235–262. doi: 10.1007/s10608-006-9118-6

Siegle, G. J., Price, R. B., Jones, N. P., Ghinassi, F., Painter, T., & Thase, M. E. (2014). You gotta work at it: Pupillary indices of task focus are prognostic for response to a neurocognitive intervention for rumination in depression. *Clinical Psychological Science*, *2*, doi: 10.1177/2167702614536160

Tombaugh, T. N. (2006). A comprehensive review of the Paced Auditory Serial Addition

Test (PASAT). *Archives of Clinical Neuropsychology*, *21*, 53–76.

Treynor, W., Gonzalez, R., & Nolen-Hoeksema, S. (2003). Rumination reconsidered: A psychometric analysis. *Cognitive Therapy and Research*, *27*, 247–259.

Tuynman-Qua, H., de Jonghe, F., & McKenna, S. P. (1997). Quality of Life in Depression Scale (QLDS). Development, reliability, validity, responsiveness and application. *Eur Psychiatry*, *12*, 199–202.

Üstün, T., Kostanjsek, N., Chatterji, S., & Rehm, J. (2010). Measuring health and disability: Manual for WHO Disability Assessment Schedule (WHODAS 2.0), World Health Organization, Switzerland: Geneva.

Van der Does, A. J. W. (2002). *BDI-II-NL. Handleiding: De Nederlandse versie van de Beck Depression Inventory - 2nd edition*. Lisse: Harcourt Test Publishers.

Vanderhasselt, M.-A., & De Raedt, R. (2009). Impairments in cognitive control persist during remission from depression and are related to the number of past episodes: An event related potentials study. *Biological Psychology*, *81*, 169–176. doi: 10.1016/j.biopsycho.2009.03.009

Vanderhasselt, M.-A., De Raedt, R., Namur, V., Lotufo, P. A., Bensenor, I. M., Boggio, P. S., & Brunoni, A. R. (2015). Transcranial electric stimulation and neurocognitive training in clinically depressed patients: A pilot study of the effects on rumination. *Prog Neuropsychopharmacol Biol Psychiatry*, *57*, 93–99. doi: 10.1016/j.pnpbp.2014.09.015

Wagnild, G. M., & Young, H. M. (1993). Development and psychometric evaluation of the resilience scale. *Journal of Nursing Measurement*, *1*, 165–178.

Wells, A. (2000). *Emotional disorders and metacognition innovative Cognitive Therapy*. New York: Wiley.

Zimmerman, M., Martinez, J. H., Attiullah, N., Friedman, M., Toba, C., Boerescu, D. A., & Ragheb, M. (2013). A new type of scale for determining remission from depression: The Remission from Depression Questionnaire. *Journal of Psychiatric Research*, *47*, 78–82. doi: 10.1016/j.jpsychires.2012.09.006

APPENDIX

-Table 1: provides an overview of training task performance as a function of training condition

-Table 2: provides descriptives for Time 1, Time 2, and Time 3 when not taking into account ITT

Supplemental Table 1

Training task progress: Mean median ISI and accuracy rates as a function of training condition

	Training condition					
	Cognitive control (*n* = 29)			Active control (*n* = 32)		
	M ISI (ms)	*SD* ISI (ms)	*M* % correct	*M* ISI (ms)	*SD* ISI (ms)	*M* % correct
Session 1	2062	505	54.86	1011	1279	59.34
Session 2	1772	418	56.24	744	203	61.31
Session 3	1666	423	56.21	723	220	61.84
Session 4	1562	366	56.86	719	180	61.31
Session 5	1517	430	56.48	705	223	61.81
Session 6	1441	374	57.21	700	213	61.41
Session 7	1393	360	57.41	678	195	62.06
Session 8	1338	341	57.14	670	190	61.88
Session 9	1328	390	58.17	664	191	62.19
Session 10	1321	394	58.21	667	209	61.34

Note: ISI = InterStimulus Interval. Training progress measures are based on completers only, not taking intention-to-treat into account

Supplemental Table 2

Group characteristics as a function of training condition for completers only

	Training condition											
	Cognitive control						Active control					
	Time 1 (*n* = 34)		Time 2 (*n* = 29)		Time 3 (*n* = 28)		Time 1 (*n* = 34)		Time 2 (*n* = 32)		Time 3 (*n* = 29)	
Variables	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*	*M*	*SD*
Cognitive transfer measures												
Cogn. task accur.	50.82	17.89	86.94	9.71	81.31	13.32	51.03	12.91	61.93	16.56	65.82	17.69
Cogn. complaints	117.15	24.84	114.21	26.01	108.04	22.41	119.65	22.47	117.84	24.13	119.00	25.92
Primary outcome measures												
Depressive sympt.	8.77	8.65	5.45	7.29	4.32	4.46	7.27	6.28	8.84	8.51	9.28	6.88
Trait rumination	43.00	11.88	34.07	8.94	29.39	5.04	43.29	12.27	44.28	12.09	41.31	14.39
Brooding	10.29	3.77	8.14	2.30	6.96	1.53	10.35	2.91	10.56	3.21	9.62	3.26
Reflection	9.59	3.46	7.93	2.88	6.71	1.94	9.85	3.56	9.75	3.41	9.35	3.99
Secondary outcome measures												
Adaptive ER	59.15	13.34	58.17	15.61	54.25	14.94	56.65	14.31	54.94	14.19	56.10	15.23
Maladaptive ER	36.21	9.41	31.00	9.51	25.71	7.08	36.24	10.86	35.75	10.52	33.10	10.09
Quality of Life	4.24	6.28	/	/	2.86	4.07	3.32	4.55	/	/	4.66	5.31
Disability	17.23	13.73	/	/	12.58	11.45	19.66	11.41	/	/	21.51	14.44
Resilience[a]	76.41	10.37	/	/	82.07	11.58	75.50	11.32	/	/	75.46	11.16
Remission[a]	19.44	15.61	/	/	14.93	11.32	19.24	14.87	/	/	24.21	15.22
Other variables												
Credibility	0.21	2.74	0.78	2.54	/	/	-0.21	2.32	-0.47	2.57	/	/
Expectancy	0.54	2.64	0.56	2.64	/	/	-0.54	2.52	-0.52	2.62	/	/
Stressful events	1.27	1.40	0.41	0.68	0.57	0.74	1.15	1.26	0.50	0.88	0.90	1.15

Note: ER = Emotion Regulation; [a] Due to missing data for one participant, results for Resilience and Remission from depression for the follow-up assessment are based on a sample of 28 participants instead of 29 participants for the active control condition

CHAPTER 7

THE INTERPLAY BETWEEN COGNITIVE RISK AND RESILIENCE FACTORS IN REMITTED DEPRESSION: A NETWORK ANALYSIS[1]

ABSTRACT

Individuals in remission from depression are at increased risk for developing future depressive episodes. Several cognitive risk- and resilience factors have been suggested to account for this vulnerability. In the current study we explored how risk- and protective factors such as cognitive control, adaptive and maladaptive emotion regulation, residual symptomatology, and resilience relate to one another in a remitted depressed (RMD) sample. We examined the relationships between these constructs in a cross-sectional dataset of 69 RMD patients using network analyses in order to obtain a comprehensive, data-driven view on the interplay between these constructs. We subsequently present an association network, a concentration network, and a relative importance network. In all three networks, resilience formed the central hub, connecting perceived cognitive control (i.e., working memory complaints), emotion regulation, and residual symptomatology. The contribution of the behavioral measure for cognitive control in the network was negligible. Moreover, the directed relative importance network indicates bidirectional influences between these constructs, with all indicators of centrality suggesting a key role of resilience in remission from depression. These findings indicate the importance of resilience to successfully cope with stressors following remission from depression. Further in-depth studies will be essential to identify the specific underlying resilience mechanisms that may be key to successful remission from depression.

[1] Based on Hoorelbeke, K., Marchetti, I., De Schryver, M., & Koster, E.H.W. (2016). The interplay between cognitive risk and resilience factors in remitted depression: A network analysis. *Journal of Affective Disorders, 195*, 96-104. doi: 10.1016/j.jad.2016.02.001

Depression is a highly prevalent, severe mental illness that is related to substantial individual suffering (e.g., Cuijpers, de Graaf, & van Dorsselaer, 2004; Lima & Fleck, 2007). In terms of disability, estimations suggest that major depressive disorder (MDD) is among the leading causes of burden of diseases worldwide (e.g., Demyttenaere et al., 2004). Current treatment options (psychological, pharmacological, and neurostimulation interventions) are moderately successful in achieving initial symptom reduction but long-term effects are less encouraging, with research showing that recurrence of MDD (i.e., experiencing a depressive episode after having exhibited full and/or partial remission from a previous depressive episode) is high in the general population (35% after 15 years), and even higher in those treated at specialized mental health centers (60% after 5 years and 85% after 15 years; Hardeveld, Spijker, De Graaf, Nolen, & Beekman, 2010). This has led to the realization that studying individuals remitted from depression (RMD) is crucial in understanding who remains well after initial remission and who is at-risk for new depressive episodes (e.g., De Raedt & Koster, 2010; Marchetti, Koster, Sonuga-Barke, & De Raedt, 2012).

Current research has successfully identified a number of interindividual variables that seem to play a key role in risk as well as resilience in RMD. At the level of information-processing, previous depressive episodes have a negative impact on cognitive control processes (Vanderhasselt & De Raedt, 2009), which are crucial for goal-directed behavior. Importantly, cognitive control has been found to play a major role in emotion regulation, the process of influencing which emotions one has, including when and how these emotions are experienced (Gross, 1998). For instance, cognitive control impairments have been associated with maladaptive emotion regulation strategies such as rumination, self-blame, and catastrophizing (e.g., Hoorelbeke, Koster, Demeyer, Loeys, & Vanderhasselt, 2016; Joormann & Gotlib, 2008; Whitmer & Banich, 2007), known to have detrimental effects on mental well-being (Aldao & Nolen-Hoeksema, 2010; Garnefski & Kraaij, 2006). Moreover, cognitive control moderates the effects of maladaptive emotion regulation on mood in daily life, with for instance low levels of cognitive control predicting a stronger increase in negative affect following rumination (Pe, Raes, & Kuppens, 2013). Furthermore, in the context of remission from depression, impaired cognitive control has shown to predict rumination,

linking cognitive control impairments to recurrent depressive symptoms in a RMD sample (Demeyer, De Lissnyder, Koster, & De Raedt, 2012). Importantly, cognitive control impairments may also disrupt adaptive emotion regulation processes (Cohen, Daches, Mor, & Henik, 2014; Joormann & D'Avanzato, 2010; Joormann & Vanderlind, 2014), which are key to resilience and mental well-being (Gross & John, 2003; Hu et al., 2014; Kalisch, Müller, & Tüscher, 2015). Despite increasing research linking RMD to information-processing factors that are involved in emotion regulation strategies, which subsequently influence resilience or alternatively increase depressive symptoms, there are limitations to the current available research. Most importantly, research has often tested simple, unidirectional relationships between these constructs, which ignores the notion that many of the constructs involved can have reciprocal relationships. For instance, there is empirical evidence showing that levels of cognitive control can influence ruminative tendencies (Cohen, Mor, & Henik, 2015) as well as evidence that levels of rumination influence cognitive control (Philippot & Brutoux, 2008). Currently, there is very little work integrating risk- and protective factors in RMD.

In order to obtain a more comprehensive view on the interaction between information-processing and emotion regulation strategies in relation to risk and resilience we conducted a network analysis on these constructs in a RMD sample. Based on graph theory, network modeling represents an important innovation to examine the interplay between different constructs in a largely data-driven manner (Borsboom & Cramer, 2013). Within a network model each variable is represented by a node, while the edge between two nodes shows the relationship between them. Typically, studies have relied on this type of analysis to explore how observable behaviors (i.e., symptoms) relate to one another, aiming to overcome the use of unobservable, latent variables (i.e., depression) (e.g., Borsboom, Cramer, Schmittmann, Epskamp, & Waldorp, 2011; Cramer, Waldorp, van der Maas, & Borsboom, 2010; De Schryver, Vindevogel, Rasmussen, & Cramer, 2015; Fried, 2015; McNally et al., 2014). However, network modeling can also be employed to decipher the interrelationship between constructs (i.e., structural network analysis) and, in turn, explore the nomological universe in which the different constructs are placed (Costantini et al., 2015b). To do so, relying on weighted and directed networks represents a great advancement, in that it is

possible to obtain a fine-grained representation of the centrality (i.e., the extent to which a construct plays a central role in the network) of all the constructs considered and the possible directionality among them (Borsboom & Cramer, 2013; Costantini et al., 2015a).

In order to gain further insight in the mechanisms underlying remission from depression, we propose the use of this latter approach to examine how key constructs in the context of vulnerability for depression and resilience are related in a RMD sample. For this purpose, based on the literature, we selected four key risk factors (cognitive control impairments, working memory complaints, maladaptive emotion regulation, and residual depressive symptomatology) and two protective factors (adaptive emotion regulation and resilience) for the network analyses: (1) At the level of information-processing we obtained information about cognitive control measured with a well-validated performance based task, the Paced Auditory Serial Addition Task (PASAT; Gronwall, 1977; for a review see Tombaugh, 2006), and (2) an indicator of experienced working memory complaints, the Working Memory scale of the Behavior Rating Inventory of Executive Function (BRIEF-WM; Roth, Lance, Isquith, Fischer, & Giancola, 2013). Previous studies with MDD and other clinical samples indicate that self-reported cognitive functioning in daily life and performance on cognitive tasks may capture different aspects of cognitive control, as they are not necessarily associated with each other and may differ in their predictive value for well-being and symptomatology (Chan et al., 2008; Middleton, Denney, Lynch, & Parmenter, 2006; Mowla et al., 2008; Svendsen, Kessing, Munkholm, Vinberg, & Miskowiak, 2012). Furthermore, the Cognitive Emotion Regulation Questionnaire (CERQ; Garnefski, Kraaij, & Spinhoven, 2001) was used to assess a broad range of emotion regulation strategies, which allows calculation of compound scores for (3) adaptive and (4) maladaptive emotion regulation processes. (5) The Remission from Depression Questionnaire (RDQ; Zimmerman et al., 2013) was used as an indicator of residual symptoms following (partial) remission from depression given that previous work indicates that residual symptomatology increases the chance of recurrence of depressive episodes (e.g., Solomon et al., 2000). This questionnaire provides a more nuanced assessment of remission than standard measures of depressive symptomatology as it combines

assessment of residual depressive- and related symptoms with indicators of functioning such as sense of well-being. (6) Finally, given the importance of resilience to mental health (e.g., Griffiths et al., 2015), resilience was selected as a protective factor for the network analysis. Resilience – connoting "inner strength, competence, optimism, flexibility, and the ability to cope effectively when faced with adversity" (Wagnild, 2009, p. 105) – was assessed using the Resilience Scale (RS; Portzky, Wagnild, De Bacquer, & Audenaert, 2010; Wagnild & Young, 1993). This self-report measure is based on five characteristics assumed to be central to resilience: perseverance, equanimity, meaningfulness, being self-reliant, and the realization that each person is unique (for a review, see Wagnild, 2009).

In line with previous literature (Costantini et al., 2015a; McNally et al., 2014), we relied on different types of network models to obtain a more comprehensive representation of factors related to remission from depression. First, we examined simple correlational patterns (i.e, association network). Second, the underlying structure of the network was examined by means of a concentration network, where the correlations between every pair of variables were controlled for all the other variables of the network. Third, we examined a relative importance network to index predictive directionality within cross-sectional data, although this does not necessarily imply causality (McNally et al., 2014). Based on the literature we expected to find a model depicting reciprocal relationships between cognitive control and emotion regulation. Maladaptive emotion regulation strategies would link cognitive control impairments to increased residual symptomatology, whereas adaptive emotion regulation strategies would link cognitive control to resilience, which should show the opposite relation to residual symptomatology.

METHOD

Participants

The sample consisted of 69 RMD patients that were recruited for a cognitive control training study registered as NCT02407652 at ClinicalTrials.Gov. The protocol of

this training study was published online (Hoorelbeke, Faelens, Behiels, & Koster, 2015). For our network analyses, baseline measures were used from the 68 participants of the training study plus one additional participant that was only willing to contribute to the correlational study. To be eligible for participation in this study, participants should be aged 23 – 65, show a history of MDD and report being in (partial) remission for at least six months. A history of comorbid disorders was allowed, with the exception of severe substance abuse, psychosis and bipolar disorder. However, participants should not meet criteria for a clinical diagnosis at time of assessment nor report neurological impairments. Use of antidepressant medication and psychotherapeutic maintenance treatment was allowed. Sample characteristics are reported in Table 1. Participants received a financial reimbursement for their participation to the training study. This study was approved by the local ethical committee of Ghent University.

Table 1. Sample characteristics

	RMD patients (*n* = 69)
Mean age (SD)	47.13 (11.46)
Gender (male : female)	23 : 46
Mean age of onset (SD)	27.36 (12.76)
Mean self-reported amount of depressive episodes (SD)	3.28 (4.23)
Mean self-reported episode length in months (SD)	6.96 (4.64)
Mean time since previous episode in years (SD)	6.12 (6.34)
% reporting recurrent MDD	74%
% currently on antidepressant medication	42%
% reporting maintenance contact with psychologist	9%
% reporting maintenance contact with psychiatrist	13%

Apparatus and Material

The cognitive task was run using the INQUISIT Millisecond software package on a Dell Dimension 4600 computer with a 72 Hz, 17-inch color monitor. Statistical analyses were performed in R version 3.2.2.

Screening instruments. Eligibility for participation to the study was screened using a two-phased, in time separated, protocol. First, interested candidates were contacted by telephone to give practical information concerning the study and to

screen for eligibility using a selection of relevant questions of the screening version of the Mini-International Neuropsychiatric Interview (MINI Screening version; Sheehan et al., 1989; Van Vliet & De Beurs, 2007). Next, participants' eligibility was re-assessed by a clinical psychologist using the MINI Screening version and relevant modules of the corresponding structured clinical interview (MINI structured interview; Sheehan et al., 1989) at the Faculty of Psychology and Educational Science of Ghent University. By default, all participants completed the module on (current and lifetime) depressive episodes. Based on the individual responses to the MINI Screening version during the second phase, relevant modules of the MINI structured interview were added to rule out the presence of other current diagnoses.

Questionnaires. The Working Memory subscale of the Behavior Rating Inventory of Executive Function Adult version (BRIEF-WM; Roth et al., 2013; Scholte & Noens, 2011) assesses working memory complaints, which was used as an indicator of *perceived cognitive control* (range: 8 – 24; e.g., "I find it difficult to concentrate on tasks (e.g., while doing chores, reading, work)"). Adaptive and maladaptive emotion regulation was assessed using the Cognitive Emotion Regulation Questionnaire (CERQ; Garnefski et al., 2001). In line with Vanderhasselt et al. (2014) we calculated two sum scores: (1) *adaptive emotion regulation* (range: 20 – 100; e.g., "I think I can learn something from the situation") was computed using the subscales acceptance, refocus on planning, positive refocus, positive reappraisal, and putting into perspective, whereas (2) *maladaptive emotion regulation* (range: 16 – 80; e.g., "I feel that I am the one to blame for it") was computed using the subscales self-blame, blaming others, rumination, and catastrophizing. Remission was assessed using the Remission of Depression Questionnaire (RDQ, range: 0 – 82; e.g., "I felt sad or depressed"; Peeters, Nicolson, Wichers, & Hacker, 2013; Zimmerman et al., 2013), which combines indicators of depressive residual symptoms and related symptoms with indicators of functioning (e.g., well-being). Provided that a higher score on this scale is indicative for more pathological processes, for convenience we will consistently refer to it as *residual depressive symptoms*. *Resilience* was assessed using the Resilience Scale (RS, range: 25 – 100, e.g., "I am determined", "I can usually find something to laugh about"; Portzky et al., 2010; Wagnild & Young, 1993). The self-report measures for working memory

complaints, adaptive and maladaptive emotion regulation, resilience and residual depressive symptoms demonstrated proper reliability in our sample, with a Cronbach's Alpha of .88, .92, .87, .91, and .96 respectively. For all questionnaires but the RS and the CERQ compound measure for adaptive emotion regulation, a higher score reflects the presence of more symptoms or maladaptive processes. As this study is part of a more extensive training study, other questionnaires were assessed which will not be discussed here.

Cognitive control task. Participants performed three blocks of the non-adaptive Paced Auditory Serial Addition task (PASAT; Gronwall, 1977; for a review, see Tombaugh, 2006) containing 60 trials each. During this task participants listened to a series of digits and had to continuously respond to the sum of the last two digits. Task difficulty increased over the three blocks, using inter stimulus intervals of 3000, 2000 and 1500 ms respectively. The total accuracy score served as a *behavioral indicator of cognitive control*. The split-half reliability of this measure (Spearman-Brown corrected) was .95.

Procedure

The data were collected during the baseline assessment of a cognitive control training study (see Hoorelbeke et al., 2015 for the full protocol). Participants were recruited drawing on an existing data-base of potentially interested candidates (n = 23), and using flyers that were placed in 106 drugstores in Ghent area, advertisements in popular magazines and national newspapers. After a telephone screening, potential participants were invited for a second screening, including a more extensive structured clinical interview at the Faculty of Psychology and Educational Sciences of Ghent University. Candidates that met the inclusion criteria then gave informed consent, completed the questionnaires and completed the cognitive task. Debriefing and reimbursement took place at the end of participation to the training study.

Data Analysis

After inspecting the descriptive statistics and zero-order correlations among the variables of interest, three types of networks were computed using the R package

qgraph (Epskamp, Cramer, Waldorp, Schmittmann, & Borsboom, 2012). Importantly, each network was displayed in accordance to the Fruchterman and Reingold's (1991) algorithm, whereby strongly related nodes are positioned in the middle of the figure, while poorly correlated ones appear in the periphery. We proceeded as follows.

We first computed the association network with all the variables of interest being included (the nodes) and the edges representing zero-order correlations (Borsboom & Cramer, 2013). In both the association and concentration network, node size reflects the (relative) importance of a variable in the network in terms of centrality. The thickness and color saturation of the edge signify the magnitude of the correlation, while green edges represent positive correlations and red edges represent negative correlations. From this, it follows that the association network is weighted and undirected. Although informative, the association network only approximates the underlying structure of the network, in that the association between two nodes could be due to shared connections to a third node, rather than representing a real influence between the two nodes (Borsboom & Cramer, 2013).

To address this concern, we built a concentration network (Cox & Wermuth, 1993), where the association between every pair of nodes was controlled for the influence of all the other variables. By doing so, it is relatively probable that the remaining (partial) correlations reflect relations that are likely/common in the population on which the network analysis has been done (Borsboom & Cramer, 2013). Moreover, sparse networks (i.e., networks characterized by less edges than the maximum possible) are to be preferred, in that they are simpler to interpret and more stable (Costantini et al., 2015a). However, in weighted networks, two nodes are not connected if and only if the weight of the connection is zero, whereas ordinary least squares (OLS) approach virtually never reports estimations exactly amounting to zero. In order to overcome this problem, the adaptive LASSO method represents a widely accepted procedure (Costantini et al., 2015a). Adaptive LASSO method is a technique that assigns different penalties to different weights and causes small weights to automatically shrink to zero (Zou, 2006), thereby producing a more parsimonious and sparse model. Importantly, adaptive LASSO outperforms other types of estimation in terms of reduced false positives (Kraemer, Schaefer, & Boulesteix, 2009). Adaptive

LASSO partial correlations were computed using the R package *parcor* (Kraemer et al., 2009).

Then, we computed a relative importance network, including the variables that emerged as linked in the adaptive LASSO concentration network. In a relative importance network, each edge represents the relative importance weights of node X in predicting node Y, after controlling for all the other nodes (McNally et al., 2014; Robinaugh, LeBlanc, Vuletich, & McNally, 2014). In other words, relative importance weight quantifies the amount of explained variance attributable to each predictor, after controlling for multicollinearity (Johnson, 2000), and it ranges between 0 and 1. This procedure was repeated for every node of the network. The resulting network was weighted and, importantly, directed. Thus, not only does relative importance analysis provide specific weights, but also directionality. However, it is of crucial importance to note that directionality of these weights represents directionality of the predictions and does not imply causality. To compute non-normalized relative importance weights, we used the *lmg* metric as provided by the R package *relaimpo* (Groemping, 2006).

Furthermore, in order to qualify the importance of each node in the relative importance network, we calculated four indexes of centrality: *betweenness*, *closeness*, *instrength*, and *outstrength* (Borsboom & Cramer, 2013; Costantini et al., 2015a). Betweenness refers to the number of times that a specific node lies on the shortest path between two other nodes, whereas closeness is computed as the inverse of the sum of the total length of all the shortest path lengths between a specific node and the rest of the network. Instrength is calculated as the sum of all the directed weights accounting for a specific node and being originated by all the other nodes of the network, while outstrength summarizes the total influence that a certain node exerts on all the other nodes. In terms of interpretation, betweenness indexes how efficiently a node connects to other nodes, while closeness represents the average distance from a specific node to all other nodes. Additionally, outstrength quantifies the extent to which a certain variable is expected to influence connected variables in the network rather than being influenced by these other variables (instrength). In the relative importance network, we choose to vary the node size as a function of outstrength. Together, these centrality indexes point out the variable(s) whose manipulation is most

likely to influence the rest of the network, and, by representing different aspects of node centrality, higher levels of each index reflect higher node centrality. All the centrality indexes were computed by means of the R package *qgraph* (Epskamp et al., 2012).

RESULTS

Descriptive statistics of the variables of interest are reported in Table 2. The association network (Figure 1) highlights that all the nodes were related to one another, with resilience, residual depressive symptoms (RDQ), and self-reported working memory complaints (BRIEF-WM) showing the strongest connectivity and being positioned at the center of the network. In general, resilience showed the strongest correlations compared to RDQ and BRIEF-WM, therefore suggesting a possible primary role in the network. Surprisingly, PASAT accuracy index was unrelated to BRIEF-WM (r = .06), maladaptive emotion regulation strategies (r = .03), and RDQ (r = .09), and weakly and negatively correlated to resilience (r = -.21) and adaptive emotion regulation strategies (r = -.26).

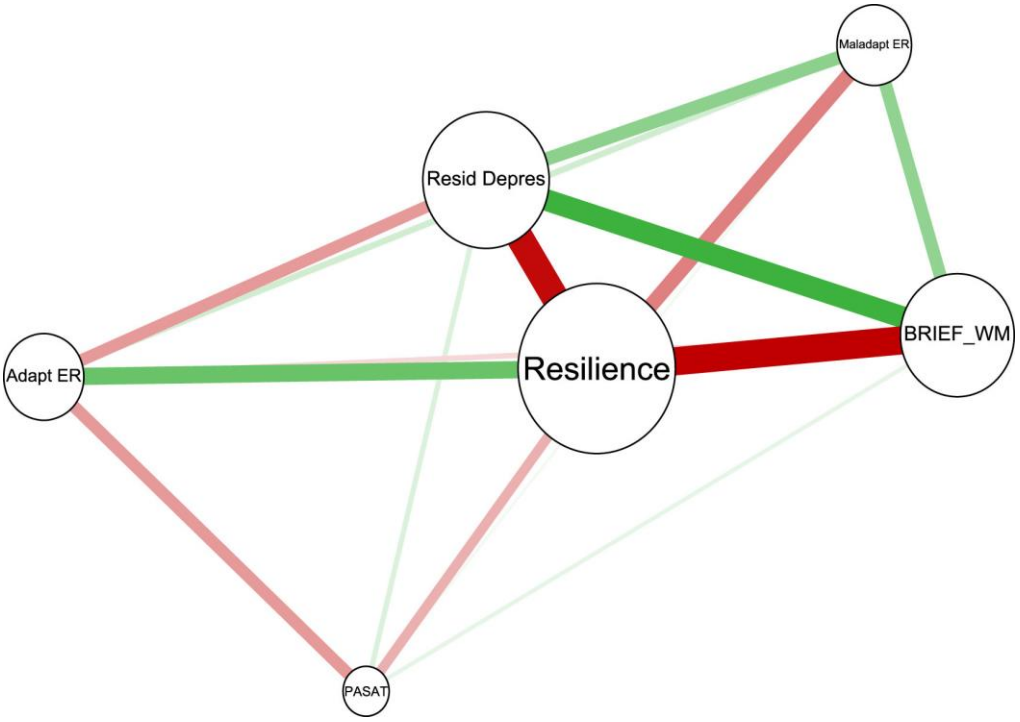


Figure 1. Association network

Table 2. Descriptive statistics, zero-order correlations, and adaptive LASSO partial correlations

	M ± SD	min - max	BRIEF_WM	PASAT_ACC	Adaptive Emotion Regulation Strategies	Maladaptive Emotion Regulation Strategies	Resilience	Residual Depressive Symptoms
BRIEF_WM	14.03 ± 3.99	8 - 22	1	.06	-.10	.28	-.66	.50
PASAT_ACC	0.51 ± 0.16	0.12 - 0.9	0	1	-.26	.03	-.21	.09
Adaptive Emotion Regulation Strategies (CERQ)	57.97 ± 13.70	31 - 89	0	0	1	.12	.39	-.26
Maladaptive Emotion Regulation Strategies (CERQ)	36.16 ± 10.02	16 – 61	0	0	0	1	-.33	.30
Resilience	76.16 ± 10.84	52 - 94	-.52	0	.26	-.21	1	-.64
Residual Depressive Symptoms	19.22 ± 15.05	0 - 56	0	0	0	0	-.41	1

Note. Zero-order correlations are reported above the diagonal and adaptive LASSO partial correlations are reported below the diagonal. BRIEF_WM = self-reported cognitive control ; PASAT_ACC = PASAT accuracy, performance on the behavioral measure for cognitive control; CERQ = Cognitive Emotion Regulation Questionnaire

In order to shed light on which nodes exert real influences rather than spurious ones (Borsboom & Cramer, 2013; Costantini et al., 2015a), the adaptive LASSO concentration network (Figure 2) was built to refine the model suggested by the association network. Interestingly, resilience emerged to be the main hub of the network, in that it connected all the variables, which were not connected otherwise (Table 3). When estimated with adaptive LASSO, resilience appeared to be strongly related to BRIEF-WM (*pr* = -.52) and RDQ (*pr* = -.41), and weakly to moderately related to maladaptive and adaptive emotion regulation strategies (*pr* = -.21, and *pr* = .26, respectively). Moreover, the PASAT accuracy index emerged to be unrelated to the rest of the nodes (i.e., sparse network), therefore suggesting that PASAT task performance does not play a substantial role in accounting for resilience, residual depressive symptoms, and (mal)adaptive emotion regulation strategies in RMD.

