Accepted for publication in *Brain and Cognition*

RUNNING HEAD: DEPRESSIVE BROODING: THE PROCESSING OF NEGATIVE INFORMATION

How brooding minds inhibit negative material: an event-related fMRI study

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5248 words (without abstract, acknowledgments, & references)

DEPRESSIVE BROODING: THE PROCESSING OF NEGATIVE INFORMATION

Highlights

The tendency to use depressive brooding was measured in a sample of healthy volunteers

Brooding tendencies are not related to behavioral outcomes of inhibitory control

Brooding tendencies are positively related to neural activation in the anterior cingulate cortex

Brooding tendencies affect performance efficiency but not performance effectiveness

Abstract

Depressive brooding -a passive ruminative focus on one's problems, negative mood and their consequences- is a thinking style that places individuals at a greater risk to develop future psychopathology. In this study, we investigated whether inter-individual differences in depressive brooding are related to neural differences underlying the inhibition of a dominant response towards negative information in favor of the concurrent (positive) response. To exclude the possibility that information processes would be confounded by sustained negative mood or enhanced stress responses, a sample of thirty never-depressed healthy individuals was selected. The Cued Emotional Control Task (CECT) was used to index the ability to enhance cognitive control when encountering a negative stimulus associated with an incompatible stimulus-response mapping. Individual brooding scores were not related to behavioral performances on the CECT. On the other hand, whole brain analyses demonstrated that trait depressive brooding scores were positively associated with activation in the posterior parts of the dorsal anterior cingulate cortex (pdACC) while successfully inhibiting a response to negative relative to positive information. These findings demonstrate that brooding minds need to recruit more pdACC activation when inhibiting a dominant response towards negative information (in favor of a response towards positive), although they are performing similarly as low brooders at the behavioral level. Future research should investigate whether and how these brooding related neural adjustments in healthy volunteers are related to future psychopathology.

Keywords: Depressive brooding – rumination – fMRI - cognitive control –ACC

227 words

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The experience of positive thoughts and feelings is crucial for well-being. Yet, after confrontation with a life stressor (e.g., job loss) most people will initially develop negative thoughts and feelings. Fortunately, human beings have a unique ability to yield control over these initial thoughts and feelings in order to regulate their emotions. However, individuals differ considerably in these higher-level thought processes (Gross, 1998). One of the most detrimental thinking styles in response to negative mood is 'depressive brooding', which is a passive ruminative focus on one's problems, negative mood and their consequences (Treynor, Gonzalez, & Nolen-Hoeksema, 2003; Joormann, Dkane, & Gotlib, 2006). Although brooding can be healthy and not all brooders will ever experience clinical depression, they demonstrate a tendency to get caught up in vicious circles on negative self-referential thoughts. Because this thinking style appears to be a stable risk factor for developing depressive mood in the future (Nolan, Roberts, & Gotlib, 1998; Nolen-Hoeksema, 2000), ever more research is currently exploring fundamental mechanisms at the level of attentional control that might influence this maladaptive response (e.g. Koster, De Lissnyder, Derakshan, & De Raedt, 2011).

In this endeavor, researchers have investigated how in everyday life habitual brooders process information in order to disengage from and/or inhibit negative material. This information processing approach focuses on the use of cognitive control, which allows us to adapt our behavior depending on the personal or task goals. Former studies have established that habitual brooders demonstrate impaired cognitive control for inhibiting and disengaging from negative information (e.g., Whitmer & Banich, 2007;

De Lissnyder, Derakshan, De Raedt, & Koster, in press; De Lissnyder, Koster, & De Raedt, in press; De Lissnyder, Koster, Derakshan, & De Raedt, 2010; Berman et al., 2011). Cognitive impairments in habitual brooders may serve as a pitfall mechanism underlying the development of sustained negative feelings (De Raedt & Koster, 2010; Koster et al., 2012). In other words, given that a life stressor initially triggers negative thoughts and feelings, habitual brooders may experience difficulties disengaging from this negative content, which may lead to recurrent thoughts that feature negative ideas about the self, the world, and the future. Therefore, identifying cognitive mechanisms associated with depressive brooding might help in understanding the etiology and maintenance of negative mood and depression (Berman et al., 2011). Nonetheless, the majority of these studies are based on individuals with already elevated depressive brooding scores, comparing groups of depressed patients versus healthy controls. As a result, these studies focus merely on the consequences of enhanced rumination/depression and consider the control sample as a homogeneous group. However, in a sample of healthy never-depressed individuals, inter-individual differences in everyday use of depressive brooding might reveal specific cognitive mechanisms associated with this detrimental thinking style, even before these healthy brooders might develop sustained negative mood and dysfunctional cognitions (Joormann, Yoon, & Zetsche, 2007).

