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The traumatized brain

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A Comparison of Cortical and Subcortical Gray Matter in Dissociative Identity Disorder, Posttraumatic Stress Disorder and Healthy Controls

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Chapter

4

Submitted for publication

Abstract

Background: The etiology of dissociative identity disorder (DID), previously known as multiple personality disorder, remains a subject of debate. Limited neuroscientific research allows this debate to continue. While some assume an iatrogenetic origin, clinical observation and research suggest that DID is a trauma-related disorder and a severe form of posttraumatic stress disorder (PTSD). A direct whole-brain anatomical comparison between the two groups could test this last hypothesis. In this study we investigate the neuroanatomical differences between DID, PTSD and healthy controls (HC).

Method: Brain structural magnetic resonance images were acquired from 17 DID and 16 PTSD patients and 28 HC. All participants were matched for gender, age and education. Cortical and subcortical gray matter volumetric measures were extracted and were compared between groups.

Results: In DID and PTSD patients the cortical gray matter volume was found to be similarly smaller for the whole-brain, frontal, temporal and insular cortices, compared to HC. The subcortical measures revealed that DID patients had smaller hippocampal and larger caudate and pallidum volumes relative to HC and had larger putamen and pallidum volumes relative to PTSD patients. We propose that this large dorsal striatum volume in DID may be related to the involvement of this structure in switching between and maintenance of identity states and/or memory.

Conclusions: On the basis of the similarities between DID and PTSD patients, and their joint differences relative to HC in cortical morphological changes, our study supports a trauma-related etiology for DID. These findings are of clinical importance and have potential for translation into patient's benefit.

Introduction

Dissociative identity disorder (DID) is a mental disorder that, according to DSM-IV, is characterized by the presence of two or more different identity states that recurrently take control of a person's behavior and consciousness. Dissociative amnesia, depersonalization, derealization, and sensori-motor dissociative symptoms are other characteristic features of this disorder.

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, 1993, Van der Hart et al., 2006). In this view DID is thought to be a severe form of posttraumatic stress disorder (PTSD) (Spiegel, 1984). *The non-trauma-related* model (Giesbrecht et al., 2008, Merckelbach and Muris, 2001) is also referred to as the sociocognitive (Spanos, 1996) or fantasy model (Dalenberg et al., 2012) and assumes that DID is due to simulation, suggestive psychotherapy and/or sociocultural influences and is mediated by high fantasy proneness. A recent literature review evaluated the evidence for the trauma-related and fantasy models and reported that when fantasy proneness is controlled pathological dissociation still is predictive of a trauma history (Dalenberg et al., 2012).

Neurobiological studies in DID are scarce (for review see Dalenberg et al., 2012, Reinders, 2008) and functional brain imaging studies have reported widespread findings throughout the brain (Elzinga et al., 2007, Sar et al., 2007, Savoy et al., 2012, Tsai et al., 1999). Reinders et al. (2003, 2006 and 2012) reported that different prototypical (Van der Hart et al., 2006) dissociative identity states in DID are associated with different brain activation patterns when confronted with trauma-related cues, proposing the involvement of mainly the cortical posterior-association-areas (PAA) and subcortical amygdala and subparts of dorsal-striatum (i.e. the caudate and putamen) in the psychopathology of DID. In addition, their most recent neuroimaging study revealed that DID is not linked to

fantasy proneness (Reinders et al., 2012).

Volumetric neuroimaging studies of DID have focused on region-of-interest (ROI) analyses rather than whole-brain assessments. It has been reported that, compared to healthy-controls (HC), DID patients have a smaller parahippocampal cortex (Ehling et al., 2008), hippocampus (Ehling et al., 2008, Irle et al., 2009, Tsai et al., 1999, Vermetten et al., 2006) and amygdala (Ehling et al., 2008, Irle et al., 2009, Vermetten et al., 2006), although one study reported preserved amygdalar and hippocampal size in a sample of combined dissociative amnesia and DID patients (Weniger et al., 2008). Volumetric studies in PTSD have reported smaller gray matter (GM) volume of the hippocampus (Bremner et al., 2003, Kasai et al., 2008), and the insula (Kasai et al., 2008), frontal (Geuze et al., 2008) and temporal (Woodward et al., 2009) cortices and anterior cingulate cortex (ACC) (Kasai et al., 2008), whereas findings regarding amygdalar volume have been inconsistent (Kuo et al., 2012, Weniger et al., 2008).

The current study aims to investigate the hypothesis that DID is related to PTSD by comparing whole-brain cortical and subcortical GM morphology in DID patients to age, gender and education matched PTSD patients and HC. Based on previous studies we hypothesized that DID and PTSD groups would show (i) similarities in the GM abnormalities in the frontal, temporal and insular cortices, and (ii) differences in the parietal cortex GM abnormalities. In addition, at a subcortical level we expected to find smaller (iii) hippocampal and (iv) amygdalar volumes in both PTSD and DID patients compared to HC.

Methods

Subjects

Sixty-five females participated in this study: seventeen DID patients, sixteen PTSD patients and thirty-two HC. All subjects were matched for age, education and Western European ancestry. DID and PTSD patients were recruited via mental healthcare institutions and internet advertisements. The diagnosis of DID was assessed by one of the two DID experts (E.N. or N.D.) using the Structural Clinical

Interview for DSM-IV Dissociative Disorders (SCID-D)(Boon and Draijer, 1993, Steinberg, 1993) and PTSD comorbidity was determined using the PTSD section of the SCID-D. All DID patients met the criteria for either comorbid PTSD (82.35%) or PTSD in-remission (17.65%). PTSD patients were diagnosed by researchers E.V. and M.G. using the Clinician Administered PTSD Scale (CAPS) interview (Blake et al., 1995). Only PTSD patients with inter-personal trauma were included.

Exclusion criteria for DID and PTSD patients were: age outside 18-65, pregnancy, systemic/neurological illness, claustrophobia, presence of metal implants and alcohol/drug abuse. HC were recruited through advertisements in local newspapers. Exclusion criteria for HC were: the presence of dissociative-symptoms, as determined with the Dissociative Experiences Scale (DES) (Bernstein and Putnam, 1986) and Somatoform Dissociation Questionnaire (SDQ-20) (Nijenhuis et al., 1996), a high score on the Traumatic Experience Checklist (TEC) (Nijenhuis et al., 2002) or mental illness in the past or at present. After complete description of the study to the subjects, written informed consent was obtained according to procedures approved by the Medical Ethical Committee (METc) of the University Medical Center Groningen (UMCG) and of the Amsterdam Medical Center (AMC).

Image acquisition

Participants were scanned on a 3T magnetic resonance imaging (MRI) scanner (Philips Medical Systems, Best, NL) in one of the participating centers in The Netherlands (UMCG and AMC). The samples were balanced over the two centers (ten DID patients, ten PTSD patients and nineteen HC were scanned at UMCG), and a reproducibility study was conducted that resulted in an optimized structural MRI protocol with a high reproducibility between the two centers (Chalavi et al., 2012). The details of this protocol were: MPRAGE-sequence, TR=9.95ms, TE=5.6ms, flip-angle=8°, slice thickness=1mm isotropic-voxel, number of slices=160, total scan-time=10m14s.