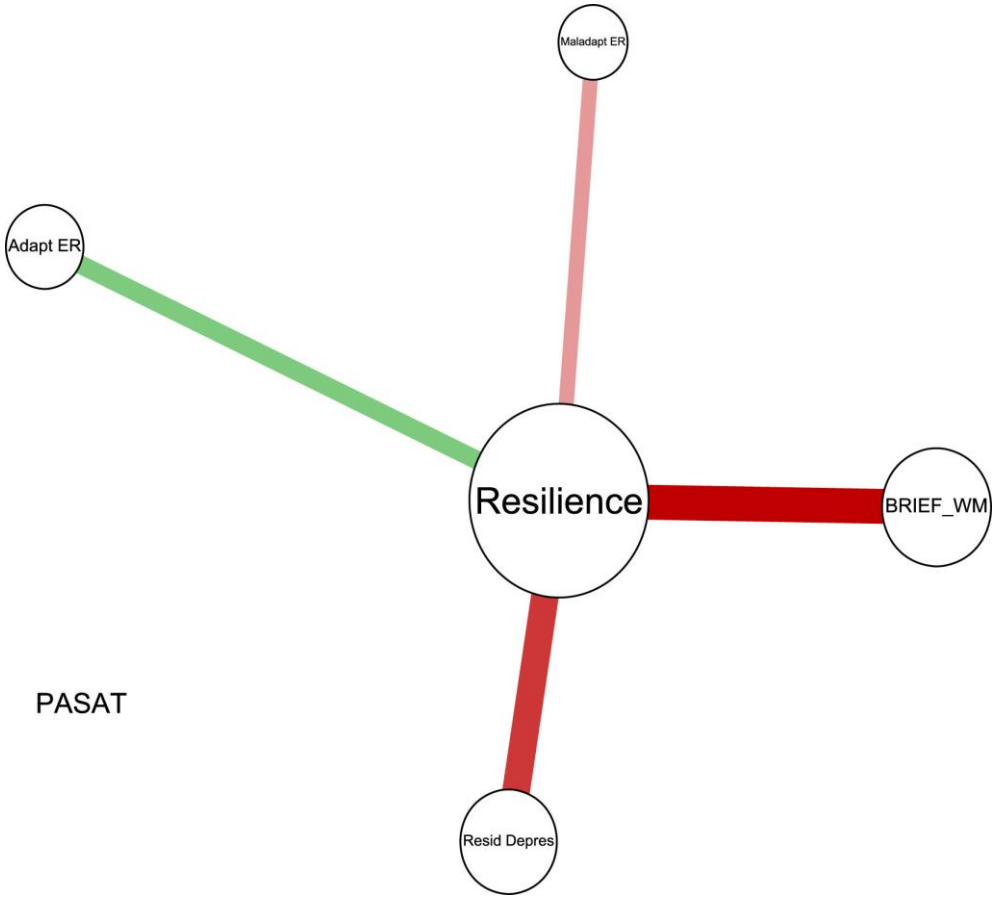


Figure 2. Adaptive LASSO concentration network

Table 3. Relative importance weights (non-normalized)

		Outcome (Y)				
		BRIEF_WM	Adaptive Emotion Regulation Strategies (CERQ)	Maladaptive Emotion Regulation Strategies (CERQ)	Resilience	Residual Depressive Symptoms
Predictors ($X_{1,\ldots,n}$)	BRIEF_WM	-	.02	.03	.27	.12
	Adaptive Emotion Regulation Strategies (CERQ)	.02	-	.05	.11	.03
	Maladaptive Emotion Regulation Strategies (CERQ)	.03	.04	-	.05	.04
	Resilience	.31	.15	.07	-	.24
	Residual Depressive Symptoms	.12	.04	.04	.21	-
	R^2	.48	.25	.19	.64	.43

Note. BRIEF_WM = self-reported cognitive control ; CERQ = Cognitive Emotion Regulation Questionnaire

Finally, the directed relative importance network (Figure 3)[2] was constructed including all the variables that emerged as related to other nodes of the network in the concentration network. Thus, PASAT accuracy was excluded. Importantly, the directed relative importance network highlighted that resilience was the main hub of the network, in that it exerted a major influence on all the other nodes, as confirmed by centrality analysis (Figure 4; Table 4). In fact, resilience showed the highest levels of betweenness, closeness, and strength. In keeping with this, unlike all the other nodes, resilience had higher outstrength values (0.77) than instrength values (0.64). In other words, although the other nodes accounted for 64% of the resilience variance, resilience – in turn – could explain about 77% variance of the other variables, across different regression models. This seems to imply that, although highly related to all the other constructs, resilience exerted a larger influence on the rest of the network than vice versa.[3]

[2] In contrast to the association network and adaptive LASSO concentration network where green represents a positive association and red a negative association, no such distinction can be made in relative importance networks. That is, here all edges represent amount of variance, therefore no negative values (i.e., red edges) are allowed.

[3] In order to determine stability of these findings (i.e., the central role of resilience), a post-hoc association network, adaptive LASSO concentration network and relative importance network was generated using alternative operationalizations of residual symptomatology (depressive symptomatology, assessed using the Beck Depression Inventory 2nd edition), adaptive- (positive appraisal, assessed using the Cognitive Emotion Regulation Questionnaire) and maladaptive emotion regulation (Brooding, assessed using the Ruminative Response Scale). This provided similar results, demonstrating the central role of resilience in remitted depressed patients. These models have been added as Figures 1, 2, and 3 in Appendix.

Table 4. Centrality indexes – Relative importance network

	Betweenness	Closeness	Instrength	Outstrength
BRIEF_WM	0	0.03	0.48	0.44
Adaptive Emotion Regulation Strategies (CERQ)	0	0.02	0.26	0.21
Maladaptive Emotion Regulation Strategies (CERQ)	0	0.01	0.19	0.17
Resilience	10	0.04	0.64	0.77
Residual symptoms	0	0.02	0.43	0.41

Note. BRIEF_WM = self-reported cognitive control; CERQ = Cognitive Emotion Regulation Questionnaire

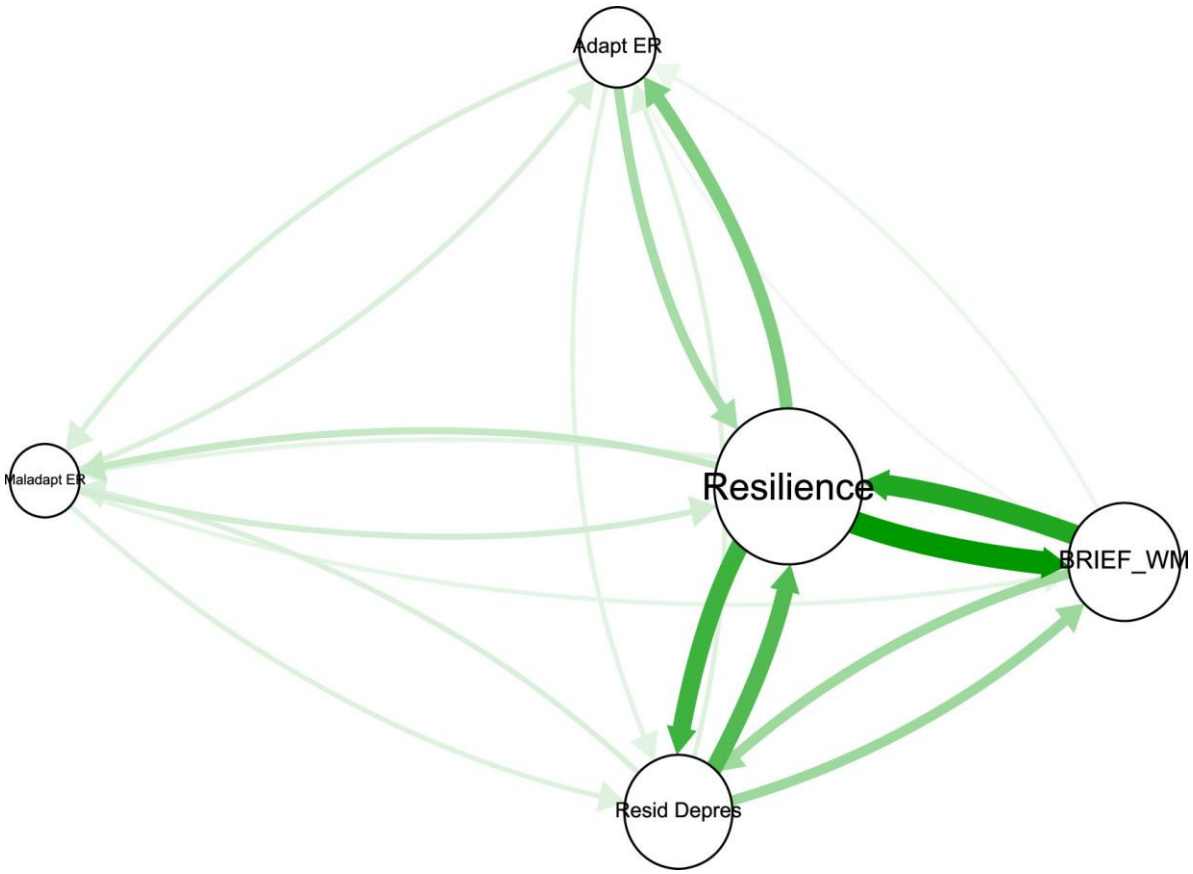


Figure 3. Directed relative importance network

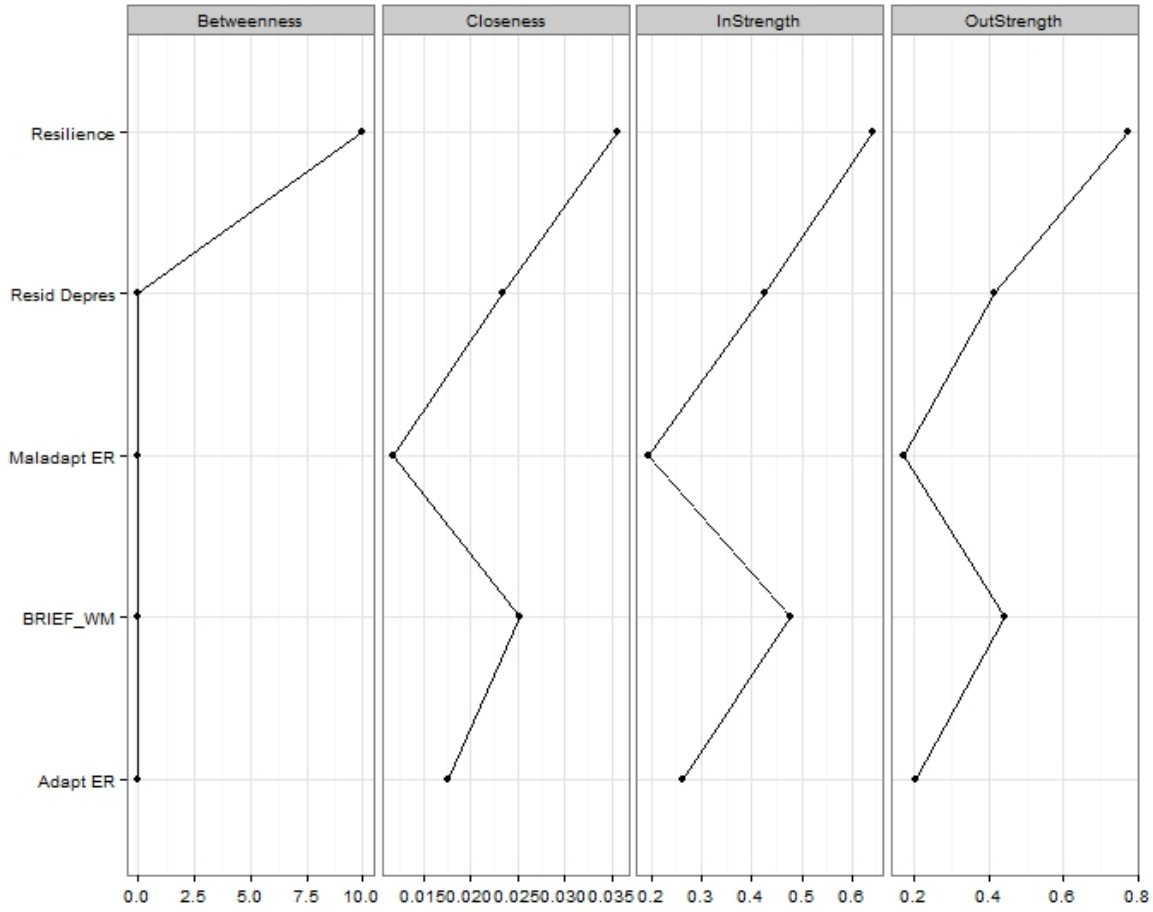


Figure 4. Indexes of centrality

DISCUSSION

Provided that individuals who remit from depression have a larger chance to develop new depressive episodes, we aimed to obtain a comprehensive view on how risk- and protective factors relate in this population. Based on previous work we identified cognitive control, adaptive and maladaptive emotion regulation as well as resilience and residual depressive symptoms as key constructs. The relationships between these constructs were examined using network analyses in order to obtain a comprehensive, data-driven view on the interplay between these constructs. We will below discuss the main results in relation to the different type of network analyses applied in the current study.

The association network revealed that resilience forms a key hub, showing a strong negative association with residual depressive symptomatology and working memory complaints. That is, participants with high resilience scores are likely to report fewer residual depressive symptoms and working memory complaints. Furthermore, resilience showed a moderate positive association with adaptive emotion regulation strategies and a negative association with maladaptive emotion regulation strategies. Moreover, the latter construct showed a moderate positive association with residual depressive symptomatology. Finally, working memory complaints showed a strong association with residual depressive symptoms. All other edges of the association network represented minor associations ($r < .30$).

The adaptive LASSO concentration network confirmed the central role of resilience in the network, in that resilience was related to a number of key variables in RMD such as adaptive and maladaptive emotion regulation, residual depressive symptoms, and self-reported working memory complaints. Moreover, after the correlations between every pair of variables were controlled for all the other variables of the network, the remaining constructs in the network were only indirectly connected to one another via resilience, whereas the direct associations between the other constructs disappeared (e.g., maladaptive emotion regulation and residual symptomatology). The absence of an association between performance-based and self-reported working memory performance is in line with previous literature (e.g., Mowla et al., 2008; Svendsen et al., 2012). However, in contrast to our expectations, the PASAT node had no edges in the adaptive LASSO concentration network, indicating that associations between PASAT task performance and the other constructs in the network were negligible. Importantly, self-reported working memory functioning was strongly associated with resilience in this network, linking experienced cognitive functioning indirectly to emotion regulation and residual depressed symptoms.

Subsequently, the directed relative importance network clearly showed bidirectional influences among the constructs. Interestingly, the indexes indicated that resilience played a central and key role in RMD, in that its influence over the other variables was stronger than the reverse influences of the other variables in the network on resilience. The stability of these findings was confirmed using additional

operationalizations for some of the key constructs (e.g., 'brooding' as indicator of maladaptive emotion regulation, 'positive appraisal' as indicator of adaptive emotion regulation, and an alternative measure for 'depressive symptomatology'; see Appendix Figures 1, 2, and 3). Provided a dynamic conceptualization of resilience as a protective factor that may be insufficiently represented in remitted depressed patients (Waugh & Koster, 2015), these findings suggest that manipulating resilience may be an efficient way to increase other protective factors (e.g., adaptive emotion regulation), as well as decrease risk factors for recurrent depression (e.g., cognitive dysfunctioning, maladaptive emotion regulation, and residual symptomatology). This is in line with recent views on the importance of resilience in stable remission from depression (Garland et al., 2010; Waugh & Koster, 2015).

Importantly, these findings are not fully in line with the hypothesis that emotion regulation strategies would be important predictors of resilience. Furthermore, in contrast to our prediction, the lack of inclusion of the PASAT in the final model indicates that this specific measure of cognitive control did not significantly contribute to the resilience network, although these findings might be task-specific. Furthermore, the lack of such contribution to the network may be due to the specific operationalization of cognitive control as a behavioral measure whereas all other constructs are assessed using self-report measures. In contrast, self-reported cognitive control (i.e., working memory complaints) contributed to emotion regulation processes and remission, but mostly via the central hub resilience. Several factors may have contributed to this discrepancy between the current findings and our hypothesis based on the literature. First, previous studies have typically used standard analytical techniques to investigate relationships between constructs, testing specific directed models (e.g., De Lissnyder et al., 2012; Demeyer et al., 2012). In contrast, we used a data-driven approach. Because the models are empirically rather than theoretically derived, the solutions might be sample-specific. Second, the behavioral measure for cognitive control relied on neutral stimuli, whereas in previous studies effects were often found using emotional relevant stimuli (e.g., De Lissnyder et al., 2012; Demeyer et al., 2012; Joormann & Gotlib, 2008; Pe et al., 2013). It would be interesting for future studies to include several indicators of

cognitive control (e.g., updating, inhibition) over neutral and emotional information to further test how this factor is related to resilience and remission.

At the theoretical level, the current findings are of interest in directing attention to the mechanisms that play a major role in remitted depressed individuals. Especially given that individuals who have recovered from depression still face significant stressors, frequently due to consequences of having experienced a depressive episode (e.g., unemployment, loss of social roles, etc.). These stressors may interact with cognitive and neurobiological vulnerability factors to predict recurrence of depression (e.g., De Raedt & Koster, 2010), stressing the considerable role of resilience to maintain remission. For instance, previous studies have shown that depression is associated with impaired stress- and emotional reactivity (Burke, Davis, Otte, & Mohr, 2005; Bylsma, Morris, & Rottenberg, 2008), which may continue during remission (e.g., O'Hara, Armeli, Boynton, & Tennen, 2014). In line with these findings, Waugh and Koster (2015) argue that stress recovery, positivity or promotion, and flexible application of coping responses – among other intra- or interpersonal factors contributing to resilience – may play an important role in preventing recurrence of depressive symptoms (but also see Southwick, Vythilingam, & Charney, 2005). These factors match the operationalization of resilience in this study, in line with Wagnild (2009), referring to concepts such as optimism, effectively coping with adversity, and flexibility.

In this context, it is noteworthy that one influential framework for resilience, the broaden-and-build theory, proposes that positive emotions may play an important protective role, as they broaden cognitive and behavioral processes (Fredrickson, 2001; Fredrickson, Tugade, Waugh, & Larkin, 2003). This may foster adaptive emotion regulation processes and prevent psychopathological processes from occurring. Given the bidirectional nature of these processes, this may then further increase resilience. Indeed, research indicates that levels of positive affect moderate the detrimental effects of stressful events on mood in daily life and may even buffer negative effects of genetic vulnerability for depression (e.g., Wichers et al., 2007). This resilience model is in line with our network models, showing stronger outstrength than relative instrength values for our central hub, resilience, which connected perceived working memory functioning (i.e., working memory complaints) and adaptive emotion regulation with

residual depressive symptoms in our RMD sample. This indicates the importance of directly targeting resilience next to focusing on specific vulnerabilities. At the clinical level, it is interesting to note that the central role of resilience also parallels an increased interest in treatments that focus on resilience (Garland et al., 2010; Geschwind, Peeters, Drukker, van Os, & Wichers, 2011; Keng, Smoski, & Robins, 2011; Waugh & Koster, 2015). Indeed, our findings indicate that patients may benefit from interventions targeting resilience mechanisms. Among more common cognitive behavioral interventions (e.g., Songprakun & McCann, 2012; Steinhardt & Dolbier, 2008), Waugh and Koster (2015) argue that patients may benefit from well-being training, stress inoculation training, meditation and mindfulness-based cognitive therapy (for a meta-analytical review on the efficacy of resilience training programs, see Leppin et al., 2014).

To our knowledge this study is the first to provide a data-driven test of how key constructs such as (perceived) cognitive control, emotion regulation processes, and resilience relate to remission from depression in a RMD population. However, several limitations should be taken into account. A first and most important limitation is the cross-sectional nature of the data. Although the analytical techniques deployed here give an indication of direction of associations, this does not allow drawing conclusions concerning the causal nature of these relationships. Related to this, our network models visualize how key constructs such as cognitive control, (mal)adaptive emotion regulation, resilience and residual depressive symptoms relate at one certain moment in time following (partial) recovery from depression. However, the observed relations may behave in a different manner when observed over multiple time points. Future studies should take this into account, for instance using experience sampling and an experimental approach (Hoorelbeke et al., 2016). Third, the selected nodes for the network were theory-driven and limited to a fixed set of key constructs in the literature pertaining cognitive vulnerability for depression. It is possible that the network is currently overlooking additional nodes which may link factors such as cognitive control to resilience in RMD. Fourth, given that we only included one behavioral measure, the lack of contribution of the behavioral measure for cognitive control to the network – while self-reported working memory functioning was included in the network – is not

fully conclusive given that effects may be task-specific. For this purpose, future studies exploring how cognitive control relates to other proposed risk- and protective factors in remitted depressed patients should deploy multiple measures of cognitive control. Furthermore, repeated studies are necessary to identify rather stable connections, focusing on the generalization both within and between different populations (De Schryver et al., 2015). Fifth, we relied on a broad indicator of resilience. Given its central role, future in-depth prospective studies are essential to further elucidate the specific resilience facet(s) that may be key to successful remission from depression.

Summary

The current study explored how several cognitive processes relate to remission of depression in a RMD sample. The relationships between cognitive control, experienced cognitive functioning, (mal)adaptive emotion regulation, resilience, and residual depressive symptomatology were examined cross-sectionally using network analyses in order to obtain a comprehensive, data-driven view on the interplay between these constructs. Over a series of network models, resilience was found to be a central hub consistently linking working memory complaints and emotion regulation processes to residual symptoms. However, performance on the Paced Auditory Serial Addition task, a behavioral measure of cognitive control, was unrelated to the other variables. These findings indicate the importance of resilience to successfully cope with stressors following remission from depression.

ACKNOWLEDGEMENTS

This research was supported by a Special Research Fund (BOF) of Ghent University awarded to Kristof Hoorelbeke (B/13808/01) and by Grant BOF10/GOA/014 for a Concerted Research Action of Ghent University awarded to Ernst Koster. Igor Marchetti is a postdoctoral research fellow of the Research Foundation Flanders (FWO; FWO14/PDO/115). Maarten De Schryver was supported by Grant BOF09/01M00209 awarded to Jan De Houwer.

REFERENCES

Aldao, A., & Nolen-Hoeksema, S. (2010). Specificity of cognitive emotion regulation strategies: A transdiagnostic examination. *Behav. Res. Ther., 48*, 974–983.

Borsboom, D., & Cramer, A.O.J. (2013). Network analysis: An integrative approach to the structure of psychopathology. *Annu. Rev. Clin. Psychol., 9*, 91–121. doi:10.1146/annurev-clinpsy-050212-185608

Borsboom, D., Cramer, A.O.J., Schmittmann, V.D., Epskamp, S., & Waldorp, L.J. (2011). The small world of psychopathology. *PLoS One, 6,* e27407. doi:10.1371/journal.pone.0027407

Burke, H.M., Davis, M.C., Otte, C., & Mohr, D.C. (2005). Depression and cortisol responses to psychological stress: A meta-analysis. *Psychoneuroendocrinology, 30*, 846–856.

Bylsma, L.M., Morris, B.H., & Rottenberg, J. (2008). A meta-analysis of emotional reactivity in major depressive disorder. *Clin. Psychol. Rev., 28*, 676–691.

Chan, R.C.K., Wang, Y., Ma, Z., Hong, X.H., Yuan, Y.B., Yu, X., . . . Gong, Q.Y. (2008). Objective measures of prospective memory do not correlate with subjective complaints in schizophrenia. *Schizophr. Res., 103*, 229–239.

Cohen, N., Daches, S., Mor, N., & Henik, A. (2014). Inhibition of negative content - A shared process in rumination and reappraisal. *Front. Psychol., 5*, 662.

Cohen, N., Mor, N., & Henik, A. (2015). Linking executive control and emotional response: A training procedure to reduce rumination. *Clin. Psychol. Sci., 3*, 15–25. doi:10.1177/2167702614530114

Costantini, G., Epskamp, S., Borsboom, D., Perugini, M., Mottus, R., Waldorp, L.J., & Cramer, A.O.J. (2015a). State of the aRt personality research: A tutorial on network analysis of personality data in R. *J. Res. Pers., 54*, 13–29.

Costantini, G., Richetin, J., Borsboom, D., Fried, E.I., Rhemtulla, M., & Perugini, M. (2015b). Development of indirect measures of conscientiousness: Combining a facets approach and network analysis. *Eur. J. Pers., 29*, 548–567. doi:10.1002/per.2014

Cox, D.R., & Wermuth, N. (1993). Linear dependencies represented by chain graphs. *Stat. Sci., 8*, 204–218.

Cramer, A.O.J., Waldorp, L.J., van der Maas, H.L.J., & Borsboom, D. (2010). Comorbidity: A network perspective. *Behav. Brain Sci., 33*, 137–193. doi:10.1017/S0140525X09991567

Cuijpers, P., de Graaf, R., & van Dorsselaer, S. (2004). Minor depression: risk profiles, functional disability, health care use and risk of developing major depression. *J. Affect. Disord., 79*, 71–79.

De Lissnyder, E., Koster, E.H.W., Goubert, L., Onraedt, T., Vanderhasselt, M.A., & De Raedt, R. (2012). Cognitive control moderates the association between stress and rumination. *J. Behav. Ther. Exp. Psychiatry, 43,* 519–525. doi:10.1016/j.jbtep.2011.07.004

De Raedt, R., & Koster, E.H.W. (2010). Understanding vulnerability for depression from a cognitive neuroscience perspective: A reappraisal of attentional factors and a new conceptual framework. *Cogn. Affect. Behav. Neurosci., 10*, 50–70. doi:10.3758/cabn.10.1.50

Demeyer, I., De Lissnyder, E., Koster, E.H.W., & De Raedt, R. (2012). Rumination mediates the relationship between impaired cognitive control for emotional information and depressive symptoms: A prospective study in remitted depressed adults. *Behav. Res. Ther., 50*, 292–297. doi:10.1016/j.brat.2012.02.012

Demyttenaere, K., Bruffaerts, R., Posada-Villa, J., Gasquet, I., Kovess, V., Lepine, J.P., . . . Chatterji, S. (2004). Prevalence, severity, and unmet need for treatment of mental disorders in the World Health Organization World Mental Health Surveys. *J. Am. Med. Assoc., 291*, 2581–2590.

