## Abstract

Neuroimaging studies conducted in PTSD patients who have undergone various psychological treatments have provided evidence of modifications in cerebral blood flow (single photon emission computer tomography, SPECT), neuronal volume and density (magnetic resonance imaging, MRI), and, more recently, brain electric signal (electroencephalography, EEG). However, to date the number of such studies is still far too limited since only a few psychotherapies have been investigated using SPECT and MRI. In this respect, a recent study designed to monitor psychotherapy-related neurobiological changes is expected to pave the way for a new concept in PTSD treatment investigations. The purpose of this chapter is to review the results of functional and structural changes being reported in PTSD treatments.
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Abstract
Neuroimaging studies conducted in PTSD patients who have undergone various psychological treatments have provided evidence of modifications in cerebral blood flow (single photon emission computer tomography, SPECT), neuronal volume and density (magnetic resonance imaging, MRI), and, more recently, brain electric signal (electroencephalography, EEG). However, to date the number of such studies is still far too limited since only a few psychotherapies have been investigated using SPECT and MRI. In this respect, a recent study designed to monitor psychotherapy-related neurobiological changes is expected to pave the way for a new concept in PTSD treatment investigations. The purpose of this chapter is to review the results of functional and structural changes being reported in PTSD treatments during the period from 1999 to 2012, to present a critical review and to analyze the reported pathophysiological changes.
Posttraumatic stress disorder (PTSD) is a clinical condition that may affect victims of major psychological trauma and is one of the major causes of mental suffering. Initially defined in DSM-III in 1980, PTSD is a dysfunctional learning disorder with derangement of memory and mood regulation, leading to a fear-conditioned response elicited by internal or external cues associated with the traumatic situation that is recalled in flashbacks with involuntary vivid replays, concomitant autonomic reactions, and negative feelings. This oppressive tendency to reexperience the trauma leads to avoidance of reminders, irritability, and social and emotional withdrawal (American Psychiatric Association 1994). The recurring traumatic memory acts as a new traumatic experience that activates the brain networks engaged in a fear response, thus resulting in the body’s emotional reactions of autonomic arousal. It is estimated that in the general population of the USA, there is a lifetime prevalence of PTSD of 1.3–9% (Breslau et al. 1991; Kessler 2000; Breslau 2001; Davidson et al. 2002), which makes PTSD the fourth most common psychiatric disorder (Breslau et al. 1991). Drawing on such evidence, a large survey conducted in six European countries (Belgium, France, Germany, Italy, Spain, and the Netherlands) by way of face-to-face interviews administered to 21,425 participants showed that the general prevalence of PTSD was 1.1% (95% confidence interval = 1.0–1.3). The highest prevalence was reported in the Netherlands (2.63%), whereas the lowest was found in Spain (0.56%) (Darves-Bornoz et al. 2008).

Recent studies have shown that psychological trauma can cause anatomical and functional changes in specific areas of the brain associated with the onset of PTSD symptoms. These alterations occur in those areas of the brain implicated in trauma psychology and in symptoms onset. As a result, metabolic and morphological changes in the brain can be identified during the symptomatic phase of the disease, and also, each area involved in the complex mechanism underlying the processing of emotions and psychological traumas can be assigned a specific role.

Functional and structural studies have shown significant neuropathological alterations in patients with PTSD, particularly during the autobiographical reliving (script) of the trauma. Most of these studies included in a review (Bremner 2007) led to the identification of metabolic and morphological changes occurring in the brain when the disease becomes symptomatic, thus helping to associate a function with each specific area involved in the processing of emotions and psychological traumas.

However, to date no functional neuroimaging study has succeeded in investigating PTSD and its related psychotherapies with accurate time resolution. The real-time firing of brain neurons responding to external psychotherapy-induced stimuli, along with the effects of such stimuli on brain activation/deactivation, was recorded before and after treatment. This has restricted the findings to static conditions without describing in detail the dynamics of regional neuronal synchronization during psychotherapy sessions, an essential step in the comprehension of their functional mechanism. One of the tools that might potentially help to overcome the limiting
methodological factors is the EEG, resulting in a time resolution of milliseconds and having an acceptable capability to identify the sources of activity in the 3D brain space, especially with a medium to high-density array of electrodes.

