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Divergent Change Mechanisms in Trauma-Focused and Non-Trauma-Focused Therapies for Post-Traumatic Stress Disorder (PTSD)

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Abstract

Both trauma-focused (TF) and non-trauma-focused (N-TF) therapies are associated with partial PTSD remission for about half of completers. However, there may be unique neural mechanisms underlying symptom reductions in TF vs. N-TF therapies. Multiple neuroimaging studies suggest that PTSD is associated with increased amygdala activation and decreased anterior cingulate cortex (ACC) activation, relative to healthy controls. In TF therapies, improvements in PTSD symptoms have been associated with a reversal of this pattern: reduced amygdala activation and increased ACC activation, which may indicate an increase in top-down regulation. In contrast, in N-TF therapies, improvements in PTSD symptoms have been associated with reductions in both amygdala and ACC activation, which may suggest reduced bottom-up reactivity and thus a lesser need for top-down regulation. As a reduction in bottom-up reactivity might plausibly represent a more stable, long-term mechanism of symptom reduction (requiring fewer active cognitive resources), it is suggested in this paper that future research should test the hypothesis that N-TF therapies are associated with longer lasting PTSD symptom reductions.

Keywords: posttraumatic, trauma, exposure, EMDR, psychodynamic.

Résumé

Les études de neuroimagerie indiquent que le trouble de stress post-traumatique (TSPT) est associé à une augmentation de l'activité de l'amygdale et à une réduction de l'activité du cortex cingulaire antérieur (CCA). Quoique les deux types de thérapie pour le TSPT, focalisée sur le trauma (FT) vs. non-focalisée (N-FT), ont été associées à court-terme à une rémission partielle du TSPT pour la moitié des sujets, des mécanismes divergents semblent être sous-jacents à leur efficacité. Avec les thérapies FT, les améliorations symptomatiques du TSPT ont été associées à une inversion du pattern usuel de réponses neuronales du TSPT non-traité : l'activation réduite de l'amygdale et l'activation accrue du CCA, suggérant une augmentation du contrôle top-down des émotions et de l'anxiété. Inversement, avec les thérapies N-FT, les améliorations symptomatiques ont été associées à la réduction conjointe de l'activation de l'amygdale et du CCA, suggérant une réduction de la réactivité bottom-up menant à un moindre besoin de régulation top-down. Comme la réduction de la réactivité émotive pourrait plausiblement consister en un mécanisme plus stable à long-terme (requérant moins de ressources pour être maintenues), il est suggéré que les études futures vérifient si la réduction conjointe de l'activation de l'amygdale et du CCA est associée à des effets thérapeutiques durables.

Mots-clés : post-traumatique, cingulaire, trauma, exposition, EMDR, psychodynamique.

Therapeutic approaches for treating PTSD can be divided into two major types: trauma-focused (TF) and non-trauma-focused (N-TF) therapies. TF therapies, such as prolonged exposure (PE) and eye movement desensitization and reprocessing (EMDR), involve re-experiencing traumatic events as intensely as possible as well as altering cognitions about trauma (Foa, Keane, & Friedman, 2004; Shapiro, 1995). In contrast, N-TF therapies for PTSD entail developing a therapeutic relationship, reducing anxiety, enhancing self-care, altering cognitions, linking meaningful traumatic details to pre-existing conflicts, and uncovering and resolving pre-existing emotional issues (Horowitz, 2001). In N-TF therapies, the details of traumatic events may be reviewed along with dysphoric emotions, but only if individuals have already demonstrated a capacity to continue self-reflective work while experiencing dysphoric emotions and if a solid therapeutic relationship has also been established (Gaston, 1995; Horowitz, 2001). Therefore, TF and N-TF therapies for PTSD proceed differently and their effects are likely to involve different mechanisms of change.

In this article, we briefly review findings on the efficacy of TF and N-TF therapies for PTSD. We then examine recent evidence from neuroimaging studies that suggest divergent mechanisms associated with TF and N-TF therapies. Finally, we discuss the possibility that differences in neural mechanisms may relate to differences in the long-term stability of therapeutic outcomes.