88 **Table 4.1.** Demographical and clinical characteristics of the participants

	Mean(SD)			ANOVA/ χ^2		Post hoc <i>P</i> -Values		
	DID (n=17)	PTSD (n=16)	HC (n=28)	Statistic	<i>P</i> -Value	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Demographics								
Age, years	43.82(9.85)	40.75(12.05)	41.75(12.29)	F(2,58)=0.31	0.74			
Education, years	14.88(0.99)	14.94(0.85)	15.04(1.20)	F(2,58)=0.11	0.89			
Handedness, n (%right)	14(87.50%)	15(93.75%)	27(96.43%)	$\chi^2(2)= 1.31$	0.52			
Medication history								
<i>Antipsychotics: n(typical,atypical)</i>	past:2(1,1), current:8(2,6) ^a	past: 0 current: 0	past: 0 current: 0					
<i>Anti-epileptics: n</i>	past:1 current:3	past: 0 current: 0	past: 0 current: 0					
<i>Antidepressant: n</i>	past: 2 current:10	past: 0 current: 2	past: 0 current: 0					
Clinical measures								
Depersonalization (CDS)								
<i>frequency</i>	1.91(0.51)	0.85(0.44)	0.26(0.30)	F(2,57)=87.00	<0.001*	<0.001*	<0.001*	<0.001*
<i>duration</i>	2.73(0.70)	1.37(0.72)	0.44(0.47)	F(2,57)=74.66	<0.001*	<0.001*	<0.001*	<0.001*
<i>total score</i>	134.77(33.46)	64.56(32.70)	20.57(21.31)	F(2,57)=86.56	<0.001*	<0.001*	<0.001*	<0.001*
Dissociation								
<i>Psychoform (DES)</i>	54.41(16.18)	22.18(13.83)	7.12(11.54)	F(2,58)=64.63	<0.001*	<0.001*	<0.001*	<0.001*
<i>Somatoform (SDQ-20)</i>	57.06(17.26)	32.69(13.43)	22.71(4.19)	F(2,58)=45.94	<0.001*	<0.001*	<0.001*	<0.001*

Table 4.1 (cont.). Demographical and clinical characteristics of the participants

	Mean(SD)			ANOVA/ χ^2		Post hoc <i>P</i> -Values		
	DID (n=17)	PTSD (n=16)	HC (n=28)	Statistic	<i>P</i> -Value	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Traumatic Experience Checklist (TEC)								
<i>emotional neglect</i>	12.23(3.15)	7.50(5.82)	2.07(4.13)	F(2,58)=28.84	<0.001*	<0.001*	0.002*	<0.001*
<i>emotional abuse</i>	11.06(4.11)	6.81(5.36)	0.36(1.34)	F(2,58)=49.51	<0.001*	<0.001*	0.001*	<0.001*
<i>physical abuse</i>	10.76(4.56)	3.69(4.19)	0.96(3.10)	F(2,58)=34.82	<0.001*	<0.001*	<0.001*	0.006*
<i>sexual harassment</i>	8.76(5.32)	2.56(2.58)	0.50(1.26)	F(2,58)=35.80	<0.001*	<0.001*	<0.001*	0.042*
<i>sexual abuse</i>	9.18(5.14)	2.37(3.07)	0.07(0.38)	F(2,58)=45.54	<0.001*	<0.001*	<0.001*	0.025*
<i>total trauma score</i>	17.53(4.08)	11.06(4.01)	2.25(2.43)	F(2,58)=124.21	<0.001*	<0.001*	<0.001*	<0.001*

^a one DID patient used typical antipsychotics in the past but stopped and was using atypical antipsychotics at the time of the MRI scan. Another DID patient was using atypical antipsychotics in the past but was not using any antipsychotics at the time of the MRI scan.

* *P*-value≤0.05

Two brain scans were collected from each subject whenever possible (fifteen DID patients and fourteen HC). Where both scans were artifact-free, the first scan was used, resulting in the ultimate exclusion of four scans from HC. This left seventeen DID, sixteen PTSD and twenty-eight HC scans for morphological analyses.

Demographical and clinical assessments

Table 4.1 lists demographical and clinical characteristics of the participants. DID patients filled in the questionnaires in their most predominant identity state. Depersonalization and dissociative symptoms were evaluated using the Cambridge Depersonalization Scale (CDS) (Sierra and Berrios, 2000), DES and SDQ-20. Reports of potentially traumatizing experiences were assessed using the TEC. Participants' psychotropic medication was not discontinued in this study (Table 4.1). All HC were free of present and past psychiatric medication. CDS data from one HC was missing.

Image analysis

FreeSurfer (v5.0) (<http://surfer.nmr.mgh.harvard.edu>) was used to examine different morphological measurements of GM: cortical volume (mm^3), cortical surface area (mm^2), cortical thickness (mm) and subcortical volume (mm^3). All the images were analyzed using the same version of FreeSurfer to avoid a bias due to cross version differences (Gronenschild et al., 2012). To summarize, image processing included: motion correction, skull stripping, Talairach transformation, segmentation of the subcortical white-matter (WM) and deep GM structures, intensity normalization, tessellation of the GM/WM boundary and finally, surface deformation following intensity gradients to optimally place the GM/WM and GM/cerebrospinal fluid (CSF) borders at the location where the greatest shift in intensity defines the transition to the other tissue class. Once the cortical models were completed a refinement procedure was applied to obtain a representation of the GM/WM boundary. This surface was subsequently deformed outwards to obtain an explicit representation of the pial surface, which was then divided into

distinct cortical regions. The parcellation labelled cortical sulci and gyri, and then cortical surface area and cortical thickness values were calculated in the 34 regions per hemisphere. Cortical surface area was calculated as the sum of the areas of each tessellation falling within each region. Cortical thickness was calculated as the average distance between the GM/WM boundary and the GM/CSF boundary within each region. Cortical thickness and cortical surface area can provide complementary information (Panizzon et al., 2009). Cortical volume, which is by definition the product of thickness and surface area, combines the morphological properties of both cortical surface area and cortical thickness (Panizzon et al., 2009). Each subcortical voxel was assigned one of about 40 labels by the automatic subcortical segmentation, after which subcortical volumes for each structure were extracted (Dale et al., 1999, Fischl and Dale, 2000, Fischl et al., 2004).

Volumetric measurements

FreeSurfer extracts several volumetric measurements from each brain image. In order to provide robust protection against type-I error and to satisfy the assumption for multivariate analysis of variance, which states that the number of cases in each category must be larger than the number of dependent variables, both cortical and subcortical measurements were reduced in dimensionality by creating superparcels similar to Woodward et al. (2009). For cortical measurements, left, right and total (sum of left and right) superparcels were defined for the frontal, parietal, temporal, occipital and insular cortices and whole-brain cortex (Table 4.2). For subcortical volumes, left, right and total (sum of left and right) volumes of all the segmented GM subcortical structures, i.e. thalamus, caudate, putamen, pallidum, hippocampus, amygdala, nucleus accumbens and ventral diencephalon, were extracted. Whole-brain subcortical GM volume was defined as the sum of the volumes of all the above-mentioned GM subcortical structures.

Chapter 4

Table 4.2. *Superparcel formation for cortical measurements*

Superparcel name	Cortical parcels
Frontal	Caudal and rostral middle frontal, lateral and medial orbito frontal, pars opercularis, pars triangularis and pars orbitalis of the inferior frontal, paracentral, precentral, superior frontal, frontal pole, caudal and rostral anterior cingulate
Parietal	Superior and inferior parietal, postcentral, precuneus, isthmus and posterior cingulate, supramarginal.
Temporal	Superior, middle and inferior temporal, temporal pole, transverse temporal, banks of the superior temporal sulcus, parahippocampal, entorhinal, fusiform
Occipital	Lateral occipital, cuneus, lingual, peri-calcarine
Insula	Insula
Whole-brain	Sum of the five superparcels (Frontal, Parietal, Temporal, occipital, Insula)

Statistical analyses

All statistical analyses were conducted using SPSS 18.0. For both cortical and subcortical morphological measures an F test was conducted for the main effect of group on the total measurements (Omnibus test). In this test, group and center were used as categorical predictors, and age and parenchymal volume (total GM + total WM) as continuous predictors. Subsequently, for each superparcel and subcortical GM area pairwise t -tests were performed on the total measures for: i) DID vs. HC, ii) DID vs. PTSD and iii) PTSD vs. HC. As post-hoc analysis, pairwise t -tests were performed on the left and right volumetric measurements. To protect against type-I error, multiple comparison correction was applied using Bonferroni-Holm for both the Omnibus test (to correct for number of measurements) and pairwise comparisons (to correct for the number of groups).

