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Functional Dissociative Seizures and Borderline Personality Disorder: Review of their Psychological and Neurobiological Relationships

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Abstract

Functional Dissociative Seizures (FDS) are conversion disorders with seizures that present as paroxysmal events associated with disruptive changes in behavior, thought or emotion. On the other hand, Borderline Personality Disorder (BPD) is defined as "a pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity, beginning by early adulthood and present in various contexts." The psychiatric profile of FDS patients is highly complex. Among psychiatric comorbidities, personality disorders occurred in 71.43% of cases. Furthermore, BPD was the most common among personality disorders seen in these patients, with a frequency ranging from 10% to 69%, depending on the study. In this manuscript, we carried out a state-of-the-art review to provide a critical approach to the extensive literature about FDS and BPD. We believe that the similarities in emotion regulation strategies and brain structures and functions (specifically the amygdala, hippocampus, insula, prefrontal cortex, and anterior cingulate cortex) between FDS and BPD may shed some light on the understanding of the relationship between these two disorders.

Highlights

- Borderline Personality Disorder (BPD) frequency in Functional Dissociative Seizures (FDS) patients varied from 10% to 69%
- Under-regulation of affect (present in BPD patients) tend to cause positive conversion symptoms, such as FDS
- Similar variations in amygdala, hippocampus, insula, prefrontal cortex and anterior cingulate cortex may explain their relationship

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Introduction

Functional Dissociative Seizures (FDS), formerly known as Psychogenic nonepileptic seizures (PNES), are a type of conversion disorder with seizures that present as paroxysms events (sudden, violent, uncontrollable) associated with disruptive changes in behavior, thought, or emotion. During FDS, the normal functioning of the central nervous system is altered, and self-control is reduced. Frequently mistaken for epilepsy, FDS has no relationship with ictal discharges on the electroencephalogram. FDS is identified when medical explanations (such as epilepsy) have been dismissed, and psychological mechanisms are involved in their emergence [1,2].

Borderline Personality Disorder (BPD), on the other hand, is defined as "a pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity, beginning by early adulthood and present in a variety of contexts, as indicated by": frantic efforts to avoid real or imagined abandonment; a pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation; identity disturbance; impulsivity in areas that are potentially self-damaging; recurrent suicidal behavior, or self-mutilating behavior; affective instability due to a marked reactivity of mood; chronic feelings of emptiness; inappropriate, intense anger or difficulty controlling anger; transient, stress-related paranoid ideation or severe dissociative symptoms [2]. Effective, evidence-based treatments, such as Dialectical Behavior Therapy (DBT) and Cognitive Behavioral Therapy (CBT), are available to manage the symptoms of borderline personality disorder [3].

The psychiatric profile of FDS patients is highly complex. Among psychiatric comorbidities, Axis I psychiatric disorders were the most frequent, occurring in almost 100% of PNES patients. In addition, personality disorders were also present, with a frequency of 71.43% in FDS. Furthermore, among personality disorders, Cluster B Personality Disorders (in which BPD is the most predominant) were the most common (42,86%) [1].

The prevalence of BPD in the general population is 1.6% [4]. However, this number tends to rise in FDS patients. It varies from study to study reviewed (from 10% to 69%), but its frequency is always higher than in control groups **(Table 1)**.

According to one study, 50,6% of FDS patients "showed a broad pattern of maladaptive personality traits across all four higher order dimensions" of the DAPP-BQ (emotional dysregulation, dissocial behavior, inhibitedness, and compulsivity). This pattern resembles the one seen in patients with borderline personality disorder, adding evidence to the relationship between BPD and FDS [5].

This article presents an updated review of the psychological and biological basis of both FDS and BPD. We aim to understand the relationship between the two in the reviewed publications.

Table 1: Prevalence of BPD in FDS and ES patients.

