Investigating new process-focused treatments for posttraumatic stress disorder : attentional bias modification and mindfulness-based cognitive therapy

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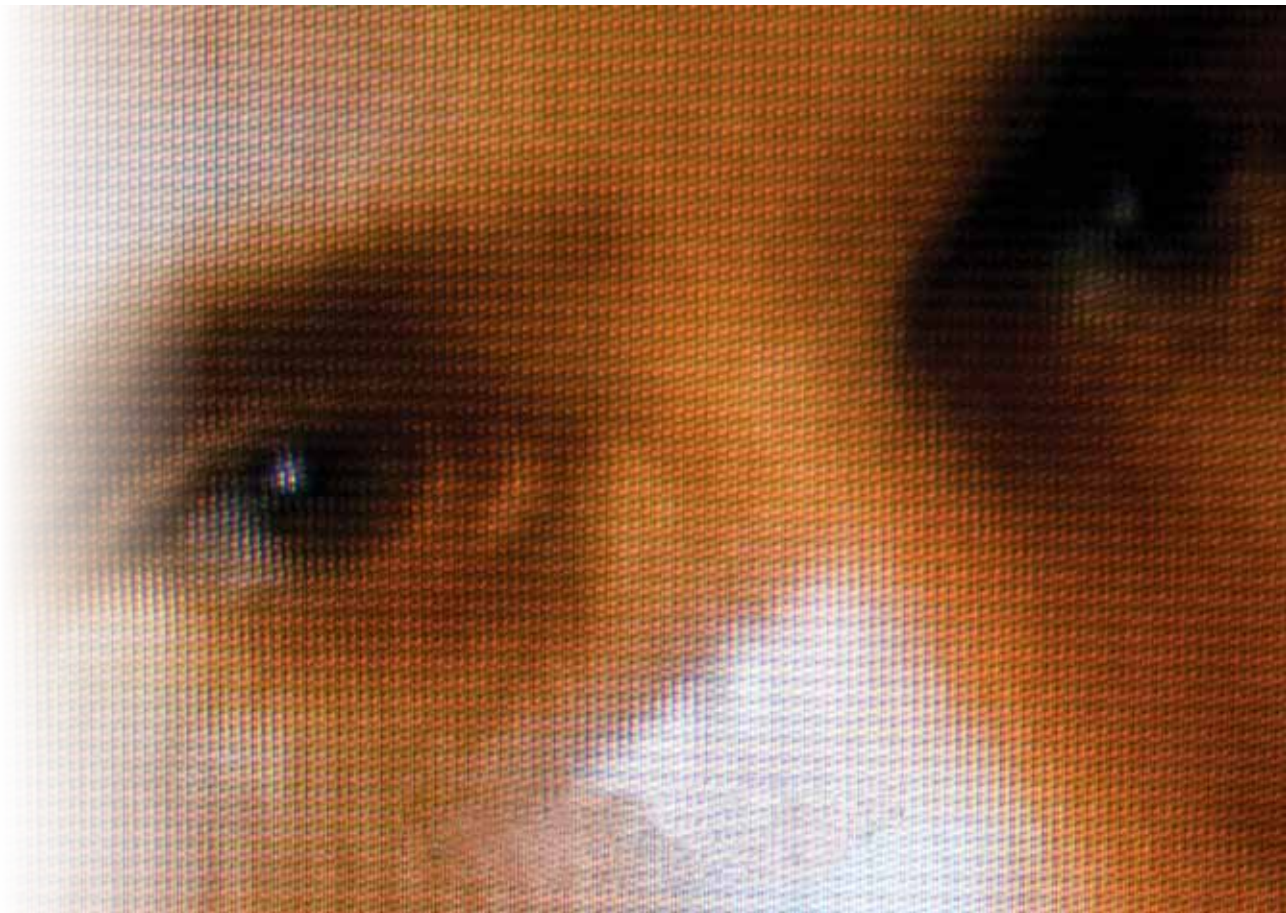
General discussion