To investigate inter-individual differences in habitual depressive brooding in healthy individuals, neural correlates might provide crucial information about subtle differences in functional cognitive processes. Although neuroimaging research on inter-individual differences in healthy people is scarce, Ray and colleagues (2005) reported

that a tendency to ruminate was associated with increased amygdala activation during the up-regulation of negative emotions in healthy volunteers. Amygdala activation, which is increased when confronted with negative arousing stimuli (Zald, 2003), is a key neural area within the ventral (limbic) system. The anterior cingulate cortex (ACC), can be seen as a bridge between ventral areas (for emotion processing) and dorsal areas related to cognitive control processing (Bush, Luu, & Posner, 2000). In healthy, never-depressed individuals amygdala hyper-activation initiates a negative feedback signal to the dorsal areas (Siegle, Steinhauer, Thase, Stenger, Carter, 2002; Taylor & Fragopanagos, 2005), resulting in increased dorsal activation to down-regulate the amygdala and prevent the development of negative affect. Within the dorsal system, dorsal ACC activation usually reflects the need to exert additional top-down control in the face of conflict or error, signalling to the dorsolateral prefrontal cortex (DLPFC) to modify the distribution of processing resources (Hopfinger, Buonocore, & Mangun, 2000; Macdonald Cohen, Stenger & Carter, 2000). This interplay between ventral (emotion) and dorsal (cognition) systems is crucial for adequate cognitive regulation over emotions. Interestingly, inter-individual differences in depressive brooding scores have been found to be positively related to activation in the right DLPFC during disengaging from negative as compared to positive information (Vanderhasselt, Kühn, & De Raedt, 2011). These data provide evidence that individuals scoring high on brooding have to recruit more DLPFC activation (i.e. more activation in the dorsal system) in order to successfully disengage from negative information.

Importantly, in this latter study of Vanderhasselt et al. (2011), participants were asked to simply withhold a dominant response to emotional information using a go/nogo

paradigm. However, given that high brooders demonstrate a tendency to brood over negative information, the process to inhibit a dominant (or habitual) response towards negative material in favor of an alternative response towards positive material, may provide more fine grained information on the functional neurocognitive mechanisms underlying depressive brooding. This is vital because depressive brooders are known to passively and recurrently process negative thoughts and feelings, once these have been generated by a negative life event. This passive ruminative focus on negative material (e.g., one's problems, negative mood and their consequences) is associated with a difficulty to move towards positive content and possibly underlies or enhances sustained depressive mood and future psychopathology. In order to explore the cognitive and neural processes specifically associated to depressive brooding as a trait thinking style, it is important to investigate this functional cognitive process in healthy volunteers who report a habitual tendency to brood over negative thoughts and feelings, but who have never been depressed so far. All together, the aim of this study was to investigate whether habitual depressive brooding tendencies in clinically healthy individuals are related to the ability to inhibit a dominant response following emotional information in order to engage a response towards the opposite emotion. Functional imaging data were collected during the Cued Emotional Control Task (CECT, see Figure 1, Vanderhasselt et al., 2012). In this paradigm, one (out of three) cue types requires participants to exert additional cognitive control in order to inhibit a dominant response to the emotional stimulus in favor of a concurrent/alternative response (for example, when participants are required to process sad faces but had to categorize them as positive). In other words, in this cue type a task-appropriate response conflicts

with a dominant alternative response. This condition elicits the maximum emotional interference - and hence conflict - at the behavioral level. For the current study, we expected inter-individual differences in habitual depressive brooding scores to be reflected in neural activation during a successfully inhibition of a dominant response when encountering a negative stimulus with incongruent stimulus-response mapping as compared to a dominant response of naming negative information. This emotional conflict, created by a task-relevant response that is incongruent with the facial emotional expression, is known to recruit the dorsal ACC activation, a neural region implicated in the facilitation of task-appropriate response selection and conflict monitoring (Botvinick, Braver, Barch, Carter, & Cohen, 2001; Egner & Hirsch, 2005; Etkin, Egner & Kalisch, 2011). Therefore, we expected a positive relation in these ACC areas known for their role in emotional conflict resolution with brooding scores of a sample of well-functioning individuals.

Methods

Participants

Postings on the university website were used to recruit a group of 30 female participants with a mean age of 21.07 (*SD* = 2.36, [18-30]). This is a different but comparable sample of subjects as in the study of Vanderhasselt et al. (2011) (no overlap of participants). All participants were right-handed, medication free (except for birth control pills) and eligible for fMRI research. The Dutch version of the Beck Depression Inventory (BDI-II; Beck, Steer, & Brown, 1996; Dutch translation: van der Does, 2002) was administered to screen for depressive symptoms (exclusion if score > 13; Mean=4.20; *SD*=4.72). A semi-structured interview, the Mini-International

Neuropsychiatric Interview (M.I.N.I; Sheehan et al., 1997), was administered by a trained psychiatrist (CB) in order to exclude (a history of) psychopathology (axis I and II) and/or neurological conditions.

Material

Self-report measures of mood and affect. The Ruminative Response Scale was used to measure depressive brooding (Nolen-Hoeksema& Morrow, 1991; Treynor et al., 2003). The Dutch version of the RRS (Raes & Hermans, 2007; Schoofs, Hermans & Raes, 2010; RRS-NL) is a 22-item self-report measure and consists of items that describe responses to a depressed mood that are focused on the self, symptoms, or consequences of depressed mood. Participants are asked to indicate how often they engage in these responses using a four-point Likert scale ranging from 1 (almost never) to 4 (almost always). A factor analysis of the RRS has identified a depressive brooding subscale (5 items). The subscale assesses the degree to which individuals passively focus on depressive symptoms, the reasons for their distress, and a passive comparison of one's current situation with some unachieved standards. An example of an item is "think about a recent situation, wishing it had gone better". The RRS can also be used to assess a measure of reflective pondering, which is, compared to depressive brooding, a more adaptive form of rumination. The RRS is a reliable and valid measure of rumination with good psychometric properties (Treynor et al., 2003).

