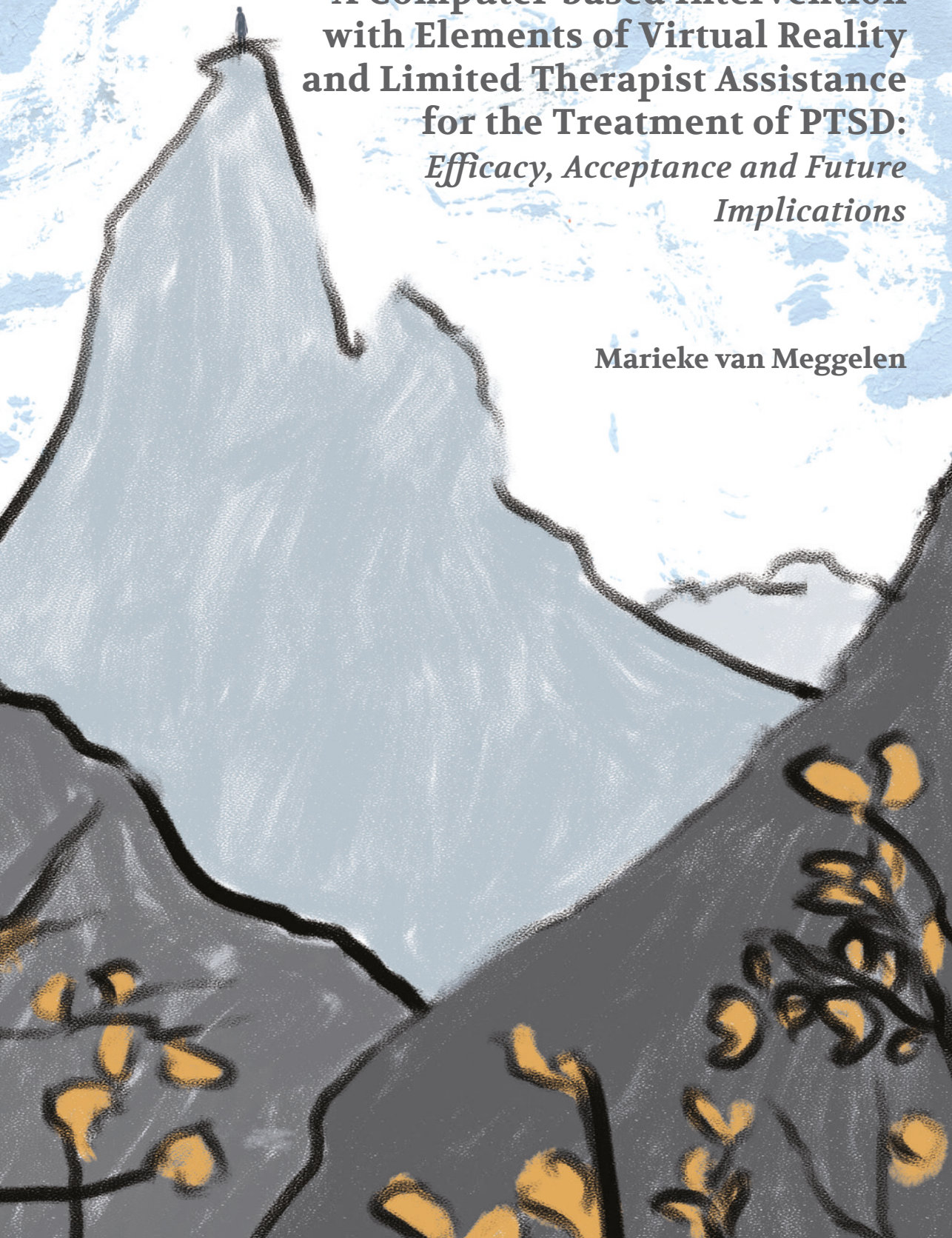
A Computer-based Intervention with Elements of Virtual Reality and Limited Therapist Assistance for the Treatment of PTSD:

Efficacy, Acceptance and Future Implications

Marieke van Meggelen



A Computer-based Intervention with Elements of Virtual Reality and Limited Therapist Assistance for the Treatment of PTSD:

Efficacy, Acceptance and Future Implications

Marieke van Meggelen

Cover design by Elisa Calamita, persoonlijkproefschrift.nl
Layout by Elisa Calamita, persoonlijkproefschrift.nl
Printing: Ridderprint BV | www.ridderprint.nl
ISBN: 978-94-6375-491-0

The research presented in this dissertation was funded by NWO as part of the Virtual eCoaching and Storytelling technology for post-traumatic stress disorder treatment (VESP) project (no. 314-99-104).

A Computer-based Intervention with Elements of Virtual Reality and Limited Therapist Assistance for the Treatment of PTSD:

Efficacy, Acceptance and Future Implications

Een computergestuurde interventie met elementen van Virtual Reality en beperkte therapeut ondersteuning voor de behandeling van PTSS: Werkzaamheid, acceptatie en toekomstig gebruik

PROEFSCHRIFT

ter verkrijging van de graad van doctor aan
de Erasmus Universiteit Rotterdam

op gezag van de rector magnificus

Prof. dr. R.C.M.E. Engels

en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden
op 15 november 2019 om 13:30

door

Marieke van Meggelen
geboren te Leiden

Erasmus University Rotterdam

Promotiecommissie

Promotoren:

Prof. dr. I.H.A. Franken
Prof. dr. C. van der Heiden
Prof. dr. N. Morina

Overige leden van de commissie:

Prof. dr. R.C.M.E. Engels
Prof. dr. M.J. Wieser
Prof. dr. A. van Minnen

Copromotor:

dr. ir. W.P. Brinkman

Contents

1

General Introduction

"Every day my father picked me up from primary school so I didn't have to walk home alone. Every day he stopped and parked the car, so he could rape me before we arrived home."

Angela, a 51-year old victim of childhood sexual abuse

Introduction

Some experiences from the past haunt people for many years. In the United Stated the lifetime prevalence of exposure to a potential traumatic event is estimated between 50% and 70% (Kessler, Sonnega, Bromet, Hughges, & Nelson, 1995; Resnick, 1993). In a minority of cases, traumatic experiences induce a post-traumatic stress disorder (PTSD). The estimated lifetime prevalence of PTSD in the United States is estimated between 6.8% and 12.3% (Kilpatrick et al., 2013; Kessler, Berglund, Demler, Merikangas, & Walters, 2005; Kessler et al., 1995; Resnick, et al. 1993). In European countries the estimates tend to be lower, whereas results show a lifetime prevalence of PTSD of 1.9% (Alonso et al., 2004). However, in countries with a recent history of war (such as Kosovo, Iran, Cambodia, Croatia and Lebanon), no less than one fourth of the population is estimated to suffer from PTSD and/or depression (Morina, Stam, Pollet, & Priebe, 2018). The impact of PTSD can be widespread and its effects on daily life are tremendous. After a potential traumatic event, people with PTSD typically re-experience the traumatic event unwantedly by memory flashbacks or nightmares. Also, they feel anxious, are irritable, and avoid memories of the event (American Psychiatric Association, 2013). In general, the majority of individuals with PTSD fail to recover even after many years (Morina, Wicherts, Lobbrecht, & Priebe, 2014). Cognitive behavioral therapy (CBT) approaches have been widely examined and approved for the treatment of PTSD for diverse types of trauma (Bradley, Greene, Russ, Dutra, & Westen, 2005). Trauma focused CBT, together with Eye Movement Desensitization Reprocessing (EMDR), is currently regarded as the most effective psychological treatment for PTSD (Cusack et al., 2016; Morina, Koerssen & Pollet, 2016). Trauma focused CBT's focus on the memory of the trauma and/or its meaning (Morina et al., 2016). In trauma focused therapies exposure to the traumatic memories or cues for the traumatic event often plays an important role in reducing symptoms of PTSD (Rauch & Foa, 2006). In EMDR, the patient is asked to hold the distressing image in mind, along with the associated negative cognition and bodily sensations, while engaging in saccadic eye movements. The current standard of both CBT's and EMDR consists of at least 8 to 12 weekly sessions with a therapist lasting 60 to 90 minutes (Cusack et al., 2016) and can therefore be seen as therapist intensive. The current approaches however, seem to have an insufficient reach amongst help seeking individuals.

Seeking help and barriers

Although there are effective psychological treatments available, only a minority of the people who could benefit from these treatments receive help. It is reported that less than a third of American people with any mental disorder receive mental health service within one year (Regier, Narrow, Rae, Manderscheid, Locke, Goodwin, 1993). Also, Hoge et al. (2004) studied over 6000 subjects of four U.S. combat infantry units and found that only 23-40% of the respondents that met criteria for a mental disorder, sought help. Lewis et al. (2005) have reported that only 18.9% of rape victims in a National Women's Study sought formal or informal help for their PTSD or major depressive episode. There are good reasons to assume that in general barriers to seek and receive help when one suffers from mental health problems, are high. Amongst other things these numbers reflect fear of stigmatization, fear to be seen as weak or to be treated differently (e.g., Regier, Narrow, Rae, Manderscheid, Locke, Goodwin, 1993; Hoge et al., 2004). Besides this, a well-known problem in mental health care is that of waiting lists. When people do get cross their initial restraints and seek help, they often get caught up in waiting times of several months, which are currently commonplace. These waiting times have even resulted in numerous reports warranting change (e.g., Mental Health Foundation [MHA, 2018]; Nederlandse Zorg Autoriteit [NZA, 2017]). From a global perspective, factors as confined access to mental health care due to long travel distances or financial restraints and a limited number of available therapists are current. Altogether, the above indicates the need for interventions that may improve the effectiveness, cost-effectiveness, and accessibility for individuals with PTSD.

As mentioned before, exposing the patients to the traumatic memories or cues for the traumatic event plays an important role in effective treatments for PTSD. Exposure can be offered imaginary (i.e., by thinking about a traumatic event) or in vivo (e.g., by creating an actual real life confrontation with [elements of a] a traumatic event). Another way to offer exposure therapy is by Virtual Reality Exposure Therapy (VRET). VRET uses computer-generated environments to simulate feared stimuli. In these virtual environments, users can be systematically exposed to specific stimuli within a contextually relevant setting, for example a warzone or airplane for soldiers with war-related PTSD (Parsons & Rizzo, 2008). Over the years virtual reality systems have become less costly, more available, and generally more user-friendly (Parsons & Rizzo, 2008). This has led to more applications for the treatment of anxiety disorders, resulting in several studies describing positive treatment outcomes for several disorders, among which PTSD (e.g., Carl et al., 2018).

When looking for manners to enlarge treatment accessibility, computerized and internet-based interventions need to be considered. These interventions are often known

for their ability to reach large groups of people. They have several benefits compared to traditional therapy; often they are personalized and tailored to the needs of a diverse group of users, they can reach a large population at relatively low cost and they can be used from a person's own home (Amstadter. Broman-Fulks, Zinzow, Ruggiero, & Cercone, 2009). This could potentially overcome many of the barriers mentioned above. Generally, computer-based interventions yield comparable effect sizes as traditional psychosocial interventions in the treatment of depression and anxiety (Carlbring, Andersson, Cuijpers, Riper, & Hedman-Lagerlöf, 2018). Differences exist in the extent to which assistance is offered during these interventions (e.g., no, administrative, or therapist assistance; Richards & Richardson, 2009). Interventions that require only limited therapist involvement can potentially improve cost-effectiveness. By now the efficacy of internet health interventions in general has been validated for a number of health problems such as social anxiety (Kampmann, Emmelkamp, & Morina, 2016), depression (e.g ., Kenwright, Liness, Marks, 2001; Marks, Kenwright, McDonough, Whittaker, & Mataix-Cols, 2004) and post-traumatic stress disorder (PTSD, e.g., Carlbring et al., 2018; Heber et al., 2017; Karyotaki et al., 2018). Nevertheless, several challenges lay ahead.

First of all, studying the efficacy of these interventions is an ongoing process in which we have to keep asking ourselves whether we offer help seeking individuals the most sufficient treatment options. Another challenge is the acceptance of this form of treatment by both patients and therapists. The International Society for Research on Internet Interventions (ISRII; Ritterband et al., 2006) describes the enhanced level of acceptance by government and medical insurers of the feasibility and value of diverse computer-based interventions, such as Beating the Blues for depressive disorders (e.g., Kenwright et al., 2001; Marks et al., 2004) and Fear Fighter for anxiety disorders (McCrone et al., 2004; Proudfoot et al., 2004). They also mention this acceptance as an essential step in establishing this mode of treatment delivery (via computers and the internet) and recommend that, along with investigating how these interventions compare with more traditional forms of treatment delivery, also their acceptance in the community should be studied.

Multi Modal Memory Restructuring (3MR) system

This dissertation examines the efficacy, acceptance and future implications of a computer-based trauma intervention with elements of VR and limited therapist involvement for the treatment of PTSD, offered via the *Multi Modal Memory Restructuring* (*3MR*) system. The *3MR* system was originally designed by Brinkman, Vermetten, Van de Steen, and

Neerincx (2011) and is a software application which focuses on the restructuring and relearning of past events. The *3MR* system allows people to visualize past events using personal photos, narrative texts, online geographical maps and patient-created 3D virtual worlds. The *3MR* system consists of a period overview and a diary, which contains the tools 'Text', 'Images', 'Website', 'Media', 'Webcam' and '3D world'. The *3MR* system and an accompanying therapy manual are used to guide patients through 12 therapy sessions targeting the traumatic memories of the participant.

The aims of this dissertation

The current dissertation describes a series of four studies, which overall aim to investigate the efficacy, acceptance and future implications of the *3MR* intervention for the treatment of PTSD. **Chapter 2** describes the current state of art of the field of VRET for the treatment of PTSD and forms the starting point of this dissertation. In a meta-analysis we analyzed ten clinical trials that compared VRET with active or inactive control conditions among patients with PTSD. This information provides a basis for **Chapter 3** in which we study the efficacy of the *3MR* intervention in a randomized controlled trial (RCT) amongst traumatized victims of childhood sexual abuse (CSA) and war veterans. We compared the effects of the *3MR* intervention to those of more regular treatment methods ('treatment as usual' [TAU]), which consisted of evidence-based approaches such as imaginal exposure, EMDR, or narrative exposure therapy. After this, **Chapter 4** is aimed at gathering more detailed knowledge about the working mechanisms of the *3MR* intervention, since this is considered useful for future research and possible utilization in mental health care. For that purpose, the added value of the multimedia tools of the *3MR* system to writing exercises that were aimed at reducing distress, negative affect and intrusions as a result of a negative but not traumatic memory were studied in another RCT amongst a healthy student population. Finally, **Chapter 5** provides first indications into the patients' and therapists' acceptance of the *3MR* intervention and elaborates on the future implications of these findings.

2

Virtual Reality Exposure Therapy for the Treatment of PTSD: A Meta-Analysis

This chapter is submitted as:
Van Meggelen, M., Morina, N., Van der Heiden, C., Brinkman, W.P., Arends, L.R., & Franken, I.H.A.

(submitted). Virtual Reality Exposure Therapy for the Treatment of PTSD: A Meta-Analysis

Abstract

Over the last decades multiple studies have found promising outcomes using Virtual Reality Exposure Therapy (VRET) for the treatment of post-traumatic stress disorder (PTSD). We conducted a meta-analytic review of clinical trials that compared VRET with active or inactive control conditions among patients with PTSD. Overall, 337 records were found in the Scopus database and ten of these met our inclusion criteria. Results suggest that VRET conditions do not differ from the active treatment conditions regarding decrease of symptoms of PTSD (g = -0.136 [-0.391; 0.118], n.s. [p = .294]). Compared to inactive treatment conditions, VRET did significantly better (g = 0.545 [0.257; 0.832], p < .001). For comorbid depression, a similar pattern was seen (VRET vs. active control, g = -0.059 [-0.414; 0.296], n.s. p = .744 and VRET vs. inactive control [g = 0.499 (0.206; 0.793), p = .001]). These findings support the therapeutic value of VRET in the treatment of PTSD. However, the findings are confined by a limited number of includable studies, which all differed widely in terms of VRET intervention, control condition, sample size and study design. Therefore, future research should be aimed at overcoming these limitations.

Keywords: *Virtual Reality, posttraumatic stress disorder, treatment outcome, meta-analysis, depression*

Introduction

Waking up haunted by nightmares, paralyzed by anxiety, and hindered by excessive vigilance; a post-traumatic stress disorder (PTSD) can be widespread and the effects can have a detrimental impact on daily life. In the United States the lifetime prevalence of exposure to a potential traumatic event is estimated between 50 and 70% (Kessler, Sonnega, Bromet, Hughges, & Nelson, 1995; Resnick, 1993). Only a minority of people with a history of traumatic experiences develop PTSD afterwards. The estimated lifetime prevalence of PTSD in the United States is estimated between 6.8% and 12.3% (Kilpatrick et al., 2013; Kessler, Berglund, Demler, Merikangas, & Walters, 2005; Kessler et al., 1995; Resnick, et al. 1993). In European countries, the estimates tend to be lower; results from the European Study of the Epidemiology of Mental Disorders show a lifetime prevalence of PTSD of 1.9% (Alonso et al., 2004). However, in countries with a recent history of war (such as Kosovo, Iran, Cambodia, Croatia and Lebanon), about one fourth of the population is estimated to suffer from PTSD and/or depression (Morina, Stam, Pollet, & Priebe, 2018). Individuals with PTSD often also suffer from comorbid psychiatric disorders. In particular, depression has been reported as a common comorbid disorder, with estimates that about half of individuals with PTSD also suffer from depression (Flory & Yehuda, 2015).

Cognitive behavioral therapy (CBT) approaches have been widely examined and approved for the treatment of PTSD for diverse types of trauma (e.g., adult/childhood sexual abuse, combat exposure; Bradley, Greene, Russ, Dutra, & Westen, 2005). Trauma focused CBT, together with EMDR, is currently regarded as the most effective psychological treatment for PTSD (Cusack et al., 2016; Morina, Koerssen & Pollet, 2016). One of the key elements of CBT is the exposure to the traumatic stimuli or memory (Rauch & Foa, 2006). There are several methods to achieve exposure and exposure in vivo is found to have greater efficacy when compared to imaginable exposure, especially when treating specific phobias (Emmelkamp, 2003). Despite the advances in the treatment of PTSD, in general more than one third of the people that suffer from PTSD fail to recover even after many years. This effect is seen in both people who seek help and those who do not (Kessler et al., 1995). Also, therapy drop-out rates are high, sometimes even up to 45% (Schottenbauer, Glass, Arnkoff, Tendick, & Hafter Gray, 2008). Additionally, barriers to seek mental health care generally seem high: less than a third of American people with any mental disorder receive mental health service within one year (Regier, Narrow, Rae, Manderscheid, Locke, Goodwin, 1993). More specifically, Hoge et al. (2004) found that amongst 6201 subjects of four U.S. combat infantry units (deployed either to Iraq or Afghanistan) only 23-40% of the respondents that met criteria for a mental disorder, sought help. Similarly, Lewis et al. (2005) reported that only 18.9% of rape

victims in a National Women's Study sought formal or informal help for their PTSD or major depressive episode.

The above indicates the need for easily accessible effective methods to treat PTSD. Technological innovations, such as Virtual Reality Exposure Therapy (VRET), might meet that need. Unlike the above-mentioned traditional forms of exposure therapy, which utilize imaginal, in vivo, or interoceptive stimuli, VRET uses computer-generated environments to simulate feared stimuli. In these virtual environments users can be systematically exposed to specific stimuli within a contextually relevant setting, for example a warzone or airplane for soldiers with war-related PTSD (Parsons & Rizzo, 2008). During the last decades, virtual reality systems have become less costly, more available and generally more user-friendly (Parsons & Rizzo, 2008), leading to more applicability in treating anxiety disorders. This has resulted in positive treatment outcomes for the treatment of anxiety disorders (e.g., Morina, IJntema, Meyerbröker & Emmelkamp, 2015) and PTSD in particular (e.g., Gamito et al., 2010; Parsons & Rizzo, 2008). VRET, in comparison to exposure in vivo, has several advantages such as that it provides the possibility of generating gradual assignments (sequence and intensity of treatment), and of creating idiosyncratic exposure (Powers & Emmelkamp, 2007).

VRET is usually offered using a head-mounted display (HMD) equipment and virtual reality systems specific for the patient target groups. The first publications on VRET for PTSD emerged in the late 90's and focused on Vietnam veterans and accompanying scenery (e.g., Rothbaum et al. 1999). Ever since the field of VRET for PTSD has broaden. For example, Difede et al. (2007) use a scenery of lower Manhattan and computer simulation of the September 11th attacks on the WTC in treatment of traumatized civilians and disaster workers exposed to these attacks. Gamito et al. (2010) use a VRET world consisting of a footpath surrounded by dense vegetation with the option of adding ambush, mortar and evacuation cues, to resemble experiences of Portugese elderly war veterans. Ultimately, Virtual Iraq and Afghanistan (Gerardi, Rothbaum, Ressler, Heekin, & Rizzo, 2008; Rizzo et al., 2010) are examples of VRET worlds developed especially for American military personnel who have served in the U.S. government's OEF (2001) and OIF (2003) operations in the Middle East. These interventions underline the broad range of possibilities that VRET equipments have at its disposal, since they include auditory stimuli (e.g., weapon fire, helicopter flyovers and radio), visual stimuli (night vision, wounded civilians and wrecked vehicles), olfactory stimuli (e.g., burning rubber, diesel fuel) and even tactile stimuli (i.e., vibration). Also the patient uses a hand-held controller to move forward within the environment. However, other utilities with for example a computer screen are used as well. An example is the unspecific virtual environment *EMMA's World*, designed to promote emotional processing (Baños, Guillen, Quero, Garcia-Palacios, Alcaniz, & Botella, 2011; Botella, Garcia-Palacios, Guillen, Baños,

Quero, & Alcaniz, 2010). EMMA's World consists of EMMA's Room, the Book of Life and several virtual surroundings. Following the patient's emotions, time of day and the weather in the virtual world can be adjusted (Botella et al. 2010).

The current meta-analysis provides an updated review on the efficacy of VRET interventions for the treatment of PTSD. In a systematic review, Gonçalves et al. (2012) included ten studies that used VRET to conduct exposure in CBT treatment for PTSD. They found that VRET for the treatment of PTSD is potentially promising, but still a new field of research with several limitations (e.g., only few studies available in the literature, no standardized number of therapy sessions and the non-use of intent-to-treat analysis). Nelson (2013) indicated similar results comparing six studies on the efficacy of VRET for the treatment of service members and war veterans of the U.S. Army. Also, Motraghi, Seim, Meyer, & Morissette (2013) conducted a literature review on this topic. They included nine unique studies and concluded that VRET may serve as a preferable treatment alternative for individuals avoiding treatment due to stigmatization, and may further offer a greater verisimilitude to traumatic scenarios, which possibly improves extinction and habituation to both discrete as contextual stimuli. These reviews report promising results, but also highlight limitations. For example, Gonçalves et al. (2012) included only four randomized controlled trials (RCTs) with very small sample sizes (ranging from 10 [$n = 2$] to a maximum of 20 participants [$n = 1$]). Motraghi et al. (2013) warranted that further research should use well-specified randomization procedures, assessor blinding, and monitoring of treatment adherence. These indications are in line with findings of Page and Coxon (2016) highlighting the perception that the strength of the evidence base of VRET treatments is weakened by three key methodological limitations; a) the use of small sample sizes, b) a lack of appropriate control groups, and c) a lack of RCTs ([a] e.g., McLay et al., 2014; Castro et al., 2014; Morina et al., 2015, [b] e.g., Nelson, 2013; McCann et al., 2014, and [c] e.g., Nelson, 2013; McCann et al., 2014). Especially for studies on the treatment of PTSD, the limitations are more likely to be present (Page & Coxon, 2016). To illustrate the topic of sample size in this field of research; in their meta-analysis on the efficacy of VRET for the treatment of anxiety and specific phobias, Parsons and Rizzo (2008) included 21 studies (including two studies focusing on VRET for PTSD) and concluded that although the reported effect sizes were high (e.g., $r = 0.82$ for PTSD), in future research sample sizes should not be lower than 30 participants in order to achieve adequate power (≥ 0.80).

To date, no meta-analysis has been conducted on the efficacy of VRET in the treatment of PTSD. Therefore, the scope of the current study is to examine the efficacy of VRET for PTSD using a meta-analytic approach. To this end, we focused on clinical trials that reported treatment outcome data comparing VRET with any kind of comparison group. It is expected that VRET interventions will gain better results in reducing PTSD

symptoms than inactive control conditions. With respect to the comparison to active control conditions, we expect no significant differences between the conditions.

Method

Identification and selection of studies

The literature search was conducted by the first author (MM). A comprehensive search strategy was used by searching Scopus 1996 to January, 2018. The following search terms were used: "posttraumatic stress disorder", "PTSD" AND "VR", "virtual", "computer simulation", "computer application", "human machine systems", "internet-based", "computer-based", "computerized" AND "treatment", "therapy", " intervention" OR "exposure" AND "outcome", compared", "comparison" OR "control". These terms were searched in key words, title or abstract. To ensure the search was comprehensive, we looked at references cited in each of the identified articles. Special attention was paid to previous aggregated literature on this topic (e.g., literature and methodological reviews) to make sure no key articles were missed-out. We included peer reviewed journal articles on the effects of VRET for the treatment of PTSD in a controlled setting. Accordingly, we included trials that compared VRET with an 'active' (other treatment, such as CBT or EMDR) or 'inactive' (such as Waitlist or Minimal Attention [MA]) comparison group.

Data coding

Information on the following variables was coded: (1) Population (e.g., military, civilian); (2) study design (e.g., randomized controlled trial, parallel case series); (3) control condition ('active' vs. 'inactive'); (4) type of VRET intervention ('VRET with HMD' vs. 'elements of VRET'); (5) dependent variables (e.g., 'PTSD measurement' [CAPS, PCL-R]), (6) sample size (total N, experimental group N, control group N), (7) demographics (age, gender), and (8) summary statistics required for analysis (i.e., M/SD Pre PTSD score condition VR/EXP, M/SD Post PTSD score condition VR/EXP).

Quality Assessment

Two independent assessors (MM and NM) assessed the quality of the trials based on what was reported in the included publications. To this end, we used a checklist constructed by Cuijpers, van Straten, Bohlmeijer, Hollon, and Andersson (2010) and adjusted by Smit et al. (2012). This checklist has been used in meta-analyses on the efficacy of psychotherapy for PTSD (e.g., Morina, Lancee, & Arntz, 2017). The original criteria by Cuijpers et al. (2010) were based on an authoritative review of empirically supported psychotherapies (Chambless & Hollon, 1998), and on the criteria proposed by

the Cochrane Collaboration to assess the methodological validity of a study by Higgins and Green (2006; Cuijpers et al. 2010). Studies were rated using the following questions: 'Was the diagnosis determined using a semi-structured interview?', 'Was a treatment manual used?', 'Were therapists trained either specifically for the study or in a general training?', 'Was treatment integrity checked by supervision and/or recordings and/or standardized instruments?', 'Were data analyzed with intent-to-treat analysis?', 'Was it a randomized study?', 'Was randomization done by an independent third person (or computer or sealed envelopes)?', 'Were blinded assessors used for interviews?', and 'Were dropouts adequately reported?'. Items were rated on a scale ranging from -1 (Not Applicable, NA) to in some cases 3 (YES). For example the question 'Were drop-outs reported adequately?' could be rated as -1. NA (e.g., retrospective study), 0. Unknown, 1. NO, 2. YES, but not distinguishing type of dropout, or 3. YES (distinguishing treatment & study dropout). Initial inter-rater agreement was 97.3%, and the reviewers met to resolve the few scoring discrepancies by discussing the criteria as suggested by Cuijpers et al. (2010).

Statistical analysis

Random effects models were used to compute summarize effect sizes for all the outcome measures studied, thereby taking heterogeneity across studies into account (DerSimonian & Laird, 1986; Van Houwelingen, Arends, & Stijnen, 2002). Hedges' *g* was reported since this effect size provides a better estimate of effect sizes based on small samples as compared to Cohen's *d* (Field & Gillet, 2010). Hedges' *g* was interpreted conservatively according to Cohen (1988), with 0.2 indicating a small, 0.5 a medium, and 0.8 a large effect. Hedges' *g*s from different studies were pooled to calculate the benefit of VRET compared to an 'active' (other treatment, such as CBT or EMDR) or 'inactive' (Waitlist, Minimal Attention [MA]) comparison group on the measurement of symptoms of PTSD and of symptoms of depression. Of the ten included studies, two studies (Gamito et al. [2010] and Reger & Gahm [2016]) describe two comparison groups besides the VRET condition; an active and inactive control group. To encounter for these groups, these studies were entered twice into analysis, once with the active control ('author'_a), once with the inactive ('author'_b).

Subgroup analyses and sensitivity analyses were performed to understand the 'robustness' of the data and to find possible sources for study heterogeneity. In the subgroup analyses, the following study characteristics were compared: Difference in population (e.g., active duty soldiers or veteran vs. civilian), study design (e.g., RCT vs. parallel case series) and the comparison between different PTSD measurements used (e.g., CAPS vs. PCL-R).

To define the extent of publication bias, the Duval and Tweedie trim-and-fill test (Duval & Tweedie, 2000) and the Egger test (Egger, Smith, Schneider, & Minder, 1997) were applied to quantify the level of bias. All analyses were performed with Comprehensive Meta-Analysis statistical software (version 2.2.064; Biostat, Englewood, NJ).

Results

Overall search findings

The initial search led to 337 hits. A title and abstract review of these hits excluded 305 hits. However, full text assessment of the remaining 32 hits revealed that seven articles did not include a control group, two reported preliminary data better represented in a later (and therefore included) article, one described the same sample as represented in another article describing the PTSD subsample of that group (which was therefore included), four described case studies and six were non-experimental reviews or editorials. Furthermore, two articles did not have a PTSD measurement as primary outcome measure. Altogether, ten studies met inclusion criteria and could therefore be included. Studies included are randomized controlled trials ($n = 7$), a semi randomized controlled trial ($n = 1$), a head to head randomized trial ($n = 1$) and a parallel case series ($n = 1$). Most studies examined active duty soldiers or veterans ($n = 7$), and three studies a civilian trauma population (see Figure 1 for more information). Details about the included studies can be found in Table 1.