Results

Demographics

The three groups did not significantly differ with respect to age, education or handedness (Table 4.1). Depersonalization and dissociative symptoms were significantly higher in DID compared to HC and PTSD. PTSD patients also reported higher depersonalization and dissociative symptoms compared to HC. Potentially traumatic experiences (as measured using the TEC) were significantly higher in DID compared to HC and PTSD. The TEC scores were also higher for PTSD patients compared to HC.

Volumetric measurements

Cortical volume

A significant main effect of group was found in cortical volumes of the whole-brain, frontal, temporal and insula superparcels (Table 4.3). Pairwise tests revealed that compared to HC, DID patients had smaller cortical volume of the whole-brain, both hemispheres, and total left and right frontal and temporal, left parietal, and total and left insula superparcels. PTSD patients had smaller cortical volume of the whole-brain, both hemispheres, and total, left and right frontal and temporal and total and left insula superparcels (Figure 4.1). No significant difference was found when comparing cortical volumes of DID and PTSD.

Cortical surface area

Significant differences between the groups were found in cortical surface area of the frontal and insula superparcels (Table 4.4). Pairwise tests revealed smaller cortical surface area of the right frontal and left insula superparcels in DID relative to HC. Compared to HC, PTSD patients had smaller cortical surface area of the whole-brain, both hemispheres, left and right frontal and temporal, and left insula superparcels. No significant differences were found when comparing the cortical surface areas of DID and PTSD.

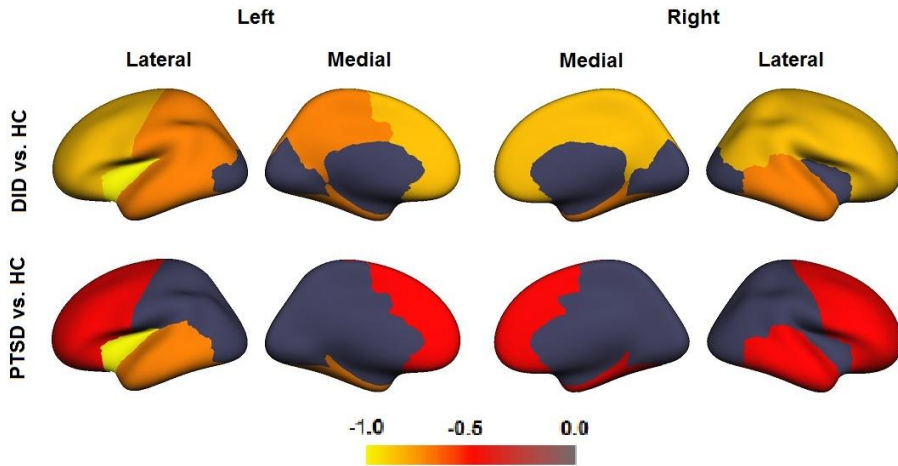


Figure 4.1. Cortical maps displaying the Cohen's *d* effect sizes of the superparcels that showed a significant cortical volume difference in the contrasts DID vs. HC (upper row) or PTSD vs. HC (bottom row). DID= dissociative identity disorder; PTSD= posttraumatic stress disorder; HC= healthy controls.

Cortical thickness

The omnibus tests and the pairwise tests did not show any significant effect of group on cortical thickness measurements.

Subcortical volume

Volumes of the hippocampus, putamen and pallidum differed significantly between the groups (Table 4.5). Pairwise tests showed smaller total, left and right hippocampal volumes in DID as compared to HC (Figure 4.2). In addition, larger total and left caudate, and total and right pallidum volumes were found in DID relative to HC. DID was found to have larger total, left and right putamen and total and right pallidum volumes as compared to PTSD. PTSD and HC groups did not differ significantly with regard to subcortical measurements.

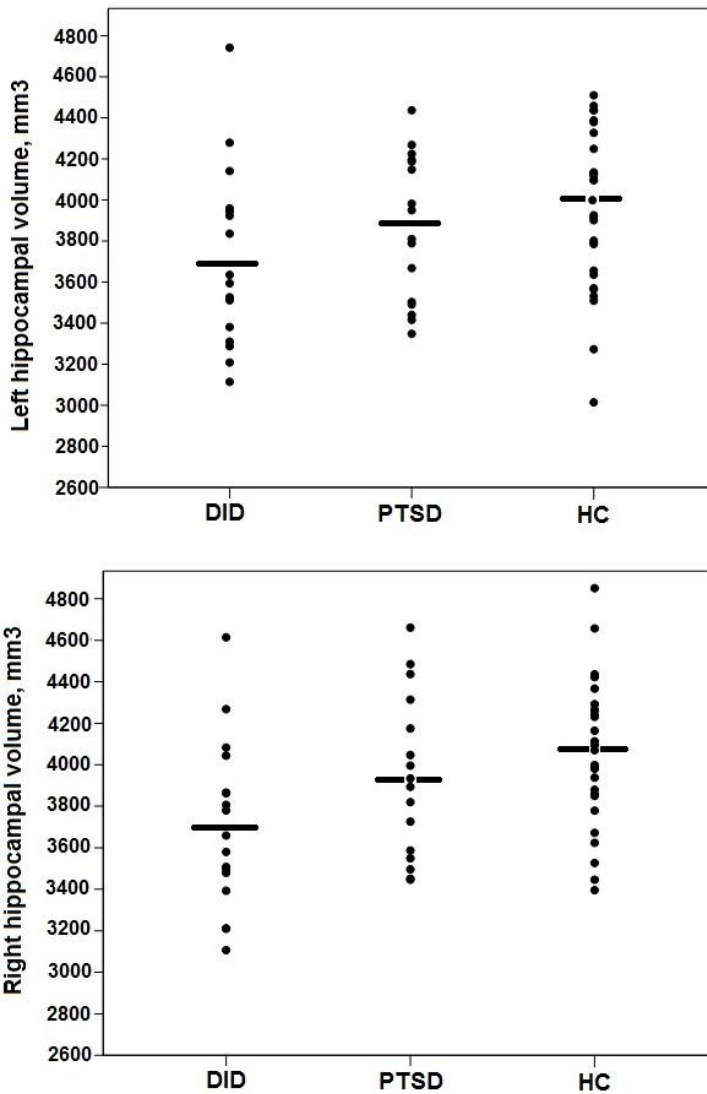


Figure 4.2. Left and right hippocampal volumes in DID, PTSD and HC. The bold horizontal lines indicate mean values and the dots represent the individual hippocampal volumes. DID= dissociative identity disorder; PTSD= posttraumatic stress disorder; HC= healthy controls.

