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Similar cortical but not subcortical gray matter abnormalities in women with posttraumatic stress disorder with versus without dissociative identity disorder

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ABSTRACT

Neuroanatomical evidence on the relationship between posttraumatic stress disorder (PTSD) and dissociative disorders is still lacking. We acquired brain structural magnetic resonance imaging (MRI) scans from 17 patients with dissociative identity disorder (DID) and co-morbid PTSD (DID-PTSD) and 16 patients with PTSD but without DID (PTSD-only), and 32 healthy controls (HC), and compared their whole-brain cortical and subcortical gray matter (GM) morphological measurements. Associations between GM measurements and severity of dissociative and depersonalization/derealization symptoms or lifetime traumatizing events were evaluated in the patient groups. DID-PTSD and PTSD-only patients, compared with HC, had similarly smaller cortical GM volumes of the whole brain and of frontal, temporal and insular cortices. DID-PTSD patients additionally showed smaller hippocampal and larger pallidum volumes relative to HC, and larger putamen and pallidum volumes relative to PTSD-only. Severity of lifetime traumatizing events and volume of the hippocampus were negatively correlated. Severity of dissociative and depersonalization/derealization symptoms correlated positively with volume of the putamen and pallidum, and negatively with volume of the inferior parietal cortex. Shared abnormal brain structures in DID-PTSD and PTSD-only, small hippocampal volume in DID-PTSD, more severe lifetime traumatizing events in DID-PTSD compared with PTSD-only, and negative correlations between lifetime traumatizing events and hippocampal volume suggest a trauma-related etiology for DID. Our results provide neurobiological evidence for the side-by-side nosological classification of PTSD and DID in the DSM-5.

1. Introduction

A proportion of individuals develop posttraumatic stress disorder (PTSD) following potentially traumatizing events. Confronted with reminders of these events, many individuals with PTSD become hyperaroused, experience flashbacks and relive their traumatic experiences (Lanius et al., 2010). These symptoms have also been referred to as 'positive' dissociative symptoms (Nijenhuis and van der Hart, 2011). However, some individuals become hypoaroused, emotionally numb, and experience depersonalization and derealization (Lanius et al., 2010). These symptoms have been referred to as 'negative' dissociative symptoms (Nijenhuis and van der Hart, 2011). The latter pattern would particularly characterize PTSD patients who have experienced prolonged traumatizing events such as chronic childhood physical and psychological abuse. Whereas some predominantly respond with hyperarousal and others with hypoarousal, still others alternate between the two (Van der Hart et al., 2006; Lanius et al., 2010). Although several imaging studies have investigated the neuroanatomical correlates of PTSD (Bremner et al., 2003; Geuze et al., 2008; Kasai et al., 2008; Woodward et al., 2009), the neuroanatomical correlates of dissociative symptoms in relation to lifetime potentially traumatizing events remain unclear.

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The recent nosological classification in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) has placed PTSD in the trauma- and stressor-related disorders (TSRD) category, right before the dissociative disorders (DD) category "to indicate the close relationship between them" (Spiegel et al., 2013). Among dissociative disorders, dissociative identity disorder (DID) is the most severe one, and it shares many of the features described for PTSD. DID is further characterized by a disruption of identity by two or more distinct "personality states", a discontinuity in the sense of self, impaired recall of everyday events or important personal information, and/or traumatizing events that are inconsistent with ordinary forgetting. In individuals with DID, symptoms such as dissociative amnesia, depersonalization/derealization, and sensorimotor negative dissociative symptoms can cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. Interestingly, PTSD has been conceptualized as a "simple dissociative disorder" (Van der Hart et al., 2006), and DID as a severe childhood-onset PTSD (Boon and Draijer, 1993a, 1993b; Putnam, 1997; Van der Hart et al., 2006; Spiegel et al., 2013). However, empirical neurobiological evidence for such an intimate relationship is lacking.

Abundant clinical observations and retrospective correlational research suggest that DID is related to a history of severe and chronic childhood traumatization (Chu and Dill, 1990; Boon and Draijer, 1993b; Mulder et al., 1998; Draijer and Langeland, 1999; Van der Hart et al., 2006; Nijenhuis and Den Boer, 2009). However, there is still an ongoing debate about the etiology of DID (Dalenberg et al., 2012, 2014; Paris, 2012; Brand et al., 2013; Martinez-Taboas et al., 2013; Lynn et al., 2014). Two competing models concerning the etiology of DID have been put forward (Dalenberg et al., 2012; Reinders et al., 2012). *The trauma-related* model indicates that DID is causally related to early childhood traumatization by a combination of factors such as disorganized attachment, lack of affect regulation by caregivers, and chronic and severe neglect and abuse (Boon and Draijer, 1993a; Van der Hart et al., 2006). In this model, DID is comprehended as a childhood onset posttraumatic disorder. This model accommodates the fact that more than 90% of the DID patients meet the criteria for PTSD (Rodewald et al., 2011). Conversely, *the non-trauma-related* model (Lilienfeld et al., 1999; Merckelbach and Muris, 2001; Piper and Merskey, 2004; Giesbrecht et al., 2008), which is also referred to as the sociocognitive (Spanos, 1996) or fantasy model (Dalenberg et al., 2012), assumes that DID is due to simulation, suggestive psychotherapy and/or sociocultural influences and is mediated by high fantasy proneness. Neurobiological research testing these models has been called for by proponents of both models (Brand, 2012; Paris, 2012) as it can help clarify the etiology and nature of DID, which will eventually help diagnoses and treatment of these patients.

