Memory traces of trauma: Neurocognitive aspects of and therapeutic approaches for posttraumatic stress disorder
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Chapter 10

Discussion

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10.1 Overview

The aim of this thesis was to investigate important aspects of memory and information processing in patients with PTSD, and to examine therapeutic approaches for targeting traumatic memories. The following research questions were addressed:

- Are neurocognitive deficits in trauma survivors and PTSD patients specifically related to PTSD, or also to its clinical correlates such as major depression and sleep disturbances?
- What are the effects of BEP and EMDR on PTSD and its clinical correlates, and is there a difference in response pattern?
- Do neurocognitive disturbances in PTSD change over the course of trauma-focused psychotherapy?
- Can predictors be identified for treatment success in trauma-focused psychotherapy? Do neurocognitive and neuroendocrine aspects of PTSD and hotspots in trauma memories contribute to treatment response?

In this final chapter, findings of the previous chapters will be discussed. A summary of the main findings of the studies is provided, followed by the strengths and limitations of the randomized controlled trial and the cross-sectional study in disaster survivors. We further address the findings of the studies in the light of recent studies and developments, theories about PTSD, and explanations of the working mechanisms of the therapies. The chapter concludes with implications of the studies for clinical practice and recommendations for future research.

10.2 Main findings

*Are neurocognitive deficits in trauma survivors and PTSD patients specifically related to PTSD, or also to its clinical correlates such as major depression and sleep disturbances?*

Baseline data of the randomized controlled trial provided the opportunity to compare neurocognitive performance of PTSD patients with and without MDD. Verbal memory performance proved to be significantly more impaired in PTSD patients with major depression than in PTSD patients without major depression, expressed in more impairment of learning and retrieval of separate words. No differences were found for the group with...
PTSD and MDD in the domains of verbal recognition, retrieval of a coherent paragraph, mental processing speed, shifting of attention, selective attention, or cognitive interference, compared to the group of PTSD patients without MDD. Medium-sized effects were found for group differences on verbal memory for separate words.

The cross-sectional study in disaster survivors showed that PTSD symptoms, depressive symptoms and sleep disturbances independently contributed to sustained attention performance two years after the disaster. The variables age, education, depressive symptoms and sleep disturbances all contributed to sustained attention in these disaster survivors, but correlations between PTSD symptoms and sustained attention performance were still significant for the least difficult subtests after controlling for these variables.

**What are the effects of BEP and EMDR on PTSD and its clinical correlates, and is there a difference in response pattern?**

In the randomized controlled trial, BEP and EMDR were found to be equally effective in reducing PTSD symptom severity, but speed of change was different in these psychotherapeutic treatments. Findings regarding the response pattern indicated that EMDR led to a significantly sharper decrease in PTSD symptoms than BEP. Additional analyses correcting for session duration still yielded this result. Dropout rates were similar for both treatments (29% for EMDR; 36% for BEP). Both treatments yielded large improvement effect sizes for both self-reported and clinician-rated PTSD, indicating that the majority of the participants benefitted from these treatments. The PTSD diagnosis remained present for 10% of the enrolled patients post-treatment. The treatments also had positive effects on comorbid psychiatric disorders and symptoms. MDD was present in 60% of the patients enrolled in our trial, and was diagnosed in 16% of the patients at the endpoint of our trial. Anxiety disorders other than PTSD were present in 16% of the patients before treatment, and were diagnosed in 11% of the patients at the treatment’s conclusion. Improvement effect sizes were also large for self-reported depressive and general anxiety symptoms. These effects were obtained faster in EMDR, and were similar in both treatment conditions at the endpoint.

A case report on one of the patients in the trial suggested that EMDR may also be an efficacious treatment for patients with concurrent PTSD and OCD. Successful processing of the trauma resulted in decreased anxiety when coping with trauma reminders, and subsequently decreased the need for obsessive compulsive symptoms. EMDR in this case facilitated...
the application of exposure and response prevention techniques for OCD symptoms.

Do neurocognitive disturbances in PTSD change over the course of trauma-focused psychotherapy?

