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### ► To cite this version:

Ali Amad, Joaquim Radua, Guillaume Vaiva, Steve Cr Williams, Thomas Fovet. Similarities between borderline personality disorder and post traumatic stress disorder: Evidence from resting-state meta-analysis. *Neuroscience and Biobehavioral Reviews*, 2019, 105, pp.52 - 59. 10.1016/j.neubiorev.2019.07.018 . hal-03487832

**HAL Id: hal-03487832**

**<https://hal.science/hal-03487832>**

Submitted on 20 Jul 2022

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# Similarities between Borderline Personality Disorder and Post traumatic Stress Disorder: evidence from Resting-State Meta-Analysis

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## **Abstract**

Borderline personality disorder (BPD) and post-traumatic stress disorder (PTSD) are common psychiatric disorders. The nature of the relationship between BPD and PTSD remains controversial, but it has been suggested that these disorders should be brought closer because of their many similarities.

We thus performed a quantitative meta-analysis of resting-state functional imaging to assess similarities in the brain activation across BPD and PTSD diagnostic groups.

Overlap analyses revealed decreased activation in the left and right precuneus of both BPD and PTSD groups when compared to control subjects. BPD showed significant increased, but PTSD showed decreased activation, relative to control subjects, in the anterior cingulate/paracingulate gyri and in the left superior frontal gyrus. Complementary overlap analyses on a subgroup of studies with similar sex and age distribution partially confirmed the main results as the same pattern of functional activation in the anterior cingulate and in the left superior frontal gyrus were found.

Our findings are in agreement with the hypothesis that BPD and PTSD share common neuropathological pathways.

## **Key-words**

borderline personality disorder; post-traumatic stress disorder; resting state; age-dependant neuroplasticity; trauma

## INTRODUCTION

Borderline personality disorder (BPD) is a common mental disorder characterized by a pervasive pattern of emotional lability, impulsivity, interpersonal difficulties, identity disturbances, and disturbed cognition (e.g., depersonalization, derealization, and hallucinations) (Lieb et al., 2004). BPD is estimated to occur in 0.5–5.9% of the general population (Grant et al., 2008; Lenzenweger et al., 2007) and is likely to be diagnosed in early adulthood (Lenzenweger et al., 2007). Follow-up studies show a decrease in impulsivity with age (Stevenson et al., 2003; Zanarini et al., 2007), but associated mood disorders and interpersonal difficulties appear to be persistent and chronic (Zanarini et al., 2007). BPD is commonly comorbid with other psychiatric disorders, notably mood disorders, anxiety disorders, substance abuse, and other personality disorders (Skodol et al., 2002; Tomko et al., 2013).

Post-traumatic stress disorder (PTSD) can develop following exposure to extremely traumatic events (e.g. physical and sexual assaults, accidents, natural disasters). PTSD is characterized by the persistence of intense, distressing, and fearfully avoided reactions to reminders of the triggering event, alteration of mood and cognition, distressing and intrusive memories and nightmares of the trauma, irritability and hypervigilance. PTSD occurs in 5–10% of the population and is also associated with suicidal behaviour (Shalev et al., 2017; Yehuda et al., 2015). Both BPD and PTSD are associated with high mortality and morbidity, due to suicide, frequent hospitalization, substance use, psychiatric comorbidity, considerable economic burden and poor quality of interpersonal relationships (Bisson et al., 2015; Skodol et al., 2002).

The nature of the relationship between BPD and PTSD remains controversial but several arguments suggest that these disorders should be brought closer because of their many similarities (Cloitre et al., 2014; Frías and Palma, 2015; Gunderson and Sabo, 1993; Lewis and Grenyer, 2009). First, BPD and PTSD share numerous clinical features, particularly major disturbances in emotional and affect regulation, impulse control, reality testing, interpersonal relationships, self-evaluation and

sense of identity (Gunderson and Sabo, 1993; Lewis and Grenyer, 2009; Resick et al., 2012). **Second**, the role of trauma is obviously essential for PTSD but it also plays a major role in BPD. Indeed, the prevalence of childhood trauma is so frequently associated with BPD (either neglect (92%), sexual abuse (40%-70%) or physical abuse (25%-73%) (Zanarini et al., 2002)) that a causal relationship can be suggested (Ball and Links, 2009). Individuals with BPD are also probably vulnerable to develop PTSD (Golier et al., 2003). Furthermore, recent studies seem to indicate that BPD shares a genetic vulnerability with PTSD as FKBP5 variants –an important functional regulator of the glucocorticoid receptor complex– are associated with PTSD (Zannas and Binder, 2014)– and BPD (Amad et al., 2019; Martín-Blanco et al., 2015), which appears to be consistent with the hypothalamus–pituitary–adrenal (HPA) axis dysregulation highlighted in both disorders (de Kloet et al., 2006; Drews et al., 2019; Schumacher et al., 2019; Wingenfeld et al., 2010). Finally, from a neuro-functional perspective, BPD and PTSD are supposed to share the same abnormalities. Indeed, abnormalities in fronto-limbic networks, particularly a limbic hyperactivity and a diminished recruitment of frontal brain regions, have been suggested for both BPD and PTSD (Krause-Utz et al., 2014; Patel et al., 2012). Interestingly, BPD and PTSD recently showed, in several resting-state functional meta-analysis some common features. Both disorders were associated with an increased activity in inferior and superior frontal gyrus, respectively involved in response inhibition, working memory and attention (Amad and Radua, 2017; Wang et al., 2016). In the same studies, resting-state activation in other regions were found to be differently associated to both disorders such as the anterior cingulate cortex that showed an increased activation in BPD versus healthy controls, but a decreased activation in PTSD versus healthy controls.

