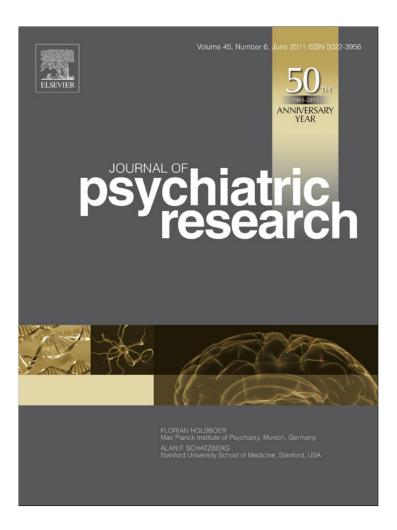
Provided for non-commercial research and education use. Not for reproduction, distribution or commercial use.



This article appeared in a journal published by Elsevier. The attached copy is furnished to the author for internal non-commercial research and education use, including for instruction at the authors institution and sharing with colleagues.

Other uses, including reproduction and distribution, or selling or licensing copies, or posting to personal, institutional or third party websites are prohibited.

In most cases authors are permitted to post their version of the article (e.g. in Word or Tex form) to their personal website or institutional repository. Authors requiring further information regarding Elsevier's archiving and manuscript policies are encouraged to visit:

http://www.elsevier.com/copyright

Journal of Psychiatric Research 45 (2011) 727-734



Contents lists available at ScienceDirect

Journal of Psychiatric Research



journal homepage: www.elsevier.com/locate/psychires

Police officers under attack: Resilience implications of an fMRI study

Julio F.P. Peres^{a,*}, Bernd Foerster^b, Leandro G. Santana^c, Mauricio Domingues Fereira^c, Antonia G. Nasello^d, Mariângela Savoia^d, Alexander Moreira-Almeida^e, Henrique Lederman^a

^a Department of Diagnostic Imaging – Radiologia Clinica Universidade Federal de Sao Paulo, Escola Paulista de Medicina, SP, Brazil ^b Philips Medical Systems, USA

^c Sao Paulo State Militarized Police Force, Brazil ^d Faculty of Medical Sciences, Santa Casa de Sao Paulo, Brazil

^e School of Medicine, Universidade Federal de Juiz de Fora, Minas Gerais, Brazil

ARTICLE INFO

Article history: Received 30 July 2010 Received in revised form 22 September 2010 Accepted 2 November 2010

Keywords: PTSD Police Psychotherapy Resilience Neuroimaging fMRI

ABSTRACT

Objective: Crime is now a top-priority public-health issue in many urban areas. Sao Paulo's state police force was the target of gunfire attack on an unprecedented scale. Several officers were killed or wounded, and many more were affected by psychological trauma. We investigated the brain activity underlying trauma, the coping effect of psychotherapy, and resilience in a highly homogenous sample that experienced the same traumatic event. The design applied was a between-group comparison of cerebral blood-oxygenation-level-dependent signals and symptom scores of police officers with and without partial Posttraumatic Stress Disorder (pPTSD).

Method: We used functional magnetic resonance imaging (fMRI) to investigate the retrieval of traumatic memories of 36 volunteers divided in three groups: (1) pPTSD policemen submitted to psychotherapy; (2) pPTSD policemen on the wait list; and (3) symptom-free (resilient) policemen. All participants were given a baseline fMRI scan and a follow-up scan some 40 days later. Not given psychotherapy, groups 2 and 3 were controls.

Results: Group 1 showed 37% fewer PTSD symptoms post-psychotherapy and their scores and neural expressions were comparable to Group 3 resilient policemen. A marked increased in medial prefrontal cortex (mPFC) activity was concomitant with decreased amygdala activity during traumatic memory retrieval in both resilient and pPTSD participants (after psychotherapy) and these findings were associated with symptom attenuation.

Conclusions: Our results provide neurophysiological evidence of resilience in a high-risk group for PTSD. 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.

© 2010 Elsevier Ltd. All rights reserved.

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). Lifetime prevalence of PTSDtriggering traumatic events may be as much as 50-90%, and actual

E-mail address: julioperes@yahoo.com (J.F.P. Peres).

prevalence in the general population is about 8% (Kessler et al., 1995; Vieweg et al., 2006), while partial PTSD (pPTSD) in an at-risk group exposed to combat such as Vietnam veterans has 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 sub-threshold PTSD was introduced to describe subsyndromal forms of PTSD (Blanchard et al., 1995; Stein et al., 1997).

Crime is now one of the most frequent causes of death in many countries. Coping with stressful and life-threatening situations is part of policing so officers are routinely exposed to critical-incident stressors in the line of duty. Although active policemen are understudied relative to other traumatized samples, this population may be critical to our understanding of responses to traumatic stressors

^{*} Corresponding author. Rua Maestro Cardim 887, Sao Paulo - SP, Brazil, Postal Code 01323-001, fax: +55 11 3284 8929.