Author (Year) Country	Patients with FDS		Patients with ES		p value	Method
	n	Prevalence	n	Prevalence		
Binzer et al. (2004) Denmark [51]	n=20	35%	n=20	5%	<0.05	SCID-I, **SCID-II**, GAF Scale
Direk et al. (2012) Turkey [52]	35	40%	35	5,7%	<0.001	Psychiatric assessment, SCID-I, **SCID-II** (conducted by a qualified psychiatrist)
D'Alessio et al. (2006) Argentina [53]	24	33% (BPD and other Cluster B Personality Disorders)	19 (PNES patients with comorbid Epilepsy)	21% (BPD and other Cluster B Personality Disorders)	Not stated	Psychiatric assessment, SCID-I, **SCID-II**
Galimberti et al. (2003) Italy [54]	n=31	10%	n=31	3%	<0.001	Psychologic assessment, I.Q. evaluation, CBA, SCID P., **SCID-II**
Harden et al. (2009) Miami, USA [55]	n=16	69%	n=16	30%	0.007	**SCID-II**
Jawad et al. (1995) Wales [56]	n=46	13%	n=50 (psychiatric patients)	4%	0.1	DMI, BDI, **SCID**
Rady et al. (2021) Egypt [57]	33	66,7%	33	27,3%	0.001	MINI, **SCID-II**, Goldberg's IPIP Big Five personality questionnaire
Salinsky et al. (2018) USA [58]	n=71	40.90%	n=63	22.60%	0.03	Psychologic/ Psychiatric assessment, SCID-I, **SCID-II**, PCL, BDI-II, Combat Exposure Scale, PSEQ, TOMM, MMPI-2-RF
Scévola et al. (2013) Argentina [1]	35	42,86% (BPD and other Cluster B Personality Disorders)	49 (DRE)	18,37% (BPD and other Cluster B Personality Disorders)	0.02	Psychiatric assessment, SCID-I, **SCID-II**, GAF Scale
Stone et al. (2004) Sweden [50]	20	35%	30	7%	<0.05	Standardized Interview, SCID-I, **SCID-II**, GAF Scale, Egna Minnen Beträffande Uppfostran Self-Rating Inventory

Note: BDI: Beck Depression Inventory; CBA: Cognitive Behavioral Assessment; DMI: Defense Mechanisms Inventory; ES: Epileptic Seizures; FDS: Functional Dissociative Seizures; GAF: Global Assessment of Functioning; IQ: Intelligence Quotient; IPIP: International Personality Item Pool; MINI: Mini-International Neuropsychiatric Interview; MMPI-2-RF: Multiphasic Personality Inventory-2 Restructured Form; PSEQ: Patient Seizure Etiology Questionnaire; SCID: Structured Clinical Interview for Personality Disorders; SCID P: Structured Clinical Interview for DSM-III-R-Patient Version; TOMM: Test of Memory Malingering

Methods

We aim to produce a thorough review of FDS patients with BPD. The search strategy was made through PubMed using the following terms: ((FDS) OR (Functional Dissociative Seizure) OR (PNES) OR (Psychogenic Nonepileptic Seizures) OR (BPD) OR (Borderline Personality Disorder)) AND ((Amygdala) OR (Hippocampus) OR (Insula) OR (PFC) OR (Prefrontal Cortex)). Additionally, we undertook a hand search of references cited in selected papers. The chosen articles comprise the years 1995 to 2021.

A general framework

Conklin and colleagues state that maladaptive affect regulation strategies, characteristic of BPD patients, represent efforts to escape overwhelming or intolerable emotions [6]. Meanwhile, Yen et al. claim that BPD patients are more likely to have intense affective experiencing and report poor control of their intense emotions [7]. These descriptions of emotional control are consistent with the under-regulation of affect strategies, which, according to del Río-Casanova et al., are predominant in BPD patients [8]. Under-regulation is the inability to regulate intense emotions, such as re-experiencing traumatic events, anger, and hyperarousal, resulting in excitatory states and increased emotional responsivity. It is characterized by a decrease in the Orbitofrontal Cortex (OFC) and Ventromedial Prefrontal Cortex (vmPFC) activity, which, in turn, reduces its inhibition over limbic regions (such as the amygdala and the hippocampus), leading to a declined activation in body awareness-related areas, causing dissociative episodes.

