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PTSD, Neuroimaging and Psychotherapy: A Fruitful Encounter

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1. Introduction

Most of us have dealt with a traumatic event of some kind such as loss, accident, or illness, or will be dealing with one at some point in our lives. Psychological trauma is closely related to the development of posttraumatic stress disorder (PTSD), involving three sets of symptoms: (i) reliving trauma (traumatic memories, nightmares, intrusive thoughts); (ii) emotional avoidance/numbness (affective distance, emotional anaesthesia); and (iii) increased arousal (irritability, insomnia and hypervigilance) (American Psychiatric Association, 1994). Lifetime prevalence of PTSD-triggering traumatic events may be as much as 50–90%, and actual prevalence in the general population is about 8% (Kessler et al., 1995; Vieweg et al., 2006), while partial PTSD (pPTSD) in an at-risk groups have been estimated at approximately 30% (Weiss et al., 1992). After noting that individuals who do not meet the full set of diagnostic criteria for PTSD may suffer from clinically significant symptoms of PTSD (Weiss et al., 1992), the concept of pPTSD or subthreshold PTSD was introduced to describe subsyndromal forms of PTSD (Blanchard et al., 1995; Stein et al. 1997). Thus, exposure to traumatic stressors and psychological trauma is widespread, with a wide range of cognitive and behavioral responses/outcomes among trauma survivors (Peres et al., 2009; 2011).

One of the main psychological sequelae of traumatic experiences is conditioning of specific fears. In addition to PTSD, traumatic events can significantly influence major depression, somatoform disorders, panic and anxiety disorders, obsessive-compulsive disorders, phobic disorders, and substance abuse (Peres et al., 2009). Although traumatic events are associated with PTSD in the literature, traumatized people do not meet DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, 4th Edition) criteria for PTSD in many cases and often present a range of psychoform or somatoform symptoms. Considerable overlap in symptoms and disease comorbidity has been noted for medically unexplained symptoms in the primary care setting, such as chronic fatigue syndrome, low back pain, irritable bowel syndrome, primary headaches, fibromyalgia, temporomandibular joint disorder, major depression, panic attacks, and PTSD (Peres et al., 2009). Epidemiologic surveys increasingly point to a relation between exposure to traumatic events and more health care utilization, adverse health outcomes, onset of specific diseases, and premature death (Corrigan et al., 2005; Keane et al., 2006). Certain characteristics of traumas, particularly peritraumatic cognitive response and related cognitions, appear to heighten the risk for PTSD (Peres et al.,

2009). How people process stressors may be critical in determining whether or not trauma will be experienced, as well as the different constellation of symptoms if traumatization is characterized.

A single traumatic event can be processed in very different ways by individuals who experienced the same traumatic episode (Peres et al., 2005; 2011). The psychopathological signs of trauma are not static over time, nor is the form of the expression of traumatic memories. This fluidity is a consequence of the sensitization that is driven by reminders of the traumatic event and the vulnerability of memory to being modified with repeated recall (Peres et al., 2008; 2011). The sensitization of neural pathways involved in this reactivity is central to understanding the neurobiology of PTSD. The purpose of this chapter is to attempt to integrate both neuroimaging and psychotherapeutic findings in relation to PTSD, so that integration might bring greater efficacy to the treatment of psychologically traumatized patients.

2. A single disorder with many different facets

In life-threatening situations, mammals tend to react in two ways: "fight or flight" or "freezing". In light of adaptive evolutionary theory, both types of responses lead to adaptive gains for survivors. The defensive cascade animal model shows that several animals flee from or confront other predators, whereas others “pretend” to be dead when captured (Broman-Fulks et al., 2006). More than 100 studies have pointed to a distinction between simple and complex PTSD; therefore, some researchers have sought to include the dissociative subtype in the DSM-V (van der Kolk, 2006). Although based on recent literature, "freeze, flight, fight, fright, faint" provides a more comprehensive description of the human acute stress response sequence than current descriptions (Bracha et al., 2004). Two main behavioral systems are involved in PTSD: (1) hyperstimulation of sympathetic reactivity with expressive activity of the adrenergic system typically involved in fight or flight responses, and (2) dissociation with parasympathetic reactivity involved in freeze responses (Bremner et al., 2003). Supporting these two PTSD subtypes is a model of risk factors for PTSD developed after a study with a group of acutely burned people. Two pathways to PTSD were discerned: 1) from the size of the burn and level of pain following the acute anxiety, and then to PTSD; and 2) from the size of the burn to the level of acute dissociation following the burn, and then to PTSD. Together these pathways accounted for almost 60% of variance in PTSD symptoms and constituted a model with excellent fit indices. These findings support a model of complex etiology for childhood PTSD in which two independent pathways may be mediated by different biobehavioral systems (Saxe et al., 2005). Similar results were found in a different sample of sexually abused children. Independent pathways—anxiety/arousal and dissociation—through which sexually abused children are likely to develop later PTSD symptoms, accounted for about 57% of variance in PTSD symptoms (Kaplow et al., 2005). The finding that high levels of dissociative symptoms may be related to suppression of autonomic physiological responses to stress supports Bremner’s conceptualization of dissociative symptoms as comprising one of two subtypes of the acute stress response, differing physiologically as well as subjectively from a predominantly hyperarousal or intrusive symptom response (Creamer et al., 2005). The dissociative subtype may be seen in adults with a history of sexual abuse during childhood who present a consistent picture of dissociative amnesia, which occurs more often in victims

of interpersonal violence during childhood than in combat soldiers and accident victims (who do not present hyperarousal symptoms).

2.1 Subtype I

In a situation of unknown risk, heart and visceral alterations point to autonomous nervous system hyperactivity, whereas a subjective state of arousal potentiates an immediate search for syntheses and parameters for generating behavior. Peripheral and metabolic alterations (eg, tachycardia, mydriasis) reflect hyperactivity of the sympathetic nervous system and the hypothalamus-hypophysis-adrenal (HPA) axis leading to an immediate self-preservation response (Peres et al., 2007). Neurofunctional studies with hyperarousal PTSD patients using symptom provocation paradigms (in most cases, the retrieval of traumatic memories) suggest that the difficulty of synthesizing, classifying, and integrating a traumatic memory in narrative form may be related to the decreased activity of the prefrontal cortex involved in reducing negative feedback from the activity of the amygdala (Shin et al., 2004). Studies have implicated the HPA and the sympathetic-adrenal-medullar stress axes as key components of this pathogenic process (Boscarino et al., 2006). The relationship between anxiety level and performance is no longer advantageous after a certain point. Self-generated information flooding into sensory pathways affects the perceptual processing of data from surroundings, thus hampering the ability to formulate new hypotheses and syntheses.

Trauma-related studies involving epinephrine (E), norepinephrine (NE), and serotonin (5-HT) suggested that alterations in NE, E, and 5-HT may have relevance for symptoms commonly seen in survivors with PTSD, including hypervigilance, exaggerated startle, irritability, impulsivity, aggression, and intrusive memories (Southwick et al., 1999). Studies related to the role of NE in arousal, orienting to novel stimuli, selective attention, and vigilance demonstrated heightened noradrenergic neuronal reactivity, increased □-2 receptor sensitivity and exaggerated arousal in organisms that have been exposed to chronic uncontrollable stress. The way an individual cognitively processes a traumatic event may trigger an anxious/arousal or a dissociative reaction.

2.2 Subtype II

Tonic immobility (TI) is a possible component of the fear response characterized by freezing or immobility in situations involving extreme fear coupled with physical restraint, and is observed in 30% to 40% of rape victims (Kaplow et al., 2005). A study of TI in victims of childhood sexual abuse (CSA)—female undergraduates (n = 39) and female psychiatric inpatients (n = 41)—showed that more than 52% of all participants reported TI in response to CSA. TI reports were associated with greater current psychological impairment (Heidt et al., 2005) and may be typical not only of rape and sexual abuse victims, but other kinds of directly experienced traumas as well (Bados et al., 2008).