To investigate the relationship between BPD and PTSD from a neuro-functional perspective, we performed a functional quantitative meta-analysis to compare results across diagnostic groups and to assess functional similarities that may reflect common neuropathological pathways in these disorders.

## MATERIAL AND METHODS

All brain imaging studies of the resting-state studies which have compared brain activation in patients with BPD or PTSD versus healthy controls were included in two separate meta-analyses (one for BPD and one for PTSD). To identify eligible studies, a systematic search, in respect to the PRISMA statement (Moher et al., 2009), was conducted on the Medline and ISI Web of Knowledge up to April 2018 using the following search term combinations: (1) “neuroimaging”, “fMRI”, “PET”, “ALFF”, “ReHo”, “rCBF”, (2) “resting-state”, “default network” and (3) the terms “borderline personality disorder” or “post-traumatic stress disorder”. Reviews and meta-analyses were cross-referenced to identify studies that were missed in the literature searches.

Studies were only selected according to the following inclusion criteria: 1) studies were published in an English-language peer-reviewed journal; 2) used at least one of the functional imaging techniques (fMRI, PET, or SPECT), 3) enrolled patients with BPD or PTSD compared to controls, 4) performed a whole brain analysis and reported activation coordinates in standard space (MNI or Talairach), 5) the diagnosis was made according to the current diagnostic criteria for both disorders. Also, we ensured that the same threshold throughout the whole brain was used within each included study, in order to avoid bias toward liberally thresholded brain regions. Authors were contacted for unpublished data including t-maps from the original studies. Article titles and the abstracts of studies identified from the searches were screened and excluded for the following reasons: not written in English, used seed-voxel-based analysis procedures, reported only region of interest results, review article, opinion, or hypothesis article; and samples with a disorder other than BPD or PTSD. The literature search strategy is summarised in the flow chart presented in **Supplementary Figures 1 and 2**.

The functional neuroimaging meta-analyses were performed using the anisotropic effect size version of Seed-based D Mapping (formerly Signed Differential Mapping, AES-SDM, [www.sdmproject.com](http://www.sdmproject.com)) (Radua et al., 2014, 2012). This method allows the inclusion of both peak

information (coordinates and t-values) and statistical parametric maps to create whole-brain effect size and variance maps, which are then used to perform voxel-wise random effects meta-analyses.

Peak coordinates and effect-sizes (e.g. t-values or z-scores) of statistically significant differences between patients and controls at the whole-brain level were extracted from each dataset. A standard MNI map of the resting-state differences was then separately recreated for each dataset using an anisotropic Gaussian kernel. The mean map was finally generated by voxel-wise calculation of the random-effects mean of the dataset maps, weighted by the sample size, intra-dataset variability, and between-dataset heterogeneity. All analyses were conducted using the grey matter template included in AES-SDM (template sampling size of 2x2x2 mm<sup>3</sup> voxels). The default SDM kernel size and thresholds were used (full width at half maximum [FWHM] = 20 mm,  $p < 0.005$ , peak Z value of  $>1$ , cluster size of  $>10$ ). To assess heterogeneity between studies, I<sup>2</sup> values were extracted from the meta-analytic peaks and interpreted according to (Higgins and Green, 2011). Jackknife sensitivity analyses, consisting of iteratively repeating the meta-analysis excluding one study at a time, were also conducted, for both BPD and PTSD, to examine the robustness of the main meta-analytic output. Meta-regression analyses were performed to study the effects of age and gender. These analyses were thresholded more conservatively ( $p < 0.0005$ ) to minimize spurious findings. Publication bias was also examined by using the Egger test.

The multimodal analysis function of the AES-SDM statistical package also allows conjunction analyses to be performed, which enabled us to identify regions where both patient groups show common differences with respect to controls, while taking into account error in the estimation of the magnitude of these differences (Radua et al., 2013). The default parameters of SDM were used (peak  $p < 0.00025$ , cluster size of  $>10$ ).

The main meta-analyses were performed for BPD and all the PTSD studies. Importantly, neural activity abnormalities in patients with PTSD compared to controls can appear dramatically different depending on whether individuals without trauma exposure (non-trauma exposed controls; NTC) or individuals with trauma exposure who did not develop PTSD (trauma-exposed controls; TEC)

are employed as experimental controls (Disner et al., 2018). To account for such heterogeneity, the analyses were also performed using, both by merging all the PTSD studies and by performing separate analysis according to the control group. Finally, as BPD and PTSD patients represent different socio-demographic characteristics, especially for age and gender, we conducted a subgroup analysis of studies with similar sex and age distribution (more than half females and mean age less than 40 years).

## RESULTS

### *Studies characteristics*

#### *Borderline personality disorder*

Nine studies comparing patients and healthy controls (**Supplementary Table 1**) were included. These studies included a total of 235 patients and 214 healthy controls. Patients' mean age was 28,5 years (SD=5.3) and 86.5 % were female. The mean age of healthy control participants was 30.4 years (SD=6.3), and 83.6 % were female. No information about the history of trauma and its characteristics (age and type) was available.

#### *Post-traumatic stress disorder*

Eighteen studies comparing patients and healthy controls (**Supplementary Table 2**) were included. These studies included a total of 433 patients and 619 healthy controls. Patients' mean age was 39.4 years (SD=8.78) and 41.3 % were female. The mean age of healthy control participants was 40.5 years (SD=7.8), and 39.4 % were female.

### *Meta-analysis*

#### *BPD vs healthy controls*

Functional differences in BPD relative to healthy controls are shown in **Table 1** and **Figure 1**.

We found an increased activation in patients with BPD relative to healthy controls in the anterior cingulate, paracingulate gyri and in the left inferior frontal gyrus. Reduced activation was found in the right precuneus. Heterogeneity between studies was substantial in the anterior cingulate cortex ( $I^2 = 63\%$ ), moderate in the left inferior gyrus ( $I^2 = 47\%$ ) and was not seen in the right precuneus.