Measures of memory and executive functioning, administered both before and after treatment in the randomized controlled trial, showed significant improvements over the course of both treatments. Medium-sized improvements were found for verbal memory of a coherent paragraph. Improvements in other domains, such as verbal memory for separate words, psychomotor speed, selective attention, divided attention and cognitive interference were more modest, but also significant. Greater PTSD symptom decrease was related to better post-treatment neurocognitive performance on almost all measures, but we could not confirm any relationship between decrease of PTSD symptoms and increase in neurocognitive performance. PTSD patients with comorbid MDD improved more on cognitive interference tasks than PTSD patients without MDD. Similar neurocognitive changes were found for patients who were on serotonergic antidepressants and those who were not.

Can predictors be identified for treatment success in trauma-focused psychotherapy? Do neuropsychological and neuroendocrine aspects of PTSD and hotspots in trauma memories contribute to treatment response?

Verbal memory for emotionally neutral material, measured before treatment in the trial, proved to have a strong effect on treatment success. Poorer baseline performance on tasks of encoding, short-term and long-term recall of words and recall of a coherent paragraph were associated with less decrease in self-reported PTSD, for both treatment conditions. These effects were independent of baseline severity of PTSD symptoms and major depression. The strongest effects were found for delayed recall measures. Based on their pre-treatment long-term cued retrieval of words, 75.6% of the patients could be correctly classified as responder, with a sensitivity of 74.1% and a specificity of 88.9%.

From the patients who completed BEP in the trial, subgroups of the most successful and least successful treatments were selected based on their decrease in PTSD symptom severity. Subsequently, audio recordings of the imaginal exposure sessions of these treatments were assessed for the presence of hotspots and the associated emotions, cognitions, and characteristics. The mean number of hotspots did not differ between the
successful and unsuccessful treatments, but hotspots were more frequently addressed by the therapist in successful treatments. Moreover, more characteristics of hotspots, such as an audible change in affect, were present in successful treatments than in unsuccessful ones.

In another subgroup of patients, biomarkers of PTSD were investigated before their treatment in the trial with the aim of exploring their potential as a predictor for treatment success. A more suppressed cortisol curve after administration of dexamethasone significantly predicted greater PTSD decrease in trauma-focused psychotherapy, controlling for the effects of several potential mediators. Basal early morning cortisol and dehydroepiandosterone were not found to be associated with treatment outcome.

10.3 Methodological considerations: strengths and limitations

Strengths

The study had a strong design. This enabled a methodologically sound comparison of the two trauma-focused psychotherapy protocols and made it possible to study response patterns. Protocol adherence, treatment integrity checks, intention-to-treat analyses, the use of structured clinical interviews, weekly assessment of symptoms, and independent assessment of outcome contributed to the soundness of the results. A further strength of the study was the clinical relevance, taken into account by some features of a ‘practical trial’, defined as a randomized trial that combines elements of both efficacy and effectiveness designs (Schnurr, 2007). Inclusion of a heterogeneous trauma population, the cultural diversity of the sample, treatment duration dependent on patients’ recovery, and the use of non-expert therapists added to the generalizability of the results to clinical practice. This enhances the relevance of our study for making clinical decisions. Further strengths were the relatively large group of patients we included, and the administration of a wide range of predictive and outcome variables, including neurocognitive tests for verbal memory and attention, and neuroendocrine measures for a subgroup of the participants in the trial.
Limitations

Design

Limitations related to the design of the trial are mostly related to the features of effectiveness designs that we applied, which enhance generalizability but pose potential threats to internal validity. The choice to let the treatment duration depend on the patients’ recovery, as applied in clinical practice, provided a challenge for the timing of the trial’s post-assessments. We chose to schedule the first post-assessment after 6 sessions in the BEP condition and after the whole EMDR treatment, which on average was also 6 sessions. In some BEP treatments, the exposure lasted longer than the 6th session, but nevertheless the first post-assessment took place at this point in time. It is a limitation of our study that this time point was variable for EMDR but not for BEP. Also, the session duration was 30-45 minutes longer in EMDR than in BEP. Equal session durations would have allowed for a more fair comparison of the treatments. This is the reason why we performed an additional analysis to correct for session duration for the primary outcome. The session durations we implemented were standard in clinical care and were therefore applied as such. Another limitation was the allowance of concurrent treatments to a certain extent. Although our aim was to keep the pharmacological treatment as stable as possible, pharmacological treatments and changes in pharmacological treatment may have contributed to the treatment effects in a minority of the patients. Non-trauma-focused therapies may also have had an additional effect. To some extent, this may be related to the large-sized effects we found.