The Under-regulation of the affect mechanism is hypothesized to cause positive conversion symptoms, characterized by excessive activity manifested by tremors, aberrant movements, and functional dissociative seizures [9]. Adding to this, Roberts & Reuber affirm that FDS may respond to intolerable panic, anger, frustration, guilt, fatigue, or other experiences, which matches the under-regulation definition [10]. FDS patients presented higher levels of dissociation (compared to Epilepsy) in both aspects proposed by Brown [11]: detachment, which entails psychological distancing from one's environment, and compartmentalization, which involves a compromise in function, as in paralysis or other somatoform conditions including FDS [10].

Biological Basis

This part of the review describes the results of neuroimaging studies done on FDS and BPD patients highlighting their similarities and differences. It has been divided into five parts, explaining variations in five brain regions: amygdala, hippocampus, insula, Prefrontal Cortex (PFC), and Anterior Cingulate Cortex (ACC). **Table 2** summarizes these neuroimaging studies, their results, and their techniques.

Amygdala

The amygdala is an almond-shaped structure with a central role in behavioral (integrating input signals and initiating activities related to them), vegetative, and endocrine activities. The most widely known function of the amygdala is in the modulation of fear, memory, and attention [12]. Its structure can be found altered in both FDS and BPD patients.

Various studies have studied amygdala variations in FDS and BPD patients. However, we only found one similarity between both disorders: greater amygdalar connectivity with the left precentral gyrus (motor control region) [13,14]. According to the authors, a stronger coupling between emotion and motor control regions may lead to a stronger increase in dissociation. This, in turn, may allow for the manifestation of involuntary motor symptoms, as previously described.

Besides, multiple studies described changes in the amygdala in FDS patients. Resting-State Functional Magnetic Resonance Imaging (RS fMRI) studies found hypo-reactivity in the bilateral amygdala, increased Functional Connectivity (FC) between the amygdala and the left precentral, inferior, and middle frontal gyri, and greater inhibitory effects from the amygdala on the left insula, inferior frontal gyri, dorsolateral, PFC, precentral gyrus, and Supplementary Motor Areas (SMA) [14,15]. A Single-Photon Emission Computerized Tomography (SPECT) found a decreased regional cerebral blood flow in the right amygdala [16].

Variations in the amygdala were also found in BPD patients. Many structural neuroimaging studies encountered a reduced Gray Matter Volume (GMV) in this structure [17-20].

Regarding functional neuroimaging studies, results tended to vary. In two studies by Hazlett et al. and Krause-Utz et al. [21,22], patients underwent Functional Magnetic Resonance Imaging (fMRI) scanning while viewing pleasant, neutral, and unpleasant pictures. BPD patients showed an increased amygdala activation while viewing unpleasant pictures, compared to Healthy Control (HC). BPD patients showed increased amygdala connectivity with numerous brain regions as well, such as the left insula, left precentral gyrus, right thalamus, right anterior cingulate [13], dorsolateral PFC, hippocampus [23], right superior/middle temporal gyrus, right middle occipital gyrus, left inferior parietal lobule and left claustrum [24]. Krause-Utz et al. [25] also found no or less amygdalar habituation in BPD patients compared to HC.

Table 2: Affected Brain Structures in FDS and BPD.