#### *PTSD vs healthy controls*

Functional differences in PTSD relative to healthy controls are shown in **Table 2** and **Figure 2**.

We found an increased activation in patients with PTSD relative to healthy controls in the left supramarginal, the right anterior insula, the left cerebellum, the right parahippocampal gyrus, the right dorso-lateral prefrontal cortex (dlPFC) and the median cingulate and paracingulate gyri. Reduced activations in patients with PTSD relative to healthy controls were found in the right Heschl

gyrus, the right lingual gyrus and inferior and middle frontal gyri. Heterogeneity between studies was low for all the brain regions found significant ( $I^2 < 25\%$ ). **The results of the meta-analysis performed by separating the control group in TEC and NTC are detailed in Table 3 and 4.**

### ***Reliability analysis***

Jackknife sensitivity analyses showed that the main findings were highly replicable across combinations of datasets for both disorders. Indeed, the increased activity in BPD patients in anterior cingulate cortex and left inferior frontal gyrus were robust as they were significant in all but one combination. Results in the right precuneus were preserved throughout all combinations of the data sets. The activation in patients with PTSD were also highly replicable, being preserved in 16 of 24 combinations of the data sets. See **Supplementary Table 3 and 4** for details.

### ***Age and gender effects***

For BPD, meta-regression analysis suggested that a higher percentage of females had significantly increased activation in the left inferior frontal gyrus (MNI coordinates = -44, 42, 10; SDM = 2.697;  $p < 0.0001$ , 78 voxels) and in the anterior cingulate (MNI coordinates = 6,44,12 ; SDM = 2.444 ;  $p < 0.0001$ ; 51 voxels) and a decreased activation the middle occipital gyrus (MNI coordinates = 34,-72,30; SDM = -2.739,  $p < 0.0001$ ; 726 voxels). Age was associated with an increased activation in the right middle occipital gyrus (MNI coordinates = 34, -72, 32; SDM =2.802,  $p < 0.0001$ , 758 voxels) and a decreased activation in the middle frontal gyrus (MNI coordinates = -44,44,10; SDM = -2.470;  $p < 0.0001$ ; 172 voxels).

For PTSD, meta-regression analysis suggested that a higher percentage of females had significantly increased activation in the right fusiform gyrus (MNI coordinates = 20,-38,-14; SDM = 6.166;  $p \sim 0$ ; 143 voxels) and in the superior temporal gyrus (MNI coordinates = 48,12,-16; SDM = 5.629;  $p \sim 0$ ; 109 voxels) and a decrease in the left angular gyrus (MNI coordinates = -42,-62,34; SDM = -5.493;  $p \sim 0$ ; 45 voxels). Age was associated with an increased activation in the right supplementary area (MNI coordinates = 10,-2,46; SDM = 4.518;  $p \sim 0$ ; 1401 voxels) and in the right frontal superior gyrus (MNI coordinates = 22,-2,48; SDM = 2.170;  $p < 0.0001$ ; 25 voxels) and a

decreased activation in the left olfactory cortex (MNI coordinates = -18,4,-14; SDM = -2.018,  $p < 0.0001$ ; 381voxels) and in the left lingual gyrus (MNI coordinates = -16,-98,-12; SDM = -1.546;  $p < 0.0001$ ; 127 voxels).

### ***Publication bias analysis***

For BPD, there was no publication bias for these clusters ( $p$ -values for Egger tests  $> 0.15$ ). For PTSD, only the cluster encompassing the dlPFC showed a publication bias ( $p = 0.003$ ).

### ***Overlap analyses***

Overlap analyses (**Figure 3**) revealed a significant shared decreased activation in both BPD and PTSD groups relative to control subjects in left and right precuneus (MNI coordinates = 0, -46, 38; 606 voxels). BPD showed significant increased, but PTSD decreased activation relative to control subjects in the anterior cingulate/paracingulate gyri and in the left superior frontal gyrus (MNI coordinates = 2, 44, 20; 1205 voxels). The overlap analyses by using specifically TEC or NTC for PTSD studies are presented in **Tables 5 and 6**.

Complementary overlap analyses were also performed on a subgroup which only included studies with more than half females and a mean age of less than 40 years. Several regions were identified where BPD showed significant increased but PTSD decreased activation relative to control subjects in the anterior cingulate/paracingulate gyri and in the left superior frontal gyrus (MNI coordinates = 2, 38, 0; 506 voxels), but also in the left insula and inferior frontal gyrus (MNI coordinates = -36, 12, 6; 2169 voxels) and in the left hippocampus (MNI coordinates = -26, -8, -24; 340 voxels).

## DISCUSSION

Here, we report findings from two distinct resting-state functional meta-analyses conducted in BPD and PTSD. For BPD, we found an increased activity in patients relative to healthy controls in the anterior cingulate cortex (ACC) and in the left inferior frontal gyrus, and a reduced activity in the right precuneus, which complements previously published functional meta-analyses using the same method (Amad and Radua, 2017; Visintin et al., 2016). These results contrast with the established fronto-limbic hypothesis of BPD which postulates a decreased activity of frontal brain regions and a limbic hyperactivity. In fact, the brain regions found here may correspond to specific networks involved in pain processing (Kluetsch et al., 2012) and dissociative states (*i.e.* disintegration of perception, consciousness, identity and memory). Dissociation, characterized by subjective detachment from overwhelming emotional experience during and after a trauma, is known to be frequently found (up to two thirds) of BPD patients (Vermetten and Spiegel, 2014). Interestingly, the regions identified here have been associated in participants with PTSD while in dissociative states (Lanius et al., 2002). We also found an increased activity in the left inferior frontal gyrus a critical brain region for response inhibition and for successful implementation of inhibitory control over motor responses (Swick et al., 2008) which has also been associated with attention-deficit/hyperactivity disorder (ADHD) (van Rooij et al., 2015) another disorder characterised by impulsivity and which is often associated with BPD. **Finally, one can also suggest that, as several studies about functional neuroimaging findings of emotion processing tasks have shown some evidence of the fronto-limbic hypothesis (Schulze et al., 2016), the resting-state imaging may not be the most accurate modality to demonstrate or refute it.**