^{0022-3956/\$ -} see front matter © 2010 Elsevier Ltd. All rights reserved. doi:10.1016/j.jpsychires.2010.11.004

(Kessler et al., 1995; Vieweg et al., 2006; Weiss et al., 1992). A criminal organization attacked the State of Sao Paulo Militarized Police Force on an unprecedented scale in the period May 12–23, 2006, and many officers were killed or wounded in firefights. Some were traumatized, while others remained symptom free.

Whether an event is traumatic or not will depend on an individual's perceptual neural-circuitry processing and underlying resilience, which is the ability to cope effectively and adapt in the face of loss, hardship or adversity (Bonanno, 2004; Block and Kremen, 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, 2004; Florian et al., 1995). Neuroscientists have yet to comprehensively research this field. 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), (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).

Two basic issues yet to be addressed are the reasons for most trauma survivors not developing PTSD and the predictors of positive outcomes in traumatized victims (Shin et al., 2005, 2006). All the police officers in our sample had come under fire and seen colleagues being shot, so our study offered a unique opportunity to investigate victims who were all affected by the same traumatic event, which they reported as watching wounded colleagues dying after pleading for help. The study controlled all five variables listed above and was conducted 3 months after the criminal attacks, so there was sufficient time for a confident diagnosis of PTSD. In order to address the object of the study – brain activity underlying trauma, psychotherapy effect and resilience – we used functional magnetic resonance imaging (fMRI) to detect alterations in brain activity related to overcoming trauma after psychotherapy.

Since we had screened for startle response and hypervigilance (Fig. 1) as prevalent symptoms, we hypothesized that pPTSD policemen would present an exaggerated amygdala response pattern (Bremner, 2003) during traumatic memory retrieval prior to psychotherapy. On the other hand, we predicted that resilient policemen and pPTSD policemen would show increased PFC activation after psychotherapy. Based on studies that have suggested that lower cortisol levels in traumatized victims and combat veterans (Yehuda et al., 1995) pose a risk factor for PTSD, we hypothesized that

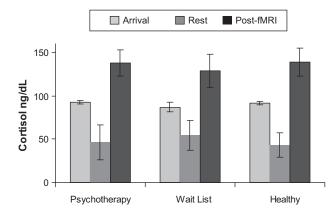


Fig. 1. Samples of saliva cortisol were collected using the non-invasive Salivette-Sarstedt method on three occasions: (i) on arrival at the neuroimaging center (ii) after 30 min in repose, and (iii) 15 min after concluding the fMRI scan. All salivary samples were obtained from 6pm to 8pm.

pPTSD policemen would present lower cortisol levels than healthy (symptom-free) policemen.

2. Methods

2.1. Participants

We initially examined 97 police officers, all targeted in the wave of gunfire attacks prior to the study, of whom 29.6% developed pPTSD. Twenty-four of them with pPTSD and 12 healthy (resilient) men were randomly selected for the study. All 36 policemen studied (mean age 28.2, SD = 3.2) were free of comorbidities; there were no differences in recency of the stressor and all had experienced the same event, which caused trauma for some, but not others (Table 1). According to Blanchard et al. (1995) and Stein et al. (1997) we considered pPTSD subjects as those who presented fewer than the required number of DSM-IV criterion B, or C or D symptoms for full PTSD. The pPTSD individuals selected for the study did not present symptoms in the

Table 1

Demographic characteristics of the 36 policemen.

	pPTSD Psychotherapy group $(n = 12)$		Healthy group $(n = 12)$		
Gender (male/female)	12/0	12/0	12/0		
Cerebral dominance (right/non-right)	12/0	12/0	12/0		
Marital status (single/married)	8/4	5/7	6/6		
Age subjects	31.2/5.8/	27.6/3.9/	28.2/7.8/		
(years/months) (mean/SD/range)	24-36	23-31	25-38		
Comorbidities (with/ without)	0/12	0/12	0/12		
Psychotropic medication (with/without)	0/12	0/12	0/12		
Age of memories (months/days)	3.5	3.10	3.15		
Education (secondary school/university)	12/0	12/0	12/0		
Type of trauma (criminal attack/others)	12/0	12/0	12/0		
Previous traumatic events scoring over 10 (Impact Event Scale)	0	0	0		

Summary of demographic characteristics of all pPTSD subjects (24) and healthy subjects (12). SD, Standard deviation.

avoidance and numbing cluster of the Clinician Administered PTSD Scale for DSM-IV (CAPS; Blake et al., 1990), but did present re-experiencing and hyperarousal clusters. In the present study specifically, pPTSD subjects had the same recurrent traumatic memories (criterion B), hypervigilance and exaggerated startle response (criterion D) as prevalent symptoms, but presented sub-threshold symptoms for criterion C - numbing of general responsiveness - thus not meeting full DSM-IV criteria for PTSD. Police officers with dissociative expression (criterion C) – which is an important confounding variable found in neuroimaging studies of PTSD patients (Shin et al., 2005, 2006; Peres et al., 2008) – were excluded. Moreover, to test whether volunteers' responses were dissociative or hypervigilant, and to ensure sample homogeneity (Griffin et al., 1997; Lanius et al., 2002, 2006), we monitored heart rate before the study and during fMRI scans, as well as saliva cortisol expression, since its measures differed significantly in its relationship to dissociation versus hypervigilant PTSD subjects (Simeon et al., 2008) (Fig. 1). Samples of saliva cortisol were collected using the non-invasive Salivette-Sarstedt method (Kirschbaum and Hellhammer, 1994; Poll et al., 2007). Only hyperresponsive volunteers were selected for the study. After giving informed written consent, subjects were divided in three groups: (1) pPTSD policemen subjected to Exposure and Cognitive Restructuring Therapy (ECRT; Marks et al., 1998), (2) pPTSD policemen not yet subjected to psychotherapy (wait-list), and (3) healthy (resilient) policemen.

