

Neuro-functional alterations due to PTSD after environmental disasters: fMRI evidence and clinical suggestions

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Summary

Introduction

The post-traumatic stress disorder is an important clinical challenge. The present work was aimed at assessing the specific neural network showing functional changes in people suffering from post-traumatic stress disorders (PTSD) as a consequence of a natural disaster.

Methods

To pursue this aim we will perform a meta-analysis of fMRI studies of PTSD after natural disasters using Activation likelihood estimation (ALE).

Using ALE's inclusion criteria, we selected 22 individual experiments investigating the PTSD due to natural disasters.

Results

ALE analysis showed activation foci in superior and inferior frontal gyrus, insula and lingual gyrus in the right hemisphere. The

PTSD due to natural disasters modifies a cerebral network involved in learning spatial sequences in the environmental space. This neuro-functional alteration suggests the presence of selective cognitive deficits in visuo-spatial and navigational memory that could reduce the individual's capability to cope the emergency situation.

Discussion and conclusions

The PTSD due to natural disasters differs from that caused by other traumatic events altering in selective way the lingual gyrus, an important structure involved in topographical memory. This trauma-specific effect suggests the importance to develop specific treatment aimed at the PTSD's resolution.

Key words

PTSD • Post-traumatic stress disorders • Psychological therapies focused on trauma • Emergency Psychology • Natural disaster • Earthquake • Topographical memory • Topographical orientation

Introduction

A traumatic event, where there was a severe injury or a threat (or a perceived threat) to the physical integrity of individual involved, may produce a common behavioural, psychological, biological and social pattern of responses called "post-traumatic stress disorder" (PTSD) ². The PTSD is characterized by the following symptoms: i) re-experiencing the trauma through intrusive distressing recollections of the event, flashbacks, and nightmares; ii) Avoidance of places, people, and activities that are reminders of the trauma; iii) negative alterations in cognitions and mood, such as persistent and exaggerated negative beliefs or expectations about oneself, others, or the world (i.e., persistent guilt or shame; emotional numbness; diminished interest or participation in significant activities; inability to remember an important aspect of the traumatic events); iv) Increased arousal such as sleeping and concentrating difficulty, reckless or self-destructive behaviour hypervigilance, and being easily irritated and angered ³.

To receive a diagnosis of PTSD, the individuals have to show these symptoms for more than a month after the event and to become chronic they have to persist for at least three months ⁴. Even though PTSD may occur and may be considered a common disorder after being exposed to a life-threatening situation (i.e., physical attack, domestic violence, sexual abuse, car accident, the experience of unexpected or sudden death of a friend or relative, natural disaster, terroristic attack), not all survivors will show PTSD. Indeed, many of them will exhibit resilient responses or brief subclinical symptoms or consequences that fall outside of diagnostic criteria. Large scale disasters can have a multitude of effects upon a community: from economic to social, from physical to psychological. The impacts on health of direct or indirect exposure to a traumatic event could be exhibited in the middle and long term as a consequence of the entire disruption of the health infrastructure of the city, the loss of social support and of a normal life.

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For such a reason, a crucial aspect of disaster mental health response during the early post-impact phase is the identification of individuals at risk for long-term problems². Victims may be classified into at least four groups according to the type of their involvement and their functions: i) primary victims who have been directly exposed to the disaster; ii) secondary victims, who have not been directly affected, but who mourn a close relative who is part of the primary victims or who witnessed the traumatizing events; iii) third-level victims, such as rescuers (i.e., health personnel, fireworkers, policemen) who intervene on the scene and have witnessed traumatizing experiences; iv) fourth-level victims, the general public or community members, who were not physically present at the scene but suffered by proxy when exposed to the media information⁵.

In the last few years, the number of natural disasters has increased significantly, a recent review by Ripoll Gallardo et al.⁶ reported that, only in the 2014, 324 natural disasters have been occurred, which 10% constituted by earthquakes.

The L'Aquila population exposed to the earthquake of 6th April 2009 appears to be one of the most studied from multiple perspectives. In particular, it was observed to investigate the trauma effects on health to short and medium-term⁷. There are some previous trauma conditions that may predispose individuals to the persistence of stress symptoms, but also the type of exposure, as well as the following experience may contribute to be at risk of subsequent PTSD (e.g., survivors to mass-destruction phenomena; complicated mourning; loss of the family and of the community; survivors already exposed to previous traumatic experience; loss of the employment; financial loss etc.)⁷⁻¹¹. Also individual factors may contribute to the development of subsequent chronic psychological disorders (i.e., female gender, personality, genetic factors, low-educational level; epigenetics vulnerability; previous psychiatric disorders; whether the trauma took place during childhood or adulthood; degree of exposure; close proximity with the epicentre of the earthquake; physical injuries and trapped experience; the loss of home and relocation after the disaster^{7 12-22}. Concerning the age, for instance, people over 50 show a greater sensitivity to the stressful event exhibiting a greater maladaptive response²¹. Women show a greater sensitivity to the trauma²³, adopting more negative coping strategies²⁴. Furthermore, the incidence of complete PTSD is higher in women with respect to men^{7 25}.