Regarding PTSD, our results are also highly consistent with a recent resting-state functional meta-analysis using the same method (Wang et al., 2016), even after adding 3 new neuroimaging studies. We found an increased activation in the anterior insula, the cerebellum, the cingulate and paracingulate gyri and the parahippocampal gyrus and a decreased activation in the Heschl and lingual gyri. When the analyses were performed with specific control groups (*i.e.* NTC or TEC), our

results also confirmed previous studies: PTSD patients show (i) increased activation in the anterior insula and decreased activation in the dorso-medial prefrontal cortex when compared with NTC, (ii) increased activation in the ventro-medial prefrontal cortex when compared with TEC (Wang et al., 2016).

In this study, we have also directly compared BPD and PTSD to identify common and distinct patterns of functional modulations. We showed that the two conditions share similar patterns of decreased activation in left and right precuneus. We have also identified that the anterior cingulate/paracingulate gyri and left superior frontal gyrus are affected in both conditions (increased activation for BPD patients and decreased activation for PTSD subjects, relative to control subjects). These results were partially confirmed by complementary analysis on a more homogeneous subgroup regarding age and gender and when the analyses were performed using specific control groups (TEC or NTC).

Reduced activation in precuneus was found in both BPD and PTSD. The precuneus, which is part of the medial parietal cortex, plays a central role to link the limbic structures with parietal regions. This region is also involved in autobiographical memory and in self-referential processing, namely first-person perspective and experience of agency (Cavanna and Trimble, 2006). Precuneus activity has been demonstrated as related to trauma memory generalization (Hayes et al., 2011), and flashbacks (Whalley et al., 2013). Thus, alterations in the precuneus found in BPD and PTSD patients may be related to altered self-referential and memory processes, such as memory deficits, intrusions or flashbacks.

Anterior cingulate/paracingulate gyri and left superior frontal gyrus were also identified to be affected in both conditions. The anterior cingulate gyrus is part of the medial prefrontal cortex (PFC) which exerts inhibitory control over stress responses and emotional reactivity partly through connections with the amygdala. Interestingly, patients with PTSD also exhibit decreased ACC volumes (Bromis et al., 2018), that seem to be consequences of the course of PTSD rather than a pre-existing risk factor (Kasai et al., 2008). Functional imaging studies involving patients with PTSD also found

decreased activation of the medial PFC in response to trauma stimuli, such as trauma scripts, combat pictures and sounds, trauma-unrelated negative narratives, fearful faces, emotional stroop (for review see (Sherin and Nemeroff, 2011)). Even if there are discordant findings, reduced activation of the medial PFC was associated with PTSD symptom severity in several studies. Successful SSRI treatment has also been shown to restore medial PFC activation patterns (Shin et al., 2006). Regarding BPD, higher levels of glutamate in the ACC were found in patients when compared with healthy controls, and there are positive correlations between glutamate levels and impulsivity (Hoerst et al., 2010). It has also been shown that the hyperactivation of ACC was correlated with hippocampal activity, abnormal functioning of the memory system, poorer performance in retrieval tasks related to traumatic or emotionally significant memories (Schmahl et al., 2004).

We believe that our results are in line with the hypothesis that the conceptual interface between BPD and PTSD could be highlighted by the '*age-dependent neuroplasticity*' framework (Amad et al., 2016) which postulates that the same experience can differentially affect the brain plasticity depending on one's age (Kolb and Gibb, 2014). In this perspective, it has then been proposed that trauma during childhood could favour the development of BPD (Amad et al., 2014) while trauma in adulthood could increase the risk of PTSD (Amad et al., 2016). However, this hypothesis could not be tested since no BPD studies included data about the trauma history of these patients. Interestingly, there is a current debate about the distinction between PTSD, BPD and complex PTSD (PTSD plus several symptoms such as emotional dysregulation, negative self-cognitions and interpersonal relationship problems). Complex PTSD has even been recently proposed as a distinct clinical entity in the WHO International Classification of Diseases, 11th version. It has also recently been suggested that the relationship between these three disorders could follow a continuum of trauma and biological severity on a spectrum of common clinical features. These disorders could then be classified together under trauma-related disorders instead of distinct clinical diagnoses (Giourou et al., 2018). However, one of the most frequent, and important, criticism when

considering BPD as a trauma spectrum disorder is that the existence of trauma is not necessary or sufficient to explain the development of the disorder (Lewis and Grenyer, 2009).

