Modification of Cognitive Biases Related to Posttraumatic Stress:

A Systematic Review and Research Agenda

Marcella L. Woud[a]

Johan Verwoerd[b]

Julie Krans[c]

a. Mental Health Research and Treatment Center, Department of Psychology, Ruhr-Universität Bochum, Massenbergstrasse 9-13, 44787 Bochum, Germany. Tel.: +49 (0) 2343221502. E-mail: Marcella.Woud@rub.de

b. Department of Clinical Psychology, University of Groningen, Grote Kruisstraat 2-1, 9712 TS, Groningen, The Netherlands. Tel.: +31 (0) 503637615. E-mail: J.R.L.Verwoerd@rug.nl

c. Behavior, Health and Psychopathology, Faculty of Psychology and Educational Sciences, KU Leuven. Tiensestraat 102, 3000 Leuven, Belgium. Tel.: +32 (0) 16 37 30 76. Email: julie.krans@kuleuven.be

Corresponding author: Marcella L. Woud, Mental Health Research and Treatment Center, Department of Psychology, Ruhr-Universität Bochum, Massenbergstrasse 9-13, 44787 Bochum, Germany. E-mail: Marcella.Woud@rub.de. Tel.: +49 (0) 2343221502. Fax: +49 (0) 2343214369.

Abstract

Cognitive models of Posttraumatic Stress Disorder (PTSD) postulate that cognitive biases in attention, interpretation, and memory represent key factors involved in the onset and maintenance of PTSD. Developments in experimental research demonstrate that it may be possible to manipulate such biases by means of Cognitive Bias Modification (CBM). In the present paper, we summarize studies assessing cognitive biases in posttraumatic stress to serve as a theoretical and methodological background. However, our main aim was to provide an overview of the scientific literature on CBM in (analogue) posttraumatic stress. Results of our systematic literature review showed that most CBM studies targeted attentional and interpretation biases (attention: five studies; interpretation: three studies), and one study modified memory biases. Overall, results showed that CBM can indeed modify cognitive biases and affect (analog) trauma symptoms in a training congruent manner. Interpretation bias procedures seemed effective in analog samples, and memory bias training proved preliminary success in a clinical PTSD sample. Studies of attention bias modification provided more mixed results. This heterogeneous picture may be explained by differences in the type of population or variations in the CBM procedure. Therefore, we sketched a detailed research agenda targeting the challenges for CBM in posttraumatic stress.

Keywords: posttraumatic stress disorder (PTSD); cognitive biases; cognitive bias modification (CBM); attention; interpretation; appraisal; memory

Posttraumatic Stress Disorder (PTSD) is a psychological reaction following one or several traumatic events. According to the Diagnostic and Statistical Manual of Mental Disorders-5th edition (DSM 5, 2013), PTSD is characterized by four symptom groups: (a) Involuntary memories of the trauma such as intrusions or nightmares; (b) Persistent avoidance of stimuli associated with the traumatic event; (c) Negative alterations in cognitions and mood that are associated with the trauma; and (d) Alterations in arousal and reactivity that are associated with the trauma. Research suggests that most victims recover spontaneously (e.g., Foa & Riggs, 1995). However, for 10-15% of the victims, the symptoms persist (e.g., Foa & Rothbaum, 1998; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995), depending on various external (e.g., the type of trauma) and intrapersonal factors (e.g., emotion regulation skills, cognitive biases). If the symptoms persist for more than a month, the diagnosis of PTSD can be given.

To elucidate the specific contribution of cognitive factors to the development and maintenance of PTSD, several information processing theories have been proposed in the past 30 years (e.g., Brewin, Dalgleish, & Joseph, 1996; Dalgleish, 2004; Ehlers & Clark, 2000; Foa, Steketee, & Rothbaum, 1989). These theories converge on the idea that PTSD symptoms can be explained best by alterations or dysfunctions in cognitive processing. Three specific cognitive biases have been identified in emotional disorders (for reviews, see e.g., Barry, Vervliet, & Hermans, 2015; Hirsch, Meeten, Krahé, & Reeder, 2016; Mathews & MacLeod, 2005), which can be also found in the context of PTSD (for review, see e.g., Buckley, Blanchard, & Neill, 2000; Johnson, Bomyea, & Lang, in press): attention, interpretation, and memory biases. According to the cognitive model of Ehlers and Clark (2000), cognitive biases for trauma-relevant information contribute to a sense of 'current threat', which (partly) determines the degree to which an individual will spontaneously recover from the traumatic experience.

Current research shows that cognitive biases are correlated with PTSD symptomatology. However, it remains unclear whether cognitive biases causally contribute to PTSD (Kraemer, 1997). Developments within experimental research demonstrate that cognitive biases may be manipulated by means of Cognitive Bias Modification (CBM; cf: Koster, Fox, & MacLeod, 2009; Woud & Becker, 2014). There is a substantial and promising body of research on CBM in emotional disorders which is summarized in various reviews and meta-analyses (e.g., Cristea, Kok, & Cuijpers, 2015; Hallion & Ruscio, 2011; MacLeod & Mathews, 2012). Importantly, there is also a growing body of CBM research in the field of psychological trauma. To the best of our knowledge, this evidence has not previously been reviewed. Hence, the main aim of the present review is to provide a systematic overview of CBM research in the field of PTSD and (analogue) trauma. Before presenting these results we will first provide an illustrative overview of exemplary studies assessing cognitive biases in psychological trauma. This overview defines the type of cognitive biases we are interested in to serve as a background for the reader.

Current evidence for cognitive biases in PTSD

Attention

This section summarizes studies assessing biased attention in PTSD, structured according to the paradigms commonly used to measure attentional processes.

Emotional Stroop task. In the emotional Stroop task (ES; Cisler et al., 2011; Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & IJzerdoorn, 2007), participants are exposed to printed color words that may or may not be related to their traumatic experience. Participants are instructed to ignore the words' meaning and instead name the words' print color. Longer response latencies for trauma-related or anxiety-related versus other color words reflect trauma-

specific and general-threat-related attentional bias, respectively. Literature reviews on ES effects reveal different conclusions. Based on a qualitative review in dissertation abstracts (Kimble, Frueh, & Marks, 2009) and a meta-analysis (Cisler & Koster, 2010), evidence for trauma-specific attentional bias in PTSD appears to be scarce. As reported by Cisler and Koster (2010), evidence generally shows biased responding for trauma-relevant words both in PTSD patients and trauma-exposed controls when these groups are compared with healthy controls. An interim summary of research revealed that interference effects for trauma-relevant words can be best explained by trauma-exposure alone (Cisler & Koster, 2010; van Bockstale et al., 2014). To conclude: various studies suggest that the ES paradigm as index of attention bias is unable to detect enhanced processing of trauma-related or general threat-related information in PTSD.

Dot probe task. In the dot probe task (MacLeod, Mathews, & Tata, 1986), a fixation cross is presented in the middle of a computer screen. Subsequently, two cues appear simultaneously left and right or top and bottom of the fixation cross. One of the cues is trauma- or threat-related, the other neutral. After a short presentation (e.g., 500 ms, 1000 ms), one of the cues is replaced by a target stimulus. Participants are instructed to respond to this target as fast as possible. Hence, an attentional bias is inferred from faster reaction times on trials were a target replaces a trauma cue (congruent trials) compared to trials where the target appears at the opposite location (incongruent trials) (Van Bockstaele et al., 2014). For instance, Naim et al. (2014) tested a sample of motor vehicle accident survivors within 24h of hospital admission. A dot probe task was used including threat-neutral word pair combinations. Strength of the cueing effect (the difference in reaction times of congruent minus incongruent trials) as an index of attentional bias towards threat predicted PTSD three months later. This example follows the general pattern of evidence presented in earlier reviews (Bar-Haim et al., 2007; van Bockstaele

et al., 2014), suggesting that the majority of studies do find that attention bias as measured with the dot probe is correlated with PTSD. Yet, with this paradigm, it is difficult to disentangle whether attention bias effects in PTSD reflect difficulty to disengage from threat, avoidance from threat, or facilitated attention towards theat. Furthermore, few studies have tested PTSD-related attention bias using trauma-specific stimuli.