A first aid is strongly suggested for helping people in managing initial and transitory symptoms of post-traumatic stress and for preventing long-standing clinical signs⁴. Several psychological therapies have been proposed in the PTSD treatment: cognitive therapy^{26 27},

therapies with a psychodynamic approach²⁸ and EMDR (Eye Movement Desensitization and Reprocessing)²⁹. The trauma focused therapies are considered the most effective in the trauma reprocessing and among elective therapies for PTSD there are cognitive-behavioural therapy and EMDR^{4 30-35}.

A recent meta-analysis on neuro-functional correlates of different types of PTSD showed as a distinction should be made in accordance to the type of traumatic event. Boccia et al.³⁶ reported that PTSD caused by physical assaults is associated with neural alteration of cerebral area known to be involved in the processing of skeletomotor orientation to the noxious stimuli (i.e., middle cingulate cortex), while the combat-related trauma is associated to a cerebral network involved in memory, emotional processing and monitoring internal body states (i.e., hippocampus, anterior and posterior cingulate cortex and bilateral insula) and the PTSD following natural disasters modify cerebral areas involved in spatial and environmental representation (i.e., parahippocampal cortex). The evidence that different traumatic event may modify different neuro-functional brain areas suggest a specific trauma dimension that may provide useful cues to the PTSD treatment. On the other hand, this finding is in line with behavioural findings showing that stress traumatic reactions may differ due to the type of traumatic event. Indeed, Schuster et al.³⁷ reported that in cases of technological or natural disasters or major terrorist attacks, the tendency is to increase mutual contacts and look for reassurance in others.

In the present study investigated the presence of a neuro-functional alteration correlates to the post-traumatic stress disorder following natural disaster (PTSD-ND). To pursue this aim, we performed an Activation likelihood estimation (ALE) analysis, which allows for coordinate-based meta-analyses of neuroimaging data¹.

Methods

Studies/samples

Studies selection was performed using BrainMap Functional database and PubMed. Inclusion criteria for papers were: 1) use of functional magnetic resonance imaging (fMRI) or positron emission tomography (PET); 2) inclusion of coordinates of activation foci, either in Montreal Neurological Institute (MNI) or Talairach reference space; 3) inclusion of peak activations derived from comparisons between patients diagnosed with PTSD and healthy age- and educational-matched controls; 4) the traumatic event was a natural or an environmental disaster.

Thus, we selected 22 studies described in 14 papers³⁸⁻⁵¹ (see Table I for details about number of participants and

on the type of experiment performed) which investigated the neural correlates of PTSD after a natural disaster, with a total of 163 foci of activation.

Activation likelihood estimation (ALE) analysis

Activation likelihood estimation (ALE) was performed on activation-location coordinates from selected studies⁵². ALE models the uncertainty in localization of activation foci using Gaussian distribution⁴⁵ and analyses the probability that a voxel will contain at least one of the activation foci; it is calculated at each voxel and results in a thresholded ALE map. In other words, ALE assesses the overlap between foci by modeling the probability distributions centered at the coordinates of each one¹.

In the present study, we performed an ALE analysis to determine whether a consistent neural substrate of PTSD due to natural disasters exists.

The ALE meta-analysis was performed using GingerALE 2.3.6 (brainmap.org) with MNI coordinates (Talairach coordinates were automatically converted into MNI coordinates by GingerALE.). According to Eickhoff et al.'s¹ modified procedure, the ALE values of each voxel in the brain were computed and a test was performed to determine the null distribution of the ALE statistic of each voxel. The FWHM value was automatically computed because this parameter is empirically determined¹.

The thresholded ALE map was computed using p values from the previous step and a False Discovery Rate (FDR) at the 0.05 level of significance (Tom Nichol's FDR algorithm). Moreover, a minimum cluster size of 200 mm³ was chosen.

A cluster analysis was performed on the thresholded map. The ALE results were registered on an MNI-normalized template using Mricron (<http://www.mccauslandcenter.sc.edu/mricron/index.html>).