One of the main limitations of this study corresponds to the very different socio-demographic characteristics of BPD and PTSD patients included, especially for age and gender as highlighted by the meta-regression analysis. Accordingly, we conducted a complementary analysis focusing on studies with more than half females and a mean age of less than 40 years. This complementary analysis partially confirmed our main results as we found the same pattern of functional activation in the ACC and in the left superior frontal gyrus between BPD and PTSD. Another possible limitation is the use of different statistical approaches such as independent component analysis, regional homogeneity, etc. to assess resting-state in the different studies included (Kühn and Gallinat, 2013). As soon as more resting-state studies on BPD and PTSD patients are published, new analysis should be performed including studies with the same statistical approach and future research will also need to confirm our results. Cautious interpretation is also needed because BPD and PTSD have a potentially high clinical heterogeneity and have been associated with many comorbidities, such as depression which can have a significant effect on the resting brain activity (e.g. (Mulders et al., 2015)). Unfortunately, data presented in the different studies included in these meta-analyses did not allow to include these potential confounding factors in our analyses. Our results therefore can hardly be attributed solely to BPD or PTSD. In the same way, no sufficient information about medication was available to perform complementary analysis. Future functional neuroimaging research in this field should directly compare BPD and PTSD patients in studies specifically designed to compare these populations using appropriate paradigms (e.g. task or resting-state). The participants included should be carefully assessed to explore specific dimensions and refined phenotypes (e.g., type and number of trauma, age of exposure, psychotic features or impulsivity). From an epidemiological point of view, the clinical profile of BPD patients with and without a history of childhood abuse could also be directly compared as it seems that the clinical profiles of BPD patients appear to differ according to the severity of childhood trauma (Zanarini et

al., 2002). Ideally, these analyses would be performed in large well-characterized epidemiological cohorts powerful enough to detect BPD patients without a history of trauma. Lastly, genetic studies could also help to highlight the similarities/differences between BPD and PTSD, by, for example, comparing shared polygenic risk between these disorders.

In conclusion, this study sheds new light on the neurobiology of BPD, which has been little investigated despite its high prevalence (0.5–5.9% of the general population) and severity (Amad et al., 2014) whilst also highlighting the functional similarities between BPD and PTSD. Our findings help reinforce the hypothesis that BPD shares conceptual and phenomenological similarities with PTSD. One difference between these disorders could be the age at which trauma occurs, differentially affecting the resting brain function and thus the psychiatric symptoms (Amad et al., 2016).

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## FIGURES AND TABLES CAPTIONS

**Figure 1.** Regions of increased (red) and decreased (blue) activation at rest in patients with borderline personality disorder compared with healthy controls. Statistical maps are thresholded at  $p < 0.005$  and  $k > 10$ .

**Figure 2.** Regions of increased (red) and decreased (blue) activation at rest in patients with posttraumatic stress disorder compared with healthy controls. Statistical maps are thresholded at  $p < 0.005$  and  $k > 10$ .

**Figure 3.** Clusters showing significant shared decreased activation in both BPD and PTSD (purple) groups relative to control subjects in left and right precuneus (MNI coordinates: 0, -46, 38; 606 voxels). Other regions (in green) were also identified where BPD showed significant increased but PTSD decreased activation relative to control subjects in the anterior cingulate/paracingulate gyri and in the left superior frontal gyrus (MNI coordinates: 2, 44, 20; 1205 voxels).

**Table 1.** Clusters showing differences between BPD and healthy controls.

**Table 2.** Clusters showing differences between PTSD and all healthy controls.

**Table 3.** Clusters showing differences between PTSD and trauma exposed controls (TEC).

**Table 4:** Clusters showing differences between PTSD and non-trauma exposed controls (NTC).

**Table 5.** Clusters showing similar activation in BPD and PTSD (trauma exposed controls, TEC).

**Table 6.** Clusters showing similar activation in BPD and PTSD (non-trauma exposed controls, NTC).

**Conflict of interests**

The authors declare no potential conflict of interest.

**Contributors**

AA, JR, TF participated in the conception and design of the study; AA and TF participated in the acquisition of data; AA, JR, TF performed the analyses; AA and TF wrote the first draft of the manuscript. All authors participated in the writing and revision of the successive drafts of the manuscript and approved the final version.

**Role of the Funding source**

No funding source to declare.

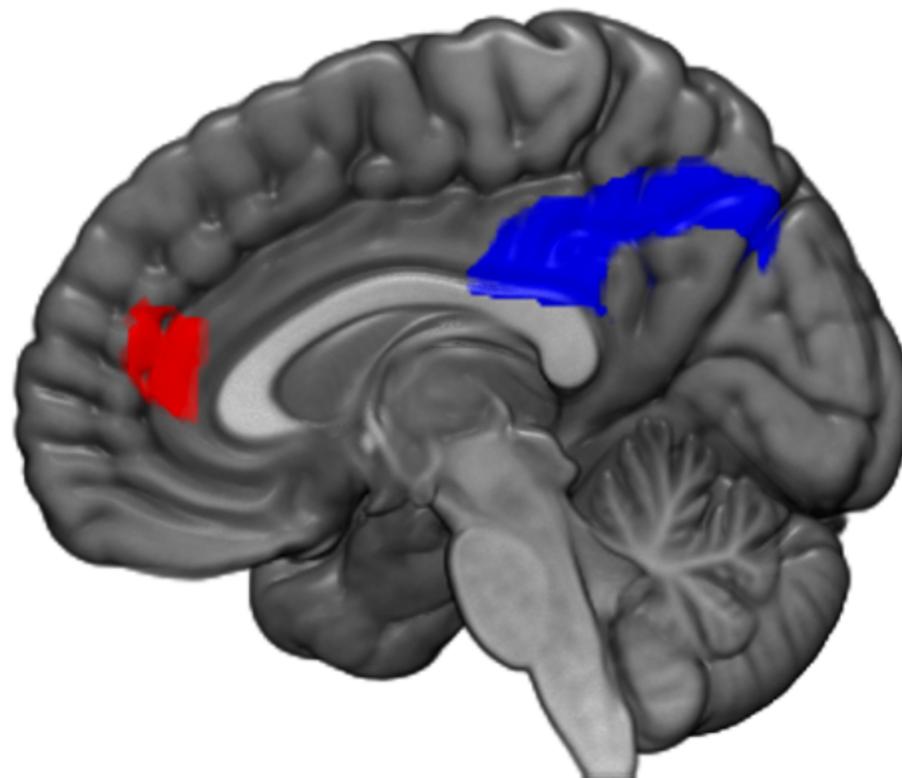
**Acknowledgements**

No Acknowledgement

Left inferior frontal gyrus



Anterior cingulate / paracingulate gyri (red)  
Precuneus (blue)

