Behavioural Brain Research 270 (2014) 307–315

Contents lists available at ScienceDirect

Behavioural Brain Research

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

Review

Anatomical deficits in adult posttraumatic stress disorder: A meta-analysis of voxel-based morphometry studies

Yajing Meng[a,b,1], Changjian Qiu[a,1], Hongru Zhu[a], Sunima Lama[c], Su Lui[c,*], Qiyong Gong[c], Wei Zhang[a,b,*]

[a] West China Mental Health Center, West China Hospital of Sichuan University, Chengdu, China
[b] State Key Laboratory of Biotherapy, Psychiatric Laboratory, West China Hospital, Sichuan University, Chengdu, Sichuan, China
[c] Huaxi MR Research Center (HMRRC), Department of Radiology, West China Hospital of Sichuan University, Chengdu, China

HIGHLIGHTS

- We report the meta-analyses of the structural abnormalities by 20 VBM studies in PTSD.
- The PTSD patients had significantly smaller regions compared with trauma-exposed healthy subjects including the left ACC, the left insula and the right parahippocampal gyrus.
- The clinician-administered PTSD scale scores were negatively correlated with GM in the left ACC and positively correlated with GM in the left insula.
- The PTSD patients who experienced accidental or non-accidental disasters were likely to be impaired in different regions.

ARTICLE INFO

Article history:
Received 23 April 2014
Received in revised form 12 May 2014
Accepted 15 May 2014
Available online 23 May 2014

Keywords:
Posttraumatic stress disorder (PTSD)
Meta-analyses
Voxel-based morphometry (VBM)
Anterior cingulate cortex (ACC)
Insular cortex
Disaster type

ABSTRACT

Evidence from previous anatomical studies indicate that widespread brain regions are involved in the pathogenesis of posttraumatic stress disorder (PTSD). The aim of the present study was to quantitatively integrate the literature on structural abnormalities seen on individuals with PTSD. Twenty voxel-based analysis studies were analysed through a comprehensive series of meta-analyses. Compared with healthy controls, PTSD patients showed a significant reduction in grey matter (GM) in the left anterior cingulate gyrus (ACC) at the whole-brain level. Several brain regions, including the left ACC, the left insula and the right parahippocampal gyrus were significantly smaller in individuals with PTSD than in trauma-exposed healthy subjects. Furthermore, the clinician-administered PTSD scale scores were negatively correlated with GM in the left ACC and positively correlated with GM in the left insula. In addition, PTSD patients who experienced accidental or non-accidental trauma had anatomical changes in different brain regions. These results suggest that the smaller ACC and insular cortex within the limbic-prefrontal circuit contribute to the pathogenesis of PTSD. Moreover, the PTSD patients with different types of trauma may have different cerebral deficits.

Contents

* Corresponding authors at: West China Hospital, Sichuan University, Guoxue Lane 37, Chengdu 610041, Sichuan, China. Tel.: +86 28 85422005/+86 28 85423960; fax: +86 28 85582944/+86 28 85423503.
E-mail addresses: lusuwcums@hotmail.com (S. Lui), weizhanghx@163.com, weizhang27@163.com (W. Zhang).
[1] Contributed equally to this work.

http://dx.doi.org/10.1016/j.bbr.2014.05.021
0166-4328/

1. Introduction

Posttraumatic stress disorder (PTSD) is described as a condition in which the process of recovery from trauma is impeded [1]. Despite its serious impact on the population, the pathogenesis of PTSD is unclear. Using Pavlovian fear conditioning as a model for understanding the underlying mechanisms of pathological fear responses [1–3], one of the popular hypothesis suggested that PTSD might reflect strong associative learning akin to such conditioning [4]. In this model, the amygdala and medial prefrontal cortex (mPFC, encompassing the anterior cingulated cortex (ACC)), which comprise the core of the limbic system, has been associated with distinguishing and processing of threatening stimuli and encoding fear-based memories [5,6]. Impaired ACC function is one of the most robust neuroimaging finding in PTSD [7], and the reduction in grey matter density (GMD) in the ACC is consistent with this neurocircuitry model [8].