Cued Emotional Conflict Task (CECT). The CECT was programmed using E-prime software (Psychology Software Tools Inc, Pittsburgh, Pennsylvania). Each trial started with one of two word cues ("actual" or "opposite") presented for 500 ms (Figure 1). After the presentation of the cue word, a fixed interval of 2000 ms separated the

presentation of the cue from the target. The target was either a happy or sad face presented in the center of the screen. The inter-trial interval was jittered between 4000 and 6000 ms (in 500ms steps). Throughout the remainder of the manuscript, effects are described by “cue-facial emotion” pairs (e.g., “opposite-happy” refers to the opposite cue followed by a happy face, which requires pressing the button labeled with “sad”).

Twelve faces (6 female and 6 male actors) from the Karolinska Directed Emotional Faces dataset (KDEF, Lundqvist, Flykt, & Ohman, 1998) were used as stimuli. Each face was shown in a happy or sad expression (matched for arousal based on the validation of Goeleven, De Raedt, Leyman, &Verschuere, 2008). After the CECT, participants rated the faces for valence and arousal using 9-point Likert scales (*valence*: 1=unhappy, 5=neutral, 9=happy; *arousal*: 1=calm, 5=intermediate, 9=excited). Paired *t*-tests revealed that participants rated the happy faces (6.54±0.88) as more positive relative to the sad faces (3.36±0.91), $t(30)=10.74$, $p<0.001$. Ratings of arousal were not different between happy (3.39±1.62) and sad (3.37±1.68) faces, $t(30)=.002$, $p>0.05$.

Participants completed 16 practice trials (using five faces not shown in the experimental blocks), followed by 6 blocks of 36 trials. Each block contained eighteen trials for each cue (2 cues: 36 trials). In each block, 12 trials were not followed by a target face but instead a blank screen (1/3 of all trials). This made it possible to separate the cue from target phase for imaging results, in order to solely investigate cognitive control in response to the emotional stimulus in the target phase.

For the target, this resulted in a total number of six trials for each cue (2) x face (2) combination per block (24 targets per block). Participants were instructed to respond as quickly and accurately as possible immediately after the presentation of the

emotional face. The assignment of labels to the two response buttons was counterbalanced across participants.

[Insert Figure 1 over here]

Image acquisition. The study was carried out on a 3T MRI scanner (Philips Achieva, Best, The Netherlands) equipped with a transmit/receive head coil. We measured 6 consecutive sessions with each 108 SE-EPI volumes (TR/TE=3000/70 ms, flip angle=90°, 24 slices, slice thickness/gap=4.0/1.0 mm, size=128x128, in plane resolution=1.80x1.80 mm, duration 5 min 33 sec) covering the whole brain. A T1-weighted structural scan (3D IR-TFE, TI/TR/TE=1501/12/3.81 milliseconds, flip angle=10°, matrix=256x256, in plane resolution=1.0x1.0 mm, 100 slices, slice thickness 2.0 mm, duration 6 minutes 24 seconds) of the whole head was performed. During functional magnetic resonance imaging, the trial information of the CECT was back-projected onto a flat screen positioned at the subject's feet and viewed via a mirror mounted on the head coil.

Procedure

All participants were initially screened for inclusion/exclusion criteria and gave written informed consent prior to the study. Subsequently, the emotional CECT was administered in the fMRI scanner. Finally, participants rated all the experimental faces on valence and arousal and filled in the RRS questionnaire. This experiment was part of a larger project investigating other neuro-cognitive markers. The study protocol was approved by the local Medical Ethics Committee of the University Hospital (UZBrussel) of the Vrije Universiteit Brussel (VUB). All participants received financial compensation.

Data analytic plan.

The self-report and behavioral data were analyzed with SPSS 15. For the behavioral data, a within subjects ANOVA with *Cue* (Opposite, Actual) x *Emotion* (Sad, Happy) was performed for both (1) Reaction Times (RT) for correct responses, and (2) the number of errors. To answer the question as to how performance during the CECT is associated with individual differences in depressive brooding tendencies, we correlated the RT and errors to all four CECT trials with scores for depressive brooding on the RRS.

The fMRI data were analyzed with statistical parametric mapping using SPM 5 software (Wellcome Department of Cognitive Neurology, London, UK). The fMRI time series were realigned to their first volume to correct for head movements. After the realignment step, a slice time correction, normalization into the standard anatomical space (EPI MNI template) and smoothing with an 8 mm Gaussian kernel were performed. The anatomical scan was normalized to the standard anatomical space (T1 MNI template) to be used as anatomical underlay for the results.