De Schryver, M., Vindevogel, S., Rasmussen, A.E., & Cramer, A.O. (2015). Unpacking constructs: A network approach for studying war exposure, daily stressors and Post-Traumatic Stress Disorder. *Front. Psychol., 6*. doi: 10.3389/fpsyg.2015.01896

Epskamp, S., Cramer, A.O.J., Waldorp, L.J., Schmittmann, V.D., & Borsboom, D. (2012). Qgraph: Network visualizations of relationships in psychometric data. *J. Stat. Softw., 48*, 1–18.

Fredrickson, B.L. (2001). The role of positive emotions in positive psychology - The broaden-and-build theory of positive emotions. *Am. Psychol., 56*, 218–226.

Fredrickson, B.L., Tugade, M.M., Waugh, C.E., & Larkin, G.R. (2003). What good are positive emotions in crises? A prospective study of resilience and emotions

following the terrorist attacks on the United States on September 11th, 2001. *J. Pers. Soc. Psychol., 84*, 365–376.

Fried, E.I. (2015). Problematic assumptions have slowed down depression research: Why symptoms, not syndromes are the way forward. *Front. Psychol., 6*, 309.

Fruchterman, T.M.J., & Reingold, E.M. (1991). Graph drawing by force-directed placement. *Softw. - Pract. Exp., 21*, 1129–1164. doi:10.1002/spe.4380211102

Garland, E.L., Fredrickson, B., Kring, A.M., Johnson, D.P., Meyer, P.S., & Penn, D.L. (2010). Upward spirals of positive emotions counter downward spirals of negativity: Insights from the broaden-and-build theory and affective neuroscience on the treatment of emotion dysfunctions and deficits in psychopathology. *Clin. Psychol. Rev., 30*, 849–864. doi:10.1016/j.cpr.2010.03.002

Garnefski, N., & Kraaij, V. (2006). Relationships between cognitive emotion regulation strategies and depressive symptoms: A comparative study of five specific samples. *Pers. Individ. Dif., 40*, 1659–1669.

Garnefski, N., Kraaij, V., & Spinhoven, P. (2001). Negative life events, cognitive emotion regulation and emotional problems. *Pers. Individ. Dif., 30*, 1311–1327. doi:10.1016/s0191-8869(00)00113-6

Geschwind, N., Peeters, F., Drukker, M., van Os, J., & Wichers, M. (2011). Mindfulness training increases momentary positive emotions and reward experience in adults vulnerable to depression: A randomized controlled trial. *J. Consult. Clin. Psychol., 79*, 618–628.

Griffiths, F. E., Boardman, F. K., Chondros, P., Dowrick, C. F., Densley, K., Hegarty, K. L., & Gunn, J. (2015). The effect of strategies of personal resilience on depression recovery in an Australian cohort: A mixed methods study. *Health, 19*, 86-106.

Groemping, U. (2006). Relative importance for linear regression in R: The package relaimpo. *J. Stat. Softw., 17*. doi:10.18637/jss.v017.i01

Gronwall, D.M.A. (1977). Paced Auditory Serial Addition Task - Measure of recovery from concussion. *Percept. Mot. Skills, 44*, 367–373.

Gross, J.J. (1998). The emerging field of emotion regulation: An integrative review. *Rev. Gen. Psychol., 2*, 271–299. doi:1089-2680/98/$3.00

Gross, J.J., & John, O.P. (2003). Individual differences in two emotion regulation processes: Implications for affect, relationships, and well-being. *J. Pers. Soc.*

Psychol., 85, 348–362. doi:10.1037/0022-3514.85.2.348

Hardeveld, F., Spijker, J., De Graaf, R., Nolen, W.A., & Beekman, A.T.F. (2010). Prevalence and predictors of recurrence of major depressive disorder in the adult population. *Acta Psychiatr. Scand., 122*, 184–191. doi:10.1111/j.1600-0447.2009.01519.x

Hoorelbeke, K., Faelens, L., Behiels, J., & Koster, E.H.W. (2015). Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Protocol for a randomized controlled trial. *BMC Psychiatry, 15*, 125.

Hoorelbeke, K., Koster, E.H.W., Demeyer, I., Loeys, T., & Vanderhasselt, M-A. (2016). Effects of cognitive control training on the dynamics of (mal)adaptive emotion regulation in daily life. *Emotion, 16,* 945-956. doi: 10.1037/emo0000169

Hu, T.Q., Zhang, D.J., Wang, J.L., Mistry, R., Ran, G.M., & Wang, X.Q. (2014). Relation between emotion regulation and mental health: A meta-analysis review. *Psychol. Rep., 114*, 341–362. doi:10.2466/03.20.PR0.114k22w4

Johnson, J.W. (2000). A heuristic method for estimating the relative weight of predictor variables in multiple regression. *Multivariate Behav. Res., 35*, 1–19. doi:10.1207/S15327906MBR3501_1

Joormann, J., & D'Avanzato, C. (2010). Emotion regulation in depression: Examining the role of cognitive processes. *Cogn. Emot., 24*, 913–939. doi:10.1080/02699931003784939

Joormann, J., & Gotlib, I.H. (2008). Updating the contents of working memory in depression: Interference from irrelevant negative material. *J. Abnorm. Psychol., 117*, 182–192. doi:10.1037/0021-843x.117.1.182

Joormann, J., & Vanderlind, M.W. (2014). Emotion regulation in depression: The role of biased cognition and reduced cognitive control. *Clin. Psychol. Sci., 2*, 402–421. doi:10.1177/2167702614536163

Kalisch, R., Müller, M.B., & Tüscher, O. (2015). A conceptual framework for the neurobiological study of resilience. *Behav. Brain Sci., 38*, 1–79. doi:10.1017/S0140525X1400082X, e0

Keng, S.L., Smoski, M.J., & Robins, C.J. (2011). Effects of mindfulness on psychological health: A review of empirical studies. *Clin. Psychol. Rev., 31*, 1041–1056.

Kraemer, N., Schaefer, J., & Boulesteix, A.-L. (2009). Regularized estimation of large-

scale gene regulatory networks with Gaussian graphical models. *BMC Bioinformatics, 10*, 384. doi:10.1186/1471-2105-10-384

Leppin, A.L., Bora, P.R., Tilburt, J.C., Gionfriddo, M.R., Zeballos-Palacios, C., Dulohery, M.M., . . . Montori, V.M. (2014). The efficacy of resiliency training programs: A systematic review and meta-analysis of randomized trials. *PLoS ONE, 9*, e111420. doi: 10.1371/journal.pone.0111420

Lima, A.F.B.D., & Fleck, M.P.D. (2007). Subsyndromal depression: An impact on quality of life? *J. Affect. Disord., 100*, 163–169.

Marchetti, I., Koster, E.H.W., Sonuga-Barke, E.J.S., & De Raedt, R. (2012). The Default Mode Network and recurrent depression: A neurobiological model of cognitive risk factors. *Neuropsychol. Rev., 22*, 229–251. doi:10.1007/s11065-012-9199-9

McNally, R.J., Robinaugh, D.J., Wu, G.W.Y., Wang, L., Deserno, M.K., & Borsboom, D. (2014). Mental disorders as causal systems: A network approach to posttraumatic stress disorder. *Clin. Psychol. Sci.* doi:10.1177/2167702614553230

Middleton, L.S., Denney, D.R., Lynch, S.G., & Parmenter, B. (2006). The relationship between perceived and objective cognitive functioning in multiple sclerosis. *Arch. Clin. Neuropsychol., 21*, 487–494.

Mowla, A., Ashkani, H., Ghanizadeh, A., Dehbozorgi, G.R., Sabayan, B., & Chohedri, A.H. (2008). Do memory complaints represent impaired memory performance in patients with major depressive disorder? *Depress. Anxiety, 25*, E92–E96. doi:10.1002/da.20343

O'Hara, R.E., Armeli, S., Boynton, M.H., & Tennen, H. (2014). Emotional stress-reactivity and positive affect among college students: The role of depression history. *Emotion, 14*, 193–202.

Pe, M.L., Raes, F., & Kuppens, P. (2013). The cognitive building blocks of emotion regulation: Ability to update working memory moderates the efficacy of rumination and reappraisal on emotion. *PLoS One, 8*, 12. doi:10.1371/journal.pone.0069071

Peeters, F., Nicolson, N., Wichers, M., & Hacker, P. (2013). Remission of Depression Questionnaire - Dutch translation (RDQ-NL).

Philippot, P., & Brutoux, F. (2008). Induced rumination dampens executive processes in dysphoric young adults. *J. Behav. Ther. Exp. Psychiatry, 39*, 219–227.

doi:10.1016/j.jbtep.2007.07.001

Portzky, M., Wagnild, G., De Bacquer, D., & Audenaert, K. (2010). Psychometric evaluation of the Dutch Resilience Scale RS-nl on 3265 healthy participants: a confirmation of the association between age and resilience found with the Swedish version. *Scand. J. Caring Sci., 24*, 86–92. doi:10.1111/j.1471-6712.2010.00841.x

Robinaugh, D.J., LeBlanc, N.J., Vuletich, H.A., & McNally, R.J. (2014). Network analysis of persistent complex bereavement disorder in conjugally bereaved adults. *J. Abnorm. Psychol., 123*, 510–522. doi:10.1037/abn0000002

Roth, R.M., Lance, C.E., Isquith, P.K., Fischer, A.S., & Giancola, P.R. (2013). Confirmatory factor analysis of the Behavior Rating Inventory of Executive Function-Adult version in healthy adults and application to attention-deficit/hyperactivity disorder. *Arch. Clin. Neuropsychol., 28*, 425–434. doi:10.1093/arclin/act031

Scholte, E., & Noens, I. (2011). BRIEF-A Handleiding: Vragenlijst executieve functies voor volwassenen. Hogrefe, Amsterdam.

Sheehan, D. V, Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., . . . Dunbar, G.C. (1989). The Mini-International Neuropsychiatric Interview (MINI): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J. Clin. Psychiatry, 59*, 22–33.

Solomon, D.A., Keller, M.B., Leon, A.C., Mueller, T.I., Lavori, P.W., Shea, M.T., . . . Endicott, J. (2000). Multiple recurrences of major depressive disorder. *Am. J. Psychiatry, 157*, 229-233.

Songprakun, W., & McCann, T. (2012). Effectiveness of a self-help manual on the promotion of resilience in individuals with depression in Thailand: A randomised controlled trial. *BMC Psych., 12*:12.

Southwick, S. M., Vythilingam, M., & Charney, D. S. (2005). The psychobiology of depression and resilience to stress: Implications for prevention and treatment. *Annu. Rev. Clin. Psychol., 1,* 255-91.

Steinhardt, M., & Dolbier, C. (2008). Evaluation of a resilience intervention to enhance coping strategies and protective factors and decrease symptomatology. *J. Am. Coll. Health, 56*, 445-453.

Svendsen, A.M., Kessing, L. V, Munkholm, K., Vinberg, M., & Miskowiak, K.W. (2012). Is

there an association between subjective and objective measures of cognitive function in patients with affective disorders? *Nord. J. Psychiatry, 66*, 248–253.

Tombaugh, T.N. (2006). A comprehensive review of the Paced Auditory Serial Addition Test (PASAT). *Arch. Clin. Neuropsychol., 21*, 53–76.

Van Vliet, I.M., & De Beurs, E. (2007). Het Mini Internationaal Neuropsychiatrisch Interview (MINI): Een kort gestructureerd diagnostisch psychiatrisch interview voor DSM-IV en ICD-10-stoornissen. *Tijdschr. Psychiatr., 49*, 393–397.

Vanderhasselt, M.-A., & De Raedt, R. (2009). Impairments in cognitive control persist during remission from depression and are related to the number of past episodes: An event related potentials study. *Biol. Psychol., 81*, 169–176.

Vanderhasselt, M.-A., Koster, E.H.W., Onraedt, T., Bruyneel, L., Goubert, L., & De Raedt, R. (2014). Adaptive cognitive emotion regulation moderates the relationship between dysfunctional attitudes and depressive symptoms during a stressful life period: A prospective study. *J. Behav. Ther. Exp. Psychiatry, 45*, 291–296. doi:10.1016/j.jbtep.2014.01.003

Wagnild, G.M., & Young, H.M. (1993). Development and psychometric evaluation of the resilience scale. *J. Nurs. Meas., 1*, 165–178.

Wagnild, R. N. (2009). A review of the Resilience Scale. *J. Nurs. Meas., 17*, 105-113.

Waugh, C.E., & Koster, E.H.W. (2015). A resilience framework for promoting stable remission from depression. *Clin. Psychol. Rev., 41*, 49–60. doi:10.1016/j.cpr.2014.05.004

Whitmer, A.J., & Banich, M.T. (2007). Inhibition versus switching deficits in different forms of rumination. *Psychol. Sci., 18*, 546–553.

Wichers, M.C., Myin-Germeys, I., Jacobs, N., Peeters, F., Kenis, G., Derom, C., . . . van Os, J. (2007). Evidence that moment-to-moment variation in positive emotions buffer genetic risk for depression: a momentary assessment twin study. *Acta Psychiatr. Scand., 115*, 451–457.

Zimmerman, M., Martinez, J.H., Attiullah, N., Friedman, M., Toba, C., Boerescu, D.A., & Ragheb, M. (2013). A new type of scale for determining remission from depression: The Remission from Depression Questionnaire. *J. Psychiatr. Res., 47*, 78–82. doi:10.1016/j.jpsychires.2012.09.006

Zou, H. (2006). The adaptive lasso and its oracle properties. *J. Am. Stat. Assoc., 101*,

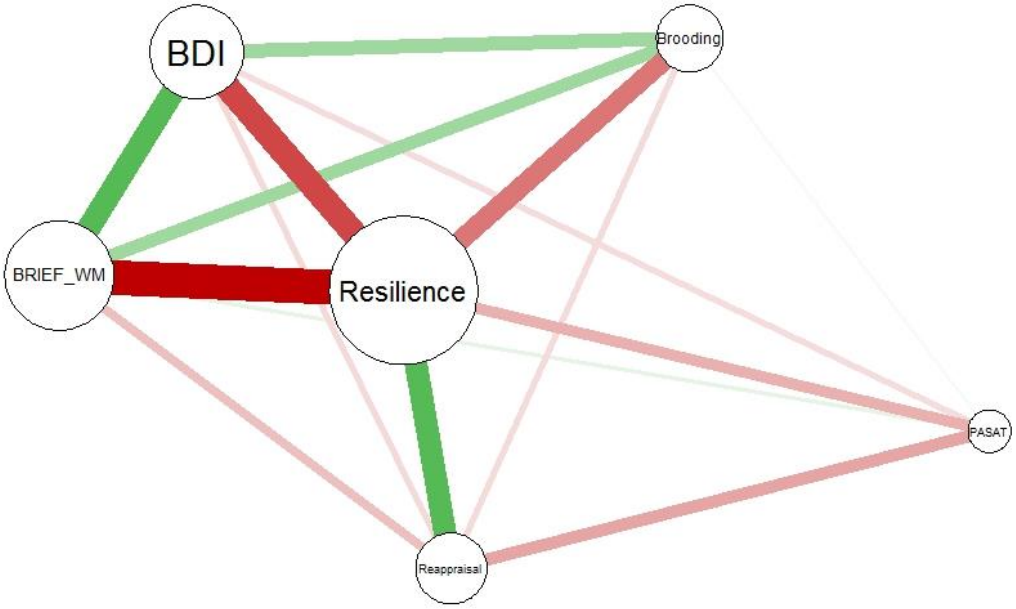
1418–1429. doi:10.1198/016214506000000735

APPENDIX

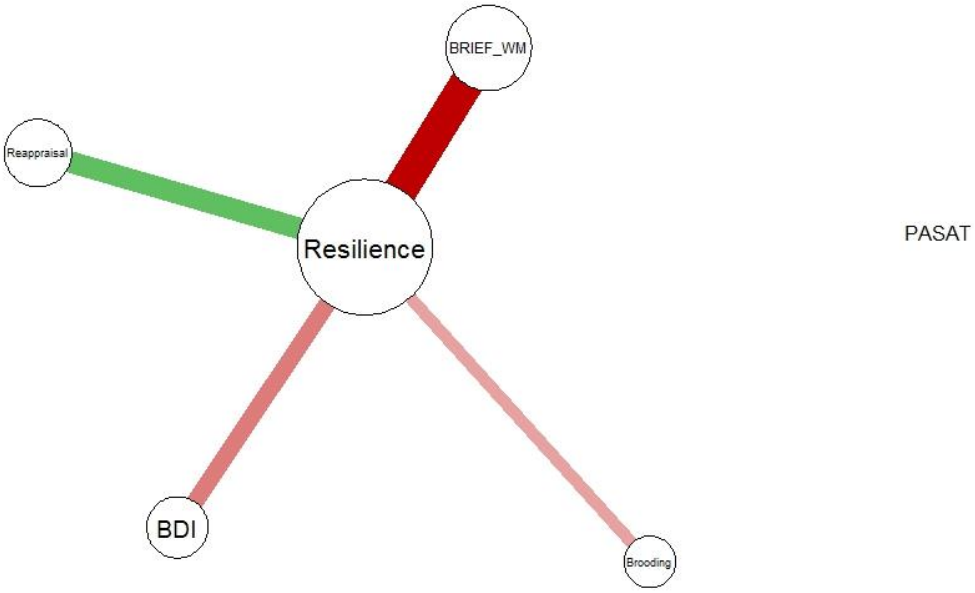
-Figure 1: provides an Association network containing alternative operationalizations of residual depressive symptomatology (BDI-II instead of RDQ scores), maladaptive emotion regulation (RRS Brooding instead of CERQ maladaptive emotion regulation compound scores), and adaptive emotion regulation (CERQ positive reappraisal subscale instead of CERQ adaptive emotion regulation compound scores)

-Figure 2: provides the Adaptive LASSO concentration network for the model containing the alternative measures of (mal)adaptive emotion regulation and residual symptomatology

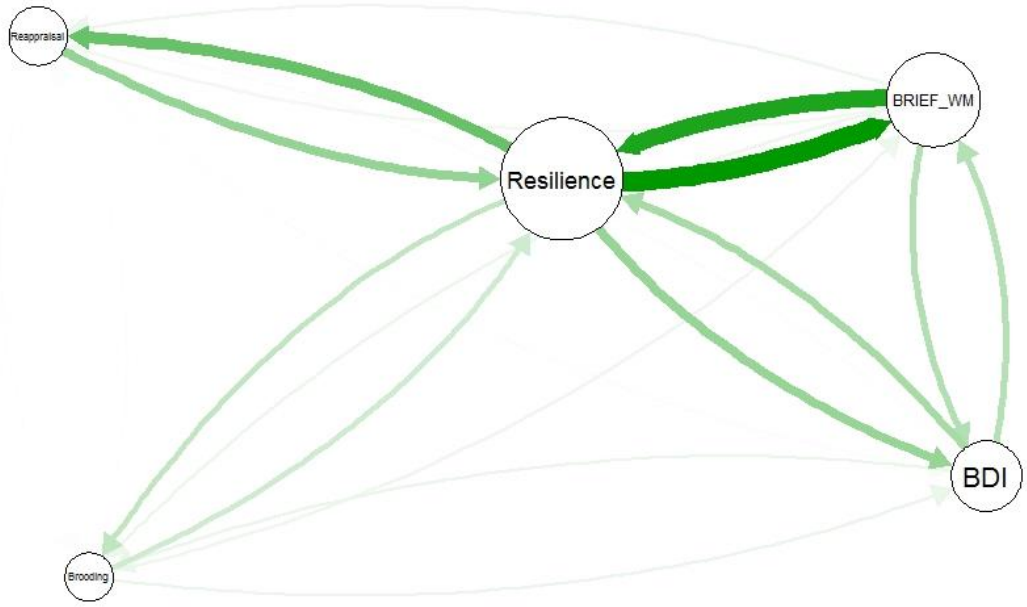
-Figure 3: provides the Directed relative importance network for the model containing the alternative measures of (mal)adaptive emotion regulation and residual symptomatology



Supplemental Figure 1. Association network



Supplemental Figure 2. Adaptive LASSO concentration network



Supplemental Figure 3. Directed relative importance network

CHAPTER 8

GENERAL DISCUSSION

Previous studies suggest that cognitive control deficits form a risk factor for the development and maintenance of depressive symptomatology (Joormann & D'Avanzato, 2010; Joormann & Vanderlind, 2014; Joormann & Stanton, 2016), a mechanism which is proposed to be mediated by maladaptive emotion regulation (e.g., depressive rumination; Demeyer, De Lissnyder, Koster, & De Raedt, 2012; Hsu et al., 2015). Early studies exploring effects of cognitive control training on clinical outcomes have rendered promising results, showing beneficial effects on depressive rumination and depressive symptomatology in MDD patients (e.g., Siegle, Ghinassi, & Thase, 2007). However, a number of methodological limitations of earlier studies limit the inferences that can be drawn regarding the causal involvement of cognitive control in depression, leaving important questions concerning the mechanisms underlying far transfer effects unresolved. Furthermore, early training studies have mainly focused on the application of cognitive control training in the context of treatment of depression (curative), whereas cognitive control training may also hold potential as a preventive intervention for depression. Addressing these questions could have important implications on both a theoretical (i.e., increasing our understanding of the etiology of depression, processes underlying emotion regulation, etc.) and clinical level (given the individual and societal impact of mood disorders). Hence, the main goal of this PhD was to test the causal influence of cognitive control in depression vulnerability, exploring the preventive potential of cognitive control training and the mechanisms that may underlie earlier reported training effects on depressive symptomatology.

For this purpose, we conducted several empirical studies testing the impact of cognitive control training on indicators of depression vulnerability, exploring effects of

training in controlled lab settings as well as in daily life (Chapter 3 – 6). Furthermore, as the literature on this research line expanded, we conducted a systematic review uniting various cognitive control training studies in the context of depression vulnerability that were published before the 16th of August 2016 (Chapter 2). Finally, in order to gain further insight into the mechanisms underlying remission from depression, we used network analysis to examine how key constructs in the context of cognitive vulnerability for depression and resilience are related following remission from depression (Chapter 7).

COGNITIVE CONTROL AND DEPRESSION VULNERABILITY: A STORY OF CAUSALITY

Evidence from our Empirical Studies

First, we conducted an experimental study exploring effects of cognitive control training on stress reactivity and depressive rumination in trait ruminators (Chapter 3; Hoorelbeke, Koster, Vanderhasselt, Callewaert, & Demeyer, 2015). Comparing two weeks of adaptive PASAT training to an active control condition, we found beneficial effects on self-reported affect and cognition in response to a lab stressor. That is, during a stress induction procedure in the lab the active control training group reported a significant reduction in positive thoughts and an increase in self-reported negative affect. In contrast, the amount of positive thoughts and negative affect remained stable in the adaptive PASAT training condition.

Providing a second test of the preventive potential of cognitive control training in the context of depression vulnerability, we proceeded to explore effects of cognitive control training on depressive rumination in response to a naturalistic stressor. For this purpose, effects of cognitive control training on depressive rumination were assessed at four weeks follow-up during the examination period. Controlling for elapsed time since the previous exam – i.e., the ruminative response elicited due to a stressor diminishes over time (cfr. Grant & Beck, 2010) – participants in the adaptive PASAT training condition reported a significant reduction in depressive rumination, which was not the case for the active control group. Interestingly, responsiveness to the lab stressor was

associated with change in depressive rumination from baseline to four weeks follow-up (Chapter 3).

These findings suggest that cognitive control is causally involved in depressive rumination, where reduced rumination is likely to translate into increased resilience to stressful events (i.e., diminished cognitive vulnerability). Alternatively, the observed effects of cognitive control training in terms of reduced stress reactivity in response to a lab stressor and naturalistic stressor may (partially) be due to increased or more efficient use of adaptive emotion regulation strategies such as positive (re)appraisal. Hence, in a second empirical study we explored effects of cognitive control training on depressive rumination and positive appraisal as indicators of adaptive and maladaptive emotion regulation in a convenience sample (Chapter 4; Hoorelbeke, Koster, Demeyer, Loeys, & Vanderhasselt, 2016). In line with the previous study, effects of cognitive control training on emotion regulation were first assessed in response to a lab stressor, which again was followed by assessment of training effects on emotion regulation in a more ecologically valid, naturalistic context. For the latter purpose, we relied on experience sampling methodology to test effects of cognitive control training on the dynamics of emotion regulation in daily life.

In contrast to our expectations, cognitive control training only affected the use of maladaptive emotion regulation strategies, whereas we did not find beneficial effects of cognitive control training on adaptive emotion regulation strategies in lab context or daily life. That is, both groups did not differ in the ability to reappraise a negative autobiographical memory in the lab context following training. Furthermore, in healthy students cognitive control training did not affect the deployment or efficacy of positive appraisal in daily life during a period of seven days following training. Instead, we observed a marginally significant cross-level interaction for deployment of rumination (p = .06), indicating that low levels of positive affect in daily life triggered less depressive rumination in the adaptive PASAT training condition compared to the active control group. Importantly, in line with the Response Styles Theory (Nolen-Hoeksema, 1991; Nolen-Hoeksema & Morrow, 1991) engaging in depressive rumination was predictive for subsequent mood deterioration, as indicated by a decrease in positive affect and increase in negative affect.

Taken together, in line with findings from previous prospective (e.g., Demeyer et al., 2012; Zetsche & Joormann, 2011) and experimental studies (e.g., Siegle et al., 2007, 2014), our results provide evidence for the hypothesis that higher levels of cognitive control reduce the chance of responding to stressful events with perseverative negative thinking such as depressive rumination (Chapters 3 & 4; Hoorelbeke et al., 2015; Hoorelbeke, Koster, et al., 2016). In this context, it is likely that the training effects reported in these first empirical studies in healthy or at-risk students provide an underestimation of the true preventive potential of cognitive control training due to sample characteristics. For instance, our observed effect size regarding depressive rumination is lower than effect sizes typically reported for MDD patients in adaptive PASAT training studies (e.g., Siegle et al., 2007, 2014). However, simultaneously, effects of training reported in these early studies are likely to be biased by methodological features such as lack of blinding and adequate control conditions. As a result, to provide a more stringent test of the causal involvement of cognitive control in depression vulnerability, we conducted a pre-registered double-blind randomized controlled trial study testing the effects of cognitive control training on depression vulnerability in a clinical population, namely, remitted depressed patients (RMD, Chapters 5 & 6; Hoorelbeke, Faelens, Behiels, & Koster, 2015; Hoorelbeke & Koster, 2017).

Confirming our previous findings, two weeks of adaptive PASAT training showed beneficial effects on depressive rumination (RRS Brooding) and depressive symptomatology (BDI-II) in RMD patients using intention-to-treat analysis (Hoorelbeke & Koster, 2017). Effects were observed immediately following training and remained present at three months follow-up. Similar findings were observed using alternative indicators of maladaptive emotion regulation (CERQ) and residual depressive symptomatology (RDQ). Importantly, intention-to-treat analysis also revealed beneficial effects of adaptive PASAT training on self-reported resilience at three months follow-up. Furthermore, completers of the training procedure reported reduced disability three months following training, suggesting that effects of preventative cognitive control training extend to broader indicators of functioning in RMD patients.

Lessons Learned from the Cognitive Control Training Literature

Taken together, our empirical studies demonstrate the causal involvement of cognitive control in depression vulnerability and resilience, with effects of training being more profound in high risk groups. Interestingly, our systematic review of the broader cognitive control training literature supports this hypothesis (Chapter 2; Koster, Hoorelbeke, Onraedt, Owens, & Derakshan, 2017). That is, not taking into account studies using single-session manipulations, 47% (*n* = 7) of all identified studies exploring beneficial effects of cognitive control training on indicators of cognitive vulnerability for depression in *non-clinical samples* (i.e., healthy or at-risk student- or convenience samples) provided evidence in support of the preventative potential of cognitive control training. Here, beneficial effects were reported for indicators of cognitive vulnerability such as emotional reactivity, emotion regulation, negative mood, cognitive complaints, and/or depressive symptomatology (e.g., Calkins, McMorran, Siegle, & Otto, 2015; Cohen et al., 2016; Gavelin, Boraxbekk, Stenlund, Järvholm, & Neely, 2015; Hoorelbeke et al., 2015; Schweizer, Grahn, Hampshire, Mobbs, & Dalgleish, 2013; Schweizer, Hampshire, & Dalgleish, 2011; Takeuchi et al., 2014). Additionally, at least 33% (*n* = 5) of studies using healthy or at-risk samples reported findings that provide mixed support for this hypothesis, showing beneficial effects on some but not on other indicators of depression vulnerability (e.g., Calkins & Otto, 2013; Daches & Mor, 2014; Hoorelbeke, Koster et al., 2016; Owens, Koster, & Derakshan, 2013; Xiu, Zhou, & Jiang, 2016). Note that in some of these studies chances of finding clear transfer effects on depression vulnerability were limited due to design features such as suboptimal sample characteristics to address this question. For instance, Calkins and Otto (2013) found beneficial effects of cognitive control training on mood in absence of beneficial effects on depressive symptomatology. However, participants were pre-selected to show elevated obsessive compulsive symptoms and low depressive symptomatology. Furthermore, some of these studies used healthy convenience samples which are less likely to exhibit depression vulnerability (e.g., Hoorelbeke, Koster et al., 2016; Xiu et al., 2016).