Clinical Efficacy of TF and N-TF Therapies for PTSD

Several meta-analyses of randomized clinical trials (RCT) have been conducted to determine the short-term efficacy of various therapies for PTSD. One meta-analysis (Bradley, Greene, Russ, Dutra, & Western, 2005) concluded that all therapies examined (PE, EMDR, cognitive therapy, anxiety management, supportive therapy, and dynamic therapy) were equally efficacious, with 56% of partial PTSD remission and 44% of clinical improvement in all participants. In comparison to a wait-list condition, the average effect size was 1.11. No significant differences between TF therapies and N-TF therapies were observed. A more recent meta-analysis (Powers, Halpern, Ferenschak, Gillihan, & Foa, 2010) concluded that TF therapies (PE, EMDR) and N-TF therapies (traditional cognitive-behavioral therapy) were equally effective. A third meta-analysis (Barrera, Mott, Hofstein, & Teng, 2013) specifically examined the efficacy of cognitive therapy, with and without an exposure (TF) component, and no difference was found. Therefore, findings appear to converge on the conclusion that TF and N-TF therapies have similar short-term efficacy.

It is worth noting that N-TF therapies, such as supportive and dynamic therapy, have also been used as control placebos in some studies (see Powers et al., 2010). In such studies, important limitations have been placed, however, upon the administration of these therapies. For example, supportive therapists were instructed to refrain from addressing any aspect of the traumatic event (see Foa, Rothbaum, Riggs, & Murdock, 1991) and dynamic therapy was provided after only 2 days of training (see Gilboa-Schechtman et al., 2010). These constraints significantly undermine any conclusions one can draw with regard to the efficacy of these therapies. As indicated by some authors (Benish, Imel, & Wampold, 2008), such control therapies are not *bona fide* therapies because they do not reflect how N-TF therapies are conducted by clinicians. To remedy this situation, a meta-analysis was conducted on the efficacy of *bone fide* therapies only for treating PTSD (Benish et al., 2008). No was found difference between TF-therapies and *bona fide* N-TF therapies. Finally, although little studied, when provided by well-trained therapists, brief dynamic therapy designed to treat PTSD has been shown to be superior to a wait-list control condition (Krupnick, 2002) and to be equally efficacious to TF therapies (Brom, Kleber, & Defares, 1989).

Therefore, both TF and N-TF therapies seem to be equally efficacious in treating PTSD. In the short-term, they are all associated with partial PTSD remission although substantial symptoms remain (Bradley et al., 2005).Given that they entail different therapeutic strategies, TF and N-TF therapies could, however, plausibly be associated with unique mechanisms of change. We will now review a range of neuroimaging findings that appear to support this possibility.

Neural Correlates of PTSD Reductions in TF vs. N-TF Therapies

A considerable number of studies have examined the neural correlates of PTSD itself. One meta-analysis of such studies recently concluded that, relative to healthy controls, PTSD was associated with increased amygdala activation as well as reduced activation in both the medial prefrontal cortex and anterior cingulate cortex (ACC) (Patel, Spreng, Shin, & Girard, 2012). Other studies also appear to support this general pattern of findings upon presentation of trauma-related cues (see Lanius et al., 2010). The amygdala is thought to play an important role in unconsciously appraising the emotional significance of perceived stimuli, and in generating emotional reactions in response to these appraisals (Bernston, Bechara, Damasio, Tranel, &

Cacioppo, 2007; Davis & Whalen, 2001; Koenig & Grafman, 2009). Such emotional reactions include the automatic initiation of autonomic/behavioral responses as well as biases in attention, memory, and decision-making. In contrast, the ACC has been implicated in the mental representation of emotion and in several aspects of emotional regulation, as well as the induction of analgesic placebo effect (Etkin, Egner, & Kalisch 2011; Lane, Weihs, Herring, Hishaw, & Smith, 2015). Because the ACC has been implicated in top-down inhibition of anxiety-related amygdala activity (Etkin et al., 2011), greater amygdala activation paired with reduced ACC activation in PTSD may indicate increased bottom-up emotional reactivity (within the amygdala), deficient top-down regulation (within the ACC), or both. Recent neuroimaging findings may shed some light on the neural mechanisms involved in PTSD reductions in both TF and N-TF therapies.