Visual search paradigm. In a lexical decision variant of the visual search paradigm, participants are presented with arrays of distracters consisting of several trauma-related or neutral stimuli and a single target stimulus (trauma-related or neutral) that has to be detected and identified. Facilitated engagement of attention is inferred by speeded responding to trauma-related targets compared to non-trauma related targets. Delayed disengagement is measured by comparing trials where a non-trauma target has to be detected in arrays with several trauma-related distracters with trials in which trauma-related targets have to be searched for in arrays of non-trauma distracters. Pineles et al. (2007, 2009) compared sexual trauma victims high and low on PTSD symptoms (2009) and Vietnam-era veterans with high and low scores on PTSD symptoms (2007) on attention facilitation and delayed disengagement. Results of both studies showed that the high PTSD participants were characterized by delayed disengagement from trauma-related stimuli compared to trauma-exposed controls. No evidence was found for PTSD-related facilitated engagement with trauma stimuli. In the second study, it was found that group differences in attentional bias were specific for trauma-related words: Individuals with PTSD and trauma-exposed controls did not show different patterns of responding for general threat words and neutral words. As no other empirical studies have been conducted apart from the ones described here, it is possible to tentatively conclude that the visual search paradigm is able to detect a correlation between attention bias and having a PTSD diagnosis. This evidence points

towards a PTSD-related difficulty to disengage attention from trauma-related word stimuli. No evidence was found for facilitated engagement within PTSD groups.

RSVP task. In the rapid serial visual presentation (RSVP) temporal attentional bias can be assessed by comparing the capacity of trauma-related, general anxiety-related and neutral stimuli to impair subsequent target processing. In a recent study (Olatunji, Armstrong, McHugo, & Zald, 2013), veterans with PTSD, trauma-exposed veterans without PTSD and healthy controls were instructed to identify the rotation of neutral target image as quickly as possible. Distracters preceded the target and consisted of combat-related, disgust, positive, or neutral images. Results showed impaired target detection in the veterans with PTSD after combat-related distracters were presented shortly (200 ms) before the target stimulus. The PTSD group did not differ from the trauma-exposed control group and the healthy controls on trials with disgust, positive and neutral distracters. In summary, although evidence using this paradigm is still scarce (i.e., Olatunji et al., 2013; see also Amir, Taylor, Bomyea, Badour, 2009), results are in line with the studies presented for the dot probe and visual search paradigms showing a specific relationship between attention bias and PTSD.

Brief summary. Taken together, several studies investigating the role of trauma-related and general-threat related attention bias in PTSD using the dot probe, visual search, and RSVP paradigms generally support the idea that long-term persistence of PTSD symptoms after trauma exposure can be explained in part by alterations or dysfunctions in cognitive processing. The ES paradigm has been shown to differentiate between trauma-exposed individuals (both PTSD and non-PTSD) and healthy control participants, but could not detect specific information processing abnormalities related to PTSD.

Interpretation

This section will first summarize findings obtained via the Post Traumatic Cognitions Inventory (PTCI; Foa et al., 1999), and then present studies assessing biased interpretations in PTSD, structured according to the paradigms commonly used to measure these processes.

Post Traumatic Cognitions Inventory. The PTCI (Foa et al., 1999) assesses dysfunctional appraisals of trauma-related symptomatology. It contains three subscales: dysfunctional cognitions about the self, the world, and self-blame. Its reliability for the full scale is excellent, and excellent – good for the subscales (e.g., Foa et al., 1999). Various studies showed that dysfunctional cognitions assessed with the PTCI are associated with PTSD symptomatology and severity. To illustrate, in Foa et al.'s study (1999), all three subscales were positively correlated with PTSD severity, and they discriminated between traumatized individuals with and without PTSD. More recently, Kleim et al. (2013) demonstrated that a reduction in dysfunctional appraisals was predictive of symptom reduction during trauma-focused CBT. However, symptom reduction was not predictive of a reduction in dysfunctional appraisals (for additional studies, see e.g., Ehlers, Clark, Hackmann, McManus, & Fennell, 2005; Hagenaars, van Minnen, & de Rooij, 2010). Prospective longitudinal studies further support the role of dysfunctional appraisals in PTSD. In Bryant and Guthrie's studies (2005, 2007) trainee fire-fighters completed the PTCI before exposure to trauma situations and were assessed for PTSD symptomatology after six months (Bryant & Guthrie, 2005) and after four years (Bryant & Guthrie, 2007) of firefighting duty. Pre-trauma scores of the PTCI self-subscale were particularly predictive of subsequent PTSD symptoms (for related studies, see e.g., Ehring, Ehlers, & Glucksman, 2008; Kleim Ehlers, & Glucksman, 2007). The PTCI therefore appears to be an adequate instrument to assess dysfunctional appraisals when using correlational and prospective approaches.

Sentence completion task. The sentence completion task involves the presentation of sentences that do not yet have an ending. The sentences are ambiguous such that one possible meaning could be a trauma-related interpretation. Kimble et al. (2002) showed that combat veterans with PTSD generated more trauma-related endings than combat veterans without PTSD. In another study, Kimble et al. (2012) presented ambiguous sentence stems that were completed with either a threatening, expected, or unexpected ending. Participants had to indicate whether a sentence made sense. During the task, participants' event-related potentials were assessed (N400) too. Results showed that participants with PTSD, compared to those without PTSD, showed significantly smaller N400s in response to threatening sentence endings, suggesting that PTSD patients exhibited enhanced expectations for threat-related interpretations. To summarize, these results show that the sentence completion task successfully distinguished between potentially trauma-exposed individuals with and without a PTSD diagnosis, and that participants' performance is related to trauma-relevant physiological processing.

Homograph task. Amir, Coles, and Foa (2002) employed a homograph paradigm during which participants were presented with sentences that were followed by a cue word. Participants were asked to indicate whether sentence and cue word matched. Half of the target sentences ended with a homograph, of which half had a threatening meaning and the other half a nonthreatening meaning. The other half of the target sentences ended with a non-homograph. Results showed that participants with PTSD, compared to participants without PTSD, were slower to reject sentence word combinations that included homographs with a possible threatening meaning than sentence word combinations that included non-homographs. This suggests that PTSD patients are unable to inhibit the potentially negative meaning of the

homographs, making the homograph task a very suitable approach to assess (subtle) interpretation biases related to trauma-relevant information.

Visual task. Trauma-related interpretations have also been assessed with visual stimuli. In the study by Elwood, Williams, Olatunji, and Lohr (2007), women with and without a history of assault were exposed to film clips depicting threatening, positive, and neutral situations. The clips' outcome was ambiguous, and it was the participants' task to rate these clips on predictability, controllability, perception of escalations, and valence. Women with a history of assault rated the threatening film clips as more predictable and more quickly increasing in danger than women without assault experiences. These results show that visually-presented ambiguous trauma-relevant information also has the potential to elicit interpretation biases.

Brief summary. To summarize, these data indicate a potentially crucial role for dysfunctional, trauma-related appraisals and interpretations. That is, the data robustly show that such dysfunctional cognitive processing is correlated with and predictive of trauma-relevant symptomatology (for a review on interpretation biases in emotional disorder, see e.g., Hirsch et al., 2016; Schoth & Liossi, 2017; and for PTSD specifically, see Johnson et al., 2017). Importantly, these findings are independent of the research paradigm (e.g., questionnaires vs. reaction-time based paradigms) and stimuli modality used (e.g., verbal vs. visual material). Dysfunctional, trauma-related appraisals may therefore provide a target process for modification. In particular, verbal based processes such as measured by the PTCI or sentence-completion task may provide a useful starting point.