Symptom provocation paradigms are an extremely useful and powerful way of delineating the functional anatomy of the traumatic memory that characterizes PTSD. Changes in local activations in response to specific tasks point to neural processing dysfunctions. In this respect, autobiographical trauma-script exposure (Pavic et al. 2003; Lindauer et al. 2004; Pagani et al. 2005) or audio and visual trauma-related stimuli (Liberzon et al. 1999; Zubieta et al. 1999) proved to be a valid approach to elicit cerebral blood flow (CBF) changes in PTSD, and improved technical and methodological features have made neuroimaging studies particularly suitable in in vivo investigations into the neurobiology of emotions. It is worth noting that since the neutral script administered to the patient is experienced as a new procedure, stress levels can rise and/or attention levels can be below normal levels and, finally, that the resting state may differ from one investigation to the next. To some extent, the above factors are responsible for inconsistency across PTSD research results.

In the review by Francati et al. (2007), in which functional studies on PTSD were evaluated, it is worth noting that, in general, SPECT studies include a larger sample of patients (on average 16 compared with 9 for positron emission tomography, PET, and functional MRI, fMRI, studies) and a broader spectrum of traumatic events. In fact, of the reviewed 99mTc-HMPAO SPECT studies, four out of eight did not include combat-related or sexual abuse studies, whereas this was true for only 5 out of 30 PET and fMRI studies. The need for recruiting larger cohorts of subjects is partially due to the lower spatial and time resolution of SPECT as compared to PET and fMRI leading to the need for a larger number of investigated subjects to reach comparably reliable results. Moreover, whereas in the past most PTSD studies were carried out on veterans and abused women and children, now there is a tendency to investigate traumas related more to daily life and social problems.

Research has helped to identify the brain regions that may play a key role in the pathophysiology of PTSD: the amygdala, the medial prefrontal cortex (mPFC), and the hippocampus. The amygdala appears to be involved when dealing with threat-related stimuli (Morris et al. 1998; Whalen et al. 1998; Davis and Whalen 2001) and plays a role in the process of fear conditioning (LeDoux 2000; Davis and Whalen 2001). As PTSD patients are very sensitive to potential threats from the surrounding environment and are prone to acquire conditioned fear (Orr et al. 2000; Peri et al. 2000), an amygdala hyperactivation has been suggested in this clinical condition. Another region of interest is the mPFC that is connected to the amygdala and is involved in the extinction of fear conditioning (Quirk et al. 2000; Milad and Quirk 2002). In fact, patients with PTSD show a significant response to fear in their everyday life and exhibit reduced extinction of conditioned fear (Orr et al. 2000; Rothbaum et al. 2001). Lastly, a further region of interest is the hippocampus, which is involved in memory processes (Eichenbaum 2000; Corcoran and Maren 2001). Interestingly, it has been demonstrated that PTSD is associated with memory impairment and abnormal hippocampal functions.
More specifically, amygdala hyperresponsivity in PTSD has been shown during the presentation of traumatic narratives (Rauch et al. 1996; Shin et al. 2004a) and combat sounds (Liberzon et al. 1999; Pissiota et al. 2002). In patients with PTSD, the amygdala also appears to show significant responses to affective material not strictly associated to personal traumas, such as fearful facial expressions. Interestingly, the activity of the amygdala is positively correlated with PTSD symptom severity (Shin et al. 2004a) and self-reported anxiety (Pissiota et al. 2002; Fredrikson and Furmark 2003). However, it is worth noting that some studies of PTSD failed to detect any amygdala activation during symptomatic states (Bremner et al. 1997). Failure to replicate this finding has been related to methodological divergences between studies and to scientific and technical limitations such as relatively poor spatial and temporal resolution (e.g., in SPECT), small sample sizes of patients and controls involved in the studies, and inappropriate paradigm to induce symptoms.

Various neuroimaging studies in PTSD consistently showed a decreased activation and/or a failure to activate the mPFC, including anterior cingulate cortex and medial frontal gyrus. Such evidence occurred when patients were listening to traumatic narratives (Lindauer et al. 2004; Shin et al. 2004a; Britton et al. 2005) and were exposed to combat pictures or sounds (Bremner et al. 1999b). Some studies have reported that mPFC activation is inversely related to PTSD symptom severity (Shin et al. 2004a; Britton et al. 2005). Although the majority of studies have shown a diminished activation of mPFC in PTSD, a few studies have shown different results, such as both increased and decreased activation in this region (Shin et al. 1997) or increased activation (Rauch et al. 1996; Zubieta et al. 1999; Sachinvala et al. 2000). Possible explanations for such discrepancies may depend on the specific technique used or on technical properties’ heterogeneity. Another explanation accounts for the presence of a dissociative state of the participants during experiments.