Affected Brain Structure	FDS			BPD		
	Paper	Affected Structure	Technique	Paper	Affected Structure	Technique
Amygdala	Allendorfer et al. (2019)	Hyporeactivity in left/right amygdala. Greater right amygdalar connectivity to left precentral and inferior/middle frontal gyri	RS fMRI	Depping et al. (2016)	Reduced GMV in the amygdala	SBM
	Amiri et al. (2021)	Left amygdala has greater inhibitory effects on the left insula, inferior frontal gyri, dorsolateral PFC, precentral gyrus, and SMA	RS fMRI	Hazlett et al. (2012)	Greater amygdalar reactivity and prolonged activation	fMRI during processing of neutral, pleasant, and unpleasant pictures from the IAPS

	Gallucci-Neto et al. (2021)	Decreased regional cerebral blood flow in the right amygdala	SPECT with 99mTc-ethyl cysteinate dimer	Krause-Utz et al. (2012)	Bilateral amygdala activity during emotional distraction	fMRI during performance of an emotional working memory task
				Krause-Utz, Elzinga, et al. (2014)	Increased connectivity of amygdala with left insula, left precentral gyrus, right thalamus, and right anterior cingulate during emotional distraction	fMRI during performance of an emotional working memory task
				Krause-Utz, Veer, et al. (2014)	Greater amygdala connectivity with dorsolateral PFC and hippocampus	RS fMRI
				Krause-Utz et al. (2016)	Compared to HC patients, there was no amygdala habituation	fMRI during a differential delay aversive conditioning paradigm
				Krause-Utz et al. (2018)	Stronger coupling of the amygdala with right superior/middle temporal gyrus, right middle occipital gyrus, left inferior parietal lobule and left claustrum. Those BPD patients exposed to a dissociation script showed reduced bilateral amygdala activity	fMRI combining script-driven imagery with a subsequent EWMT
				Niedtfeld I et al. (2013)	Smaller GMV in the amygdala	Structural MRI
				Richter et al. (2014)	Decrease in the right amygdala volume	VBM
				Yu et al. (2019)	Decreased GMV and GMD in the bilateral Amygdala	VBM Meta- Analysis
Hippocampus	Johnstone et al. (2016)	Smaller left hippocampal volume in patients who had experienced sexual abuse	MRI	Depping et al. (2016)	Reduced GMV in the hippocampus and parahippocampus	SBM
				Krause-Utz, Elzinga, et al. (2014)	Greater amygdalar connectivity with hippocampus	RS fMRI
				Niedtfeld I et al. (2013)	Smaller GMV in the hippocampus	Structural MRI
				Richter et al. (2014)	Decrease in the hippocampus volume bilaterally	VBM
				Rossi et al. (2012)	Decreased volumes of the bilateral hippocampi	MRI
Insula	Amiri et al. (2021)	Increased inhibition of the left insula by the amygdala, ACC and precentral gyrus	RS fMRI	Krauch et al. (2018)	Increased activation in the left posterior insula	fMRI during script-driven imagery paradigm
	Li et al. (2015)	Stronger FC between insular subregions and sensorimotor network, lingual gyrus, superior parietal gyrus and putamen	RS fMRI	Mortensen et al. (2016)	Reduced brain activity in the right mid insula	fMRI during a Posner task
				Takahashi et al. (2009)	BPD participants who had had violent episodes over the previous 6 months, had a smaller insular cortex bilaterally	MRI
				Zhou et al. (2017)	Less surface area and GMV in left anterior insula	MRI
PFC	Ding et al. (2014)	Decreased long range FC in right medial PFC	fMRI	Aguilar-Ortiz et al. (2018)	GMV reduction in the dorsolateral PFC bilaterally	VBM
	Li, Li, et al. (2015)	Increased fALFF and increased FC in the dorsolateral PFC	RS fMRI	Depping et al. (2016)	Reduced GMV in the dorsolateral PFC	SBM