The primary objective of the RCT was to compare the effects of two active treatments. However, regarding the study on neurocognitive changes in response to treatment, a control group not receiving treatment would have allowed for more certainty regarding the causal role of trauma-focused psychotherapy in the improvements we found. Even though we used different versions of the neurocognitive tests pre- and post-treatment, it cannot be completely ruled out that practice effects played a role in the improvement of neurocognitive functioning over time. It was felt to be unethical to have a waitlist control group for the duration of the treatments in the study (i.e. 4 months), and thereby withholding evidence-based interventions from them for this period. Moreover, for the primary objective of the RCT to compare the effects of the treatments, it is deemed unwise to include a control group that does not account for important
factors such as therapist commitment and belief in the treatment (Bradley, Greene, Russ, Dutra, & Westen, 2005).

For the explorative studies on hotspots and neuroendocrine predictors of treatment response in various subgroups of the participants, small numbers may have led to insufficient statistical power to detect all the effects.

**Dropout from therapy and assessments**

Both treatments in the trial suffered from treatment dropout and assessment dropout. No differences were found in percentages of dropout between the treatment conditions, but 32.5% of patients did not complete the treatment they were assigned. This rate is comparable with those of other trials (Hembree et al., 2003; Schnurr et al., 2007; Schottenbauer, Glass, Arnkoff, Tendick, & Gray, 2008). Ten percent of patients dropped out before treatment, which may indicate motivational problems to start trauma therapy. Non-attendance of assessments was somewhat higher than in other trials, particularly for BEP. This non-attendance of assessments occurred more often in patients who had dropped out of treatment. Some results, for instance the neurocognitive improvements, may therefore be more reflective of changes in treatment completers.

**Generalisability**

Although the participants recruited for this trial were treatment-seeking patients at our clinic and efforts were made to maximize external validity, some selection criteria could not be avoided. This poses some limitations for the generalizability of the results. Results are therefore not necessarily representative for PTSD patients who are acutely suicidal, or who endorse diagnostic criteria for severe major depressive disorder, severe alcohol or drug dependence, lifetime psychotic disorders, and severe personality disorders. These exclusion criteria were common when the trial was started. In the mean time, there are indications that PTSD patients with a high level of borderline personality characteristics also benefit significantly from trauma-focused interventions (Feeny, Zoellner, & Foa, 2002; Clarke, Rizvi, & Resick, 2008) and stabilizing group interventions (Dorrepaal et al., 2012). Alcohol and substance related disorders do not necessarily preclude the application of trauma-focused interventions either (e.g., Hien, Campbell, Ruglass, Hu, & Killeen, 2010), nor does a chart diagnosis of psychosis (van den Berg & van der Gaag, 2012). The relatively strict exclusion criteria in the current trial may be associated with our large improvement effect sizes (Bradley et al., 2005).
Strengths and limitations of the study in disaster survivors

Strengths of the cross-sectional study in disaster survivors were that this was the first study to investigate sustained attention in such a population, and the participants stemmed from a community sample not necessarily seeking treatment. Limitations are that only one aspect of attention was assessed in the study, instead of multiple neurocognitive domains, and that the study may not be representative for other disaster survivors. Important characteristics of disasters (e.g., geographical location, resource loss) and survivors (e.g., age, socioeconomic status) vary and may be of influence on neuropsychological performance of survivors.

10.4 Relevance of the findings

Can the feeling of safety originating from adequate memory functioning be restored by treatment? Do anxiety, depression and stress responses normalize after treatment?