Emotional factors play a role in many reflex TI manifestations referred to as *feigning death*. Whether orienting and defense responses provide a valid model in humans has yet to be proven, but the dissociative response in certain trauma cases resembles animal TI. Bovin and colleagues (2008) asked whether TI mediates relations between perceived inescapability, peritraumatic fear, and PTSD symptom severity among sexual assault survivors. Their findings indicated that TI fully mediated relations between perceived inescapability and overall PTSD symptom severity, as well as re-experiencing and

avoidance/numbing symptom clusters. Beyond the hyperarousal PTSD model, TI may be a pathway through which trauma survivors develop severe PTSD symptoms. Supporting this hypothesis, psychophysiological changes associated with peritraumatic dissociation in female recent-rape victims were studied, as well as the relation between these changes and PTSD symptoms. Individuals in the high peritraumatic dissociation group showed a significantly different pattern of physiological responses from those in the low dissociation group. There was suppression of autonomic physiological responses in the former group, which also showed a discrepancy between self-reports of distress and objective physiological indicators in the laboratory setting (low heart rate and skin conductance), whereas high measures of subjective suffering were observed while volunteers talked about rape. On the other hand, the low dissociation group showed increased sympathetic system response (heart rate and skin conductance) during the same task. These findings support the hypothesis that in addition to the anxiety/arousal subtype, there is a dissociative subtype of persons with PTSD symptoms who exhibit diminished physiological reactivity (Griffing et al., 2006). Another study found that female rape victims with acute PTSD who scored high on the Peritraumatic Dissociative Experiences Questionnaire exhibited suppression of physiological responses during exposure to trauma-related stimuli (Kaufman et al., 2002).

Routes to traumatic amnesia from dissociative detachment (loss of emotional content leading to loss of factual content) and from dissociative compartmentalization (failure in integration) are frequent in PTSD subtype II patients. Women with high disability pain were more likely to have experienced child abuse, adult sexual assault, more severe spousal abuse, lifetime abuse-related injuries, and PTSD symptoms.

Neuroimaging studies found distinct neural reciprocities for the two types of responses. The first pattern of sympathetic excitability involved attenuation of medial-prefrontal cortex activity and heightened amygdala activity leading to continuous autonomic arousal and state of alert. The second pattern (dissociative) showed heightened activity of the medial-prefrontal cortex resulting in inhibition of amygdala activity, blunting the sympathetic response and leading to emotional numbing (Peres et al., 2011).

3. Neuroimaging studies of sufferers of traumatic memories

Single photon emission computed tomography (SPECT), positron emission tomography (PET), and functional magnetic resonance imaging (fMRI) neuroimaging techniques have provided information about the dynamics of brain activity in sufferers of traumatic memories. The neural substrates underlying traumatic memories have been induced with personalised narrative trauma scripts, images, sounds and virtual reality equipment. The diversity of findings and the heterogeneity of symptomatology amongst people suffering psychological traumas suggest it may not be possible to identify one specific neural circuit underlying PTSD. Nevertheless, neuroimaging studies of symptom provocation have identified some consistent patterns, including reduced left hemisphere activity, and hypo perfusion in the anterior cingulate (AC), dorsolateral prefrontal cortex, hippocampus, and Broca's area. Other areas have shown consistently increased activation, including the parahippocampal gyrus, posterior cingulate, and amygdale. Less consistent findings include bilateral reduction in activation of the thalamus and fusiform gyrus, and increase in activation of the right insula and cerebellum (Peres et al., 2005).

Rauch and colleagues (1996) were the first to use PET and personalised script-driven imagery to temporarily provoke symptoms in individuals with PTSD. The study revealed

increased perfusion in limbic and paralimbic structures of the right hemisphere, including the orbit frontal cortex, insular cortex, anterior temporal pole, and middle temporal cortex. Broca's area in the left inferior frontal cortex showed significantly decreased blood flow during provocation of traumatic memories, though not all studies have replicated this finding (McFarlane et al., 1997; Peres et al., 2007).

There is consensus that limbic and paralimbic regions are involved in the expression of emotional memories (Grillon et al., 1996; Shalev et al., 2000; Shalev, 2002; Moscovitch et al., 2005). More specifically, activation of the amygdala and anterior paralimbic structures is implicated in the processing of negative emotions such as fear. Studies of war veterans with PTSD, during visualisation of combat images showed increased activation of the anterior ventral cingulate gyrus and right amygdala, and reduced activity in Broca's area (Shin et al., 1999; Pissiota et al., 2002) A SPECT study by Liberzon and colleagues (1999) using combat veterans with and without PTSD and healthy controls, found left amygdala activation in response to combat sounds in PTSD patients only, but no amygdala activity in response to neutral sounds. Similarly, Rauch and colleagues (2000) found that people with PTSD showed greater activation of the right amygdala when shown frightening faces, compared to the controls.

PET has been used to study veterans to measure patterns of neural activity associated with traumatic images and sounds. Decrease in activity of the left prefrontal cortex (PFC) and anterior cingulate cortex of those individuals has also been demonstrated (Bremner et al., 1999). In another study with war veterans, fMRI was used to measure changes in activation of the left anterior cingulate cortex in response to a cognitive activation model – counting stroop for combat-related, negative, and neutral words (Shin et al., 2001). Individuals with PTSD showed decreased activity in the left PFC and AC when compared to the control group. In contrast, other SPECT studies of war veterans, did not find differential activity in these regions in response to trauma-related stimuli in PTSD, but found increased activity in the middle prefrontal cortex that was not correlated with symptoms (Shin et al., 1999; Zubieta et al., 1999). Two PET studies of women victims of childhood sexual abuse utilized directed scripts of neutral images and events related to the trauma (Bremner et al., 2002; Bremner et al., 1999). The scripts evoked memories of abuse experiences in all women, and resulted in increased bilateral activation of the posterior cingulate and motor cortex, but there was no differential activity in the middle prefrontal cortex or AC in women with PTSD relative to controls. Liberzon and colleagues (1999) and Zubieta and colleagues (1999) conducted a SPECT using similar methodology, involving war veterans with PTSD, publishing findings on PFC activity, which appeared to modulate the response to fear. In contrast to the typical findings, a regional increase in blood flow (not decrease) was found in PFC in individuals with PTSD. This discrepancy may that relate to the selection of this region in a region-of-interest analysis, which was derived from a separate control group or a confounding variable of a dissociative subtype of PTSD. Lanius and colleagues (2004), using a script-driven symptom provocation paradigm, have observed greater activity in the right posterior cingulate, right parietal lobe, and right occipital lobe, in PTSD and less activity in the left hemisphere. These findings support the suggestion of the inherently nonverbal nature of traumatic memory recall in PTSD subjects, compared to a more verbal pattern of traumatic memory recall in subjects without PTSD.

Despite some inconsistencies, there are reproducible neuroimaging findings in studies of traumatic memories. Functional neuroimaging has revealed greater activation of the right

amygdala and anterior paralimbic regions, structures which are known to be involved in processing negative emotions, deactivation of the Broca's area and other non-limbic cortical regions, and decreased activity of the left PFC and cingulate cortex in response to trauma-related stimuli in individuals with PTSD (Hull et al., 2002; Pitman et al., 2001; Peres et al., 2007).

However, there is also evidence to suggest that the failure of the medial prefrontal cortex/anterior cingulate network to regulate amygdala activity may extend beyond the situations of threat reminders associated with traumatic memory (Bremner et al., 1999), as these circuits are also implicated in the processing of facial expression and affect (Phillips et al., 1997), and have been found to be abnormal in PTSD (Rauch et al., 2000; Felmingham et al., 2003). The exact nature of the disruption of the networks in PTSD is unclear, but such findings suggest that there is an abnormality in the networks involved in these processing affective states. The finding of Felmingham and colleagues (2003) was of particular interest, and demonstrated less ability to differentiate between fearful and resting facial expression in PTSD, possibly reflective of the emotional numbing symptom in PTSD, which has disruptive socially implications.

Williams and colleagues (2005) explored the time course of activations associated with processing of fearful faces in PTSD and found that while traumatic emotions had a primary impact on the medial prefrontal systems, there was also a breakdown of the laterality of AC responses, which intensified with repeated exposure. The lack of coupling of the amygdala and AC in the PTSD subjects may account for the disruption of spatio-temporal activity observed in this disorder.

Another body of research has examined the processing of non-trauma-related stimuli in PTSD (Semple et al., 1993; Weber et al., 2005). This line of research is of particular interest for two reasons. It explores the question as to whether there are differences between PTSD subjects and controls in their ability to manage their day-to-day environment (Clark et al., 2003). PTSD patients demonstrated reduced activity in the left dorsolateral and inferior parietal cortex, indicative of decreased recruitment of these key areas involved in verbal working memory updating. Event-related potential (ERP) data from these same subjects (Weber et al., 2005) showed an abnormal pattern of cortical source activity during this updating process in PTSD, with a strong reduction in left fronto-parietal activity, systems involved in attention, working memory and interactions with medial temporal areas during episodic memory. The abnormalities that have been identified raise the question as to whether the difficulties that individuals with PTSD have dealing with traumatic reminders may, in part, reflect a more pervasive abnormality of information processing (McFarlane et al., 1997). There is extensive work demonstrating ERP abnormalities in PTSD (Karl et al., 2006).