Yehuda and LeDoux suggested that the amygdala's ability to control fear responses to threatening stimuli was regulated by the hippocampus and mPFC [1]. Another hypothesis views the hippocampus as the core structure in the aetiology of PTSD because of its critical role in learning, memory, stress regulation and activation of the hypothalamic–pituitary–adrenal axis [9]. This theory was supported by a substantial number of cross-sectional regions of interest (ROI)-based structural studies and evidences which revealed reduced hippocampal volumes in PTSD [10–15]. Anatomical and functional deficits in the parahippocampal gyrus (PHG) were also found to be related with dissociation symptoms, such as re-experiencing events and flashbacks [16] and the performance of active working memory recall [17]. Another region that has been proposed to be involved in PTSD is the insular cortex, the changes of which have been associated with the severity of PTSD symptoms [14]. The insular cortex may also be involved in heightened detection of bodily arousal during the anticipation of aversive images and in response to fearful facial expressions, painful stimuli and memories [18–20].

To summarise findings from anatomical studies [6,21,22], several meta-analyses of structural magnetic resonance imaging (MRI) studies in PTSD were conducted. A reduced volume was identified in several regions, including the hippocampus [23–27], cingulate gyrus and amygdala [12,28]. These findings suggested that widespread regions within the brain are involved in the pathogenesis of PTSD, prompting researchers to study brain changes in PTSD patients at the whole-brain level. Recently, voxel-based morphometry (VBM) involves a voxel-wise comparison of the local concentration of grey matter between two groups of subjects at the whole-brain level [29]. GM density or volume (GMD/GMV) is a useful parameter for determining the quantity of regional GM [30]. VBM has been demonstrated to be more sensitive and more easily applied than the ROI method [31]. In addition, VBM has been widely used to quantify structural brain changes associated with PTSD at the whole-brain level (Table 1).

However, to date, no study has summarised findings from/that involves automated methods such as VBM/DARTEL (Diffeomorphic Anatomical Registration Through Exponentiated Lie algebra) or automated segmentation, which can overcome certain drawbacks of manual segmentation [32], among PTSD patients, trauma-exposed subjects and healthy controls. For meta-analysis of the coordinate information reported in VBM studies, new methods such as activation likelihood estimation (ALE) [33] and signed differential mapping (SDM) [34] were developed to identify brain regions that consistently showed an effect of interest. Unlike a meta-analysis of ROI neuroimaging studies which relatively is based on priority and subjectivity, a meta-analysis of VBM studies can provide a global and independent view of anatomical deficits in PTSD. Compared with other peak-probability meta-analysis methods such as ALE [35], effect-size SDM (ES-SDM) is a valid and reliable coordinate-based method that can be improved by including/using statistical parametric mapping.

In view of the heterogeneity of individuals with PTSD resulting from various traumatic experiences, several researchers have proposed that different types of trauma may result in different PTSD symptoms [36–38]. However there are other researchers who do not support this idea [39]. Given that there are few relevant studies, the specific types of trauma most strongly associated with PTSD and the brain structure morphological correlates of PTSD is not fully understood.

The aim of the current study was to quantitatively integrate the literature through a comprehensive series of meta-analyses of the structural abnormalities revealed by VBM studies of individuals with PTSD. Two hypotheses are addressed here: (1) PTSD is associated with widespread GM deficits involving limbic neurocircuitry that are not found in traumatised individuals, and (2) different types of trauma affect the GM in PTSD patients in different ways.

2. Methods

2.1. Literature survey: Inclusion and exclusion criteria

Using PubMed, Google Scholar and the Cochrane library database, we searched for English-language, structural MRI studies on PTSD that were published between January 2000 and March 2013.The keywords included during the search was PTSD (e.g., PTSD or posttraumatic stress disorder or trauma or stress), and VBM (e.g., VBM or voxel or volume or density or concentration or GM or morphometry or DARTEL or MRI). The abstracts of the initially identified articles were reviewed to select papers for full-text review.