Comparing the effects of the treatments in the trial to meta-analyses (Bradley et al., 2005; Bisson et al., 2007), effect sizes of BEP are comparable to those of TF-CBT and those of EMDR are larger than in previous studies and meta-analyses. Effect sizes of BEP in our trial from pre- to post-treatment (average Cohen’s $d$ 1.75) were also somewhat larger than in other RCTs investigating BEP in comparison to waiting list or a minimal attention condition (average Cohen’s $d$ of 1.30 – 1.62, Gersons, Carlier, Lamberts, & van der Kolk, 2000; Lindauer et al., 2005; Schnyder, Müller, Maercker, & Wittmann, 2011). Both treatments also yielded large effect sizes regarding comorbid depressive symptoms and general anxiety symptoms. Only 10% of the participants in our trial kept endorsing the diagnostic criteria for a PTSD diagnosis, whereas Bradley et al. (2005) found that 33% of treatment completers and 44% of patients who entered treatment still met criteria for PTSD in their meta-analysis. Overall, the treatments investigated in our trial thus produced substantial improvements in symptomatology. However, this study did not specifically focus on the symptoms which remain after treatment, which can also lead to significant constraints in daily functioning. A study of BEP in 511 police officers who completed the treatment closely investigated the residual symptoms (Smit et al., in press). Although only 1.3% of the police officers met full criteria for PTSD post-treatment, remaining PTSD symptoms were present in almost 60% of them. Subjective concentration difficulties were the most prevalent residual symptom in 16.4 % of the police officers. This indicates that the ‘memory traces’ of trauma in sustained attention are not
gone completely should we rely on the opinion of the trauma survivor. These remaining concentration difficulties may contribute to less than optimal daily memory functioning. Also, there may be a tendency for the patients who do not get better to drop out of treatment. Our dropout analysis indeed showed that dropouts were more likely to have less symptom improvement over the first sessions of the therapy than the patients who stayed in the trial at that point. Furthermore, patients who dropped out of treatment were younger and were more likely to stem from minority ethnic groups.

In contrast with the subjective experience of concentration difficulties as a residual symptom, we found significant improvements on more objective neurocognitive tests over the course of treatment. Verbal memory for a coherent paragraph improved most from pre- to post-treatment, and verbal learning and memory for separate words, divided attention, cognitive interference, selective attention and psychomotor speed improved as well. These neuropsychological improvements are in line with changes in brain activation patterns found by other studies over the course of trauma-focused treatments. Normalized activity in the prefrontal cortex was reported after EMDR and BEP, and some studies have also found decreased limbic activation (Levin, Lazrove, & van der Kolk, 1999; Lansing, Amen, Hanks, & Rudy, 2005; Oh & Choi, 2007; Lindauer et al., 2008). In EMDR responders, increased hippocampal volumes were found (Bossini, Fagioli, & Castrogiovanni, 2007), as well as increased posterior cingulate, anterior insula, and right parahippocampal gyrus volumes (Nardo et al., 2010). In an EEG study, Pagani et al. (2012) found a shift in cortical firing from prefrontal and limbic regions at the start of EMDR, to fusiform and visual cortex at the end of the therapy. Psychotherapy for PTSD seems to normalize the fear network in PTSD by engaging executive functions in the prefrontal cortex and thereby inhibiting emotional responses in limbic structures (LeDoux, 2002; Quide, Witteveen, El-Hage, Veltman, & Olff, 2011). A recent study by Thomaes et al. (2012) found that symptom improvement after trauma therapy also coincided with functional changes in the anterior cingulate cortex and insula when processing emotional material.

How can the differential treatment speed be explained, and which working mechanisms are involved in BEP and EMDR?

EMDR in our trial led to a significantly sharper decline in PTSD symptoms than BEP, and this effect remained after controlling for session duration in an additional analysis. As mentioned in paragraph 1.1, BEP and EMDR
target the traumatic memories in a different way and this is a likely explanation for this differential treatment effect. Detailed exposure to the memory of the trauma takes place in BEP, whereas in EMDR, short exposure moments to the hotspots in the memory of the trauma are interrupted by distracting stimulation and followed by free associations. These differences in the exposure procedure may explain why EMDR works faster. A remarkable outcome of the RCT is that the treatments lead to similar results after both interventions are finished, although they are approaching the trauma memory quite differently.

Several memory theories have offered explanations for the working mechanisms in trauma-focused interventions. A general explanation for trauma-focused psychotherapy with exposure and cognitive restructuring components comes from dual representation theory (Brewin, 2005). Brewin assumes that trauma treatment involves both the image-based memory system (SAM) and the verbal memory system. According to this theory, a form of imaginal exposure reduces re-experiencing symptoms and cognitive restructuring techniques target beliefs that the person has about him- or herself and the world. When the trauma survivor deliberately maintains attention on the content of the flashbacks, and no longer tries to avoid them, information that is only present in the SAM system is presumed to be re-encoded in the VAM system. By this process, the memories are assigned a spatial and temporal context. Trauma survivors will then be able to place their memory in the past, and to recognize that the threat is no longer present. This reduces the need for flashbacks and nightmares, and thereby leads to PTSD symptom reduction.