For each subject, we estimated condition effects using the general linear model (Friston, Harrison, Penny, 2003). We modelled our 2 regressors for the *cue*: “opposite” and “actual”; and 4 regressors of interest for the *target*: “opposite-sad”, “opposite-happy”, “actual-sad” and “actual-happy” as separate boxcar functions convolved with 3 basic functions: the canonical HRF and its temporal and dispersion derivatives. Besides the presentation time of the cue (including the cues followed by a blank screen) and the target, the model also contained the six movement parameters (3 translation, 3 rotation) as confounds (no participant was excluded because of excessive head movements).

This model was applied to the activation time series in each voxel (Friston et al., 2003). Significant activation peak voxels were analysed with the Talairach Client - Version 2.4.2 (Lancaster et al., 1997, 2000).

We generated contrast (% signal change) maps and *t*-statistic maps corresponding to the contrasts for the target (we have no hypothesis regarding the cue): “opposite-sad vs. actual-sad”; “opposite-happy vs. actual-happy”; opposite-sad vs. opposite-happy”, & “actual-sad vs. actual-happy”. Because the accuracy rates were high (see Results), only correct responses were included in the analyses.

First, we examined whether participants recruited more activation in areas associated to cognitive control when they had to respond with the opposite emotion compared to the actual emotion (cue: “opposite vs. actual). A paired t-test was performed between the contrast [opposite-sad vs. opposite-happy] and [actual-sad vs. actual-happy].

To answer our research question as to how brain activation, as measured during the CECT, is associated with individual differences in brooding tendencies, separate whole brain regression analyses were performed in SPM 5. We were specifically interested in brooding-related differences in activation during the ‘inhibition of negative information’ versus the ‘naming negative information’ (opposite-sad vs. actual-sad), and we also tested ‘inhibiting positive information’ versus the ‘naming of positive information’ (opposite-happy vs. actual-happy). These analyses were performed to confirm that the differences were based on cognitive control for negative material, and not the processing of negative or positive material. Most important, we related inter-individual brooding scores to the ‘inhibition of negative information’ versus the ‘inhibition of

positive information', always towards the opposite emotion (opposite-sad vs. opposite-happy). Each of the contrasts was used separately as dependent factor and the individual scores on depressive brooding served as covariate.

To control for type I and type II errors, we used AlphaSim as implemented in the SPM REST toolbox (restfmri.net/forum/) to determine the peak intensity and cluster extend threshold based on Monte Carlo simulations (Poline, Worsley, Evans, & Friston, 1997; Ward, 2000) to have a cluster-level corrected significance of $p<0.05$. Based on these simulations, a cluster extend threshold (Ke) of 66 voxels and a voxel significance threshold of $p<.005$ was determined.

Results

Self-report data

The mean brooding score was 9.60 (*SD*=3.39; [5-18]). The mean reflection score, the other subscale of the RRS, was 8.23 (*SD*=3.04; [5-16]). The mean BDI score was 4.20 (SD=4.72; [0-13]), both brooding and BDI were not significantly correlated, $r(30)=.26$, $p>.1$. Reflection and brooding scores, on the other hand, were positively correlated, $r(30)=.53$, $p=.002$. The mean scores of the brooding and reflection subscales are not significantly different from the mean scores in our prior study (Vanderhasselt et al., 2011), $p>.1$. Moreover, the mean brooding and reflection scores of this sample are within the range of one standard deviation from the mean scores of brooding and reflection of a study using two large samples (N>400) of nonclinical volunteers (Schoofs et al., 2010). The internal consistencies of these questionnaires (and subscales) was good, cronbach's $\alpha = > .8$.

Behavioral data

A within subjects ANOVA with *Cue* (Opposite, Actual) x *Emotion* (Sad, Happy) for RT revealed a main effect of *Cue*, $F(1,29)=159.66$, $p<.001$, $\eta_p^2=0.85$, with slower RT after "opposite" compared to the "actual" cues (*p*s<.001). A main effect of *Emotion,* $F(1,29)=9.45$, $p<.015$, $\eta_p^2=0.25$, indicated that RTs for sad faces were generally slower than those for happy faces (*p*s<.05). Moreover, a significant two-way interaction emerged, $F(1,29)=20.89$, $p<.001$, $\eta_p^2=0.42$. Paired *t*-tests revealed that participants were faster in naming the actual emotion of a happy compared to a sad face [actual-happy (658.03±122.94) < actual-sad (738.40±165.21), *p*<.001], and were slower in naming the opposite emotion of a happy compared to a sad face [opposite-happy (857.76.03±177.01) > opposite-sad (833.40±169.89), *p*<.05].

Overall, accuracy rates for all four CECT trial types were relatively high (actual-sad=93.72 % ± 4.08; actual-happy=97.49 % ± 3.31; opposite-sad=94.09 % ± 4.96; opposite-happy = 90.00 % ± 5.60). A within subjects ANOVA with *Cue* (Opposite, Actual) x *Emotion* (Sad, Happy) for the number of errors revealed a main effect of *Cue*, $F(1,29)=49.17$, $p<.001$, $\eta_p^2=0.62$, due to more errors after "opposite" compared to the "actual" cues (*p*s<.001). No other main or interaction effects yielded a significant effect (*p*s>.05).

Related to our research question, we observed no correlations between inter-individual differences in brooding tendencies and RT for each of the CECT trial types separately, *β*s<.63, *p*s>.31. Moreover, there was no association between brooding scores and the number of errors on each of the CECT trial types, *p*s>.50.