One of the challenges in interpreting these data is understanding the extent to which such changes are indicative of primary pathology in the processing of traumatic memories or whether they are part of compensatory changes which would represent partial resilience - the ability to overcome difficulties and build a satisfactory quality of life - to trauma exposure. Britton and colleagues (2005) found decreased activation to the amygdala to the neutral memories in PTSD and increased activation to the traumatic reminders in both PTSD and trauma exposed individuals who did not develop PTSD. In general, the pattern of activation for PTSD patients was midway between those for combat-exposed and non-traumatized controls, indicating they may have partial or less effective regulation of amygdala activation than combat-exposed controls. PTSD patients also showed a failure of activation in the AC and diminished medial prefrontal cortex activity in response to

traumatic memories. These findings emphasise that the interaction between neural circuits, rather than activity of specific neuroanatomical regions is central to understanding the neurobiology of PTSD. The AC is of importance in the monitoring of emotional experience (Bush et al., 2000) and the greater intensity of negative emotions in PTSD may represent a failure of this region to exert appropriate top down inhibition (Britton et al., 2005).

One interesting study (investigated the temporal dynamics of amygdala activity in PTSD, and found increased early amygdala responses, which in the left hemisphere correlated with symptom severity (Protopopescu et al., 2005). PTSD patients also failed to show the normal pattern of habituation to threat-related words (unrelated to trauma), and instead showed a pattern suggestive of sensitization. In summary, this pattern of reactivity and increasing responsiveness to threat stimuli in PTSD provides valuable neurobiological insights into the difficulty that patients have in modulating their reactivity. Chung and colleagues (2006) in a SPECT study in a resting condition, found increased blood flow in limbic regions and decreased perfusion in the superior frontal gyrus and parietal and temporal regions in PTSD, further suggesting general dysregulation of regions involved in memory and emotion in PTSD.

An fMRI study explored the processing of social cognitions associated with empathy judgments in PTSD (Farrow et al., 2005). Participants were scanned pre- and post- modified cognitive behavioural therapy, with healthy people showing increased activation in the left middle temporal gyrus associated with empathy judgments and posterior cingulate gyrus activation associated with forgivability judgments. In patients, activity of regions activated by empathy and forgivability judgments increased as PTSD symptoms resolved, suggesting networks that might underpin the symptoms of social withdrawal and emotional numbing.

Intense or overwhelming experiences may trigger different responses, and studies have shown interindividual variability in the processing of life events and basic emotions (Eugene et al., 2003). Rather than simply passively registering reality, acquisition of information is conceived as an intrinsically active dynamic process of deconstruction and reconstruction of the external world on the basis of patterns of stimulations exciting the sensory receptors (Palmer et al., 2004). Sensory data from the outside world are deconstructed and used to build percepts, or perceptual representations. In order to cope with enormous amounts of sensory information being processed simultaneously - to generate adaptive behavior on the basis of this information - the nervous system has to collect them in a single percept. This process of building a representation (known as the "binding problem") gives rise to a perceptual unit, or synthesis, which depends on neural activity manifesting a state of spatial-temporal coherence to define the percept produced, even though it may be spread across several cortical circuits. A sensory stimulation pattern may generate one synthesis in a certain neutral situation but another very different one in situations in which these stimuli are accompanied by emotionally valenced events. The forming of atypical perceptual syntheses associated with events of highly emotional content may be related to several of the perceptual disorders involved in PTSD. For instance, dissociated PTSD subjects have distorted body perceptions (Griffin et al., 1997). The traumatized individuals' perceptive "binding" may occur in a dysfunctional manner: the nervous system may not succeed in grouping - or synthesizing - sensory information gathered from the environment in a coherent and functional manner. Strategies for altering maladapted syntheses/bindings formed by traumatic events may provide an important tool for exposure and cognitive restructuring therapy. For instance, a traumatized individual

may use new associations (new "pathways" - or neural circuitry) based on their own experiences of solving problems to constitute perceptual "bindings".

Whether an event is traumatic or not will depend on an individual's perceptual neural-circuitry processing and underlying resilience - significantly influenced by subjectivity (Creamer et al., 2005) - which is the ability to cope effectively and adapt in the face of loss, hardship or adversity (Bonanno et al., 2004.; Block et al.., 1996). Resilient individuals reported fewer posttraumatic symptoms after combat and showed greater ability to optimize emotional functioning through the use of alternative cognitive strategies (Bonanno et al., 2004; Florian et al., 1995). Neuroscientists have yet to comprehensively research this field (Peres et al., 2011). Examining neural mechanisms underlying psychological trauma or resilience is difficult given the heterogeneous symptoms and peculiarities of traumatic memories (key symptoms of PTSD). There are several methodological challenges and complex factors to control such as: (i) traumatized individuals typically present various comorbidities (e.g. major depression, substance abuse, etc.), (ii) traumatic events of different kinds (violence, accidents, loss, etc.) involve distinct sensory levels and modalities of memories (visual, tactile, olfactory, auditory, affective), (iii) different PTSD symptoms and emotions may accompany specific neural interactions during retrieval of traumatic memories (e.g. dissociative experiences are psychoneurophysiologically different from hyperarousal experiences, thus it is now clear that the division of PTSD into more specific subtypes is necessary in future diagnostic manuals to better categorise patterns of symptomatology and the respective neural substrates involved), (iv) the heterogeneous nature of trauma may pose difficulties when inducing reproducible responses in patients, or comparable activations in healthy control subjects, (v) the recency of the memories being studied is often different (memory expression may be modified over time, causing changes in the neural substrates involved). In the last ten years, however, neuroimaging research has yielded important information on heightened amygdala responsivity in PTSD patients during symptomatic states, and has found that medial prefrontal cortex (mPFC) responsivity is inversely associated with PTSD-symptom severity (Shin et al., 2006). Nevertheless, the directionality of the PFC to amygdala-activity correlation has been inconsistent: negative in PTSD cases but positive in controls, suggesting coupling only in psychopathology (Shin et al., 2005; Peres et al., 2008; 2011).

3.1 Comprehending neuroimaging findings

As advances are made in interpreting the meaning of neuroimaging findings, this work may lead to important refinements of therapeutic interventions for the treatment of traumatized patients (Peres et al., 2008). Clinical studies suggest that abnormalities in interpretation, synthesis, and integration of emotionally salient episodes play a crucial role in experiences being received as traumatic (Van Der Kolk, 1997).

Decreased hippocampal volume, often associated with PTSD, may have etiological significance for dissociation and errors in interpretation of information related to threats (Gilbertson et al., 2002). Moreover, reduction or blockage of hippocampal integrative function can fragment the various aspects of the memory of the traumatic experience into body sensations, smells, and sounds that seem strange and separate from other life experiences (Van Der Kolk, 1997). It has been proposed previously that impaired hippocampal functional may contribute to the fragmentation of experience in patients with PTSD (Lamprecht et al., 2002).

People exposed to personalised narratives of their trauma who have PTSD demonstrate a different pattern of activation, highlighting networks that are more associated with affective processing and less associated with linguistic representation. It appears that disruption of activity in the left frontal region is of particular importance in PTSD (Pissiota et al., 2002; Van Der Kolk, 1997) and the propensity to engage right hemisphere networks. It has been suggested that the left hemisphere sequentially organizes information and is responsible for problem solving and categorization operations (Hull et al., 2002; Van Der Kolk, 1997), which may explain why traumatic memories are experienced as 'belonging to the present', as brain regions necessary for sequencing and categorizing experiences are not adequately activated (Peres et al., 2007; 2011).

Individuals with PTSD were examined with SPECT before and after treatment with Eye Movement Desensitization and Reprocessing (Levin et al., 1999). Post-treatment, there was increased activity in the AC and left frontal lobe, perhaps influencing neuronal activity in the areas implicated in PTSD, particularly the left hemisphere. The finding of Farrow and colleagues (2005) further indicated that post-treatment there was greater activation of left hemisphere pathways associated with empathetic responses, with concomitant symptomatic improvement in PTSD.