Table 4.3. Statistical results for cortical volume (mm³)

Superparcel	Total/ side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Effect size [^])		
			DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Whole-brain	total	0.002**	446401(37257)	452332(37169)	468430(28543)	0.003** (-0.67)	0.98(-0.16)	0.003** (-0.49)
	left		222674(18165)	225741(18497)	234336(14676)	0.001** (-0.71)	0.91(-0.17)	0.001** (-0.52)
	right		223727(19168)	226591(18820)	234094(14003)	0.009** (-0.63)	0.99(-0.15)	0.011** (-0.46)
Frontal	total	0.003**	167141(16312)	169937(17707)	176665(10572)	0.002** (-0.71)	0.79(-0.16)	0.007** (-0.48)
	left		83709(7489)	85356(8528)	88555(5548)	0.001** (-0.74)	0.74(-0.21)	0.005** (-0.45)
	right		83431(8863)	84581(9253)	88110(5173)	0.006** (-0.67)	0.85(-0.13)	0.012** (-0.49)
Parietal	total	0.19	121424(8372)	124058(8490)	126517(9795)	0.084(-0.56)	0.62(-0.31)	0.24(-0.27)
	left		60021(3960)	61775(4731)	63019(5287)	0.041* (-0.65)	0.43(-0.40)	0.24(-0.25)
	right		61403(4545)	62283(3926)	63497(4702)	0.20(-0.45)	0.88(-0.21)	0.28(-0.28)
Temporal	total	0.016**	100784(9853)	101619(8226)	105858(7498)	0.031* (-0.58)	0.65(-0.09)	0.010** (-0.54)
	left		50669(5019)	50664(4021)	53209(3967)	0.038* (-0.57)	0.36(0.00)	0.003** (-0.64)
	right		50114(4873)	50955(4315)	52648(3719)	0.039* (-0.59)	0.95(-0.18)	0.050* (-0.42)
Occipital	total	0.39	43885(4534)	43524(4401)	45340(4850)	0.51(-0.31)	0.50(0.08)	0.17(-0.39)
	left		21900(2596)	21569(2068)	22552(2541)	0.69(-0.25)	0.36(0.14)	0.16(-0.43)
	right		21985(2062)	21955(2449)	22788(2513)	0.41(-0.35)	0.72(0.01)	0.24(-0.34)
Insula	total	0.002**	13165(1000)	13192(1068)	14047(1042)	0.010** (-0.86)	0.45(-0.03)	0.001** (-0.81)
	left		6373(579)	6376(523)	6999(446)	<0.001** (-1.22)	0.66(-0.01)	<0.001** (-1.29)
	right		6792(526)	6816(661)	7048(704)	0.51(-0.42)	0.41(-0.04)	0.12(-0.34)

DID= dissociative identity disorder; PTSD= posttraumatic stress disorder; HC= healthy controls.

** Corrected for multiple comparison; * Uncorrected for multiple comparisons (P-value<=0.05); ^ Cohen's d effect size

Table 4.4. Statistical results for cortical surface area (mm²)

Superparcel	Total/ side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Effect size [^])		
			DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Whole-brain	total	0.091	162433(12472)	162318(11870)	166157(11612)	0.15(-0.31)	0.49(0.01)	0.042* (-0.33)
	left		81060(6187)	81138(5922)	82813(5722)	0.16(-0.79)	0.52(-0.30)	0.050* (-0.48)
	right		81372(6320)	81180(5965)	83344(5917)	0.14(-0.05)	0.47(-0.04)	0.035* (-0.01)
Frontal	total	0.019*	59526(5360)	59487(5105)	61592(4019)	0.048* (-0.44)	0.46(0.01)	0.010** (-0.46)
	left		29732(2649)	29820(2443)	29794(2736)	0.072(-0.39)	0.57(-0.03)	0.025* (-0.37)
	right		29794(2736)	30939(2039)	29666(2678)	0.034* (-0.48)	0.38(0.05)	0.005** (-0.54)
Parietal	total	0.54	46110(3080)	46595(3098)	46828(3688)	0.31(-0.21)	0.89(-0.16)	0.44(-0.07)
	left		22705(1426)	23085(1622)	23132(1855)	0.21(-0.26)	0.78(-0.25)	0.41(-0.03)
	right		23404(1690)	23509(1542)	23695(1893)	0.45(-0.16)	0.99(-0.07)	0.50(-0.11)
Temporal	total	0.072	31819(2786)	31570(2608)	32474(2418)	0.28(-0.25)	0.23(0.09)	0.024* (-0.36)
	left		16160(1399)	15999(1409)	16409(1268)	0.47(-0.19)	0.22(0.11)	0.046* (-0.31)
	right		15658(1419)	15570(1237)	16065(1199)	0.16(-0.31)	0.28(0.07)	0.015** (-0.41)
Occipital	total	0.55	20536(1962)	20258(1914)	20669(2489)	0.74(-0.06)	0.50(0.14)	0.30(-0.19)
	left		10300(1075)	10111(948)	10314(1270)	0.91(-0.01)	0.44(0.19)	0.34(-0.18)
	right		10235(940)	10147(999)	10354(1278)	0.60(-0.11)	0.59(0.09)	0.29(-0.18)
Insula	total	0.035*	4442(272)	4406(257)	4593(366)	0.12(-0.47)	0.32(0.13)	0.013** (-0.60)
	left		2162(173)	2120(104)	2304(185)	0.005** (-0.79)	0.39(-0.30)	0.001** (-0.48)
	right		2279(131)	2286(214)	2288(230)	0.99(-0.05)	0.38(-0.04)	0.32(-0.01)

DID= dissociative identity disorder; PTSD= posttraumatic stress disorder; HC= healthy controls.

** Corrected for multiple comparison; * Uncorrected for multiple comparisons (P-value<=0.05); [^] Cohen's d effect size

8 **Table 4.5.** *Statistical results for subcortical volume (mm³)*

Subcortical structure	Total/ side	Omnibus test	Mean(SD)			Group comparisons: <i>P</i> -Value (Effect size [^])		
			DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Whole-brain	total	0.22	54297(3897)	53597(4691)	54373(2956)	0.27(-0.02)	0.087 (0.16)	0.40 (-0.20)
	left		27162(2052)	26827(2396)	27207(1571)	0.29(-0.02)	0.10 (0.15)	0.41 (-0.19)
	right		27134(1886)	26769(2322)	27165(1448)	0.27(-0.02)	0.094 (0.17)	0.43 (-0.21)
Hippocampus	total	0.030*	7404(789)	7804(723)	8016(709)	0.008** (-0.82)	0.12 (-0.53)	0.38 (-0.30)
	left		3700(428)	3866(355)	3951(387)	0.040* (-0.62)	0.24 (-0.42)	0.47 (-0.23)
	right		3704(400)	3938(391)	4065(353)	0.003** (-0.96)	0.070 (-0.59)	0.33 (-0.34)
Amygdala	total	0.99	3092(346)	3134(328)	3150(371)	0.96(-0.16)	0.99 (-0.12)	0.97 (-0.05)
	left		1544(175)	1561(180)	1584(198)	0.71(-0.21)	0.84 (-0.10)	0.56 (-0.12)
	right		1548(205)	1573(170)	1565(184)	0.79(-0.09)	0.84 (-0.13)	0.64 (0.05)
Caudate	total	0.082	7385(849)	7037(1005)	7071(632)	0.031* (0.42)	0.095 (0.38)	0.79 (-0.04)
	left		3601(406)	3441(500)	3439(323)	0.024* (0.44)	0.092 (0.35)	0.73 (0.00)
	right		3783(462)	3596(518)	3631(328)	0.052(0.38)	0.11 (0.38)	0.86 (-0.08)
Putamen	total	0.039*	10891(1120)	10408(1379)	10764(933)	0.17(0.12)	0.011** (0.39)	0.12 (-0.31)
	left		5542(621)	5313(702)	5513(469)	0.27(0.05)	0.016** (0.35)	0.098 (-0.34)
	right		5349(544)	5095(694)	5251(504)	0.13(0.19)	0.018* (0.41)	0.21 (-0.26)
Pallidum	total	0.033*	3247(306)	3072(408)	3128(301)	0.034* (0.39)	0.015** (0.49)	0.50 (-0.16)
	left		1771(189)	1704(253)	1740(181)	0.21(0.17)	0.083 (0.30)	0.45 (-0.17)
	right		1475(148)	1368(161)	1387(146)	0.003** (0.60)	0.003** (0.69)	0.67 (-0.12)