Brain imaging data

Whole brain analyses. For an overview of the results of the regression analysis see Table 1. Paired *t*-tests were performed for trials where participants needed to inhibit a dominant response to emotional information versus trials were they needed to simply name the emotion contrast [opposite-sad vs. opposite-happy] > [actual-sad vs. actual-happy]). Results demonstrated significantly more neuronal activity in the right prefrontal areas (DLPFC: BA 9, BA 46) during opposite trials.

Regression analyses confined to individual scores on depressive brooding. For an overview of the results of the regression analysis see Table 2. When inter-individual brooding scores were related to the whole-brain contrast for opposite-sad vs. actual-sad (inhibiting compared to engaging to a dominant response following negative information), we observed a positive correlation within the left anterior cingulate cortex (ACC, see Table 2). Peak activation was located in the posterior part of the left dorsal ACC (BA 24, based on MNI brain atlas). According to Etkin et al. (2011), this is the posterior dorsal (pd)ACC. When inter-individual brooding scores were correlated with the whole-brain contrast for opposite-happy vs. actual-happy, we observed a negative correlation within a similarly located cluster of voxels in the left pdACC and the postcentral gyrus (see Table 2). Most important, we investigated brooding-related differences in activation during the inhibition of negative versus the inhibition of positive information, always towards the opposite emotion (opposite-sad vs. opposite-happy). Whole-brain contrast demonstrated a positive correlation again within the same pdACC neural cluster (cluster size=107; Figure 2). A scatter plot of the extracted contrast values ruled out the possibility of the correlation being driven by outliers. It is important to note

that the cluster of the left anterior cingulate cortex activation was similar over each regression analysis described above. Finally, we also observed a positive correlation within the post central gyrus (cluster size=96). These findings confirm that more attention was required for high brooders when inhibiting negative compared to positive information. No other brain areas yielded significant voxels (Ke > 66).

[Insert Table 1/2 and Figure over here]

Correlations with reflection scores, the other subscale of the RRS, with the different contrasts revealed no interpretable cluster of brain activation (i.e., no cluster was larger than 66 voxels). In addition, similar correlations with BDI scores revealed only white matter cerebral activation. Therefore, all these correlations suggest that the association between inhibiting negative/positive information and dACC activation patterns is specific for participants with elevated depressive brooding scores. For all of these correlations with brooding tendencies, we observed no voxels within the DLPFC or other prefrontal brain regions.

Discussion

The aim of the current study was to investigate how inter-individual differences in depressive brooding are related to neural correlates of conflict processing in response to emotional information. We selected a sample of healthy participants, without confounds of negative mood or prior depressive episodes, to investigate functional cognitive mechanisms associated with depressive brooding.

Behavioral data revealed that, overall, participants were biased towards positive information: they were (1) faster in naming the actual valence, but (2) slower in naming

the opposite valence in response to an emotionally positive stimulus (both relative to a response to negative information). This tendency in healthy non-depressed individuals to attend to positive information is in line with several studies (for a review, see Murphy & Isaacowitz, 2008). At the neural level, participants recruited more dorsal activation when inhibiting a dominant response to an emotional stimulus as compared to simply giving the emotional response (no interaction with emotion was observed).

Inter-individual differences in depressive brooding scores were not correlated with behavioral performances on CECT trials. In contrast, whole brain analyses revealed that the contrast maps were correlated with individual differences in depressive brooding. The higher the depressive brooding scores, the more activation in the dACC when inhibiting a response to negative relative to positive information. Specifically, depressive brooding was positively associated with a cluster of voxels within the posterior part of the dACC (pdACC, Etkins et al., 2011) when responding with the opposite emotion following a sad face relative to responding to the opposite emotion of a happy face (contrast opposite-sad vs. opposite-sad). Moreover, brooding scores were positively correlated with neural activation within the pdACC during the inhibition relative to the naming of negative information (contrast opposite-sad vs. actual-sad) which defeats the possibility that brooding is solely associated with the processing of negative information. Interestingly, brooding scores were also negatively correlated during the inhibition (relative to the naming) of a dominant response to positive information (opposite-happy vs. actual-happy). This means that high brooders needed less pdACC activation when inhibiting a dominant response to positive facial expressions in order to move towards negative information. This is the reverse pattern as compared to the

inhibition of negative information, and underscores the emotional specificity of our brooding related observations. For this latter contrast, we also observed activation in the postcentral gyrus, which is the primary somatosensory gyrus. At this point, it remains unclear why this region was activated during a pure cognitive control task using emotional facial expressions. Finally, the correlation of reflection (a more adaptive ruminative response) and BDI (an indication of depressive symptoms) with brain activation during the CECT did not yield any significant cluster of voxels that are associated to depressive brooding. This means that the neural activation within the pdACC during the inhibition of a dominant response towards positive and negative information seem typically for depressive brooding, and not for depressive symptoms.