During exposure to traumatic narratives, several studies have also shown a decline in activation in Broca's area of the left inferior frontal gyrus. Shin and colleagues (1999) verified that only individuals with PTSD exhibited a failure of activation in Broca's area and the AC. Other studies have also identified significantly decreased activity in Broca's area, and are perhaps linked with the difficulty PTSD individuals have in assimilating the traumatic event into a narrative structure (Hull et al., 2002; Peres et al., 2007; 2011).

The PFC and AC have been shown to be deactivated during retrieval of traumatic memories in patients with PTSD. These structures may inhibit responses to emotional stimuli (Bryant et al., 2005; Gilboa et al., 2004). In addition, dysfunction of dorsolateral PFC may mediate problems with language, cognition and integration of verbal expression with emotions. Decreased PFC activity may extinguish response to the symptoms of PTSD, attenuating the negative feedback of amygdala activity (Bremner et al., 2002; Nutt et al., 2004; Peres et al., 2007; 2011).

However, studies that have examined the temporal dynamics of these neural networks suggest that one of the key factors in PTSD is a progressive sensitisation and increasing responsivity to non-specific threat stimuli, even in a brief period of time (Protopopescu et al., 2005). The failure to adaptively process threat suggests that in PTSD, there is a propensity for increasing strength of affective responses with time, which disrupts the modulation of affect. Such neuroimaging findings highlight the experience of patients and underscore the disruptions of processing of the external world. Further evidence for a pervasive problem of information processing of non-trauma related stimuli in PTSD (Clark et al., 2003; Karl et al., 2006) suggests that treatment needs to address this aspect of the phenomenology of the disorder. The sense of being confused and aroused by the external world goes beyond specific reminders of the trauma.

Although neuroimaging studies of PTSD are still in an "embryonic" stage, disruption of hippocampal function, deactivation of Broca's area, the left hemisphere, and prefrontal cortex are consistently implicated in the pathophysiology of PTSD, expressed as a difficulty in synthesizing, categorizing, and integrating the traumatic memory (Peres et al., 2008). The subtle impact of the processing of facial expression may impact on the sense of engagement

and empathy in the therapeutic setting. These abnormalities occur against the background of a more pervasive disruption of information processing in PTSD of stimuli unrelated to the trauma. These limitations should be considered as an important factor challenging the capacity of these patients to engage in the therapeutic process.

3.1.1 Trauma and memory systems

Trauma, in its Greek etymological root, means lesion caused by an external agent. The term psychic trauma was firstly coined by Freud (1895) during his studies on the aetiology of neurosis, in which he stated that psychic traumatism is characterized by excessive excitement related to an individual's tolerance and capacity to integrate and psychically elaborate this stimulus. However, characterization of an event as traumatic does not depend only on the stressor stimulus, and there is no single human response to the same traumatic events or a "universal reaction to trauma" (Jones et al., 2003). The search to understand idiosyncratic responses to trauma has turned to the contribution of personality factors (Bonanno et al., 2004), with the way people process the stressor event appearing to be a critical factor in determining whether an event will be encoded as traumatic or not (Peres et al., 2007).

There are several complex memory systems involved, including declarative memory (Peres et al., 2005). Emotional memories interact with the neural substrates of declarative memory (Erk et al.,1998). Clinical observations clearly demonstrate that unpleasant emotional memories (charged with sadness, disgust, fear, or rage) can lead to maladaptive changes, such as distortions of perception, assessment, and judgment (Fivush et al., 1998). Although such distortions may not characterize a traumatic event, unpleasant emotional memories can remain vivid over time, and serve as references for expression of avoidance behaviours. In contrast, an event of greater emotional impact that is perceived as traumatic can lead to abnormal memory phenomena that are typical of PTSD, including the extreme imprinting of the experience, fragmentation of memories for the event, partial forgetfulness, or even amnesia (Lamprecht et al., 2002; Van Der Kolk, 1997). Studies of adults with a history of sexual abuse during childhood present with a consistent picture of dissociative amnesia, occurring more often in victims of interpersonal violence during childhood than in combat soldiers and accident victims (Williams et al., 1995). Amnesias for emotional and cognitive content appear to be related to the age at which the trauma occurred, as well as the constancy of the stressor event, with younger the age and prolonged duration of the traumatic stressor associated with greater probability of significant amnesia (Loftus et al., 1999). Thus, terrifying experiences can either totally resist integration, or can be etched in an “indelible” manner in a person's memory, and under many circumstances, traumatized individuals report a combination of these two phenomena. For example, in studies of posttraumatic nightmares, some individuals reported they repeatedly experienced the same traumatic scenes without change over a 15-year period. It is curious to note that few patients describe their perceptions as exact representations of sensations experienced at the time of the trauma (Van Der Kolk, 1997; 2006). The permeability of traumatic memories, to cultural influences and changes of their expression over time has been demonstrated (Jones et al., 2003).

Van der Kolk (1997) investigated the differences in recovering memories of traumatic experiences from recovering memories of significant but non-traumatic events. Non-

traumatic memory recall was associated with narratives and was without strong sensorial manifestation. In contrast, 78% of individuals questioned about traumatic memories from both childhood and adult traumas, initially reported not having any memory of the event and were unable to give an account of what happened. Regardless of the age at which the trauma occurred, all individuals stated that they initially "remembered" the trauma in the form of sensorial flashbacks, such as visual, olfactory, affective, or auditory impressions, with the awareness and capacity to describe what actually happened developing over time. This study demonstrated the key distinction between the recovery of the traumatic and emotional events was the relative absence of any narrative expression of the traumatic memory.

Functional neuroimaging studies suggest that explicit retrieval is preferentially associated with increased activity in prefrontal and medial temporal regions (Schacter et al., 1998), and the phenomenological awareness that accompanies episodic memories may arise within the hippocampal-frontal memory system. This information has to be bound together to be retrievable as a conscious memory, and the hippocampus is critical to this binding function (Verfaellie et al., 1997). Studies point to an important distinction between hippocampally-dependent and non hippocampally-dependent forms of memory that are affected differently by extreme stress (Brewin et al., 2001; 2003). One form, termed verbally accessible memory (VAM) supports ordinary autobiographical memories that can be modified and interact with other autobiographical knowledge, so that the trauma is represented within a personal context comprising past, present, and future. These traumatic memories are influenced by information that the individual has encoded before, during, and after the traumatic event, and that received sufficient conscious processing to be transferred to long-term memory in a form that can explicitly retrieved and verbally communicated. Another form, termed situationally accessible memory (SAM), contains information that has been obtained from lower-level perceptual processing of the traumatic scene (e.g. visuospatial information that has received little conscious processing) (Hellawell et al., 2002) and from the person's bodily (e.g. autonomic, motor) responses. This form of memory is consistent with the phenomenon of trauma-related 'flashbacks' that are a characteristic of severely traumatized people. Because SAMs do not involve verbal representations, these memories are difficult to communicate and may not therefore interact with other autobiographical knowledge. During periods of intense emotion, reduction of hippocampally-dependent processing of information and formation of SAMs may result in increased probability of amygdala reactivity to trauma reminders and the person experiencing a sense of current threat. A longitudinal study (Peace et al., 2004) of the reliability of memories for trauma and other emotional experiences, demonstrated that traumatic memory imagery tended to persist with no apparent decrement, whereas emotional memories were subject to considerable distortion over time. The findings converge on the non-hippocampally dependent nature of traumatic memories, and suggest a tendency of these memories to resist change with the passage of time. Nevertheless, it is clear that that at any time multiple memory systems are activated simultaneously and in parallel and findings suggest that these systems may interact (Poldrack et al., 2003; McDonald et al., 2004). One treatment study, using an exposure and cognitive restructuring process, suggest an interaction between SAM and VAM systems (Peres et al., 2007).

Clinical observation indicates that the narrative organization of mnemonic content, will assist its permeability to change. If an event, once charged with emotions, can be integrated into an individual's autobiographical memory, it tends not to be available anymore as a

separate and immutable entity. The memory becomes modified by associated experiences, emotional context and a state of consciousness during the recall process (Peres et al., 2005). Breuer and Freud asserted that bringing early traumatic material to consciousness would allow "abreaction" and quick remission of symptoms, with psychotheraputic approaches favouring the retrieving the mis-stored memory and integrating this memory with narratives. This re-working consisted of building cross-links between the traumatic memory and other memories and thoughts, believed to reintegrate the isolated traumatic memory into "normal" memory systems (Freud, 1895).