General Discussion

Effect of ABM: RCT and case series

We tested the therapeutic effect of ABM in a large RCT in patients with PTSD. The effect of ABM on symptoms or on AB was not significantly larger than the effect in the control condition, which led us to conclude that the presently tested version of ABM is not effective in PTSD. One could argue that both conditions were effective, since the control condition may not have been neutral. The control condition – in fact an extended version of the assessment version of the Dot-probe test – is equivalent to training people at a 50/50 contingency. For individuals who have an attentional bias towards threat, this might work as a low-dose treatment. But in fact the effect sizes of the improvement in both conditions were even somewhat smaller than the effect sizes of pill-placebo in pharmacotherapy trials of chronic PTSD (Marshall, Beebe, Oldham, & Zaninelli, 2001; Davidson, Rothbaum, van der Kolk, Sikes, & Farfel, 2001; Brady et al., 2000).
Our findings are disappointing, since positive effects of ABM had been shown in GAD and SAD (Amir, Beard, Burns, & Bomyea, 2009a; Amir et al., 2009b; Schmidt, Richey, Buckner, & Timpano, 2009) and attentional bias to threat is also a feature of PTSD (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & Van IJzendoorn, 2007). Several explanations could account for these negative results, and will be discussed in detail further below.
However, just after we first analyzed the results of our RCT, Amir (2010) reported on two studies with positive effects of ABM in PTSD patients (male veterans) in a conference presentation. The preliminary outcomes of an open trial with 13 patients were presented, together with the results of another 13 patients participating in an RCT. ABM was individualized (self-selected stimuli) and verbal stimuli were used. On a PTSD self-report questionnaire, patients in the ABM condition demonstrated significant effects of the training, and patients in the control condition showed no response. In addition, a recent meta-analysis (Hakamata et al., 2010) suggested that ABM with verbal stimuli might outperform ABM with pictorial stimuli. We then decided to further investigate the hypothesis that individualized, verbal ABM would generate more positive clinical results in patients with PTSD (also male combat veterans). We tried to replicate the study of Amir in a case series design (N = 6). But again, we found no effect of ABM on any of the outcome measures (symptoms or AB).

The second research aim of our RCT was to investigate the tolerability and acceptability of ABM. Since 13.4% declined participation, we concluded that the acceptability of ABM was moderate. Regarding tolerability, the mean drop-out rate (25.2%) was comparable to drop-out rates in traditional treatments for PTSD (i.e. Cognitive Behavioral Therapy, CBT) (Schottenbauer et al., 2008). We had expected lower drop-out rates, since ABM is short and could be carried out at home. Also, the

attrition rates in the three reported clinical trials (Amir et al., 2009a; Amir et al., 2009b; Schmidt et al., 2009) ranged from 0-8%. However, in only one of these studies, a flowchart according to the Consolidated Standards of Reporting Trials (CONSORT) guidelines was presented (Amir et al., 2009b). Moreover, in all three studies participants were paid for their participation (Beard, 2011). It is therefore likely that attrition in our study is a realistic representation of the acceptability of ABM in the 'real world', when patients do not receive a financial incentive.

Possible explanations for the lack of effect of ABM

The large difference in outcomes is difficult to explain. In the three mentioned clinical trials on SAD and GAD effect sizes as large as 1.4 are reported, compared to an effect size of 0.4 for the placebo condition, a difference of 1.0. Our effect sizes were 0.66 (ABM) and 0.46 (control condition), a difference of only 0.2.

Methodological issues

The role of attentional bias in ABM

Our sample size is considerably larger than most studies, so lack of power is not a likely explanation. In our study, no overall AB at pre-treatment was observed. Reviewers of our paper indicated that this absence of AB explains the disappointing clinical results; when no attentional vigilance is present, ABM seems redundant.

Of course, we had expected to find AB in our sample. However, we aimed at evaluating the treatment as it is being advocated - for *any* patient with PTSD, not just for 'patients with PTSD who also have attentional bias'. For this reason, AB was not an inclusion criterion. Serotonergic dysfunction for example, is also never used as a criterion to start treatment with selective serotonin reuptake inhibitors (SSRIs). Furthermore, since we did not test our version of the DPT in a control group, we can not compare our results to healthy controls. Possibly a control group might have demonstrated AB towards neutral stimuli, which would indicate that AB in patients with PTSD is characterized by automatic avoidance of neutral stimuli.

Attentional bias modification is based on three assumptions; 1. particular patient groups have specific biases in their attention; 2. this bias can be modified by training; and 3. changing this bias will have an effect on symptoms. Each of these assumptions has been tested in previous research, including the assumption that patients with PTSD have an attentional bias to threat. Yet, since AB is always reported on group level (patients vs. controls), it cannot be concluded that every individual patient has a positive bias score to threat.

In addition, in only one of the previous clinical ABM studies, AB data at the start of the treatment were reported (Amir et al., 2009b) and the positive clinical results were reached despite the demonstrated lack of AB on group level. Furthermore, we performed a post-hoc analysis with patients with positive AB (> 5 ms, n = 46), but no effect of ABM was demonstrated in this subgroup.

Although extensive research has linked AB towards threat (vigilance) to anxiety and anxiety disorders (Williams, Mathews, & MacLeod, 1996; Bar-Haim et al., 2007), attentional *avoidance* is also reported in several studies, associated with specific time-intervals of the presented stimuli (Cisler & Koster, 2010). In line with the vigilance-avoidance theory (Mogg, Bradley, Miles, & Dixon, 2004), anxious individuals are thought to have a specific pattern of fast vigilance of threatening stimuli (i.e., within < 500 ms), followed by avoidance of threatening stimuli. However, several studies observed threat avoidance in anxiety with the same time-interval (500 ms) as used in our studies (e.g. Mansell, Clark, Ehlers, & Chen, 1999; Musa, Lepine, Clark, Mansell, & Ehlers, 2003; Chen, Ehlers, Clark, & Mansell, 2002; Pine et al., 2005, Monk et al., 2006, Putman, 2011).