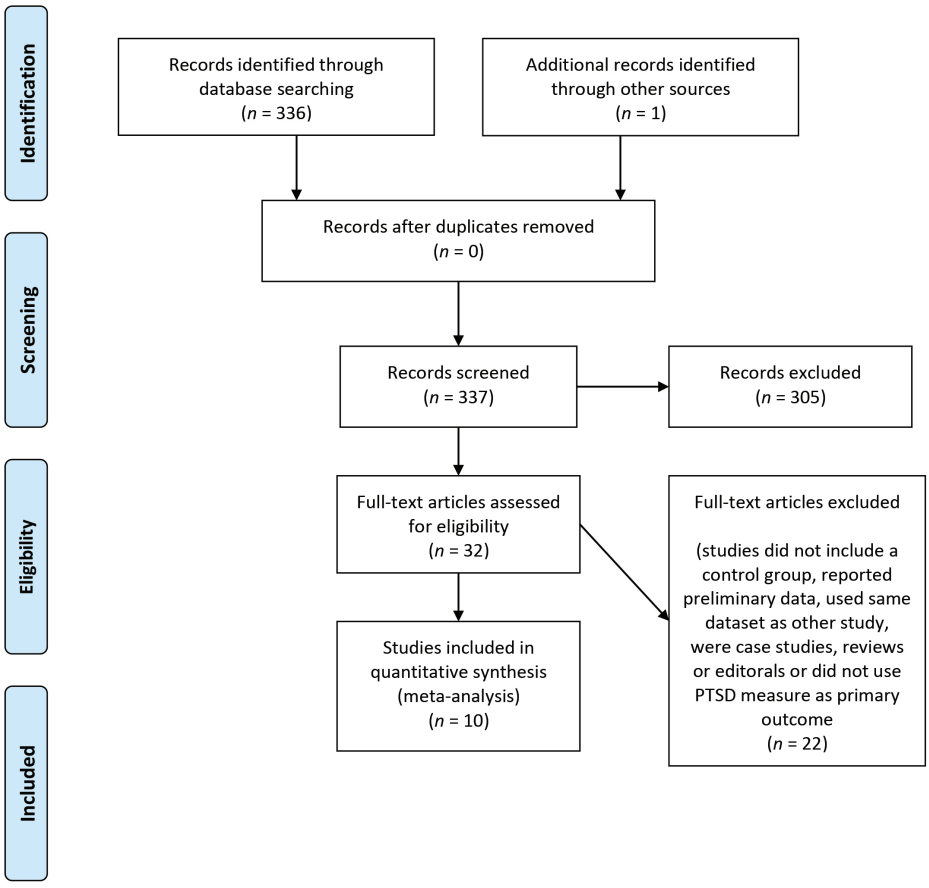


Figure 1: PRISMA Flowchart of the process of identifying and selecting studies.

Table 1: VRET Comparison Studies for PTSD

Study	Participants	Male gender %	Study design	VRET environment & equipment	Control condition	PTSD measures	Total N
Baŝoğlu (2007)	Civilians who experienced an earthquake	13%	RCT	Earthquake simulator	Repeated Assessments (RA)	CAPS total	31
Botella (2010)	Civilians who experienced car accidents, robbery, assault or domestic violence	20%	RCT	Customized symbols and personalized imagery with projectors and screen, wireless pad and speakers	Cognitive Behavioral Therapy (CBT)	CAPS total	10
Difede (2007)	Civilians and disaster workers exposed to 9/11 terrorist attacks	86%	Semi RCT	VR Helmet and tracking system with a scenery of lower Manhattan	Waitlist (WL)	CAPS total	18
Gamito (2010)	Portugese colonial war veterans	100%	RCT	VR HMD with three types of cues Ambush (A), Mortar (M), and Evacuation (E)	Imaginal Exposure (IE)/ Waitlist (WL)	CAPS total	10
McLay (2017)	Active duty military in Iraq and Afghanistan	96%	Head-to-head randomized trial	VR HMD with joystick controller and a version of Virtual Iraq or Afghanistan	Control Exposure Therapy (CET)	CAPS total	85
McLay (2010)	Active duty military in Iraq	100%	Parallel case series	VR HMD with joystick controller and a version of Virtual Iraq or Afghanistan	Exposure Therapy (ET)	PTSD Checklist (PCL) Military (M)	10
McLay (2011)	Active duty military in Iraq and Afghanistan	95%	RCT	VR HMD with joystick controller and a version of Virtual Iraq or Afghanistan	Treatment As Usual (TAU)	CAPS total	20
Ready (2010)	Vietnam veterans	100%	RCT	VR HMD with audio, joystick controller (two versions of a Vietnam war scenery)	Present-Centered Therapy (PCT)	CAPS total	11
Miyahira (2012)	Active duty military in Iraq and Afghanistan	94.5%	RCT	VR HMD with tracking, 3D computer generated-combat environment	Minimal Attention (MA)	CAPS total	22
Reger (2016)	Active duty soldiers with PTSD from deployments to Iraq and Afghanistan	96%	RCT	VR HMD with inertia cube orientation tracker, headphones, bass shaker speakers platform and a version of Virtual Iraq or Afghanistan	Prolonged Exposure (PE) / Minimal Attention-Waitlist (MA-WL)	CAPS total (week)	162

Note: CAPS = *Clinician Administered PTSD Scale*; *RCT = Randomized Controlled Trial; VR HMD = Virtual Reality Head Mounted Display*

Quality Assessment Outcome

Table 2 describes the primary outcomes of the quality assessment conducted by two independent raters (NM and MM). The results indicate a good satisfactory level of quality for most of the publications, with five publications (50%) receiving an average item score of two or higher. On average six out of nine items were coded with a mean of higher than two. The three items rated less favorably were: independent randomization (M = 0.9), check of treatment integrity (M = 1.1), and blinded assessment (M = 1.5).

Table 2: Evaluation of Treatment Comparison Studies Using a Variation on Cuijpers et al. (2010)

	Diagnosis semi structured interview	Use of treatment manual	Therapist training	Treatment integrity check	Use of intent-to-treat analysis	Randomization	Randomization by 3rd person/party	Blinded assessors	Report of dropout
Baŝoğlu et al. (2007)	2	2	3	1	3	3	3	2	3
Botella et al. (2010)	2	2	2	2	0	3	0	0	3
Difede et al. (2007)	3	2	3	2	1	2	0	2	3
Gamito et al. (2010)	2	0	0	0	0	3	0	1	3
McLay et al. (2017)	2	3	3	2	3	2	1	3	3
McLay et al. (2010)	1	3	2	1	3	1	-1	-1	3
McLay et al. (2011)	2	3	2	0	1	3	3	2	3
Ready et al. (2010)	2	0	0	0	1	3	0	3	3
Miyahira et al. (2012)	2	0	3	0	1	3	0	0	3
Reger et al. (2016)	3	3	3	3	3	3	3	3	3

Note: 0 = NO / Unknown; 1 = NO; 2 = YES, but; 3 = YES; -1 = Not Applicable (NA)

The effect of treatment on symptoms of PTSD

When comparing the VRET conditions with the seven active treatment conditions, there was no significant difference between VRET and the comparison groups on the measurement of symptoms of PTSD (g = -0.136 [-0.391; 0.118], n.s. [p = .294]). See Figure 1.

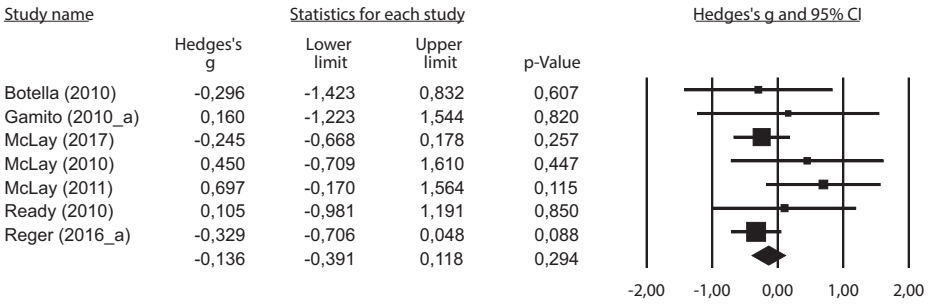


*Figure 1: Forest plot of effect sizes comparing experimental conditions to active control conditions (*n = *7) at posttreatment PTSD measurement*

Furthermore, the comparison of VRET conditions to the five inactive treatment conditions led to a medium effect in favor of VRET (g = 0.545 [0.257; 0.832], p < .001). See Figure 2.

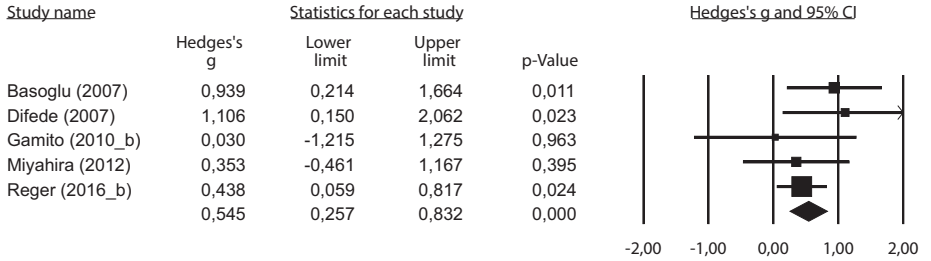


*Figure 2: Forest plot of effect sizes comparing experimental conditions to inactive control conditions (*n = *5) at posttreatment PTSD measurement*

The effects of treatment of symptoms of depression

Five out of ten studies also provided outcome data of depression measurements. When comparing the VRET conditions with the two active treatment conditions, there was no significant difference between VRET and the comparison groups on the measurement of symptoms of depression (g = -0.059 [-0.414; 0.296], n.s. p = .744). See Figure 3.

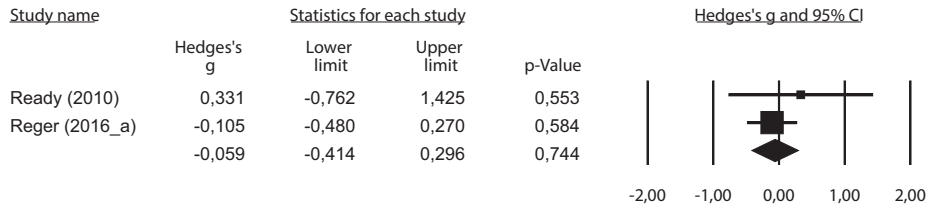


*Figure 3: Forest plot of effect sizes comparing experimental conditions to active control conditions (*n = *2) at posttreatment depression measurement*

However, when comparing the VRET conditions with the four inactive treatment conditions, there was a significant difference between VRET and the comparison groups on the measurement of symptoms of depression (g = 0.499 [0.206; 0.793], p = .001). This was a medium effect in favor of VRET. See Figure 4.

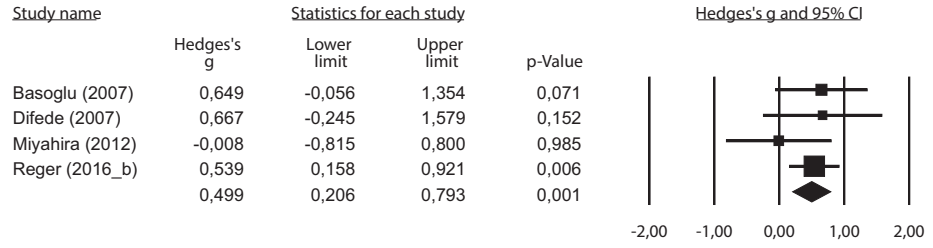


*Figure 4: Forest plot of effect sizes comparing experimental conditions to inactive control conditions (*n = *4) at posttreatment depression measurement*

Additional analyses

There were no significant subgroup differences between the pooled effect sizes of the active duty or veterans population versus the civilian/other population, nor between the parallel case series design versus RCT, nor between CAPS total versus PCL-M.

Publication bias

We assessed publication bias for the seven studies comparing VRET to active treatment conditions regarding symptoms of PTSD through visual inspection of the funnel plot. This provided some indication for publication bias. Trim and fill procedure introduced three studies to the left side, but after this adjustment the effect only got stronger from g = -0.136 (-0.391; 0.118), n.s. (p = .294) to g = -0.252 (-0.578; 0.073), n.s., Egger's regression intercept (t[5] = 2.12, p = .088). There was no publication bias detected considering the comparison of VRET conditions to the five inactive treatment conditions regarding symptoms of PTSD (Egger's regression intercept [t(3) = .40, p = .717]).

Since there were only two studies involved for the comparison of the VRET conditions to the active treatment conditions in terms of depression symptoms, no publication bias could be calculated here. Furthermore, there was hardly any publication bias detected when comparing the VRET conditions with the four inactive treatment conditions considering depression symptoms; the effect barely changed after adjustment for publication bias (trim and fill procedures suggested one imputed study on the left side), from g = 0.499 [0.206; 0.793], p = .001 into g = 0.480 [0.201; 0.759], p = .001, Egger's regression intercept: t[2] = 0.377, p = .742. Overall, publication bias did not seem to influence the outcomes of this meta-analysis.

Discussion

This meta-analysis reviewed the current available literature on the efficacy of VRET interventions for the treatment of PTSD. During the last decades, VRET systems have become less costly, more available and generally more user-friendly (Parsons & Rizzo, 2008), leading to more applicability in treating anxiety disorders. This has resulted in positive treatment outcomes for the treatment of anxiety disorders (e.g. Morina et al., 2015) and PTSD in particular (e.g. Gamito et al., 2010; Parsons & Rizzo, 2008). Although almost two decades have passed since the first studies on VRET interventions for the treatment of PTSD have appeared (e.g. Rothbaum et al., 1999), this field is still in a relatively early stage of research. The number of randomized controlled trials on VRET is limited, the existing trials mostly consist of small sample sizes and there exists a lack of standardized treatment methods (e.g. Gonçalves et al., 2012; Nelson, 2013; Motraghi et al., 2013; Page

& Coxon, 2016). For this reason, this meta-analysis focuses on all studies that investigated the efficacy of VRET for PTSD in comparison to any kind of control condition.

Considering the results of this meta-analysis, we hypothesized that looking at the decrease of PTSD symptoms over time, VRET conditions would do significantly better than inactive control conditions, but equally good compared to active control conditions. Our results suggest that when VRET is compared to active control conditions, indeed no differences in treatment efficacy between VRET and active conditions could be observed. Our second finding is that VRET significantly outperformed the inactive control conditions, as expected. Compared to placement on a waitlist (WL) or doing as less as possible (MA), VRET seems significantly more effective in reducing PTSD symptoms. We found the same pattern of results for comorbid depression, but these data were only reported in five out of ten included studies. These results do not appoint VRET as a replacement for other trauma-focused therapies, but do highlight the added value of VRET as a good alternative for people with PTSD who might be hesitant or not able to receive regular trauma-focused therapy.

This meta-analysis has several limitations. First, only ten studies met eligibility criteria and were included in this meta-analysis. Only five out of ten studies provided depression outcome data besides the data on PTSD symptoms. Second, although deliberately put together, the included studies in this meta-analysis are very diverse. A possible point of critique can be that this meta-analysis employs liberal inclusion criteria resulting in a very heterogeneous sample of included studies, all using very different techniques. However, it does give a representative display of an emerging research field, which is inevitably associated with different approaches in terms of techniques, sample size, and number of therapy sessions for example. Focusing on the added value of using a meta-analytic approach for the first time in synthesizing the current available study data, we do consider this unavoidable.

Furthermore, although quality assessment showed an overall satisfactory level of study set up, most studies use small sample sizes. If we follow the criterion set by Parsons and Rizzo (2008) and assume that sample sizes that are below 30 participants are considered small, only three out of ten included studies would have satisfactory sample sizes ($n = \geq 30$). Ultimately, this warrants the need for larger controlled studies on the efficacy of VRET. However, this meta-analysis also shows a positive trend with larger sample sizes in recent studies, for example Reger et al. (2016; $n = 162$) and McLay et. al. (2017; $n = 85$).

In view of future research, this meta-analysis underlines the findings of previous overview articles (e.g., Gonçalves et al., 2012; Nelson, 2013; Mothragi et al., 2014; Page & Coxon, 2016), that although results of VRET for PTSD are promising, larger sample sizes, more controlled studies and standardized treatment methods and studies are needed. However, it also shows that over time VRET for PTSD consistently shows positive treatment results and it seems that recent studies already tend to show an increase of sample sizes. Therefore, it is appropriate to conclude this review with a very hopeful note for future developments.

3

A Randomized Controlled Trial on the Efficacy of a Computer-based Intervention with Elements of Virtual Reality and Limited Therapist Assistance for the Treatment of Post-traumatic Stress Disorder

This chapter is submitted as:
Van Meggelen, M., Morina, N., Van der Heiden, C., Brinkman, W.P., Yocarini, I.E., ... & Franken, I.H.A.

(submitted). A Randomized Controlled Trial on the Efficacy of a Computer-based Intervention with Elements of Virtual Reality and Limited Therapist Assistance for the Treatment of Post-traumatic Stress Disorder

Abstract

Although well-established therapies for post-traumatic stress disorder (PTSD) exist, barriers to seek mental health care are high. Technology-based interventions may play a role in improving the effectiveness, cost-effectiveness, and reach of efforts to treat, especially when therapist availability is low. The goal of the current randomized controlled trial was to evaluate the efficacy of a computer-based trauma intervention with elements of virtual reality (VR; *3MR* system) and limited therapist involvement for the treatment of PTSD in a childhood sexual abuse (CSA) and veteran sample and to compare this to 'treatment as usual' (TAU). TAU consisted of evidence-based approaches such as imaginal exposure, EMDR, or narrative exposure therapy. A total of 44 patients with PTSD were included. Patients were randomly assigned to either 12 sessions of *3MR* intervention or TAU. Self-report questionnaires (PCL-5, BDI-II, and OQ-45-2) and a semi-structured clinical interview (M.I.N.I. 5.0.0.) were administered to measure symptoms of PTSD and depression and scores of overall well-being at pre, post, and a three month follow-up measurement. Results show that symptoms of PTSD and depression both significantly decreased between pre and post measurements (after 12 sessions *3MR* or TAU). There was no significant difference found between the two treatment conditions. Similar results were found for the increase of overall well-being. Finally, both treatment conditions produced similar remission rates of PTSD and depression. The computer-based *3MR* intervention seems effective for the treatment of PTSD and similarly effective to evidence-based PTSD treatments. Therefore, *3MR* may constitute an appropriate treatment alternative, especially when therapist availability is lowered and the intention to enlarge reach of treatment efforts and improve cost-effectiveness are present.

Keywords: *Post-traumatic stress disorder, treatment, intervention, computer-based, computer-controlled, VR, low therapist assistance, veterans, childhood sexual abuse*

Introduction

Around 7-8% of all people suffer from the effects of a post-traumatic stress disorder (PTSD) during their life (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; De Vries & Olff, 2009). After a potential traumatic event such as a sexual assault, or violent experiences during war, people with PTSD typically re-experience the traumatic event unwantedly by means of memory flashbacks or nightmares. Also, they feel anxious, are irritable, and avoid memories of the event (American Psychiatric Association, 2013). Research shows that sexual abuse and rape are the most common causes of PTSD amongst women (Kessler et al., 1995), while for men, this is exposure to direct war violence (Kessler et al., 1995). Childhood sexual abuse (CSA), defined as sexual contact involving an adult and a child, has been reported in large numbers by both men and women (Forns, Pereda, Gomez-Benito, & Guilera, 2009). A meta-analysis comparing more than 200 studies shows that prevalence numbers worldwide for girls are between 16.4%-19.7% and for boys between 6.6%-8% (Stoltenborgh, Van IJzendoorn, Euser, & Bakermans-Kranenburg, 2011). Considering exposure to direct war violence, Fulton et al. (2015) reported a prevalence of 23% for PTSD amongst Operation Enduring Freedom (OEF) / Operation Iraqi Freedom (OIF) veterans. Dirkzwager and Bramsen (2008) found that amongst Dutch veterans prevalence numbers of PTSD due to traumatic war experiences range from 2%-8%. They also found that around 15% of the veterans experience symptoms of PTSD, but do not meet the criteria for a full diagnosis. Epidemiological surveys further indicate that about one fourth of civilian war survivors suffer from PTSD (Morina, Stam, Pollet, & Priebe, 2018).

In general, the majority of individuals with PTSD fail to recover even after many years (Morina, Wicherts, Lobbrecht, & Priebe, 2014). Also, barriers to seek mental health care are high. Less than a third of American people with any mental disorder receive mental health service within one year (Regier, Narrow, Rae, Manderscheid, Locke, Goodwin, 1993). Hoge et al. (2004) found that amongst 6000 subjects of four U.S. combat infantry units, only 23-40% of the respondents that met criteria for a mental disorder, sought help. Lewis et al. (2005) reported that only 18.9% of rape victims in a National Women's Study sought formal or informal help for their PTSD or major depressive episode. Besides this, a well-known issue in mental health care is that of waiting lists. Waiting times of several months are commonplace, and have resulted in numerous reports warranting change (e.g., Mental Health Foundation [MHA, 2018]; Nederlandse Zorg Autoriteit [NZA, 2017]).

There are widely examined and approved therapies for PTSD, such as cognitive behavioral therapy ([CBT], Cusack et al., 2016). In CBT, exposure to the traumatic memories or cues for the traumatic event often plays an important role in reducing symptoms of PTSD (Rauch & Foa, 2006). In general, exposure in vivo (e.g., confronting

fear of spiders by approaching real spiders) is found to have the best efficacy when for example compared to imaginary exposure (i.e., thinking about a fearful spider in the case of fear of spiders), especially when treating specific phobias (Emmelkamp, 2003). However, for PTSD treatment, exposure in vivo might often be difficult to establish, mainly due to practical reasons such as high costs (e.g., travelling to other countries). Also, it might be dangerous to return to the original surroundings of the traumatic event (i.e., in case of a warzone).

To summarize, there is need for interventions that may improve the effectiveness, cost-effectiveness, and accessibility for individuals with PTSD. When looking at innovative manners to offer exposure therapy, Virtual Reality Exposure Therapy (VRET) seems promising. VRET uses computer-generated environments to simulate feared stimuli. In these virtual environments, users can be systematically exposed to specific stimuli within a contextually relevant setting, for example a warzone or airplane for soldiers with war-related PTSD (Parsons & Rizzo, 2008). Over the years virtual reality systems have become less costly, more available, and generally more user-friendly (Parsons & Rizzo, 2008). This has led to more applications for the treatment of anxiety disorders, resulting in several studies describing positive treatment outcomes for several disorders, among which PTSD (e.g., Carl et al., 2018). Indeed, in a recent meta-analysis, Van Meggelen, Morina, Van der Heiden, Arends, and Franken (submitted) compared ten clinical trials on the efficacy of VRET for the treatment of PTSD. They found that VRET for PTSD significantly outperformed inactive control conditions and did not differ from active control conditions. However, these results are confined by a limited number of relevant trials.

Considering the need for accessible treatments, computer-based interventions are known for their ability to reach large groups of people. This type of intervention has several benefits compared to traditional therapy; they are often personalized and tailored to the needs of a diverse group of users, they can reach a large population at relatively low cost and they can be used from a person's own home (Amstadter. Broman-Fulks, Zinzow, Ruggiero, & Cercone, 2009). Generally, computerized interventions yield comparable effect sizes as traditional psychosocial interventions in the treatment of depression and anxiety (Amstadter et al., 2009; Carlbring, Westling, Ljungstrand, Ekselius, & Andersson, 2001; Proudfoot et al., 2003; Proudfoot et al., 2004). Differences exist in to what extend assistance is offered during these interventions (e.g., no, administrative or therapist assistance; Richards & Richardson, 2009). Interventions that require limited therapist involvement can potentially improve cost-effectiveness.

The current study examined the efficacy of a computer-based trauma intervention with elements of VR and limited therapist involvement for the treatment of PTSD, offered via the *Multi Modal Memory Restructuring* (*3MR*) system. The *3MR* system was originally

designed by Brinkman, Vermetten, Van de Steen, and Neerincx (2011), and is a software application, which focuses on the restructuring and relearning of past events. The *3MR* system allows people to visualize past events using personal photos, narrative texts, online geographical maps and patient-created 3D virtual worlds.

The goal of the current randomized controlled trial was to (1) evaluate the efficacy of a computer-based trauma intervention with elements of VR (*3MR* system) and limited therapist assistance for the treatment of PTSD in a CSA and veteran sample; and (2) to compare this to 'treatment as usual' (TAU). We therefore tested whether the treatments significantly decreased symptoms of PTSD, and if the outcome of the *3MR* treatment was different from TAU.

Method

Procedure

Patients were either victims of childhood sexual abuse (CSA) or war veterans. They enrolled for treatment via the specialized mental health care centers of PsyQ (locations Rotterdam-Kralingen, Spijkenisse, and The Hague), Reinier van Arkel (Psychotrauma Centrum Zuid-Nederland), and the ambulatory of the Erasmus University Rotterdam (Department of Clinical Psychology). Potential participants that presumably met in- and exclusion criteria were given a detailed information sheet about the project. There were at least five days between the first and second consultation so that potential participants had the chance to (re-)consider whether they truly wanted to participate in this study. If individuals were interested in participation, they filled in an informed consent. After consent the in- and exclusion criteria were checked in an extensive interview by telephone (see 2.2 Participants and flow).

This study had a randomized controlled design. The control condition was 'treatment as usual' (TAU). Randomization was conducted after inclusion (see 2.4 Participant assessment and randomization). Participants were assessed at pre-treatment, post-treatment, and follow up measurements. The first follow-up assessment was conducted at 3 months post-treatment and consisted of a repetition of the primary and secondary outcome measures and a semi-structured clinical interview to respectively determine PTSD and depression symptom levels and overall well-being and check the criteria for meeting the diagnosis of PTSD and/or depression. At 12-months post treatment, another follow-up measurement was conducted, this assessment is ongoing and is not further described in the present study. Between the last session of the *3MR* system and the 3-month follow-up participants were instructed to not seek other forms of therapy unless indicated by the therapist. In the control condition, this restriction was not given due to practical reasons. Participants

were not compensated for their contribution to the study and were free to leave the study at any time and (in the *3MR* condition) receive TAU instead.

The procedures of this study were approved by the Medical Ethical Research Committee (MERC) of the Erasmus Medical Center in Rotterdam (MEC-NL46279.078.13) and pre-registered via ClinicalTrials.gov (Protocol Record CI1-12-S028-1).

Participants and flow

Victims of CSA could have either single or multiple/recurrent traumatic experiences. Experiences that occurred between 0-18 years old were considered 'childhood sexual abuse'. Recruited veterans presumably served (a) Dutch military mission(s) in Lebanon, Bosnia-Herzegovina, Iraq, or Afghanistan. Participants were excluded if they met criteria for a current bipolar disorder, current psychotic episode, if they were actively suicidal (defined as 'high risk' according to the Mini International Neuropsychiatric Interview Plus - Dutch Version 5.0.0 [MINI Plus 5.0.0., Sheehan et al., 1997; Van Vliet, Leroy, & Van Meegen, 2000]), or scored a total score of ≥ 40 on the *Dissociative Experiences Scale* (DES, Bernstein & Putnam, 1986). Co-morbidity as such was not an exclusion criterion, but PTSD had to be the primary diagnosis[1] according to the MINI Plus 5.0.0. Use of medication was no exclusion criterion, provided that dose was stable for at least two weeks at the beginning of the therapy, remained stable throughout therapy, and was closely monitored.

Following pre-screening, a total of 83 patients were referred via the participating mental health care centers. Of the 83 individuals that were contacted by the researchers, 48 registered interest in the study. Of these 48 individuals, three did not meet in- and exclusion criteria and one could not join the study due to practical reasons (not able to follow therapy sessions at home). See Figure 1 for a flow of the participants through the trial.

Participants were aged between 20 and 62 years, with an average age of 39 years. Forty-eight percent was female, 47.7% had previously followed therapy, and 43.2% took prescription drugs during the study period. See Table 1 for participant descriptives specified per treatment condition (*3MR* and TAU). Table 2 shows that independent samples *t*-tests revealed no significant baseline differences between conditions. A total of 14 patients dropped out of the study. See also Figure 1 and section 4.3 Drop-out analysis. Thirteen individuals could be classified as therapy drop-out, whereas one individual dropped out because of practical reasons. See Figure 1.

---

1 Initially, it was agreed to include patients that met criteria for the diagnosis of PTSD and/or Depression (according to the M.I.N.I. 5.0.0.) as primary diagnosis. However, since recruitment took place at the trauma departments of the participating mental health care centers, only one patient did not meet criteria for the diagnosis of PTSD (only for Depression) at initial screening and inclusion. Therefore, the main focus of the article is on PTSD (e.g., background, introduction, discussion).