Results

The ALE meta-analysis showed clusters of consistent activations in the insula (cluster 1), in the lingual gyrus (cluster 3), in the inferior frontal gyrus (cluster 4) and in the superior frontal gyrus (cluster 2) of the right hemisphere (Figure 1, Table I).

Discussion

The aim of the present study was to investigate the neuro-functional alterations in individuals affected by PTSD following a natural disaster (PTSD ND), for verifying the existence of specific brain functional areas related to the type of traumatic event.

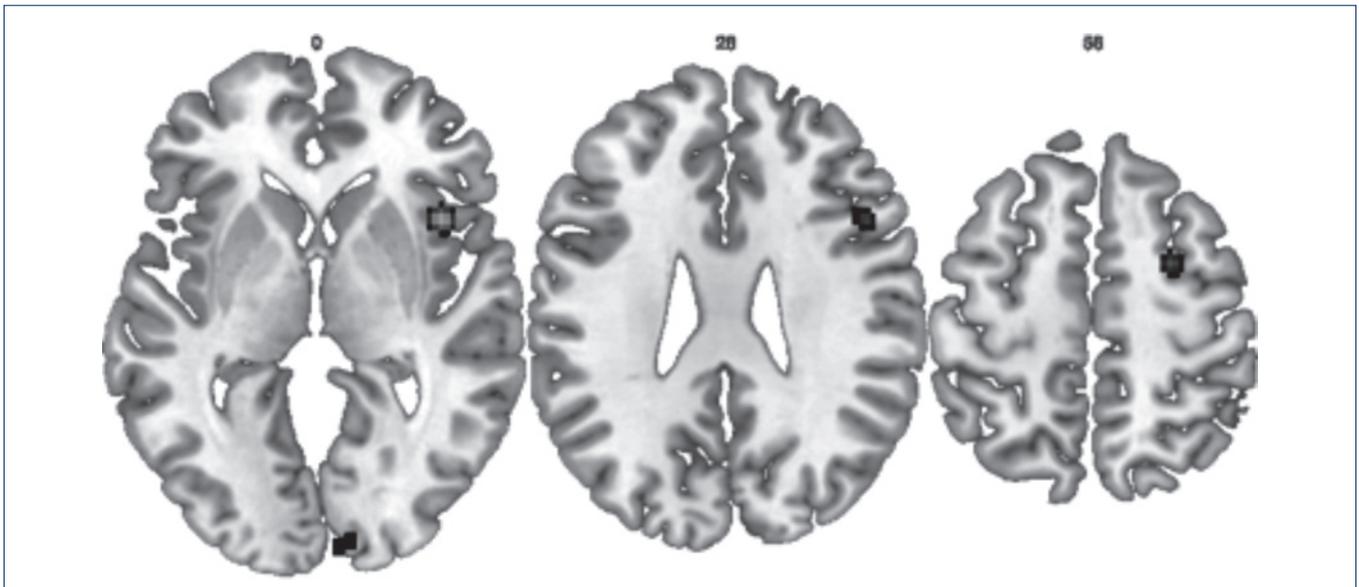
PTSD is the only major mental disorder with a known cause, that is, an event that threatens one's physical in-

tegrity or that of others and induces a response of intense fear, helplessness or horror⁵³. Although different studies have showed common neural mechanisms underpinning PTSD symptomatology, including intrusive memories of the traumatic event, avoidance of reminders of it, emotional numbing and hyperarousal⁵³, no previous study (except for a first exploration by Boccia et al.³⁶) has assessed the effect of different traumatic events on the brain mechanisms underlying PTSD. Clinical evidence suggests that different traumatic events interact with individual factors (i.e., personality, gender and genetic factors) leading to different physical and behavioural outcomes as well as a different prevalence of PTSD⁵⁴⁻⁵⁷.

To this purpose we have performed an ALE meta-analysis on the selected studies for showing the cerebral areas involved in PTSD-ND. We found that a specific networks of areas, including insula, lingual gyrus, right inferior and superior frontal gyri are associated to the PTSD-ND. These set of areas have been recently found related to different spatial abilities: specifically, lingual gyrus and insula are involved with learning sequences in the navigational space, with specific and complementary contributes⁵⁸. Indeed, inferior frontal gyrus is involved in the mental rotation of 3-D objects and letters of the alphabet⁵⁹ and the superior frontal gyrus is involved in working memory and more specifically in the maintaining of spatial orientation⁶⁰.