Attentional bias in PTSD

Although the preponderance of evidence shows that PTSD is associated with automatic attention to threat (vigilance) (Williams et al., 1996, Bar-Haim et al., 2007), attentional avoidance has also been observed, for instance in maltreated children (Pine et al., 2005). Avoidance of angry and threatening faces was found to be related to a history of physical abuse and to PTSD symptoms. Moreover, experiential avoidance is one of the diagnostic criteria of PTSD (APA, 2000); PTSD is typically associated with attentional tendencies away from threatening stimuli.

Two studies used the DPT with pictorial stimuli in trauma victims (Elsesser, Sartory, & Tackenberg, 2004; Elsesser, Sartory, & Tackenberg, 2005). Although not all participants had PTSD, the mixed results (respectively avoidance and absence of AB) seem in line with our findings. Another study demonstrated that AB towards *positive* stimuli (i.e. happy faces) mediated the relationship between traumatic experiences and PTSD symptoms (avoidance) in adult survivors of childhood maltreatment with and without PTSD (Fani, Bradley-Davino, Ressler, & McClure-Tone, 2011).

However, a recent longitudinal study on risk factors associated with the development of PTSD, again identified attentional vigilance to threat during combat employment as a risk factor for PTSD development (Wald et al., 2013). The results also indicated that AB interacts with other risk factors, and that AB is differentially related to different phases in the development of PTSD.

Taken together, it seems that the direction of attentional bias depends strongly on various methodological variables (e.g., stimulus-type, cue-target delay) but the separate influence of these parameters has not been sufficiently investigated. In addition, it is very likely that AB interacts with other cognitive biases and risk factors. The relationship between AB and PTSD clearly is more complicated than formerly thought.

This seems in line with the results of a close inspection of the phenomenon of AB in PTSD as measured by the emotional Stroop task (EST) (Kimble, 2009). In 92% of the reviewed dissertations and in 56% of the publications in peer reviewed journals, the effect is not demonstrated, despite general consensus. It has been suggested that these results are due to the Stroop task and illustrate that more appropriate

experimental tasks (e.g., the Dot-probe Test) should be used to assess the relationship between PTSD and AB (Bardeen & Orcutt, 2011). However, it cannot be ruled out that publication bias is as strong for research with the DPT. A review on AB in PTSD as measured with the DPT including dissertation abstracts and peer reviewed journals is needed to clarify this issue.

Reliability of the Dot-probe Test

Another problem in ABM research is the lack of validated cognitive measures. For example; concerns have been raised on the reliability of the DPT (Schmuckle, 2005; Staugaard, 2009). In our case series (Schoorl, Putman, Mooren, Van Der Werff, & Van Der Does, 2013) the pattern of intra-individual change in AB as measured with the DPT also indicates problems with the test-retest validity. Improving reliability of widely used cognitive measures or developing new cognitive tasks that are first validated before dissemination seems mandatory (Mauer & Borkenau, 2007). Without such reliable measurements, any positive clinical outcomes of ABM can not be attributed to a change in AB.

ABM and the nature of anxiety disorders

The absence of therapeutic effects might fit with theoretical considerations that positive effects of ABM depend on the 'specifity' of the anxiety disorder (Reese, Mc Nally, Najmi, & Amir, 2010). Some anxiety disorders are more stimulus-driven (e.g., phobias, PTSD) than others (e.g., GAD, SAD). ABM might have more effect in 'general' anxiety disorders, characterized by ruminative symptoms, and not in 'specific' anxiety disorders, like phobias. In (non-clinical) spider-fearful individuals ABM reduced attentional bias only temporarily and anxiety was not reduced (Reese et al., 2010). However, rumination and worry are also important features of PTSD and function as a cognitive avoidance strategy (Ehlers & Steil, 1995; Bomyea, Risbrough, & Lang, 2012). Furthermore, posttraumatic anxiety is also strongly related to abstract ''general'' themes (e.g., 'anything bad can happen to me anytime'), in contrast with specific phobias.

About 70% of our PTSD patients also suffered from a depressive episode. This depression comorbidity is very common, but might account for the lack of positive results of ABM in PTSD. Studies in this area reported mixed results. AB in mood disorders has been demonstrated at later stages of information processing (e.g., 1500 ms) (see Mogg & Bradley, 2005, for a review). Recent outcomes of a study using a spatial cueing task found no difference in AB between trauma-exposed participants with and without PTSD and healthy controls, but a group effect was evident between depressed and non-depressed individuals (Hauschildt, Wittekind, Moritz, Kellner, & Jelinek, 2013). Moreover, null results of ABM in a small sample of patients with major depressive disorder (MDD) have been reported, and post-hoc analysis suggested that ABM can even be counterproductive in patients with severe depressive symptoms (Baert, De Raedt, Schacht, & Koster, 2010). Six different