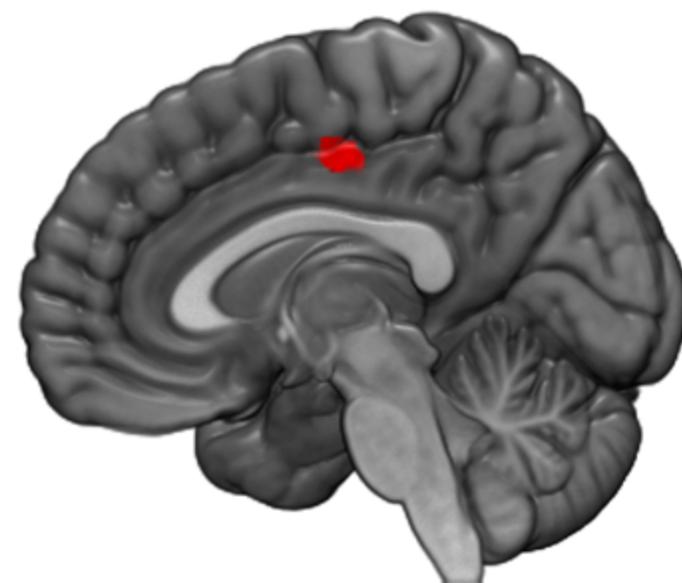
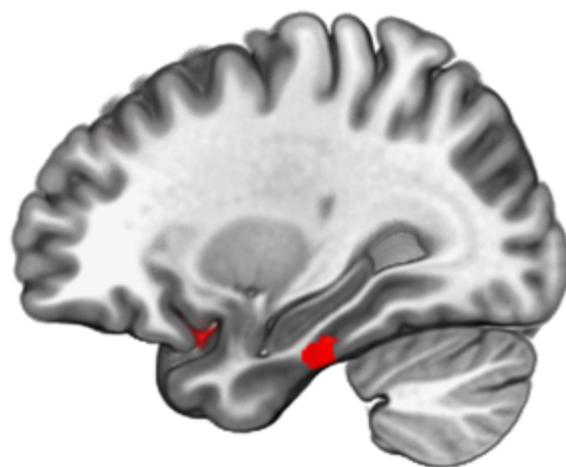
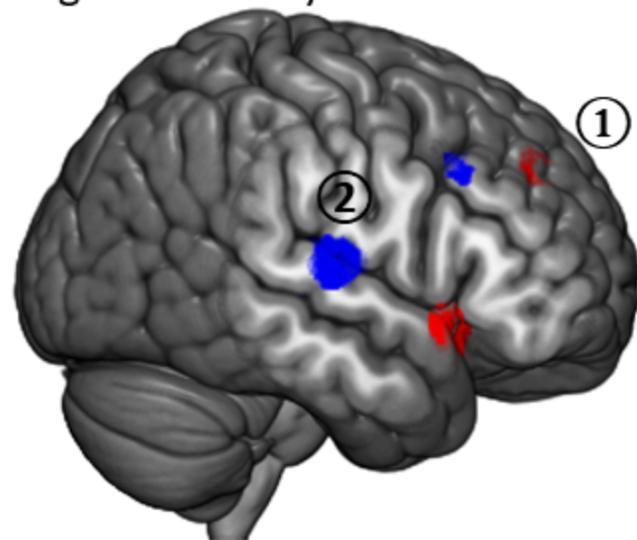


① Right dorsolateral Prefrontal cortex

Right anterior insula

Median cingulate / paracingulate gyri

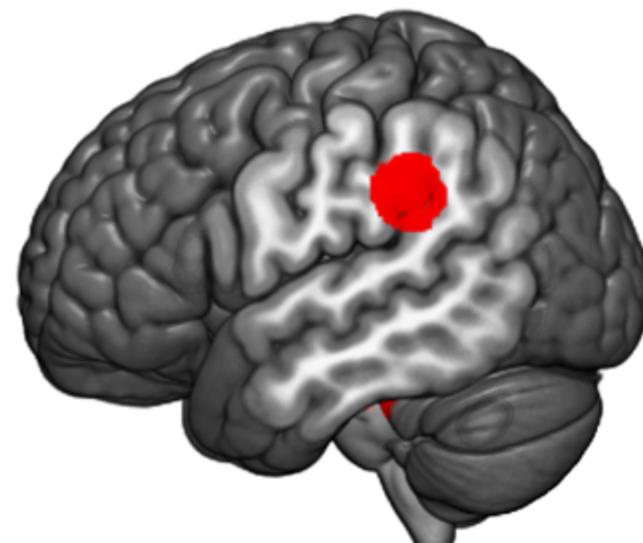
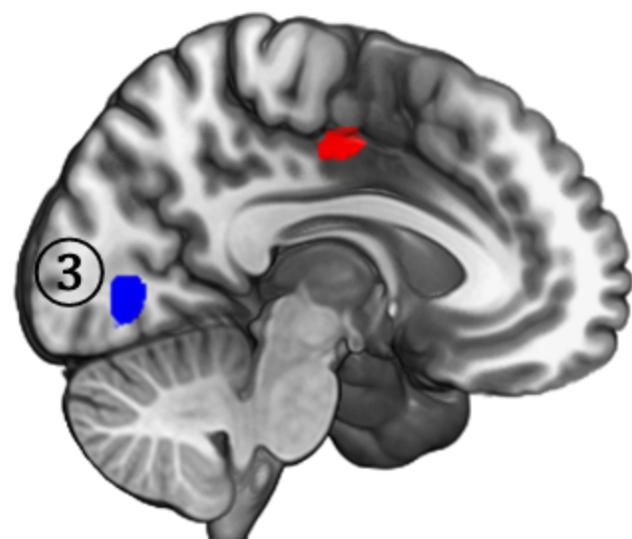
② Right Heschl Gyrus