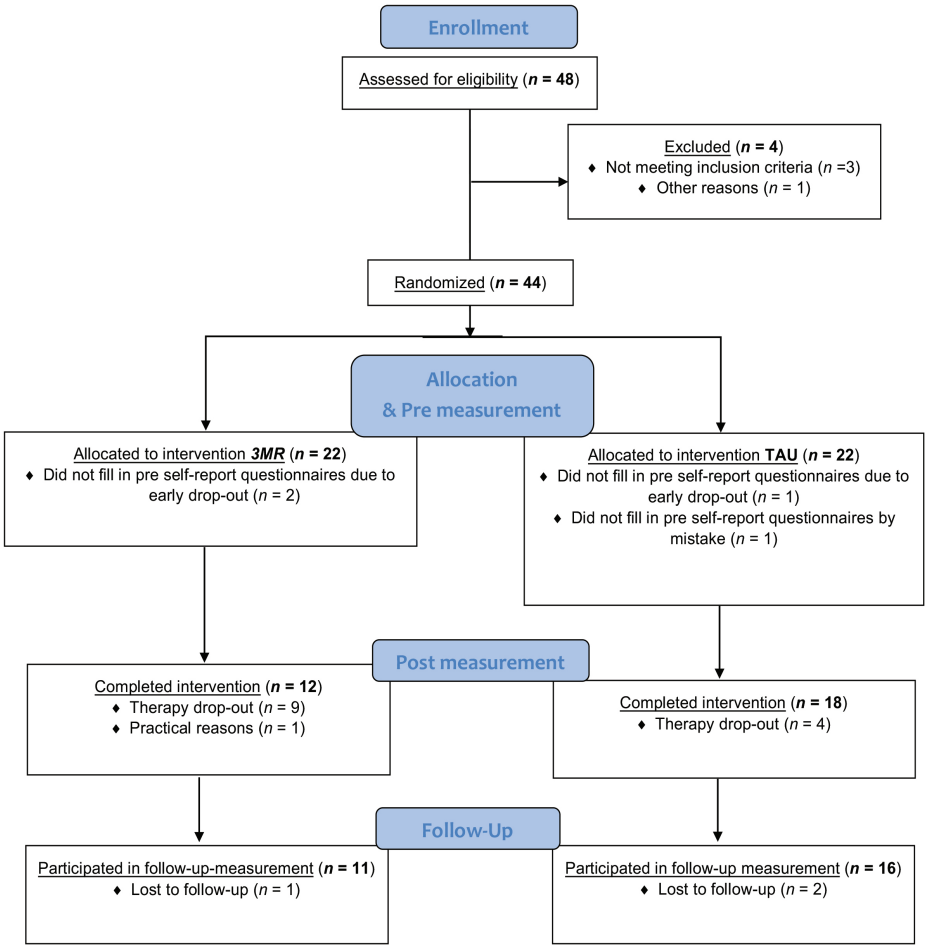


Figure 1: Flow chart of participants through the study

Table 1: Descriptive statistics of patients in 3MR and TAU conditions

Condition	*N*	Age* *M (SD)*	Male gender %	Trauma group (CSA or veteran)	Previous therapy %	Medication** %	Pre PCL-5 *M (SD)*	Pre BDI-II *M (SD)*	Pre OQ-45-2 *M (SD)*
3MR	22	42.05 (12.15)	50.0%	54.5% CSA 45.5% Veteran	59.1%	48.8%	45.45 (13.41)	25.56 (7.92)	85.10 (25.32)
TAU	22	36.55 (10.43)	55.5%	54.5% CSA 45.5% Veteran	40.1%	51.2%	49.10 (10.22)	28.95 (9.37)	86.40 (16.56)

Note: **Missing age and pre measurement PCL-5, BDI-I-II and OQ-45-2 data* n = *4 (*3MR *[*n = *20], TAU [*n = *20]). **Missing Medication data* n = *1 (*3MR *[*n = *21], TAU [*n = *22]). CSA = Childhood Sexual Abuse; PCL-5 = PTSD Checklist for the DSM 5; BDI-II-NL = Beck Depression Inventory – Second Edition; OQ-45-2 = Outcome Questionnaire – 45 – Second Edition;* 3MR = *Multi Modal Memory Restructuring; TAU = Treatment as Usual*

Table 2: Independent samples t-test baseline (pre) differences between 3MR and TAU condition

	t	*df*	*p*
*Age**	-1.536	38	0.133
Gender	-0.295	42	0.769
Trauma group	0.000	42	1.000
Previous therapy	-1.198	42	0.238
*Medication***	0.167	41	0.868
PCL-5	0.968	38	0.399
BDI-II	1.240	38	0.223
OQ-45-2	0.192	38	0.849

Note: *Missing age and pre measurement PCL-5, BDI-I-II and OQ-45-2 data* n = *4 (*3MR *[*n = *20], TAU [*n = *20]). **Missing Medication data* n = *1 (*3MR *[*n = *21], TAU [*n = *22]).* 3MR = *Multi Modal Memory Restructuring; TAU = Treatment as Usual; PCL-5 = PTSD Checklist for the DSM 5; BDI-II-NL = Beck Depression Inventory - Second Edition; OQ-45-2 = Outcome Questionnaire – 45 – Second Edition*

Participant assessment and randomization

Patients were screened and measured by independent, but not blinded, assessors**.** Eligible patients were randomized assigned to two conditions by an independent researcher via a random-numbers table and its allocation sequence was computer-generated. A stratified randomization procedure was employed for clients with CSA or war related PTSD. Patients were assigned to groups by the first author (MM) following the assessment of inclusion and exclusion criteria and randomization.

Measures

Assessment of the in- and exclusion criteria included a semi-structured clinical interview and a self-report questionnaire administered by trained psychologists and master Psychology students over the telephone. The semi-structured clinical interview was also assessed at post and follow-up measurements. Primary and secondary outcome measures were assessed via online self-report questionnaires at pre-, post- and 3-month follow-up measurements.

Semi-structured clinical interview

To assess primary diagnosis of PTSD and/or depression, the Dutch version of the *M.I.N.I. Plus 5.0.0* was administered (M.I.N.I. Plus 5.0.0.; Sheehan et al., 1997; M.I.N.I. Plus 5.0.0 NL [Dutch version] Van Vliet, Leroy, & Van Meegen, 2000). The M.I.N.I. Plus 5.0.0. is a structured clinical interview used to assess Axis I Disorders according to DSM IV. All questions are yes/no questions and based on the answers, it is determined whether the

patient meets the criteria for a certain disorder (e.g., "In the past month, have you avoided thinking about the event, or have you avoided things that remind you of the event?"). The MINI 5.0.0. has excellent interrater reliability ($\kappa > .75$), very good test-Retest reliability ($\kappa > .75$), as well as validity (Sheehan et al., 1997).

Self-report questionnaires

The *Dissociative Experiences Scale* (DES) (Bernstein & Putnam, 1986) was used to measure dissociative experiences that the participant may be suffering from due to the PTSD. The DES consists of 28 self-report items rated on a scale of 0 to 100. Subjects indicate to what extent they experience certain symptoms such as amnesia. An example item is "Some people have the experience of finding themselves in a place and having no idea how they got there. Select a number to show during what percentage of the time this happens to you." The DES has good test-retest reliability ($r = .84$) and split-half reliability ($r = .71$-$.96$), as well as good internal consistency and construct validity ($p = .64$) (Bernstein & Putnam, 1986).

Self-reported symptoms of PTSD were assessed using the *PTSD checklist for the DSM 5* with LEC and extended Criterion A (PCL-5, Blevins, Weathers, Davis, Witte, & Domino, 2015; Boeschoten, Bakker, Jongedijk, & Ollf, in preparation). The PCL-5 is a 20-item self-report measure assessing the symptoms of PTSD according to the DSM 5. An example item is "In the past month, how much were you bothered by repeated, disturbing, and unwanted memories of the stressful experience?" on a scale of 0 (*not at all*) to 4 (*extremely*). The PCL-5 was found to have strong internal consistency ($\alpha = .94$), test-retest reliability ($r = .82$), and convergent ($rs = .74$ to $.85$) and discriminant (rs = .31 to .60) validity (Blevins et al., 2015).

The *Beck Depression Inventory – Second Edition* (BDI-II; Beck, Steer, & Brown, 1996; BDI-II-NL [Dutch version] Van der Does, 2002) is a 21-item self-report instrument that assesses severity of depression. Each item has four options ranging from 0 ('not present') to 3 ('present all the time') within the previous two weeks. Higher scores indicate a more severe depression. An example item is "I don't feel I am worse than anybody else - I am critical of myself for my weaknesses or mistakes - I blame myself all the time for my faults - I blame myself for everything bad that happens". The BDI-II has shown good internal consistency reliability ($\alpha = .93$ amongst college students, $\alpha = .92$ amongst outpatients, Beck et al., 1996).

Overall well-being was assessed using the *Outcome Questionnaire – 45 – Second Edition* (OQ-45-2, Lambert et al., 1996). It measures symptom distress (SD), interpersonal relationships (IR) and difficulties in social roles (SR). The participant indicates how often the statements applied to them in the past week on a scale of 0 ('never') to 4 ('almost all the time'). An example item is "I have difficulty concentrating". It has been shown to have

good test-retest reliability (r = .79), good internal consistency reliability (r = .92) as well as good concurrent validity (α = .68-.80) in Dutch clinical populations (De Jong et al., 2007).

Apparatus

The *Multi Modal Memory Restructuring* (*3MR*) system is a software application, which focuses on the restructuring and relearning of past events and can be operated by the patient without or with minimal therapist assistance. The *3MR* system allows people to visualize past events using personal photos, narrative texts, online geographical maps, and patient-created 3D virtual worlds. Patients view the *3MR* application on their computer screen. In this trial there was no use of Head Mounted Displays.

The *3MR* system consists of a period overview and a diary, which contains the tools 'Text', 'Images', 'Website', 'Media', 'Webcam' and '3D world'. The *3MR* system and an accompanying therapy manual were used to guide patients through 12 therapy sessions targeting the traumatic memories of the patients. During sessions, patients completed assignments which were described in the therapy manual (abbreviated version shown here) varying from 'Search for the location of this event on Google Maps, use Google Street view and answer the following questions; "Where is this?", "What happened here?", "What feeling does looking back at this location give you?", to 'Do you have pictures you have on your computer (add these via the tool 'Images') or in hard copy (add these via the tool 'Webcam') that date from that time period? Then now answer the following questions; "Which people are on this picture?", "Why is this picture important to illustrate your memory?". The assignments build up to the construction of a personalized 3D environment, reflecting the actual traumatic memory of the participant with the use of corresponding 3D items. In the 3D world builder several pre-selectable formats existed (e.g., a 'desert' environment in the military version, and a 'room' environment in the CSA version). Patients added items to these environments from a library, which contains hundreds of specific items such as vehicles, houses, soldiers and civilians in the military version, and coaches, tables, closets and beds in the CSA version. While looking at this personal created virtual 3D environment patients answered classical exposure questions from the therapy manual, such as 'What do you see looking at this situation?', 'What do you hear?', 'What do you smell?'. After use of the 3D world, patients were instructed to distance themselves from the memory by actively zooming out of the 3D environment before closing it.

Patients install the *3MR* system on their own PC or laptop. The *3MR* system runs at any PC or laptop that has a *32* or *64* bit version of Windows XP, Windows Vista or Windows 7, Windows Internet Explorer 6 or higher, a processor with a clock speed of at least 1 GHz, 512 MB of intern memory (RAM), 2 GB of free hard disk space and a graphical card which supports OpenGL. The therapy manual that contained 12 therapy

sessions was handed-out in hardcopy. Illustrative screenshots of the application are available online [doi:10.4121/uuid:cacc5b31-047e-4e88-b341-cff18d76de49].

Treatment

3MR intervention

Patients randomly assigned to the *3MR* group received a one-hour face-to-face introduction appointment with a trained therapist to be introduced to the *3MR* system and treatment manual. The treatment rationale was explained thoroughly and especially the importance of non-avoiding was discussed and highlighted. Treatment sessions were scheduled two times per week. After this introduction appointment, patients autonomously followed through the 12 sessions of *3MR* intervention at home with use of the treatment manual. At session six, the participant was called by the therapist to check progress and to see whether there were any questions or problems. During the *3MR* intervention the therapist could be contacted by the patient by e-mail or telephone and he or she offered feedback or help when requested. In practice, extra requests for therapist assistance were not often done and therapist assistance remained mostly confined to the mid-term contact moment initiated by the therapist at session six.

Treatment as Usual

The control condition consisted of 'treatment as usual' (TAU), which in this trial was a trauma-focused intervention for PTSD (i.e., Imaginal Exposure [IE], Eye Movement Desensitization and Reprocessing [EMDR], or Narrative Exposure Therapy [NET]). These approaches are applied as TAU because they are known to lead to high effect-sizes (e.g., Cusack et al., 2016) and are recommended in guidelines from different institutions (e.g., American Psychological Association [APA], and ISTSS; Cusack et al., 2016). A total of 22 certified psychologists working at the Psychotrauma departments of PsyQ, Reinier van Arkel and the ambulatory of the Erasmus University Rotterdam were involved in TAU and/or *3MR* therapy assistance. The post measurement was conducted after 12 *3MR* or TAU therapy sessions. For ethical reasons ongoing TAU's were not forced to be determined after this point; whether or not patients had followed additional TAU during the period between the post measurement and the follow-up measurement was recorded at the three month follow-up registration.

Data analysis

To include patients with one or more missed measurements and to fit the nested data structure of multiple measurements within a participant, a multilevel model (also known as mixed random effect model) was used to analyze the data. Hereby, pre, post, and 3-month follow-up measurements of the PTSD and depression symptoms are defined at Level 1 and patients at Level 2, with condition (*3MR* or TAU) as a Level 2 predictor variable (see e.g., Hox (2010); for a general overview of multilevel analysis procedures). In multilevel models, random effects are included in addition to fixed effects to account for the dependencies between the levels. All data preparation and analyses were performed in R (R Core Team, 2018) using the nlme package (Pinheir, Bates, DebRoy, & Sarkar, 2018) or SPSS 25.

Different models were fitted to the PCL-5, BDI-II, and OQ-45-2 scores after which the fit of the models were compared to each other by testing the difference in deviance across models. First a baseline model (M0) was fitted to the data with random intercepts. In the second model (M1) the Level 1 predictor time was added to the model. In the third model (M2) the Level 2 predictor condition was added to the model. The fourth model (M3) was further extended by adding random slopes for time. Finally, the fourth model (M4) also included a cross-level interaction of time at Level 1 and condition at Level 2 to assess whether the effect of time varied across conditions.

The baseline model (M0) was first used to assess whether multilevel analysis was required by testing if the variance at Level 2 was significant. The intraclass correlation, calculated using: ICC $=\rho = \frac{\sigma_{u0}^2}{\sigma_{u0}^2 + \sigma_e^2}$, where σ_{u0}^2 is the variance of the random person intercept and σ_e^2 is the variance of residual error, was consequently calculated using the baseline models' results as an indication of the proportion of total variance explained by the patient variation at Level 2. Next, the rest of the models were fitted and parameter estimates were reported. The fit of the models was compared using the deviance statistic and a significance test on the difference in deviance. For the best fitting model, post hoc analysis were performed to evaluate the specific decrease in symptoms from the pre to post measurement, and post to follow up measurement using a Tukey HSD test to correct for multiple comparisons. Also, residuals were inspected to assess the model's assumptions of normality and linearity. Unless otherwise reported residuals of the best fitting model met these assumptions.

Furthermore, the dichotomous data of the M.I.N.I. Plus 5.0.0. NL were studied using descriptive statistics (diagnosis PTSD and/or current depression YES/NO) on pre, post, and follow-up measurements.

Considering missing data; of three dropped out patients only pre diagnostic data according to the M.I.N.I. Plus 5.0.0. NL were available (which means no questionnaire

data at all). Of one participant no pre questionnaire data were available, but post questionnaire data and pre, post and follow-up M.I.N.I. Plus 5.0.0. NL data were available. Also, of one participant no post and follow-up questionnaire data were available, but pre questionnaire data and pre and post M.I.N.I. Plus 5.0.0. NL data were available. All questionnaire data were taken into account with use of the multi-level analysis. All available M.I.N.I. Plus 5.0.0. NL data were used in the descriptive analysis. In all other analyses the available *n* is noted when relevant. See also Figure 1 for a flow chart of participants through the study.

Results

Multi-level analysis

Table 3 shows the descriptive statistics of the symptom scales (PCL-5, BDI-II and OQ-45-2) in both treatment conditions (*3MR* and TAU). Figure 2 to 4 illustrate the individual patient trajectories over time for the three symptom scales and show there is individual variability in the symptom changes over time in both treatment conditions. Results of the statistical analyses showed that for all three symptom scales a multilevel model with random intercepts fitted the data (i.e., variance at Level 2 was significant), where $ICC_{PCL-5} = 0.47$, $ICC_{BDI-II} = 0.62$ and $ICC_{OQ-45-2} = 0.65$.

Table 3: Descriptives per scale per measurement moment and condition

Scale	Time	TAU condition					*3MR* condition				
		Mean	SD	Min	Max	Missing	Mean	SD	Min	Max	Missing
PCL-5	Pre	49.10	10.22	33	68	1	45.45	13.41	18	68	
	Post	33.13	18.61	8	65	6	22	18.75	3	68	8
	Follow up	36.15	20.15	3	62	8	28.50	19.02	5	59	10
BDI-II	Pre	28.95	9.37	8	52	1	25.55	7.92	14	44	
	Post	23.4	12.56	5	45	6	14.08	9.75	2	37	8
	Follow up	23	12.82	0	43	8	15.30	10.26	5	34	10
OQ-45-2	Pre	86.4	16.56	53	111	1	85.10	25.32	14	148	
	Post	77.07	31.30	31	113	6	61	22.3	28	102	8
	Follow up	76.62	35.86	8	122	8	64.10	22.82	27	96	10

3MR = *Multi Modal Memory Restructuring; TAU = Treatment as Usual; PCL-5 = PTSD Checklist for the DSM 5; BDI-II-NL = Beck Depression Inventory - Second Edition; OQ-45-2 = Outcome Questionnaire – 45 – Second Edition*

PCL-5

Comparing the fitted models on the PCL-5 scores showed that the fourth model (M3: random intercepts and slopes for time, with Level 1 predictor time, and Level 2 predictor condition) fitted best (see Table 4). In this model a significant average decrease of PCL-5 scores was observed across the measurement moments. From the pre to post measurement, PCL-5 scores decreased by 18.55 points on average (t [47] = -7.14, $p < 0.001$). The decrease from the pre to the follow-up measurement was slightly less as PCL-5 scores decreased 12.49 points on average (t [47] = -4.42, $p < 0.001$). Post-hoc analyses showed that this is due to the small increase in the average PCL-5 scores from the post to follow-up measurement of 6.06 points, which was not statistically significant (t [47] = -2.05, $p = 0.111$). Note that the variances of the random slopes for measurement moment were statistically significant in this model, implying that the slopes for the measurement moments vary across patients. This is also evident by the different patterns across measurement moments displayed in Figure 2. In this model, the PCL-5 scores differed -2.88 points on average across the two conditions, however this difference was not statistically significant (t [39] = -0.78, $p = 0.442$). These results show no indication of a difference in the average decrease of PTSD symptoms between the TAU and *3MR* condition.

BDI-II

For the BDI-II scores, a likelihood ratio test to compare the fitted models showed that the second model (M1: random intercepts with Level 1 predictor time) fitted best (see Table 5). In this model, a significant average decrease of BDI-II scores was observed across the measurement moments. From the pre to post measurement, BDI-II scores decreased by 7.81 points on average (t [55.42] = -5.24, $p < 0.001$), while the decrease in BDI-II scores was 6.65 on average from the pre to follow-up measurements (t [55.91] = -4.24, $p < 0.001$). Subsequent post-hoc analysis showed that from the post to follow-up measurement an increase of 1.15 points in the average BDI-II scores was observed, which was not statistically significant (t [51.8] = -0.71, $p = 0.757$). As including a fixed effect of condition or interaction effect between measurement moment and condition did not result in a better model fit, the results revealed no indication of a difference in the average decrease of depression symptoms between the TAU and *3MR* condition.

Table 4: Parameter estimates (se between brackets) and model fit statistics per model for PCL-5 scores

		M0	M1	Stand.[1]	M2	M3	Stand.	M4
Fixed part	Intercept	38.95 (2.47)***	47.03 (2.51)***		49.42 (3.36)***	48.53 (2.62)***		48.68 (2.63)***
	Pre-post		-18.77 (2.54)***	-0.84	-18.89 (2.54)***	-18.55 (2.60)***	-0.83	-16.93 (3.51)***
	Pre-FU[2]		-13.08 (2.67)***	-0.58	-13.21 (2.68)***	-12.49 (2.83)***	-0.56	-12.45 (3.85)***
	Condition				-4.84 (4.55)	-2.88 (3.71)	-0.13	-3.23 (3.75)
	Interaction Pre-post							-3.63 (5.25)
	Interaction Pre-FU							-0.09 (5.84)
Random part	σ_e^2	156.69	90.50		91.07	17.36		17.68
	σ_{u0}^2	179.69	164.21		161.64	124.32		124.36
	σ_{u1}^2					148.51		148.88
	$\underline{\sigma_{u2}^2}$					157.72		166.61
Likelihood ratio test[2]			42.73***		1.17	15.58**		0.62

*M0: baseline model with random intercepts and Level 1 predictor time. M1: M0 + Level 2 predictor condition. M2: M1 + random slopes for time. M3:M2 + cross-level interaction effect of time and condition. [1]Stand.: Standardized coefficients of fixed effects. ***p < 0.001. **p < 0.01.*
Note: R^2 *was not reported as expanding the model did not result in a significant better fit. [2]FU = Follow-up.*

Table 5: Parameter estimates (se between brackets) and model fit statistics per model for BDI-II scores

		M0	M1	Stand.	M2	M3	M4
Fixed part	Intercept	23.7(1.57)***	27.22 (1.61)***		29.66 (2.12)***	29.04	28.84 (1.91)***
	Pre-post		-7.81 (1.49)***	-0.56	-7.92 (1.49)***	-7.88 (1.63)***	-6.59 (2.21)**
	Pre-FU		-6.65 (1.57)***	-0.48	-6.77 (1.57)***	-6.39 (1.64)***	-4.90 (2.20)*
	Condition				-4.94 (2.90)	-3.66 (2.69)	-3.29 (2.72)
	Interaction Pre-post						-3.00 (3.29)
	Interaction Pre-FU						-3.47 (3.32)
Random part	σ_e^2	46.80	30.87		31.06	7.19	7.28
	σ_{u0}^2	75.66	73.85		69.07	69.19	67.21
	σ_{u1}^2					57.60	57.95
	σ_{u2}^2					52.32	52.80
Likelihood ratio test[2]			26.92***		2.92	6.47	1.28

M0: baseline model with random intercepts and Level 1 predictor time. M1: M0 + Level 2 predictor condition. M2: M1 + random slopes for time. M3: M2 + cross-level interaction effect of time and condition. [1]Stand.: Standardized coefficients of fixed effects.
*** $p < 0.001$. ** $p < 0.01$. * $p < 0.05$. *Note:* R^2 *was not reported as expanding the model did not result in a significant better fit.*
[2]FU = Follow-up.

OQ-45-2

Finally, for the OQ-45-2 scores, the second model (M1: random intercepts with Level 1 predictor time) was also the best fitting model. Here, a significant average decrease of OQ-45-2 scores was observed across the measurement moments. From the pre to post measurement OQ-45-2 scores decreased 14.49 points on average (t [47] = -3.85, $p < 0.001$). From the pre to follow-up measurement a decrease of 12.37 OQ-45-2 points on average was observed (t [47] = -3.13, $p < 0.001$). Post-hoc tests showed that the slight increase in OQ-45-2 scores of 2.12 points on average was not statistically significant (t [47 = -0.52, $p = 0.863$). Similar to previous results, these results reveal no indication of a difference in the average decrease of OQ-45-2 scores across the TAU and *3MR* condition.

M.I.N.I. Plus 5.0.0. NL

Descriptive statistics of the M.I.N.I. Plus 5.0.0. NL data show that at post measurement 81.1% of the completers in the *3MR* condition (n = 12) no longer met criteria for the diagnosis of PTSD, and 72.2% of the completers in the TAU condition (n = 18). In the *3MR* condition, 75% of the completers that met diagnostic criteria for depression at pre measurement no longer met criteria at post measurement. In the TAU condition this was 50%. In both conditions one participant that did not meet diagnostic criteria at pre measurement, did meet criteria at post measurement. At the three month follow-up measurement, in the *3MR* condition (n = 11) 18.2% of the completers met criteria for PTSD and/or depression. In the TAU condition (n = 16) this was 25% both for PTSD and depression. In the TAU condition two patients relapsed into prior diagnosis of PTSD and one into prior diagnosis of depression. In the *3MR* condition two patients relapsed into prior diagnosis of PTSD and one participant met criteria for depression only at the follow-up measurement.

Drop-out analysis

Drop-out analysis revealed that drop-outs (available data n = 11) tented to score somewhat but not significantly different than completers (available data n = 29) on pre measurements of the PCL-5 (dropout M = 49.91, SD = 13.12, completers M = 46.28, SD = 11.49, $t(38)$ = -0.859, p = 0.396), BDI-II-NL (dropout M = 29.19, SD = 6.21, completers M = 26.52, SD = 9.51, $t(38)$ = -0.859, p = 0.396) and OQ45-2 (dropout M = 94.36, SD = 20.76, completers M = 82.48, SD = 20.68, $t(38)$ = -1.621, p = 0.113). When comparing treatment conditions, the *3MR* condition suffered from a higher drop-out rate (45%) than the TAU condition (18%). This effect was noticeable but not significant χ^2 (1) = 3.771; p = 0.104). Furthermore, slightly more patients in the CSA group dropped out than in the military group (CSA = 37.5%, military = 25%).

Table 6: Parameter estimates (se between brackets) and model fit statistics per model for OQ-45-2 scores

		M0	M1	Stand.	M2	M3	M4
Fixed part	Intercept	79.06 (3.81)***	85.54 (3.98)***		87.45 (5.41)***	85.96 (4.69)***	85.97 (4.70)***
	Pre-post		-14.49 (3.76)***		-14.56 (3.77)***	-13.92 (3.73)***	-11.25 (5.04)*
	Pre-FU		-12.37 (3.96)***		-12.44 (3.97)**	-11.08 (4.55)*	-10.53 (6.23)
	Condition				-3.87 (7.40)	-0.77 (6.67)	-0.87 (6.69)
	Interaction Pre-post						-6.05 (7.53)
	Interaction Pre-FU						-1.26 (9.43)
Random part	σ_e^2	245.86	197.07		197.93	43.98	44.58
	σ_{u0}^2	461.22	443.08		449.90	408.62	408.94
	σ_{u1}^2					285.96	287.13
	$\underline{\sigma_{u2}^2}$					424.23	450.89
Likelihood ratio test[2]			16.09***		0.29	9.61	0.85

M0: baseline model with random intercepts and Level 1 predictor time. M1: M0 + Level 2 predictor condition. M2: M1 + random slopes for time. M3: M2 + cross-level interaction effect of time and condition. [1]Stand.: Standardized coefficients of fixed effects.
*** $p < 0.001$. ** $p < 0.01$. * $p < 0.05$. *Note:* R^2 *was not reported as expanding the model did not result in a significant better fit.*
[2]*FU = Follow-up.*

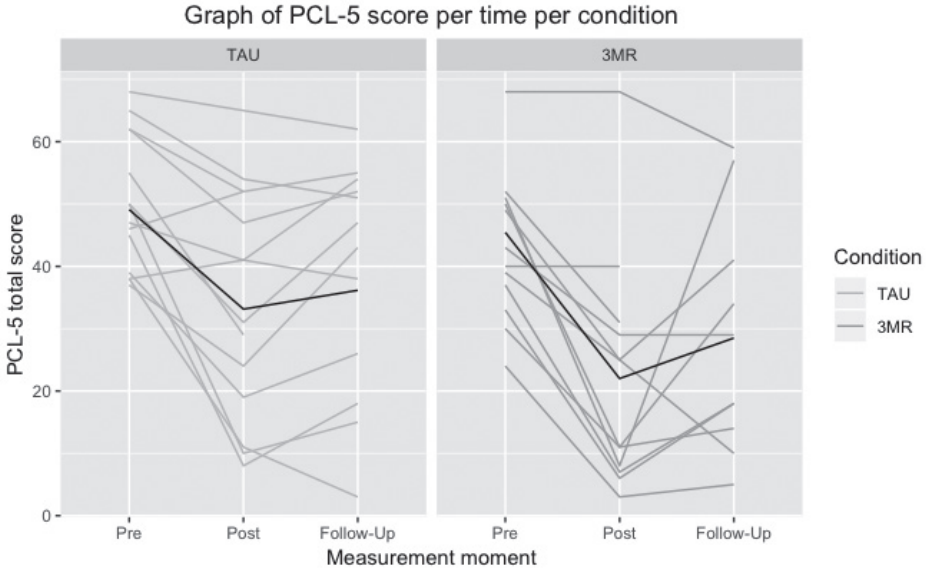


Figure 2: Individual participant trajectories over time for the PCL-5 in both treatment conditions, with the dark line representing the mean scores

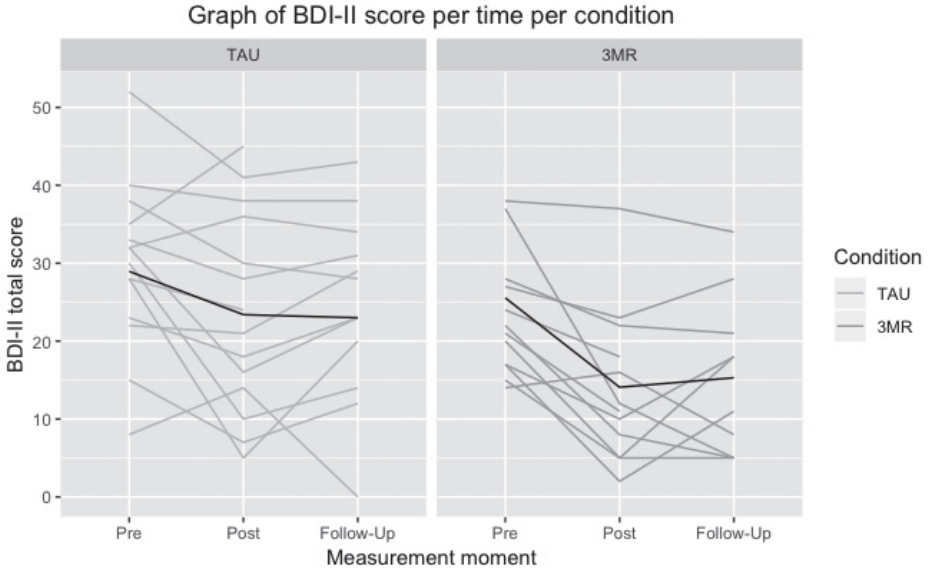


Figure 3: Individual patient trajectories over time for the BDI-II in both treatment conditions, with the dark line representing the mean scores

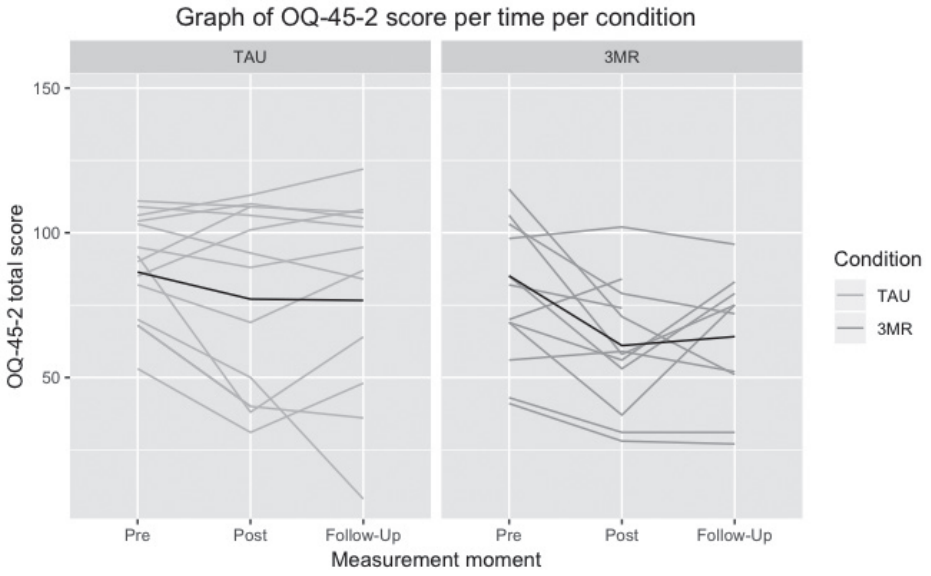


Figure 4: Individual patient trajectories over time for the OQ-45-2 in both treatment conditions, with the dark line representing the mean scores

Discussion

This paper describes a randomized controlled trial to evaluate the efficacy of a computer-based trauma intervention with elements of VR (*3MR* system) and limited therapist assistance for the treatment of PTSD in a sample of 44 CSA and veteran patients. The *3MR* intervention was compared to 'treatment as usual' (TAU), which consisted of evidence-based trauma focused therapy such as IE, EMDR, or NET. Results show that symptoms of both PTSD and depression significantly decreased between pre and post measurements (after 12 sessions of respectively *3MR* or TAU), and that there was no indication found for a difference between the two treatment conditions. Similarly, overall well-being also increased following treatment. Data of the semi-structured clinical interviews indicate that in both treatment conditions diagnoses of PTSD and depression declined from pre to post measurements. Overall, both *3MR* and TAU show significant reduction in symptoms of PTSD and depression, and an increase in overall well-being, and no differences were found between the two interventions in terms of efficacy.