Brooding scores were consistently associated to a cluster of voxels within the posterior parts of the left dorsal ACC (BA 24). This latter brain structure is implicated in the detection of conflict and response inhibition, and is usually activated when the presented stimulus interferences with the goal relevant response (Botvinick et al., 2001; Egner & Hirsch, 2005). Moreover, the pdACC region is implicated in top-down forms of attentional regulation (Etkin et al., 2011), both for emotional and non emotional information. Therefore, based on the present neuroimaging findings, it might be that task-irrelevant negative information interferes more in high versus low depressive brooders, even in never depressed individuals. As a result, high depressive brooders might need more mental resources to successfully inhibit a dominant response to negative information and move towards goal relevant positive content. These results lend further support to the conclusions of research showing that higher rumination scores were associated to a behavioral difficulty to inhibit the processing of emotionally

negative material, both in healthy volunteers and depressed patients (Joormann & Gotlib, 2010; Joormann, 2006).

It is interesting to observe that healthy volunteers that report a tendency to brood over negative information need to recruit more neural activation within the dorsal circuitry when inhibiting negative information (in order to move towards positive), but behaviorally perform as good as low brooders. Prior studies have shown preserved behavioral performance together with enhanced neural activation within regions associated with cognitive control in major depressed patients compared with healthy controls (Harvey et al., 2005; Wagner et al., 2006; Langenecker et al., 2007). These findings have been explained in the context of reduced cognitive efficiency versus effectiveness (Derakshan, Ansari, Hansard, Shoker, & Eysenck, 2009). More specifically in the current study, habitual brooders seem less efficient when employing neural regions associated to cognitive control, especially when inhibiting a dominant response to negative information. This is because high brooders needed more activation in the pdACC when inhibiting negative information, but this augmented neural activation was not associated to better behavioral performance (e.g., no association with behavioral speed in high brooders). This means that for the same effectiveness of apparent behavioral performance, high brooders (as compared to low brooders) were less efficient in using neural regions that are typically associated to inhibitory control (e.g., dorsal system).

A flourishing literature is pointing at a crucial mechanism of cognitive inhibition underlying rumination (Koster et al., 2011), which in turn predicts the onset of depressive episodes (Nolan et al., 1998). Cognitive (inhibitory) control is however

considered neurobiologically heterogeneous and associated with distinctive neural pathways (Joormann et al., 2007; Dillon & Pizzagalli, 2007). Neural activation therefore largely depends on the experimental task that is being used. As a result, although the current findings are in line with our prior neuroimaging study (Vanderhasselt et al., 2011) (e.g., brooding scores are positively associated with neural activation in the dorsal system), the neural activation appeared in a different region of the dorsal circuitry (DLPFC vs. pdACC). This dissimilarity might be a result of different task designs and dependent variables that were being used in both studies. The current task design is related to conflict processing (which is typically related to the ACC), whereas the paradigm we used in our former study was used to test cognitive inhibition (without a response towards other material). The added value of this study is that, besides the fact that it replicates the general findings of our prior study, it also shows emotion specific findings for depressive brooding: (1) more neural activation when inhibiting a dominant response to negative in favor of positive information, but (2) less neural activation when inhibiting a dominant response to positive in favor of negative information. This emotion specific finding highlights the interaction between cognition and emotion in depressive brooding.

As mentioned in the introduction, the processing of negative information in healthy volunteers who report to ruminate has been associated with increased amygdala activation (Ray et al., 2005), a crucial brain region within the ventral circuitry. According to the mediation hypothesis (Wager et al., 2008), dorsal regions send feedback signals to the ventral system in order to suppress emotional processing (Taylor & Fragopaganos, 2005). Indeed, a large number of studies suggest that the

dorsal system initiates emotion regulation by down-regulating of the amygdala (e.g., Siegle, Thompson, Carter, Steinhauer, & Thase, 2007), and that a failure to inhibit amygdala activation by dorsal systems is associated with a cognitive bias to negative (threatening) information (Fales et al., 2008). Moreover, major depressive disorder is characterized by a failure of dorsal areas to regulate ventral emotion producing systems (Mayberg, 1997; Phillips, Drevets, Rauch, & Lane, 2003). Our findings regarding brooding related activation in the dorsal circuitry suggest that high brooders need to recruit more cognitive control to inhibit a response to negative information, and consequently down-regulate amygdala activation that is activated during the processing of negative information. This neural compensation to successfully inhibit a dominant/habitual response to negative information might be a mechanism to effectively evade negative vicious cycles (a cognitive style that makes individuals vulnerable to develop sustained negative mood). Therefore, future research should focus on the functional connectivity between DLPFC/dACC and limbic regions in order to investigate the emotion-cognition interplay underlying depressive brooding as a trait thinking style in depressed and non-depressed volunteers. Moreover, it might be interesting to investigate whether these functional interactions between dorsal and ventral systems predict future psychopathology, even in never depressed healthy volunteers that report a tendency to brood over negative thoughts and feelings. Finally, given that we are the first to report brooding related neural activation during this specific cognitive control task, it is challenging to interpret the specific lateralization pattern of our results. However, the fact that cognitive control deficits in depressed patients have been related to the left hemisphere (Holmes & Pizzagalli, 2008a,b) and that depressed individuals show the

tendency to brood might explain our lateralized results. Future research should further investigate the association between depressive brooding scores and the lateralization of neural activation in the dorsal system (e.g., functional connectivity between ACC/DLPFC and amygdala).