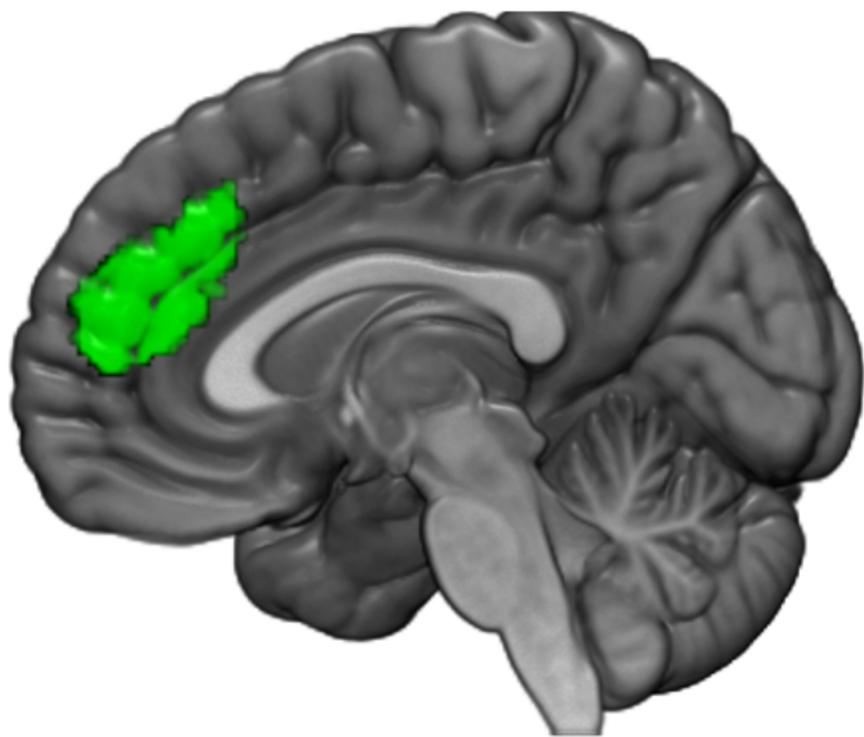
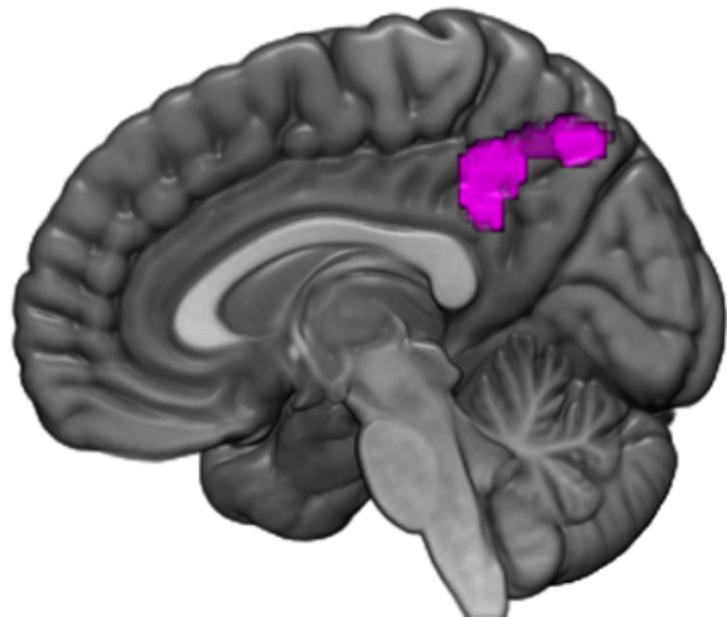
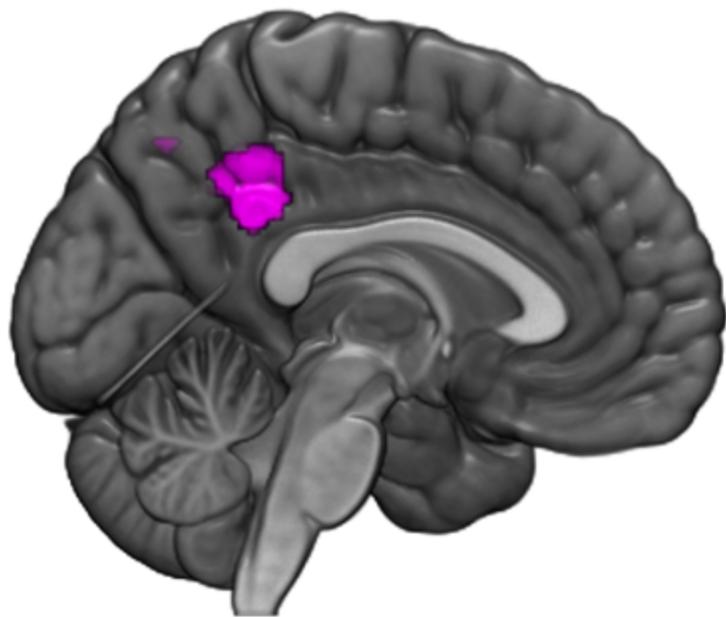


③ Right lingual Gyrus

Left cerebellum (lobule IV / V)

Left supramarginal gyrus





MNI coordinates (x, y, z)	SDM-Z	P	Cluster size / voxels	Brodman areas	Side (L/R)	Brain areas
<i>BPD &gt; Controls</i>						
-10 56 22	1.647	0.000304401	805	32	L+R	Anterior cingulate / paracingulate gyri
-54 10 16	1.371	0.002392530	113	44, 48	L	Left inferior frontal gyrus
<i>BPD &lt; Controls</i>						
6 -62 44	-2.268	0.000009835	2043	7	R	Precuneus