For cognitive control training studies including *patient samples* (i.e., clinically depressed or previously depressed patients), beneficial effects were reported in 57% (*n* = 8) of identified cases (e.g., Alvarez, Sotres, León, Estrella, & Sosa, 2008; Brunoni et al.,

2014; Hoorelbeke & Koster, 2017; Iacoviello et al., 2014; Morimoto et al., 2014; Segrave, Arnold, Hoy, & Fitzgerald, 2014; Siegle et al., 2007; Vanderhasselt et al., 2015). Furthermore, an additional study (7%) reported mixed effects on depression vulnerability, observing beneficial effects on depressive rumination in absence of immediate effects on depressive symptomatology (Siegle et al., 2014). However, Siegle and colleagues (2014) did observe beneficial effects of cognitive control training on outpatient day-treatment visits at one year follow-up, suggesting long-term beneficial effects on depressive symptomatology in MDD patients.

In contrast, 20% (*n* = 3) and 36% (*n* = 5) of the studies selected for inclusion in the systematic review strictly reported *null-findings* regarding effects on depression vulnerability in healthy / at-risk (Moshier, Molokotos, Stein, & Otto, 2015; Onraedt & Koster, 2014, study 1 and 2) or patient samples respectively (Bowie et al., 2013; Elgamal, McKinnon, Ramakrishnan, Joffe, & MacQueen, 2007; Moshier, 2015; Trapp, Engel, Hajak, Lautenbacher, & Gallhofer, 2016; Wanmaker, Geraerts, & Franken, 2015). While critically reviewing this literature, we noted that some of the reported null-findings may be attributable to methodological features. For instance, some of these studies have relied on very limited sample sizes, not being able to detect moderate effects of cognitive control training in clinically depressed patients (e.g., *d* = 0.67; Trapp et al., 2016). Moreover, in addition to exploring effects of cognitive control training using potentially underpowered designs (e.g., CCT [*n* = 12] vs. active controls [*n* = 12] vs. healthy controls [*n* = 22], Elgamal et al., 2007; CCT + behavioral activation [*n* = 21] vs. active controls + behavioral activation [*n* = 13], Moshier, 2015), a significant percentage of training studies reporting null-results have relied on a limited amount of training sessions (e.g., 3 sessions, Moshier et al., 2015; 4 sessions, Moshier, 2015; 6 sessions / one week, Onraedt & Koster, 2014, study 1 and 2). This may have been insufficient to detect stable effects of cognitive control training over time. Furthermore, some cognitive control training studies in MDD patients simply did not directly assess effects of training on rumination or depressive symptomatology (e.g., Bowie et al., 2013). Taken together, this leaves only one study (Wanmaker et al., 2015) presenting null-findings following extensive cognitive control training (24 sessions of dual n-back + symmetry span training, using neutral stimuli) using a sufficiently powered sample to

detect moderate effects of cognitive control training (CCT: *n* = 36, active controls: *n* = 39). Here, it would be interesting to test whether the absence of training effects are considered to be 'in support of the null-hypothesis' or 'inconclusive' (cfr. infra, Bayesian analysis).

The 21 studies in which beneficial effects of cognitive control training were reported in terms of reducing vulnerability for depression typically relied on more *extensive training procedures*. Not taking into account the study of Alvarez and colleagues (2008) in which training length was contingent on the time necessary to reach training goals, and the study of Morimoto and colleagues (2014) in which participants were exposed to 30 hours of cognitive control training, the other 19 studies reporting beneficial training effects on average used 12.32 training sessions with 79% of the studies using ≥ 6 training sessions and 58% using ≥ 10 training sessions (the amount of sessions used in our experimental studies). Furthermore, often one training session would include exposure to multiple training tasks. These findings illustrate the importance of *training intensity* for effects of cognitive control training to occur.

Another interesting observation in this context is that, among the cognitive control training studies reporting beneficial effects on depression vulnerability (*n* = 21), the multitude of training studies (71%, *n* = 15) relied on cognitive control training procedures which were argued to train *cognitive control over emotional information*. That is, either using a cognitive control training procedure containing emotional stimuli (23.81%, *n* = 5; e.g., Iacoviello et al., 2008; Schweizer et al., 2013; Owens et al., 2013) *or* training cognitive control in a highly frustrating / emotion eliciting task context[1] (47.62%, *n* = 10; e.g., Siegle et al., 2007, 2014). In contrast, again not taking into account single-session manipulations, none of the studies reporting null-findings for cognitive control training on depression vulnerability used emotional stimuli during the training procedure. Furthermore, only two studies (25%) used a training procedure which is believed to target cognitive control over emotional information given the frustrating task context (Moshier, 2015; Moshier et al., 2015). This raises the important question

[1] For some of the cognitive control training paradigms using neutral stimuli, it has been argued that – although using neutral stimuli – cognitive control is trained over emotional information given the frustrating task context (e.g., PASAT; Gronwall, 1997).

whether effects of cognitive control training may be improved by explicitly training control over emotional information, which may resemble the cognitive mechanism underlying depression vulnerability more closely. Interestingly, two studies directly tested this hypothesis, providing (preliminary) evidence that training cognitive control over emotional information would be more effective in terms of reducing vulnerability for depression than training cognitive control over neutral information. For instance, comparing a group completing an affective modification of the dual n-back training task with a neutral dual n-back training condition and an active control condition over a period of 20 days, Schweizer and colleagues (2011) found the emotional dual n-back training group to report greater transfer effects to emotional Stroop task performance compared to the neutral training group. Similarly, Iacoviello and colleagues (2014) compared effects of an emotional n-back training with an n-back training using neutral stimuli, showing selective far transfer effects to indicators of memory bias in the affective training condition only, and marginally stronger effects of affective training on depressive symptoms.

Overall, these findings suggest that transfer effects to indicators of depression vulnerability are most likely to be found given that following criteria are met: (a) The study is sufficiently powered to detect small to moderate effects (Motter et al., 2016), taking into account differences in population characteristics regarding depression vulnerability (i.e., differences between healthy, at-risk, MDD, and RMD samples regarding the to be expected outcome of manipulation of cognitive vulnerability for depression). For instance, in at-risk groups cognitive vulnerability is most apparent in response to stressors; (b) Cognitive control is trained over emotional information, using emotional stimuli or an emotion eliciting task context; and (c) Given sufficient exposure to the training procedure (i.e., training intensity).

Exploring Mechanisms Underlying Training Effects: A Stepwise Approach

As discussed above based on the existing cognitive control training literature, several design features and methodological considerations may contribute to (lack of) transfer effects for emotional outcomes. Throughout our empirical studies we consistently exposed participants to 10 sessions of adaptive PASAT training over a two-

week period, where effects were compared to an active control training. Training cognitive control in an emotion eliciting (frustrating) task context using this procedure yielded several interesting effects on indicators of depression vulnerability. During this process, several efforts were made to elucidate the specific mechanisms underlying the observed far transfer effects, linking emotional transfer to cognitive control.

First, in each of our experimental studies, cognitive control training was compared to an *active control condition* in which more general cognitive functions were trained without placing a high load on cognitive control / working memory functioning (e.g., Harrison et al., 2013; Redick et al., 2013). In order to control for motivational effects of undergoing training (i.e., placebo effects), we assessed whether both training groups showed an increase in training task performance over time. Indeed, in all of our experimental studies, both training conditions showed a significant improvement in training task performance over the ten sessions (Chapters 3 – 6; Hoorelbeke et al., 2015; Hoorelbeke, Koster et al., 2016; Hoorelbeke & Koster, 2017). Furthermore, in the randomized controlled trial study we provided psycho-education regarding cognitive training and monitored credibility and expectancy of the cognitive training approaches used (Chapters 5 – 6). Here, cognitive training condition did not have a differential impact on self-reported credibility or expectancy. Furthermore, both training conditions did not differ in the extent to which participants believed being allocated to a 'placebo condition' (Chapter 6; Hoorelbeke & Koster, 2017). These findings suggest that the reported effects on outcomes of depression vulnerability are unlikely to stem from only motivational effects of undergoing training.

Second, before exploring effects of cognitive control training on emotional outcomes, we assessed *transfer to closely related cognitive processes* (e.g., indicators of cognitive control task performance, indicators of working memory capacity, self-reported executive functioning). Importantly, we observed transfer effects of adaptive PASAT training on several indicators of cognitive control. For instance, we observed a tendency for increased dual n-back performance following cognitive control training in healthy students (Chapter 4; Hoorelbeke, Koster, et al., 2016). Here, improvements in cognitive control were predicted by prior cognitive control levels. Furthermore, RMD patients in the cognitive control training condition performed significantly better than

the active control condition on the non-adaptive PASAT assessment task immediately following training (Chapter 6; Hoorelbeke & Koster, 2017). This is in line with findings reported in cognitive control training studies included in our systematic review (Chapter 2; Koster, Hoorelbeke, et al., 2016), in which beneficial transfer effects were observed in healthy / at-risk and MDD samples for a multitude of transfer measures. For instance, near transfer effects on cognitive control were reported using n-back assessment tasks (Gavelin et al., 2015; Schweizer et al., 2013; Xiu et al., 2016), the non-adaptive PASAT task (Siegle et al., 2007, 2014), and several modifications of the Stroop Color-Word task (Morimoto et al., 2014; Schwiezer et al., 2011). Furthermore, transfer of cognitive control training has been established to several indicators of working memory functioning, such as the Letter Memory Running Span task (Gavelin et al., 2015), several versions of the Digit Span task (Elgamal et al., 2007; Schweizer et al., 2011), the Reading Span task (Wanmaker et al., 2015), and the Change Detection Paradigm (Owens et al., 2013). Moreover, beneficial effects of cognitive control training have been observed on verbal learning and memory (Bowie et al., 2013; Elgamal et al., 2007). In addition, some studies even showed far transfer effects on indicators of cognitive functioning such as intelligence (e.g., Raven's progressive matrices, Gavelin et al., 2015; Schweizer et al., 2011; WAIS, Alvarez et al., 2008).

In contrast, we did not find differential cognitive transfer effects of adaptive PASAT training in trait ruminators using an indicator of working memory capacity (Chapter 3; Hoorelbeke et al., 2015). Although we observed an overall increase in automated O-Span task performance following training, both groups did not significantly differ. We propose that this finding is attributable to task- and sample characteristics, where ceiling effects may have hampered finding differential training effects. Additionally, it is possible that improvements in automated O-Span task performance in both conditions reflect improvements in different cognitive functions (updating and inhibition, attention, etc.). Similarly, ceiling effects may have limited the observed cognitive transfer effects in the healthy student sample (Chapter 4; Hoorelbeke, Koster, et al., 2016).

Interestingly, some studies reported beneficial effects of cognitive control training on cognitive complaints (e.g., Gavelin et al., 2015). This is in line with findings

from our randomized controlled trial study, where – in addition to effects on behavioral measures for cognitive transfer – RMD patients who completed the training procedure also reported a marginal significant increase in executive functioning from baseline to post-training (i.e., a reduction in self-reported cognitive complaints; Chapter 6; Hoorelbeke & Koster, 2017).

Third, we assessed *stability of cognitive transfer effects*. That is, it has been suggested that improved cognitive functioning underlies the observed long-term beneficial effects of adaptive PASAT training (e.g., Siegle et al., 2014). However, previous studies did not empirically test whether cognitive transfer effects remain stable following adaptive PASAT training. Here, in order to support the hypothesis that improved cognitive functioning via training may affect cognitive vulnerability in the long term, cognitive control training should elicit long-term cognitive transfer effects. For this purpose, cognitive transfer effects were assessed immediately following training and at three months follow-up in RMD patients in our randomized controlled trial study (Chapter 6; Hoorelbeke & Koster, 2017). Importantly, training related improvements in cognitive control remained present at three months follow-up. Participants in the cognitive control training condition performed significantly better on the non-adaptive PASAT task at each time point. Additionally, the cognitive control training group reported a significant reduction in cognitive complaints from post-training until three months follow-up.

Fourth, when comparing training conditions and demonstrating cognitive transfer, there is always the possibility that differences in emotional outcomes may result from subtle *differences in training procedures* which *may act as confounding factors*. For instance, in the context of adaptive PASAT training for depression vulnerability, one could argue that differential training effects on emotional outcomes may arise from potential differences in training conditions, such as difficulty of the tasks or differences in exposure to stress and rumination during the training task. To control for this potential 'mastery experience' or 'stress inoculation' effect, depressive rumination during training and effects of training on perceived competence and mood were assessed following each online session in two of our empirical studies (Chapters 4 – 6; Hoorelbeke & Koster, 2017; Hoorelbeke, Koster, et al., 2016). Importantly, no

differential effects of training condition were found in the healthy student sample (Chapter 4; Hoorelbeke, Koster, et al., 2016). Furthermore, effects of cognitive control training on depressive rumination and depressive symptomatology remained significant in RMD patients after controlling for change in process measures of training task experience (Chapter 6; Hoorelbeke & Koster, 2017), allowing us to rule out these confounding effects.

In order to test the assumption of causality, it is also important to *explore how cognitive and emotional transfer effects relate to one another* (but see Moreau, Kirk, & Waldie, 2016). We have done this on several occasions (e.g., Hoorelbeke et al., 2015; Hoorelbeke & Koster, 2017). For instance, in the study with trait ruminators increased working memory functioning predicted less depression vulnerability (ruminative brooding) and higher self-reported resilience following training, while controlling for baseline levels of brooding or resilience respectively (Chapter 3; Hoorelbeke et al., 2015). This was only the case for the cognitive control training condition, which may suggest that improvements on the automated O-Span task reflect increased cognitive control in the cognitive control training condition, whereas in the other condition, improved automated O-Span task performance may have been due to more general improvements in cognitive functioning which play a less central role in depression vulnerability (cfr. supra). Furthermore, improvements in cognitive control predicted lower depressive rumination and depressive symptomatology in RMD patients (Chapter 6; Hoorelbeke & Koster, 2017). Importantly, several studies included in our systematic review (Chapter 2; Koster et al., 2017) have reported similar associations between improvements in training- or cognitive transfer task performance and outcomes of depression vulnerability (e.g., Brunoni et al., 2014; Calkins et al., 2015; Calkins & Otto, 2013; Morimoto et al., 2014; Onraedt & Koster, 2014, Study 1; Segrave et al., 2014; Vanderhasselt et al., 2015).

Finally, our randomized controlled trial study was set-up to test a specific hypothesis regarding the underlying mechanisms of far transfer effects. Here, it has been assumed that cognitive control training affects depressive symptomatology via its impact on ruminative thinking (*mediation hypothesis*; Siegle et al., 2007, 2014). Hence, we tested whether improvements in cognitive control task performance from baseline

to post-training could predict depressive symptomatology at three months follow-up, via post-training brooding. While controlling for baseline depressive symptomatology and brooding, we found evidence for partial mediation (Chapter 6; Hoorelbeke & Koster, 2017). That is, increased cognitive control places one at reduced risk to respond to stressful events with depressive rumination, which translates into lower future depressive symptoms. Here, it is likely that other to be identified mediators contribute to this effect.

Taken into account the efforts made to tie emotional transfer effects to cognitive processes, we believe this PhD provides firm evidence for the causal involvement of cognitive control in depression vulnerability. In contrast, fostering adaptive emotion regulation has proven to be a more challenging endeavor.

Lack of Transfer Effects: Evidence for Absence?

Although relatively successful in targeting indicators of depression vulnerability, we consistently failed to observe beneficial effects of adaptive PASAT training on use of adaptive emotion regulation strategies such as positive appraisal as indicators of resilience (Chapters 4 & 6; Hoorelbeke & Koster, 2017; Hoorelbeke, Koster, et al. 2016). Importantly, failures to reject the null-hypothesis are inconclusive as they do not provide evidence for the hypothesis that cognitive control training does *not* affect adaptive emotion regulation (Kruschke, 2011; Mulder & Wagenmakers, 2016). Strength of evidence for the null-hypothesis can be tested using Bayesian analysis.[2] Given that emotion regulation deficits are more likely to occur in clinical samples than in healthy student samples, we conducted a post-hoc Bayesian comparison of training effects on adaptive emotion regulation for the RMD patient sample. The results of this analysis

[2] Bayesian statistics rely on likelihood ratios, with Bayes Factors (BFs) reflecting the probability of the data given one hypothesis compared to the probability of the data given another hypothesis (Jeffreys, 1961), allowing comparison of strength of evidence for the null-hypothesis. Here, strength of evidence for the alternative [BF(10)] or null-hypothesis [BF(01)] can be interpreted as "no evidence for any hypothesis" (BF = 1), "anecdotal" (BF = 1 – 3), "substantial" (BF = 3 – 10), "strong" (BF = 10 – 30), "very strong" (BF = 30 – 100), or "extreme" (BF > 100; Jeffreys, 1961; Wagenmakers, Wetzels, Borsboom, & van der Maas, 2011). The BFs presented in this text were calculated in JASP 0.8.1 (Love et al., 2015) using two-sided Bayesian *t*-tests on Δ-scores (e.g., Fang, Hoorelbeke, et al., 2017) from baseline to three months follow-up. We assumed a Cauchy distribution as a prior (e.g., Wetzels, Matzke, Lee, Rouder, Iverson, & Wagenmakers, 2011) and performed a robustness check to establish that the findings are unspecific to the choice of prior.

favor the null-hypothesis by a factor of 3.10 for adaptive emotion regulation, whereas results for maladaptive emotion regulation strategies are 7.83 times more likely to occur under the alternative hypothesis of training effects.

These findings confirm that cognitive control training only impacted use of maladaptive emotion regulation strategies. Several factors may account for these results: First, it has been argued that difficulties with adaptive emotion regulation strategies are only apparent in severely disturbed clinical samples (e.g., Dillon & Pizzagalli, 2013) whereas we explored effects in healthy students or patients in remission. Second, although training cognitive control may reduce the chance of responding to stressors with perseverative negative thinking, this does not necessarily imply that the subject will have acquired necessary skills or insights to adopt more adaptive emotion regulation strategies. Here, meta-cognitions regarding emotion regulation strategies may play an important role as well as ability and prior experience with adaptive emotion regulation strategies. For this purpose, combining cognitive control training with emotion regulation training would be interesting. For instance, a recent study focused on the combination of cognitive control training and mindfulness, suggesting superior effects of a combined approach for worrying (Course-Choi, Saville, & Derakshan, 2017). It is currently unclear however if similar efforts would also show transfer to indicators of adaptive emotion regulation.

Furthermore, the above presented evidence for absence of transfer effects on adaptive emotion regulation (as an indicator of resilience, Kalish et al., 2016), does not rule out the possibility that effects of cognitive control training exceed depression vulnerability. Indeed, beneficial effects were observed on self-reported resilience in the remitted depressed patient sample (Hoorelbeke & Koster, 2017). Specifically, Bayesian re-analysis of our data provides strong evidence for the effects of cognitive control training on resilience, BF(10) = 33.43. Here, future studies exploring mediating factors underlying transfer effects are crucial to enhance our understanding of the role of cognitive control in resilience.

Clinical Implications

The finding that cognitive control is causally involved in vulnerability for depression has important clinical implications. That is, our empirical studies and systematic review indicate that cognitive control training forms an interesting intervention in terms of vulnerability reduction in at-risk groups (e.g., trait ruminators, remitted depressed patients) and clinically depressed patients. Hence, given sufficient practice, cognitive control training could be used to selectively target depressive rumination. An important advantage of this intervention technique is that it can be easily disseminated online, targeting vulnerability mechanisms in a cost effective manner. Note that, although cognitive control has shown beneficial effects in MDD samples, these effects were typically obtained in combination with existing (psychotherapeutic or pharmacological) interventions. As a result, cognitive control training should be treated as an add-on intervention in clinically depressed samples. Furthermore, before cognitive control training can readily be implemented in clinical practice, several questions remain to be addressed (e.g., amount of sessions needed, different types of cognitive control training, role of affective context, stability of effects, influence of booster sessions, interactions with existing treatments, etc.).

For instance, our current knowledge regarding moderators of training effects is limited. Here, previous work suggests the importance of task engagement (Siegle et al., 2014). Hence, fostering motivation to engage in training while stimulating cognitive control as efficiently as possible forms an important challenge for cognitive control training studies in the context of depression vulnerability. This difficulty is also reflected by high drop-out levels obtained in some of the presented studies (e.g., Hoorelbeke, Koster, et al., 2016). What this is concerned, psycho-education and carefully selected gamification techniques may form interesting additions to existing cognitive control training procedures. For instance, drop-out levels were minimal in our last study in which a psycho-education component was added to the cognitive control training procedure (Chapter 6; Hoorelbeke & Koster, 2017). Similarly, Anguera, Gunning, and Areán (2016) reported low drop-out levels for a gamified cognitive control training in patients suffering from late life depression. Following four weeks of training, participants in the gamified cognitive control training condition demonstrated enhanced cognitive functioning compared to the control condition receiving problem

solving therapy. Moreover, gamified cognitive control training and problem solving therapy shared similar beneficial effects on depression severity, which remained stable at one month follow-up. In a second study, Areán and colleagues (2016) compared effects of gamified cognitive control training and problem solving therapy with a control condition in which participants only received health tips. The complete study was administered online using mobile apps. For patients with moderate levels of depression severity, the gamified cognitive control training condition and problem solving therapy condition both performed better in terms of remission from depression than the control condition. However, mobile administration of gamified cognitive control training was characterized by high attrition rates before starting the first training session, especially among patients showing high levels of depressive symptomatology (Areán et al., 2016).

Hence, fostering motivation to engage in cognitive training and adhere to the training protocol forms an important challenge for internet-delivered preventive interventions for depression. For this purpose, we recently conducted a user requirements analysis for the adaptive PASAT training procedure based on focus groups with RMD patients (Vervaeke, Van Looy, Hoorelbeke, Baeken, & Koster, in preparation). This resulted in specific recommendations regarding the configuration of training (e.g., flexible deployment of sessions, session length), technological and personal requirements (e.g., availability of the training on different platforms and devices), and motivating factors (e.g., psycho-education, gamification elements such as performance monitoring, feedback, reinforcing game-elements, etc.). Interestingly, meta-analytical findings regarding the effectiveness of E-health interventions suggest that therapist support may improve the effectiveness of internet-delivered interventions (Spek et al., 2007). As a result, we conducted interviews with clinicians regarding the requirements for implementation of cognitive control training in clinical practice (Vervaeke et al., in preparation). Mental health workers pointed out the need for clinical workshops regarding use of cognitive control training, and support of policy makers, in addition to a training platform that is easy in use and provides the possibility of online clinical assessment and monitoring of improvement during and following therapy, without increasing the administrative load of clinicians. Based on these findings, we are

currently setting up an online platform containing a gamified modification of the adaptive PASAT training (PrevenD Project).

Another important question is what preventive interventions for depression should ideally target in addition to cognitive control impairments. In Chapter 7 we presented a cross-sectional study in which network models were applied to explore how cognitive vulnerability and protective factors contribute to remission following depression. Results of this study suggest a central role for resilience, linking (mal)adaptive emotion regulation and subjective cognitive control to residual depressive symptomatology (Hoorelbeke, Marchetti, De Schryver, & Koster, 2016). In contrast, a behavioral indicator for cognitive control was removed from the models. We propose this may be due to method variance between the predictors. Nonetheless, the findings suggest that stimulating resilience may be the most efficient way to modify the network of protective and vulnerability factors following remission from depression. However, note that subjective cognitive control (working memory complaints) was ranked second on the centrality indexes of the model (e.g., Closeness, Instrength, and Outstrength; see Chapter 7 Table 4). This is in line with the observation that improvements in working memory functioning predict increased resilience (Chapter 3; Hoorelbeke et al., 2015) and the reported beneficial effects of cognitive control training on indicators of depression vulnerability *and* resilience (Chapter 6; Hoorelbeke & Koster, 2017). However, it is unclear how cognitive control training relates to other resilience focused interventions (e.g., Leppin et al., 2014; Songprakun & McCann, 2012; Steinhardt & Dolbier, 2008; for a review, see Waugh & Koster, 2015). Here, it could be the case that different preventive interventions may complement one another in reducing vulnerability for emotional disorders (e.g., mindfulness + cognitive control training; Course-Choi et al., 2017).

Taken together, although the literature pertaining the preventative potential of cognitive control training has evolved considerably recent years, several steps still need to be undertaken before being able to implement cognitive control training as a preventive intervention for depression. In the next section we provide guidelines regarding how future studies may address this need.

LIMITATIONS AND FUTURE RESEARCH DIRECTIONS

Throughout this dissertation we have undertaken several initiatives to increase our understanding of the causal involvement of cognitive control in depression vulnerability. Nonetheless, in addition to previous studies mentioned above, the studies presented in this dissertation have their own limitations and have raised additional questions which should be addressed in future studies. For instance, the current studies have relied on relatively limited sample sizes, following-up participants over relatively short periods of time. Moreover, we have mainly focused on the effects of cognitive control training on emotional outcomes, paying limited attention to the neuropsychological mechanisms underlying transfer effects, or the specific cognitive control processes involved in adaptive PASAT performance. Furthermore, effects were typically assessed using behavioral and self-report measures, whereas it would be interesting to explore effects of training on multiple levels, for instance, combining self-report and behavioral measures with psychophysiological measures and neuroimaging techniques. Hence, several recommendations can be made to increase our understanding of the involvement of cognitive control processes in depression vulnerability and resilience:

First, a substantial amount of cognitive control training studies have relied on suboptimal designs. For this purpose, in our systematic review of the literature (Chapter 2; Koster et al., 2017), we presented general desiderata for future studies aimed to improve the quality of the cognitive control training literature and inferences that can be drawn from it. Table 1 presents a summary of these general recommendations aimed at improving our understanding of transfer effects, mediating, and moderating factors. Specifically, next to cognitive control training studies demonstrating sound methodological characteristics for replication purposes of earlier reported training effects, there is a strong need for large scale studies set-up to identify potential moderators of training effects. In this context, candidates are objective and subjective cognitive control deficits (cognitive task performance, cognitive complaints), trait rumination, (residual) depressive symptomatology, number of depressive episodes, etc. Increased knowledge of moderators of training effects would ideally lead to a set of

(contra)indications for cognitive control training for depression. Furthermore, identifying (sub)groups of patients that (do not) seem to benefit from cognitive control training would allow further tailoring of training in order to increase the effectiveness of targeted cognitive control interventions.

Table 1. Recommendations for future research

Increasing understanding of transfer effects
1. Pre-register efforts to establish transfer effects
2. Use a sample size that allows to at least detect changes of moderate magnitude on the primary outcome measure(s)
3. Use multiple training sessions
4. Foster task engagement (e.g., using psycho-education)
5. Training should be targeting cognitive functioning in a task context that may elicit cognitive processes directly involved in repetitive negative thinking (e.g., frustrating task context)
6. Transfer effects should be assessed in a similar task context relevant to the cognitive mechanisms involved in the emotional outcome(s)
7. Use training paradigms for which cognitive transfer has already been demonstrated or include multiple measures of transfer
8. Explore the relation between cognitive and emotional transfer
9. Integrate indicators of neurophysiological mechanisms of depression vulnerability on multiple levels
10. Examine how change in cognitive control is related to change in the emotional outcome measure(s)
11. Use follow-up assessments to pick up training effects and to explore stability of transfer effects
12. Train samples that allow sufficient improvement in cognitive control and show sufficient heterogeneity regarding the emotional outcome(s)
13. For different training procedures and populations, taking into account potential moderators, set-up designs allowing to determine the number of sessions needed to establish transfer on cognitive and emotional outcomes
Increasing understanding of underlying mechanisms
14. Include measures of potential mediating variables
15. Include multiple time points in order to examine mediation
16. Compare training effects using an adequate comparator condition (e.g., active control) to ensure mechanisms can be linked to cognitive control
Increasing understanding of moderators of training effects
17. Conduct confirmatory research to replicate the moderators that have been observed
18. Moderator analysis requires sufficient data (cfr. sample size)
19. Explore the influence of specific clinical moderators that have a high likelihood of influencing efficacy of training
20. Assess cognitive impairments on multiple levels

Note: This table was adopted from Supplemental material added to Koster, Hoorelbeke, Onraedt, Owens, and Derakshan (2017; Chapter 2 of this dissertation).