versions of ABM for dysphoria were tested in a case series design and none of these versions had any consistent effect on AB (Kruijt, Putman, & Van Der Does, 2013).
However, in an influential meta-analysis, (Bar-Haim et al., 2007), it was concluded that ''whether or not participants with depression were included in the anxious group did not modulate the attentional bias effect''. In addition, in the ABM-study on GAD (Amir et al., 2009a) the positive effects of ABM treatment were not limited to anxiety but extended to depressive symptoms, implying that these symptoms might also be sensitive to attentional bias manipulation. Furthermore, comorbid MDD is not necessarily a reason for other PTSD therapies to fail; for example, no difference in effect of PTSD treatment (CBT) in patients with or without comorbid depression was observed (Tarrier, Sommerfield, Pilgrim, & Faragher, 2000).
New data may be available soon that hopefully clarify these matters. At clinicaltrials.gov, the main register where clinical trials are recorded before the onset to objectively evaluate the outcomes; two RCTs investigating ABM in combat veterans with PTSD were announced by Dr. Amir in 2008. Since preliminary findings were reportedly positive (Amir, 2010), we look forward to compare the designs and outcomes with our results.

Progression in ABM research

Another potential explanation for our null results can be that ABM only targets AB, whereas other forms of cognitive bias (e.g., interpretation bias) might also play a role in the development and maintenance of anxiety disorders (Hallion & Ruscio, 2011; Beard, 2011). This would be in line with research (Hirsch, Clark, & Mathews, 2006-Hallion) and theoretical models (e.g., Ouimet, Gawronski, & Dozois, 2009; Eysenck, Santos, Derakshan, & Calvo, 2007) that indicate that mood and anxiety disorders are characterized by a broad range of cognitive biases. Future research could focus on changing multiple cognitive biases to generate more positive effect on symptoms.
Thus, at this point, it seems too early to identify the active factors of ABM and other cognitive bias modification research (Beard, 2011). Moreover, the acceptability of CBM might not be sufficient. In our trial, we observed that patients found the treatment boring and tiring. Although we excluded one patient who literally fell asleep during ABM, we have doubts about some other participants' level of compliance. We did not observe patients who ostensibly malperformed on the DPT – the DPT RT data did not show unusual patterns either – and without doubt all patients hoped to benefit. However, subtle ways to avoid looking at the pictures, fatigue, dissociative phenomena and the severity of PTSD symptoms could have had an impact on the efficacy of ABM. Explicit instructions have been suggested to enhance performance, but might not solve the involuntary problems with task performance (Beard, 2011; Hallion & Ruscio, 2011).

Comparison with recent ABM results

As mentioned above, only one of the three successful clinical trials was reported in accordance with the CONSORT guidelines. None was pre-registered at a clinical trial

database. This means that the primary outcome measures were also not preregistered, making it possible that the researchers have capitalized on chance. For example, close examination of the ABM trial in GAD that is generally presented as a positive trial (Amir et al., 2009a) reveals that there were no improvements on a worry scale that is generally used as primary outcome measure (Emmelkamp, 2012). Furthermore, other unregistered studies probably exist, with either positive or negative results (Beard, 2011; Emmelkamp, 2012).

The present RCT is the first study carried out with a clinical PTSD sample representative of most mental health care settings ('real world' setting). Previous studies in GAD and SAD were pilot studies and included younger and more highly educated patients. The sample size of these studies was also notably smaller. Our results therefore seem of clinical relevance.

Other negative results of ABM in SAD have been reported recently (Boetcher, Berger, & Renneberg, 2012; Carlbring et al., 2012; Neubauer et al., 2012). These negative findings are primarily discussed as problems attributed to the internet delivery of ABM, as opposed to the laboratory setting used in the studies with positive clinical findings (Amir et al., 2009a; Amir et al., 2009b; Schmidt et al., 2009). Technical problems, disturbances during the training or a different stress level (e.g. AB ''not activated'') in the home setting are suggested to have lead to the different outcomes.

These explanations seem at least insufficient, since earlier positive results of internet-delivered ABM have also been reported (Malcolm 2003, reported in MacLeod & Rutherford, 2004; MacLeod, Soong, Rutherford, & Campbell, 2007; See, MacLeod, & Bridle, 2009). Furthermore, it does not resolve another failure to replicate positive effects on AB and anxious reactivity of a single session of ABM delivered in the laboratory (Julian, Beard, Schmidt, Powers, & Smits, 2012, in an attempt to replicate Amir et al., 2008).

Our study was not a direct replication, but a conceptual replication of the Amir and Schmidt studies. As with other conceptual replications, the chances of publication of these null results in a journal are much smaller then when positive effects are found. As described by Pashler & Harris (2012), failing conceptual replications seem to generate a typical reaction; the researchers are prone to attribute null results to deviations from the original method (e.g., internet-delivered, see above). Although our results might not directly contradict the positive results originally reported, the outcomes at least question the robustness of the underlying effect.