Table 4.5 (cont.). Statistical results for subcortical volume (mm3)

Subcortical structure	Total/ side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Effect size [^])		
			DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Nucleus Accumbens	total	0.26	1248(190)	1230(202)	1323(159)	0.19 (-0.43)	0.88 (0.09)	0.16 (-0.52)
	left		588(103)	584(86)	647(101)	0.060 (-0.58)	0.90 (0.04)	0.088 (-0.67)
	right		660(99)	646(131)	676(86)	0.76 (-0.17)	0.68 (0.12)	0.46 (-0.28)
Thalamus	total	0.32	12930(973)	12735(1229)	12791(1047)	0.15 (0.14)	0.24(0.18)	0.92(-0.05)
	left		6365(501)	6303(686)	6318(556)	0.18(0.09)	0.38(0.10)	0.74(-0.02)
	right		6565(486)	6431(567)	6473(540)	0.15(0.18)	0.17(0.25)	0.89(-0.08)
Ventral diencephalon	total	0.91	8097(876)	8172(656)	8127(520)	0.66(-0.04)	0.88(-0.10)	0.80(0.08)
	left		4048(474)	4118(360)	4115(312)	0.30(0.11)	0.54(-0.01)	0.74(0.15)
	right		4049(424)	4054(327)	4012(241)	0.86(-0.17)	0.78(-0.17)	0.89(0.01)

DID= dissociative identity disorder; PTSD= posttraumatic stress disorder; HC= healthy controls.

*** Corrected for multiple comparison; * Uncorrected for multiple comparisons (P-value<=0.05); ^ Cohen's d effect size*

Discussion

Our study is the first to examine whole-brain GM abnormalities in DID patients and to compare them to age- and education-matched PTSD patients and HC. Our results revealed differences in cortical and subcortical GM in DID patients compared to HC. At a cortical level these differences were similar to those found in PTSD patients compared to HC. Our results are of both clinical and neurobiological importance and suggest a trauma-related nature of DID.

Cortical gray matter

Our findings of smaller whole-brain cortical volume and surface area in DID and PTSD compared to HC (Tables 4.3 and 4.4) are in agreement with prior volumetric studies in PTSD (Woodward et al., 2009). Cortical volume measurements combine morphological properties of cortical surface area and cortical thickness. In this study, despite observing cortical thinning in several individual cortical regions (Supplementary Table ST4.1), total cortical volume abnormalities in DID and PTSD were mainly driven by differences of cortical surface area. These differences could reflect influences of genetic (Yoon et al., 2012) as well as gene-environmental factors in the etiology of DID and PTSD. More research is needed to investigate these possibilities. In the remainder of the discussion we use the term “cortical GM” for cortical volume, surface area and thickness. Exploratory detailed analyses compared cortical GM of individual brain regions within the superparcels between the groups and results are presented in Table ST4.1 and discussed below.

Frontal cortex

Cortical GM of the frontal superparcel was significantly smaller in DID and PTSD patients compared to HC. GM differences were most prominent in the orbitofrontal and adjacent caudal ACC, and superior frontal cortex, whereas precentral, pars-triangularis and caudal ACC GM volumes were smaller in DID relative to PTSD (Supplementary Table ST4.1).

Smaller cortical GM of the frontal cortices has been reported in traumatized individuals (Geuze et al., 2008). Several neuroimaging studies have also highlighted GM abnormalities of the ACC in PTSD patients and adults with a history of childhood maltreatment (Kasai et al., 2008). In addition, Forrest (2001) proposed involvement of the orbitofrontal cortex in the etiology of DID. In terms of this neurodevelopmental model of DID, an early abusive and neglectful care-giving environment compromises the maturation of the orbitofrontal cortex, which leads to difficulty integrating self-representations into a unified self.

Parietal cortex

The left parietal superparcel and specifically the left inferior parietal cortex and bilateral posterior cingulate cortex were found to have smaller cortical GM in DID compared to HC. The left inferior parietal cortical GM was also smaller in DID relative to PTSD (Supplementary Table ST4.1).

It has been shown that different prototypical (Van der Hart et al., 2006) dissociative identity states in DID have different activation patterns in the posterior association areas (PAA) (Reinders et al., 2003, 2012). These cortical regions integrate sensory information from different modalities. Functional or structural alterations in this brain region can affect the integration of somatosensory, visual, auditory or vestibular perceptions. It has been suggested that disturbed integration of different sensory perceptions in the temporal-parietal junction and parietal cortex are causally related to dissociative symptoms (Reinders et al., 2003) and out-of-body experiences (Blanke and Arzy, 2005). Post-hoc correlation analyses revealed correlations between patients' left inferior parietal GM volume (normalized for whole-brain volume) and depersonalization (Simeon et al., 2000) (CDS: Spearman's- $\rho=-0.342$; $p=0.050$), and dissociative symptoms (DES: Spearman's- $\rho=-0.352$; $p=0.045$). This can indicate that this brain region plays an important role in the symptomatology of DID (Reinders et al., 2003, 2012).

Temporal cortex

Cortical GM of the temporal superparcel was found to be smaller in both DID and

PTSD patients relative to HC. In the DID group, this was driven by smaller inferior-temporal and superior-temporal regions and in PTSD by smaller superior, middle and inferior temporal regions (Supplementary Table ST4.1). These findings are in accord with prior PTSD studies (Geuze et al., 2008, Woodward et al., 2009) and have been linked to cognitive and memory deficits (Francati et al., 2007) and dissociative-symptoms (Geuze et al., 2008).

Insular cortex

Smaller cortical GM of the insula was found in both DID and PTSD patients compared to HC. The insula has been implicated in interoceptive awareness of emotional states (Craig, 2003) and has been indicated as an important node in the functional network for emotion regulation in dissociative PTSD (Lanius et al., 2010) and DID (Reinders et al., 2003, Reinders et al., 2012).

Subcortical volume

Hippocampus

Smaller bilateral hippocampal volume was found in DID compared to HC (see Figure 4.2) which is in line with previous neuroimaging reports of smaller hippocampal volume in DID (Ehling et al., 2008, Irlé et al., 2009, Tsai et al., 1999, Vermetten et al., 2006). A previous volumetric study in DID by Vermetten et al.(2006) was criticized as having shown age-dependent rather than genuine smaller hippocampal volume (Smeets et al., 2006). However, the findings of Vermetten et al.(2006) are corroborated by the current study in which subjects were carefully matched for age, gender and education. Smaller hippocampal volume in DID, compared to HC, can be a result of prolonged exposure to stress hormones given the high density of hippocampal glucocorticoid receptors (Sapolsky, 1993). Alternatively, it has been hypothesized that smaller hippocampal volume can be a predisposing factor for the development of, rather than a result of, trauma-related disorders (Gilbertson et al., 2002) or the result of an interaction between genetic and environmental influences. Given the cross-sectional design of this study, our results do not provide evidence for either hypothesis.