Recent neuroimaging findings have begun to shed light on the neural mechanisms associated with PTSD symptom reductions in both TF and N-TF therapies. In one meta-analysis (Thomaes, Dorrepaal, Draijer, Jansma, Veltman, & van Balkom, 2014), PTSD reduction was mostly associated with a reversal in the neural pattern observed in PTSD itself. That is, participants showed reduced amygdala activation and greater ACC activation after therapy. It is worth noting, however, that all but one of the studies included in this meta-analysis examined the effects of TF therapies (PE, EMDR, and cognitive-behavioral therapy with a PE component). For example, in a study examining the efficacy of cognitive-behavioral therapy with PE (Felmingham et al., 2007), a negative correlation($r = -.85$) was found between amygdala activation and PTSD reduction at post-test, while a positive correlation ($r = .84$) was found between ACC activation and PTSD reduction. The more PTSD symptoms had decreased, the less activated the amygdala was and the more activated the ACC was upon trauma-related stimulation, suggesting top-down inhibition.

However, one study in this meta-analysis reported a divergent pattern of neural responses (Thomaes et al., 2012). This was the only study included that examined the neural correlates of N-TF therapies: treatment-as-usual (TAU) and a combination of cognitive-behavioral stabilizing therapy plus TAU. At post-test, dorsal ACC activation was reduced in the stabilizing therapy plus TAU only, and there was a significant positive correlation between PTSD reduction and decreased ACC activation across both therapies. In this study, PTSD reduction was thus paired with reduced ACC activation, which represents a unique pattern of neural responses compared to that observed in studies of TF therapies. One further neuroimaging study examined the neural correlates of PTSD remission in N-TF therapies (Dickie, Brunet, Akerib, & Armory, 2011) and it was not included in the above meta-analysis (Thomaes et al., 2014). In this study, almost all participants received dynamic integrative therapy (Gaston, 1995). At 6 to 9 months within therapy, CAPS scores were found to correlate with amygdala activation ($r = 0.51$) upon trauma-related stimulation and PTSD reductions were found to correlate with reductions in sgACC activation for emotional memory ($r = 0.85$); the greater the PTSD reductions were, the greater the reductions in ACC activation (E.W.E. Dickie, personal communications, August 2014 and June 2015). Together, these recent neuroimaging findings could be interpreted to suggest that PTSD remission in N-TF therapies is associated with a decreased bottom-up emotional reactivity within the amygdala, thus reducing the need to engage top-down inhibition within the ACC.

Interestingly, a similar association between symptom reduction and reduced activation in both amygdala and ACC has also been found in dynamic therapy for depression (Buchheim et al., 2012). Furthermore, the efficacy of dynamic therapy of panic disorder was also found to be associated with reduced amygdala activation and a trend toward reduced prefrontal activation in hospitalized patients, as compared to healthy controls, upon presentation of negative emotional cues (Beutel, Starkb, Panc, Silbersweigd, & Dietricha, 2010). With specific phobia, reduced ACC activation was associated with complete remission after psycho-education and gradual exposure (Straube, Glauer, Dilger, Mentzel, & Miltner., 2006). Therefore, there seems to be a trend within the effects of N-TF therapies for other mental disorders that is consistent with the pattern observed in the few recent studies of the neural correlates of PTSD described above.

Thus, in N-TF therapies, PTSD reduction may be associated with a decreased tendency for the amygdala to generate emotions due to greater ACC activation inhibiting emotions. Recent findings support the hypothesis that TF therapies and N-TF therapies involve different mechanisms of change.