In this light, it is not surprising that the possibility that ABM is an ineffective treatment for SAD is not even suggested in the recent RCTs. This brought Emmelkamp (2012) to write a commentary with the sole purpose ''to discuss other potential reasons for these negative results'', advising against further investigating (internet-delivered) ABM. The theoretical background for a lack of robust evidence for ABM is also discussed, since the author found no evidence that other effective treatments coincide with a reduction in AB. His conclusion is that if the working mechanism of ABM is not clear, it is premature to apply ABM clinically.

The tendency to diminish the impact of null results is also mirrored in the conclusions of one of the two meta-analyses on ABM (Hallion & Ruscio, 2011), in which the authors found strong evidence for publication bias in the field of ABM research.

One can only speculate on the background of this bias in the field of Cognitive Bias research. Since ABM treatment stems from experimental research, researchers might not have much experience with clinical standards in research (e.g., CONSORT guidelines). Also, as Emmelkamp (2012) points out, the field of experimental psychology might be in need for clinical applications to valorize their research area.

Whatever the reasons for the problems with ABM research, disseminating ABM to clinical patients is not yet appropriate. More importantly, based on our results and results of the recent studies on SAD, the commercial exploitation of (internet-delivered) ABM in this phase seems premature if not unethical. A website like www.managingyouranxiety.com (accessed March 7th, 2013) where patients can buy time-limited access to DPT training programs is very premature.

Limitations and recommendations for further research

In our RCT, the patients with PTSD formed a rather heterogeneous sample; some patients suffered from childhood traumas and others were traumatized later in life. It is often theorized that there is a difference in attentional bias between those with versus those without childhood trauma, since these subgroups also present different symptoms (McCauly et al., 2003). However, we analyzed the data of the first 71 patients of our sample (35 with childhood trauma) and found no significantly different AB in these subgroups (Tjaarda, 2011). As mentioned above, one study investigated AB in adult survivors of childhood maltreatment with and without PTSD (Fani et al., 2011). Only AB towards positive stimuli (i.e., happy faces) was found to mediate the relationship between the traumatic events and PTSD symptoms.

We aimed to test a representative clinical sample, and we therefore did not exclude patients based on the nature of the traumatic event they experienced. The stimuli material consisted of various threatening scenes (e.g., a man holding a gun, a car accident), and have not been equally relevant for all patients. However, in our case series, we specifically tested the effect of personalized ABM in a homogeneous sample of male veterans (Chapter 4), leading to similar disappointing outcomes.

Attentional control and attentional bias

In our large clinical PTSD sample, AC was found to moderate the relationship between PTSD symptoms and AB (Chapter 3). Patients high in PTSD and low in AC showed attentional avoidance and no association between AB and PTSD was observed in patients with medium or high levels of AC. These outcomes may have important implications: high AC might buffer against the development of AB in PTSD, and low or medium levels of AC are a potential risk factor for AB in PTSD.

Theoretical implications

Our results seem to validate theoretical considerations on the interplay between AC and AB (Eysenck et al., 2007); in our study, AC was indeed found to play a crucial role in the relation between bottom-up information processing and (PTSD-related) anxiety. PTSD patients with greater AC seem able to inhibit reflexive attentional processes, and this is in line with earlier empirical evidence that validated these relationships (Derryberry & Reed, 2002; Bardeen & Orcutt, 2011; Putman, Arias-Garcia, Pantazi, & Van Schie, 2012). Thus, our outcomes extend earlier results to a patient population, thereby forming the first step in closing the gap between experimental research and clinical studies.

Interesting in this light are the results of an analogue study investigating three different forms of ABM (training towards or away from threatening stimuli and a control condition) in socially anxious students. Compared to the controls, participants in both training conditions experienced less anxiety in response to a subsequent social stress task (Klumpp & Amir, 2010). It was suggested that ABM, regardless of the direction of the training, primarily affects AC; ABM might have facilitated AC, thereby enabling disengagement from the task-irrelevant stimuli and limiting the impact of threatening information in anxiety.

In any case, when considering AB as a dysfunctional attentional reaction related to anxiety, high AC is hypothesized to play a correcting or inhibiting role in AB. It seems mandatory that the specific relationship between the protective function of attentional control, attentional bias and anxiety should be further examined in clinical samples to elaborate on the relationships and relevance. With more evidence for a moderating effect of AC, a comprehensive rationale that can account for different bias effects (e.g., inhibiting vigilance or avoidance) could be developed and tested.

Furthermore, AC is measured through self report only (mostly ACS) in the abovementioned studies. At this point, extending AC studies with more behavioral measures is recommended, to strengthen both theory and empirical evidence.

Developmental impact of AC

The capacity to use attentional resources likely originates in prefrontal cortical regions (Bishop, Jenkins, & Lawrence, 2007). AC is considered to both regulate posterior attentional systems and to underlie subsequent behavioral output.