Another memory theory was specifically formulated to explain the effects of EMDR. This working memory account is currently the most plausible explanation for how EMDR works. It states that the eye movements offered shortly after imaginal exposure to the hotspot of the trauma tax the working memory of the trauma survivor, and thereby reduce the vividness and emotionality of the memories (Andrade, Kavanagh, & Baddeley, 1997; Gunter & Bodner, 2008; Engelhard, van Uijen, & van den Hout, 2010). It is assumed that the dual task of keeping the emotional memory in mind and performing the eye movements creates a psychological distance and leads to de-arousal, which eventually leads to PTSD symptom decrease. The eye movements task thus has an incremental value in EMDR (Lee & Cuijpers, 2013), in contrast with previous analyses and thoughts on this matter (e.g., Davidson & Parker, 2001). The working memory account is based on the multi-component model of working memory by Baddeley and colleagues (Baddeley & Hitch, 1974; Repovs &
Baddeley, 2006). Several experiments have proven that one can apply several other tasks that tax working memory instead of eye movements, such as drawing a complex figure and arithmetic assignments. This makes it likely that the component of the working memory that these tasks draw on is the central executive.

Which factors facilitate or hinder the processing of traumatic memories and normalization of anxiety?

Several findings of the studies in this thesis are in line with dual representation theory formulated by Brewin and colleagues (Brewin, Dalgleish, & Joseph, 1996; Brewin & Holmes, 2003). This specifically applies to factors that proved to be important for treatment success in BEP and EMDR. First, we found that several aspects of verbal memory were related to treatment outcome. The degree to which the verbal memory system is deregulated thus seems to indicate to which extent patients will be able to benefit from trauma-focused psychotherapy. Our finding of a poorer treatment response in patients with more restricted verbal memory performance led us to believe that higher-order learning and meaning-making capabilities will be limited for both emotionally neutral and trauma-related information. These underlying processes can therefore hamper the processing of trauma memories and reconsolidation. In terms of dual representation theory, this would mean that reencoding of the trauma memories from SAM into VAM and assignment of a spatial and temporal context to the memory of the trauma would not adequately take place.

Second, our explorative findings on the association between repeatedly focusing on hotspots in imaginal exposure sessions and successful treatment can be explained by dual representation theory. According to this theory, hotspots correspond to the moments where there is maximal functional separation between visuospatial and verbal processing, leading to a large discrepancy between the contents of the VAM and SAM memory systems (Brewin, 2005). Repeatedly focusing on hotspots during imaginal exposure may be necessary for successful reencoding of all potential retrieval cues into the VAM, to prevent the recurrence of flashbacks.

Apart from the above factors which can be related to dual representation theory, we also found preliminary evidence that a more flattened cortisol morning curve in response to dexamethasone was a biomarker for better treatment response to trauma-focused interventions. This points to the important role of the sensitivity of the HPA axis and the enhanced negative feedback loop in PTSD, which is one of the most
consistent neuroendocrine findings in PTSD populations. Thus, patients with the neuroendocrine picture that is most characteristic of PTSD also respond better to trauma-focused psychotherapy, whereas basal cortisol and DHEA levels do not seem to predict treatment response. This corresponds with previous research in BEP and TF-CBT (Olff, de Vries, Güzelcan, Assies, & Gersons, 2007; Yehuda et al., 2009).

In summary, we have identified some neurocognitive and neuroendocrine characteristics and autobiographical memory correlates to be associated with treatment response. These factors seem to make stronger contributions to treatment response in trauma-focused psychotherapies than certain demographic and clinical factors in our study. Previous research has already noted that demographic and clinical predictors tend to differ across populations, interventions, and outcome measures studied (Karatzias et al., 2007).

Do the results inform us about the concept of PTSD?
With the release of the DSM-5, it is interesting to note that the hotspots in trauma memories in our explorative pilot study were accompanied by a large proportion of emotions not present in criterion A2 of the DSM-IV. DSM A2-emotions were only present in 34% of these moments of emotional impact. Fear, helplessness, or horror in the direct aftermath of traumatic events were found to be only weak predictors of later PTSD, and other posttraumatic emotional responses, such as guilt, shame and anger, also predicted PTSD (Brewin, Andrews, & Valentine, 2000; Andrews, Brewin, Rose, & Kirk, 2000; Feeny, Zoellner, & Foa, 2000). Moreover, anger may negatively impact treatment success (Foa, Riggs, Massie, & Yarczower, 1995; Forbes, Creamer, Hawthorne, Allen, & McHugh, 2003; Forbes et al., 2008), while guilt may positively influence treatment response (Rizvi, Vogt, & Resick, 2009). Taken together, the studies mentioned here suggest that it may be a valid discussion to eliminate criterion A2 from the PTSD diagnosis in DSM-5, because a range of other emotions may be more important for who will go on to develop PTSD after a trauma. Our pilot findings on hotspots cannot contribute to the role of these emotions in the development of PTSD, but we found preliminary evidence that addressing hotspots with non DSM-IV A2 emotions is important for treatment response in trauma-focused psychotherapy. It may enhance the treatment outcome to focus on these other emotions, instead of only on fear which is now mostly the case in TF-CBT and cognitive processing therapy. Furthermore, the role of one of these emotions, anger, has been given a
more prominent position in the PTSD symptom criterion of reckless and destructive behavior expected to appear in DSM-5.