Memory

Given the complexity of memory processes in trauma, it is safe to say that there is no such thing as *the* memory bias in PTSD. We have made an attempt to come to a thoughtful and

functional, yet necessarily limited, definition that is mostly pragmatic in light of the purpose of this article. By 'memory bias' we refer to an individual's tendency to, intentionally or unintentionally, recall certain autobiographical memories over other autobiographical memories, in a non-random fashion. Harvey and colleagues outlined several memory processes involved in PTSD: selective memory, overgeneral memory, avoidant encoding and retrieval, and working memory (Harvey, Watkins, Mansell, & Shafran, 2004, Chapter 3). To avoid circular reasoning, we will not label memory phenomena that are part of the PTSD symptoms as memory biases (i.e., intrusive memories and amnesia). Further, processes of avoidant encoding (e.g., dissociation) and avoidant retrieval lack conceptual clarity and empirical support, respectively (e.g., Harvey et al., 2004), and will therefore be excluded too. Finally, working memory may facilitate a memory bias by limiting capacity to counter the bias but, in our view, does not constitute a bias per se and will therefore not be included here. Therefore, we limited our scope to implicit and explicit memory biases of overgeneral and selective recall that can potentially be targeted via cognitive bias modification.

The memory literature is less consistent in the paradigms that have been used to study memory bias than it is for attention and interpretation bias. With the exception of overgeneral memory, which is typically assessed with a cue-word paradigm, no 'holy grail' for the assessment of memory biases exists. There are almost as many methodological approaches as there are studies. Structuring the memory bias section according to methodological paradigm would therefore hinder readability and clarity of this paper. Therefore, the section on memory bias will be organized according to the different type of biases rather than the paradigms used to assess the biases.

Overgeneral memory. Autobiographical memories can be retrieved at different levels of specificity (Conway & Pleydell-Pearce, 2000). Specific memories are of events that occurred in a specific place at a specific time, lasting no longer than one day (e.g., dinner with friends last Saturday). Overgeneral memory refers to the inability to recall specific memories (Williams & Broadbent, 1986) and has mostly been studied in the context of depression (for a review see Williams et al., 2007). Generally, findings indicate that overgeneral memory can predict the development of PTSD after trauma (for a review, see Moore & Zoellner, 2007), and that it increases risk for PTSD by 20% (Kleim & Ehlers, 2008). The most commonly used measure of overgeneral memory is the Autobiographical Memory Task (AMT; Williams & Broadbent, 1986), in which participants are presented with cue words and are asked to recall a specific memory in response to this cue word (typically within 30 seconds). The proportion of specific memories on this task is taken as an index of overgeneral memory.

Apart from one study with burn victims (Willebrand et al., 2002), all cross-sectional studies found evidence for a link between overgeneral memory and PTSD symptoms (e.g., McNally, Lasko, Macklin, & Pitman, 1995; Moradi et al., 2008; Wessel, Merckelbach, & Dekkers, 2002). For example, male Vietnam veterans with and without PTSD were asked to recall a specific memory where they exhibited a positive trait or a negative trait (McNally et al., 1995). Participants with PTSD retrieved fewer specific memories and showed longer response latencies for positive traits than non-PTSD controls. PTSD veterans wearing regalia retrieved fewer specific memories than PTSD participants who were not wearing regalia and controls, with no significant difference between the latter two groups.

Prospective studies (e.g., Boelen, Huntjens, & Van den Hout, 2014; Bryant, Sutherland, & Guthrie, 2007; Harvey, Bryant, & Dang, 1998) generally provide additional support for the

value of overgeneral memory in predicting PTSD symptoms. In one study in male trainee firefighters, memory specificity in response to positive cue words, but not to negative cue words or non-specific memories, negatively predicted posttraumatic stress symptoms and depressive symptoms approximately 49 months later (Bryant et al., 2007). In a prospective longitudinal study in assault victims, participants with a diagnosis of ASD recalled more assault-related memories in response to negative cue words, and a lower proportion of specific memories than non-ASD participants at two weeks, and this predicted PTSD and depression at six months (Kleim & Ehlers, 2008).

Selective memory bias. Whereas overgeneral memory refers to a quality of the retrieval process (resulting in a specific or non-specific memory), selective memory refers to the content of the memory instead (i.e., trauma-related or not). Selective memory bias can be distinguished for implicit memory and explicit memory. In implicit memory, no conscious recollection of the memory is necessary, but the participant's response is clearly influenced by the memory representation. If the implicit effect is greater for trauma-related information than other information, this would indicate an implicit memory bias (Harvey et al., 2004). In explicit memory, participants are asked to consciously recall a memory. The outcome of this retrieval process indicates whether a selective memory bias is present by studying the content of the recalled memories. Several paradigms have been adopted to study implicit memory bias in PTSD: tachistoscopic identification (Paunovic, Lundh, & Öst, 2003), noise judgement task (Amir, McNally, & Wiegartz, 1996), word-stem completion (Golier, Yehuda, Lupien, & Harvey, 2003), and picture-clarity ratings (Amir, Leiner, & Bomyea, 2010). Overall, the empirical data does not seem to indicate that there is an implicit memory bias in PTSD. Only two studies reported an implicit memory bias for trauma-related information in PTSD (Amir et

al., 1996, 2010). The first included a very small sample size (14 veterans) and therefore warrants replication in a larger sample. The second study had a larger sample size but did not diagnose PTSD, which makes generalizability to clinical PTSD difficult. Interestingly, these two studies did not assess implicit memory with verbal stimuli, but with ratings of noise and picture-clarity ratings. This implies that implicit memory bias may only be found indirectly, that is, in a different modality than the encoded stimuli.

With the exception of one (Amir et al., 2010), studies on selective memory bias generally report evidence for a trauma-related explicit memory bias in PTSD. For example, using word lists, it was found that Vietnam veterans with PTSD recall a higher proportion of Vietnam-related and negative emotional words than neutral control words compared to non-PTSD veterans (Vrana, Roodman, & Beckham, 1995), that Holocaust survivors with PTSD recalled more Holocaust-related words than survivors without PTSD (Golier et al., 2003), and PTSD patients recalled more trauma-related words than non-PTSD participants (Paunovic, Lundh, & Öst, 2002). Using recognition tasks it was found that crime victims had poorer recognition performance for faces (pictures) that they rated as non-hostile compared to a control group (Paunovic et al., 2003). Finally, using the AMT, participants with PTSD recalled more trauma-related autobiographical memories in response to cue words than trauma victims without PTSD (Sutherland & Bryant, 2008). Studies on overgeneral memory that also report some data on selective memory (but not necessarily direct statistical tests of selective memory bias) generally indicate support for trauma-related selective memory (e.g., McNally, Litz, Prassas, & Shin, 1994; Schönfeld, Ehlers, Böllinghaus, & Rief, 2007; but see Harvey et al., 1998 for a null finding).

Overgeneral memory and selective memory bias. There is a clear lack of studies on the relation between overgeneral memory and selective memory bias in trauma. In the one study we could find, bereaved participants were administered a standard AMT and a trait version of the AMT in a telephone interview (Boelen, Huntjens, Van Deursen, & Van den Hout, 2010). The trait-version requires participants to recall a memory where they exhibited the trait represented by the cue word. Selective recall of loss-related memories on the standard AMT was not associated with grief, PTSD, or depression when controlling for background variables such as age and kinship. On the trait AMT, however, a loss-related selective memory bias was positively associated with symptoms of complicated grief, PTSD, and depression, but only for specific memory responses.