2.2. Symptom measures

Two blinded researchers examined the three groups before the first and after the second fMRI scan. The Structured Clinical Interview from DSM IV (SCID; First et al., 1995) and the Clinician-Administered PTSD Scale (CAPS; Blake et al., 1990) were applied to all participants. In addition, the following standardized evaluations were self-administered after each fMRI scan: the Beck Depression Inventory (Beck et al., 1961), the Beck Anxiety Inventory (Beck et al., 1988), and Impact of Event Scale (Horowitz et al., 1979), Dissociative Experiences Scale (Fiszman et al., 2004) and Resilience Quotient Test (Reivich and Shatte, 2002/validated by Barbosa, 2006). Because most participants reported that spirituality/religiousness was an important factor in their lives we also used the Brief Religious Coping (RCOPE; Pargament et al., 2000) and Duke Religious Index (DUREL; Koenig et al., 1997).

2.3. Sensory modalities of traumatic memories

The Traumatic Memory Inventory (TMI; Hopper and van der Kolk, 2001) was used to evaluate and classify the basic characteristics of traumatic, pleasant and neutral memories. This inventory evaluates the intensity and vivacity of five modalities of traumatic memory (visual, affective, tactile, olfactory, auditory, and narrative), and may be used to assess their evolution over time. Thus, pPTSD subjects underwent the same type of assessment prior to treatment as a baseline control condition, and following ECRT as a post-treatment condition. Policemen in control groups 2 and 3 were administered the TMI twice in forty days.

2.4. Standardizing the stressor event and activation paradigm

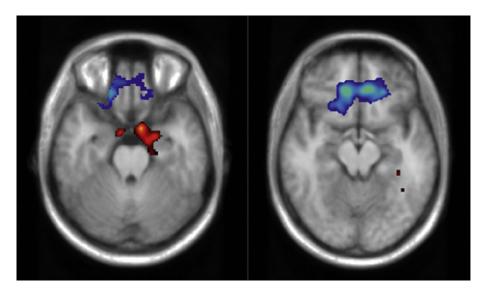
The policemen taking part were all officers involved in deadly shooting incidents during the concerted wave of attacks, for whom this was the stressor event of major emotional impact (Table 1). When interviewed, they unanimously referred to the particular events they described as the most traumatic: seeing wounded colleagues pleading for help, or even dying, during the firefights. A real-life recording of policemen under fire followed by death was used as paradigm to evoke the traumatic memory. The policemen selected for the study were those who, on listening to this stimulus, presented faster heart rates (adrenergic response) rather than lower ones (dissociative response) varying 20% or more from their baseline rates. All the policemen had a repertoire of pleasant memories on a beach and neutral memories of an off-the-air television. White noise (like an off-the-air television) and the sound of waves on a beach with similar frequencies to the traumatic-event recording (500–100,000 Hz) were used as neutral and pleasant stimuli respectively. The frequencies of all auditory paradigms (neutral, pleasant and traumatic) were also matched. All three memories were from the same period as the traumatic episode which occurred 3 months prior to the study.

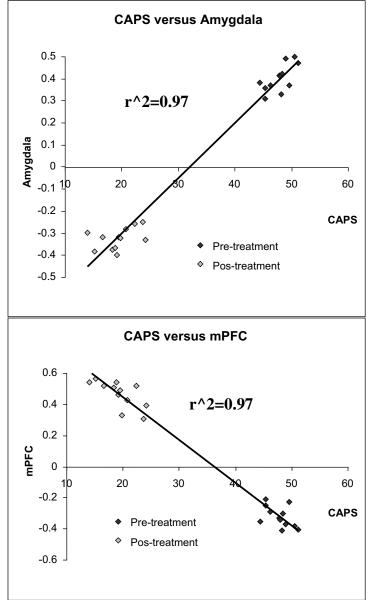
2.5. Psychological rehabilitation program

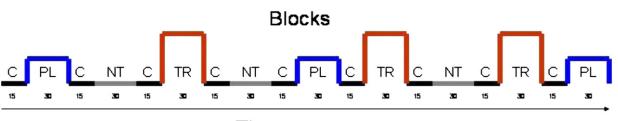
Exposure-based therapy and cognitive restructuring (ETCR) led to PTSD patients showing marked improvements that were stable over time (Marks et al., 1998; Peres et al., 2007; Bryant et al., 2008). Exposure-based therapy in particular is often indicated as the psychological treatment of choice for patients with traumatic memories (Weiss et al., 1992; Bonanno, 2004; Peres et al., 2008). Our research team had applied the ETCR procedure as standard treatment for trauma victims, which helped them attain psychological growth on the basis of their negative experiences (Peres et al., 2007). The police force's Social and Legal Assistance Center issued mental health rehabilitation guidelines for policemen involved in life-threatening incidents based on psychological assessments of officers involved in any incident that causes or may cause psychological trauma. Its 28-day multidisciplinary psychological rehabilitation program involves ETCR groups (Marks et al., 1998; Peres et al., 2007), art therapy and ecological walks.