				Mortensen et al. (2016)	Reduced brain activity in the right rostrolateral PFC and bilaterally in the ventromedial PFC	fMRI during a Posner task
				Winter et al. (2015)	Increased activity in the dorso-lateral PFC	fMRI to measure changes in BOLD signal, combining script-driven imagery (to experimentally induce dissociation) with a subsequent emotional stroop task
				Yu et al. (2019)	Decreased GMV and GMD in the bilateral medial PFC network	VBM Meta- Analysis
ACC	Amiri et al (2021)	Left ACC has more inhibitory effects on the insula and IFG; and right ACC is more inhibited by the insula and IFG, and has a less inhibitory effect on the SMA and precentral gyrus	RS fMRI	Amad et Al. (2017)	Increased activation of the ACC	fMRI, PET, SPECT
	Arthuis et al. (2014)	Hypometabolism in bilateral ACC	FDG- PET	Depping et al. (2016)	Reduced GMV in the ACC	SBM
	Ding et al. (2014)	Increased short-range FC in the ACC	fMRI	Hoerst et al. (2010)	Higher levels of glutamate in the ACC	MRS to measure glutamate levels in the ACC
	Labate et al. (2012)	GMV reductions in right ACC	Structural MRI, VBM	Krause-Utz et al.(2014)	Diminished negative resting state FC between the dorsal ACC and the left PCC and increased negative resting state FC of the left ventral ACC with occipital cortex, lingual gyrus, and cuneus	RS fMRI
	Li et al. (2015)	Increased FC values between the SMA and the ACC	RS fMRI	Lei et al. (2019)	The left ACC exhibited increased resting state FC and abnormal structural connectivity with the right MFG and decreased resting state FC with the left MTG	RS fMRI, DTI
	Ristić et al. (2015)	Increased sulcal depth in the right rostral ACC	Structural MRI	Niedtfeld et al. (2013)	Smaller GMV in the ACC	Structural MRI
	van der Kruijs et al.(2012)	Increased functional connectivity in the ACC	RS fMRI, event-related fMRI	Wingenfeld et al. (2009)	Compared to healthy controls, there was not a significant recruitment of the ACC for negative versus neutral and individual negative versus neutral conditions	fMRI during performance of an individualized EST, with neutral, general negative words, and individual negative words
				Zhou et al (2017)	Reduced cortical thickness in left ACC	MRI

Note: ACC: Anterior Cingulate Cortex; BOLD: Blood oxygen level-dependent; BPD: Borderline Personality Disorder; EST: Emotional Stroop Task; EWMT: Emotional Working Memory Task; Falff: Fractional Amplitude of Low-Frequency Fluctuations; FC: Functional Connectivity; FDG-PET: Fluorodeoxyglucose–Positron Emission Tomography; FDS: Functional Dissociative Seizures; fMRI: Functional Magnetic Resonance Imaging; GM: Gray Matter; GMD: Gray Matter Density; GMV: Gray Matter Volume; HC: Healthy Controls; IAPS: International Affective Picture Show; IFG: Inferior Frontal Gyrus; MFG: Middle Frontal Gyrus; MRI: Magnetic Resonance Imaging; MRS: Magnetic Resonance Spectroscopy; MTG: Middle Temporal Gyrus; PCC: Posterior Cingulate Cortex; PET: Positron Emission Tomography; PFC: Prefrontal Cortex; RS fMRI: Resting State Functional Magnetic Resonance Imaging; SBM: Source-based Morphometry; SMA: Supplementary Motor Area; SPECT: Single-Photon Emission Computerized Tomography; VBM: Voxel-Based Morphometry

Hippocampus

The hippocampus is a complex structure that plays a significant role in long-term memory and learning [26]. Its structure can be found altered in both FDS and BPD patients.

According to an MRI study of a group of FDS patients with childhood trauma [27], smaller left hippocampal volumes were found in patients with a history of sexual abuse than in patients without it. Additionally, a Source-Based Morphometry (SBM) study [19] and a magnetic resonance imaging (MRI) study [17] of patients with BPD showed a reduced GMV in the hippocampus. Besides, a Voxel-Based Morphometry (VBM) study [18] and an MRI study [28] found a decrease in the hippocampus volume bilaterally. These hippocampal abnormalities can manifest as emotional regulation problems or affective instability.

Moreover, one RS fMRI study showed greater Functional Connectivity (FC) between the amygdala and the hippocampus [13]. However, this study was not replicated with FDS patients.