3.1.2 Implications of neuroimaging findings in psychotherapeutic treatment: The challenge of integration

Questions concerning the neurobiological effects of psychotherapeutic interventions are now given considerable importance within the field of psychiatry and psychology. Neuroimaging studies have provided evidence for changes in cerebral dynamics after pharmacotherapy or psychotherapy (Peres et al., 2008; Rybakowski, 2002). PET, ERP and fMRI studies have provided substantial evidence that cognitive and behavioural changes that occurred within a psychotherapeutic context can cause alterations in the regional cerebral metabolism of patients with obsessive-compulsive disorders (Schawartz et al., 1996), major depression (Brody et al., 2001), as well as in patients with social phobia (Furmark et al., 2002) and specific phobia (Paquette et al., 2003). The findings suggest that the psychotherapeutic interventions have the potential to modify dysfunctional neural circuits associated with the disorders studied (Roffman et al., 2005).

Psychological treatments are presently considered the first-line intervention of choice for sufferers of traumatic memories with PTSD (Foa et al., 2000). According to the Expert Consensus Guideline Series for treatment of PTSD (1999), exposure-based therapy was indicated as a psychological treatment of choice for flashbacks, intrusive thoughts, trauma-related fears, and avoidance. All of the multicomponent treatments that include cognitive interventions have exposure as one of their key elements (Levin et al., 1999; Marks et al., 1998; Peres et al., 2007; 2011). In fact, revisiting traumatic memories can bring therapeutic benefits, as long as a well-structured process of restructuring of the emotional content is employed (Littrell, 1998).

Ehlers and colleagues (2002) evaluated the quality and content of memories of individuals that had been through different traumatic experiences. The authors emphasized the importance of identifying, the moment of greatest emotional salience, so that associations and patterns of arousal established at that moment could be reprocessed. Conscious attention to unfolding events is likely to result in richer VAM representations, and theoretically, sustained attention to flashbacks may promote information transfer between these systems, leading more rapidly to amygdala inhibition (Brewin et al., 2003; 2005). Therefore, it is reasonable to postulate that well designed exposure and cognitive restructuring psychotherapies may enable the critical translation of the fragmented sensory elements of the traumatic memories into a more integrated, narrative representation of the memory (Peres., 2007). In this respect, psychotherapy should facilitate a new framing of the traumatic experience by reviving and strengthening memories of successful coping and self-effectiveness prior to the trauma. These memories, their respective emotional valences and states of consciousness, may be recognized and interconnected with the memory of the trauma during a restructuring session. We found that each time a patient narrated a

traumatic episode, the narrative could be structured with new cognitive and emotional elements extracted from reinforced memories of successful coping. Therefore, the reinterpretation and reconstruction of traumatic memories may lead to changes in neural networks involved, and relieve symptoms (Peres et al., 2007).

Increasingly, psychological interventions have focused on exposure-based therapies for cognitive restructuring of past events (Leskin et al., 1998), with the essential component of involving repeated exposure to memories of the traumatic stressor. Is should be noted, however, that confrontation with traumatic memories through debriefing has not been effective in treating individuals with PTSD (Marcks et al., 1998). Thus, confrontation of the memories does not appear to be sufficient to provide a therapeutic effect, but also requires the restructuring and integration of memories. A point worth noting is Breuer and Freud found prepsychoanalytic cathartic treatment alone generally ineffective, and the latter turned to a more narrative type of approach in transference based therapy (Freud et al., 1895). Moreover, we believe it is critical for narrative to involve the search for constructive lessons. Thus, psychotherapy will sensitize the traumatized individual's resilient traits by propitiating access to this repertoire from their pre-trauma life history. Good examples of successful coping by individuals who drew lessons from their traumatic experiences and so developed their resilience may be also provide models for trauma victims when developing new types of cognitive processing.

3.1.3 Memory reconstruction

There is consensus that emotionally-charged memories are not static, but rather, are interpretations, new reconstituted versions of the original event (Damasio., et al 2002). Loftus and colleagues (1999) observed the imprecise nature of remembering by examining the phenomenon of false memories. It has also been demonstrated that responses to traumas are guided by emotional beliefs, independently of the precision of the information (Peres et al., 2007; McNally et al., 2003). Thus, neuroscience findings provide crucial insight for psychotherapy, highlighting that emotionally-charged memories are peculiar representations of an event, distant from the original episode, but salient in their significance for the individual.

We postulate that the re-interpretation and reconstruction of traumatic memories can be used with exposure and cognitive restructuring psychotherapies, to alleviate some of the distressing symptoms of PTSD, by changing the nature of the representations of the traumatic event. It is therefore, crucial to consider that the most important modulators of the acquisition, formation, and evocation of traumatic memories are the emotions involved and the individuals' conscious access to the memories (Baddelev et al., 2000; Dolan et al., 2002). The retrieval of traumatic memories, whether spontaneous or provoked, occurs in an altered state of consciousness. Vermetten and Bremner (Vermetten et al., 2004) reviewed remarkable similarities in neuroimaging studies of traumatic recall and hypnotic processes. The same brain structures – thalamus, hippocampus, amygdala, medial prefrontal cortex, and anterior cingulate cortex – were involved in both research lines. We propose that therapeutic interventions focussing on emotions and the conscious processing of these events will modulate the memory for these events, effectively changing the interactions between underlying neural networks. It is argued that this shift of consciousness, will results in changes in the perception of the same event (Dietrich et al., 2003). Retrieval and interpretation of the original altered states of consciousness also permit the transformation

of "early" traumatic memory into "later" explicit memory (Brenneis et al., 1996). In accordance, Breuer suggested hypnosis might be useful to access and modulate that altered state of consciousness and remobilize memory systems for the purpose of cross linking them with narrative memory functions (Freud et al., 1895). Other work supports the idea that the use of altered states of consciousness can be an effective tool in the formation of new patterns of perception involving thought, feelings, and behaviour (Horowitz et al., 1972; Kasorow et al., 1999). By re-experiencing the trauma in different states of consciousness and, consequently, acquiring different perceptions of the same traumatic event, the individual may efficiently transfer information from the non-hippocampally-dependent memory store to the hippocampally-based memory system (Peres et al., 2007; Peres et al., 2005). In many cases, the trauma per se must be accessed before mourning can proceed. In this respect, Pierre Janet's hypnotherapy and its approach based on a dissociation model has been used satisfactorily for cases in which traumatic grief occurs when psychological trauma obstructs mourning (van der Hart et al., 1990).

Psychotherapy can be informed by the neuroimaging literature in relation to the difficulties PTSD patients have with processing both trauma-related and trauma-neutral information. The challenge is to be able to grasp the experience of an individual whose registration of the environment is fundamentally different from normal perception, and explore the attribution of meaning. Neuroimaging research highlights that a large component of a patient's cognitive and affective experience, has changed their capacity to create meaning and manage their perceptions of those experiences, particularly with regard to interpretations of their current environment. The challenge of the psychotherapy is to draw the patient out of this world by facilitating changes in perception and meaning.

When a traumatic memory can be reconstructed and reintegrated in this way, it loses intensity and evolves from a traumatic memory into an emotional one. Psychotherapy can facilitate the search for a narrative and integrated translation of the traumatic event, so the experience can be understood and conveyed in communicable language. We argue that psychotherapeutic interventions involving exposure and cognitive restructuring, and accommodating the altered states of consciousness during traumatic memory retrieval, will make an important contribution to the treatment of PTSD. Moreover, other psychotherapeutic strategies related to mirror neurons can offer a satisfactory outcome of traumatized people submitted to psychotherapy, as follows.