So far, there are only a few studies on brain morphological abnormalities in DID which investigated gray matter (GM) volumetric abnormalities in only a small number of *a-priori* hypothesized regions. Compared with healthy controls (HC), patients with DID had smaller volumes of the parahippocampal cortex (Ehling et al., 2008), hippocampus (Tsai et al., 1999; Vermetten et al., 2006; Ehling et al., 2008; Irle et al., 2009) and amygdala (Vermetten et al., 2006; Ehling et al., 2008; Irle et al., 2009). To our knowledge, no neuroimaging study has yet assessed whole-brain morphology in DID. The neuroanatomical correlates of PTSD mainly point to smaller GM volume of the hippocampal formation and insula, frontal (including anterior cingulate, medial and lateral prefrontal, orbitofrontal, superior, middle and inferior frontal) cortices and temporal (including superior temporal and parahippocampal) cortices (Bremner et al., 2003; Geuze et al., 2008; Kasai et al., 2008; Weniger et al., 2008; Woodward et al., 2009; Nardo et al., 2010, 2013; Kuo et al., 2012). Furthermore, previous literature investigating the relationships between brain morphology and severity of lifetime traumatizing events, dissociative and depersonalization/derealization symptoms in both DID and PTSD patients have reported mixed findings (Stein et al., 1997; Bremner et al., 2003; Ehling et al., 2008; Nardo et al., 2010, 2013). Therefore, these relationships need to be explored further, preferably in larger samples of DID and PTSD patients than were included to date.

The current study investigated, for the first time, whole-brain cortical and subcortical GM morphological features in patients with DID and co-morbid PTSD and compared them to those of gender, education and age-matched HC and patients with PTSD. It also explored the relationship between the morphological features and severity of lifetime traumatizing events, and dissociative, and depersonalization/derealization symptoms.

We hypothesized that (1) patients with DID and co-morbid PTSD and patients with PTSD only would show GM reductions compared to controls, in the frontal cortices (including anterior cingulate, medial and lateral prefrontal, orbitofrontal, superior, middle and inferior frontal) (Geuze et al., 2008; Woodward et al., 2009; Nardo et al., 2013) and insular cortex (Kasai et al., 2008) as well as in the hippocampus and amygdala (Vermetten et al., 2006; Ehling et al., 2008); (2) Differences in GM abnormalities between the two patient groups were expected in the inferior parietal cortex (Simeon et al., 2000; Reinders et al., 2003, 2006, 2012, 2014) and the dorsal striatum (Reinders et al., 2014). Finally, (3) we expected that volume of the GM regions sensitive to the effects of stress, such as the hippocampus, would show negative correlations with severity of the lifetime traumatizing events. Furthermore, correlations with severity of dissociative symptoms were expected in the parietal cortices and the striatum, but with unknown directionality due to heterogeneity of previous findings.

2. Methods

2.1. Subjects

Sixty-five women underwent magnetic resonance imaging (MRI): 17 with a diagnosis of DID and co-morbid PTSD, 16 with a diagnosis of PTSD only and 32 HC. Participants were Caucasian and were all matched for gender, age, number of years of education (Table 1). DID patients and PTSD patients with a history of interpersonal traumatizing events were recruited via mental healthcare institutions and internet advertisements.

The diagnosis of DID was assessed by one of two DID experts (E.N. or N.D.) using the Structural Clinical Interview for DSM-IV Dissociative Disorders (SCID-D) (Boon and Draijer, 1993a; Steinberg, 1993) during which a possible PTSD co-morbidity was assessed as well. Of the DID patients, 82.35% ($n=14$) met criteria for PTSD. The remaining 17.65% ($n=3$) had PTSD symptoms, but these had become reduced with psychotherapy at the time of the MRI measurements. These three individuals were thus cases of PTSD in remission. We refer to this sample of 17 patients as "DID-PTSD". The personal therapists of the patients with DID-PTSD reported the following co-morbid disorders, based on DSM-IV classification (American Psychiatric Association, 1994): somatoform disorder ($n=2$), recurrent major depression ($n=4$), dysthymic disorder ($n=1$), trauma-related specific phobias ($n=2$), personality disorder-not otherwise specified ($n=2$), mixed personality disorders ($n=2$), borderline personality disorder symptoms ($n=3$), dependent personality disorder symptoms ($n=1$), histrionic personality disorder symptoms ($n=1$), eating disorder ($n=2$), sleeping disorder ($n=2$), and catalepsy ($n=1$).

Severity of psychoform and somatoform dissociative symptoms were evaluated using the Dissociative Experiences Scale (DES: Bernstein and Putnam (1986)) and Somatoform Dissociation Questionnaire (SDQ-20: Nijenhuis et al. (1996)), respectively. The DES is a 28-item self-report screening questionnaire on which participants indicate which percentage of time (0–100%) each statement of psychoform dissociation applies to them. The overall DES score is the average of all the item scores and ranges from 0 to 100. The SDQ-20 is a 20-item questionnaire whose items range from 1 to 5 and pertain to negative (e.g., analgesia) and positive somatoform dissociative phenomena (e.g., site-specific pain) and the total score ranges from 20 to 100. The five-item SDQ-5 (total score range: 5–25) was derived from the SDQ-20. These five items as a group discriminate best between patients with and without a dissociative disorder (Nijenhuis et al., 1997, 1998). The cut-off scores that we used for the DES and SDQ-5 were 25 and 7, respectively (Boon and Draijer, 1993b; Nijenhuis et al., 1997). Depersonalization symptoms were evaluated using the Cambridge Depersonalization Scale (CDS: Sierra and Berrios (2000)), which is a 29-item self-report measure of depersonalization experiences and is designed to explore the "frequency" (range 0–4) and "duration" (range 0–6) of depersonalization symptoms over the last 6 months. To obtain a total score, the