Divergent Mechanisms of Change in TF vs. N-TF Therapies

Firstly, it should be kept in mind that current support for the proposed difference in mechanism between TF and N-TF therapies is preliminary, if not exploratory. One major purpose of this article is to highlight the need for further empirical investigation of this possible difference, as it could have important implications for the long-term stability of symptom reduction within different PTSD therapies. That is, as we discuss below, despite the fact that both TF and N-TF therapies result in similar short-term PTSD reduction, this difference in mechanism may give reason to think that the effects of N-TF therapies will be more long-lasting.

Plausible Mechanisms of Change in TF Therapies

As highlighted above, one plausible mechanism underlying PTSD remission in TF therapies appears to be top-down inhibition of the amygdala by the ACC. This would actively counteract a strong tendency for the amygdala to generate anxiety to salient perceptual cues. Top-down control processes of this kind typically require, however, available cognitive resources to be maintained. Therefore, under high cognitive load, within conditions of sleep deprivation or high arousal, or in other conditions also known to inhibit executive functioning, it would be possible for top-down control processes to fail, potentially promoting PTSD relapse. Thus, in TF therapies, top-down regulation may represent an effective short-term solution for reducing PTSD, but this mechanism may remain continually vulnerable to disruption – and the subsequent return of PTSD symptoms.

Indeed, top-down inhibition appears to play an important role in the fear extinction process (Comte et al., 2014; Etkin et al., 2011). Extinction training is currently thought to involve the creation of a new memory, which results in the transient inhibition of the original fear memory rather than a direct modification of it (Bouton, 2004). This model serves as the basis for TF therapies given that they focus on re-experiencing traumatic events (see Foa & Riggs, 1993; Foa et al., 2004). However, conditioned fear reactions are known to recur spontaneously, a phenomenon named spontaneous recovery (Pavlov, 1927; Rescorla, 2004), and to return after a single re-introduction of the aversive stimulus, a phenomenon named reinstatement (Pavlov, 1927; Rescorla & Heth, 1975). Consequently, exposure to post-traumatic memories is likely to result in this type of transient top-down inhibition, as opposed to directly modifying the original traumatic memory. Furthermore, consistent with the phenomena of spontaneous recovery and reinstatement following extinction learning, the effects of TF therapies for PTSD have been found to gradually decay over time, diminishing from 1.08 to 0.68 (a 40% loss) within months according to one meta-analysis (Powers et al., 2010). In the only long-term follow-up study of TF therapies, PTSD symptoms were as deteriorated ($d = -.82$ and $d = -0.83$) in EMDR participants as in untreated controls after 5 years (Macklin et al., 2000).

Certain considerations may also suggest that the underlying mechanism of PE and EMDR could involve a process similar to dissociation. Suggestively, the pattern of neural responses observed in dissociative PTSD involves reduced amygdala activation and greater ACC (Lanius et al., 2010), which is similar to the neural responses associated with PTSD remission in TF therapies (Thomaes et al., 2014). Furthermore, in dissociative PTSD, one study found that greater activation in ACC was associated with conscious fear only (Felmingham et al., 2008), while the authors proposed dissociation as a regulatory strategy invoked to cope with extreme arousal in PTSD – a strategy functioning only during the conscious processing of threat.

Together, these findings could suggest that the conscious and potentially overwhelming re-experiencing of traumatic events occurring in TF therapies might inadvertently induce a dissociative process. While this interpretation remains speculative, dissociation is a mechanism closely related to divided attention, a phenomenon that is central to TF therapies and especially EMDR. Indeed, in the midst of re-experiencing a traumatic event, EMDR explicitly instructs patients to engage in a sensory dual-attention task. In addition, EMDR has also been found to trigger unusually large reductions in subjective distress (Davidson & Parker, 2001) and a sudden reduction in heart rate within seconds of the dual task (Schubert, Lee, & Drummond, 2011), two phenomena also associated with the spontaneous induction of dissociation. These types of sudden reductions in fear have also been found to have higher rates of spontaneous recurrence as compared to gradual fear reductions (Gershman, Jones, Norman, Monfils, & Niv, 2013), and this could have implications for the long-term effectiveness of TF therapies for PTSD.