Lastly, some neuroimaging studies focusing on hippocampal function in PTSD led to mixed results. Early studies reported lower activity in this region in the presence of symptoms (Bremner et al. 1999a; Shin et al. 1999), and cognitive activation studies showed a failure to recruit this neural structure during the recollection of emotional words (Bremner et al. 2003) and neutral words (Shin et al. 2004b). However, the latter study also found that blood flow in the hippocampus and parahippocampal gyri was significantly positively correlated with symptom severity.

In a recent functional connectivity study on rCBF changes during trauma versus neutral scripts (Osuch et al. 2008), the authors showed left amygdala coupling with right ACC and bilateral anterior insula, as well as coupling between the amygdala and contralateral hippocampus.

To summarize, during the last years a growing body of evidence has irrefutably demonstrated the existence of a neural model of PTSD encompassing the amygdala, the mPFC, and the hippocampus. These neural structures appear to be pathologically involved in PTSD (Shin et al. 2006). According to this model, the amygdala is typically hyperresponsive, implying an unexpected response to fear. By contrast, regions of the mPFC (including rostral anterior cingulate cortex and ventral medial frontal gyrus) are hyporesponsive, and this has been linked to a partial failure to appropriately inhibit the amygdala activity. In addition, it has been suggested that such
a hypofunction may also be related to reduced fear extinction. Lastly, hippocampal dysfunction may be associated to the declarative memory impairment typically showed in patients with PTSD. However, it is worth noting that mounting evidence suggests that the original model should be more complex than expected and should also take into due account the role played by additional neural structures, such as the dorsal anterior cingulate cortex and the insula (Shin and Liberzon 2010).

The purpose of this chapter is to present and briefly discuss significant English language articles published in the last 13 years (indexed in PubMed 1999–2012) regarding cerebral changes in patients diagnosed with PTSD for whom the neurobiological effects of various psychotherapies have been investigated by neuroimaging techniques and mostly by SPECT and structural MRI scans. A very recent EEG investigation will also be mentioned reinforcing the hypotheses suggested by previous functional neuroimaging studies.

15.2 Neuroimaging in PTSD Psychotherapies

Neuroimaging techniques have been used in an attempt to shed light on the neurobiological correlates of various psychotherapies revealing their neurobiological effects. An extensive review (Roffman et al. 2005) analyzed 14 functional neuroimaging investigations designed to measure the effects of psychotherapies on brain function. Despite a positive clinical outcome and the significant effect of behavioral, cognitive behavioral, and interpersonal therapies on brain functions, neuroanatomical changes were largely inconsistent both within-disorders and within-psychotherapies, making it impossible to draw any well-structured conclusion. However, the studies under review were conducted on a variety of experimental paradigms, methodologies, and psychotherapies, but more importantly they looked at groups of patients falling within the whole spectrum of psychiatric diagnoses, ranging from major depression to phobias and schizophrenia. Such heterogeneity accounts for the failure to identify plausible and convergent physiological mechanisms in the treatments under investigation. Consequently, this chapter will include only those articles which relate to psychotherapies used to treat PTSD.

The first study in which SPECT was used in psychotherapy research dates back to 1999, the year in which Levin et al. (1999) published a case report on a subject with PTSD treated with eye movement desensitization and reprocessing (EMDR). Upon recall of the traumatic event, SPECT showed a cerebral blood flow increase after therapy in the anterior cingulate and left frontal lobe. Unfortunately, despite extensive discussion of the positive clinical and neuropsychological outcome following the EMDR therapy, the authors only mentioned the functional effects and the design of the SPECT study (a within-subject comparison). The outcome of the SPECT examination was described, but no details were given about the type of camera, the camera resolution, or the methodology applied for image analysis and for statistical testing. However, notwithstanding the abovementioned inadequacy, this study paved the way for subsequent studies which demonstrated the feasibility of investigating brain physiology during the reliving of trauma.
Few years after, Lansing et al. (2005) investigated six psychologically traumatized police officers, before and after EMDR therapy. When the traumatic event was recalled, it was found that, after the disappearance of the clinical and psychological signs of PTSD, blood flow decreased significantly in the occipital lobe, left parietal lobe, and posterior frontal lobes and perfusion increased significantly in the left inferior frontal gyrus. The study was conducted with a high-resolution SPECT camera and with an acceptable statistical threshold, considering the low number of subjects and the experimental nature of the investigation. The most relevant results were a parallel decrease in perfusion in regions hyperaroused during the symptomatic phase and an increased blood flow in the inferior frontal cortex after EMDR. These findings indirectly confirmed the impact of EMDR on the neurobiology of PTSD, thus reversing the reduced prefrontal cortex control over the amygdalae.