2.6. Neuroimaging design

Three months after the traumatic event, we assessed the neural mechanisms underpinning the psychological process related to coping with trauma, as well as predictors of resilience, using fMRI adapted for an acoustic-cue paradigm, with two scans interspaced 40-days. Recall or retrieval was cued by three types of memories: (a) pleasant (soothing ocean-beach noise); (b) neutral (white noise from an off-the-air TV station); and (c) traumatic (real-life recording of gunfire during the wave of attacks). Group 1 was given its baseline fMRI scan with a follow-up scan after the ETCR. Control groups 2 and 3 were given baseline and follow-up scans but not therapeutic procedures. Altered hemodynamic responses - bloodoxygenation-level-dependent (BOLD) - were measured while reliving the traumatic memory recall (TR), the pleasant memory (PL) and the neutral noise (NT). Conditions TR, PL and NT were combined three times in an acquisition series. Participants were subjected to a single period of acquisition totaling 6 min and 45 s. Each series included three 30-s blocks. During both fMRI scans, participants were asked to evoke their traumatic, pleasant and neutral memories while three recordings were played through ear phones. They were asked to lie down, be still, breathe through the nose, and recall sensations and emotions associated with the traumatic and pleasant memories as vividly as possible. The block sequence was organized in random order and balanced across participants. Blocks were separated by a 15-s period as a distinct cognitive task for emotional separation from the next memory task, while participants listened and mentally ran through a countdown from 15 to 1 (Condition C). This design enabled us to examine BOLD signals related to traumatic memory in both traumatized and resilient police officers, and to discuss the clinical implications of the findings for resilience.







Time (seconds)

2.7. fMRI procedures and data analysis

FMRI data were obtained using a clinical 1.5 T MR scanner, Achieva Pulsar, Philips Medical Systems. Images were acquired with fat saturated Echo Planar Imaging (TE/TR = 50/3000 ms) in oblique axial direction (29 slices, 4 mm slice thickness, 0.5 mm gap, 96 \times 96 matrix size with a quadratic field of view of 230 mm resulting in 2.4 mm inplane resolution). T1-weighted anatomic images were obtained with a 3D TFE technique (TE/TR = 5.1/25 ms, $0.76 \times 0.76 \times 1.6$ mm³ spatial resolution). BOLD data were preprocessed and statistically analyzed using the statistical parametric mapping package SPM2, Welcome Department of Cognitive Neurology. Images were realigned for motion correction, normalized to Talairach coordinates and spatially smoothed using a 5-mm Gaussian kernel. A voxel-by-voxel statistical analysis was applied to the data, using a general linear model and block designs. Analysis included a temporal highpass filter (128 s cutoff period), a voxel threshold of P = 0.005 and a cluster threshold (corrected for multiple comparisons) Pcor = 0.05; only clusters larger than 600 mm³ were considered significant. Multiple comparison correction was performed by taking corrected p-values obtained from analysis using the SPM2 software package, which implements random-field-theory based algorithm correction (Nichols and Hayasaka, 2003). Activation patterns were overlaid on the subject's T1 structure. We used region-of-interest (ROI) analyses for orbitofrontal and prefrontal cortex, anterior cingulate cortex, insula, thalamus, amygdala, hippocampus, and parietal lobes to test our a priori hypotheses. ROIs were defined by the automated anatomical labeling masks (Tzourio-Mazoyer et al., 2002). The statistical thresholds employed were p < 0.05 (small volume corrected) for ROI analyses and p < 0.001 for whole-brain analyses. BOLD signal change was correlated with change in total CAPS score from before to after treatment, and the statistical threshold for this analysis was p < 0.01.

2.8. Correlation analysis

Pearson correlations were generated to assess the association between variations in BOLD signals of the group subjected to psychotherapy. Significance tests for the correlations were limited to the ROI structures, since these were the areas that would most likely interact with each other during the pleasant, neutral and traumatic memory retrievals. Given the sample size, all results were confirmed using Spearman Rank correlations, which were also performed between the CAPS score and percentage change in BOLD responses for relevant ROI in the psychotherapy group. Since results for both methods were similar, only Pearson correlations have been shown. In order to calculate the sample correlation coefficient (Pearson product—moment correlation coefficient) we used the equation below:

$$r = \frac{\sum X^* Y - \frac{\sum X^* \sum Y}{N}}{\sqrt{\left(\sum X^2 - \frac{(\sum X)^2}{N}\right)^* \left(\sum Y^2 - \frac{(\sum Y)^2}{N}\right)}}$$