Insula

The insula is a center of visceral information processing and interoception. It is divided into four functional regions: a sensorimotor region (mid-posterior insula), an olfactogustatory region (central insula), a socio-emotional region (anterior-ventral insula), and a cognitive region (anterior-dorsal insula). Its structure is affected in FDS and BPD [29].

Two RS fMRI studies in FDS patients have been carried out that yielded results on functional changes in the insula: in one, there was an increased inhibition of the left insula by the amygdala, the anterior cingulate cortex (ACC), and the precentral gyrus [15]; in the other, there was stronger FC between anterior ventral insula with the sensorimotor network (left postcentral gyrus and bilateral supplementary motor area) and the lingual gyrus, and stronger FC between the right anterior-dorsal insula and the posterior insula with the left superior parietal gyrus and the left putamen compared to healthy controls (HC) [30].

On the other hand, regarding insular variations in BPD patients, we found two fMRI studies. One described an increased activation in the left posterior insula [31]. The other showed reduced brain activity in the right mid-insula [32]. Furthermore, two MRI studies were found. In one, BPD participants who had had violent episodes over the previous six months had a smaller insular cortex bilaterally [33]. In the other one, there was less surface area and GMV in the left anterior insula [34]. There were, however, no overlapping changes between FDS and BPD.

Prefrontal Cortex

The PFC is a complex structure whose essential functions are the "orchestration of thoughts and actions in accordance with internal goals", encoding and retrieving memories, verbal expression, abstraction, fluency, and visual search and gaze control, among others [35,36]. Its structure can be found altered in both FDS and BPD patients.

Structural neuroimaging studies were only carried out in BPD patients, and a GMV reduction of the dorsolateral PFC was found in VBM [37] and SBM [19] imaging techniques. Furthermore, another VBM study found a decreased GMV and GMD in the bilateral medial PFC network [20].

On the contrary, functional neuroimaging studies were realized in FDS and BPD patients. One RS fMRI study on FDS patients encountered increased FC in the dorsolateral PFC [38]. These findings coincide with those carried out in BPD patients that also found increased activity in the dorsolateral PFC [39]. This area is associated with executive functions, including interference inhibition of distracting emotional stimuli and emotion down-regulation.

Furthermore, an fMRI study carried out by Mortensen et al. [32] in BPD patients found reduced brain activity in the right rostrolateral PFC and bilaterally in the ventromedial PFC. Finally, Ding et al. [40], found a decreased long-range FC in right medial PFC in FDS patients. However, there were no overlapping results between FDS and BPD patients.

Anterior Cingulate

The Anterior Cingulate Cortex (ACC) location in the brain allows it to connect with the limbic system (emotion) and the PFC (cognition). This gives it a role in integrating neural circuits for affect regulation [41]. Its structure can be found altered in both FDS and BPD patients and can be a cause of affect dysregulation in these patients.

Structural neuroimaging studies effected (such as MRI, SBM, and VBM) in FDS [42] and BPD [7,19,34] patients found GMV reductions in the ACC. It is, however, worth clarifying that this reduction was found bilaterally in two BPD studies [17,19] but lateralized to the left in another BPD study [34] and lateralized to the right in the FDS study [42]. Moreover, another structural MRI study on FDS patients found an increased sulcal depth in the right rostral ACC [43].

Several functional neuroimaging studies were also carried out in FDS and BPD patients and showed significant variations from HC. Three fMRI studies (two of which were carried out in FDS patients and the other in BPD patients) found increased activation of the ACC (40,44,45). However, the variations found in every other study were not the same in patients with BPD and FDS.

Regarding studies performed in BPD patients, one fMRI study found no significant recruitment of the ACC compared to healthy controls [46]. Two RS fMRI found diminished negative resting-state FC between the dorsal ACC and the left posterior Cingulate Cortex (PCC); increased negative resting-state FC between the left ventral ACC and the occipital cortex, lingual gyrus, and cuneus; increased resting state FC and abnormal structural connectivity between the left ACC and the right middle frontal gyrus; and decreased resting-state FC with the left middle temporal gyrus [23,47]. Lastly, Magnetic Resonance Spectroscopy (MRS) also found higher levels of glutamate in the ACC [48].