By using structural magnetic resonance imaging, Bryant et al. (2008) investigated the relationship between treatment response in PTSD and the volume of the rostral anterior cingulate cortex in three groups: patients with PTSD (n = 13), traumatized control subjects (n = 13), and healthy controls (n = 13). Patients with PTSD underwent a brief treatment of CBT (8 sessions) and were then divided into two subgroups: responders (n = 7) versus nonresponders (n = 6). MRI data showed that better response to CBT was associated with larger rACC volume. While nonresponders presented a significantly smaller rACC volume, responders had an rACC volume comparable to that of controls. The authors interpreted this interesting pattern of results by stating that larger rACC volume may allow the patient to better regulate fear during CBT and subsequently to benefit more from the psychological treatment received.

Considering the limited amount of literature available about such a compelling issue, i.e., the changes occurring in the brain in association with psychotherapies in general and the related disappearance of symptoms, our research group at the Karolinska Hospital, Sweden, attempted to identify the neurobiological events occurring at functional and anatomical level during EMDR therapy. These studies formed part of a large research project on PTSD covering Stockholm public transportation employees who had experienced a “person-under-train” incident or an assault at work (Högberg et al. 2007, 2008, clinical studies; Pagani et al. 2005, 2007; Nardo et al. 2011, SPECT studies; Looi et al. 2008, 2009; Nardo et al. 2010, MRI studies). In all the above investigations, the Structured Clinical Interview for DSM-IV Axis I Disorders (First et al. 1997) was applied as a clinical diagnosis benchmark. On the other hand, data originating from interview-based and self-rating scales constituted the basis for psychological assessment.

The project was inspired by a meta-analysis of 61 outcome trials for PTSD in which patients were treated with pharmacological and psychological therapies such as behavioral therapy, EMDR, relaxation training, hypnotherapy, and dynamic therapy (Van Etten and Taylor 1998). The study concluded that the best psychological therapies were cognitive behavioral therapy (CBT) and EMDR and that these psychotherapies were more effective than drug therapy. Thirty-two percent of patients on drugs discontinued treatment, compared with 14% of patients treated with psychological therapies. A further meta-analysis came to the conclusion that EMDR
and exposure therapies had a positive clinical outcome in the treatment of PTSD (Davidson and Parker 2001). Another study (Bradley et al. 2005) reported that in more than half of the patients who completed treatment with CBT or EMDR, overall symptoms improved. However, in all such studies, patients were monitored for less than 12 months and Bradley et al. (2005) pointed out the lack of long-term follow-up. This deficiency was overcome by Högberg et al. (2008), who reported a positive outcome from EMDR therapy 3 years after the last session.

The preliminary results from Lansing et al. (2005) were confirmed in a larger SPECT study that investigated cerebral blood flow changes following psychotherapy (Nardo et al. 2011). Fifteen patients were scanned before and after therapeutic intervention, and in order to increase the reliability and robustness of the study, a control group of 22 nonsymptomatic subjects suffering from the same trauma was included in the study. This latter methodological caveat is of great relevance, since it minimizes any possible bias in the results due to psychological heterogeneity between the two groups. Furthermore, a very strict statistical threshold was applied.