This result highlights as a natural/environmental disaster that produces significant changes in the familiar places may also modify the brain areas devoted to the learning of sequences in the navigational space. In particular, the lingual gyrus that is associated with learning of sequences in the environment. In this directions, through an fMRI paradigm, Nemmi et al.⁵⁸ have showed the activation of the lingual gyrus during the learning of a new path in a navigational (extrapersonal) space, but not when the same individual learns a path in a peripersonal space. Furthermore, the lingual gyrus has been recently associated with the learning of new environments, being more activated when individuals are asked to perform a navigational task in a recently learned environment⁶¹. This neuro-functional alteration is typical of PTSD ND and it was not observed in PTSD due to physical assaults or to combat-related trauma exposures^{35 62}. Moreover, the insula within other regions (such as dorsolateral prefrontal cortex) is thought to be involved with the processing of self-generated locomotor movements⁶³.

All traumatic events shared a behavioural pattern of responses called PTSD, as well as the feeling to an exposure to an extreme life-threatening event. However, an important distinction should be made with respect to the type of traumatic event. The natural disaster exposes an entire group of people that lived in a community and in a specific place to a disaster that is often unpredictable and

**FIGURE 1.**

Region showing neuro-functional alteration in patients who developed PTSD after natural disasters, as it results from the ALE analysis on fMRI studies.

TABLE I.

Meta-analysis studies selected.

Paper	N ^a	N. of participants with PTSD/TE	Studies ^c	fMRI Paradigm	Cluster ^b
Chen et al., 2009	24	12	1	Encoding and retrieval memory tasks	
Mazza et al., 2012	20	10	1	Affective priming task	
Hou et al., 2007	17	10/7*	7	Symptom provocation paradigm/TR-STM	
Mazza et al., 2015	17	7/10*	1	Emotional and cognitive empathy task	
Du et al., 2015	42	21	1	Graph theory analysis of resting-state fMRI	1, 2, 4
Du et al., 2016	30	16*	1	Subliminal priming with earthquake-related images on attentional control during a Stroop task	
Gong et al., 2014	121	65/56*	1	Resting-State fMRI	
Shang et al., 2014	38	18/20*	1	free Resting-State fMRI Task	3, 4
Wei et al., 2013	30	15*	2	charitable donation task	
Yin et al., 2012	126	54/72*	1	Resting-State fMRI	
Yin et al., 2011	126	54/72*	2	Resting-State fMRI	3
Mazza et al., 2013	20	10	1	Negative and neutral emotional stimuli observation during Resting-State fMRI	2
Lui et al., 2009	76	44*	1	Resting-State fMRI	1
Vidotto et al., 2014	35	10	1	Disgusting and scramble images observation task	
	PTSD N = 271				
	TE N = 312				
	C = 139				

^a N. of participants; ^b Cluster contribution (if applicable); ^c Number of experiments in each paper; * Number of participants exposed to traumatic event who did not developed PTSD.

PTSD: Post Traumatic Stress Disorder; TE: Trauma Exposure; C: Healthy controls.

difficult to contrast. The natural disaster leads to the destruction of a familiar place, to the loss of the own roots and identity due to the homelessness situation. Survivors are exposed to a long period in which they have to address all cognitive resources towards the survival itself and a new start requiring the re-learning of new environmental paths as a consequence of the destruction of the familiar places. Differently, traumatic events following motor-vehicle accidents or sexual assaults are individual disasters that expose primary and secondary victims to face an event that affects the own body perception as well as the place mental representation not any more perceived as a safe place. These traumatic experiences share with natural disasters the unpredictability element but they do not have the state of social emergency and experience typical of environmental disasters.

In the war experience, comrades in arms share the exposure to traumatic scenes, however (except for the Civil wars) they do not experience the destruction of a familiar place. Specifically, in the physical assaults and in the combat-related PTSD, there is not a neuro-functional alteration of the brain areas involved in the mental environmental representation. Until now the studies investigating cognitive and psychological disorders following PTSD are never distinguished between different traumatic events. However, from a clinical point of view, this distinction could provide useful directions.

For example, a study by Roncone et al.⁶⁴ showed the presence of memory disorders (i.e., episodic memory and verbal working memory) characterizing the acute traumatic stress disorder. Authors suggest that the presence of these deficits may reduce the capability to cope in the post-traumatic phase, preventing the recovery and increasing the possibility to develop a chronic PTSD.

Taking into account for the evidence coming from the present meta-analysis of an involvement of the lingual gyrus it is possible to hypothesize that other memory deficits involving visuo-spatial and navigational information may affect survivors. Considering that trauma focused psychological therapies use visual mental imagery for reducing intrusive thoughts, the presence of these deficits may affect the effectiveness of treatments.

These aspects should be systematically investigated in individuals with acute and chronic PTSD to promote the use of individual coping strategies and with a further purpose to implement specific psychological treatments for PTSD-ND.

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