Neuroimaging studies in FDS patients showed that the left ACC had more inhibitory effects on the insula and inferior frontal gyrus. Besides, the right ACC was more inhibited by the insula and inferior frontal gyrus and had a less inhibitory effect on the SMA and precentral gyrus [15,38]. Finally, a Fluorodeoxyglucose–Positron Emission Tomography study found ACC hypometabolism bilaterally [49].

Conclusion

In this manuscript, we carried out a state-of-the-art review to provide a critical approach to the extensive literature about FDS and BPD. We described their association by reviewing their psychological and neurobiological underpinnings. The similarities in emotion regulation strategies and brain structures and functions between FDS and BPD may shed some light on understanding the relationship between these two disorders.

Most patients with FDS present at least one current and recognizable psychiatric disorder. Even though Axis I psychiatric disorders, such as depression, are the most frequent, personality disorders are also present, with a frequency of 71.43%. Among personality disorders, Cluster B personality disorders, particularly BPD, are the most common, with their prevalence varying from 10% to 69% [1,50-58].

Emotional dysregulation and instability of interpersonal relationships, hallmarks of BPD, are frequently seen in FDS patients [8,9,59]. Interestingly, BPD and FDS patients might share a history of trauma, major depression, and Post-Traumatic Stress Disorder (PTSD) [1,60]. This leads us to think that FDS may constitute a syndrome within BPD or at least have a common etiology. If this is so, the treatments for BPD might also work for FDS, such as dialectic behavioral therapy.

This is supported by brain structural and functional similarities in FDS and BPD patients found in several neuroimaging

studies: greater connectivity between the amygdala and the left precentral gyrus may increase dissociative episodes and consequently cause positive conversive symptoms (13,14); smaller left hippocampal volumes may manifest as affective instability [17-19, 27,28]; an increase of FC in the dorsolateral PFC can lead to an increase of under-regulation of affect strategies [38,39]; and GMV reductions and increased activation of the ACC that can lead to affect dysregulation [17,19,34,40,42,45].

There are some limitations of these studies. Many of them were done with small samples to permit a meaningful generalization of conclusions, a frequent difficulty considering that FDS patients are rare. Future studies should consider a multi-center design to increase the study sample size. More extensive future studies should also consider recruiting an epilepsy population or other appropriate clinical populations as control groups, which is frequently missing in the design.

In general, studies lack a structured clinical interview aiming to have homogenous criteria for diagnosis and to measure potential medication effects. Some included patients who reported a history of complex and severe interpersonal trauma. Many patients met the criteria for comorbid anxiety disorders (e.g., PTSD), which is highly prevalent in BPD. Therefore, many of the findings may be related to interpersonal trauma per se or comorbid PTSD. Parameters relating to dissociative traits, emotional processing, and the presence of psychiatric comorbidities (anxiety, depression or the presence of Post-Traumatic Stress Disorder (PTSD)) were not formally measured in many studies, and the degree of heterogeneity was frequently not documented. The presence of all these problems might constitute critical confounding factors.

Besides, the social dimension of distractors (e.g., using interpersonal scenes versus objects as distractors) may also modulate brain connectivity, generating confounding information. Studies were generally cross-sectional rather than longitudinal, so it is difficult to identify the effects of symptoms on the brain or answer whether the observed asymmetries were genetically determined (innate) or consequent to the development of BPD or FDS symptoms. Cross-sectional comparisons do not address the longitudinal evolution of MRI findings.

As seen above, the literature is sometimes hard to read or analyze, arriving at opposite conclusions. Nevertheless, some core cerebral structures are altered in these disorders. Future studies might show a more straightforward path, but for the moment, it seems clear that FDS and BPD share brain alterations, constituting disorders of the central nervous system.

Disclosure

The authors reported no conflicts of interest for this work.

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