**Fig. 1.5.1** Three-dimensional rendering of voxels reflecting higher tracer distribution in patients before EMDR (n=15) as compared to controls (n=27). The statistically significant differences are highlighted. The first row represents the lateral aspect of the right (on the left) and of the left (on the right) hemispheres; the second row represents the inferior (on the left) and the superior (on the right) aspects of the brain (Nardo et al. 2011).
(false discovery rate correction at both voxel and cluster level) accepting the risk of false negatives due to type II statistical errors. When comparing patients with the control subjects, the significant group difference found before therapy (Fig. 15.1) disappeared after treatment. Furthermore, following therapy the responders showed significant CBF normalization in the parieto-occipital lobes, visual cortex, and hippocampus and an increased CBF in the lateral prefrontal cortex. These results were confirmed 4 years later by an MRI study highlighting decreased gray matter density in roughly the same limbic and cortical structures in nonresponders before EMDR therapy (Nardo et al. 2010).

Taken together the results of the latter two studies indicate that the decrease in regional blood flow following successful EMDR therapy was associated with the remission of symptoms such as flashbacks, intrusive and stressful memories, hallucinations, and persistent trauma reliving at somatic level. On the other hand, EMDR normalized the capability to retrieve important aspects of the trauma and improved attention levels and sense of self. Furthermore, the activation of the prefrontal cortex, which has been shown to inhibit the limbic system in response to pathological stimuli that resemble the traumatic event, recovered its inhibitory role, reducing amygdala hyperactivation and the corresponding cortical hyperarousal.

The latest SPECT EMDR study to date related to two patients suffering from a psychological traffic trauma (Oh and Choi 2007). After EMDR, the authors found an increase in cerebral perfusion in the bilateral dorsolateral prefrontal cortex and a decrease in the temporal association cortex. In addition, the SPECT scans were compared to those of a non-traumatized control group, and the findings were in line with the above indicating a tracer uptake normalization following EMDR therapy. As Levin’s first study showed, also in this case, the significance of the results is reduced by the extremely low number of patients included in the sample, as well as by relatively poor statistics ($p<0.01$). However, this study also confirmed the general neurobiological effect of EMDR, with a tendency to restore cortical control over the hyperaroused subcortical limbic structures.

In 2007 a SPECT study of 16 PTSD patients, before and after exposure to cognitive restructuring therapy and following successful psychotherapy, reported a higher activation in cortical (temporal, parietal, and prefrontal lobes) and subcortical (thalamus) regions in the left hemisphere during a script-driven provocation paradigm (Peres et al. 2007). This investigation was also performed using a low statistical threshold ($p<0.001$ uncorrected for multiple comparisons) and the results should be viewed with caution.

In the following year, Lindauer et al. (2008), using brief eclectic psychotherapy (BET), investigated the cerebral blood flow in ten traumatized police officers using SPECT and reported that, after psychotherapy with a positive clinical outcome, the activation found during the script listening at baseline was significantly lowered in the middle frontal gyrus. Furthermore, treatment efficacy, as measured by PTSD scores, correlated positively with CBF in temporal and frontal cortex. However, this study was performed with a low-resolution SPECT camera and statistical differences thresholded at the liberal level of $p<0.01$ uncorrected for multiple comparisons at
voxel level. The same group published a study in 2005 in which, using MRI, the same subjects showed a lack of volumetric changes following BET (Lindauer et al. 2005). However, the hippocampi were found to be smaller in patients than in traumatized controls, a finding often reproduced in PTSD research. The question of whether this anatomical condition is a trait (present before the index trauma) or state (following the index trauma) characteristic has not yet been clarified. In addition, due to a lack of follow-up, the study did not conclusively shed light on the effects of therapy on the subcortical structures. In fact, the relatively short duration of therapy (4 months) and the minimal time elapsed between the end of psychotherapy and the MRI (about a week) may not have been long enough to produce detectable anatomical changes, as such changes may occur only after a longer interval following successful treatment.

In summary, during the past 13 years a body of research has been carried out on humans to evaluate psychotherapies’ effectiveness, and a number of studies are focused on revealing their functional substrates despite difficulties arising from both time and spatial resolution of the selected techniques. The neurobiological grounds for psychotherapies’ effectiveness in the treatment of PTSD have been supported by SPECT studies showing that, after comparing the brain activity before and after therapy, significant changes in blood flow occur mainly in limbic areas and the prefrontal cortex. Overall, the results of these studies indicate a posttreatment reversal of the prefrontal and limbic abnormalities, which were clearly recognized at pretreatment and are a frequent neuroimaging finding in patients with PTSD. In fact, despite the relatively low spatial resolution of SPECT, the increased blood flow found at posttreatment mainly in the right middle inferior temporal gyrus may reflect a higher control over the amygdala and an increased stabilization of the pathological brain hyperactivation, resulting in a reduction in somatosensory symptoms of anxiety. These findings are consistent with clinical improvements, including depression and general affective disorders, demonstrating that psychotherapies have a significant impact on brain function and that the emergent normalized pattern of brain activity is consistent with changes that may be mitigating posttraumatic and anxiety conditions.