Second, in the cognitive control training literature, a multitude of training approaches have been put forward (e.g., Cohen et al., 2016; Daches & Mor, 2014; Jaeggi, Buschkuehl, Jonides, & Perrig, 2008; Siegle et al., 2007; Schweizer et al., 2011). Continued systematic research exploring how each of these training procedures affect specific cognitive functions may advance our understanding of training effects and may allow to apply more individually tailored cognitive control training interventions (i.e., following a diagnostic phase). For instance, using a broad cognitive control training procedure for individuals showing general cognitive control impairments, whereas it is possible that other at-risk individuals may benefit more from cognitive control training procedures specifically targeting inhibition or updating of emotional information. In addition to increased knowledge regarding moderators of training effects, taking into account these subtle differences may eventually increase the effectiveness of cognitive control training as an individually tailored preventive intervention.

Third, individual variability in effectiveness of cognitive control training may also stem from metacognitions regarding (the functionality of) emotion regulation. That is, it may be adaptive to train cognitive control in participants who do not intend to actively engage in depressive rumination, whereas participants with dysfunctional beliefs regarding rumination may recruit the increased cognitive control functions to engage more in depressive rumination, potentially increasing one's vulnerability for depression. Similarly, metacognitions regarding adaptive emotion regulation strategies may determine effects of cognitive control training on emotion regulation. Although some instruments have been modified to assess metacognition regarding rumination (e.g., de Jong-Meyer, Beck, & Riede, 2009; Gooding, Taylor, & Tarrier, 2012; Kubiak, Zahn, Siewert, Jonas, & Weber, 2014), to our knowledge as to date no instrument exists to assess emotion regulation intentions *and* goal achievement for both adaptive and maladaptive emotion regulation strategies. Hence, we are currently in the process of creating and validating an instrument specifically set-up to measure the above described processes.

Fourth, the use of gamification techniques has been proposed to increase task engagement. Although findings indicate that gamification can increase user experience of a cognitive task, this does not necessarily lead to increased task performance (Hawkins, Rae, Nesbitt, & Brown, 2013). Here, incautious use of gamification techniques may affect the emotion eliciting nature of the task, which we propose may be a central element of the adaptive PASAT training (in terms of fostering transfer to emotional outcomes of depression vulnerability). Moreover, Katz, Jaeggi, Buschkuehl, Stegman, and Shah (2014) demonstrated that adding distracting game elements such as real-time scoring can reduce training improvement. Future studies should take this into account before blindly implementing gamification techniques to existing cognitive control training paradigms. Taking this into account, we are currently preparing a study in which effects of gamification on adaptive PASAT training efficiency will be mapped (PrevenD project).

Fifth, in order to advance our understanding of the temporal sequence of training effects, future studies should explore the effects of cognitive control training in daily life using intensive experience sampling procedures. We have previously explored effects of cognitive control training on emotion regulation in daily life during one week post-training (Chapter 4; Hoorelbeke, Koster, et al., 2016). However, exploring online effects of cognitive control training on the dynamics of affect, emotion regulation, and symptomatology in daily life during the training phase may provide additional information regarding immediate effects of training. Moreover, the latter study was conducted in healthy students, whereas adopting this technique in patient samples may reveal additional effects in daily life given the extent of cognitive vulnerability for depression. Additionally, assessing the dynamic relation between affect and emotion regulation in daily life prior to training may also provide novel information regarding potential moderators of training effects. For this purpose, we are currently conducting a cognitive control training study in which RMD patients are intensively monitored over a four-week period using experience sampling, with an experimental manipulation of cognitive control in week two and three. Moreover, participants will be followed-up on a weekly basis during a period of one year following training, taking into account the need for long-term follow-up of treatment effects. Ideally, future large-scale training

studies would follow patients over multiple years, allowing survival analysis as a direct test of effects of cognitive control training in terms of relapse prevention.

Finally, only a limited amount of studies have explored how cognitive control training interventions interact with existing psychotherapeutic and psychopharmacological interventions. For instance, Bowie, Mcgurck, Mausbach, Patterson, and Harvey (2012) found that generalization of effects of cognitive remediation therapy to indicators of functioning in schizophrenia is most likely when combined with skills training. In the context of mood disorders, it is possible that cognitive control training may complement effects of existing interventions for depression such as emotion regulation training or mindfulness (e.g., Course-Choi et al., 2017; but see Moshier, 2015). However, there is the possibility that effects of cognitive control training may also be hampered by other interventions, for instance in the case of side-effects of medication. Simultaneously, more research is necessary into how cognitive control training may interact with other neuromodulation techniques (e.g., Brunoni et al., 2014; Segrave et al., 2014; Vanderhasselt et al., 2015). These questions are related to the ideal method of delivery of cognitive control training for a given individual given specific diagnostics (e.g., in daily life, amount of sessions, specific processes targeted).

GENERAL CONCLUSION

This dissertation project set out to examine the causal involvement of cognitive control in depressive rumination, providing an empirical test of the preventative potential of cognitive control training for depression vulnerability. Several empirical studies included in this dissertation provide evidence for this hypothesis, demonstrating beneficial effects of adaptive PASAT training on stress reactivity and depressive rumination. These findings were observed in both lab context and daily life, using multiple indicators of depression vulnerability (e.g., reactivity to a lab stressor, reactivity to a naturalistic stressor, dynamics of affect and emotion regulation in daily life, residual symptomatology). Although adaptive PASAT training showed promise in terms of reducing vulnerability for depression in both healthy- and at-risk student

samples, effects were most apparent in remitted depressed patients where cognitive control training was combined with psycho-education. Here, increased cognitive functioning predicted immediate beneficial effects on repetitive negative thinking, which further predicted lower future depressive symptomatology.

These findings confirm central hypotheses of theoretical frameworks on the relation between cognitive control, emotion regulation, and depression, and are in line with the state-of-the-art cognitive control training literature. Furthermore, although we repeatedly found no effects of training for self-reported use of adaptive emotion regulation strategies, effects of cognitive control training were not limited to reducing vulnerability for depression. That is, increased cognitive control was related to resilience in trait ruminators, and cognitive control training fostered resilience and impacted self-reported disability in remitted depressed patients. Importantly, network models of protective and vulnerability factors in remitted depressed patients suggest that resilience plays a central role in successful remission from depression.

Our systematic review of the recent training literature confirms that several existing cognitive control training procedures show clinical potential as preventive interventions for depression. However, before implementation of cognitive control training as a clinical intervention is desirable, several questions need to be addressed, among which the impact of interindividual differences, the role of affective context, and delivery method. Increasing our knowledge on these topics may aid in providing an individually tailored cognitive control intervention, ultimately optimizing the effectiveness of cognitive control training for depression vulnerability.

As argued throughout this dissertation, we should endeavor to further improve our understanding of the involvement of cognitive control in emotion regulation, which we believe involves conducting fundamental research into the mechanisms underlying effects of experimental manipulations of cognitive control. This necessitates future research into the neurological underpinnings of effects of cognitive control training as well as research into the dynamics of cognitive functioning, emotion regulation, and affect in daily life.

REFERENCES

Alvarez, L. M., Sotres, C. J. F., León, S. O., Estrella, J., & Sosa, S. J. J. (2008). Computer program in the treatment for major depression and cognitive impairment in university students. *Computers in Human Behavior*, *24*, 816–826. doi: 10.1016/j.chb.2007.02.013

Anguera, J. A., Gunning, F. M., & Areán, P. A. (2017). Improving late life depression and cognitive control through the use of therapeutic video game technology: A proof-of-concept randomized trial. *Depress Anxiety.* doi: 10.1002/da.22588

Areán, P. A., Hallgren, K. A., Jordan, J. T., Gazzaley, A., Atkins, D. C., Heagerty, P. J., & Anguera, J. A. (2016). The use and effectiveness of mobile apps for depression: Results from a fully remote clinical trial. *J Med Internet Res, 18*, e330. doi: 10.2196/jmir.6482

Bowie, C. R., Gupta, M., Holshausen, K., Jokic, R., Best, M., & Milev, R. (2013). Cognitive remediation for treatment-resistant depression: effects on cognition and functioning and the role of online homework. *The Journal of Nervous and Mental Disease*, *201*, 680–5. doi: 10.1097/NMD.0b013e31829c5030

Bowie, C., Mcgurk, S. R., Mausbach, B., Patterson, T. L., & Harvey, P. D. (2012). Combined cognitive remediation and functional skills training for schizophrenia: Effects on cognition, functional competence, and real-world behavior. *American Journal of Psychiatry, 169*, 710-718. doi: 10.1176/appi.ajp.2012.11091337

Brunoni, A. R., Boggio, P. S., De Raedt, R., Bensenor, I. M., Lotufo, P. A., Namur, V., … Vanderhasselt, M. A. (2014). Cognitive control therapy and transcranial direct current stimulation for depression: A randomized, double-blinded, controlled trial. *Journal of Affective Disorders*, *162*, 43–49. doi: 10.1016/j.jad.2014.03.026

Calkins, A. W., Deveney, C. M., Weitzman, M. L., Hearon, B. A., & Siegle, G. J. (2011). The effects of prior cognitive control task exposure on responses to emotional tasks in healthy participants. *Behavioural and Cognitive Psychotherapy*, *39*, 205–220. doi: 10.1017/s1352465810000652

Calkins, A. W., McMorran, K. E., Siegle, G. J., & Otto, M. W. (2015). The effects of computerized cognitive control training on community adults with depressed mood. *Behavioural and Cognitive Psychotherapy*, *43*, 578–589. doi:

10.1017/S1352465814000046

Calkins, A. W., & Otto, M. W. (2013). Testing the Boundaries of Computerized Cognitive Control Training on Symptoms of Obsessive Compulsive Disorder. *Cognitive Therapy and Research*, *37*, 587–594. doi: 10.1007/s10608-012-9496-x

Cohen, N., Margulies, D. S., Ashkenazi, S., Schaefer, A., Taubert, M., Henik, A., … Okon-Singer, H. (2016). Using executive control training to suppress amygdala reactivity to aversive information. *NeuroImage*, *125*, 1022–31. doi: 10.1016/j.neuroimage.2015.10.069

Course-Choi, J., Saville, H., & Derakshan, N. (2017). The effects of adaptive working memory training and mindfulness meditation training on processing efficiency and worry in high worriers. *Behaviour Research and Therapy, 89,* 1-13. doi: 10.1016/j.brat.2016.11.002

Daches, S., & Mor, N. (2014). Training ruminators to inhibit negative information: A preliminary report. *Cognitive Therapy and Research*, *38*, 160–171. doi: 10.1007/s10608-013-9585-5

de Jong-Meyer, R., Beck, B., & Riede, K. (2009). Relationships between rumination, worry, intolerance of uncertainty and metacognitive beliefs. *Personality and Individual Differences, 46,* 547-551. doi: 10.1016/j.paid.2008.12.010

Demeyer, I., De Lissnyder, E., Koster, E. H. W., & De Raedt, R. (2012). Rumination mediates the relationship between impaired cognitive control for emotional information and depressive symptoms: A prospective study in remitted depressed adults. *Behaviour Research and Therapy*, *50*, 292–297. doi: 10.1016/j.brat.2012.02.012

Dillon, D. G., & Pizzagalli, D. A. (2013). Evidence of successful modulation of brain activation and subjective experience during reappraisal of negative emotion in unmedicated depression. *Psychiatry Research, 212*, 99-107. doi: 10.1016/j.pscychresns.2013.01.001

Elgamal, S., McKinnon, M. C., Ramakrishnan, K., Joffe, R. T., & MacQueen, G. (2007). Successful computer-assisted cognitive remediation therapy in patients with unipolar depression: a proof of principle study. *Psychological Medicine*, *37*, 1229–38. doi: 10.1017/S0033291707001110

Fang, L., Hoorelbeke, K., Bruyneel, L., Notebaert, L., MacLeod, C., De Raedt, R., & Koster, E.H.W. (in press). Can training change attentional breadth? Failure to find transfer effects. *Psychological Research*

Gavelin, H. M., Boraxbekk, C.-J., Stenlund, T., Järvholm, L. S., & Neely, A. S. (2015). Effects of a process-based cognitive training intervention for patients with stress-related exhaustion. *Stress*, 1–11.

Gooding, P. A., Taylor, P. J., & Tarrier, N. (2012). Perceived extent and effectiveness of reflection and brooding in relation to depressed mood. *Cogn Ther Res, 36*, 282-289. doi: 10.1007/s10608-011-9367-x

Grant, D. M., & Beck, J. G. (2010). What predicts the trajectory of rumination?: A prospective evaluation. *Journal of Anxiety Disorders, 24*, 480-486. doi: 10.1016/j.janxdis.2010.03.004

Gronwall, D. M. A. (1977). Paced Auditory Serial Addition Task - Measure of recovery from concussion. *Perceptual and Motor Skills*, *44*, 367–373.

Harrison, T. L., Shipstead, Z., Hicks, K. L., Hambrick, D. Z., Redick, T. S., & Engle, R. W. (2013). Working memory training may increase working memory capacity but not fluid intelligence. *Psychological Science, 24*, 2409-2419. doi: 10.1177/0956797613492984

Hawkins, G. E., Rae, B., Nesbitt, K. V., Brown, S. D. (2013). Gamelike features might not improve data. *Behav Res Methods, 45*, 301-318. doi: 10.3758/s13428-012-0264-3

Hoorelbeke, K., Faelens, L., Behiels, J., & Koster, E. H. W. (2015). Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Protocol for a randomized controlled trial. *Bmc Psychiatry*, *15*, 125.

Hoorelbeke, K., & Koster, E. H. W. (2017). Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Evidence from a double-blind randomized controlled trial study. *Journal of Consulting and Clinical Psychology, 85,* 135–146. doi: 10.1037/ccp0000128

Hoorelbeke, K., Koster, E. H. W., Demeyer, I., Loeys, T., & Vanderhasselt, M. A. (2016). Effects of cognitive control training on the dynamics of (mal)adaptive emotion regulation in daily life. *Emotion*, *16*, 945-956. doi: 10.1037/emo0000169

Hoorelbeke, K., Koster, E. H. W., Vanderhasselt, M. A., Callewaert, S., & Demeyer, I.

(2015). The influence of cognitive control training on stress reactivity and rumination in response to a lab stressor and naturalistic stress. *Behaviour Research and Therapy*, *69*, 1–10.

Hoorelbeke, K., Marchetti, I., De Schryver, M., & Koster, E.H.W. (2016). The interplay between cognitive risk and resilience factors in remitted depression: A network analysis. *Journal of Affective Disorders, 195,* 96-104. doi: 10.1016/j.jad.2016.02.001

Hsu, K. J., Beard, C., Rifkin, L., Dillon, D. G., Pizzagalli, D. A., & Björgvinsson, T. (2015). Transdiagnostic mechanisms in depression and anxiety: The role of rumination and attentional control. *Journal of Affective Disorders*, *188*, 22–27. doi: 10.1016/j.jad.2015.08.008

Iacoviello, B., Huryk, K., Alvarez, E., Collins, K., Murrough, J., Iosifescu, D., & Charney, D. (2014). Cognitive-Emotional Training as an Intervention for Major Depressive Disorder. *Biological Psychiatry*, *75*, 119S–119S.

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Perrig, W. J. (2008). Improving fluid intelligence with training on working memory. *Proceedings of the National Academy of Sciences of the United States of America*, *105*, 6829–6833. doi: 10.1073/pnas.0801268105

Jeffres, H. (1961). *Theory of probability*. Oxford: Oxford University Press.

Joormann, J., & D'Avanzato, C. (2010). Emotion regulation in depression: Examining the role of cognitive processes. *Cognition & Emotion*, *24*, 913–939. doi: 10.1080/02699931003784939

Joormann, J., & Stanton, C. H. (2016). Examining emotion regulation in depression: A review and future directions. *Behav Res Ther, 86*, 35-49. doi: 10.1016/j.brat.2016.07.007

Joormann, J., & Vanderlind, M. W. (2014). Emotion regulation in depression: The role of biased cognition and reduced cognitive control. *Clinical Psychological Science*, *2*, 402–421. doi: 10.1177/2167702614536163

Kalisch, R., Müller, M. B., & Tüscher, O. (2015). A conceptual framework for the neurobiological study of resilience. *Behavioral and Brain Sciences, 38*, 1-79. doi: 10.1017/S0140525X1400082X,e0

Katz, B., Jaeggi, S., Buschkuehl, M., Stegman, A., & Shah, P. (2014). Differential effect of motivational features on training improvements in school-based cognitive training. *Front Hum Neurosci, 8*, 242. doi: 10.3389/fnhum.2014.00242

Koster*, E.H.W., Hoorelbeke*, K., Onraedt, T., Owens, M., & Derakshan, N. (2017). Cognitive control interventions for depression: A systematic review of findings from training studies. *Clinical Psychology Review, 53,* 79-92. doi: 10.1016/j.cpr.2017.02.002

Kruschke, J. K. (2011). Introduction to special section on Bayesian data analysis. *Perspectives on Psychological Science, 6*, 272–273.

Kubiak, T., Zahn, D., Siewert, K., Jonas, C., & Weber, H. (2014). Positive beliefs about rumination are associated with ruminative thinking and affect in daily life: Evidence for a metacognitive view on depression. *Behavioural and Cognitive Psychotherapy, 42*, 568-576. doi: 10.1017/S1352465813000325

Leppin, A.L., Bora, P.R., Tilburt, J.C., Gionfriddo, M.R., Zeballos-Palacios, C., Dulohery, M.M., . . . Montori, V.M. (2014). The efficacy of resiliency training programs: A systematic review and meta-analysis of randomized trials. *PLoS ONE, 9*, e111420. doi: 10.1371/journal.pone.0111420

Love, J., Selker, R., Marsman, M., Jamil, T., Dropmann, D., Verhagen, A. J., & Wagenmakers, E.-J. (2015). JASP [Computer software].

Moreau, D., Kirk, I. J., & Waldie, K. E. (2016). Seven pervasive statistical flaws in cognitive training interventions. *Frontiers in Human Neuroscience, 10*. Doi: 10.3389/fnhum.2016.00153

Morimoto, S. S., Wexler, B. E., Liu, J., Hu, W., Seirup, J., & Alexopoulos, G. S. (2014). Neuroplasticity-based computerized cognitive remediation for treatment-resistant geriatric depression. *Nature Communications*, *5:4579*. doi: 10.1038/ncomms5579

Moshier, S. J. (2015). *Cognitive control training as an adjunct to behavioral activation therapy in the treatment of depression*. Boston University.

Moshier, S. J., Molokotos, E. K., Stein, A. T., & Otto, M. W. (2015). Assessing the effects of depressed mood and cognitive control training on memory confidence and accuracy following repeated checking. *International Journal of Cognitive Therapy*, *8*, 206–221. doi: 10.1521/ijct_2015_8_02

Motter, J. N., Pimontel, M. A., Rindskopf, D., Devanand, D. P., Doraiswamy, M. P., & Sneed, J. R. (2016). Computerized cognitive training and functional recovery in major depressive disorder: A meta-analysis. *Journal of Affective Disorders*, *189*, 184–191. doi: 10.1016/j.ad.2015.09.022

Mulder, J., & Wagenmakers, E.-J. (2016). Editors' introduction to the special issue "Bayes factors for testing hypotheses in psychological research: Practical relevance and new developments". *Journal of Mathematical Psychology, 72*, 1-5.

Nolen-Hoeksema, S. (1991). Responses to depression and their effects on the duration of depressive episodes. *J Abnormal Psychol., 100*, 569-582.

Nolen-Hoeksema, S., & Morrow, J. (1991). A prospective study of depression and posttraumatic stress symptoms after a natural disaster - The 1989 Loma-Prieta earthquake. *Journal of Personality and Social Psychology, 61*, 115-121. doi: 10.1037/0022-3514.61.1.115

Onraedt, T., & Koster, E. H. W. (2014). Training Working Memory to Reduce Rumination. *Plos One*, *9*, 12. doi: 10.1371/journal.pone.0090632

Owens, M., Koster, E. H. W., & Derakshan, N. (2013). Improving attention control in dysphoria through cognitive training: Transfer effects on working memory capacity and filtering efficiency. *Psychophysiology*, *50*, 297–307. doi: 10.1111/psyp.12010

Redick, T. S., Shipstead, Z., Harrison, T. L., Hicks, K. L., Fried, D. E., Hambrick, D. Z., . . . Engle, R. W. (2013). No evidence of intelligence improvement after working memory training: A randomized, placebo-controlled study. *Journal of Experimental Psychology-General, 142*, 359-379. doi: 10.1037/a0029082

Schweizer, S., Grahn, J., Hampshire, A., Mobbs, D., & Dalgleish, T. (2013). Training the Emotional Brain: Improving Affective Control through Emotional Working Memory Training. *Journal of Neuroscience*, *33*, 5301–5311. doi: 10.1523/jneurosci.2593-12.2013

Schweizer, S., Hampshire, A., & Dalgleish, T. (2011). Extending Brain-Training to the Affective Domain: Increasing Cognitive and Affective Executive Control through Emotional Working Memory Training. *Plos One*, *6*, 7. doi: 10.1371/journal.pone.0024372

Segrave, R. A., Arnold, S., Hoy, K., & Fitzgerald, P. B. (2014). Concurrent cognitive

control training augments the antidepressant efficacy of tDCS: A pilot study. *Brain Stimulation*, *7*, 325–331. doi: 10.1016/j.brs.2013.12.008

Siegle, G. J., Ghinassi, F., & Thase, M. E. (2007). Neurobehavioral therapies in the 21st century: Summary of an emerging field and an extended example of cognitive control training for depression. *Cognitive Therapy and Research*, *31*, 235–262. doi: 10.1007/s10608-006-9118-6

Siegle, G. J., Price, R. B., Jones, N. P., Ghinassi, F., Painter, T., & Thase, M. E. (2014). You gotta work at it: Pupillary indices of task focus are prognostic for response to a neurocognitive intervention for rumination in depression. *Clinical Psychological Science*, *2*, 455–471. doi: 10.1177/2167702614536160

Songprakun, W., & McCann, T. (2012). Effectiveness of a self-help manual on the promotion of resilience in individuals with depression in Thailand: A randomised controlled trial. *BMC Psych., 12*:12.

Spek, V., Cuijpers, P., Nyklícek, I., Riper, H., Keyzer, J., & Pop, V. (2007). Internet-based cognitive behaviour therapy for symptoms of depression and anxiety: A meta-analysis. *Psychological Medicine, 37*, 319-328. doi: 10.1017/S0033291706008944

Steinhardt, M., & Dolbier, C. (2008). Evaluation of a resilience intervention to enhance coping strategies and protective factors and decrease symptomatology. *J. Am. Coll. Health, 56*, 445-453.

Takeuchi, H., Taki, Y., Nouchi, R., Hashizume, H., Sekiguchi, A., Kotozaki, Y., … Kawashima, R. (2013). Effects of working memory training on functional connectivity and cerebral blood flow during rest. *Cortex*, *49*, 2106–2125. doi: 10.1016/j.cortex.2012.09.007

Takeuchi, H., Taki, Y., Nouchi, R., Hashizume, H., Sekiguchi, A., Kotozaki, Y., … Kawashima, R. (2014). Working memory training improves emotional states of healthy individuals. *Frontiers in Systems Neuroscience*, *8*, 1–14. doi: 10.3389/fnsys.2014.00200

Trapp, W., Engel, S., Hajak, G., Lautenbacher, S., & Gallhofer, B. (2016). Cognitive remediation for depressed inpatients: Results of a pilot randomized controlled trial. *The Australian and New Zealand Journal of Psychiatry*, *50*, 46–55. doi: 10.1177/0004867415622271

Vanderhasselt, M.-A., De Raedt, R., Namur, V., Lotufo, P. A., Bensenor, I. M., Boggio, P.

S., & Brunoni, A. R. (2015). Transcranial electric stimulation and neurocognitive training in clinically depressed patients: A pilot study of the effects on rumination. *Prog Neuropsychopharmacol Biol Psychiatry*, *57*, 93–99. doi: 10.1016/j.pnpbp.2014.09.015

Vervaeke, J., Van Looy, J., Hoorelbeke, K., Baeken, C., & Koster, E. H. W. (in preparation). User Requirements for a Gamified Cognitive Control Training for Remitted Depressed Individuals

Wagenmakers, E.-J. (2007). A practical solution to the pervasive problems of p values. *Psychonomic Bulletin & Review, 14*, 779–804.

Wagenmakers, E.-J., Wetzels, R., Borsboom, D., & van der Maas, H. L. J. (2011). Why psychologists must change the way they analyze their data: The case of Psi: Comment on Bem (2011). *Journal of Personality and Social Psychology, 100*, 426–432.

Wanmaker, S., Geraerts, E., & Franken, I. H. A. (2015). A working memory training to decrease rumination in depressed and anxious individuals: A double-blind randomized controlled trial. *Journal of Affective Disorders*, *175*, 310–319. doi: 10.1016/j.jad.2014.12.027

Waugh, C.E., & Koster, E.H.W. (2015). A resilience framework for promoting stable remission from depression. *Clin. Psychol. Rev., 41*, 49–60. doi:10.1016/j.cpr.2014.05.004

Wetzels, R., Matzke, D., Lee, M. D., Rouder, J. N., Iverson, G. J., & Wagenmakers, E.-J. (2011). Statistical evidence in experimental psychology: An empirical comparison using 855 t tests. *Perspectives on Psychological Science, 6*, 291–298.

Xiu, L., Zhou, R., & Jiang, Y. (2016). Working memory training improves emotion regulation ability: Evidence from HRV. *Physiology and Behavior*, *155*, 25–29. doi: 10.1016/j.physbeh.2015.12.004

Zetsche, U., & Joormann, J. (2011). Components of interference control predict depressive symptoms and rumination cross-sectionally and at six months follow-up. *Journal of Behavior Therapy and Experimental Psychiatry, 42*, 65-73. doi: 10.1016/j.jbtep.2010.06.001

% Data Storage Fact Sheet "Cognitive control interventions for depression: A systematic review of findings from training studies" [Chapter 2]

% Author: Kristof Hoorelbeke

% Date: 25/04/2017

1. Contact

==========

1a. Main researcher

- name: Kristof Hoorelbeke
- address: Henri Dunantlaan 2, 9000 Ghent, Belgium
- e-mail: Kristof.Hoorelbeke@UGent.be

1b. Responsible ZAP

- name: Prof. dr. Ernst H. W. Koster
- address: Henri Dunantlaan 2, 9000 Ghent, Belgium
- e-mail: Ernst.Koster@UGent.be

If a response is not received when using the above contact details, please send an e-mail to data-ppw@UGent.be or contact Data Management, Faculty of Psychology and Educational Sciences, Henri Dunantlaan 2, 9000 Ghent, Belgium

2. Information about the datasets to which this sheet applies

==========

* Reference of the publication in which the datasets are reported:

Koster*, E. H. W., Hoorelbeke*, K., Onraedt, T., Owens, M., & Derakshan, N. (2017) Cognitive control interventions for depression: A systematic review of findings from training studies. Clinical Psychology Review, 53, 79-92. doi: 10.1016/j.cpr.2017.02.002

* Which datasets in that publication does this sheet apply to:
All datasets reported in the article (given that this is a systematic review, this refers to a list of records, the steps of the selection procedure, and reliability analysis).