3. Results

Overall, results showed that pPTSD participants (Group 1 and 2) had markedly higher levels of left-amygdala activity (Talairach -17/-6/-23, T-score = 3.4, Pcorr<0.001, voxels = 681) and decreased activity in mPFC ($\pm 10/36/-15$, T-score = -4.8, Pcorr<0.001, voxels = 1945) during traumatic memory retrieval in the first fMRI (Fig. 2). Again, increased left-amygdala activity (-17/-6/-23, Tscore = 3.4, Pcorr<0.001, voxels = 576) (Fig. 2) and decreased mPFC activity ($\pm 10/36/-15$, T-score = -4.8, Pcorr<0.001, voxels = 1623) were observed in the second fMRI of Group 2. In contrast, the mPFC BOLD response to traumatic memory retrieval was significantly greater for Group 1 than for Group 2 in the second fMRI (*P < 0.05, two-sample t test corrected for multiple comparisons), and Group-1 activation was significantly lower (more so after psychotherapy than before it) in the left amygdala (-17/-6/-23, T-score = 3.4,Pcorr < 0.001, voxels = 92). In the second fMRI, Groups 1 and 3 both showed less left-amygdala activity (-17/-6/-23, T-score = 3.4, Pcorr<0.001, voxels = 232) and increased mPFC activity ($\pm 10/36/-15$, Tscore = -4.8, Pcorr < 0.001, voxels = 1852). Differences between Group 3's first and second scans did not reach significance, which was to be expected for the resilient control group. In the same ROI, we found that all three groups activated the mPFC when retrieving pleasant memories in the first and second scans.

Whole-brain analysis and other ROIs such as anterior cingulate and insula showed no statistically significant differences. In all three groups (2 pPTSD and 1symptom-free), we observed normal release of cortisol (92.7 ng/dL, SD = 4.2) as expected for their age group and time of day. For all conditions (exept induced relaxation – condition II) the normal reference value ranges from 70 ng/dL to 170 ng/dL for the time of day when salivary samples were obtained – 6pm to 8pm (Fig. 1).

Groups 1 and 2 showed similar symptom scores on initial measures [48 ± 3.62 and 46 ± 2.70 (CAPS), 38 ± 2.63 and 35 ± 3.12 (IES), 13 ± 5.35 and 15 ± 6.45 (BDI) and 28 ± 2.54 and 31 ± 3.44 (BAI)]. Only the Group 1 subjects showed a fall of 37% or more in total CAPS score post-psychotherapy, and we also observed significant improvements in symptoms on their second measures [19 ± 5.03, p = 0.03 (CAPS), 10 ± 2.97, p = 0.04 (IES), and 11 ± 2.03, p = 0.05 (BAI)] compared with their first, whereas Group 2 showed no significant changes in its scores on the second set of measures compared with the first [46 ± 2.70 and 49 ± 4.82, p = 0.19 (CAPS),

Fig. 2. 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).

Table 2	
Inventory scores of psychotherapy and control	a

inventory scores of psychotherapy and control groups.					
pPTSD psychotherapy					
	Pre-psychotherapy	Post-psychotherapy	Significance		
CAPS	48 ± 3.62	19 ± 5.03	0.03		
IES	38 ± 2.63	10 ± 2.97	0.04		
BDI	13 ± 5.35	7 ± 3.09	0.18		
BAI	28 ± 2.54	11 ± 2.03	0.05		
pPTSD wait-list group					
	1st Measures	2nd Measures	Significance		
CAPS	43 ± 4.82	46 ± 2.70	0.19		
IES	32 ± 5.64	35 ± 3.12	0.16		
BDI	16 ± 5.61	15 ± 6.45	0.21		
BAI	29 ± 5.10	31 ± 3.44	0.09		
Healthy control group					
	1st Measures	2nd Measures	Significance		
CAPS	12 ± 6.83	14 ± 5.71	0.23		
IES	9 ± 4.47	7 ± 7.92	0.32		
BDI	6 ± 6.15	7 ± 5.33	0.29		
BAI	12 ± 3.11	10 ± 4.41	0.25		

Psychotherapy treatment response characteristics (mean \pm S.D.) (paired *t*-tests) and control groups characteristics (mean \pm S.D.) (paired *t*-tests) interspaced 40 days for the Clinician Administered PTSD Scale (CAPS), the Impact of Event Scale (IES), the Beck Depression Inventory (BDI), and the Beck Anxiety Inventory (BAI).

35 ± 3.12 and 37 ± 5.64, p = 0.16 (IES), 31 ± 3.44 and 32 ± 5.10, p = 0.09 (BAI)]. After psychotherapy, Group 1 and 3 symptom scores were comparable [19 ± 5.03 and 14 ± 5.71 (CAPS), 10 ± 2.97 and 7 ± 7.92 (IES), 11 ± 2.03 and 10 ± 4.41 (BAI)]. Group 3 scores did not show significant changes compared to the first and second measurements [12 ± 6.83 and 14 ± 5.71, p = 0.23 (CAPS), 9 ± 4.47 and 7 ± 7.92, p = 0.32 (IES), 12 ± 3.11 and 10 ± 4.41, p = 0.25 (BAI)]. Group 1's post-psychotherapy IES scores (10 ± 2.97) showed the traumatic event causing less impact than previously (38 ± 2.63), and coincided approximately with Group 3 (healthy) IES scores (9 ± 4.47) (Table 2).