Some limitations of the current study should be emphasized. First, it has to be noted that our participants were young females (18-30 years old), and that a replication in an older population without a history of depression would strengthen our interpretation. Moreover, in order to draw conclusions about the relation with the development of future psychopathology, it would be important to investigate cognitive control adjustments in a sample of healthy well-functioning volunteers, but with a higher risk to develop depression in the future (e.g. people with two depressed parents, or specific genetic markers). Moreover, a larger sample would enable to perform connectivity analyses.

In closing, the findings from the present study demonstrate that healthy individuals who report a tendency to brood over negative information show more dorsal activation when successfully inhibiting a habitual response toward negative compared to positive information. Possibly, the observed pdACC activation represents a mechanism that characterizes high depressive brooders - but who have never been depressed - who need to inhibit a habitual response when confronted with negative information in favor of a positive response. The current data link cognitive control to depressive brooding and add to the growing literature on the relationship between fundamental cognitive processes and higher order thinking styles.

Acknowledgement

This research was supported by a grant from the Scientific Fund W. GeptsUZBrussel. MAV (FWO08/PDO/168) is a postdoctoral fellow of the Research Foundation Flanders (FWO).Preparation of this paper was supported by Grant BOF10/GOA/014 for a Concerted Research Action of Ghent University (awarded to RDR). This work was also supported by the Ghent University Multidisciplinary Research Partnership “The integrative neuroscience of behavioral control”. The authors declare no conflicts of interest. The authors want to thank Maud Grol for her assistance in collecting the data.

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Table 1. Results of the whole brain analyses for the T-contrast [opposite-sad/opposite-happy] versus [actual-sad/actual-happy] at *p*(uncorrected)<.005, k ≥66 (based on AlphaSim, based on Monte Carlo simulations). For each cluster, we reported the T-value and MNI coordinates at the position of the maximum, the cluster size and the appropriate Brodmann area (BA).

Activation pattern	Cluster size	Anatomical region	Hemisphere	BA	Peak *t* value	Peak coordinates (x,y,z) (mm)
	75	Pyramis	Right	-	4.31	24 -80 -32
	86	DLPFC	Right	9	4.14	52 20 26
	168	DLPFC	Right	9/46	4.06	50 38 18
	81	Parietal lobe	Right	40	3.91	52 -34 32
	75	Cerebellum	Left	-	3.34	-24 -86 -14

Table 2: Results of the whole brain regression analysis (slope >< 0) for each of the four T-Contrasts. We listed only those clusters with a significance of *p*(corrected)<0.005 and a cluster size≥66 (based on AlphaSim, based on Monte Carlo simulations). For each cluster, we reported the T-value and MNI coordinates at the position of the maximum, the cluster size and the appropriate Brodmann Area (BA).

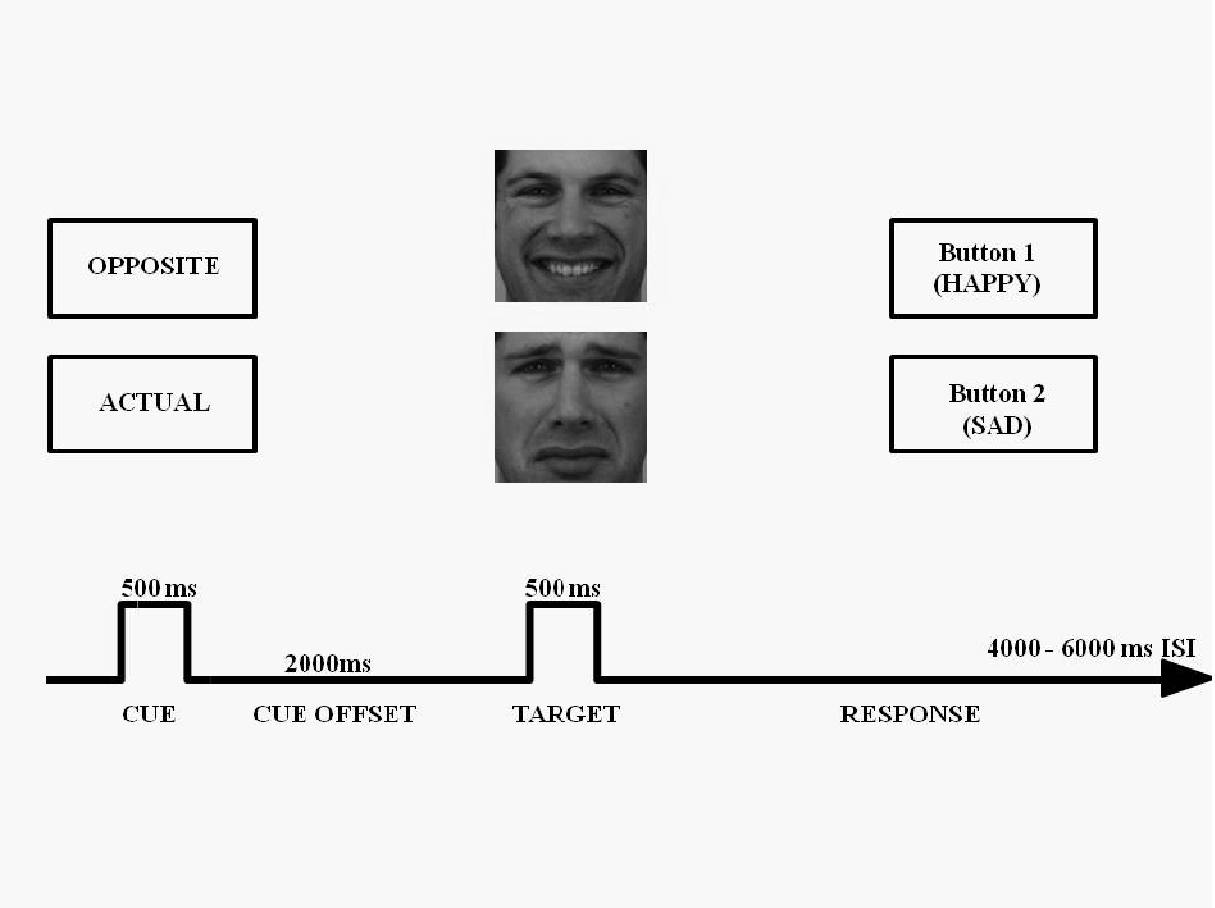
Contrast	Slope	Cluster size	Anatomical region	Hemisphere	BA	Peak T value	Peak coordinates (x,y,z) (mm)
opposite-sad vs. opposite-happy	**positive**	107	Cingulate gyrus	left	24	4.20	-14, -14, 36
		96	Postcentral Gyrus	left	3	4.01	-28, -34, 44
	negative	*NV*					
opposite-sad vs. actual-sad	**positive**	103	Cingulate Gyrus	left	31	4.22	-14, -34, 34
		76	Cingulate gyrus	left	24	4.04	-14, -14, 36
	negative	*NV*					
opposite-happy vs. actual-happy	**positive**	*NV*					
	negative	118	Cingulate gyrus	left	24	4.20	-24, -10, 34
		102	Postcentral Gyrus	left	3	4.15	-28, -34, 44
		68	Cingulate gyrus	right	24	3.75	14, -8, 30