The finding of smaller bilateral hippocampal volume is also supported by previous neuroimaging reports of smaller hippocampal volume in PTSD and victims of childhood-maltreatment (Bremner et al., 2003, Weniger et al., 2008). Interestingly, a trend was found for a smaller right hippocampal volume in DID compared to PTSD. It has been reported that chronic treatment with antidepressants increases hippocampal volume (Vermetten et al., 2003). The majority of DID patients (10 current; 2 past) and only 2 PTSD patients reported using antidepressants. Therefore the trend of a smaller hippocampal volume in DID relative to PTSD may be an underestimation of the genuine effect. Post-hoc investigation of the TEC scores revealed severe traumatic experiences between the age of 0 to 6 for the DID patients and between the age of 7 to 12 for the PTSD patients. The severity of the traumatic experiences was significantly ($p < 0.001$) higher in DID as compared to PTSD. Our finding of smaller hippocampal volume in DID as compared to PTSD might therefore be related to differences in the onset, frequency, duration and severity of traumatizing events in childhood between these groups.

Amygdala

Contrary to our hypothesis, both DID and PTSD patients showed preserved amygdalar volumes relative to HC. Although hyperactive amygdala function has been observed in DID (Reinders et al., 2003, 2006, 2012) and PTSD (Lanius et al., 2010) patients, findings regarding amygdalar GM volume have been inconsistent. Some studies have reported smaller amygdalar volume in DID (Ehling et al., 2008, Vermetten et al., 2006) and PTSD (Weniger et al., 2008), whereas others have observed preserved or larger amygdalar volume in DID (Weniger et al., 2008) or PTSD (Kuo et al., 2012, Weniger et al., 2008). However, our finding of preserved amygdalar volume does not rule out the possibility of a hyperactive amygdala.

Dorsal striatum

The caudate, putamen and pallidum form a compound structure called the dorsal striatum. In the current study, DID patients had larger caudate and pallidum compared to HC, and larger putamen and pallidum relative to PTSD. Dorsal-

striatum enlargement has been associated with using typical, but not atypical, antipsychotics (Chakos et al., 1994). In our study, three out of seventeen DID patients reported usage of typical antipsychotics. Analyses were repeated by excluding these three patients (Supplementary Table ST4.2) and a more robust enlargement of bilateral caudate volume in DID was found compared to both HC (left: $p=0.007$; right: $p=0.009$) and PTSD (left: $p=0.031$; right: $p=0.026$). The results for putamen and pallidum volumes did not change. Therefore, antipsychotic usage is unlikely to explain the dorsal-striatum enlargement in our DID group.

While admittedly speculative, we propose that our findings of abnormal dorsal striatal volume in DID compared to PTSD and HC might be related to habitual switching between identity states (Tsai et al., 1999) or maintenance of a dissociative identity state in DID (Reinders et al., 2006, 2012). A single-subject functional MRI study reported the involvement of the ventral striatum (i.e. the nucleus accumbens) during dissociative identity switching (Savoy et al., 2012). Furthermore, studies in patients with focal lesions in the dorsal striatum indicate the involvement of this structure in task switching and inhibition of irrelevant cues (Yehene et al., 2008). Another speculative explanation is related to the involvement of the dorsal striatum in memory. Evidence from studies on rodents has suggested that glucocorticoid injection into the dorsal striatum enhances memory consolidation (Quirarte et al., 2009). A recent fMRI study with healthy human participants showed that stress impaired the functioning of the hippocampal declarative memory system, which coincided with higher activation of the dorsal striatum involved in procedural memory (Schwabe and Wolf, 2012). In a PET study with DID patients, dissociative identity states fixated in trauma-related memories had more caudate and less hippocampal activation than dissociative identity states in which trauma-related memories were mentally avoided, while listening to an autobiographical trauma memory script (Reinders et al., 2003, 2006, 2012). Taking the neural activation hypotheses for dissociative identity switching, task switching, and stress related hippocampal-striatal memory retrieval switching together, we propose that the dorsal striatum is involved in the recurrent alternation between different dissociative identity states, their self-stabilization for a period of time, and

the dominance of trauma-related procedural memory for trauma-related dissociative identity states. Future studies can further test these hypotheses and replicate our findings of enlarged striatal volume.

Etiology

A high degree of similarity between DID and PTSD, as compared to HC, was found with regard to smaller cortical GM in the frontal, temporal and insular cortices, higher dissociative and depersonalization symptoms as well as greater reported exposure to potentially traumatizing events. These results suggest a trauma-related pathology for DID similar to that in PTSD and absent in HC. All DID patients in this study had PTSD comorbidity. However, compared to PTSD, the DID group had a smaller hippocampus, larger dorsal-striatum and reported higher dissociative symptoms. They also reported more potentially traumatizing events. This supports our hypothesis that DID is an extreme form of PTSD. Thus, the results of this study are in line with the trauma-related model for DID (Dalenberg et al., 2012, Reinders et al., 2012, Van der Hart et al., 2006). By contrast, the non-trauma-related model stating that DID is due to enactment or suggestive psychotherapy ('iatrogenesis') neither predicts nor explains our findings.

Some limitations of the present study should be considered. First, although the current study is thus far the only and largest whole-brain morphology study in DID and results survive multiple comparison correction, it includes a modest sample-size of 17 DID and 16 PTSD patients. Second, only female patients and controls were studied, consequently our findings cannot be extended to DID and PTSD populations in general. Third, there is a difference in psychotropic medication intake that could have affected our findings. Fourth, childhood trauma as well as neglect are retrospectively assessed and could thus be subjective and distorted.

In conclusion, our study is the first to provide evidence for cortical and subcortical GM abnormalities in DID. The similarities between DID and PTSD and their joint differences compared to HC suggest a trauma-related etiology for DID and plead against a non-trauma-related etiology. These findings thus are clinically relevant, and have definite potential for translation into patient's benefit.

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Supplemental Material for:

A Comparison of Cortical and Subcortical Gray Matter in Dissociative Identity Disorder, Posttraumatic Stress Disorder and Healthy Controls

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Chapter

4

Supplementary Table ST4.1

The results as presented in the main manuscript are based on of the volumetric measurements of the cortical GM of the superparcels. This supplementary material presents the additional analyses which were performed on the individual parcels within each superparcel in order to investigate which brain regions were driving the cortical GM differences for each GM measurement (i.e. volume, surface area and thickness) between dissociative identity disorder (DID), posttraumatic stress disorder (PTSD) and healthy controls (HC).

Supplementary Table ST4.2

The subcortical results presented in the main manuscript (Table 4.5) showed an enlargement of the areas of the dorsal striatum, i.e. the caudate, putamen and pallidum in DID as compared to HC and PTSD. In order to ascertain that these findings were genuine and not due to the use of typical antipsychotics (Chakos et al., 1994, Gur et al., 1998, Massana et al., 2005) as reported by three DID patients, we repeated the statistical analyses on the dorsal striatum volumes after excluding the three DID patients with current or past histories of typical antipsychotic use. The results are reported in Supplementary Table ST4.2.