3. Information about the provided files

==========

3a. Raw data

---

* Have the raw data been stored by the main researcher?
[X] YES / [ ] NO
If NO, please justify: /

*On which platform are the raw data stored?
1. Raw data / List of records from the systematic search in Web of Science and PubMed (Steps 1 - 3):
- [X] researcher PC: Excel file for Steps 1 - 3 [Worksheet_WOS_step 1 and 2.xlsx] [Worksheet_PuB_Step 1 and 2.xlsx] [Step3_Combined_2reviewers.xlsx]
- [ ] research group file server
- [X] other (specify): back-ups on external harddisks

2. Raw data / List of hits from snowballing and GoogleScholar search following Systematic search Step 3:
- [X] researcher PC: Excel file [Snowballing_GoogleScholar_FirstAuthors_2reviewers.xlsx]
- [ ] research group file server
- [X] other (specify): back-ups on external harddisks

3. Raw data / Overview procedure systematic review (including count of records per step and search engine, overview search procedure and criteria, overview selected articles per condition (AR, MDD, RMD)):
- [X] researcher PC: Excel file [Overview flowchart numbers.xlsx]
- [ ] research group file server
- [X] other (specify): back-ups on external harddisks

4. Raw data calculation kappa's:
- [X] researcher PC: Excel file for kappa regarding inclusion/exclusion and categorization [Berekening kappa's in en exclusie.xlsx] [Berekening kappa's inclusie categorieën.xlsx]
- [ ] research group file server
- [X] other (specify): back-ups on external harddisks

*Who has direct access to the raw data (i.e., without intervention of another person)?
For 1 to 4:
- [X] main researcher
- [ ] responsible ZAP
- [ ] all members of the research group
- [ ] all members of UGent
- [ ] other (specify): ...

4. Reproduction
==========
*Have the results been reproduced?:
[ ] YES / [X] NO
If YES, by whom (add if multiple): /

% Data Storage Fact Sheet "The influence of cognitive control training on stress reactivity and rumination in response to a lab stressor and naturalistic stress" [Chapter 3]

% Author: Kristof Hoorelbeke

% Date: 27/03/2015

1. Contact

==========

1a. Main researcher

- name: Kristof Hoorelbeke
- address: Henri Dunantlaan 2, 9000 Ghent, Belgium
- e-mail: Kristof.Hoorelbeke@UGent.be

1b. Responsible ZAP

- name: Ernst H. W. Koster
- address: Henri Dunantlaan 2, 9000 Ghent, Belgium
- e-mail: Ernst.Koster@UGent.be

If a response is not received when using the above contact details, please send an e-mail to data-ppw@UGent.be or contact Data Management, Faculty of Psychology and Educational Sciences, Henri Dunantlaan 2, 9000 Ghent, Belgium

2. Information about the datasets to which this sheet applies

==========

* Reference of the publication in which the datasets are reported:

Hoorelbeke, K., Koster, E.H.W., Vanderhasselt, M-A., Callewaert, S., & Demeyer, I. (2015). The influence of cognitive control training on stress reactivity and rumination in response to a lab stressor and naturalistic stress. *Behaviour Research and Therapy, 69*, 1-10. doi: 10.1016/j.brat.2015.03.010

* Which datasets in that publication does this sheet apply to:

All datasets reported in the article.

3. Information about the provided files

==========

3a. Raw data

---

* Have the raw data been stored by the main researcher?

[X] YES / [ ] NO

If NO, please justify: /

*On which platform are the raw data stored?

1. Raw data of questionnaires:

- [X] researcher PC: assessed on paper, scanned questionnaires and typed into an Excel-sheet for Time1 and Time2 (including the Visual Analogue Scales for the induction procedure; Time3 was assessed online)
- [ ] research group file server
- [X] other (specify): paper files for Time1 and Time2 as well as the induction procedure

2. Raw data of computer tasks:

- [X] researcher PC: Automated O-Span (pre/post), Breathing Focus Task (pre/post), Training data (Visual Search Task/Adaptive PASAT)
- [ ] research group file server
- [X] other (specify): back-ups on external harddisks

*Who has direct access to the raw data (i.e., without intervention of another person)?

For 1 and 2:

- [X] main researcher
- [ ] responsible ZAP
- [ ] all members of the research group
- [ ] all members of UGent
- [ ] other (specify): ...

3b. Other files

---

* Which other files have been stored?

- [X] file(s) describing the step-by-step transition from raw data to reported results (Dutch).

Specify: A syntax [VragenlijstenSyntax.sps] scoring the different scales accompanied with the necessary blanc dataset [Template.sav] has been provided to autoscore the questionnaires

- [X] file(s) containing cleaned data?

Specify: A file containing the cleaned data has been provided [CleanedUpData.sav]

- [X] file(s) containing results?

Specify: Outputfiles containing the main results of the manuscript have been provided [OutputArticle_part1.spv; OutputArticle_part2.spv; OutputArticle_part3.spv] from which the latter two files contain extra analyses requested by the reviewers and taken into account in the final version of the manuscript

- [X] file(s) providing proof of ethical committee

Specify: Proof of local ethical committee of Ghent University

* On which platform are these other files stored?

- [X] researcher PC
- [ ] research group file server
- [X] other (specify): back-up external harddisks

*Who has direct access to the raw data (i.e., without intervention of another person)?

- [X] main researcher
- [ ] responsible ZAP
- [ ] all members of the research group
- [ ] all members of UGent
- [ ] other (specify): ...

4. Reproduction

==========

*Have the results been reproduced?:

[ ] YES / [X] NO

If YES, by whom (add if multiple): /

% Data Storage Fact Sheet "Effects of cognitive control training on the dynamics of (mal)adaptive emotion regulation in daily life" [Chapter 4]

% Author: Kristof Hoorelbeke

% Date: 16/01/2016

1. Contact

==========

1a. Main researcher

- name: Kristof Hoorelbeke
- address: Henri Dunantlaan 2, 9000 Ghent, Belgium
- e-mail: Kristof.Hoorelbeke@UGent.be

1b. Responsible ZAP

- name: Ernst H. W. Koster
- address: Henri Dunantlaan 2, 9000 Ghent, Belgium
- e-mail: Ernst.Koster@UGent.be

If a response is not received when using the above contact details, please send an e-mail to data-ppw@UGent.be or contact Data Management, Faculty of Psychology and Educational Sciences, Henri Dunantlaan 2, 9000 Ghent, Belgium

2. Information about the datasets to which this sheet applies

==========

* Reference of the publication in which the datasets are reported:
Hoorelbeke, K., Koster, E.H.W., Demeyer, I., Loeys, T., & Vanderhasselt, M-A. (2016). Effects of cognitive control training on the dynamics of (mal)adaptive emotion regulation in daily life. *Emotion, 16*, 945-956. doi: 10.1037/emo0000169

* Which datasets in that publication does this sheet apply to:
All datasets reported in the article.

3. Information about the provided files
==========

3a. Raw data
---

* Have the raw data been stored by the main researcher?
[X] YES / [ ] NO
If NO, please justify: /

*On which platform are the raw data stored?
1. Raw data of questionnaires:
- [X] researcher PC: questionnaires were assessed on paper, typed into an Excel-sheet for Time1 and Time2 (including the Visual Analogue Scales for the induction procedure); these questionnaires have been scanned
- [ ] research group file server
- [X] other (specify): paper files for Time1 and Time2 as well as the induction procedure

2. Raw data of computer tasks:
- [X] researcher PC: Dual n-back task (pre/post), Training data (low cognitive load task/Adaptive PASAT), ESM-data (ESM self-report responses)
- [ ] research group file server
- [X] other (specify): back-ups on external harddisks

*Who has direct access to the raw data (i.e., without intervention of another person)?
For 1 and 2:

- [X] main researcher
- [ ] responsible ZAP
- [ ] all members of the research group
- [ ] all members of UGent
- [ ] other (specify): ...

3b. Other files

---

* Which other files have been stored?

- [X] files describing the step-by-step transition from raw data to reported results (Dutch).

Specify: A syntax [VragenlijstenSyntax.sps] scoring the different scales, a syntax [VAS_CCT_ESM_STUDY_REAPPRAISAL.sps] computing the VAS compound- and deltascores for the lab assessment of positive reappraisal, and a file logging decisions made while cleaning up the data (trainingdata, cognitive transfer task, ESM and questionnaires)

- [X] file(s) containing cleaned data?

Specify: A file containing the cleaned data has been provided [Data CCT Healthy.sav] (excl. ESM-component)

- [X] file(s) containing results?

Specify: Outputfiles containing the main results of the manuscript have been provided excluding the ESM-analysis [Results output.spv]

- [X] file(s) providing proof of ethical committee

Specify: Proof approval of local ethical committee of Ghent University [Approval Ethical Committee.pdf]

* On which platform are these other files stored?

- [X] researcher PC
- [ ] research group file server
- [X] other (specify): backup external harddisks

*Who has direct access to the raw data (i.e., without intervention of another person)?

- [X] main researcher
- [ ] responsible ZAP
- [ ] all members of the research group
- [ ] all members of UGent
- [ ] other (specify): ...

4. Reproduction

==========

*Have the results been reproduced?:

[ ] YES / [X] NO

If YES, by whom (add if multiple): /

% Data Storage Fact Sheet "Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Evidence from a double-blind randomized controlled trial study" [Chapter 6]

% Author: Kristof Hoorelbeke

% Date: 02/06/2016

1. Contact

==========

1a. Main researcher

- name: Kristof Hoorelbeke
- address: Henri Dunantlaan 2, 9000 Ghent, Belgium
- e-mail: Kristof.Hoorelbeke@UGent.be

1b. Responsible ZAP

- name: Prof. dr. Ernst H. W. Koster
- address: Henri Dunantlaan 2, 9000 Ghent, Belgium
- e-mail: Ernst.Koster@UGent.be

If a response is not received when using the above contact details, please send an e-mail to data-ppw@UGent.be or contact Data Management, Faculty of Psychology and Educational Sciences, Henri Dunantlaan 2, 9000 Ghent, Belgium

2. Information about the datasets to which this sheet applies

==========

* Reference of the publication in which the datasets are reported:

Hoorelbeke, K., & Koster, E.H.W. (2017). Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Effects of a randomized controlled trial. *Journal of Consulting and Clinical Psychology, 85*, 135-146. doi: 10.1037/ccp0000128

* Which datasets in that publication does this sheet apply to:

All datasets reported in the article.

3. Information about the provided files

==========

3a. Raw data

---

* Have the raw data been stored by the main researcher?

[X] YES / [ ] NO

If NO, please justify: /

*On which platform are the raw data stored?

1. Raw data of questionnaires:

- [X] researcher PC: questionnaires were assessed on paper, typed into Excel-sheets [T1.xlsx] [T2.xlsx] [T3.xlsx] and have been scanned
- [ ] research group file server
- [X] other (specify): informed consent files on paper and have been scanned

2. Raw data of cognitive transfer tasks:

- [X] researcher PC: non-adaptive PASAT task performance
[BaselinePASAT_TOTALSCORES] [PosttrainingPASAT_TOTALSCORES.xlsx]
[FollowupPASAT_TOTALSCORES.xlsx]
- [ ] research group file server
- [X] other (specify): back-ups on external harddisks

3. Raw data of cognitive training tasks:
- [X] researcher PC: non-adaptive PASAT task performance
[TrainingsdataOpgekuist.xlsx]
- [ ] research group file server
- [X] other (specify): back-ups on external harddisks

*Who has direct access to the raw data (i.e., without intervention of another person)?
For 1 to 3:
- [X] main researcher
- [ ] responsible ZAP
- [ ] all members of the research group
- [ ] all members of UGent
- [ ] other (specify): ...

3b. Other files
---
* Which other files have been stored?
- [X] files describing the step-by-step transition from raw data to reported results (Dutch).
Specify: A syntax [VragenlijstenSyntax.sps] scoring the different scales
- [X] file(s) containing cleaned data?
Specify: A file containing the cleaned data has been provided for the intention-to-treat [RCT_T1_T2_T3_ITT.sav] and completers-only analysis [RCT_T1_T2_T3_NO_ITT.sav] seperately. Similarly, a file for the cleaned training data has been provided [RCT_Trainingsdata.sav].
- [X] file(s) containing the scripts of the analyses?

Specify: Script which allows reproduction of the main findings (excluding mediation analysis, cfr. Hayes & Preacher 2004, 2008) and contains additional analyses (e.g., using transformations) [Syntax1.sps] [Syntax2.sps]

- [X] file(s) providing proof of ethical committee

Specify: Proof approval of local ethical committee of Ghent University [Approval Ethical Committee.pdf]

- [X] file(s) providing additional information regarding cleaning of raw data of training tasks [Afwijkingen in trainingsdata.xlsx] and missing data (ITT) [Missing data T3.docx]

Specify: Additional information regarding how raw training data was cleaned / filtered and how missing data at three months follow-up was handled

- [X] file(s) providing additional information regarding calculation of time spent training per training condition [TimeSpentTrainingPerCondition.xlsx]

Specify: Calculation of duration of intervention per group based on training data (based on mean median ISI per session, length of stimuli, and amount of trials)

- [X] file(s) providing a preprint version of the manuscript [Hoorelbeke & Koster 2016 JCCP.pdf] and the Supplemental material [Supplemental material.docx]

-Specify: Manuscript & Supplemental material (e.g., completers-only descriptives, training session ISI)

* On which platform are these other files stored?

- [X] researcher PC
- [ ] research group file server
- [X] other (specify): backup external harddisks

*Who has direct access to the raw data (i.e., without intervention of another person)?

- [X] main researcher
- [ ] responsible ZAP
- [ ] all members of the research group
- [ ] all members of UGent
- [ ] other (specify): ...

4. Reproduction

==========

*Have the results been reproduced?:

[ ] YES / [X] NO

If YES, by whom (add if multiple): /

% Data Storage Fact Sheet "The interplay between cognitive risk and resilience factors in remitted depression: A network analysis" [Chapter 7]

% Author: Kristof Hoorelbeke

% Date: 16/01/2016

1. Contact

==========

1a. Main researcher

- name: Kristof Hoorelbeke
- address: Henri Dunantlaan 2, 9000 Ghent, Belgium
- e-mail: Kristof.Hoorelbeke@UGent.be

1b. Responsible ZAP

- name: Ernst H. W. Koster
- address: Henri Dunantlaan 2, 9000 Ghent, Belgium
- e-mail: Ernst.Koster@UGent.be

If a response is not received when using the above contact details, please send an e-mail to data-ppw@UGent.be or contact Data Management, Faculty of Psychology and Educational Sciences, Henri Dunantlaan 2, 9000 Ghent, Belgium

2. Information about the datasets to which this sheet applies

==========

* Reference of the publication in which the datasets are reported:

Hoorelbeke, K., Marchetti, I., De Schryver, M., & Koster, E.H.W. (2016). The interplay between cognitive risk and resilience factors in remitted depression: A network analysis. *Journal of Affective Disorders, 195*, 96-104. doi: 10.1016/j.jad.2016.02.001

* Which datasets in that publication does this sheet apply to:
All datasets reported in the article.

3. Information about the provided files

==========

3a. Raw data

---

* Have the raw data been stored by the main researcher?
[X] YES / [ ] NO
If NO, please justify: /

*On which platform are the raw data stored?
1. Raw data of questionnaires:
- [X] researcher PC: questionnaires were assessed on paper, typed into an Excel-sheet [T1.xlsx]; these questionnaires have been scanned
- [ ] research group file server
- [X] other (specify): informed consent files (on paper + scanned)

2. Raw data of computer tasks:
- [X] researcher PC: non-adaptive PASAT task performance [BaselinePASAT_TOTALSCORES.xlsx]
- [ ] research group file server
- [X] other (specify): back-ups on external harddisks

*Who has direct access to the raw data (i.e., without intervention of another person)?
For 1 and 2:
- [X] main researcher
- [ ] responsible ZAP

- [ ] all members of the research group
- [ ] all members of UGent
- [ ] other (specify): ...

3b. Other files

---

* Which other files have been stored?

- [X] files describing the step-by-step transition from raw data to reported results (Dutch).

Specify: A syntax [VragenlijstenSyntaxJAD.sps] scoring the different scales

- [X] file(s) containing cleaned data?

Specify: A file containing the cleaned data has been provided [BaselineDataRCT_JAD_MS.sav]

- [X] file(s) containing the scripts of the analyses?

Specify: Script which allows reproduction of the findings [Hoorelbeke, Marchetti, De Schryver, and Koster 2016 JAD.R]

- [X] file(s) providing proof of ethical committee

Specify: Proof approval of local ethical committee of Ghent University [Approval Ethical Committee.pdf]

* On which platform are these other files stored?

- [X] researcher PC
- [ ] research group file server
- [X] other (specify): backup external harddisks

*Who has direct access to the raw data (i.e., without intervention of another person)?

- [X] main researcher
- [ ] responsible ZAP
- [ ] all members of the research group
- [ ] all members of UGent
- [ ] other (specify): ...

4. Reproduction

==========

*Have the results been reproduced?:

[X] YES / [] NO

If YES, by whom (add if multiple): dr. Igor Marchetti, dr. Maarten De Schryver

NEDERLANDSTALIGE SAMENVATTING

Depressie is een veel voorkomende stemmingsstoornis (Alonso et al., 2004; Kessler & Bromet, 2013) die gekenmerkt wordt door een toestand van aangehouden negatief affect en/of anhedonie, in combinatie met minstens drie bijkomende cognitieve, affectieve of somatische klachten die samen aanleiding geven tot significant lijden of disfunctioneren in het dagelijkse leven (American Psychiatric Association, 2013). Recente rapporten van de Wereldgezondheidszorg Organisatie suggereren dat depressie wereldwijd één van de belangrijkste bronnen van lijden vormt (World Health Organization, 2016). De maatschappelijke impact van depressie wordt onder andere gereflecteerd door de hoge kosten die gepaard gaan met deze stoornis. Zo werd in 2004 de jaarlijkse financiële impact van depressie voor Europa geschat op €118 miljard voor 21 miljoen depressieve patiënten. Dit vormde 1% van de totale Europese economie, waarvan €76 miljard te wijten was aan indirecte kosten van depressie waaronder verhoogde morbiditeit en vroegtijdige overlijdens (Sobocki, Jönsson, Angst, & Rehnberg, 2006). Uit recentere schattingen blijkt dat wereldwijd momenteel 350 miljoen mensen lijden aan een depressieve stoornis (World Health Organization, 2016).

Ondanks het feit dat bestaande psychotherapeutische en farmacologische behandelingen voor depressie effectief zijn inzake symptoomreductie op korte termijn (bijv. Cuijpers, Cristea, Karyotaki, Reijnders, & Huibers, 2016), vormt het heroptreden van depressieve episodes een ernstig probleem (bijv. Beshai, Dobson, Bockting, & Quigley, 2011; Bockting, Spinhoven, Wouters, Koeter, & Schene, 2009; Cox et al., 2012). Zo wordt de kans op herval groter naarmate iemand meer depressieve episodes meegemaakt heeft, waarbij in longitudinale studies hervalcijfers tot 80% gerapporteerd worden. Daarbij vertonen interventies die gericht zijn op hervalpreventie ruimte voor verbetering (Bockting et al., 2009; Burcusa & Iacono, 2007; Kessing, Hansen, & Andersen, 2004). Iemand met een depressieve voorgeschiedenis zal dan ook gemiddeld vijf tot negen afzonderlijke depressieve episodes doormaken doorheen zijn of haar leven (Carr & McNulty, 2016). Daarnaast zijn bestaande behandelingen weinig effectief wat betreft de aanpak van cognitieve symptomen van depressie (Gonda et al., 2015;

Gualtieri, Johnson, & Benedict, 2006; Shilyansky et al., 2016), waardoor patiënten vaak slechts partieel herstellen van een depressieve episode (en dus residuele klachten blijven vertonen, bijv. Nierenberg et al., 2010). Dergelijke restklachten hebben een predictieve waarde voor het heroptreden van depressieve episodes (Bockting, Spinhoven, Koeter, Wouters, & Schene, 2006; ten Doesschate, Bockting, Koeter, Schene, 2010). Deze bevindingen wijzen er op dat huidige behandelingen onvoldoende inspelen op onderliggende kwetsbaarheidsmechanismen voor depressie, wat gericht onderzoek naar dergelijke processen rechtvaardigt.

COGNITIEVE KWETSBAARHEID VOOR DEPRESSIE

Cognitieve theorievorming rond kwetsbaarheid voor depressie schrijft een centrale rol toe aan informatieverwerkingsprocessen (bijv. Beck, Rush, Shaw, & Emery, 1979; Bower, 1981, 1987). Zo wijst onderzoek op het belang van cognitieve emotieregulatie processen zoals ruminatie en positieve herkadering.

In de context van depressie vormt ruminatie de meest onderzochte maladaptieve emotieregulatie strategie. Deze wordt gekenmerkt door het reageren op een interne of externe stressor met gedachten waarbij de aandacht gericht wordt op de eigen depressieve klachten en de implicaties hiervan (Nolen-Hoeksema, 1991; Nolen-Hoeksema & Morrow, 1991). Daarbij wordt de nadruk met name gelegd op de perseveratieve aard van deze denkstijl, het vastlopen in repetitief negatief denken (Nolen-Hoeksema, Wisco, & Lyubomirsky, 2008). Treynor, Gonzalez, en Nolen-Hoeksema (2003) identificeerden twee subtypes van ruminatie: “brooding” (verder doorheen deze tekst naar verwezen als “depressieve ruminatie”) en “reflectie”. Met name depressieve ruminatie vormt een risicofactor voor de ontwikkeling en instandhouding van depressieve klachten (Schoofs et al., 2010; Treynor et al. 2003). Depressieve ruminatie is tevens in verhoogde mate aanwezig in risicogroepen voor het ontwikkelen van een eerste depressieve episode en blijft vaak aanwezig na het opklaren van depressieve klachten (Gibb, Grassia, Stone, Uhrlass, & McGeary, 2012; Woody et al., 2016; Woody, McGeary, & Gibb, 2014). Depressieve ruminatie vormt dan ook een

stabiele risicofactor voor depressie (voor een review, zie Nolen-Hoeksema et al., 2008; Olatunji, Naragon-Gainey, & Wolitzky-Taylor, 2013).

In tegenstelling tot depressieve ruminatie wordt positieve (her)kadering als protectieve factor tegen de ontwikkeling van psychopathologie gezien (Garnesfki & Kraaij, 2006, 2016; Garnefski, Legerstee, Kraaij, Van Den Kommer, & Teerds, 2002; Martin & Dahlen, 2005). Zo correleert positieve (her)kadering bijvoorbeeld negatief met depressieve symptomen (Kraaij, Pruymboom, & Garnefski, 2002) en wordt positieve (her)kadering typisch geassocieerd met welzijn / positief affect (Haga, Kraft, & Corby, 2009; Kraaij, Garnefski, & Schroevers, 2009; McRae, Jacobs, Ray, John, & Gross, 2012; Nowlan, Wuthrich, & Rapee, 2016), levenskwaliteit (Extremera & Rey, 2014; Li et al., 2015) en levenstevredenheid (Haga et al., 2009; McRae et al., 2012). In theoretische modellen wordt deze adaptieve emotieregulatie strategie dan ook vaak als belangrijke veerkrachtsfactor beschouwd (bijv. Kalisch, Müller, & Tüscher, 2015; McRae & Mauss, 2016).

Cognitieve controle, Emotieregulatie, en Depressie

Cognitieve controle speelt een centrale rol binnen cognitieve emotieregulatie processen (Joormann & Gotlib, 2010). Cognitieve controle verwijst naar executieve functies – zoals shiften, inhibitie van irrelevantie informatie, en updaten van informatie in het werkgeheugen (Miyake et al., 2000) – die toelaten om doelgericht gedrag te stellen. Dergelijke functies zijn cruciaal voor flexibel en efficiënt gebruik van het werkgeheugen, een cognitieve structuur met beperkte opslagcapaciteit (Baddeley & Hitch, 1974). Medisch beeldvormingsonderzoek toont aan dat positieve herkadering beroep doet op cognitieve controle (bijv. Moser, Hartwig, Moran, Jendrusina, & Kross, 2014; Ochsner, Bunge, Gross, & Gabrieli, 2002). Terwijl cognitieve controle positief correleert met adaptieve emotieregulatie strategieën zoals positieve herkadering (bijv. McRae et al., 2012), vormen cognitieve controle deficieten een risicofactor voor depressie. Moeilijkheden met het loskoppelen van (taak-irrelevante) negatieve informatie in het werkgeheugen gaat namelijk vaak gepaard met depressieve ruminatie. In verschillende cross-sectionele studies wordt bijvoorbeeld een negatieve associatie gerapporteerd tussen cognitieve controle enerzijds en ruminatie en

depressieve klachten anderzijds (bijv. Beckwé, Deroost, Koster, De Lissnyder, & De Raedt, 2014; Joormann & Gotlib, 2010; Whitmer & Banich, 2007). Daarbovenop worden cognitieve controle deficieten geobserveerd doorheen de verschillende stadia van kwetsbaarheid voor depressie, zoals bij populaties met verhoogde trekruminatie of subklinisch depressieve klachten (Beckwé et al., 2014; Joormann, 2004; Owens, Koster, & Derakshan, 2012), tijdens depressieve episoden (Joormann & Gotlib, 2010; Harvey et al., 2004; Levens & Gotlib, 2010), en na het opklaren van depressieve klachten (Levens & Gotlib, 2015; Paelecke-Habermann, Pohl, & Leplow, 2005).

Prospectieve studies bevestigen dat verminderde cognitieve controle een verhoogde kwetsbaarheid voor depressie vormt (bijv. Pe, Brose, Gotlib, & Kuppens, 2016; Pe, Raes, & Kuppens, 2013). Zo rapporteerden verschillende onderzoekers dat individuele verschillen in cognitieve controle het ontstaan en het behoud van (toekomstige) depressieve klachten en ruminatie voorspellen (Kertz, Belden, Tillman, & Luby, 2015; Zetsche & Joormann, 2011). Daarbovenop lijkt depressieve ruminatie de relatie tussen cognitieve controle en depressieve klachten te mediëren (Demeyer, De Lissnyder, Koster, & De Raedt, 2012; Hsu et al., 2015). Tevens wijst evidentie er op dat de relatie(s) tussen cognitieve controle en overige depressieve kwetsbaarheidsfactoren zoals ruminatie bidirectioneel van aard zijn (Connolly et al., 2014; Philippot & Brutoux, 2008; Vijayakumar et al., 2016; Whitmer & Gotlib, 2012). Daarbij lijkt de omvang van cognitieve controle deficieten toe te nemen naarmate patiënten meer depressieve episoden hebben meegemaakt (Vanderhasselt & De Raedt, 2009).

Deze bevindingen wijzen er op dat cognitieve controle deficieten en ruminatie elkaar mutueel versterken, wat resulteert in een toenemende depressieve kwetsbaarheid op cognitief én neurobiologisch niveau (voor reviews, zie De Raedt & Koster, 2010; Joormann & D'Avanzato, 2010; Joormann & Vanderlind, 2014). Dergelijke cross-sectionele en prospectieve bevindingen laten echter niet toe om uitspraken te doen rond de causale aard van deze relatie. Hiertoe is experimentele manipulatie van cognitieve controle noodzakelijk, bijvoorbeeld aan de hand van cognitieve controle trainingsprocedures waarbij een toename in cognitief functioneren beoogd wordt door herhaalde blootstelling aan cognitieve controle oefeningen.

Verschillende studies hebben zich reeds gebogen over de vraag rond de effectiviteit van dergelijke trainingsprocedures inzake bevordering van cognitief functioneren (bijv. Jaeggi, Buschkuehl, Jonides, & Perrig, 2008; Jaeggi, Buschkuehl, Jonides, & Shah, 2011; Klingberg et al., 2005; Klingberg, Forssberg, & Westerberg, 2002; Olesen, Westerberg, & Klingberg, 2004; Westerberg et al., 2007). Ondanks het feit dat een aantal studies inconsistente bevindingen rapporteerden met betrekking tot de mate waarin distale cognitieve processen (zoals prestatie op intelligentiematen, bijv. Harrison et al., 2013) beïnvloed kunnen worden door cognitieve controle training (voor recente reviews, zie Melby-Lervag, Redick, & Hulme, 2016; Shipstead, Redick, & Engle, 2010, 2012), wijst de huidige evidentie op de plasticiteit van cognitieve functies. Dit houdt in dat cognitieve controle training benut kan worden om functioneren op zowel het cognitieve als neurobiologische niveau te beïnvloeden (Klingberg, 2010), wat aanleiding gaf tot experimenteel onderzoek naar de rol van cognitieve processen in kwetsbaarheid voor depressie (voor een recente review, zie Mor & Daches, 2015). In deze context is het belangrijk te vermelden dat recente meta-analytische bevindingen suggereren dat cognitieve training positieve effecten op depressie-gerelateerde uitkomstmaten kan hebben (Motter et al., 2016).