Individual differences in effortful control have been found to affect the development of specific areas of cognitive functioning (Heim & Keil, 2012) and self-regulating capacities (Derryberry & Rothbart, 1997). AC is regarded as a regulating trait or temperament factor (Rothbart, Ahadi, & Evans, 2000). One study indicated that by the age of 45 months, the ability to control attention was already highly stable (Kochanska & Knaack, 2003). Reactive temperament (e.g., emotional arousibility) then can be regulated by effortful control, buffering against pathological mood and anxiety disturbances. These positive effects on self-regulation can lead to better adjustment in adulthood and enhanced psychological wellbeing (Compton, 2000; Eisenberg, Fabes, Guthrie, & Reiser, 2000).

Negative consequences of low AC can lead to diminished self-regulating of reactions on fear. This relationship, between non-emotional AC and self reported anxiety, is confirmed in children from 5-18 years old (see for a summary, Sportel, Nauta, De Hullu, De Jong, & Hartman, 2011). Children with low AC seem more susceptible to development of anxiety disorders, specifically when high in Behavioral Inhibition (BI, i.e. internalizing behavior) since AC was found to moderate the relationship between BI and a range of affective disorders in children (Sportel et al., 2011).

In individuals with low AC, poor adaptation after trauma can also be expected. One analogue study explored the associations between AC, PTSD and affective responding in trauma exposed students (Bardeen & Read, 2010). AC was found to predict recovery from trauma retelling, independent from PTSD symptoms, with greater recovery in participants high in AC.

In children, few studies also found a moderating effect of AC on the relationship between attentional reactivity and anxiety (Helzer, Connor-Smith, & Reed, 2009; Susa, Pitică, Benga, & Miclea, 2012). In the study of Susa and colleagues (2012) a stronger relationship was found between attentional focus and anxiety, than between shifting and anxiety, suggesting that specifically the ability to remain concentrated on a task buffers against AB.

Lonigan, Vasey, Phillips, & Hazen (2004) theorized that the relationship between AB and anxiety in children can be better understood when taking moderating factors into account. They suggested that high AC as a personality dimension enables high anxious children to constrain threat-related bias. The impact of AB therefore seems to depend on individual attentional control ability. When children are not able to acquire the ability to inhibit AB in childhood through AC, they might be prone to develop affective disorders (Kindt & van der Hout, 2001).

Taken together, it seems that ''cold'' cognitive factors (AC) are of crucial importance to understand the development of the relationship between "hot'' emotionally driven attentional processing of threatening information and anxiety (state or trait).

Clinical Implications

ABM

Hypothetically, AC could even explain the abovementioned mixed results reported in AB studies (e.g., great variance, difficulty to replicate results). In a review on ABM in anxiety disorders, it is also suggested that attentional control is the mechanism of change in ABM (Bar-Haim, 2010).

We performed a post-hoc analysis with high and low AC as between-subjects factor. Based on the median score in our sample, low AC was defined as below 39 points, and high AC as 39 points or more. Again, we found no effect of ABM on symptoms. To date, we are not familiar with any other study that evaluated directly the effect of AC on the effect of ABM.

In an interesting but conceptually opposite study of McEvoy and Perini (2009), CBT augmented with either attention training (ATT; Wells, 1990; 2000) or relaxation was considered equally effective in treating patients with social phobia. In ATT, the goal is on teaching patients in three phases to stay focused, learn to shift attention more flexibly and to divide attention. The authors were specifically interested in the effect of treatment on AC and hypothesized that CBT with ATT would have a larger impact on AC. This prediction was not supported, but changes in AC were associated with greater symptom improvement at post-treatment in both conditions (McEvoy & Perini, 2009).

It could also be the case that anxious participants high in AC are less likely to benefit from ABM, since they are already capable of ''correcting'' their automatic attentional tendencies (AB). In addition, particularly patients low in AC might show more pronounced treatment effects (Verwoerd, Wessel, & De Jong, 2012). Therefore, pre-treatment selection based on individual AC could be investigated as a potential valuable addition to the ABM protocol. However, clearly this assumption needs to be further investigated first. Another implication of the recent findings can be that in traditional therapies, attentional differences might indicate different treatment approaches. For example, in individuals low in AC emotionally overwhelming effects of therapy can be expected since AC affects self-regulatory capacities. Thus, a pre-treatment phase in which self-regulating skills are targeted might be of benefit for these patients.

In any case, based on theory and empirical findings so far, including measures of AC in research in both cognitive bias modification and other more traditional treatments seems valuable.

Training AC

Effortful strategies to control attention also seem more accessible for change through training (Hallion & Ruscio, 2011; Bardeen & Read, 2010). Since AC can be an early developmental protective factor, training attentional control in childhood might be of specific importance. One study indicated positive effects of AC training on cognitive functioning in children (Wass, Scerif, & Johnson, 2012).