References

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Supplementary Table ST4.1. Statistical results for cortical measurements (i.e. volume, surface area and thickness) of the individual parcel within each superparcel

Cortical parcel	Measure	Side	Omnibus test	Mean(SD)			Group comparisons: <i>P</i> -Value (Cohen's <i>d</i> effect size)		
				DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
<i>Frontal superparcel</i>									
Caudal middle frontal	volume	left	0.90	6200(1089)	6301(1227)	6274(1026)	0.94(-0.07)	0.68(-0.09)	0.69(0.02)
		right	0.49	5517(848)	5772(1101)	5854(901)	0.36(-0.39)	0.25(-0.26)	0.69(-0.08)
	surface area	left	0.67	2235(378)	2253(432)	2254(355)	0.71(-0.05)	0.62(-0.04)	0.38(0.00)
		right	0.35	1932(273)	2015(339)	2061(322)	0.16(-0.43)	0.59(-0.27)	0.48(-0.14)
	thickness	left	0.77	2.48(0.08)	2.49(0.12)	2.49(0.09)	0.96(-0.01)	0.56(-0.11)	0.49(0.10)
		right	0.82	2.53(0.10)	2.54(0.16)	2.53(0.11)	0.80(-0.07)	0.54(-0.09)	0.66(0.03)
Rostral middle frontal	volume	left	0.26	14177(1936)	13969(1892)	14632(1288)	0.51(-0.28)	0.36(0.11)	0.10(-0.42)
		right	0.66	14863(2498)	14978(2125)	15421(1588)	0.47(-0.27)	0.93(-0.05)	0.42(-0.24)
	surface area	left	0.24	5373(704)	5344(660)	5462(506)	0.44(-0.15)	0.38(0.04)	0.098(-0.20)
		right	0.43	5709(788)	5679(803)	5841(634)	0.51(-0.19)	0.54(0.04)	0.21(-0.23)
	thickness	left	0.55	2.28(0.08)	2.27(0.14)	2.30(0.14)	0.61(-0.18)	0.58(0.13)	0.27(-0.24)
		right	0.86	2.24(0.10)	2.27(0.14)	2.26(0.15)	0.74(-0.13)	0.58(-0.25)	0.78(0.10)
Lateral orbito frontal	volume	left	0.006*	7013(818)	7342(877)	7638(723)	0.002* (-0.81)	0.26(-0.39)	0.059(-0.37)
		right	0.19	6263(904)	6436(795)	6640(586)	0.074(-0.51)	0.50(-0.20)	0.30(-0.30)
	surface area	left	0.024*	2564(283)	2606(230)	2700(256)	0.037* (-0.50)	0.65(-0.16)	0.017* (-0.39)
		right	0.008*	2324(287)	2343(263)	2491(268)	0.018* (-0.60)	0.59(-0.07)	0.007* (-0.56)
	thickness	left	0.074	2.57(0.13)	2.64(0.15)	2.65(0.16)	0.023* (-0.57)	0.24(-0.52)	0.37(-0.08)
		right	0.69	2.45(0.12)	2.48(0.14)	2.44(0.15)	0.85(0.08)	0.54(-0.24)	0.39(0.28)

Supplementary Table ST4.1. (cont.) Statistical results for cortical measurements (i.e. volume, surface area and thickness) of the individual parcel within each superparcel

Cortical parcel	Measure	Side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Cohen's d effect size)		
				DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Medial orbito frontal	volume	left	0.44	4685(714)	4912(725)	5004(619)	0.20(-0.48)	0.44(-0.32)	0.68(-0.14)
		right	0.14	4876(704)	5084(731)	5238(520)	0.047*(-0.59)	0.25(-0.29)	0.49(-0.25)
	surface area	left	0.56	1802(329)	1855(237)	1850(240)	0.29(-0.17)	0.70(-0.19)	0.59(0.02)
		right	0.095	1884(243)	1900(224)	1979(206)	0.054(-0.42)	0.88(-0.07)	0.11(-0.37)
	thickness	left	0.32	2.35(0.14)	2.37(0.18)	2.40(0.13)	0.22(-0.35)	0.94(-0.08)	0.22(-0.23)
		right	0.67	2.30(0.16)	2.36(0.19)	2.34(0.11)	0.47(-0.28)	0.41(-0.30)	0.82(0.09)
Pars opercularis	volume	left	0.23	4817(1218)	4643(967)	5035(833)	0.68(-0.21)	0.23(0.16)	0.089(-0.44)
		right	0.16	4092(723)	3814(605)	4224(600)	0.59(-0.20)	0.20(0.42)	0.059(-0.68)
	surface area	left	0.21	1660(303)	1588(307)	1691(254)	0.52(-0.11)	0.27(0.24)	0.077(-0.37)
		right	0.021*	1438(216)	1286(203)	1446(200)	0.46(-0.04)	0.053(0.72)	0.006*(-0.79)
	thickness	left	0.12	2.51(0.13)	2.58(0.13)	2.60(0.11)	0.043*(-0.69)	0.24(-0.52)	0.52(-0.11)
		right	0.47	2.56(0.17)	2.64(0.19)	2.61(0.15)	0.34(-0.26)	0.24(-0.41)	0.69(0.18)
Pars orbitalis	volume	left	0.073	1894(216)	2063(246)	2106(348)	0.023*(-0.75)	0.18(-0.73)	0.43(-0.14)
		right	0.016*	2380(344)	2491(354)	2667(387)	0.007*(-0.79)	0.50(-0.32)	0.052(-0.48)
	surface area	left	0.49	595(68)	600(55)	616(89)	0.37(-0.26)	0.84(-0.08)	0.30(-0.22)
		right	0.015*	737(94)	766(89)	815(122)	0.010*(-0.72)	0.87(-0.32)	0.030*(-0.46)
	thickness	left	0.043*	2.53(0.17)	2.70(0.22)	2.70(0.25)	0.013*(-0.81)	0.15(-0.83)	0.41(-0.04)
		right	0.93	2.56(0.17)	2.60(0.20)	2.58(0.22)	0.83(-0.14)	0.72(-0.25)	0.84(0.09)

Supplementary Table ST4.1. (cont.) Statistical results for cortical measurements (i.e. volume, surface area and thickness) of the individual parcel within each superparcel

Cortical parcel	Measure	Side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Cohen's d effect size)		
				DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Pars triangularis	volume	left	0.11	3321(483)	3479(685)	3694(536)	0.064(-0.73)	0.83(-0.27)	0.11(-0.35)
		right	0.39	3782(609)	4006(600)	4080(763)	0.17(-0.43)	0.53(-0.37)	0.52(-0.11)
	surface area	left	0.16	1222(143)	1225(182)	1290(161)	0.24(-0.45)	0.47(-0.02)	0.067(-0.38)
		right	0.25	1355(202)	1390(177)	1445(232)	0.15(-0.41)	0.99(-0.18)	0.19(-0.27)
	thickness	left	0.038*	2.42(0.14)	2.53(0.22)	2.53(0.15)	0.015*(-0.74)	0.049*(-0.60)	0.89(-0.01)
		right	0.34	2.44(0.12)	2.55(0.23)	2.48(0.16)	0.62(-0.24)	0.15(-0.61)	0.26(0.36)
Paracentral	volume	left	0.22	3200(335)	3211(326)	3394(412)	0.16(-0.52)	0.91(-0.03)	0.13(-0.50)
		right	0.65	3676(523)	3796(764)	3875(366)	0.42(-0.45)	0.40(-0.19)	0.87(-0.14)
	surface area	left	0.42	1288(196)	1228(78)	1300(141)	0.72(-0.07)	0.37(0.43)	0.19(-0.65)
		right	0.99	1454(253)	1438(276)	1448(147)	0.99(0.03)	0.89(0.06)	0.88(-0.05)
	thickness	left	0.23	2.28(0.17)	2.37(0.17)	2.35(0.12)	0.11(-0.50)	0.18(-0.54)	0.98(0.13)
		right	0.016*	2.31(0.16)	2.39(0.17)	2.44(0.11)	0.004*(-0.98)	0.17(-0.50)	0.21(-0.36)
Precentral	volume	left	0.062	12480(841)	13339(1381)	13209(943)	0.068(-0.82)	0.025*(-0.77)	0.45(0.11)
		right	0.50	12349(1236)	12869(1652)	12970(1174)	0.27(-0.52)	0.34(-0.36)	0.97(-0.07)
	surface area	left	0.31	4477(216)	4681(546)	4618(318)	0.26(-0.52)	0.15(-0.53)	0.55(0.15)
		right	0.34	4544(362)	4592(459)	4674(467)	0.39(-0.31)	0.57(-0.12)	0.16(-0.18)
	thickness	left	0.58	2.54(0.14)	2.59(0.15)	2.58(0.11)	0.30(-0.33)	0.57(-0.30)	0.72(0.02)
		right	0.54	2.50(0.11)	2.56(0.16)	2.54(0.11)	0.33(-0.39)	0.34(-0.43)	0.89(0.12)