ONDERZOEKSDOELEN VAN DIT DOCTORAATSPROJECT

Dit doctoraatsproject is gericht op de toetsing van de causale rol van cognitieve controle in kwetsbaarheid voor depressie. Eerste studies waarbij effecten van cognitieve controle training op depressie-gerelateerde uitkomstmaten in kaart gebracht werden, leverden beloftevolle resultaten op. Zo rapporteerden Siegle, Ghinassi en Thase (2007) positieve effecten van een cognitieve controle training – bestaande uit de adaptieve Paced Auditory Serial Addition Task (PASAT; voor een review over de non-adaptieve versie van deze taak, zie Gronwall, 1977) en een aandachttraining – op ondermeer depressieve ruminatie en depressieve symptomatologie in klinisch depressieve patiënten. Doorheen de adaptieve PASAT taak worden participanten geconfronteerd met een reeks getallen die auditief aangeboden worden. Bij elk nieuw getal dient de participant te reageren op de som van de laatste twee gehoorde getallen.

Daarbij wordt de snelheid waarmee de getallen worden aangeboden dynamisch aangepast op basis van de prestatie van de participant doorheen de sessie. Op deze wijze wordt cognitieve controle getraind binnen een stresserende taakcontext. In een vervolgstudie vonden Siegle en collega's (2014) daarnaast positieve effecten op gebruik van ambulante hulpverlening in een periode van een jaar na uitvoering van de training. Dit wijst er op dat cognitieve controle training mogelijk stabiele effecten op (kwetsbaarheid voor) depressie kan hebben op langere termijn.

Een aantal methodologische beperkingen van deze eerste studies beperken echter de conclusies die getrokken kunnen worden inzake de causale invloed van cognitieve controle in depressie. Zo maakten deze bijvoorbeeld geen gebruik van een actieve controle conditie. Tevens lag de focus eerder op de curatieve waarde van cognitieve controle training bij de behandeling van depressie, waarbij slechts beperkte aandacht gespendeerd werd aan het onderzoeken van de mechanismen onderliggend aan deze emotionele transfereffecten, alsook de preventieve waarde van cognitieve controle training (bijv. in het kader van hervalpreventie).

Dergelijke onderzoeksvragen hebben belangrijke theoretische (bijv. kennis omtrent de etiologie van depressieve episodes, emotieregulatie processen) alsook klinische implicaties. Bijgevolg was de hoofddoelstelling van dit doctoraatsproject het testen van de causale invloed van cognitieve controle in kwetsbaarheid voor depressie, waarbij we specifiek het preventieve potentieel van cognitieve controle training in kaart brachten. Op basis van initiële beloftevolle bevindingen (Siegle et al., 2007, 2014) voerden we hiertoe verschillende empirische studies uit naar de causale invloed van cognitieve controle in kwetsbaarheid voor depressie (Hoofdstukken 3 – 6). Daarbij probeerden we systematisch de mechanismen onderliggend aan voorheen gerapporteerde trainingseffecten inzake depressieve klachten in kaart te brengen. Tevens boden we aan de hand van een systematische review een overzicht van de huidige wetenschappelijke stand van zaken rond cognitieve controle training voor depressie (Hoofdstuk 2). Daarnaast voerden we aan de hand van netwerkanalyses een cross-sectionele test uit van de relatie tussen cognitieve kwetsbaarheidsfactoren en remissie (geoperationaliseerd door residuele depressieve klachten) na het opklaren van een depressieve episode (Hoofdstuk 7).

SAMENVATTING VAN BEVINDINGEN INZAKE DE CAUSALE ROL VAN COGNITIEVE CONTROLE IN KWETSBAARHEID VOOR DEPRESSIE

Evidentie uit onze Empirische Studies

In een eerste experimentele studie bestudeerden we de invloed van cognitieve controle op stressreactiviteit en depressieve ruminatie. Hiertoe trainden we een groep studenten met een verhoogd risico op het ontwikkelen van depressieve klachten, namelijk studenten met verhoogde scores op trekruminatie (Hoofdstuk 3; Hoorelbeke, Koster, Vanderhasselt, Callewaert, & Demeyer, 2015). Daarbij werden participanten at random verdeeld over twee trainingscondities: cognitieve controle training gericht op het bevorderen van werkgeheugenprocessen, bestaande uit de adaptieve PASAT training, of een actieve controle conditie waarin gebruik gemaakt werd van een taak waarmee aandachtsprocessen getraind werden (adaptive visual search task). Beide condities voerden 10 trainingssessies uit van ongeveer 15 à 20 minuten per sessie over een periode van 14 dagen. Toegenomen werkgeheugen functioneren over deze periode op de Automated O-Span taak voorspelde een verbetering in depressieve ruminatie en veerkracht. Dit was enkel het geval voor de cognitieve controle trainingsconditie.

Na afloop van de trainingsfase werd stressreactiviteit in kaart gebracht aan de hand van een stressinductieprocedure in het lab. Hierbij kregen de participanten herhaaldelijk negatieve feedback waarbij hun prestatie vergeleken werd met een fictieve normgroep van medestudenten. Aan de hand van visueel analoge schalen voor gemoedstoestand en een gedragsmaat voor repetitief negatief denken (breathing focus task) werd de impact van de stressinductieprocedure op affect en depressieve ruminatie in kaart gebracht in het lab. Daarbij rapporteerden proefpersonen in de actieve controle conditie een negatief effect van de stressinductie procedure op zelf-gerapporteerde positieve gedachten en negatieve gemoedstoestand. Dit was niet het geval in de cognitieve controle trainingsconditie. Daarbovenop vertoonden zowel de cognitieve controle trainingsconditie als de actieve controle conditie een toename in zelf-gerapporteerde negatieve gedachten doorheen de stressinductie procedure. Deze toename was echter meer uitgesproken in de actieve controle conditie.

Vervolgens gingen we de effecten van cognitieve controle training na op perseveratief negatief denken bij blootstelling aan een naturalistische stressor. Hiertoe volgden we de effecten van cognitieve controle training op depressieve ruminatie op gedurende de examenperiode één maand na voltooiing van de trainingsprocedure. Voorgeselecteerde studenten met een verhoogde neiging tot rumineren in stressvolle situaties rapporteerden een significante daling in depressieve ruminatie van voor deelname aan de trainingsprocedure tot in de examenperiode. Daarbij controleerden we voor verlopen tijd sinds het vorige examen. Dergelijke reductie in depressieve ruminatie trad niet op in de actieve controle conditie. Daarbovenop vonden we dat stressreactiviteit bij confrontatie met de labstressor voortgezette verbetering in depressieve ruminatie voorspelde één maand later.

Deze bevindingen wijzen op de causale invloed van cognitieve controle in stressreactiviteit en ruminatie. Om een beter zicht te krijgen op de mechanismen onderliggend aan deze effecten, combineerden we vervolgens de trainingsprocedure met experience sampling (Hoofdstuk 4; Hoorelbeke, Koster, Demeyer, Loeys, & Vanderhasselt, 2016). Experience sampling is een methode waarin participanten doorheen het dagelijkse leven opgevolgd worden, bijvoorbeeld aan de hand van beknopte vragenlijsten die ingevuld worden via een smartphone. Deze methodiek heeft een hogere ecologische validiteit en laat toe gerichte hypothesen te toetsen omtrent hoe effecten van cognitieve controle training zich in het dagelijkse leven ontplooien (bijv. inzake gemoedstoestand en emotieregulatie). Daarbij verbreedden we de focus van het onderzoek tevens naar adaptieve processen als indicatoren voor veerkracht (bijv. positieve (her)kadering). Hiertoe combineerden we in onze tweede empirische studie de trainingsmethodiek met experience sampling, waarbij effecten van cognitieve controle op de dynamiek tussen affect en emotieregulatie in het dagelijkse leven in kaart gebracht werden. Daarnaast gingen we tijdens een sessie in het lab na of cognitieve controle training effect heeft op de vaardigheid tot positieve herkadering, waarbij studenten gevraagd werden een negatieve autobiografische herinnering op te roepen en deze vervolgens positief te herkaderen. Daarbij brachten we de effecten van deze geïnstrueerde herkadering op gemoedstoestand alsook de mate waarin studenten aangaven in staat te zijn te komen tot een positieve herkadering in kaart. Als

experimentele manipulatie werd opnieuw gebruik gemaakt van 10 sessies adaptieve PASAT training over een periode van twee weken. Om de impact van motivationele effecten van training verder te reduceren, ontwikkelden we voor de actieve controle conditie een nieuwe trainingstaak waarin aandachtsprocessen getraind worden zonder in sterke mate beroep te doen op het werkgeheugen. Deze taak vertoont grote gelijkenissen met de adaptieve PASAT taak, waarbij participanten in dit geval enkel dienden te reageren op het laatste gehoorde getal i.p.v. de som.

Participanten in de cognitieve controle trainingsconditie presteerden na twee weken training marginaal significant beter op de cognitieve transfertaak (een dual n-back taak) dan participanten uit de actieve controle conditie terwijl we controleerden voor interindividuele verschillen in baseline cognitieve controle. Opnieuw vonden we positieve effecten van cognitieve controle training op maladaptieve emotieregulatie. Daarbij vertoonden participanten uit de cognitieve controle trainingsconditie de neiging om minder snel over te gaan tot depressieve ruminatie bij confrontatie met lage niveaus van positief affect in het dagelijkse leven. Participanten in de actieve controle conditie vertoonden hogere niveaus van depressieve ruminatie in dergelijke omstandigheden, wat een verdere achteruitgang van gemoedstoestand voorspelt (toename in negatief affect, afname in positief affect). Dit wijst er opnieuw op dat cognitieve controle training de kans op het (onvrijwillig) vastlopen in negatieve gedachten bij confrontatie met stress kan reduceren. In tegenstelling tot onze verwachtingen vonden we echter geen positieve effecten van cognitieve controle training op gebruik en effectiviteit van positieve herkadering als adaptieve emotieregulatie strategie in het dagelijkse leven. Daarnaast had cognitieve controle training geen invloed op de vaardigheid tot of de effecten van positieve herkadering van een autobiografische negatieve herinnering in het dagelijkse leven (Hoofdstuk 4).

Deze bevindingen zijn in lijn met voorgaande prospectieve (bijv. Demeyer et al., 2012; Zetsche & Joormann, 2011) en experimentele studies (bijv. Siegle et al., 2007, 2014) die wijzen op de rol van cognitieve controle als kwetsbaarheidsfactor voor depressie. Tevens wijzen onze bevindingen op het potentieel van cognitieve controle training als preventieve interventie voor gezonde studentenpopulaties, al dan niet met een verhoogd risico op het ontwikkelen van depressieve klachten (Hoofdstukken 3 & 4).

Daarbij verlaagt toegenomen cognitieve controle de kans dat iemand reageert op een stressvolle situatie met depressieve ruminatie. Experimentele manipulatie van cognitieve controle in gezonde populaties genereert echter beperkte kansen op het vaststellen van effecten op emotionele uitkomstmaten in de context van depressie. Zo zijn bepaalde effecten mogelijks beperkt wegens 'plafondeffecten' (d.i., de populatie functioneerde reeds goed voor de experimentele manipulatie). Voorgaande studies waarbij gebruik gemaakt werd van klinische populaties rapporteren dan ook typisch grotere effecten van cognitieve controle training (bijv. Siegle et al., 2007). Daarbij dient echter steeds rekening gehouden te worden met een aantal methodologische beperkingen van deze eerste studies, waaronder ondermeer het feit dat deze niet toelieten te controleren voor motivationele effecten van cognitieve training (gebrek aan actieve controle conditie, gebrek aan blindering, enz.). Een volgende logische stap binnen dit doctoraatsproject was dan ook het toetsen van preventieve effecten van cognitieve controle training in een klinische populatie, namelijk voorheen depressieve patiënten, waarbij gebruik gemaakt werd van een meer rigoureuze methodiek waarin psycho-educatie en cognitieve controle of actieve controle training gecombineerd werden. Daartoe hanteerden we een randomized controlled trial design, waarbij zowel onderzoekers als patiënten blind waren voor de interventieconditie waartoe de patiënten at random toegewezen werden (Hoofdstuk 5; Hoorelbeke, Faelens, Behiels, & Koster, 2015). Daarbij brachten we aan de hand van intention-to-treat analyses onmiddellijke effecten alsook langere termijn effecten (drie maanden follow-up) van cognitieve controle training in kaart op primaire uitkomstmaten depressieve ruminatie en depressieve / residuele klachten. Daarnaast werden effecten op indicatoren van functioneren als secundaire uitkomstmaten in kaart gebracht (adaptieve emotieregulatie, veerkracht, ervaren hinder en levenskwaliteit).

Cognitieve controle training ging gepaard met een significante toename in cognitief functioneren op gedragsmaten voor executief functioneren (non-adaptieve PASAT assessment taak; Hoofdstuk 6; Hoorelbeke & Koster, 2017). Dit effect bleef behouden tot de laatste meting drie maanden na de trainingsprocedure. Daarnaast rapporteerden patiënten die de trainingsprocedure voltooiden een marginaal significante daling in zelf-gerapporteerde cognitieve klachten over de twee-weken-

durende trainingsprocedure heen, wat gevolgd werd door een significante daling in cognitieve klachten in de opvolgperiode tot drie maanden later. In lijn met onze vorige bevindingen rapporteerden voorheen depressieve patiënten daarnaast positieve effecten van cognitieve controle training op indicatoren voor kwetsbaarheid voor depressie. Zo rapporteerde de cognitieve controle trainingsgroep in vergelijking met de actieve controle conditie een significante daling in depressieve ruminatie (RRS) en residuele depressieve klachten (BDI-II) onmiddellijk na training. Daarnaast rapporteerden patiënten in de cognitieve controle trainingsconditie minder depressieve klachten en ruminatie drie maanden na beëindiging van de trainingsprocedure. We vonden gelijkaardige effecten voor alternatieve indicatoren voor depressieve symptomatologie (RDQ) en maladaptieve emotieregulatie (CERQ). Daarnaast had cognitieve controle training tevens positieve effecten op zelf-gerapporteerde veerkracht en voor participanten die de trainingsprocedure voltooiden tevens op zelf-gerapporteerde hinder. Deze bevindingen tonen aan dat effecten van cognitieve controle training niet beperkt zijn tot het reduceren van cognitieve kwetsbaarheid voor depressie, maar dat cognitieve controle training (al dan niet direct) tevens positieve effecten kan genereren op indicatoren voor functioneren zoals veerkracht en ervaren hinder. We vonden echter opnieuw geen positieve effecten van cognitieve controle training op adaptieve emotieregulatie processen. Post-hoc Bayesiaanse analyses van deze data boden zelfs steun voor de nulhypothese dat cognitieve controle geen effect heeft op gebruik van adaptieve emotieregulatie strategieën in voorheen depressieve patiënten. Dit is mogelijk te wijten aan de observatie dat adaptieve emotieregulatie strategieën met name verstoord zijn bij de meest disfunctionele klinische populaties, waaronder ernstig depressieve patiënten in de acute fase van de stoornis (bijv. Dillon & Pizzagalli, 2013).

We maakten tevens gebruik van de drie verschillende meetmomenten en klinische populatie om een invloedrijke theoretische hypothese rond de impact van cognitieve controle op depressie te toetsen. Zo wordt in de literatuur vaak aangenomen dat cognitieve controle met name (indirect) depressie beïnvloedt via directe effecten op maladaptieve emotieregulatie. We toetsten deze hypothese aan de hand van een mediatiemodel waarin de predictieve waarde van toegenomen cognitieve controle – dit

is, toename in prestatie op een cognitieve transfer taak doorheen de twee-weken-durende training – voor depressieve ruminatie onmiddellijk na de training en depressieve symptomatologie drie maanden later in kaart gebracht werd. Daarbij controleerden we voor de mate waarin patiënten aangaven vast te lopen in depressieve ruminatie alsook depressieve klachten ervoeren voor aanvang van de trainingsprocedure. Dit leverde evidentie op voor partiële mediatie, waarbij toename in cognitieve controle over de twee-weken-durende trainingsprocedure onmiddellijke positieve effecten op depressieve ruminatie voorspelde alsook directe langere termijn effecten op depressieve klachten. Daarbij vonden we dat het direct effect van cognitieve controle training op ruminatie verder lagere niveaus van toekomstige depressieve klachten voorspelde (indirect effect).

Evidentie uit de Recente Cognitieve Controle Trainingsliteratuur

Bovenstaande bevindingen wijzen op het potentieel van cognitieve controle training als preventieve interventie voor depressie. Dit is in lijn met recente bevindingen uit de cognitieve trainingsliteratuur. Zo identificeerden we in onze systematische review na screening van 7633 artikels in totaal 34 cognitieve controle trainingsstudies die effecten nagingen op depressie-gerelateerde uitkomstmaten (Hoofdstuk 2; Koster, Hoorelbeke, Onraedt, Owens, & Derakshan, 2017). Daarbij onderscheidden we de geselecteerde studies op basis van fase in kwetsbaarheid voor depressie (gezonde of risicopopulatie, actueel depressieve patiënten, voorheen depressieve patiënten) alsook type training, waarbij verder onderscheid gemaakt werd tussen trainingsstudies op basis van intensiteit van de trainingsprocedure alsook gebruik van emotionele versus neutrale stimuli.

Studies die gebruik maakten van één trainingssessie vertoonden weinig tot geen effecten op kwetsbaarheid voor depressie. Binnen de studies die gebruik maakten van meerdere trainingssessies rapporteerde 47% (*n* = 7) van de studies met gezonde steekproeven – al dan niet met een verhoogd risico op depressie – positieve effecten van cognitieve controle training (o.a. op stressreactiviteit, gemoedstoestand, emotieregulatie, cognitieve- en depressieve klachten; bijv. Calkins, McMorran, Siegle, & Otto, 2015; Cohen et al., 2016; Schweizer, Hampshire, & Dalgleish, 2011). 57% (*n* = 8)

van de studies die gebruik maakten van actueel- of voorheen depressieve patiënten rapporteerden tevens bevindingen in lijn met de hypothese dat cognitieve controle training effectief is ter reductie van kwetsbaarheid voor depressie (bijv. Alvarez, Sotres, León, Estrella, & Sosa, 2008; Morimoto et al., 2014). Daarnaast rapporteerde een bijkomstige 33% van de studies waarbij effecten van cognitieve controle training in gezonde participanten in kaart gebracht werden – al dan niet met een verhoogd risico op het ontwikkelen van depressieve episoden – gemengde evidentie voor bovenstaande hypothese (bijv. Calkins & Otto, 2013; Daches & Mor, 2014; Owens, Koster, & Derakshan, 2013). Voor studies die gebruik maakten van depressieve patiënten was dit 7% (Siegle et al., 2014). Daarbij werden effecten op één of meerdere kwetsbaarheidsfactoren gerapporteerd in afwezigheid van effecten op andere kwetsbaarheidsfactoren.

Uit een kritische lezing van de cognitieve controle literatuur kwam verder naar voor dat een aantal methodologische factoren mogelijks bijdroegen tot de inconsistente bevindingen in de literatuur (bijv. Elgamal, McKinnon, Ramakrishnan, Joffe, & MacQueen, 2007). Zo maakten studies die inconsistente of nulbevindingen rapporteerden vaak gebruik van designs met onvoldoende power (beperkte steekproefgrootten), wat niet toeliet om matige effecten te observeren (bijv. d = 0.67; Trapp et al., 2016). Daarnaast gebruikten een groot aantal van deze studies slechts een relatief beperkt aantal trainingssessies (bijv. Moshier, Molokotos, Stein, & Otto, 2015) en brachten sommige studies geen directe effecten van cognitieve controle training op depressieve klachten of ruminatie in kaart (bijv. Bowie et al., 2013). Studies die wel positieve effecten van cognitieve controle training terugvonden, maakten daarentegen typisch gebruik van intensievere trainingsprocedures (het gemiddelde aantal trainingssessies lag hier op 12.32), waarbij cognitieve controle met name over affectieve informatie getraind werd door gebruik van emotionele stimuli (bijv. Iacoviello et al., 2008) of via het trainen van cognitieve controle in een frustrerende / emotionerende taakomgeving (bijv. Siegle et al., 2007). Op basis van deze bevindingen maakten we specifieke aanbevelingen voor toekomstige cognitieve controle trainingsstudies (Hoofdstuk 2).

Cognitieve Controle, Cognitieve Kwetsbaarheids- / Protectieve Factoren, en Depressieve Klachten Tijdens Remissie

Om een beter zicht te krijgen op hoe cognitieve kwetsbaarheidsfactoren en protectieve factoren na het opklaren van depressieve klachten in verhouding tot elkaar staan, maakten we in Hoofdstuk 7 vervolgens gebruik van netwerkanalyses in een cross-sectionele dataset van voorheen depressieve patiënten (Hoorelbeke, Marchetti, De Schryver, & Koster, 2016). Daarbij selecteerden we een gedragsmaat voor cognitieve controle alsook zelf-gerapporteerde cognitieve controle, ruminatie, positieve herkadering, veerkracht, en residuele symptomatologie voor inclusie in een associatief netwerkmodel. Na transformatie van het model – wat toelaat de unieke relaties tussen elke variabele na te gaan en te controleren voor onstabiele / onbetrouwbare associaties – werd de gedragsmaat voor cognitieve controle uit het model gesloten. Dit was mogelijks het gevolg van methodevariantie binnen de variabelen. Alle overige variabelen maakten namelijk gebruik van zelf-rapportage. Uit drie netwerkmodellen kwam een centrale rol van veerkracht naar voor, wat achtereenvolgens (mal)adaptieve emotieregulatie en zelf-gerapporteerde cognitieve controle met residuele symptomatologie verbond. Daarbij gaven verschillende centraliteitsindices aan dat manipulatie van veerkracht de meest efficiënte manier is om het netwerk van kwetsbaarheids-, protectieve factoren, en residuele klachten in voorheen depressieve patiënten te wijzigen. We bekwamen gelijkaardige effecten bij gebruik van alternatieve maten voor adaptieve en maladaptieve emotieregulatie en depressieve klachten. Opvallend hierbij is dat in beide gevallen zelf-gerapporteerde cognitieve controle de tweede meest centrale variabele binnen het model vormde, wat in lijn is met onze eerdere bevindingen dat stimulatie van cognitieve controle een veerkracht bevorderend effect heeft (Hoofdstukken 3 & 6; Hoorelbeke et al., 2015; Hoorelbeke & Koster, 2017). Eén mogelijkheid hierbij is dat de combinatie van cognitieve controle training ter reductie van kwetsbaarheid voor depressie en interventies gericht op het bevorderen van veerkracht complementaire effecten kunnen genereren. Zo vonden Course-Choi, Saville en Derakshan (2017) bijvoorbeeld recent dat cognitieve controle training in combinatie met mindfulness effectiever is inzake aanpak van perseveratief negatief denken dan mindfulness of cognitieve controle training op zich.

IMPLICATIES VAN DE ONDERZOEKSRESULTATEN

De bevinding dat cognitieve controle een causale rol speelt in kwetsbaarheid voor depressie heeft belangrijke implicaties. Theoretisch dragen de bevindingen bij tot onze kennis omtrent de rol van informatieverwerkingsprocessen in depressie. Zo geeft dit ons beter zicht op de invloed van cognitieve controle op emotieregulatie en hoe dit bijdraagt tot verhoogde kwetsbaarheid voor depressie of eerder veerkracht. Hier bevestigen onze bevindingen voorgaand cross-sectioneel onderzoek waarin cognitieve controle deficieten typisch gepaard gaan met verhoogde rapportage van gebruik van maladaptieve emotieregulatie strategieën en minder gebruik van adaptieve strategieën (Hoofdstuk 4). Het stimuleren van cognitieve controle bevorderde dan ook emotieregulatie processen, waarbij gezonde studenten (Hoofdstuk 4), studenten met een verhoogd risico op het ontwikkelen van depressieve klachten (Hoofdstuk 3), alsook voorheen depressieve patiënten (Hoofdstuk 6) positieve effecten van cognitieve controle training rapporteerden op depressieve ruminatie. Onderzoek naar de onderliggende processen maakte hier duidelijk dat toegenomen cognitieve controle met name de kans op het vastlopen in perseveratief negatief denken zoals depressieve ruminatie reduceert bij confrontatie met stressvolle gebeurtenissen (Hoofdstukken 3 en 4). Hierbij gaat het om effecten op gebruik van emotieregulatie strategieën, eerder dan effecten op de impact van de gebruikte emotieregulatie strategie (efficiëntie van emotieregulatie; Hoofdstuk 4). Daarbij vonden we dat dit zowel direct als indirect de kans op het ontwikkelen van toekomstige depressieve klachten reduceert voor patiënten die in het verleden een depressieve episode meemaakten (Hoofdstuk 6), wat zo bestaande theoretische modellen van kwetsbaarheid voor heroptredende depressie bevestigt en uitbreidt (De Raedt & Koster, 2010). De afwezigheid van effecten op adaptieve emotieregulatie strategieën sluiten daarnaast niet uit dat cognitieve controle causaal betrokken is bij gebruik van adaptieve strategieën zoals positieve herkadering. Zo werd in de literatuur reeds opgemerkt dat deze processen met name verstoord verlopen in de meest ernstig depressieve populaties (wat buiten de scope van onze preventieve studies valt; bijv. Dillon & Pizzagalli, 2013).

Onze onderzoeksresultaten hebben tevens belangrijke klinische implicaties. Zo houdt de gepresenteerde evidentie voor de causale invloed van cognitieve controle op (kwetsbaarheid voor) depressie in dat experimentele manipulatie van cognitieve controle voor klinische doeleinden ingezet zou kunnen worden. Onze bevindingen bevestigen zo het potentieel van cognitieve controle training ter ondersteuning van bestaande interventies voor klinisch depressieve patiënten (cfr. systematische review, Hoofdstuk 2). Daarnaast bieden onze empirische studies een toets van de effectiviteit van cognitieve controle training als preventieve interventie voor risicogroepen zoals voorheen depressieve patiënten of studenten die de neiging vertonen om vast te lopen in depressieve ruminatie (Hoofdstukken 3 – 6). Dergelijke interventie heeft als voordeel dat op kostenefficiënte wijze onderliggende kwetsbaarheidsprocessen aangepakt kunnen worden. Met name de mogelijkheid tot online distributie van cognitieve controle training houdt in dat deze interventie op flexibele wijze voor grote groepen beschikbaar gesteld kan worden, waarbij deze tevens door uiteenlopende populaties benut zou kunnen worden. Cognitieve controle training vormt zo een laagdrempelige interventie. Voor klinische doeleinden dient de interventie echter steeds gezien te worden als een bijkomstige interventie (‘add-on’ interventie), waarbij aan te raden is dat klinisch depressieve patiënten daarnaast gebruik maken van het rijke arsenaal aan bestaande evidence-based interventies (psychotherapeutisch en/of farmacologisch). Een belangrijke uitdaging hierbij is het motiveren van patiënten tot initieel gebruik van de interventie alsook het volbrengen van de interventie (therapietrouw). Hiertoe is een duidelijke rationale van de eventuele doorverwijzer of onderzoeker belangrijk, mogelijks in de vorm van psycho-educatie rond cognitieve kwetsbaarheid voor depressie en cognitieve controle training. Daarnaast kan integratie van speltechnieken (gamification) bijdragen tot therapietrouw tijdens en over de verschillende trainingssessies heen.

Verschillende vragen dienen echter nog beantwoord te worden vooraleer cognitieve controle training als klinische interventie ingezet kan worden. Zo dient toekomstig onderzoek zich te buigen over de vraag naar moderatoren voor behandeleffecten en dient men te komen tot een duidelijke indicatiestelling. Andere vragen die nog beantwoord dienen te worden, zijn onder andere het ideale aantal

sessies op basis van iemands persoonlijke kwetsbaarheidsprofiel, verschillen in effectiviteit tussen verschillende versies van cognitieve controle training (bijv. aPASAT training, inhibitietraining, enz.), hoe deze varianten in te zetten op basis van het individuele kwetsbaarheidsprofiel (zorg op maat), de invloed van affectieve stimuli of taakcontext, stabiliteit van effecten (bijv. nood aan booster sessies en timing hiervan), alsook de mate waarin verschillende interventies complementair zijn aan elkaar. Zo is het waarschijnlijk dat de combinatie van cognitieve controle training met andere gerichte interventies superieur is bij de aanpak van kwetsbaarheid voor depressie (bijv. in combinatie met interventies gericht op het bevorderen van adaptieve emotieregulatie vaardigheden en aanpakken van metacognities). Recent onderzoek wijst bijvoorbeeld op superieure effecten van de combinatie van mindfulness en cognitieve controle training in vergelijking met beide interventies afzonderlijk (Course-Choi et al., 2017).