**Table 1. Clusters showing differences between BPD and healthy controls.**

MNI coordinates (x, y, z)			SDM-Z	P	Cluster size / voxels	Brodman areas	Side (L/R)	Brain areas
<i>PTSD &gt; Controls</i>								
-56	-38	32	2.346	0.000039041	584	40, 48	L	Supramarginal gyrus
48	20	-10	1.869	0.000604749	437	38	R	Anterior Insula
-26	-28	-30	1.706	0.001354516	166	30	L	Cerebellum (lobule IV / V)
-4	-12	42	1.750	0.001094818	154	23	L+R	Median cingulate / paracingulate gyri
30	-24	-30	1.689	0.001469672	80	20	R	Parahippocampal gyrus
38	42	38	1.999	0.000295222	65	9	R	dIPFC
<i>PTSD &lt; Controls</i>								
40	-20	4	-2.131	0.000078440	1625	48	R	Heschl Gyrus
20	-74	0	-2.202	0.000050783	164		R	Lingual Gyrus
52	22	38	-1.664	0.001235783	35	44	R	Inferior and Middle Frontal Gyri

**Table 2. Clusters showing differences between PTSD and all healthy controls.**

MNI coordinates (x, y, z)			SDM-Z	P	Cluster size / voxels	Brodman areas	Side (L/R)	Brain areas
<i>PTSD &gt; TEC</i>								
-52	-32	32	2.561	0.000011563	1020		L	Supramarginal Gyrus
0	50	-14	2.180	0.000144601	731	11	L	vmPFC
30	48	32	2.609	0.000008643	386	46	R	dIPFC
58	-54	24	1.665	0.001578987	296	22	R	Angular gyrus
<i>PTSD &lt; TEC</i>								
46	-18	2	-1.759	0.000753582	1111		R	Heschl Gyrus
20	-74	0	-2.897	0.000001013	322		R	Lingual Gyrus
28	-68	-18	-1.629	0.001604378	80	19	R	Cerebellum (lobule VI)
58	2	-26	-1.656	0.001384020	74	21	R	Temporo-parietal Junction
50	22	42	-1.676	0.001234770	46	44	R	Middle Frontal Gyrus
-54	18	30	-1.536	0.002774477	17	44	L	Inferior Frontal Gyrus

**Table 3.** Clusters showing differences between PTSD and trauma exposed controls (TEC).

MNI coordinates (x, y, z)			SDM-Z	P	Cluster size / voxels	Brodman areas	Side (L/R)	Brain areas
<i>PTSD &gt; NTC</i>								
28	-32	-24	2.246	0.000024676	1128	BA 20	Right	Parahippocampal Gyrus
46	20	-6	2.111	0.000076294	703		Right	Anterior Insula
-4	-14	44	1.627	0.001889586	144	BA 23	Left	Median Cingulate / Paracingulate Gyri
-20	-26	-30	1.587	0.002381325	27	30	Left	Cerebellum (lobule IV / V)
0	14	-24	1.518	0.003511727	12	11	Left	Gyrus Rectus
<i>PTSD &lt; NTC</i>								
4	54	-6	-1.664	0.001134872	236	10	Right	vmPFC
46	-76	28	-1.732	0.000762343	144	39	R	Precuneus

**Table 4:** Clusters showing differences between PTSD and non-trauma exposed controls (NTC).

MNI coordinates (x, y, z)			P	Cluster size / voxels	Brodman areas	Side (L/R)	Brain areas
<i>PTSD pos – bpd pos (increased activity in both ptsd and bpd)</i>							
-46	-6	4	< 0.00025	649	48	L	Left rolandic operculum, Left insula, Left superior temporal gyrus
56	-52	30	< 0.00025	364	39,40	R	Right angular gyrus
<i>PTSD neg – bpd neg (decreased activity in both ptsd and bpd)</i>							
None							
<i>PTSD pos – bpd neg (increased activity in ptsd and decreased in bpd)</i>							
-6	-24	30	< 0.00025	311	23	L+R	median cingulate / paracingulate gyri
<i>PTSD neg – bpd pos (decreased activity in ptsd and increased in bpd)</i>							
-4	58	22	< 0.00025	396	10, 32	L	Left superior frontal gyrus, medial
-24	50	26	< 0.00025	290	46	L	Left middle frontal gyrus, Left superior frontal gyrus, dorsolateral

**Table 5.** Clusters showing similar activation in BPD and PTSD (trauma exposed controls, TEC).

MNI coordinates (x, y, z)	P	Cluster size / voxels	Brodman areas	Side (L/R)	Brain areas
<i>PTSD pos – bpd pos (increased activity in both ptsd and bpd)</i>					
None					
<i>PTSD neg – bpd neg (decreased activity in both ptsd and bpd)</i>					
4 -72 46	< 0.00025	570	7	L+R	Precuneus
<i>PTSD pos – bpd neg (increased activity in ptsd and decreased in bpd)</i>					
24 -28 -14	< 0.00025	834			Right median network, cingulum
-2 -18 30	< 0.00025	440	23	L+R	median cingulate / paracingulate gyri
<i>PTSD neg – bpd pos (decreased activity in ptsd and increased in bpd)</i>					
4 48 4	< 0.00025	827	10, 32	L+R	Right superior frontal gyrus, medial, Left anterior cingulate / paracingulate gyri
-48 -2 2	< 0.00025	608	48	L	Left rolandic operculum

**Table 6.** Clusters showing similar activation in BPD and PTSD (non-trauma exposed controls, NTC).