These results are promising, and in line with current literature on the efficacy of interventions for PTSD that use VR. For example Carl et al. (2018) describe several interventions in their meta-analysis on RCTs for the treatment of anxiety disorders

(among which PTSD) and conclude that VRET is an effective and equal medium for exposure therapy. More specifically, in a recent meta-analysis Van Meggelen et al. (submitted) compared ten clinical trials on the efficacy of VRET for the treatment of PTSD. They found that VRET for PTSD significantly outperformed inactive control conditions and did not differ from active control conditions. Also, when considering the outcomes of computer-based interventions for the treatment of for example PTSD, our findings are in line with previous research which indicates that in general, computerized interventions yield comparable effect sizes as traditional psychosocial interventions in the treatment of depression and anxiety (Amstadter et al., 2009; Calbring et al., 2001; Proudfoot et al., 2003; Proudfoot et al., 2004).

This RCT knows several limitations. In their meta-analysis of VRET for affective and anxiety disorders, Parsons and Rizzo (2008) warrant the need for studies that exceed at least the number of 30 patients to reach adequate power. Although this RCT exceeds this number, it still examines a small number of patients and might be underpowered to detect potential differences between the conditions examined here. Therefore, trials with larger sample sizes are desired. Moreover, since significant individual differences in treatment gain are present in this trial, further insight into the question for which patients this intervention might be specifically beneficial, is warranted.

In conclusion, our data indicate that the *3MR* intervention can effectively treat PTSD and comorbid depression and may be similarly effective as evidence-based treatments for PTSD. Therefore, *3MR* may constitute an appropriate treatment alternative, especially when therapist availability is low and the intention to enlarge reach of treatment efforts and improve cost-effectiveness are present.

4

The Added Value of a Multi Modal Memory Restructuring System to Writing Exercises in Overcoming Negative Memories

This chapter is submitted as:

Van Meggelen, M., Morina, N., Van Aken, R.M., Kohlen, L.J.S.A., Tielman, M.L., Brinkman, W.P., & Franken, I.H.A.

(submitted). The Added Value of a Multi Modal Memory Restructuring System to Writing Exercises in Overcoming Negative Memories

Abstract

The computer-based trauma intervention *Multi Modal Restructuring* (*3MR*) has shown efficacy in the treatment of PTSD. This study explores the added value of the multimedia tools of the *3MR* application (e.g., 'Website', 'Media', and 'Images') in order to further elaborate on the active elements and the added value of this application in the use of overcoming negative or traumatic experiences. This study examined the added value of the multimedia tools of the *3MR* system to writing exercises that were aimed at reducing distress, negative affect and intrusions as a result of a negative but not traumatic memory in a healthy student population. A total of 55 participants was included. Participants were randomly assigned to either three sessions of writing exercises with additional use of the *3MR* multimedia tools (SWT+*3MR*) or structured writing exercises only (SWT). Multiple self-report measures were administered to assess distress evoked by the aversive memory, negative affect and intrusions on pre, post and a one month follow-up measurement. The written texts were analysed to examine quality and length of the texts. Both conditions showed a significant decrease of distress evoked by the aversive memory, negative affect as well as the *number*, *vividness* and *distress* of the reported intrusions. No differences over time nor between conditions were observed regarding the use of *positive* emotional words, *negative* emotional words, words of *insight* and words of *causation* over various sessions. However, though the length of the text during the writing sessions declined over time for both conditions, the *3MR*+SWT condition resulted in significantly less decline in written text over time and therefore a longer written text over the subsequent writing sessions.The current findings confirm the positive effects of writing exercises in overcoming negative memories. Although no substantial added value of the use of the multimedia tools of the *3MR* system was found, the application does seem to stimulate participants to keep the length of the text stable and prevent reduction in the length of the text over time.

Keywords: *Computer-based*, *intervention*, *Structured Writing Therapy*, *multi-media*, *post-traumatic stress disorder*, *text quality analysis*

Introduction

Failing an important exam, losing a friendship, or receive a job rejection are commonplace negative experiences. Some negative events however, have such an impact on those involved, that they can be considered traumatic. The lifetime prevalence of experiencing a traumatic event is 60.7% for men and 51.1% for women (Kessler, Sonnega, Bromet, Hughes & Nelson, 1995). However, most people will show resilience and recover quickly from a *potential* traumatic event. A smaller group will develop psychological problems such as a post-traumatic stress disorder (PTSD; Kessler, et al., 1995; Kilpatrick, Saunders, & Smith, 2003). The main characteristics of PTSD are recurrent intrusions, persistent avoidance of stimuli associated with the trauma, and increased arousal (American Psychological Association, 2013). There are several ways to treat PTSD. The effectiveness of Cognitive Behavioural Therapy (CBT) and Eye Movement Desensitization and Reprocessing (EMDR) for example is well established (Cusack et al., 2016). Often, *exposure* to the traumatic memories or cues for the traumatic event plays an important role in reducing symptoms of PTSD (Rauch & Foa, 2006) and reduce the impact of traumatic memories. One way of offering exposure to a traumatic event is Virtual Reality Exposure Therapy (VRET). VRET uses computer-generated environments to simulate feared stimuli. In these virtual environments, users can be systematically exposed to specific stimuli within a contextually relevant setting, for example a warzone or airplane for soldiers with war-related PTSD (Parsons & Rizzo, 2008). VRET interventions have shown promising results for the treatment of PTSD in for example active duty military personnel or veterans (e.g. McLay et al., 2017; Gamito et al., 2010). Recently, Van Meggelen et al., (submitted) compared ten clinical trials on the efficacy of VRET for the treatment of PTSD. They found that VRET for PTSD significantly outperformed inactive control conditions and did not differ from active control conditions. However, these results are confined by a limited number of relevant trials.

During the last years, increased use of computers and access to the internet have emerged another line of treatment, namely the computerized and internet-based interventions. These interventions (usually computerized CBT interventions) have shown to gain comparable effect sizes as traditional psychosocial interventions in the treatment of depression and anxiety (Carlbring, Andersson, Cuijpers, Riper, & Hedman-Lagerlöf, 2018; Amstadter, Broman-Fulks, Zinzow, Ruggiero, & Cercone, 2009; Carlbring et al., 2001; Proudfoot et al., 2003; Proudfoot et al., 2004). There are several benefits of computerized and internet based interventions compared to traditional therapy, such as that they are often personalized and tailored to the needs of a diverse group of users, they can reach a large population at relatively low cost and that they can be used from a person's own home (Amstadter et al., 2009). An example of a computerized

intervention for PTSD is the *3MR* intervention (*Multi Modal Memory Restructuring* system; Brinkman, Vermetten, Van de Steen, and Neerincx, 2011; Tielman, Neerincx, Bidarra, Kybartas, & Brinkman, 2017). The *3MR* system is a software application, which focuses on the restructuring and relearning of past events by allowing people to visualize past events using personal photos, narrative text, online geographical maps and a patient-created 3D virtual world on their own computer with only little therapist assistance. The *3MR* program consists of a period overview and a diary which contains the multimedia tools 'Text', 'Images', 'Website', 'Media', 'Webcam' and '3D world'. The *3MR* system and an accompanying therapy manual are used to guide patients through 12 therapy sessions targeting the traumatic memories of the participant. During sessions, patients make assignments which are described in a treatment manual (e.g., 'Search for the location of this event on Google Maps, use Google Street view and answer the following questions; 'Where is this?', 'What happened here?', 'What feeling does looking back at this location give you?'). The assignments build up to the construction of a personalized 3D environment, reflecting the actual traumatic memory of the participant with the use of corresponding 3D items. A recent randomized controlled trial (RCT) compared 12 sessions *3MR* to an equal amount of sessions 'treatment as usual' (TAU) that consisted of evident-based trauma-focused therapy (e.g., EMDR, Imaginary Exposure [IE], Narrative Exposure Therapy [NET]). A recent study indicated that the *3MR* intervention gained similar results as TAU in treating war veterans and childhood sexual abuse (CSA) victims for their symptoms of PTSD and depression (Van Meggelen et al., submitted).

Several years ago Lange and colleagues (Lange, Rietdijk, Hudcovicova, van den Ven, Schrieken, & Emmelkamp, 2003) were among the first to evaluate the potential of a computerized intervention for the treatment of PTSD. Based on the findings of Pennebaker (1997) the central therapeutic procedure of their intervention involved writing assignments. Structured writing assignments are comprised of writing about traumatic experiences, and the accompanying thoughts and emotions (Schoutrop, Lange, Hanewald, Davidovich, & Salomon, 2002). Numerous studies about written disclosure of stressful experiences have shown positive effects on physical and psychological health. For example, Schoutrop et al. (2002) tested the effectiveness of writing assignments on coming to terms with a traumatic experience in a controlled trial among undergraduate students. They found that the trauma-writing groups experienced fewer intrusions and showed less avoidance behavior from pre-treatment to follow-up than a waitlist control group. Also, Van Emmerik, Kamphuis, & Emmelkmap (2008) compared Structured Writing Therapy (SWT) to CBT in treating Acute Stress Disorder (ASD) and PTSD and found no differences between the two treatment conditions, implying that SWT can serve as a promising alternative for CBT. Furthermore, Ramirez and Beilock (2011) tested if expressive writing could improve the test performance of students. They found

that especially students afraid of taking tests improved their performance by expressive writing before the exam. Structured writing therefore can serve as an adequate treatment alternative for traumatic experiences, or a way to deal with negative non-traumatic experiences.

The effectiveness of written texts can be indicated by the use of emotion words by the patient. An increase in the use of positive emotional words from the first session to the last session is an indication of positive outcomes (Van Zuuren et al., 1999). Another indication of positive outcomes is the extinction of negative emotions from the first session to the last session. Further, content analyses have revealed the importance of writing style during writing exercises (Pennebaker, Mayne & Francis, 1997). There is a positive relation between the use of both insight (i.e. the use of words as "think", "know") and causation (i.e. words as "cause", "effect") words and health improvement (Pennebaker et al., 1997). Finally, the effectiveness of the writing can be evaluated by the length of the essays in total and during the individual sessions. A long essay, compared to a short essay, in particular when the written essays remain lengthy over time are associated with positive treatment outcomes (Van Zuuren et al., 1999).

In this study, we set out to explore the added value of the *3MR* program (Van Meggelen et al., submitted) when compared to structured writing assignments alone. More detailed knowledge about the working mechanisms of this intervention is useful for future research and possible utilization in mental health care. In this randomized controlled trial, the effects of three sessions of writing exercises preceded by the use of a selection of the multimedia tools of the *3MR* system (*3MR*+SWT), were compared to only writing exercises (SWT) in overcoming negative memories in a healthy student population ($n = 55$) with negative memories about stressful events. Since negative (but not traumatic) memories were studied in a healthy student population, only small changes in distress, intrusions and negative emotions on pre, post and follow-up measures were expected in favour of the *3MR*+SWT condition. We also hypothesised that use of the *3MR* multimedia tools improved both the text quality (defined by *causation*, *insight*, *positive* and *negative words*) and the length (amount of words and stability over time) of the written texts in the *3MR*+SWT condition.

Method

Procedure

Study participants were recruited via the digital study landscape of the department of Psychology of the Erasmus University Rotterdam (EUR). Recruitment was aimed at undergraduate psychology students with an aversive (non-traumatic) memory for which

they wanted to diminish the negative feelings associated with it. Given examples of negative experiences were for example an argument with a friend, a conflict in a working environment, or failing an exam. Potential participants filled in an informed consent form and were interviewed with a semi-structured clinical interview (M.I.N.I. 5.0.0.) to check exclusion criteria and exploration of the unpleasant memory. A Visual Analogue Scale (VAS) served as measure for the distress this memory evoked. Included participants were randomly assigned to the *3MR*+SWT or SWT condition. At pre measurement participants filled in a VAS scale, the Intrusion Questionnaire, the Negative Affect scale of the Positive and Negative Affect Scale (PANAS), and a short demographic questionnaire (age, gender, nationality). In a period of three weeks the participants engaged in three sessions in the Erasmus Behavioural Lab (EBL) of the Erasmus University Rotterdam.

Sessions were based on existing therapeutic writing sessions (for a description see Appendix 1). The duration of the sessions was one hour per session, which included instructions from the experimenter and filling out the self-report questionnaires. The two conditions differed in the 15 minutes prior structured writing. The *3MR*+SWT condition was given 15 minutes to use the multimedia tools of the *3MR* system to memorize and visualize their memory prior to the structured writing (30 minutes of typing text on a computer). The SWT condition was instructed to think about the negative memory for 15 minutes prior their 30 minutes of text typing on a computer (see Appendix 1).

At the start and end of each session the distress and negative emotions caused by the memory were measured with the VAS and the Negative Affect scale of the PANAS. Prior to the first and after the last session the Intrusion Questionnaire was filled in. The follow-up measurement took place one month after the last session. Participants were contacted via e-mail to fill in the VAS, the Negative Affect scale of the PANAS and Intrusion Questionnaire again.

Participants and flow

Fifty-five healthy undergraduate Psychology students (n = 55) participated in this randomized controlled trial (RCT). Participants with a negative, but non-traumatic memory, were randomly assigned to the experimental group (*3MR*+SWT) or control group (SWT). The inclusion criterion was having a negative, non-traumatic, memory which evoked a distress score of at least 50 on a Visual Analogue Scale (VAS, 0-100). Exclusion criteria were diagnosis of post-traumatic stress disorder (PTSD), current depressive disorder, current psychotic disorder, current bipolar disorder and/or high risk of suicide. To screen participants on exclusion criteria the Mini International Neuropsychiatric Interview Plus - Dutch Version 5.0.0 [MINI Plus 5.0.0., Sheehan et al., 1997; Van Vliet, Leroy, & Van Meegen, 2000]) was used.

A total of 66 potential participants were screened for eligibility. Five students were excluded based on exclusion criteria (e.g., not having a negative non-traumatic memory). Sixty-one participants ($n = 61$) were included and randomized. Fourty-nine participants ($n = 49$) were women (89.1%) and six participants were men (10.9%). Ages ranged from 17 to 33 years old with a mean age of 20.56 years ($SD = 3.51$). Of the included and randomized participants, six (n = 6) did not start the experiment. For a flow chart of participants through the study see Figure 1.

Thirty participants were included in the *3MR*+SWT condition and 31 in the SWT. Six participants did not start the experiment (see Figure 1). Available demographic characteristics ($n = 55$) are shown in Table 1. Two participants ($n = 2$) in the SWT condition and one ($n = 1$) in the *3MR*+SWT condition failed to complete the experiment and have therefore been considered as experiment drop-out.

Table 1: Demographic Characteristics of the included participants

	N	**%**
Gender	6	10.9
Male	49	89.1
Female		
Marital status	2	3.6
Married	1	1.8
Living together	53	94.5
Never married		
Age, *M* (*SD*)[a]	20.56	3.51

Note: [a] *M* = mean, *SD* = standard deviation, *n* = 55

Participant assessment and randomization

Participants were screened over the telephone by trained master Psychology students**.** Eligible participants were randomized by an independent researcher via a random-numbers table and its allocation sequence was computer-generated. Participants were randomly assigned to groups by the first author (MM) following the assessment of inclusion and exclusion criteria.

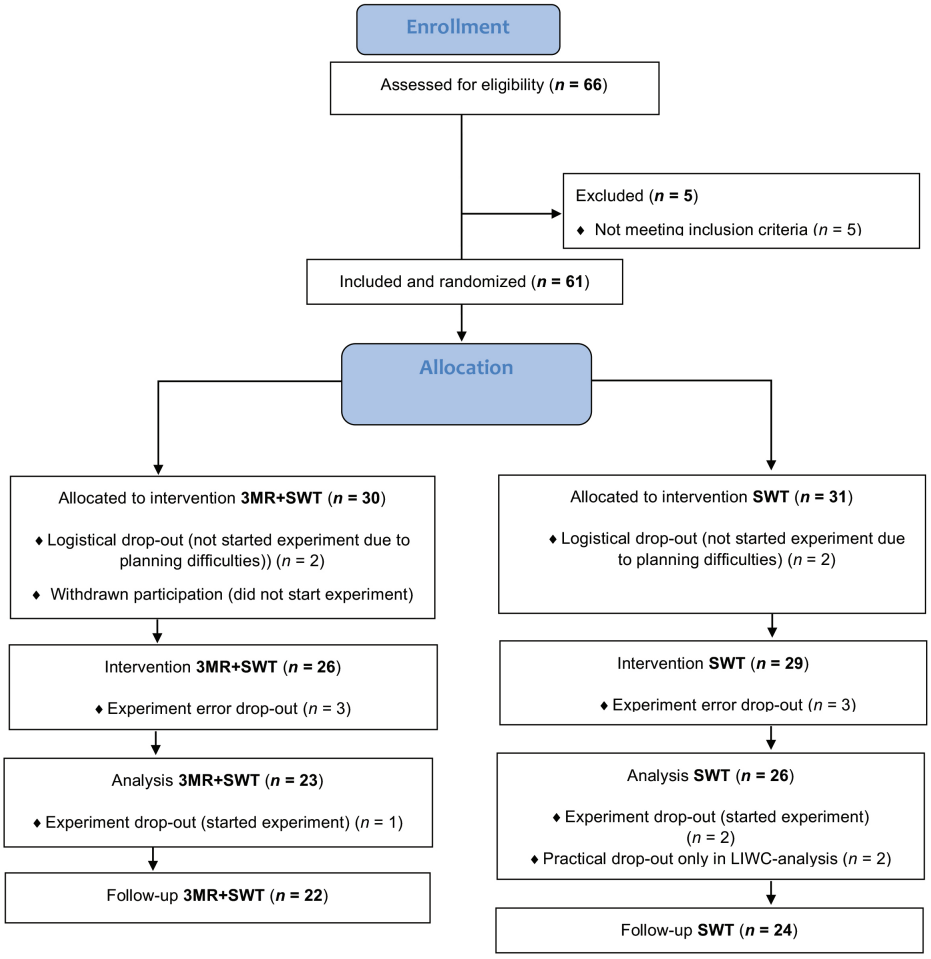


Figure 1: Flow chart of participants through the study

Material

Multi model Memory Restructuring System (3MR)

The *Multi Modal Memory Restructuring* (*3MR*) system is a software application which focuses on the restructuring and relearning of past events. The *3MR* system allows people to visualize past events using personal photos, narrative texts, online geographical maps and patient-created 3D virtual worlds (Brinkman et al., 2011; Tielman et al., 2017). Participants view the *3MR* application on their computer screen. In this study a simplified version of the *3MR2.0* version (Tielman et al., 2017) was used in which

only a period overview and a diary containing the multimedia tools 'Text', 'Images', 'Website', 'Emotion' and 'Media' were available. (For illustrative screenshots of the *3MR* applications see [doi:10.4121/uuid:cacc5b31-047e-4e88-b341-cff18d76de49]).

Linguistic Inquiry and Word Count (LIWC)

LIWC is a text analysing computer programme developed by Pennebaker, Francis and Booth (2001). The program categorises the words of the written text by counting them and calculating the percentages of the words, after placing them in the corresponding category. The LIWC has different categories, including psychological processes, emotional processes and cognitive processes. These categories are divided into subcategories. The categories that are important to get insight into the effectiveness of the written text are positive words (e.g., happy, joy), negative words (e.g., sad, angry), words of insight (e.g., because, reason), and causal word (e.g., realise, understand). To analyse the Dutch texts in this study, we used the Dutch translation of the LIWC adopted by Boot, Zijlstra and Geenen (2007).

Measures

Distress and intrusions

The *Visual Analogue Scale* (VAS) is a non-specific measurement instrument that, in the current study, measures the amount of distress a memory evokes. It measures the intensity of the distress, ranging across a continuum. The minimum score is 0 (no distress at all) and the maximum score is 100 (unbearable distress). No results of the reliability of the VAS in measuring "distress" are available. In comparison, there are results of other subjective phenomena measured with the VAS. Examples are quality of life, pain and depression. The reliability of these tests was good ranging from .60 to .99 (Boonstra, Preuper, Reneman, Posthumus & Stewart, 2008; Bijur, Silver & Gallagher, 2001; Gallagher, Bijur, Latimer & Silver, 2002). An example of a question measuring distress with a VAS is: "Now think back to your negative memory. How much distress do you experience when you think back to this memory?"**.**

To measure the intrusive memories caused by the distressing events an adapted version of the *Intrusion Questionnaire* was used (as used in Morina, Leibold & Ehring, 2013; Ehring, Fuchs, & Kläsener, 2009). This questionnaire contains 16 questions to indicate how many intrusive memories in the form of images participants' had experienced, (2) how vivid these memories were (0-100 scale), and (3) how distressing these memories were (0-100 scale). The questions focused on the *vividness* of the memory, *distress* accompanied with the memory and the *number* of intrusive memories. Examples of questions measuring

intrusions are: "How many times during the past week did you remember the negative memory in images/sounds?", "How vivid were these images/sounds?"

Negative emotions

The Positive and Negative Affect Scale (PANAS) is a self-assessment questionnaire that measures positive and negative affect (Watson, Clark & Carey, 1988). The questionnaire contains 20 items, using a 5-point Likert scale that differs in intensity (i.e., ranging from 1 'very slightly or not at all' to 5 'extremely'). Since this study examines the effects of a negative memory, the negative affect subscale is the main point of interest. Examples of adjective reflecting negative emotions are irritated, shameful and afraid. The PANAS has strong internal consistency and validity (Crawford & Henry, 2004; Leue & Lange, 2011).

Data analysis

Outcome variables were distress and intrusions, measured with the VAS and the Intrusion Questionnaire and negative emotions (measured with the Negative Affect scale of the PANAS). The VAS and the Negative Affect scale of the PANAS were measured before and after each session and at follow-up measurement. The Intrusion Questionnaire was measured before session 1, post-session 3 and at follow-up.

Moreover, the number of *emotional*, *insight* and *causation* words used by participants to describe their negative non-traumatic memory during writing exercises was reviewed (using Linguistic Inquiry and Word Count, LIWC), as well as the number of words.

To test the effect of condition on distress evoked by the negative memory, VAS scores were studied. A 7 x 2 factorial mixed design ANOVA in which time (pre-session 1, post-session 1, pre-session 2, post-session 2, VAS pre-session 3 VAS post-session 3 & follow-up) was the within-subject factor and condition (*3MR*+SWT vs. SWT) between factor, was conducted. The same analyses were conducted to look into the effect of the interventions on negative emotions (using outcome data of the Negative Scale of the PANAS).

To analyse the effects of condition on the *number*, *vividness*, and the *amount of distress* of intrusions caused by the negative memory a 3 x 2 factorial ANOVA was conducted to study three items of the Intrusion Questionnaire (item 1, 3 and 6) whereas the between-subject factor was condition (*3MR*+SWT vs. SWT) and time was the within-subject factor (pre-session 1, post Session 3, and follow-up).

Furthermore, using the text analysis program LIWC the percentages of *positive emotional*, *negative emotional*, *insight* and *causation* word usage were calculated. Thereafter a 4 x 3 x 2 mixed ANOVA was conducted to compare the percentages of negative emotion words, positive emotions words, words of insight and words of causation

used during the three writing exercises in both conditions. Condition (*3MR*+SWT vs. SWT) was between-subject factor and the within-subject factor was time (Session 1, Session 2 and Session 3) and type of word (respectively, negative emotion words, positive emotions words, insight and *causation words*).

To look into the number of words used, the total number of words used per session per condition was counted up to a total score. Next, a 3 x 2 repeated measures ANOVA was conducted to compare the frequency of words used during the three writing exercises in both conditions. The within-subject factor was time (Session 1, Session 2 and Session 3) and the between-subject factor was condition (*3MR*+SWT or SWT).

During all analyses, assumptions were checked and corrections were applied when violations of these assumptions were detected. Overall, a significance level of α .05 was used. All analyses were performed using SPSS version 25.

Results

Visual Analogue Scale (VAS)

The VAS scores were used to analyse the effect of the condition on the amount of distress a participant experienced as result of the negative memory over time. A 7 x 2 factorial mixed design ANOVA was conducted. The results indicated a significant main effect of time, F (3.57, 157.10) = 42.46, p <.001, h2 = .500. This showed that there was a significant difference between the scores measured on the different measurement moments of the VAS (see Figure 2). There has also been found an effect for time, F (1, 44) =100.23, p <.001, h2 =.695. This means that the distress measured with the VAS decreased over time. The results showed that there was a non-significant interaction effect between time and condition (F [3.67, 161.25] = 1.61, p =.179, h*2* =.035) indicating that there was no significant difference found in the amount of decrease in distress between the two conditions over time.

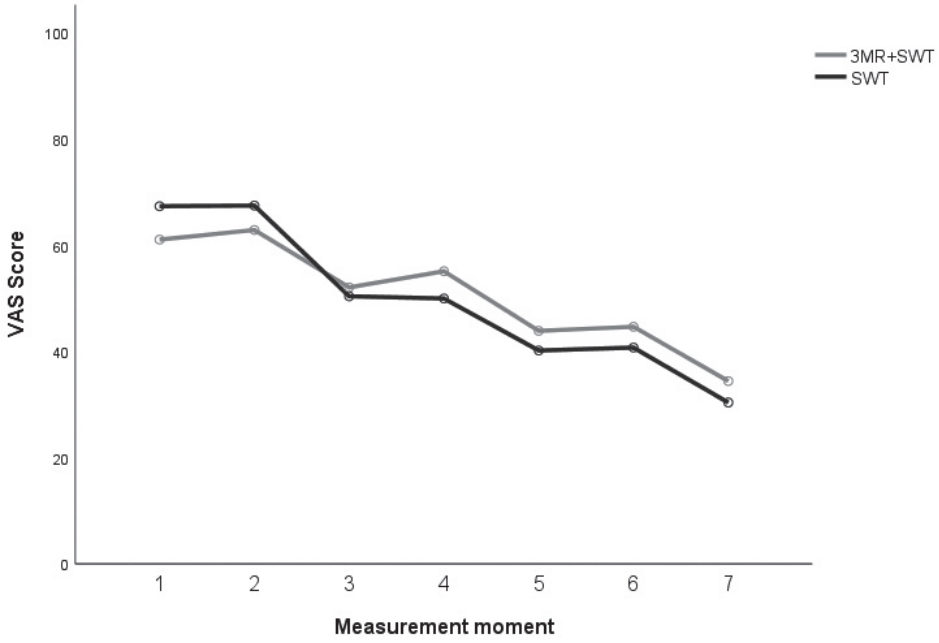


Figure 2: Mean VAS scores at all measurement moments (*pre-session 1* [1], *post-session 1* [2], *pre-session 2* [3], *post-session 2* [4], *pre-session 3* [5], *post-session 3* [6], & *follow-up* [7]) separated by condition (3MR+*SWT* and *SWT*)

Intrusion Questionnaire

To analyse the effect of condition on the degree of intrusions participants experienced according to their negative memory, three items of the Intrusion Questionnaire were studied specifically: the *number*, *vividness*, and the *amount of distress* of intrusions during the past week (question 1, 3, and 6 of the Intrusion Questionnaire respectively). A 3 x 2 factorial ANOVA was conducted. The results showed a significant main effect on the factor time on all three items (*number: F* [1.31, 57.49] = 7.33, $p < .001$, $h^2 = .143$; *vividness: F* [2, 88] = 13.00, $p < .001$, $h^2 = .228$; and *distress: F* [1.82, 79.98] = 25.94, $p < .001$, $h^2 = .365$). This indicated that there was a significant difference found between the scores on these items on the different measurement points (*pre-session 1*, *post-session 3* and *follow-up*). See Figure 3-5.