4. Mirror neurons

The mirror property of certain neurons was discovered at the University of Parma when science was once again helped by chance when Fogassi was in a laboratory, within the field of vision of a monkey subjected to a neurophysiological study, when he reached for a grape using a random gesture similar to one the monkey used to perform certain tasks. Fellow researchers observed that the same neurons in the monkey showed activation although it had not performed the motor task (Rizzolatti et al. 1996). After this surprising observation, neurophysiological research conducted by Rizzolatti and colleagues (2000; 2001) showed a class of visual-motor neurons in the monkey's premotor cortex, which were named mirror neurons. These neurons were activated when a particular action was performed or when the monkey observed a similar action being performed by another individual. Comparison between observing and performing an action involves not only the premotor cortex, but also

pathways extending to the posterior parietal lobe. The process of sensory-motor integration is supported by the frontal-parietal network, which provides an internal copy of actions observed as a means of explicitly generating the same actions. Based on these 1996 findings, European and American neuroscientists, by using different techniques in different laboratories, observed the presence of mirror properties in human neurons distributed in several other areas, such as Broca's region, which is related to verbal expression (Rizzolatti and Arbib, 1998; Rizzolatti and Craighero, 2004). Mirror neurons have been studied while subjects observe other individuals performing an action and while they themselves perform the same action, along with a number of other useful strategies. Iacoboni and colleagues (2005) conducted fMRI studies of 23 healthy individuals observing three types of visual stimuli: grasping actions without context; context itself (scenes containing objects); and grasping in two different contexts. In the last situation, the context suggested an intention associated with the action of holding or gripping something (drinking tea or cleaning a table). The actions inserted in context, compared with the two other tasks, produced a significant increase in activity in the posterior area of the lower frontal gyrus and the ventral premotor cortex. Discussion of the findings from neurofunctional studies, besides locating circuits associated with imitation and intention, has included theories of social cognition - how we interpret the world around us and therefore how we relate to events in our lives.

4.1 Mirroring and empathy

The mirror property was also observed in neurons involved in the task of simulating "mind reading". The theory of mind studies the ability to understand what is going on in other people's minds and is partly related to empathy (from the Greek empatheia, meaning 'to feel as if inside'). These neural substrata seem to facilitate certain aspects of the ability to represent other people's mental states through a conceptual system (Gallese and Goldman, 1998). Mirror neurons have been observed during cognitive processes such as social intersubjectivity, imitation, learning, empathy, and contagious behavior such as yawning or laughing (Hurley and Chater, 2005). Mirroring properties may well have been important filters or a selective mechanism for survival in our ancestral past when responding to conflict or fleeing from eminent threat. One school of thought in the neurosciences argues that mirror neurons probably influenced social skills, use of tools and language. We know that autistic individuals experience difficulty in grasping social plasticity, and this fact, together with the absence of substantive findings on the physiopathology of this disorder, plus recent findings relating to mirroring properties of certain neurons, has prompted specific research on autistic children such as Dapretto and colleagues (2006). It was found that normally developing children activated mirror neurons in the limbic system via the insula when the emotional significance of imitation was experienced and understood, but the same neural circuit was not activated in autistic children. Following these findings, further studies have suggested that autism is associated with altered neural activity patterns during imitation, which includes circuits integrating areas serving visual, proprioceptive, and emotional functions. Researchers have suggested that this deficient integration may impair social-cognitive functions in these individuals (Williams et al., 2006).

Many neuroscientists believe that mirror neurons dissolve the barrier between I and the other (Oberman et al., 2005). Singer and colleagues (2004) showed an interesting similarity in relation to the involvement of the insula, cingulate, thalamus, and cerebellum in the phenomenon of empathy. These areas were activated when an individual observes another

person feeling a painful stimulus. However, only structures involved in affective responses - rather than sensory circuits – were activated. The mirror properties of this circuit involve consciousness of the person's experiences and an emotional understanding of them, but not a precise sensory replica, since the observer does not experience the pain itself. Gallese (2006) reviewed that there was activation in the same circuits while experiencing comprehension of other people's emotions. In another fMRI study, the insula was activated when a subject experienced not only a basic emotion, such as the aversion caused by inhaling an odor, but also when the same subject visualized the face of another person feeling this aversion (Wicker et al, 2003). The wide range of neurofunctional research in humans (Peres and Nasello, 2008) means that neuroscience can now describe the activity of mirror neurons as a mechanism through which we experience empathy and recognize other individuals' intentions by observing their behavior, and mirroring this model when generating similar behavior.

4.2 Posttraumatic stress disorder, mirroring and psychotherapy

Our hypothesis is that psychotherapists may use mirror properties with PTSD patients by showing them behavioral paradigms based on individuals who successfully coped with similar traumas. On this basis, a new experimental design has been used in a recent fMRI study of traumatized individuals (Farrow et al., 2005). Thirteen patients were examined while performing three tasks that involved: (1) speculation as to another person's intention; (2) empathy; (3) decision to forgive other people; and each task was compared with the baseline involving social judgments. These PTSD individuals were subjected to a program based on behavioral therapy. Activation occurred in the same areas of the brain as those indicated in previous studies of healthy subjects, including activation in the left middle temporal as a response to empathy, and posterior cingulate in response to forgiveness decisions in post-therapy examinations. These areas were correlated with reduced PTSD symptoms. The authors suggest that time and therapy were probably the factors causing neural "normalization" in relation to these cognitive social tasks, for which PTSD individuals usually show limitations. Being able to understand other people's intentions while paying attention to their actions is a fundamental factor in social behavior. In fact, emotional numbing and social isolation are among the main PTSD symptoms (American Psychiatric Association, 1994).

Several studies have suggested that group therapy (or debriefing) is not appropriate for PTSD patients since they show no improvement, and symptoms get worse in some cases (Lewis, 2003). In the light of what we know of mirroring properties today, it is understandable that sharing painful experiences without positive models of successful coping may simply reflect and emphasize suffering instead of relieving it. On the other hand, groups such as Alcoholic Anonymous or Narcotics Anonymous bring together people seeking to end their dependency; they offer a new perspective by using repeated examples of other people coping successfully, and they have contributed to the recovery of these individuals (Vederhus and Kristensen, 2006).

Certain personality traits work to "protect" the individual during exposure to stressful events (Bonanno, 2004). One of them is self-confidence, which comprises three characteristic attitudes: the search for meaning or significance in everyday life; the notion that it is possible to affect the outcome of events; the belief that learning and development are a consequence of both positive and negative experiences. The decisive factor in developing

resilience is related to the way in which an individual perceives and processes experiences (Peres et al., 2005; 2007; 2011). Therefore sensitizing the reinforcement of resilient traits is an important aspect for psychotherapy of trauma victims, and mirror neurons may be involved in this process. Observation and simulation of coping behavior may provide individuals with models not previously apprehended by those who continue to show symptoms of the disorder, thus sensitizing their own experience of coping successfully. Although PTSD patients present a constellation of symptoms and frequently verbalize their inability to act differently, "observing" successful examples of dealing with trauma may sensitize their actions, since new behavioral paradigms may be "copied." An important element here is that psychotherapy for trauma victims should render the perception of new opportunities for generating adaptive behavior easier. In our experience, we noted that "visualizing a path in advance is a fundamental step toward taking it." However, the question is raised: is it really that simple?

The complexity of human processing obviously goes beyond simple conditioning. An important part of this process includes patients accessing their own repertories of resilient attitudes, which may reinforce strategies used in the past to overcome other difficulties experienced prior (as a child, teenager or adult) to the traumatic event (Peres et al., 2005; Peres et al., 2007). Some theories suggest that understanding others people's minds, especially their judgments and intentions, is a prerequisite for imitation and learning (Tomasello et al, 1993). Opposing this view, there is now a growing consensus among philosophers, psychologists, and neuroscientists in relation to the belief that imitation and learning are connected to perception of the other "like me" (Meltzoff, 2005). Meltzoff developed the idea that imitation and learning occur when three circumstances coincide: (1) the observer produces similar behavior to the model; (2) the perception of an action causes the observer's response; (3) equivalence between the actions of "I" and "other" plays a role in generating the response. In this respect, imitation is based on the repertoire of an observer, who identifies himself or herself with a model. Therefore, observation of examples of people who learned from their traumatic experiences and grew on that basis may occur once individuals have recognized their values, talents, and ability to recover but are still lacking a model to cope with the current trauma. In the same way that watching the behavior of professional tennis or soccer players, or any other sport, will not lead to an exact copy of their movements, but the basics may be incorporated in the observer's non-professional repertoire, examples of successfully coping will be superimposed on the treated individual's own models for coping. Internal representations of the body states associated with actions, emotions, and sensations are evoked within the observer, as if he/she would be doing a similar action or experiencing a similar emotion or sensation. Mirror neuron systems are likely to be the neural correlate of this mechanism. By means of a shared neural state realized in two different bodies, the "objectual other" becomes "another self" (Gallese, 2006). The search for therapeutic meaning through the construction of resilient narratives was correlated with higher prefrontal cortex activity and reduced PTSD symptoms (Peres et al., 2007). Therefore, it is crucial for patients to be aware that their capabilities, having been reinforced in advance, can be the basis for assimilating new specific examples of coping with trauma. In the context of exposure and cognitive restructuring therapy, films and overcoming reports may provide an opportunity to revise traumatic memories by incorporating other percepts based on healthy examples. Such cognitive faculty of