Brief summary. The studies reviewed above generally show that overgeneral memory is a predictor and risk factor (rather than an outcome) for developing PTSD after trauma (see also Williams et al., 2007, for a review of overgeneral memory in emotional disorders). In addition, overgeneral memory may be viewed as a maintaining factor, serving an avoidant function (Williams, 2006), which could prevent emotional processing of the trauma. In regard to selective memory bias, the correlational evidence indicates that an explicit (but not implicit) selective memory bias related to the traumatic event is indeed present in PTSD. It is plausible that such a bias maintains the disorder by keeping the trauma memory active (e.g., Ehlers and Clark's model for a suggestion on how this could result in a feeling of 'current threat') and by influencing how individuals experience other events – past, present, or future – in their lives (see, e.g., the concept of event centrality in trauma formulated by Berntsen and Rubin, 2007). Finally, not much is known about the interplay between overgeneral memory and selective memory bias, and clearly more research is needed on how these biases may interact.

Modification of overgeneral memory and (explicit) selective memory bias could aid in understanding the causality of these biases in (the development of) PTSD symptoms, and potentially be a useful aim for interventions.

Modification of cognitive biases in PTSD

Brief introduction to Cognitive Bias Modification (CBM)

CBM techniques have their origin in the field of experimental psychopathology research (Koster et al., 2009; Woud & Becker, 2014). Their development was motivated by assumptions that cognitive biases causally contribute to emotional disorders. Therefore, computer paradigms that had initially been used to assess cognitive biases were transformed into training paradigms. During such training, participants are exposed to an experimentally induced contingency between the disorder-relevant stimulus and a response, aiming at modifying participants' information-processing style via learning of the trained contingency (Koster et al., 2009). To illustrate, patients suffering from a social phobia can be trained to endorse more positive than negative interpretations following an ambiguous situation, or to pay more attention towards smiling faces than angry faces. According to MacLeod and Mathews (2012), CBM research is characterized by three main targets. First, CBM procedures can be used to further investigate the causal nature of cognitive biases. Second, the manipulation of cognitive biases makes it possible to examine their underlying mechanisms. Third, CBM has the potential to become an instrument of clinical value, from a therapeutic and preventative perspective. All three targets are highly relevant in the context of posttraumatic stress. Further, there is clear evidence that cognitive biases are correlated with and / or predictive of trauma-related symptomatology, which is a necessary prerequisite for research on CBM. Hence, this motivated the present systematic

literature search, which aims to give a first systematic overview of the current state of scientific knowledge within CBM approaches in (analog) posttraumatic stress.

Procedure

Literature search. The systematic review was based on recommendation of the COCRAINE manual for systematic reviews and the PRISMA guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009). The literature search was conducted in October 2015 with the following databases / search engines: PubMed and Ebsco Host (included databases: PsycINFO, PsycARTICLES, PSYNDEX: Literature and Audiovisual Media with PSYNDEX Tests). We conducted one search per cognitive bias. The keywords were as follows: i. Attention: [(Trauma* OR event*) AND ("attention* bias") AND ("cognitive bias modification" OR "bias modification" OR "bias training" OR "training" OR "modification")]; ii. Appraisal and Interpretation: [(Trauma* OR event*) AND ("interpretation bias" OR "interpretive bias" OR "appraisal bias" OR "dysfunctional appraisal" OR "negative appraisal" OR "maladaptive appraisal" OR "maladaptive beliefs" OR "reappraisal") AND ("cognitive bias modification" OR "bias modification" OR "bias training" OR "training" OR "modification")]; iii. Memory: [(Trauma* OR event*) AND (memory*) AND ("cognitive bias modification" OR "bias modification" OR "bias training" OR "training" OR "modification")].

Selection of studies: The literature searches resulted in 30 potential articles for attention, 54 for appraisal and interpretation, and 2082 for memory (for a more detailed overview, see Figure 1). For each bias, titles were screened first. Next, potentially eligible abstracts were inspected. From these abstracts, articles including potentially relevant studies were selected, and the corresponding full texts were reviewed. We applied the following criteria for the review process:

Sample: Adult patients who experienced a traumatic event (with or without PTSD diagnosis) according to the Diagnostic and Statistical Manual of Mental Disorders-IV-TR (2000). Comorbidity, except for intellectual disability, was not an exclusion criterion. Studies that included psychologically healthy adults who underwent an analog trauma induction were also included.

Trauma event: PTSD patients experienced one or more traumatic event(s). There were no restrictions concerning the type, duration, or time point of the trauma. Studies that used analog methodologies were also eligible. The analog trauma induction employed a well-established method, e.g., the trauma film paradigm (James et al., 2016; Krans, Woud, Näring, Becker, & Holmes, 2010) or highly negative pictures that proved to elicit analog trauma symptoms (e.g., intrusions).

Design: The studies contained at least one group in which one of the cognitive biases was manipulated. Pilot studies and single case series were also considered.

CBM method: Cognitive biases were directly manipulated via the training. Methods that involved an indirect bias manipulation (e.g., through working memory training) were not included.

Stimuli in CBM training: Training stimuli included PTSD-relevant stimuli (e.g., threatening word/pictorial cues, ambiguous PTSD-related sentences) and targeted PTSD-relevant cognitive processing (e.g., biases in memory specificity).

PTSD-related symptomatology as outcomes: Studies assessed PTSD-related symptomatology as described in the DSM-IV-TR (2000) or put forward in cognitive model of PTSD (e.g., Ehlers & Clark, 2000), including change in PTSD diagnosis, change in targeted bias, intrusion frequency and/or distress, PTSD-related thoughts and cognitions, avoidance, or

hyperarousal. Symptoms were assessed using (clinical) self-report, behavioral and/or physiological measures applied at least once after CBM training.

Additional interventions: Studies that included interventions other than CBM were eligible. Studies that included patients who were about to receive treatment were also eligible. Although specific information was not provided, interventions were assumed to include treatment as usual for PTSD (e.g., prolonged exposure, cognitive approaches). As we did not conduct a meta-analysis/did not calculate CBM-related effect sizes, this approach is appropriate.

These criteria resulted in a final inclusion of a total of five CBM articles for attention, three for appraisal and interpretation, and one for memory (for a brief overview and summary of the studies' design, stimuli, main outcomes, see Appendix A).

Results

Attention Bias Modification

Five published studies tested the efficacy of Attention Bias Modification (ABM) using both healthy controls and patients with a formal diagnosis of PTSD. In a first ABM study, Verwoerd, Wessel, & de Jong (2012) presented healthy undergraduates with a trauma film as an experimental analog of real-life trauma (for reviews, see James et al., 2016; Krans et al., 2009). Stills from the trauma film were presented as trauma-relevant cues in a modified spatial cuing task, together with a series of neutral control images. For participants in the ABM-training condition, all invalid trials (i.e., single cue followed by target letter on the opposite side of the screen) consisted of trauma cues whilst all valid trials (cue and following target letter share their position on the screen) consisted of neutral landscape cues. This was intended to train participants to systematically disengage from trauma reminders. Participants allocated to the

control condition were presented with a standard version of the task with trauma cues and landscape images each appearing 50% in valid and 50% in invalid trials. A single target RSVP task was used as manipulation check. Indices of attention bias were inferred by comparing errors and reaction times on control trials with trials where a trauma cue was presented as a distracter. Effects of ABM training on the symptom of intrusive memories were measured using a 3-day intrusion diary. The results indicated that in line with expectations, participants who received ABM training showed reduced interference from trauma cues on the RSVP task and reported a lower number of film-related intrusions in the diary.