The results showed a non-significant interaction effect between time *x* condition. We did not find a difference between the conditions in terms of decrease of intrusions (*number*: *F* [1.30, 57.49] = 1.146, $p = .305$, $h^2 = .025$; *vividness*: *F* [2, 88] =1.36, $p = .263$, $h^2 = .030$; and *distress*: F [1.82, 79.98] = 2.995, $p = .061$, $h^2 = .064$).

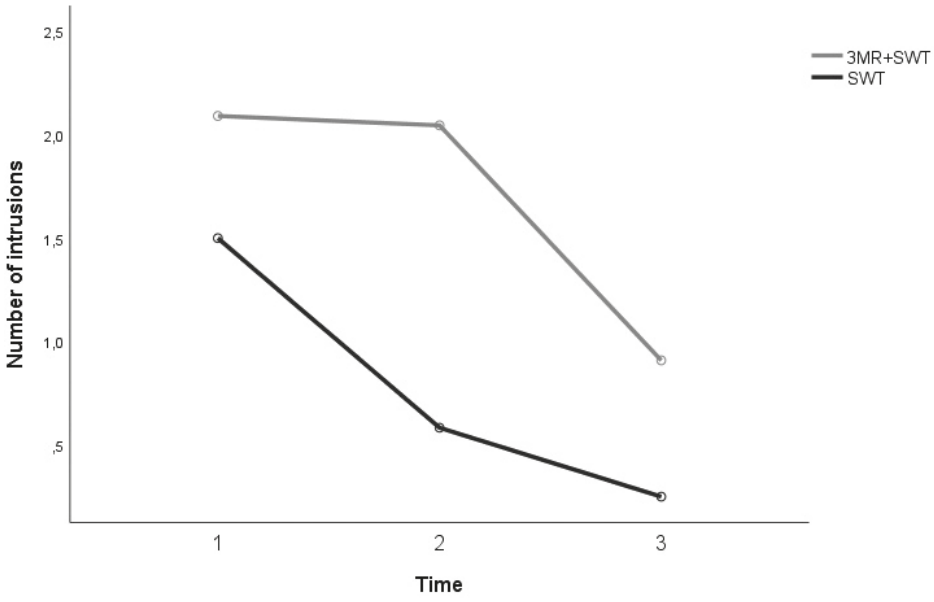


Figure 3: Number of intrusions during the past week (*pre-session 1* [1], *post-session 3* [2], and at *follow-up* [3]

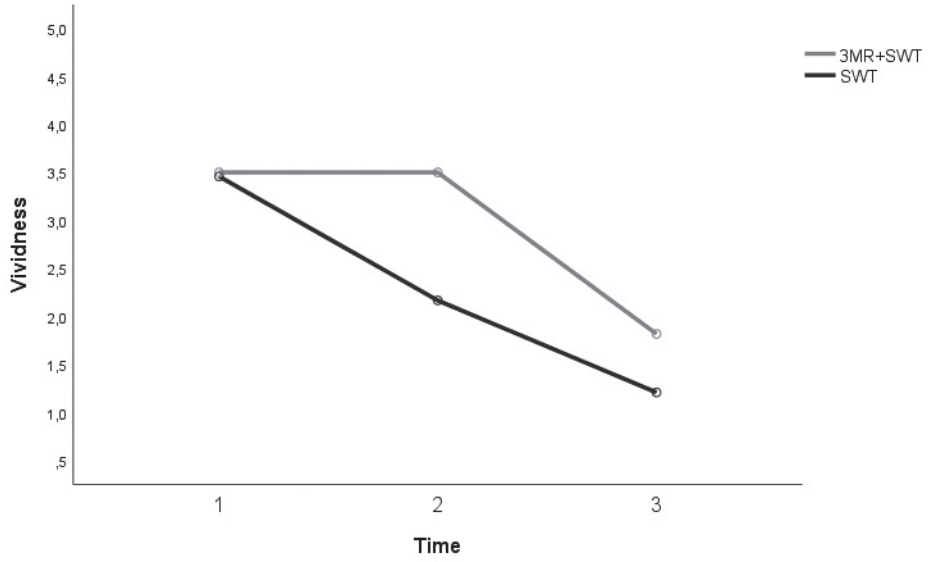


Figure 4: Vividness of the memory during the past week (*pre-session 1* [1, *post-session 3* [2] and at *follow-up* [3]

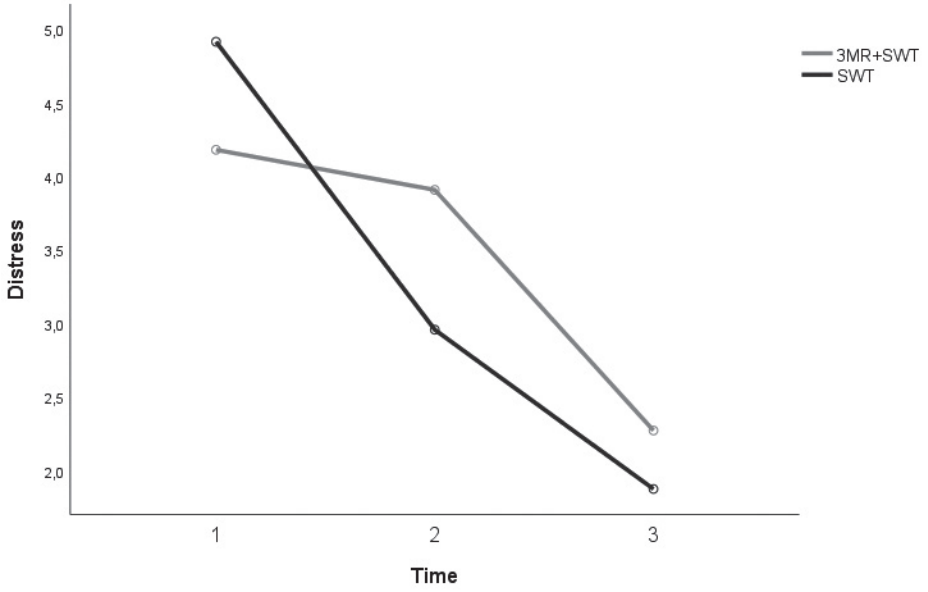


Figure 5: Distress as result of the memory during the past week (pre-session 1 *[1],* post-session 3 *[2], and at* follow-up *[3]*

Positive and Negative Affect Scale (PANAS) – Negative Affect subscale

To analyse the effect of the intervention on the amount of negative emotions as result of the aversive, non-traumatic memory, the scores of the PANAS Negative Affect subscale were examined. A 7 x 2 factorial mixed design ANOVA was conducted. The results showed a significant main effect of time, F (3.70, 162.98) = 8.80, p <.001, h*2* =.167. This indicated that we found a significant decrease between the different measurement moments on the Negative Subscale of the PANAS (see Figure 6). The interaction effect time *x* condition was non-significant. We did not find differences between conditions in terms of decrease of negative emotions measured with the PANAS Negative Affect subscale, F (3.70, 162.98) = 1.10, p =.36, h*2* = .024.

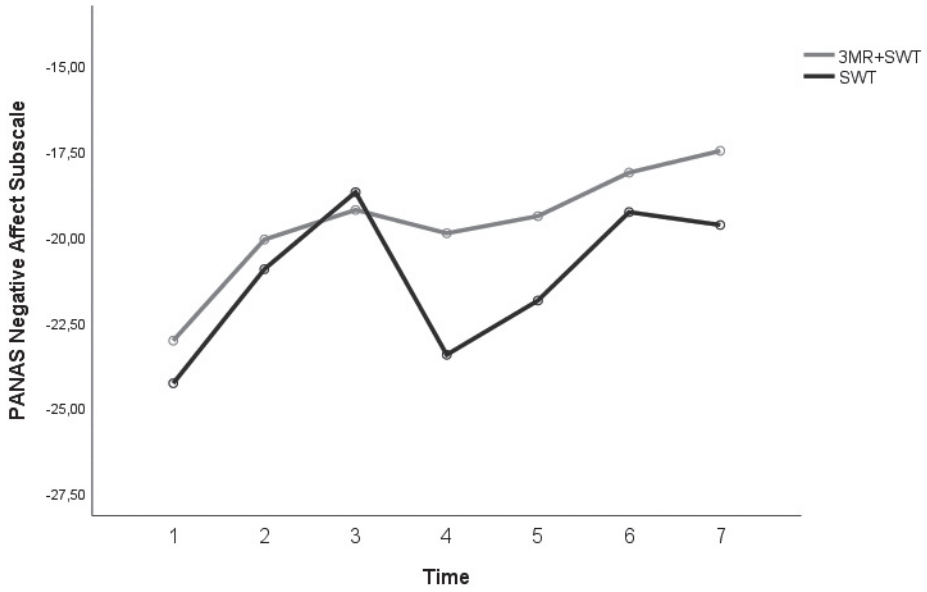


Figure 6: The mean PANAS Negative Subscale scores (pre-session 1 *[1],* post-session 1 *[2],* pre-session 2 *[3],* post-session 2 *[4],* pre-session 3 *[5],* post-session 3 *[6], &* follow-up *[7]) separated by condition (3MR*+SWT *and* SWT*)*

LIWC analyses

To analyse whether there was an effect of condition (*3MR*+SWT vs. SWT) on written text quality (i.e., the percentages of *positive emotional words*, *negative emotional words*, words of *insight* and words of *causation* participants used during writing exercises), a 4 x 3 x 2 mixed ANOVA was performed. Text analysis in LIWC revealed the percentages of these subcategories of words used by participants during the different writing assignments over time. The results showed no significant main effect on time (F [2, 84] =2.21, p = .116, h^2 = .050) which demonstrates that we did not find a difference between the use of *positive emotional words*, *negative emotional words*, words of *insight* and words of *causation* over the various sessions. The results also showed that the interaction effect between time *x* condition *x* kind of word was non-significant. This indicated that we did not find a difference between the two conditions in the percentages of types of words used over time (F [6, 252] = 1.16, p=.328, h2 =.027) and therefore in the quality of the written texts.

Word count

To analyse the average number of words participants used over time (during session 1, 2, and 3 respectively), we used a 3 x 2 repeated measures ANOVA. The results showed a significant main effect on the factor time, F (2, 88) = 9.34, p < .001, h*2* =.175 which

indicated a significant difference between sessions when looking at the amount of inserted words. The results also indicated a significant interaction effect between time *x* condition (F (2, 88) = 4.79, p = .011, h^2 = .98). This showed that there was a significant difference between the conditions (*3MR*+SWT and SWT) in the amount of words that were used over time. A graph of the analyses (see Figure 7) shows that, contrary to the *3MR*+SWT condition, the amount of words used in the SWT condition decreased after session two. (See also Table 3 for Means and Standard deviations of the word count).

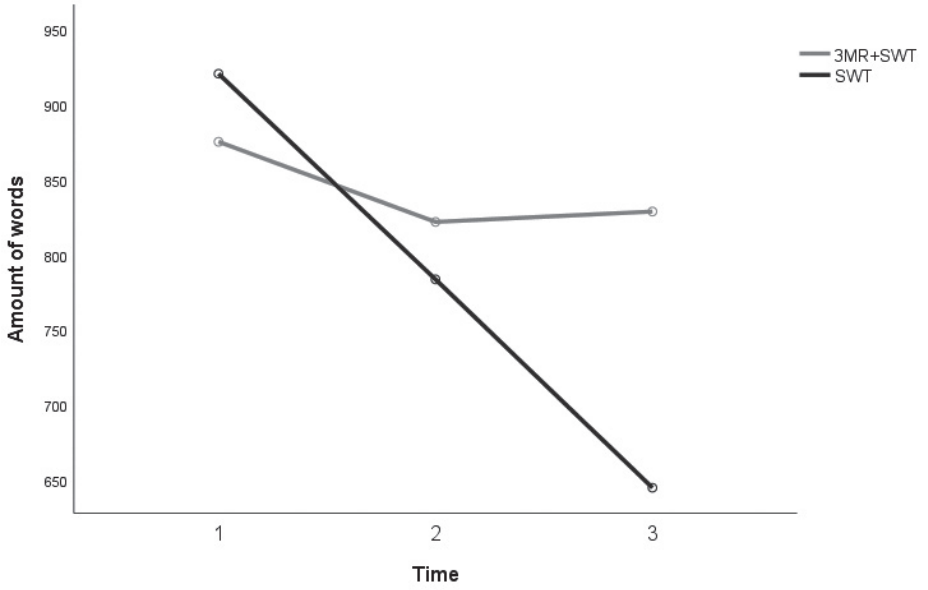


Figure 7: The amount of words used during writing exercises at session 1, session 2, and session 3.

Table 3: Means, standard deviations of inserted words during sessions 1, 2, and 3.

		M	***SD***	***N***
Word count session 1	*3MR*+SWT	875.36	283.97	22
	SWT	920.71	276.14	24
	Total	899.02	277.72	46
Words count session 2	*3MR*+SWT	821.95	336.33	22
	SWT	783.67	337.91	24
	Total	801.98	333.95	46
Word count session 3	*3MR*+SWT	828.86	317.85	22
	SWT	644.75	270.21	24
	Total	732.80	305.14	46

Note: 3MR = *Multi Modal Memory Restructuring*; SWT = *Structured Writing Therapy*

Discussion

The objective of this study was to explore the added value of the *Multi Modal Memory Restructuring* (*3MR*) system in a healthy student sample in overcoming a negative, but non-traumatic memory with the use of structured writing exercises. Overall, the research findings show a consequent pattern when looking at measures of distress, negative affect and intrusions at pre, post and follow-up measurements: both conditions seem effective in the reduction of these mild complaints over time, but no significant difference between the groups was found. A significant decrease of distress, negative affect and the *number*, *vividness* and *distress* of any intrusions was found in both conditions, showing no significant differences between the conditions. So far, these findings indicate no added value of the usage of the tools of the *3MR* system.

A second point of interest was whether the use of the multimedia tools of the *3MR* system improved the quality of the written text. Word categories that are important to get insight into the effectiveness of written text are *positive words* (e.g. happy, joy), *negative words* (e.g. sad, angry), words of *insight* (e.g. because, reason), and *causal* words (e.g. realise, understand). Although we expected to find that the quality of the written texts of the participants in the *3MR*+SWT condition would outperform the SWT condition, this was not shown. No differences over time nor between conditions were observed analysing the use of positive emotional words, negative emotional words, words of insight and words of causation over various sessions. However, another important characteristic to judge written text quality, is the number of words that is used (Van Zuuren, 1999). The length of the text during the writing sessions declined for both conditions but the decline was significantly larger in sessions two and three of the SWT condition. The *3MR* condition therefore resulted in a longer written text over the subsequent writing sessions. As seen in the content analysis of writing about traumatic events, features such as length of writing (the longer the better) and constant length of the text indicate improvements in effective writing exercises (Van Zuuren et al., 1999).

Unfortunately, this RCT is limited by a relatively small sample size. Therefore, it is possible that differences between conditions could not be detected because the study was underpowered. Moreover, the study sample consisted mainly of female, undergraduate psychology students. Therefore the findings might not be generalizable to the intended target population of the *3MR* intervention, namely patients suffering from PTSD.

In conclusion, the current findings confirm the positive effects of writing exercises in overcoming negative memories. Although no substantial evidence could be found for the added value of the use of the multimedia tools of the *3MR* system, the application does seem to stimulate participants to keep the length of the text stable and prevent reduction in the length of the text over time.

5

Patient and Therapist Acceptance of the Multi Modal Memory Restructuring System for the Treatment of Post-traumatic Stress Disorder

This chapter is submitted as:
Van Meggelen, M., Brinkman, W.P., Tielman, M.L.,
Van der Heiden, C., Morina, N., & Franken, I.H.A.

(submitted). Patient and Therapist Acceptance of the Multi Modal Memory Restructuring System for the Treatment of Post-traumatic Stress Disorder

Abstract

The efficacy of internet and computer-based interventions has been validated for a number of mental health problems, including post-traumatic stress disorder (PTSD). Possibly these interventions tackle barriers to seek mental health care and lower waiting times to receive mental health care. However, acceptance of these interventions amongst patients and therapists is a first step that is necessary to implement internet and computer-based interventions as a treatment option in mental health care. The current paper examines the patients' and therapists' acceptance of the *3MR* (Multi Modal Memory Restructuring) intervention for the treatment of PTSD in a childhood sexual abuse (CSA) and veteran sample. A subset of patients (n = 10) of a randomized controlled trial (RCT; Van Meggelen et al., submitted) filled in an adjusted version of the Application Acceptance Questionnaire (AAQ) in order to evaluate their experiences using the *3MR* system. Involved therapists (n = 15) were invited to give their opinion on the *3MR* intervention by filling in an evaluation form. Overall, patients state that they profit from the benefits of this computer-based intervention (i.e., a lower travel intensity), that they feel in control of their therapy and feel that their problems are taken seriously. They also state that the *3MR* intervention helps them to better cope with their fear, and that they do not experience stigmatization by others. In general, therapists' opinion towards the *3MR* intervention was positive, whereas most therapist state that the *3MR* intervention can be an appropriate treatment, has important benefits for their patients, and that they could recommend it to their patients. In the meanwhile, most of the therapists did also support the idea that the *3MR* intervention could only be used as an add-on to regular therapy instead of a standalone module.
The data show a primarily positive trend in the patients' and therapists' acceptance of the *3MR* intervention, which in combination with the promising treatment outcomes from the RCT (Van Meggelen et al., submitted) might form an adequate first step in the direction of future use of this computer-based intervention for the treatment of PTSD.

Keywords: *Computer-based intervention*, *trauma, PTSD*, *treatment, acceptance*, *Multi Modal Memory Restructuring*

Introduction

Computerized and internet-based interventions are known for their ability to reach large groups of people. They have several benefits compared to traditional therapy; often they are personalized and tailored to the needs of a diverse group of users, they can reach a large population at relatively low cost and they can be used from a person's own home (Amstadter, Broman-Fulks, Zinzow, Ruggiero, & Cercone, 2009). Generally, computer-based interventions for psychiatric and somatic conditions yield comparable effect sizes as traditional face to face treatment (Carlbring, Andersson, Cuijpers, Riper, & Hedman-Lagerlöf, 2018). Differences exist in the extent to which assistance is offered during these interventions (e.g., no, administrative assistance or therapist assistance; Richards & Richardson, 2009). Interventions that require only limited therapist involvement can potentially improve cost-effectiveness. The efficacy of internet health interventions in general has been validated for a number of health problems such as social anxiety (Kampmann, Emmelkamp, & Morina, 2016), depression (e.g ., Kenwright, Liness, Marks, 2001; Marks, Kenwright, McDonough, Whittaker, & Mataix-Cols, 2004) and post-traumatic stress disorder (PTSD, e.g., Carlbring et al., 2018; Heber et al., 2017; Karyotaki et al., 2018). In this article the main focus is on PTSD; approximately 7-8% of all people suffer from the effects of this disorder during their life (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; De Vries & Olff, 2009) and typically they re-experience a traumatic event unwantedly manifesting in memory flashbacks or nightmares. Also, they feel anxious, are irritable and avoid memories of the event (American Psychiatric Association, 2013). In general, the majority of individuals with PTSD do not receive treatment and fail to recover even after many years (Morina, Wicherts, Lobbrecht, & Priebe, 2014). There are widely examined and approved therapies for the treatment of PTSD, such as cognitive behavioral therapy (CBT; Cusack et al., 2016). However, barriers to seek mental health care are high, reflecting for example fear of stigmatization, to be seen as weak or to be treated differently (e.g., Regier, Narrow, Rae, Manderscheid, Locke, Goodwin, 1993; Hoge et al., 2004). Thereby, routine waiting times of several months have resulted in multiple reports warranting change (e.g., Mental Health Foundation [MHA], 2018; Nederlandse Zorg Autoriteit [NZA], 2017).

Computer- and web-based interventions may contribute to the reduction of the limitations mentioned above, especially when therapist involvement is limited. In that case, treatment can be obtained more autonomously and anonymously. These interventions can therefore possible tackle the hurdle that patients have to take in order to receive mental health care. However, acceptance of these interventions is an important factor for evaluation. In their advisory paper, the International Society for Research on Internet Interventions (ISRII; Ritterband et al., 2006) describes the

enhanced level of acceptance by government and medical insurers of the feasibility and value of diverse computer-based interventions, such as Beating the Blues for depressive disorders (e.g., Kenwright et al., 2001; Marks et al., 2004) and Fear Fighter for anxiety disorders (McCrone et al., 2004; Proudfoot et al., 2004). Ritterband et al. (2006) mention this acceptance as an essential step in establishing this mode of treatment delivery (via computers and the internet) and recommend that, along with investigating how these interventions compare with more traditional forms of treatment delivery, also their acceptance in the community should be studied.

An example of a computer-based trauma intervention with limited therapist involvement for the treatment of PTSD is the Multi Modal Memory Restructuring (*3MR*) system. The *3MR* system was originally designed by Brinkman, Vermetten, Van de Steen, and Neerincx (2011), and is a software application which focuses on the restructuring and relearning of past events. The *3MR* system allows people to visualize past events using personal photos, narrative texts, online geographical maps and patient-created 3D virtual worlds. Recently we studied the efficacy of this computer-based intervention in a childhood sexual abuse (CSA) and veteran sample of PTSD patients in a randomized controlled trial (RCT; Van Meggelen et al., submitted). The *3MR* intervention was compared to 'treatment as usual' (TAU), which consisted of recommended trauma-focused interventions for PTSD (i.e., Imaginal Exposure [IE], Eye Movement Desensitization and Reprocessing [EMDR], or Narrative Exposure Therapy [NET]). Results showed that in both treatment conditions symptoms of both PTSD and depression significantly decreased between pre and post measurements after 12 sessions and that there was no significant difference found between *3MR* or TAU. Based on these findings it was concluded that the *3MR* intervention seems effective for the treatment of PTSD and similarly effective as evidence-based treatments. Therefore it is ought to constitute an appropriate treatment alternative, especially when therapist availability is lowered and the intention to enlarge reach of treatment efforts and improve cost-effectiveness are present (Van Meggelen et al., submitted). During the implementation of our computer-based intervention with limited therapist assistance for the treatment of PTSD we encountered some doubts or even resistance amongst both patients with PTSD and trauma therapists (personal notes). This could be expected, since computer-based interventions with limited therapist assistance ask for change in roles of both the patient and the therapist when compared to more traditional psychotherapeutical approaches. For example, Feijt, De Kort, Bongers, & IJsselsteijn (2018) describe the need for therapists to adopt new behaviors in order to successfully adopt eMental Health tools in their paper on perceived drivers and barriers to the adoption of eMental Health by psychologists. Moreover, PTSD is a complex disorder, for which well established and generally intensive therapy methods exist (i.e., CBT, Cusack et al., 2016). Since the described impression

was only based on our experiences and no actual information on acceptance of this intervention was available, we decided to investigate this in a subsample of our RCT population and their therapists. The current paper examines the acceptance of the *3MR* intervention by patients and therapists. It is important to note that the results of the clinical trial were not known to patients nor therapists at the time of the assessment of this acceptance. Also, we elaborate on the implications of these findings for future use of this computer-based intervention for the treatment of PTSD.

Method & Materials

Procedure

This study represents an explorative elaboration of patients' and therapists' acceptance of the *3MR* intervention. This study was part of the 'Virtual eCoaching and Storytelling technology for Post-traumatic stress disorder treatment' (VESP) project[2], initiated by Delft University of Technology and granted by NWO, no. 314-99-104. The data used in this study were collected in the context of the randomized controlled trial (RCT) amongst patients with PTSD, which included an experimental (*3MR* intervention) and control condition (TAU). Patients either had a background in CSA or war related trauma (veterans). The general aim of the RCT was to (1) evaluate the efficacy of the *3MR* intervention; and (2) to compare this to 'treatment as usual' (TAU). A detailed description of this RCT is described in a previous paper (Van Meggelen et al., submitted). Data in the current study are analysed using descriptive statistics.

Participants

The study presented in this paper focuses on a survey completed by the experimental group of the RCT (n = 10), which was filled in half way through therapy sessions of the *3MR* intervention (i.e., at session 6 of a total of 12 sessions), and on an online survey completed by trauma therapists (n = 15) that reported their beliefs about the *3MR* intervention post involvement in the VESP project[3]. Participation in this evaluation was of free choice for both participants and therapists, therefore available data do not cover all participants of the experimental group in the RCT (n = 12) and therapists that were involved in the VESP project (approximately n = 60). Therapists came from five different

2 ii.tudelft.nl/vesp/

3 Therapists were involved in different parts of the VESP project, which means that therapists that filled in the evaluation questions were familiar with different versions of the 3MR application (i.e., version 3MR1.0 [standalone application, used in the RCT], or version 3MR2.0 [upgraded and internet-based, test phase]). For a description see Tielman, Neerincx, Bidarra, Kybartas, & Brinkman, 2017]. Illustrative screenshots of both applications are online available [doi:10.4121/uuid:cacc5b31-047e-4e88-b341-cff18d76de49])

mental health care centers in the Netherlands that were involved in the VESP project (i.e., PsyQ Parnassia Group, Reinier van Arkel Goup, GGZ Delfland, Virenze and Arq Psychotrauma Center). Seventy-three percent of the therapists that filled in the evaluation, had previously recruited one or more patients for following the *3MR* intervention.

Measures

Application Acceptance Questionnaire – 3MR

A tailored Application Acceptance Questionnaire (AAQ) is created for the evaluation of the patients' acceptance of the *3MR* system (and its accompanying therapy manual [hard copy session guide]). Questions are based on a previous version of the AAQ developed for the evaluation of the patient acceptance of a self-management support systems (SMSS) for renal transplant patients to increase their autonomy and reduce the number of hospital visits (as seen in Wang et al., 2017). The adjusted AAQ consists of ten categories: (1) Behavioral Intention, (2) Performance Expectancy, (3) Effort Expectancy, (4) Facilitating Conditions, (5) Affect, (6) Self-efficacy, (7) Trust, (8) Social Influence, (9) Concern, and (10) Component Evaluation. Original categories are preserved and category 10 is added to the original questionnaire. Questions are adjusted to fit evaluation of the *3MR* system instead of the renal transplant SMSS. Items are scored on a 7 point Likert-scale ranging from 1 ('*I totally disagree*') to 7 ('*I totally agree*'). In the current article categories 2, 3, 5, and 8 of the adjusted AAQ are explored since the other categories are less suitable for the current evaluation (e.g., Category 1) or more of interest for the system developers to upgrade the *3MR* intervention with specific feedback given by patients (e.g. Category 10).

Therapist Evaluation 3MR intervention

Therapists were invited to give their opinion about the *3MR* intervention in an online survey consisting of two general items; (1) '*I believe scientific research in mental health care is important*', (2) '*I believe technological innovations in mental health care are important*', and five *3MR*-specific items; (3) '*I believe that the* 3MR *intervention can be an appropriate treatment*', (4) '*I believe that the* 3MR *intervention can only be used as add-on on a regular treatment protocol*', (5) '*I believe the* 3MR *intervention has important benefits for my patient*', (6) '*I believe that the* 3MR *intervention will overburden my patient*', and (7) '*I would recommend my patient to follow the* 3MR *intervention*'. Items are scored on a 7 point Likert-scale ranging from 1 ('I totally disagree') to 7 ('I totally agree').

Results

Application Acceptance Questionnaire – 3MR

Performance Expectancy

The category Performance Expectancy consists of eight questions aimed at the overall interest whether patients believe that the *3MR* application can help them in decreasing their symptoms of PTSD with limited therapist assistance. Overall, patients score this category 5.9 out of 7 points. A strong majority of patients underline benefits of the way in which the *3MR* intervention is offered, namely in the comfort of their own environment (cumulated categories 6 and 7; 80%) and thereby lowered travel intensity (category 7; 90%). Also, participants feel in control of their therapy (cumulated categories 6 and 7; 90%) and experience they can follow through the *3MR* intervention autonomously and anonymously (cumulated categories 6 and 7; 90%). Also, they report that the *3MR* intervention helps them to better cope with their fears (cumulated categories 5 and 7; 80%). See Figure 1 and Table 1.

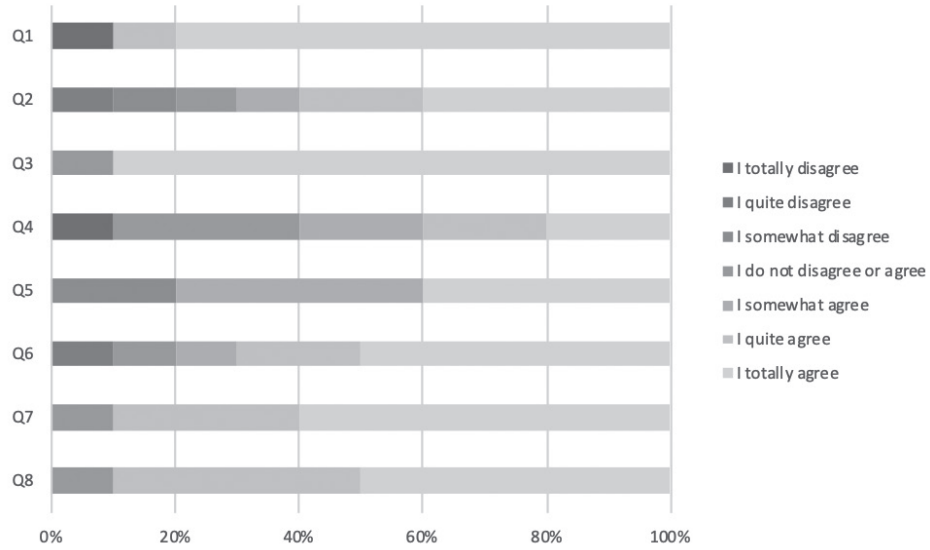


Figure 1: Stack bar chart of adjusted AAQ Performance Expectancy scale

Table 1: AAQ – 3MR Category 2. Performance Expectancy

Question	I totally disagree (1)	I quite disagree (2)	I somewhat disagree (3)	I do not agree or disagree (4)	I somewhat agree (5)	I quite agree (6)	I totally agree (7)
Q1. 'An important advantage is that I can follow this treatment in my own safe and familiar surrounding'	10%					10%	80%
Q2. 'Because I follow this treatment at home, I have more time for other things'		10%	10%	10%	10%	20%	40%
Q3. 'An important advantage of the treatment is that I don't have to travel'				10%			90%
Q4. 'Because of the treatment I tend to avoid less situations'	10%			30%	20%	20%	20%
Q5. 'The 3MR application helps me to better cope with my fear'			20%		40%		40%
Q6. 'The therapy manual gives me useful information on PTSD and the treatment'		10%		10%	10%	20%	50%
Q7. 'The 3MR application gives me control over my own treatment'				10%		30%	60%
Q8. 'Because of the 3MR application I can follow through treatment autonomous and anonymous'				10%		40%	50%

Note: 3MR = *Multi Modal Memory Restructuring*

Effort Expectancy

The category Effort Expectancy consists of six questions aimed at the overall interest in how much effort patients think using the *3MR* application costs them. Overall, patients score this category 5.3 out of 7 points. As shown in Figure 2 and Table 2 the effort rated to use the *3MR* application and accompanying therapy manual shows a very ambiguous response pattern, reflecting considerably different user experiences. Still, the majority of patients for example agrees in some degree that the *3MR* application is easy to use (cumulated categories 5, 6, and 7; 70%) and 80% (cumulated categories 6 and 7) states that it was easy for them to learn how to use the *3MR* application.