In the last 2 years, a new and groundbreaking investigation has been carried out, based on online EEG monitoring of the functional response during psychotherapy (Pagani et al. 2011, 2012). A preliminary methodological validation report describing the methodology and feasibility of this approach (Pagani et al. 2011) was recently published. To allow the experiment to be as patient friendly as possible, the EEGs in a group of ten subjects with major psychic trauma were recorded in a private practitioner’s quiet room. The activation of the human cortex in “live mode” throughout the EMDR session was compared between traumatized individuals both in the acute phase and after clinical recovery. The comparison between the patients’ EEGs recorded during the first and the last EMDR sessions showed a significantly greater activation during the latter in the temporo-occipital cortex mainly on the left side (Pagani et al. 2012). In patients after therapy, a significant decrease in the fast alpha and gamma components of the activation present in the frontoparietal cortex at the first EMDR session was also observed.
In our opinion, the importance of this latter study lies not only in the validation, through a different neuroimaging technique, of the results obtained with SPECT and PET but also in the critical importance of PTSD-related psychotherapy research. Being able to perform EEG studies in a quiet and cozy environment helps to avoid biases caused by patient discomfort and possible psychological constraints (i.e., claustrophobia, anxiety, panic) which can occur in PET or SPECT (Mazard et al. 2002).

15.3 General Discussion

The main objective of the functional studies carried out over the last 13 years has been to broaden our knowledge concerning the neurobiological mechanisms underlying successful psychotherapy. This has been pursued utilizing various methodologies (neuropsychology, SPECT, PET, MRI, and EEG) in order to identify the neuronal changes upon psychotherapy occurring in human pathophysiology, i.e., neuropsychology, blood perfusion, neuronal density, and electrical activation, following psychotherapy. This exciting journey has helped to confirm the initially sparse evidence of the association between clinical outcomes and changes in brain functions and structures following psychological treatment and has also confirmed the feasibility of real-time monitoring of cortical activations during therapy. The significant normalization of these activations at the stage of symptom disappearance can be interpreted as a neurobiological correlate of clinical recovery. This supports the hypothesis of a shift of emotive attention from limbic to cortical regions with an overwhelming cognitive and sensory role, occurring when the memory retention of the traumatic event can move from an implicit subcortical to an explicit cortical status with different regions participating in processing the experience.

In general, limbic hyperactivation in PTSD patients is paralleled by cortical hypofunction (Bremner et al. 1999a) resulting in a lack of inhibition of reaction to fear from the amygdala and lack of adequate attenuation of peripheral sympathetic and hormonal responses to stress. It has been proposed that such hyperperfusion and hyperactivity of limbic and paralimbic regions are related to stress-induced long-term potentiation between the amygdala and periaqueductal gray through the N-methyl-D-aspartate (NMDA)-mediated pathway, once a sufficient amount of glutamate is released following stressful events (Hull 2002).

It has been postulated that the critical involvement of the limbic system is connected with the emotional responsiveness to the retrieved traumatic experience elicited by symptom provocation. It is worth noting that chronic PTSD is often associated with long-term pharmacological treatment and/or alcohol and substance abuse which will further affect brain structure and function and confound the results of the investigations. In this respect, the choice of a control group is a critical factor in the global neuroimaging analysis. Subjects exposed to the same trauma as patients but not developing PTSD clinical symptoms are likely to be the best candidates to form a control group. In this case, CBF distribution differences following group comparisons will be entirely related to the disorder itself and will not be confused with possible group and trauma discrepancies nor biased by other variables.
Conclusions

In conclusion, functional and anatomical studies carried out during the last decade have yielded very promising results, supporting the evidence of neurobiological models and explaining the changes which take place following PTSD-related psychotherapies. These findings call for continued commitment to unravel the pathophysiological mechanisms underlying these effective treatments of posttraumatic stress disorder. In this respect, there is a shortage of properly controlled pre- and posttreatment neuroimaging studies investigating treatment effects in PTSD.

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