Long-term PTSD remission, with a low chance of relapse, may thus be less likely to succeed via increases in top-down control. According to the Yerkes-Dodson law regarding complex tasks, the integrative functions of the hippocampus and the prefrontal cortex are disrupted by very high anxiety (Diamond, Campbell, Park, Halonen, & Zoladz, 2007). In TF therapy, the re-experiencing of traumatic events involves very high, if not overwhelming, anxiety, and such anxiety is likely to interfere with the integrative functions of the hippocampus and the prefrontal cortex. Therefore, it may be unlikely that an integration of traumatic memories occurs in TF therapies.

Taken together, these findings suggest that the change mechanisms in TF therapies may be inhibition and possibly dissociation of traumatic memories, reducing PTSD only temporarily.

Plausible Mechanisms of Change in N-TF Therapies

N-TF therapies for PTSD differ in their therapeutic strategies from TF therapies. Dynamic therapy basically aims at establishing a therapeutic relationship and resolving emotional conflicts (Horowitz, 1976; 2001). Dysphoric emotions are experienced gradually and therapists are vigilant to prevent any overwhelming emotion, which is unlikely to induce top-down inhibition. Indeed, as mentioned above, a process causing reduced bottom-up reactivity may instead be involved. This mechanism may be more stable over time because it does not require the continual need for top-down control. In line with this contention, the effects of dynamic therapy for PTSD were found to improve over the few months after termination in the only study examining their maintenance (Brom et al., 1989), and the effects of dynamic therapy for other severe mental disorders have been repeatedly shown to increase over years according to five meta-analyses (reviewed by Shedler, 2010).

One possible mechanism of PTSD remission in N-TF therapies resides in the therapeutic relationship. Attachment theory postulates that the therapist's benevolent attitude is internalized and the subsequent secure attachment is capable of regulating emotions (Bowlby, 1988). Recent neuroimaging findings provide support for the role of secure attachment in modulating both emotions and physical pain, in a manner that does not appear to engage the ACC. Secure attachment has been found to prevent and decrease amygdala activation and to be associated with milder PTSD and PTSD prevention (reviewed in Schottenbauer, Glass, Arnkoff, Tendick, & Gray, 2008) while attachment insecurity has been found to be positively correlated with enhanced amygdala activation (Lemche et al., 2006; Norman, Lawrence, Iles, Benattayallah, & Karl, 2015). Furthermore, the priming of secure attachment during a stressful task has been found to reduce amygdala activation (Norman et al., 2015) and the priming of secure attachment in the midst of a threatening experience (physical pain) has been found to reduce ACC activation (Eisenberger et al., 2011). Finally, cues of attachment insecurity were found to activate both amygdala and ACC, while the activation of amygdala and ACC by cues of attachment insecurity was found to be reduced after dynamic therapy for depression (Buchheim, et al., 2012). Taken together, these findings suggest that the remission of symptoms in dynamic therapy, for both PTSD and depression, may be partly due to the establishment of a secure attachment via a benevolent therapeutic relationship.

Clinical Example

A case example of full PTSD remission was previously described (Gaston, 1995), after dynamic integrative psychotherapy had been employed as based on Horowitz's model (2001). The course of the PTSD symptoms is consistent with the above propositions.

When she experienced a first traumatic event, Mary was a bus driver. One night, a stabbed teenager died in her arms after a gratuitous assault. After this traumatic event, Mary had developed a very severe PTSD (including pseudo-illusions of persecution), major depressive disorder with suicidal ideations, and a conversion disorder (severe swelling of the hands and arms, so much so that she could not even dress herself). After 9 months of a dynamic and integrative psychotherapy, all PTSD and co-morbid symptoms had remitted, and Mary was back at work. One week after her return to work, a gang fight suddenly exploded in her bus, but no PTSD symptom was triggered by this event. In the ensuing years, more traumatic events happened in Mary's life.

Five years later, Mary worked as a subway conductor. In a suicidal attempt, a man threw himself onto the windshield of her cabinet, crashing it and landing on her. Mary developed PTSD, but solely in regard to the suicide (she had no intrusive symptom concerning the murder). At the employee assistance program, Mary received PE. After completing several PE sessions, Mary went back to work with some PTSD symptoms.