CONCLUSIE

Doorheen dit proefschrift gingen we na of cognitieve controle een causale rol speelt in kwetsbaarheid voor depressie. Daartoe maakten we gebruik van verschillende experimentele studies waarin cognitieve controle gemanipuleerd werd aan de hand van cognitieve training. Zo vonden we ondermeer positieve effecten van adaptieve PASAT training op cognitief functioneren, stressreactiviteit, emotieregulatie (met name depressieve ruminatie), depressieve klachten, en veerkracht. Deze effecten werden zowel in een gecontroleerde omgeving (experimenteel lab) alsook in het dagelijkse leven geobserveerd. Ondanks het feit dat we positieve effecten observeerden in zowel gezonde studenten alsook studenten met een verhoogd risico op het ontwikkelen van depressieve klachten, waren de trainingseffecten het meest uitgesproken bij voorheen depressieve patiënten. Daarnaast voerden we een systematische review uit van de cognitieve controle trainingsliteratuur. De bevindingen van deze review bevestigen dat – mits aan een aantal condities voldaan wordt – cognitieve controle training potentieel vertoont als preventieve interventie voor depressie.

REFERENTIES

Alonso, J., Angermeyer, M. C., Bernert, S., Bruffaerts, R., Brugha, T. S.,Bryson, H., ... Vollebergh, W. A. (2004). Prevalence of mental disorders in Europe: Results from the European Study of the Epidemiology of Mental Disorders (ESEMeD) project. *Acta Psychiatrica Scandinavica, 109,* 21-27. doi: 10.1111/j.1600-0047.2004.00327.x

Alvarez, L. M., Sotres, C. J. F., León, S. O., Estrella, J., & Sosa, S. J. J. (2008). Computer program in the treatment for major depression and cognitive impairment in university students. *Computers in Human Behavior*, *24*, 816–826. doi: 10.1016/j.chb.2007.02.013

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). Washington, DC: Author.

Baddeley, A. D., & Hitch, G. (1974). Working memory. In G. H. Bower (Ed.), *The psychology of learning and motivation: Advances in research and theory* (pp. 47–89). New York: Academic Press.

Beck, A. T., Rush, A. J., Shaw, B. F., & Gemery, G. (1979). *Cognitive therapy of depression.* New York: Guildford Press.

Beckwé, M., Deroost, N., Koster, E. H. W., De Lissnyder, E., & De Raedt, R. (2014). Worrying and rumination are both associated with reduced cognitive control. *Psychological Research*, *78*, 651–660. doi: 10.1007/s00426-013-0517-5

Beshai, S., Dobson, K. S., Bockting, C. L. H., & Quigley (2011). Relapse and recurrence prevention in depression: Current research and future prospects. *Clinical Psychology Review, 31*, 1349-1360. doi: 10.1016/j.cpr.2011.09.003

Bockting, C. L. H., Spinhoven, P., Koeter, M. W. J., Wouter, L. F., & Schene, A. H. (2006). Prediction of recurrence in recurrent depression and the influence of consecutive episodes on vulnerability for depression: A 2-year prospective study. *Journal of Clinical Psychiatry, 67*, 747-755.

Bockting, C. L. H., Spinhoven, P., Koeter, M. W. J., Wouter, L. F., & Schene, A. H. (2009). Long-term effects of preventive cognitive therapy in recurrent depression: A 5.5-year follow-up study. *Journal of Clinical Psychiatry, 70,* 1621-1628. doi: 10.4088/JCP.08m04784blu

Bower, G. H. (1981). Mood and memory. *American Psychologist, 36*, 129-148.

Bower, G. H. (1987). Commentary on mood and memory. *Behaviour Research and Therapy, 25,* 443-455.

Bowie, C., Mcgurk, S. R., Mausbach, B., Patterson, T. L., & Harvey, P. D. (2012). Combined cognitive remediation and functional skills training for schizophrenia: Effects on cognition, functional competence, and real-world behavior. *American Journal of Psychiatry, 169*, 710-718. doi: 10.1176/appi.ajp.2012.11091337

Burcusa, S. L., & William, G. I. (2007). Risk for recurrence in depression. *Clinical Psychology Review, 27*, 959-985. doi: 10.1016/j.cpr.2007.02.005

Calkins, A. W., McMorran, K. E., Siegle, G. J., & Otto, M. W. (2015). The effects of computerized cognitive control training on community adults with depressed mood. *Behavioural and Cognitive Psychotherapy*, *43*, 578–589. doi: 10.1017/S1352465814000046

Calkins, A. W., & Otto, M. W. (2013). Testing the Boundaries of Computerized Cognitive Control Training on Symptoms of Obsessive Compulsive Disorder. *Cognitive Therapy and Research*, *37*, 587–594. doi: 10.1007/s10608-012-9496-x

Carr, A., & McNulty, M. (2016). Depression. In A. Carr & M. McNulty (Eds.), *The handbook of Adult Clinical Psychology: An evidence-based practice approach* (265-316) New York: Routlegde.

Cohen, N., Margulies, D. S., Ashkenazi, S., Schaefer, A., Taubert, M., Henik, A., … Okon-Singer, H. (2016). Using executive control training to suppress amygdala reactivity to aversive information. *NeuroImage*, *125*, 1022–31. doi: 10.1016/j.neuroimage.2015.10.069

Connolly, S. L., Wagner, C. A., Shapero, B. G., Pendergast, L. L., Abramson, L. Y., & Alloy, L. B. (2014). Rumination prospectively predicts executive functioning impairments in adolescents. *Journal of Behavior Therapy and Experimental Psychiatry*, *45*, 46–56. doi: 10.1016/j.jbtep.2013.07.009

Course-Choi, J., Saville, H., & Derakshan, N. (2017). The effects of adaptive working memory training and mindfulness meditation training on processing efficiency and worry in high worriers. *Behaviour Research and Therapy, 89,* 1-13. doi: 10.1016/j.brat.2016.11.002

Cox, G. R., Fisher, C. A., De Silva, S., Phelan, M., Akinwale, O. P., Simmons, M. B., & Hetrick S. E.. (2012). Interventions for preventing relapse and recurrence of a depressive disorder in children and adolescents. *Cochrane Database of Systematic Reviews*, Issue 11. Art. No.: CD007504. DOI: 10.1002/14651858.CD007504.pub2

Cuijpers, P., Cristea, I. A., Karyotaki, E., Reijnders, M., & Huibers, M. J. H. (2016). How effective are cognitive behavior therapies for major depression and anxiety disorders? A meta-analytic update of the evidence. *World Psychiatry, 15,*245-258. doi: 10.1002/wps.20346

Daches, S., & Mor, N. (2014). Training ruminators to inhibit negative information: A preliminary report. *Cognitive Therapy and Research*, *38*, 160–171. doi: 10.1007/s10608-013-9585-5

De Raedt, R., & Koster, E. H. W. (2010). Understanding vulnerability for depression from a cognitive neuroscience perspective: A reappraisal of attentional factors and a new conceptual framework. *Cognitive Affective & Behavioral Neuroscience*, *10*, 50–70. doi: 10.3758/cabn.10.1.50

Demeyer, I., De Lissnyder, E., Koster, E. H. W., & De Raedt, R. (2012). Rumination mediates the relationship between impaired cognitive control for emotional information and depressive symptoms: A prospective study in remitted depressed adults. *Behaviour Research and Therapy*, *50*, 292–297. doi:10.1016/j.brat.2012.02.012

Dillon, D. G., & Pizzagalli, D. A. (2013). Evidence of successful modulation of brain activation and subjective experience during reappraisal of negative emotion in unmedicated depression. *Psychiatry Research, 212*, 99-107. doi: 10.1016/j.pscychresns.2013.01.001

Elgamal, S., McKinnon, M. C., Ramakrishnan, K., Joffe, R. T., & MacQueen, G. (2007). Successful computer-assisted cognitive remediation therapy in patients with unipolar depression: a proof of principle study. *Psychological Medicine*, *37*, 1229–38. doi: 10.1017/S0033291707001110

Extremera, N., & Rey, L. (2014). Health-related quality of life and cognitive emotion regulation strategies in the unemployed: A cross-sectional survey. Health and Quality of Life Outcomes, 12:172. doi: 10.1186/s12955-014-0172-6

Garnefski, N., & Kraaij, V. (2006). Relationships between cognitive emotion regulation strategies and depressive symptoms: A comparative study of five specific samples. Personality and Individual Differences, 40, 1659-1669. doi: 10.1016/j.paid.2005.12.009

Garnefski, N. & Kraaij, V. (2016). Specificity of relations between adolescents' cognitive emotion regulation strategies and symptoms of depression and anxiety. *Cognition & Emotion*. doi: 10.1080/02699931.2016.1232698

Garnefski, N., Legerstee, J., Kraaij, V., Van Den Kommer, T., & Teerds, J. (2002). Cognitive coping strategies and symptoms of depression and anxiety: A comparison between adolescents and adults. *Journal of Adolescence, 25,* 603-611. doi: 10.1006/jado.0507

Gibb, B. E., Grassia, M. Stone, L. B., Uhrlass, D.J., & McGeary, J. E. (2012). Brooding rumination and risk for depressive disorders in children of depressed mothers. *Journal of Abnormal Child Psychology, 40*, 317-326. doi: 10.1007/s10802-011-9554-y

Gonda, X., Pompili, M., Serafini, G., Carvalho, A. F., Rihmer, Z., & Dome, P. (2015). The role of cognitive dysfunction in the symptoms and remission from depression. *Ann Gen Psychiatry, 14*:27. doi: 10.1186/s12991-015-0068-9

Gronwall, D. M. A. (1977). Paced Auditory Serial Addition Task - Measure of recovery from concussion. *Perceptual and Motor Skills*, *44*, 367–373.

Gualtieri, C. T., Johnson, L. G., & Benedict, K. B. (2006). Neurocognition in Depression: Patients on and off medication versus healthy comparison subjects. *J Neuropsychiatry Clin Neurosci 18,* 217 – 225.

Haga, S. M., Kraft, P., & Corby, E. K. (2009). Emotion regulation: Antecedents and well-being outcomes of cognitive reappraisal and expressive suppression in cross-cultural samples. *Journal of Happiness Studies, 10*, 271-291. doi: 10.1007/s10902-007-9080-3

Harrison, T. L., Shipstead, Z., Hicks, K. L., Hambrick, D. Z., Redick, T. S., & Engle, R. W. (2013). Working memory training may increase working memory capacity but not fluid intelligence. *Psychological Science*, *24*, 2409–2419. doi: 10.1177/0956797613492984

Harvey, P. O., Le Bastard, G., Pochon, J. B., Levy, R., Allilaire, J. F., Dubois, B., & Fossti, P.

(2004). Executive functions and updating of the contents of working memory in unipolar depression. *Journal of Psychiatric Research*, *38*, 567–576. doi: 10.1016/j.jpsychires.2004.03.003

Hoorelbeke, K., Faelens, L., Behiels, J., & Koster, E. H. W. (2015). Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Protocol for a randomized controlled trial. *Bmc Psychiatry, 15.* doi: 10.1186/s12888-015-0511-0

Hoorelbeke, K., & Koster, E. H. W. (2017). Internet-delivered cognitive control training as a preventive intervention for remitted depressed patients: Evidence from a double-blind randomized controlled trial study. *Journal of Consulting and Clinical Psychology, 85,* 135–146. doi: 10.1037/ccp0000128

Hoorelbeke, K., Koster, E. H. W., Demeyer, I., Loeys, T., & Vanderhasselt, M. A. (2016). Effects of cognitive control training on the dynamics of (mal)adaptive emotion regulation in daily life. *Emotion*, *16*, 945-956. doi: 10.1037/emo0000169

Hoorelbeke, K., Koster, E. H. W., Vanderhasselt, M. A., Callewaert, S., & Demeyer, I. (2015). The influence of cognitive control training on stress reactivity and rumination in response to a lab stressor and naturalistic stress. *Behaviour Research and Therapy*, *69*, 1–10.

Hoorelbeke, K., Marchetti, I., De Schryver, M., & Koster, E.H.W. (2016). The interplay between cognitive risk and resilience factors in remitted depression: A network analysis. *Journal of Affective Disorders, 195,* 96-104. doi: 10.1016/j.jad.2016.02.001

Hsu, K. J., Beard, C., Rifkin, L., Dillon, D. G., Pizzagalli, D. A., & Björgvinsson, T. (2015). Transdiagnostic mechanisms in depression and anxiety: The role of rumination and attentional control. *Journal of Affective Disorders*, *188*, 22–27. doi: 10.1016/j.jad.2015.08.008

Iacoviello, B., Huryk, K., Alvarez, E., Collins, K., Murrough, J., Iosifescu, D., & Charney, D. (2014). Cognitive-Emotional Training as an Intervention for Major Depressive Disorder. *Biological Psychiatry*, *75*, 119S–119S.

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Perrig, W. J. (2008). Improving fluid intelligence with training on working memory. *Proceedings of the National Academy of Sciences of the United States of America*, *105*, 6829–6833. doi:

10.1073/pnas.0801268105

Jaeggi, S. M., Buschkuehl, M., Jonides, J., & Shah, P. (2011). Short- and long-term benefits of cognitive training. *Proceedings of the National Academy of Sciences of the United States of America*, *108*, 10081–10086. doi: 10.1073/pnas.1103228108

Joormann, J. (2004). Attentional bias in dysphoria: The role of inhibitory processes. *Cognition & Emotion*, *18*, 125–147. doi: 10.1080/02699930244000480

Joormann, J., & D'Avanzato, C. (2010). Emotion regulation in depression: Examining the role of cognitive processes. *Cognition & Emotion*, *24*, 913–939. doi: 10.1080/02699931003784939

Joormann, J., & Gotlib, I. H. (2010). Emotion regulation in depression: Relation to cognitive inhibition. *Cognition & Emotion, 24*, 281-298. doi: 10.1080/02699930903407948

Joormann, J., & Vanderlind, M. W. (2014). Emotion regulation in depression: The role of biased cognition and reduced cognitive control. *Clinical Psychological Science*, *2*, 402–421. doi: 10.1177/2167702614536163

Kalisch, R., Müller, M. B., & Tüscher, O. (2015). A conceptual framework for the neurobiological study of resilience. *Behavioral and Brain Sciences, 38*, 1 - 79. doi: 10.1017/S0140525X1400082X, e0

Kertz, S. J., Belden, A. C., Tillman, R., & Luby, J. (2015). Cognitive Control Deficits in Shifting and Inhibition in Preschool Age Children are Associated with Increased Depression and Anxiety Over 7.5 Years of Development. *Journal of Abnormal Child Psychology*, pp. 1–12. doi:10.1007/s10802-015-0101-0

Kessing, L. V., Hansen, M. G., & Andersen, P. K. (2004). Course of illness in depressive and bipolar disorders: Naturalistic study, 1994 – 1999. *British Journal of Psychiatry, 185*, 372-377.

Kessler, R. C., & Bromet, E. J. (2013). The epidemiology of depression. *Annu Rev Public Health, 34*, 119-138. doi: 10.1146/annurev-publhealth-031912-114409

Klingberg, T. (2010). Training and plasticity of working memory. *Trends in Cognitive Sciences*, *14*, 317–324.

Klingberg, T., Fernell, E., Olesen, P. J., Johnson, M., Gustafsson, P., Dahlström, K., … Westerberg, H. (2005). Computerized training of working memory in children with ADHD--a randomized, controlled trial. *Journal of the American Academy of Child*

and Adolescent Psychiatry, *44*, 177–86. doi: 10.1097/00004583-200502000-00010

Klingberg, T., Forssberg, H., & Westerberg, H. (2002). Training of working memory in children with ADHD. *Journal of Clinical and Experimental Neuropsychology*, *24*, 781–791. doi: 10.1076/jcen.24.6.781.8395

Koster*, E.H.W., Hoorelbeke*, K., Onraedt, T., Owens, M., & Derakshan, N. (2017). Cognitive control interventions for depression: A systematic review of findings from training studies. *Clinical Psychology Review, 53,* 79-92. doi: 10.1016/j.cpr.2017.02.002

Kraaij, V., Garnefski, N., & Schroevers, M. J. (2009). Coping, goal adjustment, and positive and negative affect in definitive infertility. *Journal of Health Psychology, 14,* 18. doi: 10.1177/1359105308097939

Levens, S. M., & Gotlib, I. H. (2010). Updating positive and negative stimuli in working memory in depression. *Journal of Experimental Psychology. General*, *139*, 654–664. doi: 10.1037/a0020283

Levens, S. M., & Gotlib, I. H. (2015). Updating emotional content in recovered depressed individuals: Evaluating deficits in emotion processing following a depressive episode. *Journal of Behavior Therapy and Experimental Psychiatry*, *48*, 156–163. doi: 10.1016/j.jbtep.2015.03.009

Li, L., Zhu, X., Yang, Y. He, J., Yi., J., Wang, Y., & Zhang, J. (2015). Cognitive emotion regulation: Characteristics and effect on quality of life in women with breast cancer. *Health and Quality of Life Outcomes, 13*:51. doi: 10.1186/s12955-015-0242-4

Martin, R. C., & Dahlen, E. R. (2005). Cognitive emotion regulation in the prediction of depression, anxiety, stress, and anger. *Personality and Individual Differences, 39*, 1249-1260. doi: 10.1016/j.paid.2005.06.004

McRae, K., Jacobs, S. E., Ray, R. D., John, O. P., & Gross, J. J. (2012). Individual differences in reappraisal ability: Links to reappraisal frequency, well-being, and cognitive control. *Journal of Research in Personality, 46,* 2-7. doi: 10.1016/j.jrp.2011.10.003

McRae, K., & Mauss, I. B. (2016). Increasing positive emotion in negative contexts: Emotional consequences, neural correlates, and implications for resilience. In J. D.

Greene, I. Morrison & M. E. P. Seligman (Eds.), Positive Neuroscience (1-37). New York: Oxford University Press.

Melby-Lervag, M., Redick, T., & Hulme, C. (2016).Working memory training does not improve performance on measures of intelligence or other measures of "far transfer": Evidence form a meta-analytic review. *Perspectives on Psychological Science, 11,* 512-534. doi: 10.1177/1745691616635612

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive Psychology*, *41*, 49–100. doi: 10.1006/cogp.1999.0734

Mor, N., & Daches, S. (2015). Ruminative Thinking: Lessons Learned From Cognitive Training. *Clinical Psychological Science*, *3*, 574–592. doi: 10.1177/2167702615578130

Morimoto, S. S., Wexler, B. E., Liu, J., Hu, W., Seirup, J., & Alexopoulos, G. S. (2014). Neuroplasticity-based computerized cognitive remediation for treatment-resistant geriatric depression. *Nature Communications*, *5:4579*. doi: 10.1038/ncomms5579

Moser, J. S., Hartwig, R., Moran, T. P., Jendrusina, A. A., & Kross, E. (2014). Neural markers of positive reappraisal and their associations with trait reappraisal and worry. *Journal of Abnormal Psychology, 123*(1), 91-105. doi: 10.1037/a0035817

Moshier, S. J., Molokotos, E. K., Stein, A. T., & Otto, M. W. (2015). Assessing the effects of depressed mood and cognitive control training on memory confidence and accuracy following repeated checking. *International Journal of Cognitive Therapy*, *8*, 206–221. doi: 10.1521/ijct_2015_8_02

Motter, J. N., Pimontel, M. A., Rindskopf, D., Devanand, D. P., Doraiswamy, M. P., & Sneed, J. R. (2016). Computerized cognitive training and functional recovery in major depressive disorder: A meta-analysis. *Journal of Affective Disorders*, *189*, 184–191. doi: 10.1016/j.ad.2015.09.022

Nierenberg, A. A., Husain, M. M., Trivedi, M. H., Fava, M., Warden, D., Wisniewski, S. R., . . . Rush A. J. (2010). Residual symptoms after remission of major depressive disorder with citalopram and risk of relapse: A STAR*D report. *Psychological Medicine, 40*, 41-50. doi: 10.1017/S0033291709006011

Nolen-Hoeksema, S. (1991). Responses to depression and their effects on the duration of depressive episodes. *Journal of Abnormal Psychology, 100,* 569-582.

Nolen-Hoeksema, S., & Morrow, J. (1991). A prospective study of depression and posttraumatic stress symptoms after a natural disaster - The 1989 Loma-Prieta earthquake. Journal of Personality and Social Psychology, 61(1), 115–121. doi: 10.1037/0022-3514.61.1.115

Nolen-Hoeksema, S., Wisco, B. E., & Lyubomirsky, S. (2008). Rethinking rumination. *Perspectives on Psychological Science, 3*, 400–424. doi: 10.1111/j.1745-6924.2008.00088.x

Nowlan, J. S., Wuthrich, V. M., & Rapee, R. M. (2016). The impact of positive reappraisal on positive (and negative) emotion among older adults. *International Psychogeriatrics, 28*, 681-693. doi: 10.1017/S1041610215002057

Ochsner, K. N., Bunge, S. A., Gross, J. J., & Gabrieli, J. D. E. (2002). Rethinking feelings: An fMRI study of the cognitive regulation of emotion. *Journal of Cognitive Neuroscience, 14*, 1215-1229. doi: 10.1162/089892902760807212

Olatunji, B. O., Naragon-Gainey, K., & Wolitzky-Taylor, K. B. (2013). Specificity of rumination in anxiety and depression: A multimodal meta-analysis. *Clinical Psychology Science and Practice, 20*, 225-257. doi: 10.1111/cpsp.12037

Olesen, P. J., Westerberg, H., & Klingberg, T. (2004). Increased prefrontal and parietal activity after training of working memory. *Nature Neuroscience*, *7*, 75–79. doi:10.1038/nn1165

Owens, M., Koster, E. H. W., & Derakshan, N. (2012). Impaired filtering of irrelevant information in dysphoria: An ERP study. *Social Cognitive and Affective Neuroscience*, *7*, 752–763. doi: 10.1093/scan/nsr050

Owens, M., Koster, E. H. W., & Derakshan, N. (2013). Improving attention control in dysphoria through cognitive training: Transfer effects on working memory capacity and filtering efficiency. *Psychophysiology*, *50*, 297–307. doi: 10.1111/psyp.12010

Paelecke-Habermann, Y., Pohl, J., & Leplow, B. (2005). Attention and executive functions in remitted major depression patients. *Journal of Affective Disorders*, *89*, 125–135. doi: 10.1016/j.jad.2005.09.006

Pe, M. L., Brose, A., Gotlib, I. H., & Kuppens, P. (2016). Affective updating ability and

stressful events interact to prospectively predict increases in depressive symptoms over time. *Emotion*, *16*, 73–82. doi:10.1037/emo0000097

Pe, M. L., Raes, F., & Kuppens, P. (2013). The cognitive building blocks of emotion regulation: Ability to update working memory moderates the efficacy of rumination and reappraisal on emotion. *Plos One*, *8*, 12. doi:10.1371/journal.pone.0069071

Philippot, P., & Brutoux, F. (2008). Induced rumination dampens executive processes in dysphoric young adults. *Journal of Behavior Therapy and Experimental Psychiatry*, *39*, 219–227. doi:10.1016/j.jbtep.2007.07.001

Schoofs, H., Hermans, D., & Raes, F. (2010). Brooding and reflection as subtypes of rumination: Evidence from confirmatory factor analysis in nonclinical samples using the Dutch Ruminative Response Scale. *Journal of psychopathology and Behavioral Assessment, 32*, 609-617. doi: 10.1007/s10862-010-9182-9

Schweizer, S., Hampshire, A., & Dalgleish, T. (2011). Extending Brain-Training to the Affective Domain: Increasing Cognitive and Affective Executive Control through Emotional Working Memory Training. *Plos One*, *6*, 7. doi: 10.1371/journal.pone.0024372

Shilyansky, C., Williams, L. M., Gyurak, A., Harris, A., Usherwood, T., & Etkin, A. (2016). Effect of antidepressant treatment on cognitive impairments associated with depression: A randomised longitudinal study. *The Lancet Psychiatry*. http://doi.org/10K1016+S2215-0366(16)00012-2

Shipstead, Z., Redick, T. S., & Engle, R. (2010). Does working memory training generalize? *Psychologica Belgica*, *17*, 245–276. doi: 10.3758/PBR.17.2.193

Shipstead, Z., Redick, T. S., & Engle, R. W. (2012). Is working memory training effective? *Psychological Bulletin*, *138*, 628–654. doi: 10.1037/a0027473

Siegle, G. J., Ghinassi, F., & Thase, M. E. (2007). Neurobehavioral therapies in the 21st century: Summary of an emerging field and an extended example of cognitive control training for depression. *Cognitive Therapy and Research, 31*(2), 235-262. doi: 10.1007/s10608-006-9118-6

Siegle, G. J., Price, R. B., Jones, N. P., Ghinassi, F., Painter, T., & Thase, M. E. (2014). You gotta work at it: Pupillary indices of task focus are prognostic for response to a

neurocognitive intervention for rumination in depression. *Clinical Psychological Science, 2*, 455-471. doi: 10.1177/2167702614536160

Sobocki, P., Jönsson, B., Angst, J., & Rehnberg, C. (2006). Cost of depression in Europe. *Journal of Mental Health Policy and Economy, 9*, 87-98.

ten Doesschate, M. C., Bockting, C. L. H., Koeter, M. W. J., & Schene, A. H. (2010). Prediction of recurrence in recurrent depression: A 5.5-year prospective study. *Journal of Clinical Psychiatry, 71,* 984-991. doi: 10.4088/JCP.08m04858blu

Trapp, W., Engel, S., Hajak, G., Lautenbacher, S., & Gallhofer, B. (2016). Cognitive remediation for depressed inpatients: Results of a pilot randomized controlled trial. *The Australian and New Zealand Journal of Psychiatry*, *50*, 46–55. doi: 10.1177/0004867415622271

Treynor, W., Gonzalez, R., & Nolen-Hoeksema, S. (2003). Rumination reconsidered: A psychometric analysis. *Cognitive Therapy and Research, 27,* 247–259.

Vanderhasselt, M.-A., & De Raedt, R. (2009). Impairments in cognitive control persist during remission from depression and are related to the number of past episodes: An event related potentials study. *Biological Psychology*, *81*, 169–176.

Vijayakumar, N., Whittle, S., Yücel, M., Byrne, M. L., Schwartz, O., Simmons, J. G., & Allen, N. B. (2016). Impaired maturation of cognitive control in adolescents who develop major depressive disorder. *Journal of Clinical Child & Adolescent Psychology*, *45*, 31–43. doi: 10.1080/15374416.2014.987381

Westerberg, H., Jacobaeus, H., Hirvikoski, T., Clevberger, P., Ostensson, M., Bartfai, A., & Klingberg, T. (2007). Computerized working memory training after stroke - A pilot study. *Brain Injury*, *21*, 21–29. doi: 10.1080/02699050601148726

Whitmer, A. J., & Banich, M. T. (2007). Inhibition versus switching deficits in different forms of rumination. *Psychological Science*, *18*(6), 546–553.

Whitmer, A. J., & Gotlib, I. H. (2012). Switching and backward inhibition in major depressive disorder: The role of rumination. *Journal of Abnormal Psychology*, *121*, 570–578. doi: 10.1037/a0027474

Woody, M. L., Kudinova, A. Y., McGeary, J. E., Knopik, V. S., Palmer, R. H. C., & Gibb, B. E. (2016). Influence of maternal depression on children's brooding rumination: Moderation by CRHR1 TAT haplotype. *Cognition & Emotion, 30*, 302-314. doi: 10.1080/02699931.2014.998631

Woody, M. L., McGeary, J. E., & Gibb, B. E. (2014). Brooding rumination and heart rate variability in women at high and low risk for depression: Group differences and moderation by COMT genotype. *Journal of Abnormal Psychology, 123*, 61-67. doi: 10.1037/a0035450

World Health Organization (2016). Depression: World Health Organization Fact sheet no 369. Accessed on 13-01-2017 from http://www.who.int/mediacentre/factsheets/fs369/en/ [Web Page].

Zetsche, U., & Joormann, J. (2011). Components of interference control predict depressive symptoms and rumination cross-sectionally and at six months follow-up. *Journal of Behavior Therapy and Experimental Psychiatry, 42*, 65–73. doi: 10.1016/j.jbtep.2010.06.001