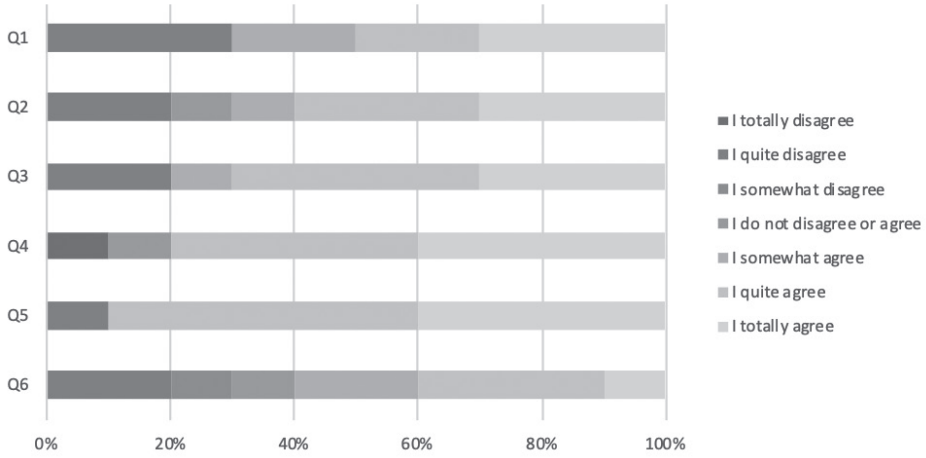


Figure 2: Stack bar chart of the adjusted AAQ Effort Expectancy scale

Table 2: AAQ – 3MR Category 3. Effort Expectancy

Question	I totally disagree (1)	I quite disagree (2)	I somewhat disagree (3)	I do not agree or disagree (4)	I somewhat agree (5)	I quite agree (6)	I totally agree (7)
Q1. 'Using the 3MR application does not cost me a lot of effort'		30%			20%	20%	30%
Q2. 'The 3MR application is easy to use'		20%		10%	10%	30%	30%
Q3. 'Using the 3MR application does not raise ambiguity'		20%			10%	40%	30%
Q4.'Learning how to use the 3MR application is easy for me'	10%			10%		40%	40%
Q5. 'Using the therapy manual does not cost me a lot of effort'		10%				50%	40%
Q6. 'Using the 3D environment [part of 3MR application, red.] *does not cost me a lot of effort'*		20%	10%	10%	20%	30%	10%

Note: 3MR = *Multi Modal Memory Restructuring*

Affect

The category Affect consists of four questions aimed at the overall interest in whether patients like working with the *3MR* application. Overall, patients score this category 5.7 out of 7 points. As shown in Figure 3 and Table 3 most patients find it interesting to use the *3MR* application (cumulated categories 6 and 7; 90%) and feel that their problems are taken seriously by using this application (cumulated categories 6 and 7; 80%).

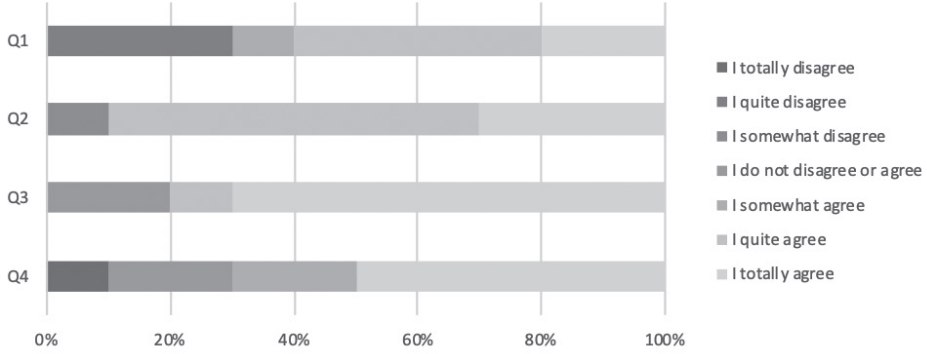


Figure 3: Stack bar chart of the adjusted AAQ Affect scale

Table 3: AAQ – 3MR Category 5. Affect

Question	I totally disagree (1)	I quite disagree (2)	I somewhat disagree (3)	I do not agree or disagree (4)	I somewhat agree (5)	I quite agree (6)	I totally agree (7)
Q1. 'I believe the 3MR application is comfortable in use'		30%			10%	40%	20%
Q2. 'I believe it is interesting to use the 3MR application'			10%			60%	30%
Q3. 'The 3MR application gives me the feeling my problem is taken seriously'				20%		10%	70%
Q4. 'The approach of the 3MR application gives me a safe feeling'	10%			20%	20%		50%

Note: 3MR = *Multi Modal Memory Restructuring*

Social Influence

The category Social Influence consists of six questions aimed at the overall interest in what patients believe other people think of the use of the *3MR* application. Overall, patients score this category 5 out of 7 points. Percentages show that a majority of patients do not think they will be judged negatively by their environment for using the *3MR* application (cumulated categories 1 and 2; 70%) and also that friends, family and other patients (should) recommend them to use the *3MR* application (cumulated categories 5, 6, and 7; respectively 70%, 70% and 80%). See Figure 4 and Table 4.

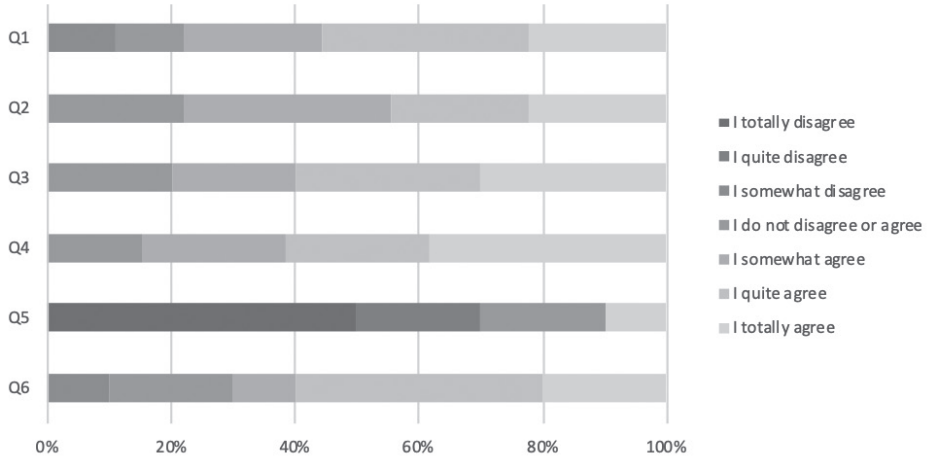


Figure 4: Stack bar chart of the adjusted AAQ Social Influence scale

Table 4: AAQ – 3MR Category 8. Social Influence

Question	I totally disagree (1)	I quite disagree (2)	I somewhat disagree (3)	I do not agree or disagree (4)	I somewhat agree (5)	I quite agree (6)	I totally agree (7)
*Q1. 'I believe my friends (should) advise me to use the 3MR application'**			10%	10%	20%	30%	20%
*Q2. 'I believe my family (should) advise me to use the 3MR application'***				20%	30%	20%	20%
Q3. 'I believe that healthcare employees in general would think that I should use the 3MR application'				20%	20%	30%	30%
Q4. 'I believe that people in my work surroundings (should) advise me to use the 3MR application'				20%	30%	30%	50%
Q5. 'I believe that my environment will judge a person who uses the 3MR application negatively'	50%	20%		20%			10%
Q6. 'I believe that other patients (should) encourage me to use the 3MR application'			10%	20%	10%	40%	20%

Note: 3MR = *Multi Modal Memory Restructuring; * Missing data* n = *1; ** Missing data* n = *1*

Therapist Evaluation 3MR intervention

Results of the general opinion part of the therapist evaluation show that off all responding therapists, 93% totally agreed with the claim that scientific research in mental health care is important. For the claim that technological innovations in mental health care are important, this was 80%. Results of the *3MR*-specific evaluation part of the therapist evaluation (see Figure 6 and Table 5) show a reasonably positive response pattern whereas most therapists in some degree agree (cumulated categories 5, 6, and 7) that the *3MR* intervention can be an appropriate treatment (86.7%), has important benefits for their patients (80%), and that they could recommend it to their patients (86.6%). However, most of the therapists seem to be prone to the idea that the *3MR* intervention could only be used as an add-on to regular therapy instead of a standalone module (cumulated categories 5, 6 and 7; 73.3%), whereas a minority somewhat disagrees with this item (category 3; 20%). Therapists are divided about the idea that the *3MR* intervention would be too much of a burden for the patient, as the response pattern on this item is divided into therapists that into some degree agree (cumulated categories 5, 6, and 7; 33.3%), disagree (cumulated categories 2 and 3; 33.4%), or are indecisive (category 4; 33.3%).

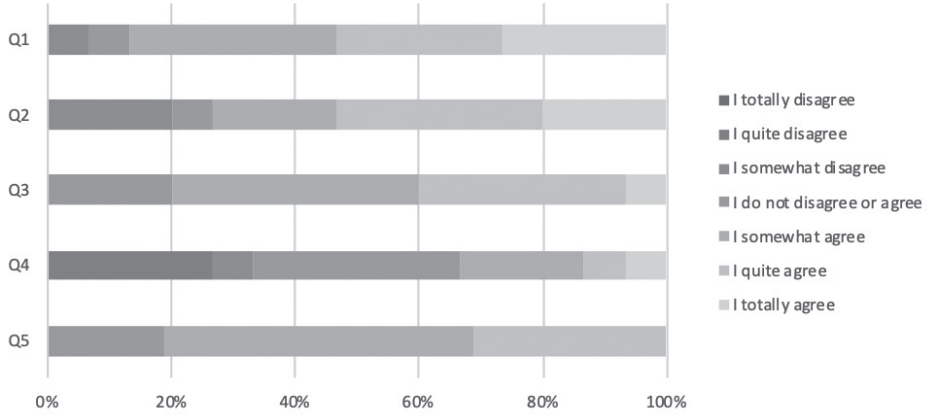


Figure 8: Stack bar chart of the 3MR-specific therapist evaluation items

Table 5: Therapist Evaluation - 3MR specific

Question	I totally disagree (1)	I quite disagree (2)	I somewhat disagree (3)	I do not agree or disagree (4)	I somewhat agree (5)	I quite agree (6)	I totally agree (7)
Q1. 'I believe that the 3MR *intervention can be an appropriate treatment'*			6.7%	6.7%	33.3%	26.7%	26.7%
Q2. 'I believe that the 3MR *intervention can only be used as add-on on a regular treatment protocol'*			20%	6.7%	20%	33.3%	20%
Q3. 'I believe the 3MR *intervention has important benefits for my patient'*				20%	40%	33.3%	6.7%
Q4. 'I believe that the 3MR *intervention will overburden my patient'*		26.7%	6.7%	33.3%	20%	6.7%	6.7%
Q5. 'I would recommend my patient to follow the 3MR *intervention'*				20%	53.3%	33.3%	

Note: 3MR = *Multi Modal Memory Restructuring*

Discussion

There are widely examined and approved therapies for the treatment of PTSD (Cusack et al., 2016). However, the majority of individuals with PTSD do not receive treatment and most of them fail to recover even after many years (Morina, Wicherts, Lobbrecht, & Priebe, 2014). Also, barriers to seek mental health care are high (Regier, Narrow, Rae, Manderscheid, Locke, Goodwin, 1993) and routine waiting times of several months have resulted in multiple reports warranting change (e.g., Mental Health Foundation [MHA], 2018; Nederlandse Zorg Autoriteit [NZA], 2017). Computer-based and internet interventions may contribute to the reduction of the issues mentioned above, especially when therapist involvement is lowered. The possibility to receive treatment in a more autonomous and anonymous manner may tackle perceived barriers to seek mental health care, such as fear of stigmatization by others. However, acceptance of these interventions is an important factor for evaluation and can contribute to clearly establishing internet and computer-based interventions as a viable and effective form of treatment (Ritterband et al., 2006).

The current paper describes the patients' and therapists' acceptance of the *3MR* intervention, a computer-based trauma intervention with limited therapist involvement for the treatment of PTSD (Brinkman et al, 2011; Van Meggelen et al., submitted). In a recent RCT the *3MR* intervention has shown efficacy in the treatment of PTSD and turned out to be similarly effective compared to evidence-based treatments (such as EMDR, IE or NET; Van Meggelen et al., submitted). To further investigate the acceptance of this intervention, evaluation data of both involved trauma patients (n = 10) and therapists (n = 15) were explored.

The data point out that in the category Performance Expectancy most of the patients underline benefits of the way in which the *3MR* intervention is offered (in the comfort of their own environment [80%] and with lowered travel intensity [90%]. Also, 80% of the therapists that filled in an evaluation questionnaire declared that they see important benefits for their patients in using this *3MR* application. A point that stands out in the category Performance Expectancy is that 90% of the patients say they feel in control of their therapy and experience that they can follow through the *3MR* intervention autonomously and anonymously. Eighty percent of the participants declares that the *3MR* intervention helps them to better cope with their fear. These indications are very promising considering the low therapist assistance that the *3MR* intervention entails. Another important point of interest (evaluated in the category Effort Expectancy) was the patient rated efforts in using the *3MR* application. However, patient data on this question show a very ambiguous response pattern. This means that there were very different user experiences reported. Nevertheless, a majority of 70% agrees in some degree that it was easy for them to use

the *3MR* application, and 80% states that learning how to use the application was not complicated for them. Data in the category Social Influence show that a majority of patients (70%) don't think they will be judged negatively by their environment for using the *3MR* application and also that other patients (should) recommend them to use the *3MR* application (80%). Especially the first finding is important, since stigmatization by others normally forms a great barrier to even seek help for mental health problems (e.g., Hoge et al., 2004). Overall, patients state that they profit from the benefit of this computer-based intervention, that they feel in control of their therapy and feel that their problems are taken seriously. They also state that the *3MR* intervention helps them to better cope with their fear, and that they do not experience stigmatization by others, as is often seen in help-seeking patients with mental health problems. The written feedback of the patients mainly concerns the '3D environment' tool of the application, about which they for example declare that it '*was not suitable for veterans that have been deployed to Lebanon, e.g., wrong vehicles, helmets etc.*', '*…my experience was at the Caribbean, and everything was based at buildings in Europe*'). This feedback can be taken into account in future adjustments of the *3MR* or similar applications.

When looking further into the therapist evaluation it can be stated that the therapists that filled in the evaluation, strongly support the importance of scientific research (93%) and technological innovations (80%) in mental health care. In general, their opinion towards the *3MR* intervention was positive, whereas most therapists state that the *3MR* intervention can be an appropriate treatment (86.7%), has important benefits for their patients (80%), and that they could recommend it to their patients (86.6%). However, most of the therapists did support the idea that the *3MR* intervention could only be used as an add-on to regular therapy instead of a standalone module (73.3%). Only a minority somewhat disagreed with this item (20%). Since therapists were divided about the idea whether the *3MR* intervention would be too much of a burden for the patient, this reasoning seems to not fully account for the noted hesitance in using the *3MR* intervention as standalone intervention. This is in line with previous findings from Feijt et al. (2018) that psychologists only like to use eMental health in combination with face-to-face sessions, since they feel that face to face contact is indispensable for the delivery of their treatment. Written feedback of the therapists ('*it is a sufficient option for the treatment of less complicated trauma complaints*', '*after the 3MR intervention there needs to be a phase in which avoidance is lowered*', '*the effects are larger with milder trauma symptoms*') indicated a somewhat hesitant feeling towards acceptance of the *3MR* intervention for the treatment of PTSD. As mentioned before, we find this hesitance for acceptance understandable, since computer-based interventions with limited therapist assistance ask for change in roles of both the patient and the therapist when compared to more traditional working methods, and PTSD is undeniably a very complex disorder.

However, results from the RCT (Van Meggelen et al., submitted) and the current patient acceptance descriptions do not endorse the need for this restraint.

Being limited to a small data set, this study provides first indications into the patients' and therapists' acceptance of the *3MR* intervention. Importantly, although the sample size of the patient evaluation was small, it does reflect the opinion of the majority of the patients that followed the *3MR* intervention in the RCT. This is different for the therapist evaluation, however, as only a small group of the potential trauma therapists participated. Arguably, these therapists represent a positive biased population as possibly therapists with a negative attitude regarding the *3MR* system did not participate in the study. On the other hand, Feijt et al. (2018) indicated that the general attitude towards computer-based interventions in the workplace seemed to be rather more disinterested than judgmental, which could also be a possible explanation for the low response rate amongst therapists. Nevertheless, the described outcomes might thus not be generalizable to the majority of trauma therapists involved in the VESP project via one of the participating mental health care centers. The current exploration of the therapist's acceptance therefore provides only limited insight into therapists' opinion about the *3MR* intervention in general.

Nevertheless, the available data show a primarily positive trend in the patients' and therapists' acceptance of the *3MR* intervention, which in combination with the promising results from the RCT (Van Meggelen et al., submitted) might form a proper basis for future use of this computer-based intervention for the treatment of PTSD, especially when patient and therapist feedback is taken into account to optimize usability and treatment outcomes.

6

Summary and conclusions

Summary of main findings

The main objective of this dissertation was to investigate the overall efficacy, acceptance and future implications of the *3MR* intervention for the treatment of PTSD. The *3MR* intervention is a computer-based trauma intervention with elements of Virtual Reality (VR) and limited therapist involvement for the treatment of PTSD, offered via the *Multi Modal Memory Restructuring* (*3MR*) system. Below, our main findings are described.

In this dissertation we started by exploring the current state of art of the field of Virtual Reality Exposure Therapy (VRET) for the treatment of PTSD in a meta-analysis. To our knowledge, no meta-analysis had been published on the efficacy of VRET in the treatment of PTSD before. We focused primarily on clinical trials that reported treatment outcome data comparing VRET with any kind of comparison group. Overall, 337 records were found in the Scopus database and ten of these met our inclusion criteria. These ten included clinical trials compared VRET with active (other treatment, such as CBT or EMDR) or inactive (such as Waitlist or Minimal Attention [MA]) control conditions among patients with PTSD. We found that VRET and active control conditions showed no significant differences in terms of efficacy (which means, reduction of symptoms of PTSD). Compared to inactive treatment conditions, VRET did significantly better. For comorbid depression, a similar pattern was seen (**Chapter 2**).

To determine the efficacy of the *3MR* intervention, we conducted a randomized controlled trial (RCT) amongst traumatized victims of childhood sexual abuse (CSA) and war veterans. In this trial we compared the effects of the *3MR* intervention to those of more regular treatment methods ('treatment as usual', TAU). TAU consisted of evidence-based approaches such as imaginal exposure, EMDR, or narrative exposure therapy. Patients enrolled for treatment via several specialized mental health care centers in The Netherlands and were offered the possibility to join this research project if inclusion criteria were met (e.g., having a primary diagnosis of PTSD due to CSA or war related trauma). A total of 44 patients with PTSD was included in the RCT. Patients were randomly assigned to either 12 sessions of *3MR* intervention or TAU. Self-report questionnaires aimed at measuring symptoms of PTSD, depression and overall well-being, and a semi-structured clinical interview pointed at the diagnoses of PTSD and depression were administered at pre, post, and a three month follow-up measurement. Results showed that symptoms of PTSD and depression both significantly decreased between pre and post measurements and that there was no significant difference found between the two treatment conditions. Similar results were found for the increase of overall well-being. Both treatment conditions produced similar remission rates of PTSD and depression (**Chapter 3**).

On this basis we wanted to gather more detailed knowledge about the specific working mechanisms of the *3MR* intervention. Therefore we conducted an RCT amongst a healthy student population directed at investigating the added value of the multimedia tools of the *3MR* system to writing exercises. A total of 55 first-year Psychology students with a negative but not traumatic memory were included to follow either three sessions of structured writing assignments preceded by 15 minutes use of the *3MR* tools (e.g., 'Website', 'Media', 'Emotions', and 'Images'; *3MR*+SWT condition), or structured writing assignments preceded by 15 minutes of thinking about the aversive memory (SWT condition). Results showed a significant decrease of distress, negative affect as well as the number, vividness and distress of the reported intrusions evoked by the aversive memory. The findings confirmed the positive effects of writing exercises in overcoming negative memories, but no substantial added value of the use of the multimedia tools of the *3MR* system was found. Nevertheless, the *3MR* application did seem to stimulate participants to keep the length of the text stable and prevent reduction in the length of the text over time, which in general is associated with positive outcomes (**Chapter 4**).

Finally, this dissertation focused on the patients' and therapists' acceptance of the *3MR* intervention. A subset of patients (n = 10) of the RCT and 15 involved trauma therapists filled in evaluation questionnaires considering their experiences with and beliefs about the *3MR* intervention. Overall, patients stated that they profited from the benefits of the *3MR* intervention (i.e., a lower travel intensity), that they felt in control of their therapy and felt that their problems were taken seriously. They also stated that the *3MR* intervention helped them to better cope with their fear, and that they did not experience stigmatization by others. In general, therapists' opinion towards the *3MR* intervention was positive as well, whereas most therapist stated that the *3MR* intervention could be an appropriate treatment, has important benefits for their patients, and that they could recommend it to their patients. In the meanwhile, most of the therapists did also support the idea that the *3MR* intervention could only be used as an add-on to regular therapy instead of a standalone module. Although compromised by a small dataset, the results showed a primarily positive trend in the patients' and therapist's acceptance of the *3MR* intervention, which in combination with the promising treatment outcomes from the RCT might form an adequate first step in the direction of future use of this computer-based intervention for the treatment of PTSD (**Chapter 5**).

Discussion and future implications

Now let us turn to the discussion of the findings that are mentioned above. Where do these findings lead us, and what future hurdles are there to take?

At this point in time, there seems no longer a way around the efficacy of VRET and computer-based interventions for the treatment of PTSD. Although obviously larger sample sizes, more controlled studies and standardized treatment methods and studies are desired, the findings in this dissertation also show that over time VRET and computer-based interventions for PTSD primarily show positive treatment results. Thereby, the need for interventions that may improve the effectiveness, cost-effectiveness, and accessibility for individuals with PTSD might have never been more topical than right now. Perceived barriers to seek help are traditionally high (Regier, Narrow, Rae, Manderscheid, Locke, Goodwin, 1993; Hoge et al., 2004; Lewis et al, 2005), but by now waiting lists in mental health care are remarkably long, indicating a growing need for trained therapists or efficient interventions with low therapist involvement to meet the needs of the current society. Also, since the general acceptance of the existence of mental health problems, for example caused by traumatic experiences, is emerging worldwide, more and more people will claim the need for psychological help. This ensures that the issues mentioned above are here to stay, unless we show flexibility and extend our current treatment approaches for PTSD.

Of course, there are still hurdles to take. As mentioned before, studying the efficacy of computer-based interventions with limited therapist assistance is an ongoing process in which we have to keep asking ourselves whether we offer help seeking individuals the most sufficient treatment options. However, another important issue in research on technological innovations such as the *3MR* intervention, is the fact that it takes generally several years to develop client focused VR or computer-based interventions, and even longer to study their efficacy in controlled trials. Most of the time technological innovations, are not that innovative anymore by the time results on their efficacy are available and implementation in clinical practice could be on the agenda. The *3MR* intervention is no exception to that matter. We need to find ways to speed up these processes, in order to better keep up with patients' needs in terms of user-friendliness of promising computer-based interventions. Also, since offering the *3MR* intervention with limited therapist assistance to a sample with a complex disorder such as PTSD raised many questions up forehand, it is considered important to note here that although not all participants benefitted from the *3MR* intervention, and a part of the sample did not manage to finish the treatment, no serious adverse events have taken place during the RCT. Nevertheless, data on especially the therapists' acceptance of *3MR* show a positive, yet hesitant attitude towards the *3MR* intervention. Recently, Feijt, De Kort, Bongers, & IJsselsteijn (2018) held in-depth interviews with psychologists on their perceived drivers and barriers in using eMental Health interventions. They describe that for example no or minimal use of these interventions can go together with the feeling of being forced to use it, or the fact that psychologists are unconvinced of the benefits of computer-based

interventions. To overcome these barriers, implementation of interventions as *3MR* in clinical practice should go together with intensive collaboration with involved therapists. Not only to convince therapists of possible benefits based on efficiency studies, but also with eye for the knowledge which is needed to implement these interventions into daily clinical practice, and the amount of time it costs to take this in for example. A last hurdle, not based on any scientific research, but on numerous conversations during the establishment of this dissertation, might be the idea that computer-based interventions are aimed at replacing therapists, which will therefore make them unnecessary in the future. Nothing could be further from the truth. Based on the current issues in mental health care which are described above, this can never be the case nor a purpose by any means. Both therapists and innovative computer-based interventions are needed to overcome boundaries to seek mental health care, to tackle waiting lists and to reach out to individuals who need psychological help after a traumatic experience. We hope that the findings of this dissertation motivate researchers, health care managers and therapists to feel that they owe it to all those people waiting for treatment on long waiting lists, living in remote areas or simply without the financial resources to access mental health care, to be open for the implementation of easy accessible computer-based interventions for the treatment of PTSD. And with this, broaden the current treatment approaches for PTSD.

R

References

Alonso, J., Angermeyer, M.C., Bernert, S., Bruffaerts, R., Brugha, T. S., Bryson, H., de Girolamo, G…& Vollebergh, W.A.M. (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.

American Psychiatric Association (2013). Diagnostic and Statistical Manual of Mental Disorders [DSM V]. Washington, D.C.: American Psychiatric Association.

Amstadter, A. B., Broman-Fulks, J., Zinzow, H., Ruggiero, K. J., & Cercone, J. (2009). Internet-based interventions for traumatic stress-related mental health problems: A review and suggestion for future research. *Clinical Psychology Review*, *29*(5), 410-420. doi: 10.1016/j.cpr.2009.04.001.

Baños, R.M., Guillen, V. Quero, S., García-Palacios, S.A, Alcaniz, M., Botella, C. (2011). A virtual reality system for the treatment of stress-related disorders: A preliminary analysis of efficacy compared to a standard cognitive behavioral program. *International Journal of Human-Computer Studies*, *69(9)*, 602-613.

Baŝoğlu, M., Şalcioğlu, E., & Livanou, M. (2007). A randomized controlled study of single-session behavioural treatment of earthquake-related post-traumatic stress disorder using an earthquake simulator. *Psychological Medicine*, *37*, 203–213. doi: 10.1017/S0033291706009123

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). Beck Depression Inventory-Second Edition manual. San Antonio, TX: The Psychological Corporation.

Bernstein, E.M., & Putnam, F.W. (1986). Development, reliability, and validity of a dissociation scale. *The Journal of Nervous and Mental Disease*, *174*(12), 727-735.

Bijur, P. E., Silver, W., & Gallagher, E. J. (2001). Reliability of the visual analog scale for measurement of acute pain. *Academic Emergency Medicine, 8*(12), 1153-1157.

Blevins, C.A., Weathers, F.W., Davis, M.T., Witte, T.K., & Domino, J.L. (2015). The Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5): Development and Initial Psychometric Evaluation. *Journal of Traumatic Stress*, *28*, 489–498. doi: 10.1002/jts.22059

Boeschoten, M.A., Bakker, A., Jongedijk, R.A. & Olff, M. (2014). PTSD checklist for the DSM-5 – Nederlandstalige versie. In voorbereiding.

Boonstra, A. M., Preuper, H. R. S., Reneman, M. F., Posthumus, J. B., & Stewart, R. E. (2008). Reliability and validity of the visual analogue scale for disability in patients with chronic musculoskeletal pain. *International Journal of Rehabilitation Research*, *31*(2), 165-169.

Boot, P., Zijlstra, H., & Geenen, R. (2007). The Dutch translation of the Linguistic Inquiry and Word Count (LIWC) 2007 dictionary. Dutch Journal of Applied Linguistics, *6*(1), 65-76.

Botella, C., Garcia-Palacios, A., Guillen, V.M., Baños, R.M., Quero, S., & Alcaniz, M. (2010). An Adaptive Display for the Treatment of Diverse Trauma PTSD Victims. *Cyberpsychology, Behavior, and Social Networking*, *13*(1), 67-71. doi: 10.1089=cyber.2009.0353

Bradley, R., Green, M. A., Russ, B. A., Dutra, M. A., & Westen, D. (2005). A Multidimensional Meta-Analysis of Psychotherapy for PTSD. *American Journal of Psychiatry*, 162, 214-227.

Brinkman, W. P., Vermetten, E., Van den Steen, M., & Neerincx, M. (2011). Cognitive Engineering of a Military Multi-Modal Memory Restructuring System. *Journal of CyberTherapy and Rehabilitation*, *4*, 83-99.