With our neurocognitive comparison study investigating PTSD patients with and without co-morbid MDD, we also hoped to contribute to the question whether PTSD with and without co-morbid MDD can be seen as separate diagnostic constructs with distinct neuropsychological profiles. Support for a somewhat more impaired verbal memory function was found in patients with PTSD + MDD, but the general neuropsychological profile was similar for both groups. Furthermore, we found some support for independent contributions of PTSD symptoms and MDD symptoms to sustained attention in disaster survivors. The evidence for distinct neuropsychological profiles is limited so far.

10.5 Clinical implications

The studies in this thesis underline treatment guidelines for PTSD (NICE, 2005; Foa, Keane, Friedman, & Cohen, 2008) that trauma-focused interventions should be the first line of treatment for patients with PTSD resulting from a single traumatic event. A history of earlier traumatic events was present in 54% of the patients, and 19% of the patients had trauma histories that can be considered ‘complex trauma’, indicating that trauma history does not need to be a reason to refrain from administration of these treatments. This study showed that BEP and EMDR both yielded large effect sizes in the reduction of PTSD symptoms, depressive symptoms and general anxiety symptoms, indicating that the majority of patients benefit from these treatments. Because both treatments were shown to be equally efficacious, with similar dropout rates and because no specific factors were shown to be differentially related to treatment outcome, we believe that patient and therapist preference can guide the choice for treatment method. Patients with a need for fast recovery from PTSD may choose for EMDR. When patients prefer more reflection on the trauma story and want to learn from the trauma, a multimodal, integrative treatment protocol such as BEP will serve them better. A general meta-analysis suggests that following patients’ preference for therapy method, format, therapist characteristics and treatment length results in better treatment outcome and less dropout (Swift, Callahan, & Vollmer, 2011).

Adhering to patient and therapist preference in the choice for a certain treatment implies that both treatments must be available in clinical settings. EMDR is widely applied and disseminated in the Netherlands and is the preferred trauma treatment for many Dutch therapists (van Minnen,
Hendriks & Olff, 2010). Less clinicians opt for TF-CBT or BEP, which may be a result of a fewer number of Dutch professionals who are trained in these treatments. Training in these therapy methods will enhance the possibility to choose this treatment option, also if the trauma survivor does not adequately recover from the first treatment that is offered. The NICE guideline (2005) advises to choose another trauma-focused intervention in case of no or only limited improvement after a specific trauma-focused intervention. Another condition for treatment of PTSD is proper identification and diagnostic assessment of PTSD patients in clinical practice. The current development of mental health care institutions to compartmentalize into departments for specific mental health problems may hinder appropriate recognition of trauma-related disorders and comorbid PTSD.

The studies in this thesis also point to the need to tailor interventions for specific groups who do not sufficiently benefit from BEP or EMDR. A first concern is the group of patients which never started treatment and the group which dropped out of treatment prematurely. Treatment dropout in our study was associated with younger age, being part of minority ethnic groups, and less symptom improvement over the first few sessions. This study was a randomized controlled trial and therefore had to strictly adhere to the treatment protocol, but in clinical practice it may be useful for these groups of patients to spend some time to build a trusting therapeutic relationship and address possible motivational problems before addressing the trauma. A second concern is the group with restricted verbal memory performance, which proved to be a strong predictor for worse treatment outcome. This is an important aspect for clinicians, as it is sometimes hard to know how much information patients ‘take home’ from the session. Administering a verbal memory test may give a more objective indication of the difficulties the patient experiences in this domain. In the future, it would be good to develop a kind of ‘mini mental state examination’ for verbal memory in PTSD patients, because memory performance varies considerably among these patients. For the people who do not sufficiently benefit from treatment, alternative or augmented treatments need to be evaluated and treatment parameters like treatment length need to be varied (Schnyder, 2005; Bradley et al., 2005). Visual memory is generally less impaired in PTSD than verbal memory (Brewin, Kleiner, Vasterling, & Field, 2007), so visual enhancers to the therapy can be useful. Other possibilities include adjusting the pace and complexity of treatment, applying a more graduated approach for trauma recall, and providing reminders of the session content and homework (Brewin, 2005).