Training AC might be beneficial throughout the life span, as one study suggests (Bherer, 2008); training attentional shifting was found to enhance executive task performance in both younger and older adults, suggesting cognitive plasticity in AC. Considering that AC is conceptualized as a temperament factor, this might be an interesting line of research.

Diverse forms of cognitive control training are designed and investigated so far. An example is the abovementioned ATT (Wells, 2000). Effects of ATT are mainly investigated in small pilot studies (e.g., Wells & Papageorgiou, 2001). Mindfulness-based interventions (first introduced as attentional control training, Teasdale et al, 1995) are even more widely applied in clinical settings. Although the positive effect of mindfulness-based therapy on attentional control is often theorized (Bishop et al., 2007, Teasdale et al., 1995), this relationship is by our knowledge not directly examined so far. We found one study exploring the effects of MBSR on performance on the Attention Network Test (ANT; Fan, McCandliss, Sommer, Raz, & Posner, 2002). This test is designed to measure three overlapping attentional subsystems: alerting, orienting and conflict monitoring. Compared to controls, participants in the MBSR condition demonstrated significantly improved orienting after the intervention, (Jha, Krompinger, & Baume, 2007). One other study reported positive effects on sustained attention (using cognitive tasks) in healthy meditators (Chambers, Lo, & Allen, 2008). In an interesting study with schoolchildren aged 7-9 years, a mindfulness practice program added to the regular school program resulted in better executive functioning in children that were less well regulated according to their teachers and parents (Flook et al., 2010).

Mindfulness and PTSD

Metacognitions: mindfulness skills and reactivity in PTSD

As hypothesized, symptoms of PTSD, mindfulness skills and reactivity were found to correlate in a large sample of clinical patients with PTSD. Moreover, mindful non-judgment was associated with anxiety sensitivity even when controlled for PTSD and depressive symptoms. Our study extended earlier results on the relationship between PTSD symptoms and an attitude of acceptance in a clinical sample (Wahbeh, Lu, & Oken, 2011; Thompson & Waltz, 2010). The sample was also heterogeneous regarding the nature of the trauma, which implies that the findings are generalizable.

Our outcomes suggest that negative metacognitions may indeed play a role in the development and maintenance of PTSD. Simply stated, the more an individual 'passes judgment' on his or her physical, emotional or cognitive reactions to a traumatic event, the higher his or her risk of developing PTSD becomes. This risk might be reduced if an accepting attitude can be developed, or is already present when a traumatic event occurs.

Our clinical results confirmed the relationship between facets of mindfulness and anxiety sensitivity that had been demonstrated in a community sample (Vujanovic,

Zvolensky, Bernstein, Feldner, & McLeish, 2007). Mindfulness is hypothesized to ''dampen'' the negative effects of anxiety sensitivity (AS) as a risk factor for psychological disturbance. High AS can lead to an automatically enrolling pattern of anxiety-driven reactions (such as catastrophyzing or panic-related arousal symptoms) when encountering a threatening situation. High mindfulness skills on the other hand might facilitate allocating attention to the here-and-now, thereby preventing these automatic patterns and creating room for disconfirmation of negative beliefs (Vujanovic et al., 2007).

Several influential theories (Brewin, Dalgleish, & Joseph, 1996; Ehlers & Clark, 2000; Foa, Steketee, & Rothbaum, 1989) have already pointed out that in traditional treatments (e.g., CBT or EMDR) negative metacognitions are not explicitly addressed. The Self-Regulatory Executive Functioning model (S-REF model; Wells & Matthews, 1996) is an attempt to combine advances in cognitive theory with treatment implications. Specifically, according to this transdiagnostic model, stimulus-driven and effortful cognitive control mechanisms, metacognitive beliefs and the interaction between these factors contribute importantly to the development of emotional disorders. The S-REF model proposes that dysfunctional cognitive processing prevent the disconfirmation of negative metacognitions (e.g., anxiety sensitivity), or inhibit positive beliefs (e.g., non-judgment). The negative beliefs in its turn are fueling maladaptive cognitive strategies. These strategies are; inflexible self-focused attention, perseverative thinking (worry, rumination), threat monitoring and inadequate coping strategies.
The clinical implications of the S-REF model are that treatments should also be focused on enhancing attentional control and targeting negative metacognitions, as is integrated in ATT (see above) and in MBCT. The results of our cross-sectional design seem to validate components of the model, since we found that a non-judgmental attitude ('belief') is independently associated with another negative metacognitive construct (AS). The interaction between mindfulness, AS and PTSD might be further evaluated in the laboratory, while experimentally manipulating mindfulness. For example, in patients with PTSD, the effect of trauma reminders on AS can be measured after a single session of mindfulness meditation, compared with controls who did not receive the intervention. Even more interestingly, in accordance with the S-REF model, investigating the relationships between AC and AS and non-judgment could add to further understanding the working mechanism of MBCT.