In an RCT conducted by Schoorl, Putman, and van Der Does (2013), 72 PTSD patients were presented with stimuli for dot probe training consisting of a series of general trauma-related cues and neutral picture cues. In the ABM version of the task, targets were systematically presented at the position of the screen previously occupied by the neutral cue, while no systematic connection between cue and target position was present in the control version. Before and after eight home-based sessions of attention training and at a 3-week follow up, attentional bias was assessed with a standard version of the dot probe task. Although PTSD symptom levels generally decreased over time, no differences were observed between patients receiving ABM or control training. Furthermore, no effect of ABM or control training was observed on attentional bias.

In a small follow up case series study using six veterans with PTSD as participants (Schoorl, Putman, Mooren, Van Der Werf, & Van Der Does, 2014), each participant was presented with a dot probe task containing individualized trauma-related words paired with neutral control words. Symptoms and attentional bias were assessed at three weekly time points prior to the ABM intervention that took place over a 2-week period. One week after the training

session(s) were completed, a follow up assessment took place. The results showed that application of this modified training paradigm with individualized trauma words did not change the main conclusion of no ABM-specific training effects from the earlier RCT.

Kuckertz et al. (2014) explored whether ABM training could be effective as adjunctive intervention to treatment in a real world setting. Participants were active-duty military members with PTSD receiving treatment at a community inpatient health unit. Assessment and ABM training versions of the dot probe paradigm consisted of general threat-neutral word pairs positioned on top and below a fixation cross. Results showed an effect of ABM training on PTSD symptom reduction on top of a general decrease in symptoms. Further, the effect of the ABM intervention was moderated by baseline levels of attentional bias with initial threat avoidance resulting in larger training effects. However, no evidence was found for a training-induced reduction in attentional bias from baseline to follow up assessment.

In a fifth study, by Khanna et al. (2015), of an original sample of 27 combat veterans with PTSD, 17 veterans completed a total of eight sessions of dot probe ABM (n = 8) or an control training condition (n = 9) within one month. For attention training, angry-neutral face pairs were presented simultaneously one above the other for a total of 160 trials. Pre- and post-training assessment of attentional bias was measured by an emotional Stroop paradigm (EST) including combat-related- negative-, and neutral words. Results of the effect of attention training on combat-related EST performance showed that somewhat unexpectedly and in contrast to some of the findings reported above, positive training effects were only observed in the control training condition. That is, reduced Stroop interference (i.e., attentional bias) for combat-related words (but not for negative and neutral words) from pre- to post-training was restricted to the control condition; no difference in combat-related Stroop performance from pre- to post training

assessment was observed in the ABM condition. The study also included pre- and post-training measures of PTSD (Clinician-Administered PTSD Scale; CAPS). In line with results reported above (e.g., Schoorl et al., 2013), there was a general decrease in symptoms from pre- to post training, which was independent of training condition.

Attention Bias Modification: Summary and conclusions

ABM as applied in the context of trauma shows a wide diversity of methods and participants, respectively. The first ABM study took advantage of the lab-based method of the trauma-film paradigm, providing rigid control over both the stressful event and the trauma cues (Verwoerd et al., 2012). That is, the film stills directly reflected the content of the earlier experience. Results showed that the ABM training was effective: Both attentional bias and intrusions were manipulated in a training congruent manner. However, none of the four studies involving PTSD patients could deliver evidence for the assumed causal role of attentional biases: a decrease in symptoms preceded by a training-induced decrease in attentional bias. Furthermore, against expectations control training resulted in a reduction in attentional bias (i.e., Khanna et al., 2015), together with an observed decrease in symptoms in both the ABM and control training (see Khanna et al., 2015; Schoorl et al., 2013, 2014). Especially the latter finding is not in line with the causal hypothesis, suggesting that researchers are still groping in the dark regarding the exact working mechanisms of ABM. To test whether the overall reduction in symptoms as observed in the clinical ABM studies is not simply the result of the passage of time, future studies should include no-task control groups to further explore the underlying mechanism of both ABM and control training. Further, results of Schoorl et al. (2013) showed that the symptom reduction in their sample was unrelated to the ABM training, rendering it rather

unlikely that the observed symptom change was a result of the ABM procedure. The observation that the ABM training did not affect attentional bias further supports this conclusion.

Based on these mixed findings so far, it is important that before conducting new time consuming and expensive RCT's, research should take advantage of validated lab-based methodologies (e.g., the trauma film paradigm) to explore ABM training in the context of trauma in a controlled and thorough manner. Such studies may compare ABM training with active and passive "wait list" control conditions, and compare the effectiveness of training stimuli directly related to the earlier (analog) trauma with training cues possessing general negative affect (e.g., angry or disgusting faces. One important direction for future research consists of developing improved training configurations for existing ABM tasks. For instance, using an analog design with non-selected participants, Clarke et al. (2017) showed that ABM training under working memory load increased the magnitude of change in attention bias when compared with a training configuration where this working memory load was omitted. Additionally, researchers should also take into account reliability issues that have been reported for the dot probe assessment task which is commonly used to measure direct effects of ABM on attention bias. That is, psychometric studies have found split-half reliability scores close to zero for attention bias indices derived from the dot probe task (i.e., incongruent trials minus congruent trials) (e.g., Kappenman, Farrens, Luck,, & Proudfit, 2014). Some studies have put forward recommendations for improved assessment of attention bias with this task that might also be important for ABM training studies (e.g., Price et al., 2014). Other research has suggested alternative approaches within dot probe analyses such as indices of attention bias variability (ABV) reflecting dynamic fluctuations of attention alternating toward and away from threat, which may occurs in participants with PTSD relative to healthy comparison subjects (e.g.,

Iacoviello et al., 2014; Naim et al., 2015). Unfortunately, a more recent psychometric evaluation of these new indices revealed similar reliability issues also implicating construct validity of ABV as it is not yet clear what these new dot probe data-derived indices actually measure (see Kruijt, Field, & Fox, 2017 for a more detailed discussion). Finally, taken into account the above mentioned reliability issues with the dot probe assessment task, an important new direction in the field of ABM will be the development of new training paradigms such as reported by Notebaert, Clark, Grafton, & Macleod (2015). This newer ABM training that consisted of matching judgements of happy and angry faces in a person identity matching task succeeded in modifying attentional bias, and had a consequent impact on emotional reactivity to an analogue laboratory stressor.

Interpretation Bias Modification

We found three papers addressing cognitive bias modification of dysfunctional appraisals and interpretations (Schartau, Dalgleish, & Dunn, 2009; Woud, Holmes, Postma, Dalgleish, & Mackintosh, 2012; Woud, Postma, Holmes, & Mackintosh, 2013). The studies by Schartau et al. (2009) trained functional appraisals related to "broad interpretation rules" (p. 16), e.g., "Bad things happen: bad things happen in the world, and I need to put them behind me and move on". All studies included healthy participants, and used both non-autobiographical (studies 1-3) and autobiographical distressing stimuli (study 4). Study 1 included an appraisal group (n = 21) and a control group (n = 20). While watching a distressing movie, the former group applied the four appraisal themes, whereas the latter group was instructed to feel the emotions elicited by the movies without trying to regulate them. Compared to the control group, the appraisal group showed reduced levels of self-reported negative emotional and psychophysiological responses. Study 2 was set up as Study 1 (appraisal group: n = 16, control

group: n = 16), however, Study 2 was spread out over two days. Here, results showed again that appraisal can reduce emotional negativity. Study 3 contained three groups, i.e., an appraisal group (n = 16), a detachment group which was instructed to think of technical issues related to the distressing movies (n = 16), and a control group similar to those used before (n = 16). Results showed that, compared to both the control groups, the appraisal group showed reduced emotional negativity. Study 4 used a distressing life event as analog trauma (appraisal group: n = 15, control group: n = 15) and again found reduced emotional negativity and intrusions in the appraisal compared to the control group.