Group 3's most salient resilience traits were self-efficacy (p = 0.05), empathy (p = 0.04) and optimism (p = 0.05). In relation to religiosity, the resilient group's scores showed significant prominence of intrinsic religiosity (p = 0.02) as posited by DUREL, and two main factors of positive religious coping with major life stressors shown by the RCOPE: (1) "I sought God's love and care" (seeking spiritual support) (p = 0.05) and (2) "I tried to put my plans into action together with God" (collaborative religious coping) (p = 0.04).

Pearson's correlation coefficients were used to test correlation between mPFC/amygdala activities and symptom scores. All correlations are reported for two-tailed p < 0.05. Only Group 1 showed a positive correlation between change in total CAPS score and change in mPFC activity ($\pm 10/36/-15$) from pre- to post-psychotherapy (r = 0.82, p = 0.02). There was also a significant positive correlation between mPFC and post-psychotherapy narrative TMI scores (r = 0.81, p = 0.03). A negative correlation was found between left-amygdala activation (-17/-6/-23) and change in total CAPS score from pre- to post-psychotherapy (r = 0.86, p = 0.04).

4. Discussion

For the first time, 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). After psychotherapy, Group 1 was comparable to Group 3 resilient policemen in terms of symptom scores and neural expressions related to traumatic memory retrieval. These 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 and Grafman, 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

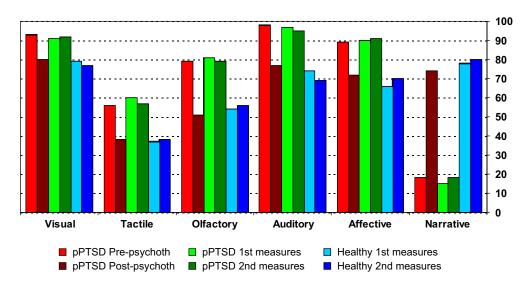


Fig. 3. Memory modality and intensity scores of traumatic memory obtained after both fMRI scans for Group 1 (red), 2 (green) and 3 (blue). Traumatic memory was affectively and sensorially less intense, and narrative scores were higher for Group 1 after psychotherapy. The sensory, affective and narrative 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.

the mPFC (Gilboa et al., 2004). Most neuroimaging studies of PTSD show reduced mPFC activity (Peres et al., 2005, 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., 2005, 2008; Shin et al., 2006), and pPTSD individuals require the same level of care (Carlier and Gersons, 1995). Neural correlations with post-psychotherapy improvement were quite marked: as CAPS and narrative TMI scores improved, mPFC activation increased and amygdala activation decreased. Group 1's increased mPFC activation correlated with postpsychotherapy 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 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 (Fig. 3). 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 (Fig. 3). Unlike the psychotherapy group, in the second set of symptom measurements, Group 2 did not show significantly better scores in terms of psychological improvement (Table 2) and the sensory modalities of traumatic memory remained similar (Fig. 3).

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 (Fig. 3) 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 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 and Kremen, 1996 Charney 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 2004) and therefore successful coping with trauma.

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 (Fig. 1), 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.

5. Conclusion

Finally, police officers are for the most part medically healthy and psychologically resilient (Neylan et al., 2005) and our findings considerably advance knowledge of the neural underpinnings of resilience, which may be learned via psychotherapy. 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) our data showed that mPFC has a key involvement in this learning process, and ECRT may influence the development of a more narrative pattern of trauma. Our sample was highly homogenous and all members experienced exactly the same traumatic event, which may well have influenced our neural substrate findings being more precise than those reported by previous studies. In particular, mPFC played a critical role in the regulation of the amygdalar complex, which strengthens the evidence for this directionality in successful coping processes.

Words are the vehicles for the therapeutic process, which is related to the attribution of meanings to past events (Peres et al., 2005). 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.

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. Together these two complementary and interdependent approaches may lead to more efficacious treatment of psychologically traumatized people.

Role of funding source

The present study did not receive any funding source and was developed with the collaboration of the authors.

Conflict of interest

None.

Acknowledgments

We thank Lisa Shin, PhD and Alexander McFarlane, MD, PhD for helpful comments on an earlier version of the manuscript, and the Psychologists Anderson Xavier, Gislaine Gil and Juliana de Resende Fonseca for they work as assistant.