Three years later, Mary was involved in a serious car accident and developed PTSD gain. Mary had intrusive symptoms pertaining to the car accident and the suicide, but not the murder. This clinical picture suggests that the traumatic memories of the murder had been integrated into her psychological structure, while the traumatic memories of the suicide were left unaltered. At the end of this second round of dynamic therapy, Mary obtained again a full PTSD remission.

In this clinical example, the N-TF therapy led to PTSD resolution and the associated traumatic memories did not resurface after the occurrence of 3 more traumatic events. In contrast, the TF therapy led to partial PTSD remission and the associated traumatic memories were reactivated by a new traumatic event.

Conclusion

While TF therapies for PTSD have been shown to be efficacious and they have gained in popularity (Sharpless & Barber, 2011), the above findings suggest a potential advantage offered by N-TF therapies for

PTSD, namely a more stable mechanism of change. The evidence reviewed above is largely preliminary, but emerging neuroimaging data suggest top-down control as a plausible mechanism in TF therapies while, in contrast, reduced bottom-up reactivity may be a plausible mechanism in N-TF therapies. As top-down control of amygdala reactivity represents a reversible mechanism capable of being disrupted in fear conditioning (see Bouton, 2004), this could explain the relatively rapid decay of effects over time after TF therapies for PTSD.

As suggested above, one plausible interpretation for both the divergent neural responses and the decay of effects over time in TF therapies is that these therapies involve the induction of reversible top-down inhibitory effects, leaving the heightened bottom-up amygdala reactivity intact. Since top-down inhibition requires the continual use of active cognitive resources, it is understandable that such a mechanism would be more prone to decay over time, explaining greater chances of PTSD relapse. In contrast, the reduction of bottom-up amygdala reactivity in N-TF therapies may be partly due to the establishment of a secure attachment based on the therapeutic relationship, a phenomenon which is likely to be more stable over time. Interestingly, reduced bottom-up amygdala reactivity also seems to occur in effective dynamic therapy for depression and panic disorder.

While bottom-up amygdala reactivity may be heightened by traumatic experiences, recent work has suggested that reducing such heightened bottom-up sensitivity may involve a process of memory reconsolidation within the medial temporal lobe (see Lane, Ryan, Nadel, & Greenberg 2014), a process which requires that arousal is neither too high nor too low. Therefore, as N-TF therapies aim at maintaining an optimal arousal level, this might facilitate the process of memory reconsolidation required to reduce the type of heightened sensitivity of the amygdala to perceptual cues associated with PTSD and, therefore, allow traumatic memories to be more adaptively integrated within the larger neuropsychological system.

It should be kept in mind that the neural correlates of PTSD remission reviewed in this paper are based on limited empirical evidence. In addition, functional neuroimaging studies are generally limited to providing correlational, as opposed to causal, information (Koenigs & Grafman, 2009). Nonetheless, neuroimaging studies remain useful tools for identifying the neural responses associated with PTSD remission and thus the mechanisms of change embedded in divergent therapeutic strategies.

In this paper, we have suggested that TF and N-TF therapies may be associated with unique mechanisms of change, as based on neuroimaging findings, and that the unique mechanisms associated with N-TF therapies could allow for more stable PTSD remission. In order to test this possibility, future research should directly investigate the long-term effects of both TF and N-TF therapies, including *bona fide* dynamic therapy, in treating PTSD.

Finally, PTSD resolution entails a full PTSD remission sustained over years. RCTs almost never report full PTSD remission, while manualized brief therapies leave individuals with substantial PTSD symptoms (Bradley et al., 2005). Therefore, although examining the neural correlates of PTSD reductions in RCTS may prove to be a useful strategy, another methodology may also be valuable. Neuroimaging research of PTSD and its recovery may benefit from examining the neural responses associated with full PTSD remission sustained over years in naturalistic settings. Mapping the neural correlates of full PTSD remission may help to identify the neural processes and mechanism of change involved in PTSD resolution.

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