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For the therapist, this may also mean that ‘hotspots’ need to be addressed repeatedly in BEP treatments. Another point of attention for the therapists may be to look for hotspots characteristics in imaginal exposure, to ensure that sufficient emotional engagement with the trauma memory takes place in BEP.

### 10.6 Future research

Regarding the effects of the treatments, one question that remains to be answered is the long term follow-up effect. The last assessment point in our trial was 12 months after the second post-assessment, and results from this assessment will follow in the near future. Few randomized studies, however, have collected data beyond that time point so the long term effects are not yet entirely clear. These data would provide information about resilience in the face of other traumatic events or life events. In addition, cost-effectiveness of the treatments deserves further study.

An important question for future research is how dropout can be minimized and treatment results maximized, in order to be able to offer more efficacious treatments to PTSD patients. Optimal session duration and frequency should be investigated. Good results have been obtained with an intensive one week treatment program, including trauma-focused interventions, for the treatment of PTSD (Ehlers et al., 2010; Hendriks, de Kleine, van Rees, Bult & van Minnen, 2010). At our clinic we have had positive experiences applying a 7-work day intensive trauma treatment program for patients with PTSD and severe comorbid conditions such as OCD. These interventions show potential and should be studied further. A related topic is at which time point interventions should be offered in order to maximize efficacy. Possibly, trauma-focused acute interventions can be helpful to prevent PTSD in the long run. Preliminary positive results have been found for a brief form of trauma-focused CBT (Rothbaum et al., 2012). The efficacy of a brief EMDR intervention applied in the acute aftermath of trauma to prevent PTSD in the long run remains to be studied.

Several topics regarding memory and neurocognitive performance are worth further investigation. In our trial we found an association between verbal memory performance and treatment outcome, but other neurocognitive variables could be related to treatment response. In light of the working memory hypothesis described earlier in this chapter, Gunter and Bodner (2008) have shown that more restricted reading span, which is a measure of executive functioning, is related to better treatment outcome in an EMDR-like procedure in students. Further research is needed to
replicate this finding in PTSD patients since it can be assumed that their working memory is more ‘taxed’ with flashbacks of traumatic events. Similarly, it is necessary to replicate findings regarding distracting tasks used in EMDR experiments in patients during the whole EMDR treatment. It could be expected that eye movements are more effective in reducing the vividness and emotionality than listening to beeps (cf. van den Hout et al., 2011; 2012). It would be interesting to compare the predictive effects of verbal versus visual memory in response to trauma-focused psychotherapy. Visual memory is less impaired in PTSD, so a weaker or absent association between verbal memory and treatment success would provide support for the dual representation theory.

In the cross-sectional study on sustained attention, subjective sleep disturbances were found to be related to sustained attention performance. It is likely that sleep disturbances affect verbal memory in PTSD patients. However, discrepancies are often found between subjective reports of sleep and objective sleep quality measured by polysomnography in PTSD (van Liempt, 2012). Relationships between objective sleep parameters and neurocognitive functioning are currently under investigation in veterans and police officers with and without PTSD as part of a collaboration between the Academic Medical Center, the University of Amsterdam, and Arq Psychotrauma Expert Group.

Findings on hotspots and HPA functioning in relation to treatment outcome in this thesis are preliminary because they were sought in subsamples of the larger trial. Replication of these findings in a larger sample is much encouraged. More statistical power would possibly allow for finding more biomarkers of treatment response. Assessment of the sensitivity of the HPA-axis by means of the dexamethasone suppression test before and after trauma-focused treatment can enhance our understanding of improved neuroendocrine functioning in response to treatment. Taken together, the proposed studies will further clarify if trauma survivors with PTSD may be able to place the psychological, neurocognitive and physiological distress, or the “memory traces of trauma”, in the past after treatment.

References


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