reinterpretation and reconstruction of emotionally charged memories may be used to good effect in exposure and cognitive restructuring therapy (Peres et al., 2007; 2011). Retrieving examples of individuals themselves being successful at other points in their lives, or highlighting other victims of psychological trauma who have managed to regain a satisfactory quality of life may ease therapeutic restructuring. Although the University of Parma monkey clearly identified with the Italian researcher's gesture, we are far from recognizing all the nuances of gestures and expressions humans derive from others and what they communicate. It is also important to remember that just as we observe and mirror the behavior of others, the same happens in relation those observing us. Our own examples of successful coping may increase awareness in our children, friends, patients, and colleagues. In this respect, Galileo Galilei left us a good example as inspiration for our "mirroring", when he said: "You cannot teach a man anything; you can only help him find it within himself." We would add that it is not a question of psychotherapists telling patients "how to do it" on an intellectual level, but rather stimulating their awareness in their ability to choose paths predictive of a better quality of life (Peres et al., 2005). We now illustrate a practical example of neuroimaging and psychotherapy integration for the benefit of traumatized patients.

5. Police officers under attack: Resilience implication of an fMRI study

For the first time, in 2011, it was possible to examine the neurofunctional reciprocities of a homogeneous set of traumatized individuals through control of complex variables (free of comorbidities and medications, no need for washout, same age of traumatic memory, same traumatic event also experienced by resilient individuals) in relation to coping (Group 1), continuity (Group 2) and spontaneous resilience to trauma (Group 3) (Peres et al., 2011). After psychotherapy, Group 1 was comparable to Group 3 resilient policemen in terms of symptom scores and neural expressions related to traumatic memory retrieval. The findings underline the importance of psychotherapy for shortening the period of suffering and/or avoiding symptoms becoming chronic – since Group 2 pPTSD policemen (not subjected to psychotherapy) continued to present the same symptoms with signs of worsening, whereas all those subjected to psychotherapy presented a reduction of at least 37% in total CAPS scores.

Evidence from neuroimaging research indicates that the PFC underlies many cognitive skills (Wood et al., 2003). Current and previous findings related to mPFC deactivation report that pPTSD and PTSD patients experience difficulty in activating this area, which is related to cognitive categorization and labeling of internal states (Peres et al., 2007; Shin et al., 2006). Higher brain regions such as the mPFC fail to diminish exaggerated arousal and distress symptoms mediated via the amygdala, and this may be related to the pathological responses found in psychologically traumatized victims (Peres et al., 2008). The hypothesis that primary pathology in PTSD may be amygdala hyper-responsivity rather than deficient mPFC suggests 'bottom-up' activation of the amygdala on the mPFC (Gilboa et al., 2004). Most neuroimaging studies of PTSD show reduced mPFC activity (Peres et al., 2007; Lanius et al., 2001), and some find increased amygdala activity during threat processing (Peres et al., 2008; Shin et al., 2006).

Integrating sensory traces of memories into structured therapeutic narratives is one of the main challenges for psychotherapies applied to trauma victims (Peres et al., 2008; Shin et al.,

2006), and pPTSD individuals require the same level of care (Carlier et al., 1995). Neural correlations with post-psychotherapy improvement were quite marked: as CAPS and narrative Traumatic Memory Inventory (TMI) scores improved, mPFC activation increased and amygdala activation decreased. Group 1's increased mPFC activation correlated with post-psychotherapy symptom improvement, which suggests that more active cognitive mPFC processing affected the resilience of pPTSD subjects. Because the PFC plays a major role in integrating cortical functioning and mediating perception and storage of memories in the cortical system, this region may be particularly important for processing traumatic memories and the subsequent development of PTSD symptoms (McFarlane et al., 2002).

Research has pointed to the nonverbal nature of traumatic memory recall in PTSD subjects, compared to a more verbal pattern of traumatic memory recall in healthy subjects (Lanius et al., 2004). Psychotherapy may help to build narratives and resilient integrated translations of fragmented traumatic memories via mPFC, and thus weaken their sensory content while strengthening them cognitively. We found that all three groups activated the mPFC while retrieving pleasant and neutral memories in the first and second scans, which suggests preservation of the declarative memory system in pPTSD subjects for non-traumatic events (Lanius et al., 2004; Peres et al., 2008). On the basis of our results for Group 1 and 2, we would postulate that diminished mPFC activity when processing stressor information during periods of intense emotional arousal heightens the probability of the amygdala being activated. It was interesting to note that increased mPFC activity was concomitant with less amygdala activity for a traumatic memory in both the "resilient" and "pPTSD after psychotherapy" groups.

The TMI scores showed that retrieval of memory of traumatic events was emotionally and sensorially less intense for Group 1 after psychotherapy. They were able to communicate their memories in a more structured narrative, like Group 3, which showed a well-defined narrative structure and low scores for sensory modalities of traumatic memory on both TMI measures. Unlike the psychotherapy group, in the second set of symptom measurements, Group 2 did not show significantly better scores in terms of psychological improvement and the sensory modalities of traumatic memory remained similar.

Previous research on correlations between CAPS and BOLD signals show that improvements in patients' symptoms were related to higher levels of PFC activity and less amygdala activity (Peres et al., 2008; Shin et al., 2006). The higher TMI narrative scores for the traumatic memory after psychotherapy were also correlated with higher levels of mPFC activity, strengthening the evidence for involvement of this region in the psychotherapy applied. The therapeutic effects may be largely due to extinction learning (Charney et al., 2004; Phelps et al., 2004), which builds a new response hierarchy and gradually replaces the previous association with fear. The similarities between Group 1 post-psychotherapy and Group 3 in relation to neural expression and symptom scores show that resilience can be developed and psychotherapy can affect this learning process.

Emotional flexibility is a critical mechanism underlying the ability of resilient people to successfully adapt to ever-changing environments (Bonanno, 2004; Block et al., 1996 Charney et al., 2004). Resilient police officers scored high on religiosity and two indicators of resilient coping were observed: seeking spiritual support and collaborative religious coping. This cognitive reserve related to supportive feelings may have influenced their resilient processing. Fear extinction is also mediated by inhibitory control of the mPFC over amygdala-based fear processes (Phelps et al., 2004) and exposure-based treatment of PTSD is thought to facilitate extinction learning (Shin et al., 2006; Charney et al., 2004) and therefore successful coping with trauma.