The study by Woud et al. (2012) applied a Cognitive Bias Modification – Appraisal (CBM-App) training after healthy participants were exposed to trauma films (N = 74). During CBM-App, participants were presented with ambiguous scenarios that ended in a to-be-completed word fragment which participants had to complete. This then produced an outcome which was consistent with either a functional (positive CBM-App, n = 37) or dysfunctional appraisal (negative CBM-App, n = 37) of the ambiguous scenario. Results showed that those trained positively appraised novel ambiguous, trauma-related scenarios more functionally than those trained negatively. Most importantly, those trained positively, compared to those trained negatively, reported fewer intrusions of the films. In a second study by Woud et al. (2013), participants first completed the CBM-App training and were then exposed to the trauma films (positive CBM: *n* = 22, negative CBM: *n* = 25). Results replicated earlier findings, i.e., those trained positively, compared to those trained negatively, reported less distress arising from their intrusive memories of the trauma film during the subsequent week.

Interpretation Bias Modification: Summary and conclusions

In the context of interpretation CBM, Schartau et al. (2009) and Woud et al. (2012, 2013) demonstrated that training functional, trauma-related appraisals before, during, or after an analog traumatic event induced training-congruent appraisal styles. Furthermore, training functional appraisals led to a reduction in intrusion frequency and distress, reduced levels of negative emotional responses, and reduced (analog) trauma-related symptomatology. Finding positive results such as these across six different studies provides promising evidence for the effectiveness of CBM training manipulating appraisals, albeit amongst healthy participants undergoing a stressful experience. Interestingly, these studies have taken two slightly different approaches to operationalizing the appraisals. The studies by Schartau et al. (2009) used appraisal rules (i.e., themes) and trained participants to be better able to see the 'bigger picture' surrounding the negative event by adopting a broader perspective that also allowed for positive information. In contrast, Woud et al. (2012, 2013) trained specific appraisals that aimed to induce a functional interpretation of the analog trauma and its consequences. Both kinds of appraisal training affected important PTSD-relevant symptoms such as intrusions. Hence, it would be interesting to directly compare both training variants in order to test whether they are in fact targeting the same processes and to examine any potential differences in their effects.

Despite these positive findings, the results' generalization is still limited as all studies used analog trauma inductions. Hence, the effects of interpretation CBM training in at-risk or clinical groups, for example, remains unknown, so conducting carefully designed studies in clinical settings could be a useful next step. The research to date also leaves many questions unanswered about the underlying mechanisms of this CBM procedure. While the studies have focused on reduction in intrusions and intrusion-linked distress, the training of more functional appraisals may also influence other PTSD maintenance factors such as avoidance, which

warrants investigation in future studies. Finally, as put forward in the section on ABM, studies including neutral control conditions are needed. For example, Woud et al. used a positive and a negative training condition, leaving it unclear whether there was in fact an induced effect of both positive and negative training, or of just one of these training conditions relative to the other.

Memory Bias Modification

To date, only one memory specificity training (MEST) has been published to target memory bias in PTSD. MEST (Raes, Williams, & Hermans, 2009) involves four one-hour weekly group sessions where participants are trained to recall specific memories in response to different cue words, and to elaborate on these by producing as much detail as possible. Between sessions, participants are given homework assignments to further train specific recall. Initially, the focus is set on positive and neutral memories, but later on negative memories are included as well. In the final session, participants are trained to become aware of the moment when their thinking becomes more general. MEST has been shown to increase memory specificity in depression (Raes et al., 2009) and some studies have found positive effects on depressive symptoms in the longer term (Neshat-Doost et al., 2013). Autobiographical memory training protocols had also previously been shown to increase memory specificity in other patient groups, e.g. schizophrenia (Blairy et al., 2008).

A pilot study tested the effect of MEST in a small sample of Iranian war veterans with PTSD. These were randomly allocated to either MEST (n = 12) or a control condition (n = 12) without any training (Moradi et al., 2014). Overgeneral memory was assessed with the AMT, and PTSD symptoms and levels of depression were assessed. Assessments were conducted before and after MEST and at 3-month follow-up. Participants in the MEST condition recalled a

higher number of specific memories on the AMT compared to the control group both after the training and at follow-up, even when controlling for PTSD and depression symptoms. Further, also when controlling for clinical symptoms, participants receiving the MEST became more specific in their memory after the training compared to baseline, and remained more specific at follow-up, whereas participants in the control condition did not change in memory specificity over time. The results for PTSD symptoms followed the same pattern. Looking at the PTSD symptom clusters, this pattern was found for intrusions and avoidance, but not hyperarousal. No effects of MEST were found on the number of war-related memories that were produced on the AMT. The authors noted that exposure to trauma memories during assessment and training may have contributed to the reduction in PTSD symptoms. Further, participants were still in the clinical range after MEST based on their PTSD scores, suggesting that MEST is not sufficient as a stand-alone therapeutic intervention to recover from PTSD.

Memory Bias Modification: Summary and conclusions

To date, the MEST as applied by Moradi et al. (2014) is the only systematic training that targets overgeneral memory bias in PTSD. Results appear promising. The format could be suitable for computerized and self-guided administration, which aligns with the idea of a low-threshold CBM format. Yet, there are still several obstacles to overcome. Moradi at al.'s study was a pilot study with a small sample and the MEST group still showed clinically significant symptoms after the training. The participants were male Iranian war veterans, which limits generalizability of the findings to other PTSD groups and females. The control group received no training, which leaves open the possibility that some kind of sham training could have led to similar results as the MEST. Hence, further studies in larger samples are needed to check the validity and increase efficacy of MEST in modifying overgeneral memory in PTSD.

MEST did not appear to be an effective training to target selective memory bias. That is, there was no effect of MEST on the number of war-related memories that were recalled on the AMT. In fact, to date no effective CBM procedures for selective memory bias have been developed or published. Therefore, there is need for a CBM method to systematically train the recall (and thereby modulate the accessibility) of trauma-related versus other (non-traumatic or threatening) information. One promising candidate may be competitive memory training (COMET; e.g., Korrelboom, Maarsingh, & Huijbrechts, 2012). This training targets negative self-esteem based on a counter conditioning procedure using selective recall. Trainees are instructed to vividly imagine positive autobiographical memories that are incongruent to their low self-esteem. The assumption is that the positive self-representations that are reflected in the memories then become more accessible and thereby associated with conditioned stimuli that previously triggered negative self-representations (i.e., counter conditioning). The COMET training is similar to MEST in that it trains people to recall the desired memories (more positive, or more specific, respectively), but in contrast to MEST, it was not designed as a memory training. To our knowledge, no study has been published on the effect of COMET on selective recall bias in PTSD, but this may be worth investigating in the future. Finally, rather than focusing on improving recall of specific or non-trauma memories, it could be worthwhile focusing on the opposite. Mechanisms of forgetting, such as retrieval-induced forgetting, could be explored for CBM potential to train memory bias in PTSD.

Modification of cognitive biases in PTSD: Summary and research agenda

Summary

Cognitive Bias Modification (CBM) techniques are a very recent and potentially promising development in the field of experimental psychopathology and clinical psychology. During the past few years, a growing body of CBM research has begun to emerge in the field of (analog) posttraumatic stress. The previous paragraphs provided a systematic overview of the state of scientific knowledge from this research. The overall findings of the reviewed CBM literature can be summarized as follows. For attention bias modification, the analog study by Verwoerd et al. (2012) showed promising results. Attention bias modification training versus control training resulted in fewer intrusions of a trauma film and reduced levels of attentional bias. However, clinical findings are less clear. For example, Kuckertz et al. (2014) found an effect of attention training on PTSD symptoms in a PTSD sample, whereas Schoorl and colleagues (2013, 2014) reported a reduction in PTSD-related symptomatology which was unrelated to CBM training condition. Furthermore, in both studies, CBM training did not affect attentional bias. For interpretation bias modification, results showed a consistent pattern across all studies: CBM interpretation training successfully induced training-congruent appraisal styles (Woud et al., 2012, 2013) and lead to a reduction in intrusion frequency and distress, reduced levels of negative emotional responses, and trauma-related symptomatology (Schartau et al., 2009, Woud et al.). However, all these studies used analog trauma inductions. For memory bias modification, only one training study with PTSD patients was identified (Moradi et al., 2014). Their Memory Specificity Training (MEST) provided promising results by showing that the MEST group reported a higher number of specific memories post-training and at 3 month follow-up, compared to baseline levels as well as a control group.