Carlbring, P., Andersson, G., Cuijpers, P., Riper, H., & Hedman-Lagerlöf, E. (2018). Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: an updated systematic review and meta-analysis. *Cognitive Behaviour Therapy*, *47*(1), 1-18.

Carlbring, P., Westling, B.E., Ljungstrand, P., Ekselius, L. Andersson, G. (2001). Treatment of panic disorder via the internet: A randomized trial of a self- help program *Behavior Therapy*, *32*(4), 751-764. doi: 10.1016/S0005-7894(01)80019-8

Castro, W. P., Sánchez M. J. R., González C. T. P., Bethencourt J. M., de la Fuente Portero J. A., Marco R. G. (2014). Cognitive-behavioral treatment and antidepressants combined with virtual reality exposure for patients with chronic agoraphobia. *International Journal of Clinical Health Psychology, 14*, 9–17. 10.1016/S1697-2600(14)70032-8

Chambless, D.L., & Hollon, S.D. (1998). Defining Empirically Supported Therapies. *Journal of Consulting and Clinical Psychology, 66*(1), 7–18.

Cohen, J. (1988). Statistical power analysis for the behavioral sciences. Hillsdale: Erlbaum.

Crawford, J. R., & Henry, J. D. (2004). The Positive and Negative Affect Schedule (PANAS): Construct validity, measurement properties and normative data in a large non-clinical sample. *British Journal of Clinical Psychology, 43*(3), 245-265.

Cuijpers, P., van Straten, A., Bohlmeijer, E., Hollon, & Andersson, S.D. (2010). The effects of psychotherapy for adult depression are overestimated: a meta-analysis of study quality and effect size. *Psychological Medicine*, *40(2)*, 211-223.

Cusack, K., Jonas, D. E., Forneris, C. A., Wines, C., Sonis, J., Middleton, J. C., ... & Weil, A. (2016). Psychological treatments for adults with posttraumatic stress disorder: A systematic review and meta-analysis. *Clinical Psychology Review*, *43*, 128-141.

De Jong, K., Nugter, A. M., Polak, M. G., Wagenborg, J. E. A., Spinhoven, P., & Heiser, W. J. (2007). The Outcome Questionnaire (OQ-45) in a Dutch Population: A Cross Cultural Validation. *Clinical Psychology and Psychotherapy*, *14*, 288-301. doi: 10.1002/cpp.529

De Vries, G. J., & Olff, M. (2009). The lifetime prevalence of traumatic events and posttraumatic stress disorder in the Netherlands. *Journal of Traumatic Stress*, *22*(4), 259- 267. doi: 10.1002/jts.20429

DerSimonian, R., & Laird, N. (1986). Meta-analysis in clinical trials. *Controlled Clinical Trials*, *7*, 177–188.

Difede, J., Cukor, J., Jayasinghe, N., Patt, I., Jedel, S., Spielman, L., Giosan, C., & Hoffman, H.G. (2007). Virtual Reality Exposure Therapy for the Treatment of Posttraumatic Stress Disorder Following September 11, 2001. *Journal of Clinical Psychiatry*, *68*(*11*), 1639-1649.

Dirkzwager, A.J.E. & Bramsen, I. (2008). Deelname aan vredesmissies: gezondheidsgevolgen en behoefte aan zorg bij veteranen en hun familie. *Bijblijven*, *24* (8), 17-26.

Duval, S., & Tweedie, R. (2000). Trim and fill: A simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. *Biometrics*, 56(2), 455–463. doi: 10.1111/j.0006-341X.2000.00455.x

Ehring, T., Fuchs, N., & Kläsener, I. (2009). The Effects of Experimentally Induced Rumination Versus Distraction on Analogue Posttraumatic Stress Symptoms. *Behavior Therapy, 40*(4), 403-413

Emmelkamp, P. M. G. (2003). Behavior therapy with adults. In M. Lambert (Ed.). *Handbook of psychotherapy and behavior change* (p. 393-446). New York: Wiley.

Egger, M., Smith, G.D., Schneider, M., & Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *British Medical Journal*, 315, 629-634.

Feijt, M.A., De Kort, Y.A.W., Bongers, I.M.B., & IJsstelsteijn, W.A. (2018). Perceived Drivers and Barriers to the Adoption of eMental Health by Psychologists: The Construction of the Levels of Adoption of eMental Health Model. *Journal of Medical Internet Research, 20*(4), 153.

Field, A. P., & Gillett, R. (2010). How to do a meta-analysis. Brit*ish Journal of Mathematical & Statistical Psychology*, *63*(3), 665-694. doi: 10.1348/000711010X502733.

Flory, J. D., & Yehuda, R. (2015). Comorbidity between post-traumatic stress disorder and major depressive disorder: alternative explanations and treatment considerations. *Dialogues in Clinical Neuroscience*, *17*(2), 141-150.

Forns, M., Pereda, N., Gomez-Benito, J., & Guilera, G. (1994). The international epidemiology of child sexual abuse: A continuation of Finkelhor. *Child Abuse and Neglect*, *6*, 331-342.

Fulton, J.J., Calhoun, P.S., Wagner, H.R., Schry, A.R., Hair, L.P., Feeling, N., Elbogen, E., & Beckham, J.C. (2015). The prevalence of posttraumatic stress disorder in Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) Veterans: A meta-analysis. *Journal of Anxiety Disorders*, *31*, 98-107.

Gallagher, E.J., Bijur, P.E., Latimer, C., & Silver, W. (2002). Reliability and Validity of a visual analog scale for acute abdominal pain in the ED. *The American Journal of Emergency Medicine*, *20*(4), 287-290.

Gamito, P., Oliveira, J., Rosa, P., Morais, D., Duarte, N., Oliveira, S., & Saraiva, T. (2010). PTSD Elderly War Veterans: A Clinical Controlled Pilot Study. *Cyber Psychology, Behavior, and Social Networking, 13*, 43-47.

Gerardi, M., Rothbaum, B.O., Ressler, K., Heekin, M., & Rizzo, A. (2008). Virtual Reality Exposure Therapy Using a Virtual Iraq: Case Report. *Journal of Traumatic Stress*, *21(2)*, 209–213.

Gonçalves, R., Pedrozo, A. L., Coutinho, E. S., Figueira, I., & Ventura, P. (2012). Efficacy of virtual reality exposure therapy in the treatment of PTSD: a systematic review. *PloS one*, *7(12)*, e48469.

Higgins, J.P.T., & Green, S. (2006). Cochrane Handbook for Systematic Reviews of Interventions 4.2.6 (updated September 2006). In The Cochrane Library, Issue 4, 2006. John Wiley & Sons, Ltd: Chichester, UK

Heber, E., Ebert, D. D., Lehr, D., Cuijpers, P., Berking, M., Nobis, S., & Riper, H. (2017). The benefit of web-and computer-based interventions for stress: a systematic review and meta-analysis. *Journal of medical Internet research*, *19*(2).

Hoge, C.W., Castro, C.A., Messer, S.C., McGurk, D., Cotting, D.I., & Koffman, R.L. (2004). Combat Duty in Iraq and Afghanistan, Mental Health Problems, and Barriers to Care. *The New England Journal of Medicine*, *351*, 13-22. doi: 10.1056/NEJMoa040603

Hox, J. J. (2010). *Multilevel analysis: Techniques and applications*. New York, NY: Routledge.

Kampmann, I.A., Emmelkamp, P.M.G., & Morina, M. (2016). Meta-analysis of technology-assisted interventions for social anxiety disorder. *Journal of Anxiety Disorders, 42*, 71-84).

Karyotaki, E., Ebert, D. D., Donkin, L., Riper, H., Twisk, J., Burger, S., ... & Geraedts, A. (2018). Do guided internet-based interventions result in clinically relevant changes for patients with depression? An individual participant data meta-analysis. *Clinical Psychology Review, 63*, 80-92.

Kenwright M., Liness, S., & Marks, I. (2001). Reducing demands on clinicians by offering computer-aided self-help for phobia/panic. Feasibility study. *British Journal of Psychiatry, 179*(5), 456–459. doi: 10.1192/bjp.179.5.456.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, *62*, 593–602.

Kessler, R. C., Sonnega, A., Bromet, E., Hughes, M., & Nelson, C. (1995). Posttraumatic stress disorder in the National Comorbidity Survey. *Archives of General Psychiatry*, *52*, 1048-1060.

Kilpatrick, D.G., Resnick, H.S, Milanak, M.E., Miller, M.W., Keyes, K.M., & Friedman, M.J. (2013). National Estimates of Exposure to Traumatic Events and PTSD Prevalence Using DSM-IV and DSM-5 Criteria. *Journal of Traumatic Stress*, *26*, 537–547.

Kilpatrick, D. G., Saunders, B. E., & Smith, D. W. (2003). Youth victimization: Prevalence and implications. Research in brief. Washington, DC: US Department of Justice, Office of Justice Programs.

Lambert, M. J., Hansen, N. B., Umphress, V., Lunnen, K., Okisshi, J., Burungame, G. M., Heufner, J. C., & Reisinger, C. R. (1996). Administration and Scoring Manual for the Outcome Questionnaire (OQ-45.2). Wilmington, DE: American Professional Credentialing Services LLC.

Lange, A., Rietdijk, D., Hudcovicova, M., Van De Ven, J. P., Schrieken, B., & Emmelkamp, P. M. (2003). Interapy: a controlled randomized trial of the standardized treatment of posttraumatic stress through the internet. *Journal of Consulting and Clinical Psychology, 71*(5), 901.

Leue, A., & Lange, S. (2011). Reliability generalization: An examination of the positive affect and negative affect schedule. *Assessment*, *18*(4), 487-501.

Lewis, S., Resnick, H.S., Ruggiero, K.J., Smith, D.W., Kilpatrick, D.G., Best, C.L., & Saunders, B.E. (2005). Assault, Psychiatric Diagnoses, and Sociodemographic Variables in Relation to Help-Seeking Behavior in a National Sample of Women. *Journal of Traumatic Stress*, *18*(2), 97–105.

Litz, B. T., Williams, L., Wang, J., Bryant, R., Engel, C.C. (2004). A Therapist-Assisted Internet Self-Help Program for Traumatic Stress. *Professional Psychology: Research and Practice*, *35*(6), 628-634.

Marks, I. M., Kenwright, M., Mcdonough, M., Whittaker, M., & Mataix-Cols, D. (2004). Saving clinicians' time by delegating routine aspects of therapy to a computer: a randomized controlled trial in phobia/panic disorder. *Psychological Medicine, 34*(1), 9–17. doi: 10.1017/S003329170300878X.

McCann, R. A., Armstrong C. M., Skopp N. A., Edwards-Stewart A., Smolenski D. J., June J. D., Metzger-Abamukong, M., Reger, G.M. (2014). Virtual reality exposure therapy for the treatment of anxiety disorders: an evaluation of research quality. *Journal of Anxiety Disorders*, *28*, 625–631. doi: 10.1016/j.janxdis.2014.05.010

McCrone P., Knapp, M., Proudfoot, J., Clash, R., Cavanagh, K., …& , Tylee, A. (2004). Cost-effectiveness of computerised cognitive-behavioural therapy for anxiety and depression in primary care: randomised controlled trial. *British Journal of Psychiatry, 185*(1), 55–62. doi: 10.1192/bjp.185.1.55.

McLay, R.N., Baird, A., Webb-Murphy, J., Deal, W., Tran, L., Anson, H., Klam, W., & Johnston, S. (2017). A Randomized, Head-to-Head Study of Virtual Reality Exposure Therapy for Posttraumatic Stress Disorder. *Cyberpsychology, Behavior, and Social Networking, 20*(4), 218-224. doi: 10.1089/cyber.2016.0554

McLay, R.N., McBrien, C., Wiederhold, M.D., & Wiederhold, B.K. (2010). Exposure Therapy with and without Virtual Reality to Treat PTSD while in the Combat Theater: A Parallel Case Series. *Cyberpsychology, Behavior and Social Networking, 13*(1), 37-42. doi: 10.1089=cyber.2009.0346

McLay, R.N., Ram, V., Murphy, J., Spira, J., Wood, D.P., Wiederhold, M.D., … Reeves, D. (2014). Effect of virtual reality PTSD treatment on mood and neurocognitive outcomes. *Cyberpsychology, Behavior and Social Networking, 17*, 439–446. doi: 10.1089/cyber.2013.0383

McLay R.N., Wood D.P., Webb-Murphy J.A., Spira, J.L., Wiederhold, M.D., Pyne, J.M., & Wiederhold B.K. (2011). A randomized, controlled trial of virtual reality-graded exposure therapy for post-traumatic stress disorder in active duty service members with combat related post-traumatic stress disorder. *Cyberpsychology, Behavior and Social Networking*, *14*, 223–229.

Mental Healthcare Foundation. (2018). *While We Are Waiting.* Retrieved from https://www.mentalhealth.org.uk/publications/while-we-are-waiting

Miyahira, S.D., Folen, R.A., Hoffman, H.G., Garcia-Palacios, A., Spira, J.L., Kawasaki, M. (2012). The Effectiveness of VR Exposure Therapy for PTSD in Returning Warfighters. *Annual Review of Cybertherapy and Telemedicine 2012*, 128-132.

Morina, N., IJntema, H., Meyerbröker, K., & Emmelkamp, P. M. (2015). Can virtual reality exposure therapy gains be generalized to real-life? A meta-analysis of studies applying behavioral assessments. *Behaviour Research and Therapy, 74*, 18-24.

Morina, N., Koerssen, R., & Pollet, T. V. (2016). Interventions for children and adolescents with posttraumatic stress disorder: A meta-analysis of comparative outcome studies. *Clinical Psychology Review*, *47*, 41-54.

Morina, N., Lancee, J., & Arntz, A. (2017). Imagery rescripting as a clinical intervention for aversive memories: A meta-analysis. *Journal of Behavior Therapy and Experimental Psychiatry*, *55*, 6-15. doi: 10.1016/j.jbtep.2016.11.003

Morina, N., Leibold, E., & Ehring, T. (2013). Vividness of general mental imagery is associated with the occurrence of intrusive memories. *Journal of Behavior Therapy and Experimental Psychiatry, 44*(2), 221-226

Morina, N., Stam, K., Pollet, T. V., & Priebe, S. (2018). Prevalence of depression and posttraumatic stress disorder in adult civilian survivors of war who stay in war- afflicted regions. A systematic review and meta-analysis of epidemiological studies. *Journal of Affective Disorders*, *239*, 328-338.

Morina, N., Wicherts, J. M., Lobbrecht, J., & Priebe, S. (2014). Remission from post- traumatic stress disorder in adults: a systematic review and meta-analysis of long term outcome studies. *Clinical Psychology Review*, *34*(3), 249-255.

Motraghi, T.E., Seim, R.W., Meyer, E.C., Morissette, S.B. (2013). Virtual Reality Exposure Therapy for the Treatment of Posttraumatic Stress Disorder: A Methodological Review Using CONSORT Guidelines. *Journal of Clinical Psychology*, *70(3)*, 197- 208.

Nederlandse Zorg Autoriteit. (2017). *Voortgangsrapportage wachttijden in de GGZ*. Retrieved from https://puc.overheid.nl/nza/doc/PUC_210611_22/1/

Nelson, R. J. (2013). Is virtual reality exposure therapy effective for service members and veterans experiencing combat-related PTSD? *Traumatology, 19*, 171–178.

Page, S., & Coxon, M. (2016). Virtual Reality Exposure Therapy for Anxiety Disorders: Small Samples and No Controls? *Frontiers in Psychology, 7*:326. doi: 10.3389/fpsyg.2016.00326

Parsons, T. & Rizzo, A. (2008). Affective outcomes of virtual reality exposure therapy for anxiety and specific phobias: A meta-analysis. *Journal of Behavior Therapy and Experimental Psychiatry*, *39*, 250-261.

Pennebaker, J. W. (1997). Writing about emotional experiences as a therapeutic process. *Psychological Science*, *8*(3), 162-166.

Pennebaker, J. W., Francis, M. E., & Booth, R. J. (2001). Linguistic inquiry and word count: LIWC 2001. Mahway: Lawrence Erlbaum Associates.

Pennebaker, J. W., Mayne, T. J., & Francis, M. E. (1997). Linguistic predictors of adaptive bereavement. *Journal of Personality and Social Psychology*, *72*(4), 863.

Pinheiro, J., Bates, D., DebRoy, S., Sarkar, D, & R Core Team. (2018). *Nlme: linear and nonlinear mixed effects models*. R package version 3.1-137. https://CRAN.R-project.org/package=nlme

Powers, M. & Emmelkamp, P. (2007). Virtual reality exposure therapy for anxiety disorders: A meta-analysis. *Journal of Anxiety Disorders, 22*, 561-569.

Proudfoot, J., Goldberg, D., Mann, A., Everitt, B., Marks, I., & Gray, J.A. (2003). Computerized, interactive, multimedia cognitive-behavioural program for anxiety and depression in general practice. *Psychological Medicine*, *33*(2), 217-227.

Proudfoot, J., Ryden, C., Everitt, B., Shapiro, D.A., Goldberg, D., Mann, A., Tylee, A., Marks, I., & Gray, J.A. (2004). Clinical efficacy of computerized cognitive-behavioural therapy for anxiety and depression in primary care: randomized controlled trial. *The British Journal of Psychiatry*, *185*, 45-54.

Ramirez, G., & Beilock, S. L. (2011). Writing about testing worries boosts exam performance in the classroom. *Science, 331*(6014), 211-213.

Rauch, S. & Foa, E. (2006). Emotional Processing Theory (EPT) and Exposure Therapy for PTSD. *Journal of Contemporary Psychotherapy*, *36*, 61-65. doi: 10.1007/s10879-006- 9008-y

Ready, D.J., Gerardi, R.J., Backscheider, A.G., Mascaro, N., Olasov Rothbaum, B. (2010) Comparing Virtual Reality Exposure Therapy to Present-Centered Therapy with 11 U.S. Vietnam Veterans with PTSD. *Cyberpsychology, Behavior, and Social Networking*, *13(1)*, 49-54. doi: 10.1089=cyber.2009.0239

Reger, M. A., & Gahm, G.A. (2016). Randomized Controlled Trial of Prolonged Exposure Using Imaginal Exposure vs. Virtual Reality Exposure in Active Duty Soldiers With Deployment-Related Posttraumatic Stress Disorder (PTSD). *Journal of Consulting and Clinical Psychology*. Advance Online Publication, doi: 10.1037/ccp0000134

Regier, D.A., Narrow, W.E., Rae, D.S., Manderscheid, R.W., Locke, B.Z., Goodwin, F.K. (1993). The de Facto US Mental and Addictive Disorders Service System Epidemiologic Catchment Area, Prospective 1-Year Prevalence Rates of Disorders and Services. *Archives of General Psychiatry*, *50*(2), 85-94. doi: 10.1001/archpsyc.1993.01820140007001

Resnick, S. H., Kilpatrick, G. D., Dansky, S. B., Saunders, E. B., & Best, L. C. (1993). Prevalence of Civilian Trauma and Posttraumatic Stress Disorder in a Representative National Sample of Women. *Journal of Consulting and Clinical Psychology, 61*(6), 984–991.

Richards. D, & Richardson, T. (2012). Computer-based psychological treatments for depression: A systematic review and meta-analysis. *Clinical Psychology Review*, *32*, 329-342.

Ritterband, L.M., Andersson, G., Christensen, H.M., Carlbring, P., & Cuijpers, P. (2006). Directions for the International Society for Research on Internet Interventions (ISRII). *Journal of Medical Internet Research*, *8*(3).

Rizzo, A., Difede, J., Rothbaum, B.O., Reger, G., Spitalnick, J., Cukor, J., & McLay, R. (2010). Development and early evaluation of the Virtual Iraq/Afghanistan exposure therapy system for combat-related PTSD. *Annals of the New York Academy of Sciences*, *1208(1)*, 114-125.

Rothbaum, B.O., Hodges, L., Alarcon, R., Ready, D., Shahar, F., Graap, K., Pair, J., Hebert, P., Gotz, D., Wills, B., & Baltzell, D. (1999). Virtual Reality exposure therapy for PTSD Vietnam Veterans: a case study. *Journal of Traumatic Stress, 12*(2), 236-271.

Schottenbauer, M.A., Glass, C.R., Arnkoff, D.B., Tendick, V., & Hafter Gray, S. (2008). Nonresponse and Dropout Rates in Outcome Studies on PTSD: Review and Methodological Considerations. *Psychiatry: Interpersonal and Biological Processes, 71*(2), 134-168. doi: 10.1521/psyc.2008.71.2.134

Schoutrop, M., Lange, A., Hanewald, G., Davidovich, U., & Salomon, H. (2002). Structured Writing and Processing Major Stressful Events: A Controlled Trial *Psychotherapy and Psychosomatics, 71*, 151-157. doi: 10.1159/000056282

Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Janavs, J., Weiller, E., Weiller, E., … & Dunbar, G.C. (1997). The validity of the Mini International Neuropsychiatric Interview (MINI) according to the SCID-P and its reliability. *European Psychiatry*, *12*, 232-41.

Smit, Y., Huibers, M. J. H., Ioannidis, J. P. A., van Dyck, R., van Tilburg, W., & Arntz, A. (2012). The effectiveness of long-term psychoanalytic psychotherapy—A meta analysis of randomized controlled trials. *Clinical Psychology Review, 32*(2), 81–92.

Smith, T.C., Ryan, M.A.K., Wingard, D.L., Slymen, D.J., Sallis, J.F., & Kritz-Silverstein, D. (2008). New Onset and Persistent Symptoms of Post-Traumatic Stress Disorder Self Reported after Deployment and Combat Exposures: Prospective Population Based US Military Cohort Study. *British Medical Journal*, *336*, 366-371.

Stoltenborgh, M., Van IJzendoorn, M., Euser, E. M., & Bakermans-Kranenburg, M. J. (2011). A Global Perspective on Child Sexual Abuse: Meta-Analysis of Prevalence Around the World. *Child Maltreat*, *16*, 79-101.

Tielman, M.L., Neerincx, M.A., Bidarra, R., Kybartas, B., Brinkman, W.P. (2017). A Therapy System for Post-Traumatic Stress Disorder Using a Virtual Agent and Storytelling to reconstruct Traumatic Memories. *Journal of Medical Systems, 41*(125).

Van Houwelingen, H. C., Arends, L. R., & Stijnen, T. (2002). Advanced methods in meta- analysis: Multivariate approach and meta-regression. *Statistics in Medicine, 21*, 589– 624.

Van Meggelen, M., Morina, N., Van der Heiden, C., Arends, L.R., & Franken, I.H.A. (submitted). Virtual Reality Exposure Therapy for the Treatment of PTSD: A Meta- Analysis.

Van Meggelen, M., Morina, N., Van der Heiden, C., Brinkman, W.P., Yocarini, I.E., … & Franken, I.H.A. (submitted). A Randomized Controlled Trial on the Efficacy of a Computer-based Intervention with Elements of Virtual Reality and Limited Therapist Assistance for the Treatment of Post-traumatic Stress Disorder.

Van den Steen, M., Brinkman, W. P., Vermetten, E., & Neerincx, M. (2010). Multi-Modal Memory Restructuring System for Patients Suffering from Combat-Related PTSD: a pilot study. *Annual Review of Cybertherapy and Telemedicine*, 208-2013.

Van Vliet, I.M., Leroy, H., van Megen., H.J.G.M. (2000). *M.I.N.I. Plus. M.I.N.I. International Neuropsychological Interview*. Nederlandse Versie 5.0.0. [Dutch Version 5.0.0] Utrecht, Netherlands: UMC

Van der Does, A.J.W. (2002). BDI-II-NL Handleiding: De Nederlandse versie van de Beck Depression Inventory—Second Edition, Enschede, Ipskamp

Van Zuuren, F. J., Schoutrop, M. J. A., Lange, A., Louis, C. M., & Slegers, J. E. M. (1999). Effective and ineffective ways of writing about traumatic experiences: a qualitative study. *Psychotherapy Research, 9*(3), 363-380.

Wang, W., Van Lint, C.L., Brinkman, W.P., Rövekamp, T.J.M., Van Dijk, S., Van der Boog, P. J. M., & Neerincx, M.A. (2017). Renal transplant patient acceptance of a self- management support system. *BMC Medical Informatics and Decision Making, 17*(58). doi: 10.1186/s12911-017-0456-y

Watson, D., Clark, L. A., & Carey, G. (1988). Positive and negative affectivity and their relation to anxiety and depressive disorders. *Journal of Abnormal Psychology, 97*(3), 346.

S

Nederlandse samenvatting

Achtergrond, Resultaten & Conclusie

"Elke dag haalde mijn vader me op van de basisschool zodat ik niet alleen naar huis hoefde te lopen. Elke dag stopten we onderweg, waarbij hij de auto parkeerde zodat hij mij kon verkrachten voordat we naar huis gingen."

Angela, een 51-jarig slachtoffer van seksueel misbruik in de kindertijd

Inleiding

Sommige ervaringen uit het verleden kunnen mensen jarenlang achtervolgen. In de Verenigde Staten (VS) wordt geschat dat tussen de 50% en 70% van de mensen ooit een potentieel traumatische ervaring meemaakt (Kessler, Sonnega, Bromet, Hughges, & Nelson, 1995; Resnick, 1993). Slechts in een minderheid van de gevallen leidt een traumatische ervaring ook tot een posttraumatische stressstoornis (PTSS). Geschat wordt dat tussen 6.8% en 12.3% van alle inwoners van de VS tijdens hun leven last krijgt van PTSS (Kilpatrick et al., 2013; Kessler, Berglund, Demler, Merikangas, & Walters, 2005; Kessler et al., 1995; Resnick, et al. 1993). In Europese landen liggen die schattingen iets lager, op 1.9% (Alonso et al., 2004). Echter, in landen met een recent oorlogsverleden (zoals Kosovo, Iran, Cambodja, Kroatië of Libanon), wordt geschat dat maar liefst een vierde van de populatie lijdt aan PTSS en/of depressie (Morina, Stam, Pollet, & Priebe, 2018). De impact van PTSS kan omvangrijk zijn en de effecten op het dagelijks leven van individuen is groot. Mensen die lijden aan PTSS hebben doorgaans last van herbelevingen in de vorm van flashbacks of nachtmerries. Ook voelen ze zich angstig, zijn ze prikkelbaar en vermijden ze herinneringen aan de traumatische gebeurtenissen (American Psychiatric Association, 2013).

Cognitief gedragstherapeutische (CGT) benaderingen zijn breed onderzocht en effectief bevonden voor de behandeling van PTSS (Bradley, Greene, Russ, Dutra, & Westen, 2005). Op dit moment wordt traumagerichte CGT samen met Eye Movement Desensitization Reprocessing (EMDR), gezien als meest effectieve psychologische behandeling voor PTSS (Cusack et al., 2016; Morina, Koerssen & Pollet, 2016).

Hulp zoeken en barrières

Hoewel er dus effectieve psychologische behandelingen voor PTSS bestaan, maakt maar een minderheid van de mensen die het nodig heeft hier gebruik van. Onderzoeken laten zien dat in het algemeen minder dan een derde van de inwoners van de VS met psychische problemen binnen een jaar hulp krijgt (Regier, Narrow, Rae, Manderscheid, Locke,

Goodwin, 1993) en dat bijvoorbeeld nog geen 19% van verkrachtingsslachtoffers formele of informele hulp zoekt voor hun PTSS of depressieklachten (Lewis et al., 2005). Er zijn dus duidelijke aanwijzingen dat in het algemeen barrières om hulp voor mentale problemen te zoeken en te ontvangen hoog zijn. Hiernaast is bekend dat, wanneer mensen wel de stap zetten om hulp te zoeken, zij vaak op lange wachtlijsten terechtkomen. Ook wereldwijd bezien spelen factoren zoals lange reisafstanden in afgelegen gebieden, een beperkt aantal beschikbare therapeuten of financiële beperkingen een rol bij de barrières die mensen ervaren bij de toegang tot de geestelijke gezondheidszorg. De bovenstaande argumenten benadrukken het belang van interventies die zowel de effectiviteit, kosteneffectiviteit, als de toegankelijkheid van de interventies voor mensen met PTSS vergroten.

In traumabehandeling speelt blootstelling aan de traumatische ervaringen vaak een grote rol. Deze 'exposure' kan doorgaans imaginair (bijvoorbeeld door te denken aan de traumatische ervaring) of in vivo (bijvoorbeeld door het creëren van een echte confrontatie met [elementen van] een traumatische ervaring) worden aangeboden.

Er is echter nog een andere manier, namelijk via *Virtual Reality Exposure Therapy* (VRET). VRET maakt gebruikt van via computers gemaakte omgevingen om gevreesde stimuli na te bootsen. In deze virtuele omgevingen kunnen gebruikers systematisch worden blootgesteld aan deze stimuli. Dit gebeurt dan in een relevante context, zoals bijvoorbeeld een oorlogsgebied of een vliegtuig bij soldaten met oorlogsgerelateerde PTSS (Parsons & Rizzo, 2008). VR systemen zijn de afgelopen jaren steeds goedkoper, gebruiksvriendelijker en makkelijker beschikbaar geworden (Parsons & Rizzo, 2008). Deze ontwikkelingen hebben ertoe geleid dat er inmiddels verschillende applicaties zijn voor de behandelingen van angststoornissen, met diverse studies die positieve behandeluitkomsten beschrijven voor onder andere PTSS (e.g., Carl et al., 2018).

Als we kijken naar manieren om de toegankelijkheid van behandelingen te vergroten, zijn computergestuurde en via internet aangeboden interventies relevant. Deze interventies staan erom bekend dat ze grote groepen mensen kunnen bereiken en ze hebben ook verschillende voordelen ten opzichte van traditionele therapieën zoals dat ze vaak gepersonaliseerd zijn en aangepast worden aan de behoeften van diverse gebruikers, meestal relatief weinig kosten en vanuit huis gebruikt kunnen worden (Broman-Fulks, Zinzow, Ruggiero, & Cercone, 2009). Over het algemeen lijken de behandelresultaten van angst- en depressieklachten vergelijkbaar met die van traditionele therapieën (Carlbring, Andersson, Cuijpers, Riper, & Hedman-Lagerlöf, 2018). Er zijn wel verschillen in de mate van de assistentie die tijdens deze interventies aangeboden wordt (bijvoorbeeld helemaal geen, alleen administratieve-, of therapeut ondersteuning; Richards & Richardson, 2009).