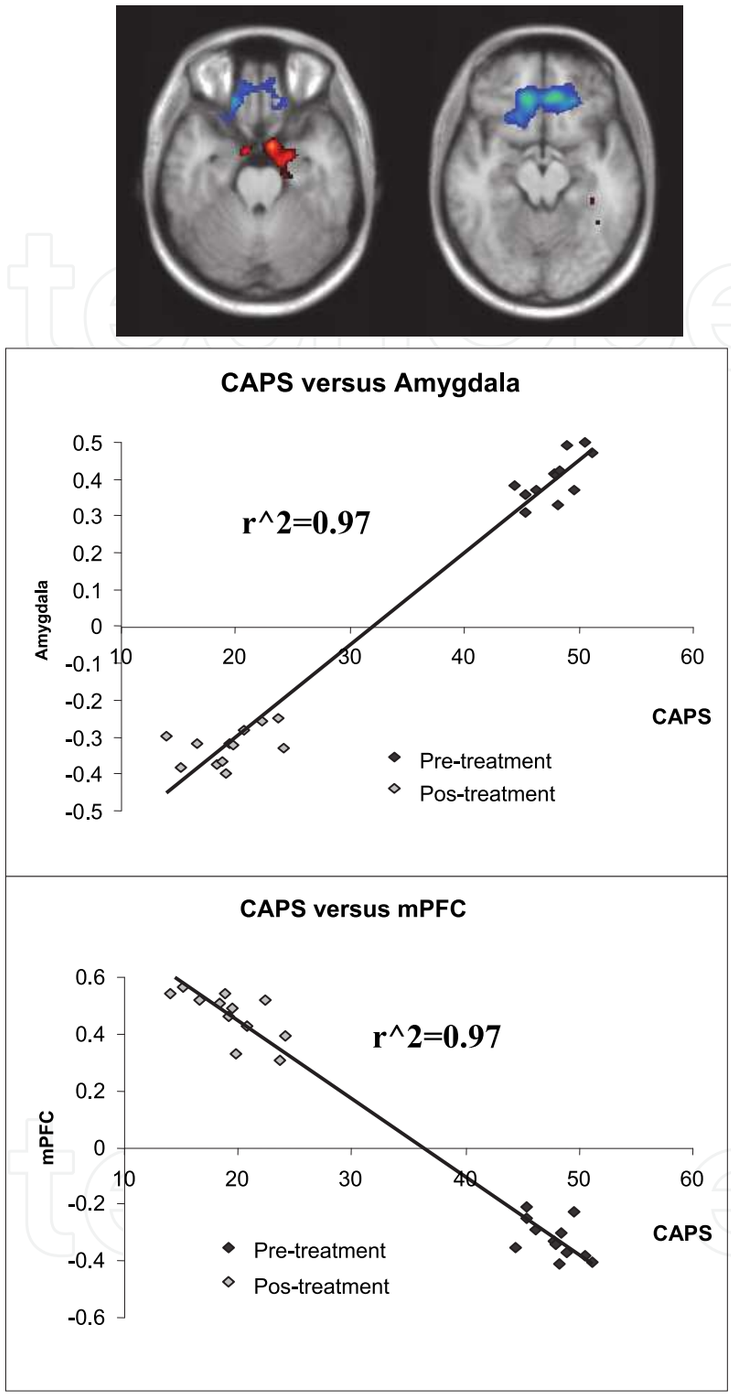

Fig.1. Correlation between changes in BOLD and changes in total severity of posttraumatic stress disorder (Clinician-Administered PTSD Scale, or CAPS) following ECRT. The functional maps display the areas where changes in BOLD activity in medial prefrontal cortex (mPFC) and amygdala correlated with changes in total CAPS score. The scatter plots display the direction of these correlations (increase in total CAPS on the horizontal axis, extent of BOLD activity on the vertical axis).

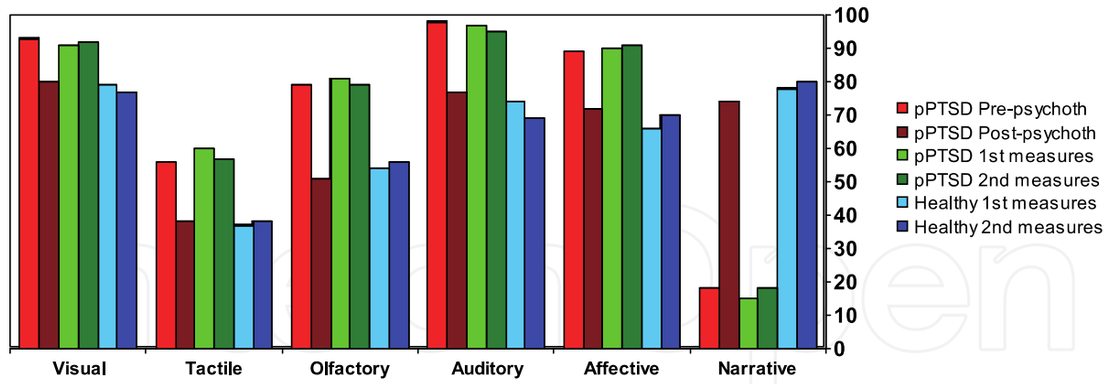

Fig.2. Memory modality and intensity scores of traumatic memory obtained after both fMRI scans for Group 1 (red), 2 (green) and 3 (blue). Traumatic memory was affectively and sensorially less intense, and narrative scores were higher for Group 1 after psychotherapy. The sensory, affective and narrative modalities of traumatic memory remained similar for Group 2 on first and second measures. Group 3 showed a well-defined narrative structure and low scores for sensory modalities of traumatic memory on both measures.

Several studies show greater suppression of cortisol release in PTSD individuals than in non-PTSDs (Yehuda et al., 1995 ; 1998; Grossman et al. 2003; Newport et al., 2004), supporting the hypothesis that PTSD is associated with enhanced negative feedback regulation of the hypothalamic-pituitary-adrenal (HPA) axis. Indeed, lower cortisol levels may also be a risk factor that affects peritraumatic reactivity and increases the likelihood of developing more pronounced PTSD symptoms (Yehuda et al., 1998; Delahanty et al., 2000). However, most studies have examined HPA axis alterations by comparing a sample of chronic, highly symptomatic PTSD patients with healthy controls (Yehuda et al., 1998; Grossman et al. 2003; Newport et al., 2004). Contrary to our hypothesis, the present study found that cortisol release was normal and as expected for the age group for both pPTSD and healthy police officers, which shows that non-chronic pPTSD police officers may not present an enhanced negative feedback regulation of the HPA axis, so a PTSD-risk factor may not be characterized if psychological assistance is provided promptly.

6. Conclusions

Psychotherapy appears efficacious in enabling sufferers of psychological trauma to better cope with the memories of their traumatic experience, with the reconstruction of the traumatic memories (Peres et al., 2007). Emotionally-charged memories are subjective representations of an event, often distorted and distant from the original episode, but salient in their significance to the individual (Creamer et al., 2005). Although there is a marked degree of inter individual variability in the processing of memory of life-events and basic emotions, we postulate that the re-interpretation and reconstruction of traumatic memories will be efficacious in relieving PTSD symptomatology. This process will influence the neural networks sub serving these experiences, leading to the formation of new memories that are less fragmented and available for narrative expression, an idea that is consistent with neuroimaging and clinical observations. Understanding the neural processes associated with successful response to psychotherapy may point to specific mechanisms that can be

modified to enhance treatment response. In accordance with previous studies (Felmingham et al., 2007; Bryant et al., 2008; Peres et al., 2007; 2011) mPFC has a key involvement in this learning process, and psychotherapy may influence the development of a more narrative pattern of trauma. Thus, the modulation of neural circuitry, involving PFC and the amygdalar complex, is a crucial aspect in the development of a psychotherapeutic approach which favours the search for narrative and integrative translations of the sensory fragmented traumatic memory. Words are the vehicles for the therapeutic process, which is related to the attribution of meanings to past events. Our data showed that the predictors of resilience were self-efficacy, empathy and optimism in addition to supportive feeling as traits that can boost resilient processing, therefore future research should address these cognitive strategies that contribute to better responses to psychotherapy (Peres et al., 2007; 2011). Further research is required for better understanding of mechanisms for processing traumatic experiences aligned with recovery in chronic PTSD samples and the same type of neuroimaging design looks promising. The work of building bridges between psychotherapy and neuroimaging must continue. Future multicentre studies addressing specific types of traumatic memories, and the age at which they were formed should be encouraged. The growing understanding of the neurobiology of emotionally-charged memories and their modulation may inform treatment of the victims of psychological trauma. Construction of coherent bridges between psychotherapy and neuroimaging must continue, in order that the two complementary and interdependent bodies of work can bring greater efficacy to the treatment of psychologically traumatized patients.

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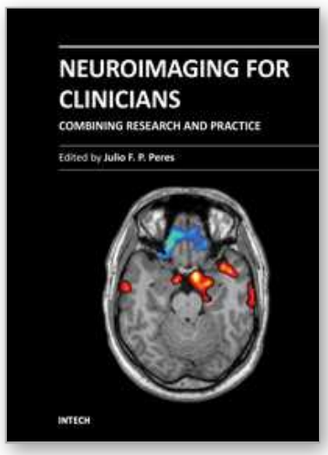

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Neuroimaging for clinicians sourced 19 chapters from some of the world's top brain-imaging researchers and clinicians to provide a timely review of the state of the art in neuroimaging, covering radiology, neurology, psychiatry, psychology, and geriatrics. Contributors from China, Brazil, France, Germany, Italy, Japan, Macedonia, Poland, Spain, South Africa, and the United States of America have collaborated enthusiastically and efficiently to create this reader-friendly but comprehensive work covering the diagnosis, pathophysiology, and effective treatment of several common health conditions, with many explanatory figures, tables and boxes to enhance legibility and make the book clinically useful. Countless hours have gone into writing these chapters, and our profound appreciation is in order for their consistent advice on the use of neuroimaging in diagnostic work-ups for conditions such as acute stroke, cell biology, ciliopathies, cognitive integration, dementia and other amnestic disorders, Post-Traumatic Stress Disorder, and many more

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