Results case series
Although several theoretical reports suggest that mindfulness-based interventions might be particularly suitable for PTSD treatment (Follete, Palm, & Pearson, 2006; Vujanovic, Niles, Pietrefesa, Schmertz, & Potter, 2011), only one open label trial investigating MBSR in PTSD patients was published so far (Kimbrough, Magyari,

Langenberg, Chesney, & Berman, 2010). The goal of our case series was to explore the feasibility and clinical effects of MBCT.
Regarding feasibility, our conclusion was two-sided. On the one hand, in the exit interviews, patients stated that they would recommend MBCT to others. In addition, potential side-effects (e.g., overwhelming emotional experiences during meditation, symptom exacerbation) were not observed in the participating patients. But on the other hand, the early drop-out rate was high. Several explanations can account for this effect, either related to mindfulness interventions specifically (e.g., early drop out; Crane & Williams, 2010) or to PTSD (e.g., patients that do not improve during treatment tend to drop out; Bradley, Green, Russ, Dutra, & Westen, 2005) or to the sample involved in the case series (chronic, possibly treatment resistant patients). These questions need to be further investigated in a next study.

The therapeutic effects of MBCT in our study were mixed. Less than half of the patients reached clinically meaningful improvements, coinciding with enhanced mindfulness skills. In the exit-interviews however, all patients reported (large) beneficial effects of MBCT. Again, this might be due to different factors (e.g., placebo effect).
Possibly, as some patients suggested, more sessions of MBCT might have resulted in a larger therapeutic effect. Other (symptom) measures might have better tapped the reported changes. But it can also not be ruled out that MBCT is not appropriate for the treatment of PTSD. We recommend further examination of MBCT first in a less chronic population.
Furthermore, as mentioned before, in addition to the outcomes of our cross-sectional study, an interesting line of research is to study the effects of MBCT on attentional control and reactivity. These constructs seem to tap underlying mechanism of change related to mindfulness interventions and might target the therapeutic effect patients reported better.

Overall conclusion

Our studies are an example of research into the potential clinical applications of cognitive science. Given the unexpected outcomes of our RCT (chapter 2), the necessity of such research in real world clinical settings cannot be made clearer. The aim of clinical research is to bridge the gap between science and practice and we hope that our studies contribute to that goal.
Although there is a distinct need for more effective treatments for PTSD, designing and testing effective novel therapies is a long and complicated process. Derived from experimental cognitive psychology, ABM seemed promising and ready for clinical dissemination. However, outside the laboratory the therapeutic effects were limited, at least for the treatment of PTSD. Even augmenting existing treatments for PTSD with ABM seems therefore redundant.

Our outcomes in the MBCT case series are mixed and the generalizibility of our results is limited because of the study design. However, the findings connecting mindfulness skills to vulnerability factors of PTSD (reactivity) indicate that some facets of mindfulness may be particularly relevant for the development and maintenance of PTSD. These outcomes provide some theoretical underpinning for the application of MBCT in the treatment of PTSD. Our case-series in chronic, possibly treatment resistant PTSD patients also formed preliminary evidence that MBCT might be effective in PTSD. Yet, its acceptability (both in patients and therapists) needs to be enhanced.

Both research in ABM and MBCT suffer from methodological problems (e.g., no pre-treatment trial registration, small sample size). At the same time, these interventions are already disseminated and advocated for diverse clinical populations. Considering the disappointing therapeutic effect of ABM in PTSD, it seems essential that researchers and clinicians first focus on well-conducted scientific research before clinical application of new treatments.
The working mechanisms of MBCT should be further validated first, to be followed with ''real world'' RCTs with valid control conditions. The clinical acceptability of MBCT in PTSD needs to be investigated in more detail and this might lead to further adjustments of the classic MBCT protocol. Also, independent measures of cognitive changes should be added to research protocols.

Although attention problems are unmistakably part of PTSD, both theoretically as clinically, the relationships between the different cognitive components and PTSD symptoms is far more complicated than commonly stated. The importance of AB in PTSD as measured with the EST is already put in perspective (Kimble, 2009), and the measurement of AB in PTSD with other cognitive measurements (e.g., the DPT) might also be more complicated than formerly theorized.
Our results support recent theoretical notions on the influence of AC on automatic attentional processing in anxiety, including in PTSD. Therefore, an important future focus in cognitive research and clinical application should be on extending evidence about the interaction between ''lower'' and ''higher'' order information processing. This fundamental research should coincide with the investigation of the effects of existing PTSD therapies on AC and the introduction of new, validated, behavioral measures of AC.
The fact that attention research is more complicated than previously thought should of course not lead to abandoning this topic. Patients with PTSD suffer from (severe) attentional problems, which can be very disabling (e.g., not being able to concentrate on work, forget important tasks etc.). Moreover, patients often report that these problems are not tackled by existing treatments. Continuing this line of research is therefore of great interest and clinical importance.

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