Op dit moment is de werkzaamheid van internet- en computergestuurde interventies gevalideerd voor verschillende gezondheidsproblemen zoals sociale angst (Kampmann, Emmelkamp, & Morina, 2016), depressie (Kenwright, Liness, Marks, 2001; Marks, Kenwright,

McDonough, Whittaker, & Mataix-Cols, 2004) en PTSS (Carlbring et al., 2018; Heber et al., 2017; Karyotaki et al., 2018). Maar natuurlijk zijn er nog steeds uitdagingen te benoemen.

Belangrijk is het gegeven dat het onderzoeken van de werkzaamheid van deze soort interventies een voortdurend proces is waarbij we ons telkens af moeten vragen of we de meest geschikte behandelingen aanbieden aan patiënten. Daarbij is de acceptatie van deze vorm van behandeling onder patiënten en behandelaren een onderwerp wat aandacht verdient. Het ISRII (International Society for Research on Internet Interventions, Ritterband et al., 2006) noemt in hun rapport over dit onderwerp acceptatie een essentieel onderdeel bij de totstandkoming van deze behandelwijzen.

Multi Modal Memory Restructuring (3MR) systeem

Dit proefschrift onderzoekt de werkzaamheid, acceptatie en het toekomstig gebruik van een computerondersteunde trauma interventie met elementen van VR en beperkte therapeut betrokkenheid voor de behandeling van PTSS, aangeboden via het *Multi Modal Memory Restructuring* (*3MR*) systeem. Het *3MR* systeem is ontwikkeld door Brinkman, Vermetten, Van de Steen, and Neerincx (2011) en is gericht op het structureren en het terugkijken op gebeurtenissen uit het verleden. Het *3MR* systeem geeft mensen de mogelijkheid om hiervoor persoonlijke foto's, teksten, online geografische kaarten en zelf gecreëerde 3D omgevingen te gebruiken. Het *3MR* systeem en een bijbehorende sessiehandleiding worden gebruikt om patiënten 12 therapiesessies uit te laten voeren die gericht zijn op het verwerken van de traumatische herinneringen van de patiënt.

Belangrijkste onderzoeksbevindingen

Dit proefschrift startte met het onderzoeken van de huidige stand van zaken van het onderzoek naar VRET voor de behandeling van PTSS. Dit is gedaan door middel van een meta-analyse. Er werden tien klinische studies geïncludeerd waarin VRET met een actieve (andere behandeling, zoals CGT of EMDR) of inactieve (zoals wachtlijst of 'minimale aandacht') controlegroep werd vergeleken en waarin uitkomstdata werden gerapporteerd. Gebleken is dat VRET en actieve controlecondities niet significant van elkaar verschilden in termen van werkzaamheid van de behandeling (wat in dit geval afname van PTSS symptomen inhield). Gegevens die VRET met inactieve controlecondities vergeleken toonden aan dat VRET het in die gevallen significant beter deed. Voor comorbide depressieklachten werd hetzelfde patroon gevonden (**Hoofdstuk 2**).

Om de werkzaamheid van de *3MR* interventie te onderzoek, is een gerandomiseerde gecontroleerde studie (RCT) uitgevoerd onder getraumatiseerde slachtoffers van seksueel

misbruik in de kindertijd en oorlogsveteranen. In deze studie zijn de effecten van de *3MR* interventie vergeleken met die van meer reguliere behandelmethoden ('treatment as usal', TAU). TAU bestond uit diverse 'evidence-based' (empirisch onderbouwde) behandelingen zoals imaginaire exposure, EMDR of narratieve exposure therapie. Een totaal van 44 patiënten met PTSS werd geïncludeerd in de RCT. Patiënten werden willekeurig toegewezen aan 12 sessies van de *3MR* interventie of TAU. Er werden op verschillende meetmomenten vragenlijsten en interviews afgenomen om symptomen van PTSS, depressie en het algemeen welzijn te meten.

De resultaten laten zien dat symptomen van PTSS en depressie allebei significant afnamen tussen de voor- en nametingen en dat er geen significante verschillen gevonden konden worden tussen de twee behandelcondities. Hetzelfde werd gevonden voor de toename van algemeen welzijn. Beide behandelcondities resulteerden in gelijke remissiecijfers voor PTSS en depressie (**Hoofdstuk 3**).

Meer inzicht in de specifieke werkzame elementen van de *3MR* interventie kunnen helpen de werkzaamheid hiervan te begrijpen. Om deze reden is nog een RCT uitgevoerd. Deze RCT richtte zich specifiek op de toegevoegde waarde van de multimedia tools van het *3MR* systeem ('Website', 'Media', 'Emoties', en 'Afbeeldingen' in het dagboekgedeelte) ten opzichte van reguliere schrijfoefeningen ('structured writing therapy', SWT) om om te gaan met negatieve ervaringen. Een totaal van 55 eerstejaars Psychologie studenten met een negatieve, maar niet-traumatische herinnering werden geïncludeerd en volgden ofwel drie sessies van gestructureerde schrijfoefeningen voorafgegaan door 15 minuten gebruik van de *3MR* tools (*3MR*+SWT conditie) ofwel drie sessies van gestructureerde schrijfoefeningen voorafgegaan door 15 minuten denken aan de negatieve herinnering (SWT conditie). Resultaten toonden een significante afname van spanning, negatief affect, evenals het aantal, de levendigheid van en de spanning veroorzaakt door intrusies over de aversieve herinnering. Deze uitkomsten bevestigen de positieve effecten die schrijfoefeningen kunnen hebben op het verwerken van negatieve herinneringen, maar geven geen indicatie voor toegevoegde waarde van het gebruik van de multimedia tools uit het *3MR* systeem. Wel werd gevonden dat het gebruik van de *3MR* applicatie deelnemers stimuleerde om de lengte van hun teksten stabiel te houden over de sessies en dus terugval van de tekstlengte over tijd tegen te gaan, wat in het algemeen wordt geassocieerd met positieve behandeluitkomsten (**Hoofdstuk 4**).

Tot slot is in dit proefschrift de patiënt- en therapeutacceptatie van de *3MR* interventie onderzocht. Een deel van de patiënten ($n = 10$) uit de RCT en 15 betrokken trauma therapeuten vulden evaluatievragenlijsten in over hun ervaringen met en mening over de *3MR* interventie. In het algemeen gaven patiënten aan dat zij baat hadden bij de voordelen van de *3MR* interventie (bijvoorbeeld een lagere reisintensiteit), dat ze zich in controle voelden over hun behandeling en dat ze voelden dat hun problemen serieus genomen werden. Ze bevestigden dat de *3MR* interventie hun hielp om beter met hun angst om te gaan en dat ze niet bang

waren voor stigmatisering door anderen. Over het geheel gezien was ook de mening van therapeuten over de *3MR* interventie positief, zij gaven aan dat ze de *3MR* interventie als een geschikte behandeloptie zien, dat ze zien dat deze belangrijke voordelen heeft voor hun patiënt en dat ze het aan zouden kunnen raden aan hun patiënten. Tegelijkertijd gaven de meeste therapeuten ook aan het idee te steunen dat de *3MR* interventie alleen als add-on bij reguliere behandeling in plaats van als een op zichzelf staande module gebruikt kan worden. Hoewel gecompromitteerd door een kleine dataset, laten de resultaten een overwegend positieve trend in de patiënt- en therapeutacceptatie van de *3MR* interventie zien. Samen met de positieve behandeluitkomsten uit de RCT kan dit een adequate eerste stap vormen in de richting van toekomstig gebruik van deze interventie voor de behandeling van PTSS (**Hoofdstuk 5**).

Discussie en toekomstig gebruik

Op dit moment lijken we niet langer om de werkzaamheid van VRET en computergestuurde interventies voor de behandeling van PTSS heen te kunnen. Hoewel er overduidelijk grotere onderzoeksgroepen, meer gecontroleerde studies en gestandaardiseerde behandelmethoden gewenst zijn, laten de bevindingen in dit proefschrift zien dat er over tijd een vooral positieve trend te zien is in de behandelresultaten met VRET en computergestuurde interventies voor de behandeling van PTSS. Daarnaast is de behoefte aan interventies die de werkzaamheid, kosten-effectiviteit en toegankelijkheid van behandelingen voor individuen met PTSS vergroten misschien wel nooit zo actueel geweest als op dit moment. Barrières die mensen ervaren bij het zoeken naar behandeling zijn traditioneel hoog (Regier, Narrow, Rae, Manderscheid, Locke, Goodwin, 1993; Hoge et al., 2004; Lewis et al, 2005), en ook zijn de wachtlijsten in de geestelijke gezondheidszorg opvallend lang, wat aangeeft dat er een toenemende behoefte is aan geschoolde therapeuten of werkzame computergestuurde interventies die weinig therapeut betrokkenheid vereisen. Daarbij komt het feit dat doordat de acceptatie van geestelijke gezondheidsproblemen (bijvoorbeeld veroorzaakt door traumatische ervaringen) steeds verder toeneemt wereldwijd, ook de vraag naar psychische hulp enkel zal toenemen. Dit bevestigt dat de bovenstaande problemen niet zomaar zullen verdwijnen, tenzij we flexibiliteit tonen en onze huidige behandelmethoden voor PTSS verbreden.

Natuurlijk zijn er in dit proces belangrijke hindernissen te nemen. Zoals eerder genoemd, is het onderzoeken van de werkzaamheid van computergestuurde interventies met beperkte therapeut assistentie een voortdurend proces waarbij we ons telkens af moeten vragen of we de meest geschikte behandelingen aanbieden aan patiënten. Maar een ander belangrijk punt is bijvoorbeeld het feit dat onderzoek naar technologische innovaties, zoals de *3MR* interventie, vaak veel tijd kost. Het kost meerdere jaren om cliëntgerichte VR of computergestuurde interventies te ontwikkelen, en zelfs nog langer om hun werkzaamheid

in gecontroleerde studies te onderzoeken. Dit resulteert erin dat technologische innovaties, niet meer zo innovatief zijn tegen de tijd dat de resultaten over de effectiviteit beschikbaar zijn en implementatie in de klinische praktijk aan de orde komt. De *3MR* interventie vormt hierop helaas geen uitzondering. We moeten manieren vinden om deze processen te versnellen, om beter aan te kunnen blijven sluiten bij de behoeftes van patiënten als het gaat om gebruiksvriendelijkheid van veelbelovende computergestuurde interventies. Ook is het zo dat het onderzoeken van de *3MR* interventie met beperkte therapeut betrokkenheid onder een patiëntgroep met zulke complexe klachten als die behorend bij PTSS, vooraf kritische vragen opriep. Daarom is het belangrijk om hier te noemen dat, hoewel niet alle patiënten profiteerden van de *3MR* interventie en het voor een deel van de onderzoeksgroep niet mogelijk bleek om de behandeling in zijn geheel te doorlopen, er geen ernstige ongewenste voorvallen ('serious adverse events') hebben plaatsgevonden tijdens de RCT. Toch laten data over vooral de therapeut acceptatie van de *3MR* interventie een positieve, maar aarzelende houding zien. Recentelijk hebben Feijt, De Kort, Bongers, & IJsselsteijn (2018) verschillende diepte interviews gehouden met psychologen over hun ervaren 'drivers' en 'barriers' als het gaat om het gebruik van eMental Health interventies. Zij beschrijven dat geen of minimaal gebruik van deze interventies onder psychologen samen kan gaan met het gevoel om hiertoe gedwongen te worden, of het feit dat men niet overtuigd is van de meerwaarde van deze interventies. Om deze barrières te overwinnen moet de implementatie van interventies zoals *3MR* in de klinische praktijk samengaan met intensieve samenwerking met betrokken therapeuten. Niet alleen om hen te overtuigen van mogelijke meerwaarde, maar ook met oog voor de kennis die er nodig is om deze interventies in de dagelijkse klinische praktijk te kunnen gebruiken, en de tijd die het kost om vertrouwd te raken met dit gebruik. Een laatste hindernis, die niet gebaseerd is op welk wetenschappelijk onderzoek dan ook, maar wel op talloze gesprekken tijdens de totstandkoming van dit proefschrift, is het idee dat computergestuurde interventies erop gericht zijn om therapeuten te vervangen, wat hen op termijn onnodig zal maken. Niets is echter minder waar. Gebaseerd op de huidige problemen binnen de geestelijke gezondheidszorg die hierboven beschreven worden, kan dit nooit het geval of een doel op zich zijn. Zowel therapeuten, als innovatieve computergestuurde interventies zijn nodig om de barrières bij het zoeken naar psychische hulp te overwinnen, om wachtlijsten te verkorten en om een hand uit te steken naar individuen die psychische hulp nodig hebben na een traumatische ervaring. Wij hopen dat de bevindingen in dit proefschrift onderzoekers, zorgmanagers en therapeuten kunnen motiveren voor het idee dat we het naar al de mensen die momenteel op een lange wachtlijst staan, in een afgelegen gebied wonen of die simpelweg niet over de financiële middelen beschikken om toegang te krijgen tot de juiste gezondheidszorg, verschuldigd zijn om open te staan voor computergestuurde interventies voor de behandeling van PTSS. En hiermee het huidige behandelaanbod voor PTSS te verbreden.

D

Dankwoord

(Acknowledgements in Dutch)

Ik kijk er al heel lang naar uit om dit onderdeel van mijn proefschrift te schrijven. Niet alleen omdat dit betekent dat het nu dan toch echt afgerond is, maar vooral omdat ik me gelukkig prijs met zoveel fijne mensen om me heen. Die wil ik hier dan ook graag bedanken.

Ingmar, bedankt voor je bereidheid om mij bij alle aspecten van dit onderzoek te helpen. Er was geen vraag die ik niet kon stellen en geen onderwerp wat niet besproken kon worden. Jouw openheid, eerlijke feedback en mensgerichtheid heb ik ontzettend gewaardeerd.

Colin, jouw kennis over wetenschappelijk onderzoek binnen de klinische praktijk is groot en vaak van waarde geweest voor dit onderzoeksproject. Ik heb veel kunnen leren van jouw ervaringen en ik bewonder jouw uitvoering van de rol van scientist practitioner.

Nexh, ik verwonder me altijd over hoeveel jij over welk wetenschappelijk onderwerp dan ook lijkt te weten. Veel dank voor jouw - zonder uitzondering - snelle en kundige feedback tijdens dit onderzoek en je bereidheid om altijd mee te denken, of je nu in Amsterdam, Wassenaar of Munster werkzaam was.

Willem-Paul, bedankt voor je begeleiding en het initiëren en leiden van het VESP project. Je hebt alle disciplines bij elkaar gehouden en was de spil tussen veel van de bijzondere samenwerkingen in dit project.

Myrthe, ik heb het erg getroffen met jou als mede PhD-student op het VESP project. Bedankt voor de fijne samenwerking, je inspanningen om een intelligente virtuele e-Coach te ontwikkelen en de gezelligheid tijdens menig presentatie samen in het land.

Dit onderzoek was niet mogelijk geweest zonder de klinische partners die deelnamen aan het VESP project. Veel dank ben ik dan ook verschuldigd aan de behandelaren van de betrokken teams bij PsyQ Parnassia Groep, de Reinier van Arkel Groep (Psychotraumacentrum Zuid-Nederland [PTC-ZN]), GGZ Delfland, Virenze, en Arq (Stichting Centrum '45). In het bijzonder mijn dank aan Gloria Gribling, Maaike Heijnis, Jeffrey van der Starre, Sandra Visser, Marijke Broekman, Elisa van Ee, Wendy Schalke, Martine van Bennekom, Lisa van Os, Tessa Zwinkels, Jan Rodenburg, Tim Wind en Jackie June ter Heide.

Zeker zoveel dank ben ik verschuldigd aan alle mensen die aan één van de beschreven onderzoeken hebben deelgenomen. In het bijzonder alle deelnemers aan de behandelstudies naar de effecten van het 3MR systeem. Ik hoop van harte dat jullie deelname aan dit onderzoek een positieve ervaring is geweest, bedankt voor jullie vertrouwen en inzet.

Alle (oud)-collega's van Klinische Psychologie: Ingmar, Colin, Pauline, Marlies, Birgit, Danielle, Linda, Marjolein, Semiha, Sanne, Susan, Matthias, Freddy, Ruth, Helen, Marianne, Guus, Kevin, Ilse, Miranda, Donna, Carmen, Nouran, Ibrahim, Ali, Sabine en Marien, bedankt dat ik van jullie mocht leren, bij jullie aan kon kloppen voor hulp en gezelligheid en natuurlijk voor de leuke uitjes en borrels tijdens de afgelopen jaren.

Veel dank ook aan de psychologen die in hun eigen tijd meewerkten aan de uitvoering van dit onderzoek en zorgvuldig onze deelnemers interviewden: Tara Vis, Ivana van Berkel, Linsey van Berkum en Sarah Hatuluwaja. Ontzettend fijn dat ik altijd op jullie kon rekenen. Ook wil ik graag Lara, Denise, Manon, Elske en Manar bedanken voor hun bijdrage aan dit onderzoek ten tijde van hun masterstudie.

Birgit Mayer en Marlies Marissen, aan jullie in het bijzonder dank voor onze samenwerking in het ambulatorium van de afdeling Klinische Psychologie. Lidia Arends, dank voor je hulp bij de meta-analyse over de effecten van Virtual Reality als behandelmethode voor PTSS. Ricardo van Aken bedankt voor je medewerking aan de studie naar de toegevoegde waarde van het 3MR systeem bij het omgaan met vervelende herinneringen. Iris Yocarini, veel dank voor je hulp bij de studie naar de werkzaamheid van het 3MR systeem, maar ook voor al die andere dingen waarbij jij als vraagbaak fungeerde of me spontaan te hulp schoot op cruciale momenten. Je was echt onmisbaar.

Lieve kamergenootjes, als ik bij aankomst op de universiteit zag dat het licht op onze kamer brandde, maakte mijn hart een sprongetje. Alleen werken is toch een stuk minder inspirerend en motiverend (maar vooral ook veel minder gezellig). Op volgorde van binnenkomst: Steven, Denise, Iris, Lara, Milou en Donna, bedankt voor alles we gedeeld hebben de afgelopen jaren. Jullie zijn super!

Denise, ik ga het missen om aan één blik boven ons beeldscherm uit genoeg te hebben. Je gaat een geweldige moeder zijn, bedankt voor je vriendschap.

Ook dank aan alle collega AiO's van DPECS. We zijn met veel en de doorstroom is gestaag, dus ik kan nooit iedereen hier opnoemen. Wel wil ik jullie graag heel erg bedanken voor de gezellige lunches, etentjes en het delen van ervaringen over de totstandkoming van onze proefschriften (of het uitblijven daarvan). A special thanks to my fellow PhD students, especially for the nice lunch gatherings, diners and for sharing our experiences on the becoming of our theses (or the absence of that).

Dank aan de Dutch-Flemish postgraduate research school for Experimental Psychopathology, het EPP, voor het aanbieden van zoveel inspirerende en leerzame seminars en de mogelijkheid om de basiscursus cognitieve gedragstherapie te volgen tijdens mijn promotietraject.

Ook dank aan de Nederlandstalige Vereniging voor Psychotrauma (NtVP) dat ik in de organisatie van de Special Interest Group 'Young Minds' mocht plaatsnemen. Mirjam Mink-Nijdam, Lieke Heesink, Alieke Reijnen, Karlijn Schols, Rafaele Huntjes en Miranda Meijer, bedankt voor de gezellige meetings en fijne samenwerking.

Bert Dijkhuizen, dank voor de mogelijkheid om naast mijn onderzoekswerk aan de EUR als psycholoog bij TwoBe te werken. Hierdoor kon ik beide werkvelden combineren en me ook als psycholoog verder ontwikkelen de afgelopen jaren. Ik heb ontzettend genoten

van mijn werkzaamheden in Pernis, Capelle aan den IJssel en op de Westblaak. Bedankt voor alle ervaring die ik heb kunnen opdoen en voor de gezelligheid van het team.

Elke, bedankt voor alle kansen die je me hebt gegeven en voor de manier waarop je me uitdaagt.

Lieve studievriendjes, Kim, Maud, Mirte, Nadia, Lianne en Ilse, bedankt voor de gezellige vrijdagen en alle andere avondjes samen!

Siri, Frank, Danielle en Joost, mijn lieve vrienden. Bedankt dat jullie er zijn, al zoveel jaren lang.

Leo, Frida, Tim, Nathalie, Isabelle en Alexander, bedankt voor jullie steun en interesse tijdens dit promotietraject!

Sabine, als collega, vriendin, ceremoniemeester en paranimf vervul je nogal wat rollen in mijn leven de afgelopen jaren! Bedankt voor jouw nooit aflatende positiviteit en energie, met jou samen worden veel dingen een stuk makkelijker. Zo ook mijn proefschrift verdedigen, hoop ik.

Lieve Sanne, je bent mijn grote zus en hebt allerlei talenten die ik niet heb (iets met structuur, maat houden en taarten bakken). Je bent me erg dierbaar en ik ben heel blij dat je mij wilt steunen tijdens de verdediging van dit proefschrift! Peter-Paul, Sophie en Fabian, bedankt voor jullie gezelligheid en verassende momenten.

Lieve pap en mam, ik kan jullie nooit genoeg bedanken voor alles wat jullie voor me betekenen en doen. Het is heel fijn dat ik zeker weet dat er altijd twee mensen zijn die onvoorwaardelijk achter me zullen staan. Ik hou van jullie.

Lieve Bas, één toevallige ontmoeting in de metro op Rotterdam CS en we zijn tien jaar verder. Bedankt voor je liefde en steun en het mooie leven wat we samen mogen leiden. Jij en onze prachtige dochters Elodie en Matilde zijn mijn grote liefdes. Mijn allerliefste meisjes, allebei geboren tijdens dit promotietraject. Door jullie zal dit boek voor mij onlosmakelijk verbonden zijn met het leven als jonge ouder (veel liefde, weinig slaap), en één van de mooiste perioden uit mijn leven. Ik hoop dat jullie altijd je dromen zullen najagen.

P

List of publications

Publications

Tielman, M.L., Neerincx, M.A., **Van Meggelen, M**., Franken, I.H.A., Brinkman, W.P. (2017) How should a virtual agent present psychoeducation? Influence of verbal and textual presentation on adherence. Technology & Health Care

Tielman, M.L., **Van Meggelen, M.**, Neerincx, M.A., Brinkman, W.P. (2015). An Ontology-based Question System for a Virtual Coach Assisting in Trauma Recollection. Proceedings of IVA 2015 - Fifteenth International Conference on Intelligent Virtual Agents

Geraerts, E.G. & **Van Meggelen, M.** (2013). Repressed and Recovered Memories. In Oxford Bibliographies in Psychology. Ed. Dana S Dunn. New York: Oxford University Press.

Submitted manuscripts

Van Meggelen, M., Morina, N., Van der Heiden, C., Brinkman, W.P., Arends, L.R., & Franken, I.H.A. Virtual Reality Exposure Therapy for the Treatment of PTSD: A Meta-Analysis

Van Meggelen, M., Morina, N., Van der Heiden, C., Brinkman, W.P., Yocarini, I.E., ... & Franken, I.H.A. A Randomized Controlled Trial on the Efficacy of a Computer-based Intervention with Elements of Virtual Reality and Limited Therapist Assistance for the Treatment of Post-traumatic Stress Disorder

Van Meggelen, M., Morina, N., Van Aken, R.M., Kohlen, L., Tielman, M.L., Brinkman, W.P., & Franken, I.H.A. The Added Value of a Multi Modal Memory Restructuring System to Writing Exercises in Overcoming Negative Memories

Van Meggelen, M., Brinkman, W.P., Tielman, M.L., Van der Heiden, C., Morina, N., & Franken, I.H.A. Patient and Therapist Acceptance of the Multi Modal Memory Restructuring System for the Treatment of Post-traumatic Stress Disorder

Presentations

Van Meggelen, M. & Franken, I.H.A. (October, 2018). *Virtual eCoaching and Storytelling technology for post-traumatic stress disorder treatment in veterans and victims of childhood sexual abuse.* Research school of Experimental Psychopathology (EPP): Symposium 'Empathy & TOM in Health and Mental Illness'. Kappellerput, Heeze, The Netherlands

Van Meggelen, M. (April, 2018). *Virtual Reality in de psychiatrie - Computergestuurde thuisbehandeling met Virtual Reality Exposure Therapy (VRET) voor de behandeling van PTSS bij veteranen en slachtoffers van seksueel misbruik in de kindertijd.* Voorjaarscongres Nederlandse Vereniging voor Psychiatrie (NVvP): Translationele uitdagingen in de psychiatrie. MECC, Maastricht, The Netherlands

Van Meggelen, M. (Augustus, 2017**).** *Virtual eCoaching and Storytelling technology for Post- traumatic stress disorder treatment (VESP) project, 3MR2.0.* Refereerbijeenkomst Stichting Centrum '45. Stichting Centrum '45, Oegstgeest, The Netherlands

Van Meggelen, M. (September, 2016). *Innovatieve behandeling voor veteranen en slachtoffers van seksueel kindermisbruik – Onderzoek doen in de praktijk*. Symposium Reinier van Arkel 'Kwaliteit door Verbinding'. Reinier van Arkel, 's Hertogenbosch, The Netherlands

Van Meggelen, M. & Tielman, M.L. (September, 2016). *Virtual eCoaching and Storytelling technology for Post-traumatic stress disorder treatment (VESP) project.* NIP Nascholingsdag 'Uw toekomst als professional in de psychologie'. Jaarbeurs, Utrecht, The Netherlands

Rodenburg, J., **Van Meggelen, M.**, & Tielman, M.L. (Juni, 2016). *Virtual Reality Exposure Therapy (VRET) voor de behandeling van PTSS bij veteranen*. Symposium GGZ Oost Brabant 'Onderzoek & Innovatie'. 't Warant, Helmond, The Netherlands

Van Meggelen, M. (September, 2016). *Virtual eCoaching and Storytelling technology for Post- traumatic stress disorder treatment (VESP) project.* Bijeenkomst Netwerk Psychotrauma Nederland (NPN). Arq, Diemen, The Netherlands

Van Meggelen, M. & Tielman, M.L. (September, 2015). *Virtual Reality Exposure Therapy (VRET) voor de behandeling van PTSS bij veteranen.* Internationaal Symposium Psychotraumacentrum Zuid-Nederland: Contextuele behandeling van complex trauma: van mensenrechten en culturele aspecten tot VR**.** Reinier van Arkel, 's Hertogenbosch, The Netherlands

Brinkman, W.P., Vermetten, E., **Van Meggelen, M**., & Tielman, M.L. (March, 2014). *Multi- Modal Memory Restructuring System (3MR).*Voorjaarssymposium Narratieve Exposure Therapie (NET). Planetarium, Amsterdam, The Netherlands

Van Meggelen, M. (October, 2012). *De rol van virtual reality behandeling bij traumaverwerking.* Symposium voor Jeugd- en Gezinsonderzoek. Hogeschool van Arnhem en Nijmegen (HAN), Nijmegen, The Netherlands

Van Meggelen, M. (November, 2012). *De toekomst van online hulp: Virtual Reality Exposure Therapy.* Congres voor Online Hulp 2012. Beatrix Theater, Utrecht, The Netherlands

Brinkman, W.P., & **Van Meggelen, M.** (April, 2012). *Computerondersteunde innovaties: toepassing voor PTSS.* Congres PTSS-en: Op weg naar maatwerk. Congrescentrum De Reehorst, Ede, The Netherlands

Poster presentations

Van Meggelen, M., Morina, N., Brinkman, W.P., Van der Heiden, C., Rodenburg, J., Geraerts, E.G., Tielman, M.L., & Franken, I.H.A. (November, 2015). *A Study on the Efficacy of Virtual Reality Exposure Therapy for Childhood Sexual Abuse related Trauma.* International Society for Traumatic Stress Studies (ISTSS). New Orleans Marriott, New Orleans, United States of America

Van Meggelen, M. & Franken, I.H.A. (June, 2015). *A Study on the Efficacy of Virtual Reality Exposure Therapy for Childhood Sexual Abuse related Trauma*'. Lustrumcongres PsyQ 'De GGZ Draait door!'. Madurodam, The Hague, The Netherlands

C

Curriculum Vitae

Marieke van Meggelen was born on February 2nd, 1989, in Leiden, The Netherlands. After completing higher general secondary education at De Lage Waard in Papendrecht and obtaining a propaedeutic diploma at the Hogeschool Rotterdam (studying International Business and Languages for one year), she started studying Psychology at the Erasmus University Rotterdam in 2007. In 2010 she received her bachelor's degree in Psychology and in 2012 she obtained her master's degree in Clinical Psychology. During and after her graduation she worked as a research assistant and a tutor in general psychology at the Institute of Psychology of the Erasmus University Rotterdam and gained clinical work experience at Stichting Centrum '45. In 2013 she started her PhD research at the Erasmus University Rotterdam. In collaboration with Delft Technical University and clinical partners including Reinier van Arkel Groep, PsyQ Parnassia Group, GGZ Delfland, and Arq she conducted several studies aimed at the clinical evaluation of a computer-based trauma intervention with elements of VR and limited therapist assistance (*3MR* intervention) for the treatment of PTSD. Together with her work in research, she worked as a psychologist (NIP certified) at Two Be Psychologenpraktijk in Rotterdam. Here she treated patients in both specialized ('SGGZ') and basic ('BGGZ') mental health care. In 2016 she successfully completed the basic course into Cognitive Behavioural Therapy (100 hours) at the RINO Group in Utrecht. During her PhD research, she participated in the education program of the Dutch-Flemish post-graduate research school for Experimental Psychopathology (EPP). Also, she reviewed empirical articles for international journals, and supervised the theses of bachelor and master Psychology students. Since 2015, she joined the organisation of the SIG 'Young Minds Psychotrauma' of the Dutch Society of Psychotrauma (Nederlandstalige Vereniging voor Psychotrauma, NtVP). The forthcoming years, Marieke aspires to continue her clinical work as well as research activities.