NV = No significant clusters emerged

Figure captions

Figure 1: Schematic overview of the Cued Emotional Conflict Task (CECT). First, a cue is presented in the center of the screen (“actual” or “opposite”), followed by a face with an emotional expression (happy or sad).

Figure 2: The significant cluster in red (BA24; xyz coordinates: -14, -14, 36) from the positive regression analysis for the opposite-sad / opposite-happy in relation to individual brooding scores at (*p*(corrected)<.005 and a cluster size≥ 66 voxels.



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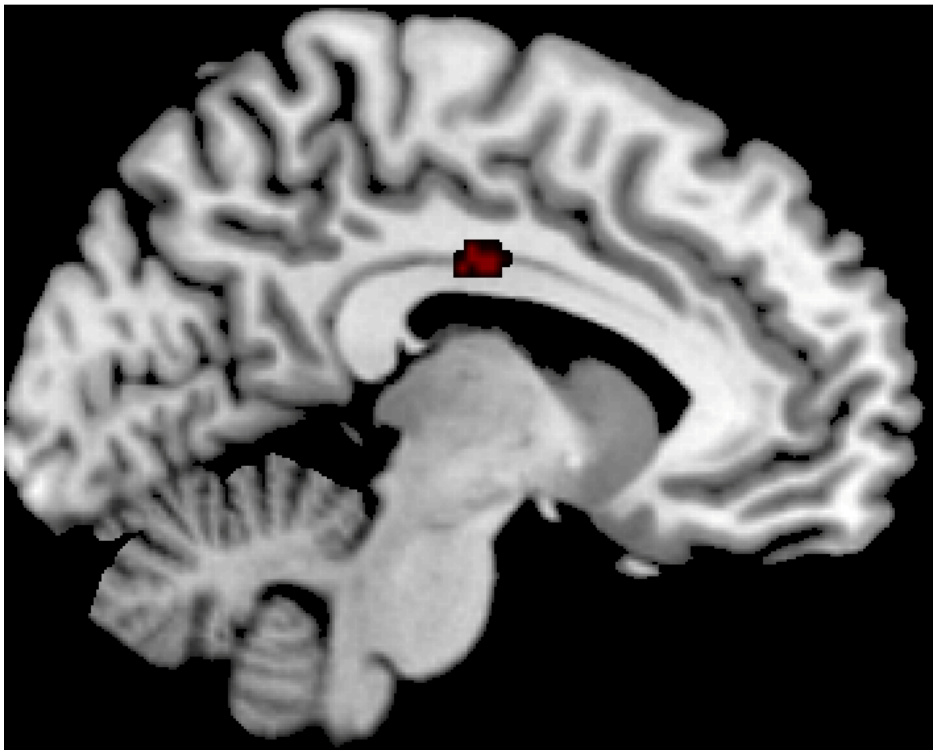

Figure 2: The significant cluster in red (-14, -14, 36, BA 24 according to MNI atlas) from the positive regression analysis for the opposite-sad / opposite-happy in relation to individual brooding scores at (*p*(corrected)<.005 and a cluster size≥ 66 voxels.