References

- Barbosa GS. Validação e Aplicação do Questionário do Índice de Resiliência: Adulto Reivich-Shatté [Validation and application of the Reivich-Shatté Adult Resilience Index]. Doctoral thesis of the Clinical Psychology postgraduate program at PUC-SP, Brazil 2006.
- Beck AT, Epstein N, Brown G. An inventory for measuring clinical anxiety: psychometric properties. Journal of Consulting and Clinical Psychology 1988;56:893-7.
- Beck AT, Ward CH, Mendelson M, Mock JE, Erbaugh JK. An inventory for measuring depression. Archives of General Psychiatry 1961;4:561–71.
 Blake D, Weathers F, Nagy D, Kaloupek G, Klauminzer D, Charney D, et al. Clinician-
- Blake D, Weathers F, Nagy D, Kaloupek G, Klauminzer D, Charney D, et al. Clinician-Administered PTSD Scale (CAPS). Boston MA: National Center for Post-Traumatic Stress Disorder, Behavioural Science Division Boston-VA; 1990.
- Blanchard EB, Hickling EJ, Vollmer AJ, Loos WR, Buckley TC, Jaccard JJ. Short-term follow-up of post-traumatic stress symptoms in motor vehicle accident victims. Behaviour Research and Therapy 1995;33:369–77.
- Block J, Kremen AM. IQ and ego-resiliency: conceptual and empirical connections and separateness. Journal of Personality and Social Psychology 1996;70(2):349–61.
- Bonanno GA. Loss, trauma, and human resilience: have we underestimated the human capacity to thrive after extremely aversive events? American Psychology 2004;59(1):20–8.
- Bremner JD. Functional neuroanatomical correlates of traumatic stress revisited 7 years later, this time with data. Psychopharmacology Bulletin 2003;37:6–27.
- Bryant RA, Felmingham K, Kemp A, Das P, Hughes G, Peduto A, et al. Amygdala and ventral anterior cingulate activation predicts treatment response to cognitive behaviour therapy for post-traumatic stress disorder. Psychological Medicine 2008;38(4):555–61.
- Carlier IV, Gersons BP. Partial posttraumatic stress disorder (PTSD): the issue of psychological scars and the ocurrence of PTSD symptoms. The Journal of Nervous and Mental Disease 1995;183(2):107–9.
- Charney DS. Psychobiological mechanisms of resilience and vulnerability: implications for successful adaptation to extreme stress. American Journal of Psychiatry 2004;161(2):195–216.
- Psychiatry 2004;161(2):195–216. Delahanty DL, Raimonde AJ, Spoonster E. Initial posttraumatic urinary cortisol levels predict subsequent PTSD symptoms in motor vehicle accident victims. Biological Psychiatry 2000;48(9):940–7.
- Felmingham K, Kemp A, Williams L, Das P, Hughes G, Peduto A, et al. Changes in anterior cingulate and amygdala after cognitive behavior therapy of posttraumatic stress disorder. Psychological Science 2007;18(2):127–9.
- First MB, Spitzer RL, Gibbon M, Williams JBW. Structured clinical Interview for DSM-IV. New York: New York State Psychiatric Institute, Biometrics Research Department; 1995.
- Fiszman A, Cabizuca M, Lanfredi C, Figueira I. The cross-cultural adaptation to Portuguese of the dissociative experiences scale for screening and quantifying dissociative phenomena. Revista Brasileira de Psiquiatria 2004;26(3):164–73.
- Florian V, Mikulincer M, Taubman O. Does hardiness contribute to mental health during a stressful real-life situation? The roles of appraisal and coping. Journal of Personality and Social Psychology 1995;68(4):687–95.
- Gilboa A, Shalev AY, Laor L, Lester H, Louzoun Y, Chisin R, et al. Functional connectivity of the prefrontal cortex and the amygdala in posttraumatic stress disorder. Biological Psychiatry 2004;55:263–72.
- Griffin MG, Resick PA, Mechanic MB. Objective assessment of peritraumatic dissociation: psychophysiological indicators. American Journal of Psychiatry 1997;154(8):1081–8.
- Grossman R, Yehuda R, New A, Schmeidler J, Silverman J, Mitropoulou V, et al. Dexamethasone suppression test findings in subjects with personality disorders: associations with posttraumatic stress disorder and major depression. American Journal of Psychiatry 2003;160(7):1291–8.
- Hopper JW, van der Kolk BA. 2(8). Retrieving, assessing and classifying traumatic memories: a preliminary report on three case studies of a new standardized method, vol. 4. New York: The Haworth Maltreatment and Trauma Press; 2001.
- Horowitz M, Wilner N, Alvarez W. Impact of event scale: a measure of subjective stress. Psychosomatric Medicine 1979;41:209–18.
- Kessler RC, Sonnega A, Bromet E, Hughes M, Nelson CB. Posttraumatic stress disorder in the national comorbidity survey. Archives of General Psychiatry 1995;52:1048–60.