To summarize, all three CBM procedures generally showed that cognitive biases can be manipulated by means of CBM and that this has an effect on (analog) trauma symptoms.

However, to date, the overall findings do not appear to present a clear unified picture. Given that the field of CBM is still very young, this can be expected. Nevertheless, it highlights current challenges for the research field. For example, interpretation bias CBM seems more effective than attention bias procedures. Regarding the latter, most studies applied the dot probe task as a training procedure. However, studies differed in terms of how exactly they operationalized the training, for example in the type of stimuli, or the number of trials, and such subtle variations might have an impact on the effectiveness of the training procedure. Further, all analog experimental studies to date provided the expected results. In contrast, clinical results were less straightforward. The fact that clinical samples are more heterogeneous than healthy samples could be a possible explanation. Another possibility is that analog studies with weak results are more difficult to publish than clinical studies with weak results. For the moment, these remaining issues are a matter of empirical scrutiny.

Research agenda

The following section aims to provide a research agenda for CBM research in posttraumatic stress. The first part considers the current state of research through the lens of the broader CBM field and how this can be applied or improved for PTSD. The second part takes the clinical picture of PTSD as a starting point and considers how CBM could be helpful in targeting thus far unaddressed issues or symptoms in PTSD. All suggestions partly emerge from our evaluation of the current state of research on CBM in PTSD; however, we also provide some more general suggestions.

Suggestions from considering CBM as a research method. Our suggestions for this section emerge from our evaluation of the present literature review and concern CBM as a research method in PTSD. However, we also include suggestions from recent developments in the

general CBM field. The first suggestion concern the difference between bias change and symptom change. Two issues are particularly important: First, before any change in PTSD-related symptomatology can be expected, a change in the targeted cognitive bias needs to be established, and to do so, a manipulation check needs to be included (Clarke, Notebaert, & MacLeod, 2014). Five out of the 13 studies that we reviewed included a pre- and post-training bias assessment in order to test the effect of the CBM training on the intended bias and thereby included the required manipulation check (Moradi et al., 2014; Kannah et al., 2015; Kuckertz et al., 2014; Schoorl et al., 2013, 2014). The Moradi et al. (2014) study indeed showed the expected change, i.e., more specific memories in the MEST group compared to baseline and to a control group. However, the other studies failed to demonstrate training-congruent bias changes. The studies by Woud et al. (2012, 2013) only assessed cognitive biases post-training, whereas Schartau et al. (2009) did not include a bias assessment at all. Therefore, future research should systematically include a pre-post manipulation check as only then changes in PTSD symptomatology can be shown to be related to the training. Further, validity between measures is an important issue. Manipulation checks are used to test the training's success, and the operationalization of these manipulation checks is often closely matched to the training's operationalization. However, finding the expected result pattern on the manipulation check task does not mean that the targeted, underlying processes have also been changed (e.g., the MEST might train improvements in the AMT but does it really change specificity?). Hence, studies may need more distinct training and outcome measures in order to examine this important issue more thoroughly. Another important point is related to the inclusion of a mediation analysis. The finding that a change in bias is accompanied by a change in symptoms does not imply that the bias change is related to symptom change. Hence, mediation analyses are needed to test this.

Illustrating this point, Schoorl et al. (2013) was the only study conducting such an analysis. However, results showed that the symptom reduction in their sample was unrelated to the CBM training. As such, future research should include mediation analyses in order to confirm that symptom change is indeed related to the theoretically proposed cognitive change. Another recommendation for follow-up research is related to disorder specificity. That is, not all studies used a clinical control group or employed disorder unspecific stimulus material. Hence, if CBM indeed changes disorder specific, dysfunctional cognitive processing, both these issues have to be taken into account when designing a study. On the other hand, however, it would be also of crucial interest to test CBM's potential from a transdiagnostic perspective.

A further suggestion is to include outcome measures that go beyond self-report. Almost all of the present CBM studies relied on self-report measures, which are characterized by a number of well-known disadvantages, i.e., self-report measures may not measure the fundamental characteristics underlying PTSD symptoms (e.g., uncontrollability and intrusive nature of intrusions) and are sensitive to demand biases. Hence, self-report measures should be supplemented with more objective measures. Schartau et al. (2009) is the only study that included a more objective outcome measure and showed that the appraisal training had an effect on heart rate and galvanic skin response. Given that PTSD is characterized by physiological reactions that indicate heightened arousal, adding physiological markers would truly broaden the spectrum of CBM effects. In line with this is another important issue. As put forward by Hertel and Mathews (2011), outcome measures are needed that show robust far-transfer effects. That is, it is essential to show that CBM effects also transfer to different types of contexts and stimuli.

Furthermore, it is important to study the interaction between the different cognitive biases. In the depression and social anxiety literature a more holistic approach has been taken with the combined cognitive bias hypothesis (e.g., Everaert, Koster, & Derakshan, 2012; Hirsch, Clark, & Mathews, 2006). According to this hypothesis, cognitive biases interact and influence each other). From a CBM perspective it would be important to test whether a change in one cognitive bias also leads to a corresponding change in another cognitive bias. However, this would require a clear theoretical framework in which to formulate these interactive hypotheses. The cognitive model by Ehlers and Clark (2000) could provide a useful starting point here. To illustrate, this models postulates that dysfunctional appraisals that deem the experience of intrusive memories as dangerous could result in overaccessibility of trauma-related memories (selective recall) through thought suppression efforts. Thus, properly designed interpretation bias modification training should affect selective memory bias. Another starting point could be the CaRFAX model (Willliams, 2006). It proposes that overgeneral memory, at least in depression, can result from attention during a memory search being 'captured' by concern-related autobiographical information which then triggers ruminative processes. This terminates the memory search prematurely, resulting in the recall of a non-specific memory. This suggests that a stronger threat-related attentional bias is related to more overgeneral memory, which gives rise to the hypothesis that properly designed attention bias modification training could affect overgeneral memory bias.

Finally, as the number of CBM studies in PTSD is still relatively small, we encourage additional analog and clinical research to further advance our understanding of the potential of CBM in posttraumatic stress. Analog studies should examine the mechanisms underlying CBM via experimental approaches, including systematic research on the effects of different types of

CBM procedures on cognitive, behavioral, and physiological outcome measures in the different biases. Further, potential moderators and mediators of the training's effects should be examined. Clinical studies should involve clinical trials, preferably RCTs, to test the translational potential of CBM, whether in adjunct to existing treatments, or as a stand-alone intervention "module".

