Degrading traumatic memories, a functional MRI study in PTSD

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Anxiety disorders and symptoms
Study type	Interventional

Summary

ID

NL-OMON40084

Source
ToetsingOnline

Brief title
Degrading traumatic memories

Condition

- Anxiety disorders and symptoms

Synonym
posttraumatic stress disorder or anxiety disorder, PTSD

Research involving
Human

Sponsors and support

Primary sponsor: VUmc, Vakgroep Psychiatrie
Source(s) of monetary or material Support: Ministerie van OC&W,De Hersenstichting

Intervention

Keyword: Functional MRI, Posttraumatic stress disorder, PTSD, Traumatic memories, Working memory

Outcome measures

Primary outcome

Subjective vividness and emotionality of negative emotional memories and

related neural activation (percentage BOLD

signal change) during memory recall.

Secondary outcome

cognitive functioning/working memory (n-back task)

Study description

Background summary

About 9-18% of trauma-exposed persons suffer from posttraumatic stress disorder (PTSD). Its hallmark symptoms are intrusive, vivid traumatic memories (e.g., flashbacks, nightmares; APA, 2001). How does one recover from such disturbing images?
Eye Movement Reprocessing and Desensitization (EMDR) is a *treatment of choice* for PTSD in (inter)national clinical guidelines based on meta-analyses. A crucial component of EMDR is that patients recall traumatic memories while simultaneously making horizontal EM induced by the therapist*s finger moving across the patient*s visual field. A meta-analysis of clinical studies has shown that EM adds to EMDR*s effectiveness (Lee & Cuijpers, 2011). This is corroborated by analogue laboratory studies by the applicant (Engelhard et al., 2010a,,b, 2011a-c; van den Hout et al., 2010, 2011a-c) and others (e.g., Gunter & Bodner, 2008), who showed that EM during recall of an emotional autobiographical memory reduces its vividness and emotionality, whereas merely recalling the memory for a similar time does not. These effects were found after the EM intervention when memories are recalled again, and up to one week later. It has been unclear, however, why EM is effective, which has been the topic of much scientific debate.
Recent findings provide a fresh perspective on the mechanisms involved. They support a *working-memory* (WM) theory, which states that the two tasks (EM and recall) compete for limited-capacity WM resources, which reduces image

vividness and emotionality (Gunter & Bodner, 2008). Experimental data fit well with this theory: (1) other taxing dual-tasks are also effective, (2) a dose-response relationship was found between WM-taxing and its effects, and (3) EM also reduces affects future-oriented images (flashforwards) (van den Hout & Engelhard, 2011). A prominent hypothesis for the long-term effects of EM(DR) is that memories become labile during recall, and due to EM, visual images become degraded. This memory degrading is thought to persist upon future recalls, since memory recall is affected by the nature of earlier recalls (Baddeley & Andrade, 2000).
However, nearly all studies relied on self-report ratings of vividness and emotional intensity, which are prone to demand bias and self-representation strategies. So far, no ('objective') neurobiological methods have been used.

Study objective

To extend our understanding of brain mechanisms involved in intrusive memory degrading by eye movement during recall of traumatic memories in the treatment of PTSD.
Brain areas involved in visual imagery are well-documented, and comprise the primary visual cortex (V1; Kosslyn ea, 2001). In patients with PTSD, personalized traumatic narratives activate not only the visual imagery areas, but also the brain fear circuit (e.g., amygdala; Shin ea, 2004), which is accompanied with decreased activation in medial prefrontal cortex (mPFC) regions involved in emotion perception (dorsomedial PFC, anterior cingulate cortex; Shin ea, 2004). We hypothesize that if recall+EM, relative to recall only, degrades traumatic memories, this should be associated with reduced V1 activation, increased activation in implicated mPFC regions, and reduced coupling between V1 and emotional brain areas (e.g., amygdala) during memory recall. We will explore whether WM areas (e.g., bilateral dorsolateral PFC, left ventrolateral PFC; Curtis & D'Esposito, 2003) will be implicated more during recall+EM than recall only, and whether activation in these areas is associated with larger effects (decreases in vividness/emotionality, reduced V1 activation, reduced V1-amygdala coupling).

Study design

Randomized controlled within-subject trial (cf. van den Hout ea, 2011c combined with trauma script driven imagery, Lanius 2010)

Intervention

Eye Movement Reprocessing and Desensitization (EMDR) is an effective treatment for posttraumatic stress disorder (PTSD), during which the patient recalls traumatic memories while performing eye movement (EM). EM adds to the treatment*s effectiveness, but it has been unclear how this might work. Recent studies (M van den Hout, I.M. Engelhart) support a *working-memory* (WM)

theory, stating that the two tasks (EM and memory recall) compete for limited-capacity WM resources, reducing memory vividness and emotionality.

Study burden and risks

The intervention is non-therapeutic to the subjects. On the study day participants will have a 60-minutes MRI session during which they will recall traumatic events while performing eye movements. At pre- and post-tests, participants will be exposed to script-driven imagery (SDI). This protocol has been used for over 20 years now in PTSD patients (since the study of Pitman ea 1987) and almost 15 years during neuroimaging (since Lanius ea 1997) and has been well tolerated. This type of paradigm can occasionally give patients uncomfortable feelings of anxiety and distress by reliving of their traumatic experiences. During and after the scan procedure a debriefing will be held to cover this. This is performed by the main executor of the scan protocol, i.e. the psychiatrist experienced with (complex) PTSD patients (Drs. K. Thomaes, MD). There is a research assistant to serve the scanner so that the psychiatrist can concentrate on the care for the patients. Patients are already familiar with her before scanning, through preparational sessions (a week before the scan sessions a psychologist which is experienced in making trauma scripts and the psychiatrist will make the trauma scripts with the patients). All patients will be familiar with the EMDR procedure before scanning through test sessions with their own therapists. SDI is a symptom provocation and the principal investigators of this study have long experience with symptom provocation in the scanner (Thomaes: early traumatized PTSD patients with comorbid personality disorders, which are far more complex patients than included in the present study, and 1 in 33 patients had a panic attack; OA van den Heuvel in anxiety and mood disordered patients; it has been revealed that patients had n rarely a panic attack and not more frequently than healthy controls). In all, we consider the risk to the subjects to be low. Functional MRI is a commonly used technique which is considered to be safe if you follow the safety instructions (e.g. no metal objects in the MRI room) and contraindications (e.g. no metal implants, no pregnant no seriously claustrophobic patients in the MRI).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Adult with age between 18 and 65 years
2. Diagnosis of PTSD (DSM-IV)
3. Single or multiple separate traumatic events (type I trauma)

Exclusion criteria

1. Repeated sexual and/or physical abuse (type II trauma)
2. Psychotic and substance-use disorders
3. Confounding medical conditions
4. Past month psychotropic/cardiovascular medication use.
5. Contra-indications for MRI scanning (metal inplants, pregnancy, claustrophobia)

Study design

Design

Study type: Interventional

Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-06-2013
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO

Date:	28-05-2013
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL42728.029.12