- Kirschbaum C, Hellhammer DH. Salivary cortisol in psychoneuroendocrine research: recent developments and applications. Psychoneuroendocinology 1994;19:313–33.
- Koenig H, Parkerson Jr GR, Meador KG. Religion index for psychiatric research. American Journal of Psychiatry 1997;154(6):885–6.
- Lanius RA, Bluhm R, Lanius U, Pain C. A review of neuroimaging studies in PTSD: heterogeneity of response to symptom provocation. Journal of Psychiatric Research 2006;40(8):709–29.
- Lanius RA, Williamson PC, Boksman K, Densmore M, Gupta M, Neufeld RW, et al. Brain activation during script-driven imagery induced dissociative responses in PTSD: a functional magnetic resonance imaging investigation. Biol Psychiatry 2002;52(4):305–11.
- Lanius RA, Williamson PC, Densmore M, Boksman K, Gupta MA, Neufeld RW, et al. Neural correlates of traumatic memories in posttraumatic stress disorder: a functional MRI investigation. American Journal of Psychiatry 2001;158(11):1920–2.
- Lanius RA, Williamson PC, Densmore M, Boksman K, Neufeld RW, Gati JS, et al. The nature of traumatic memories: a 4-T FMRI functional connectivity analysis. American Journal of Psychiatry 2004;161(1):36–44.
- Marks I, Lovell K, Noshirvani H, Livanou M, Thrasher S. Treatment of posttraumatic stress disorder by exposure and/or cognitive restructuring: a controlled study. Archives of General Psychiatry 1998;55:317–25.
- McFarlane AC, Yehuda R, Clark CR. Biologic models of traumatic memories and posttraumatic stress disorder. The role of neural networks. Psychiatric Clinics of North America 2002;25(2):253–70.
- Newport DJ, Heim C, Bonsall R, Miller AH, Nemeroff CB. Pituitary-adrenal responses to standard and low-dose dexamethasone suppression tests in adult survivors of child abuse. Biological Psychiatry 2004;55(1):10–20.
- Neylan TC, Brunet A, Pole N, Best SR, Metzler TJ, Yehuda R, et al. PTSD symptoms predict waking salivary cortisol levels in police officers. Psychoneuroendocrinology 2005;30(4):373–81.
- Nichols T, Hayasaka S. Controlling the familywise error rate in functional neuroimaging: a comparative review. Statistical Methods in Medical Research 2003;12:419–46.
- Pargament KI, Koenig HG, Perez LM. The many methods of religious coping: development and initial validation of the RCOPE. Journal of Clinical Psychology 2000;56(4):519-43.
- Peres JF, McFarlane A, Nasello AG, Moores KA. Traumatic memories: bridging the gap between functional neuroimaging and psychotherapy. Australian New Zealand Journal of Psychiatry 2008;42(6):478–88.
- Peres J, Mercante J, Nasello AG. Psychological dynamics affecting traumatic memories: implications in psychotherapy. Psychology and Psychotherapy: Theory. Research and Practice 2005;78(4):431–47.Peres JF, Newberg AB, Mercante JP, Simão M, Albuquerque VE, Peres MJ, et al. Cerebral
- Peres JF, Newberg AB, Mercante JP, Simão M, Albuquerque VE, Peres MJ, et al. Cerebral blood flow changes during retrieval of traumatic memories before and after psychotherapy: a SPECT study. Psychological Medicine 2007;37(10):1481–91.
- Phelps EA, Delgado MR, Nearing KI, LeDoux JE. Extinction learning in humans: role of the amygdala and vmPFC. Neuron 2004;43(6):897–905.
- Poll EM, Kreitschmann-Andermahr I, Langejuergen Y, Stanzel S, Gilsbach JM, Gressner A, et al. Saliva collection method affects predictability of serum cortisol. Clinica Chimica Acta 2007;382(1–2):15–9.
- Reivich K, Shatte A. The resilience factor: 7 essential skills for overcoming life's inevitable obstacles. New York USA: Brodway Books Random House; 2002.
- Shin LM, Rauch SL, Pitman RK. Amygdala, medial prefrontal cortex, and hippocampal function in PTSD. Annals of the New York Academy of Sciences 2006;1071:67–79.
- Shin LM, Wright CI, Cannistraro PA, Wedig MM, McMullin K, Martis B. A functional magnetic resonance imaging study of amygdala and medial prefrontal cortex responses to overtly presented fearful faces in posttraumatic stressdisorder. Archives of General Psychiatry 2005;62:273–81.
- Simeon D, Yehuda R, Knutelska M, Schmeidler J. Dissociation versus posttraumatic stress: cortisol and physiological correlates in adults highly exposed to the World Trade Center attack on 9/11. Psychiatry Res 2008 Dec 15;161(3):325–9.
- Stein MB, Walker JR, Hazen AL, Forde DR. Full and partial posttraumatic stress disorder: findings from a community survey. Am J Psychiatry 1997;154(8):1114–9.
- Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, et al. Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. Neuroimage 2002;15(1):273–89.
- Vieweg WV, Julius DA, Fernandez A, Beatty-Brooks M, Hettema JM, Pandurangi AK. Posttraumatic stress disorder: clinical features, pathophysiology, and treatment. American Journal of Medicine 2006;119(5):383–90.
- Weiss DS, Marmar CR, Schlenger WE, Fairbank JA, Jordan BK, Hough RL, et al. The prevalence of lifetime and partial stress disorder in Vietnam theater veterans. Journal of Traumatic Stress 1992;5(3):365–76.
- Wood JN, Grafman J. Human prefrontal cortex: processing and representational perspectives. Nature Review Neuroscience 2003;4(2):139–47.
- Yehuda R, Boisoneau D, Lowy MT, Giller Jr EL. Dose-response changes in plasma cortisol and lymphocyte glucocorticoid receptors following dexamethasone administration in combat veterans with and without posttraumatic stress disorder. Archives of General Psychiatry 1995;52(7):583–93.
- Yehuda R, McFarlane AC, Shalev AY. Predicting the development of posttraumatic stress disorder from the acute response to a traumatic event. Biol Psychiatry 1998;44(12):1305–13.

734