Suggestions from considering the particular features of PTSD. Our suggestions for this section emerges from the perspective of PTSD, i.e., we take the particular clinical characteristics of PTSD as a starting point for follow-up research that could increase the relevance and effectiveness of CBM for PTSD specifically. The emergence of PTSD is associated with the occurrence of a traumatic event at a specific point in time, but PTSD cannot be formally diagnosed until one month after the trauma. This means that intervention research in PTSD can focus on prevention of the disorder (in the direct aftermath of trauma, or even before the trauma in case of at-risk groups) as well as on the treatment of PTSD once it becomes chronic. The clinical studies in the present review (Moradi et al., 2014; Kannah et al., 2015; Kuckertz et al., 2014; Schoorl et al., 2013, 2014) applied CBM as a potential therapeutic instrument after the PTSD diagnosis had been confirmed. In addition, CBM may also aid in the primary prevention (in at-risk groups such as soldiers, police, or fire fighters) and secondary prevention (in the first month after trauma) of PTSD and PTSD symptoms. The analog studies by Schartau et al. (2009) and Woud et al. (2012, 2013) could be regarded as first steps in this direction. Woud et al. (2012, 2013) applied the CBM training before and directly after participants were exposed to a trauma film. Results showed that participants who were trained positively reported fewer intrusions and intrusion distress compared to participants who were trained negatively. The study by Schartau et al. (2009) required participants to apply the instructed functional appraisals while watching a trauma film / thinking back to a personal

negative event. This training was also successful, showing that functional appraisal lead to reduced emotional negativity. Hence, these promising analog studies provide a starting point for investigating CBM as a potential primary and secondary intervention for people who will be likely to experience or have just experienced a real-life traumatic event.

PTSD is also characterized by high comorbidity (e.g., Brady, Killeen, Brewerton, & Lucerini, 2000). Hence, it will be useful to investigate whether CBM generalizes to a wider range of symptoms, especially symptoms of depression as there is a large overlap in the symptoms of PTSD and depression. The study by Kuckertz et al. (2014) was the only study that examined CBM effects on symptoms other than those of posttraumatic stress and found that the attention bias modification training also reduced depressive symptoms.

A final suggestion concerns the nature of the traumatic experience. PTSD patients highly differ in the type of trauma. For example, some patients experienced multiple traumas over a long period of time, whereas others experienced one single traumatic event. It is unknown yet whether different types or severities of trauma are associated with different patterns of cognitive biases. If so, the relevance of the different training types may vary according to trauma characteristics. For example, interpretation-focused CBM could potentially be more suitable for chronic interpersonal traumas that are characterized by negative self-related cognitions. This remains an empirical question for future research, however, the basic observation that PTSD is heterogeneous means that care must be taken in generalizing results from a specific trauma population to PTSD more broadly. [1]

General conclusions

In this paper a systematic literature search was conducted to provide an overview of CBM in PTSD and analog trauma. CBM procedures can indeed modify cognitive biases and affect (analog) trauma symptoms. Specifically, interpretation CBM seems effective in analog samples, and overgeneral memory bias training proved preliminary success in a clinical PTSD sample. Studies of attentional bias provide more mixed results. Thus, the overall findings do not present a homogenous picture. This may be explained by differences in the type of population or variations in the CBM procedure. Hence, we sketched a research agenda which addressed the challenges for CBM. This includes systematic investigations of the change in the targeted cognitive bias and its relation to symptom change. Moreover, self-report measures should be complemented, e.g., by psychophysiological markers, and the interaction between the different cognitive biases should be examined in order to build a comprehensive framework of cognitive biases in PTSD. The potential of CBM as primary and secondary prevention intervention should be investigated in addition to a treatment add-on function, and (effects on) comorbid psychopathology. Finally, the type of trauma should be taken into account when designing future studies.

The current literature on CBM in PTSD provides preliminary evidence that cognitive biases causally contribute to trauma-relevant symptomatology. CBM also has the potential of providing specific interventions to target these biases in PTSD. Of course, additional research is needed to further advance our understanding of the causal role of these cognitive biases in posttraumatic stress and PTSD. Whether CBM approaches can be usefully integrated into existing frameworks for PTSD treatment and how best to do so remain questions for future research.

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Footnote

1. We would like thank the reviewers for the valuable suggestions for the research agenda.

PRISMA flow diagram of systematic literature search on attentional bias:

PRISMA flow diagram of systematic literature search on interpretation bias:

PRISMA flow diagram of systematic literature search on memory bias:

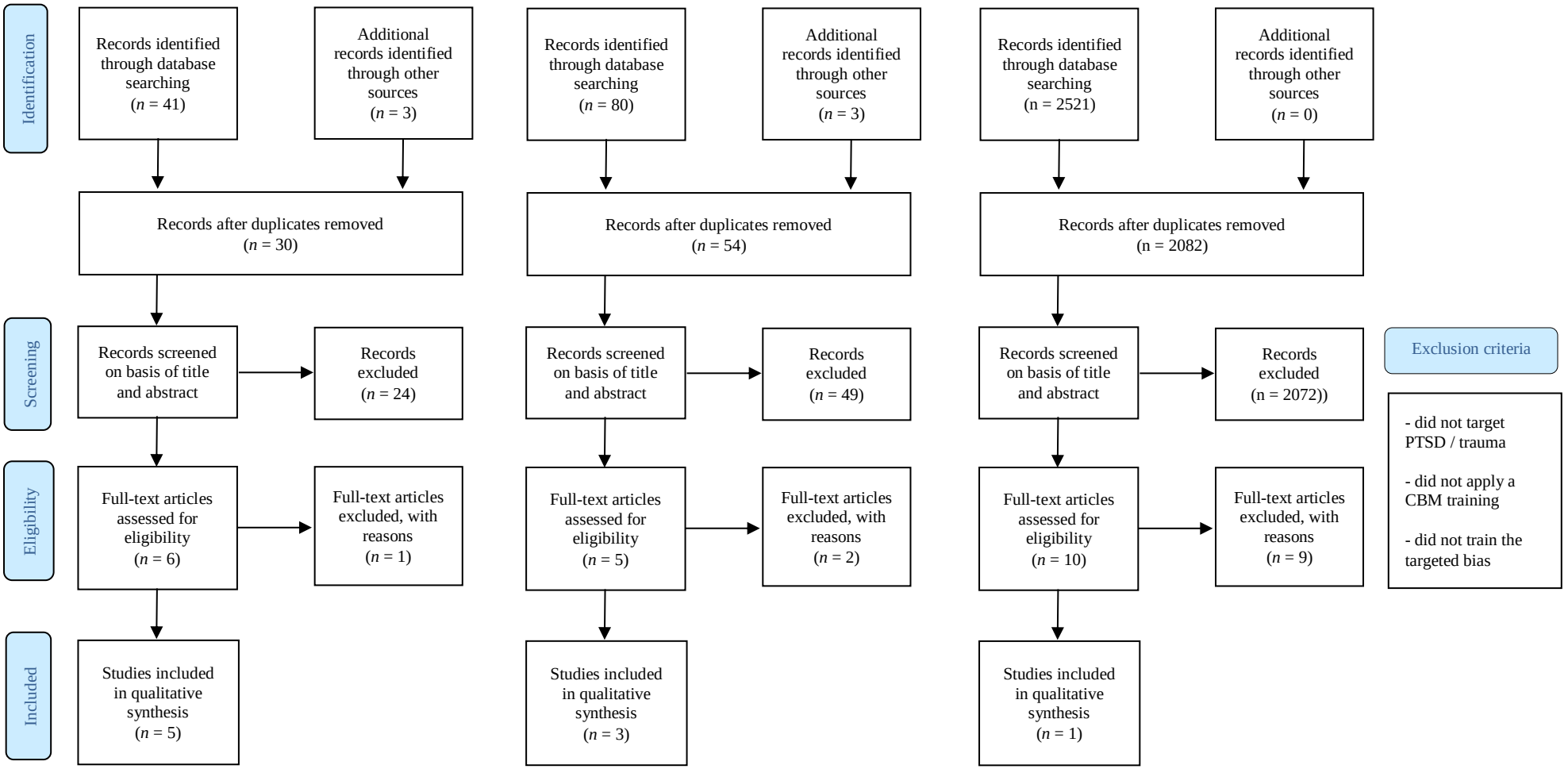

Figure 1
Overview systematic literature search per cognitive bias following the PRISMA Guidlines (see Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097).