Supplementary Table ST4.1. (cont.) Statistical results for cortical measurements (i.e. volume, surface area and thickness) of the individual parcel within each superparcel

Cortical parcel	Measure	Side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Cohen's d effect size)		
				DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Superior frontal	volume	left	0.005*	20683(1948)	20819(1880)	22144(2035)	0.015* (-0.73)	0.57(-0.07)	0.003* (-0.68)
		right	0.013*	20744(2322)	20319(2151)	21673(2008)	0.24(-0.43)	0.089(0.19)	0.003* (-0.65)
	surface area	left	0.033*	6807(667)	6777(489)	7107(610)	0.052(-0.47)	0.61(0.05)	0.021* (-0.60)
		right	0.014*	6751(728)	6583(453)	6919(596)	0.13(-0.25)	0.15(0.28)	0.004* (-0.64)
	thickness	left	0.58	2.61(0.09)	2.65(0.16)	2.66(0.14)	0.30(-0.38)	0.61(-0.29)	0.69(-0.05)
		right	0.47	2.62(0.10)	2.65(0.18)	2.67(0.11)	0.28(-0.45)	0.95(-0.16)	0.35(-0.19)
Frontal pole	volume	left	0.49	686(142)	682(133)	725(107)	0.43(-0.31)	0.75(0.03)	0.26(-0.36)
		right	0.18	920(208)	887(138)	970(147)	0.17(-0.28)	0.75(0.19)	0.096(-0.58)
	surface area	left	0.88	184(38)	182(38)	188(33)	0.79(-0.10)	0.82(0.06)	0.62(-0.16)
		right	0.27	261(61)	256(42)	277(42)	0.28(-0.30)	0.64(0.09)	0.13(-0.48)
	thickness	left	0.16	2.68(0.17)	2.65(0.18)	2.79(0.23)	0.065(-0.53)	0.55(-0.27)	0.28(-0.19)
		right	0.90	2.61(0.21)	2.74(0.27)	2.63(0.25)	0.67(-0.09)	0.74(-0.17)	0.97(0.06)
Caudal anterior cingulate	volume	left	0.92	1912(501)	1906(361)	1938(534)	0.71(-0.05)	0.98(0.01)	0.74(-0.07)
		right	0.035*	1938(456)	1939(633)	2287(415)	0.034* (-0.80)	0.91(0.00)	0.029* (-0.66)
	surface area	left	0.28	687(156)	634(93)	689(167)	0.67(-0.01)	0.28(0.42)	0.11(-0.42)
		right	0.028*	733(168)	711(177)	823(132)	0.058(-0.60)	0.50(0.13)	0.015* (-0.72)
	thickness	left	0.020*	2.48(0.20)	2.65(0.19)	2.56(0.20)	0.098(-0.37)	0.006* (-0.90)	0.12(0.53)
		right	0.35	2.38(0.12)	2.66(0.19)	2.47(0.22)	0.18(-0.53)	0.26(-0.42)	0.98(-0.05)

Supplementary Table ST4.1. (cont.) Statistical results for cortical measurements (i.e. volume, surface area and thickness) of the individual parcel within each superparcel

Cortical parcel	Measure	Side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Cohen's d effect size)		
				DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Rostral anterior cingulate	volume	left	0.74	2637(393)	2684(395)	2758(542)	0.48(-0.26)	0.91(-0.12)	0.57(-0.16)
		right	0.67	2026(554)	2184(506)	2205(449)	0.43(-0.36)	0.42(-0.30)	0.89(-0.04)
	surface area	left	0.37	831(139)	842(96)	880(197)	0.29(-0.29)	0.99(-0.09)	0.27(-0.26)
		right	0.39	669 (164)	701(150)	717(141)	0.18(-0.32)	0.65(-0.20)	0.48(-0.11)
	thickness	left	0.96	2.82(0.17)	2.46(0.26)	2.80(0.19)	0.88(0.09)	0.79(0.05)	0.88(0.04)
		right	0.60	2.66(0.22)	2.81(0.20)	2.69(0.16)	0.76(-0.15)	0.33(-0.30)	0.44(0.09)
<i>Parietal superparcel</i>									
Superior parietal	volume	left	0.56	13663(1140)	13277(1590)	13548(1574)	0.65(0.08)	0.29(0.28)	0.45(-0.17)
		right	0.18	13694(1336)	13375(984)	13153(1313)	0.069(0.41)	0.21(0.28)	0.69(0.19)
	surface area	left	0.67	5354(455)	5196(703)	5191(633)	0.52(0.30)	0.39(0.27)	0.71(0.01)
		right	0.45	5363(573)	5298(488)	5158(492)	0.22(0.38)	0.66(0.12)	0.52(0.28)
	thickness	left	0.42	2.26(0.07)	2.28(0.09)	2.31(0.12)	0.19(-0.42)	0.56(-0.18)	0.55(-0.24)
		right	0.85	2.25(0.11)	2.23(0.09)	2.24(0.13)	0.76(0.09)	0.58(0.18)	0.74(-0.07)
Inferior parietal	volume	left	0.003*	11304(1314)	13057(1325)	12980(1706)	0.002* (-1.11)	0.005* (-1.33)	0.97(0.05)
		right	0.36	14193(1639)	14677(1350)	15176(1792)	0.15(-0.57)	0.44(-0.32)	0.58(-0.32)
	surface area	left	0.005*	4098(447)	4594(469)	4468(456)	0.005* (-0.82)	0.004* (-1.08)	0.49(0.27)
		right	0.35	5022(508)	5118(436)	5254(592)	0.15(-0.42)	0.60(-0.20)	0.47(-0.26)
	thickness	left	0.025*	2.44(0.08)	2.52(0.12)	2.55(0.13)	0.007* (-0.98)	0.090(-0.76)	0.47(-0.21)
		right	0.56	2.49(0.10)	2.54(0.13)	2.53(0.15)	0.31(-0.30)	0.40(-0.39)	0.99(0.06)

Supplementary Table ST4.1. (cont.) Statistical results for cortical measurements (i.e. volume, surface area and thickness) of the individual parcel within each superparcel

Cortical parcel	Measure	Side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Cohen's d effect size)		
				DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Postcentral	volume	left	0.27	9328(1427)	9709(1154)	10058(1080)	0.11(-0.58)	0.57(-0.30)	0.35(-0.31)
		right	0.26	8786(967)	9187(1324)	9360(893)	0.10(-0.62)	0.26(-0.35)	0.71(-0.16)
	surface area	left	0.25	3830(374)	3872(367)	3984(382)	0.18(-0.41)	0.87(-0.11)	0.16(-0.30)
		right	0.45	3679(242)	3796(472)	3818(337)	0.22(-0.48)	0.71(-0.33)	0.48(-0.06)
	thickness	left	0.23	2.12(0.15)	2.18(0.12)	2.19(0.12)	0.089(-0.52)	0.33(-0.48)	0.59(-0.05)
		right	0.75	2.13(0.15)	2.15(0.11)	2.16(0.13)	0.46(-0.22)	0.78(-0.17)	0.69(-0.07)
Precuneus	volume	left	0.64	9462(782)	9659(959)	9800(1007)	0.36(-0.38)	0.79(-0.23)	0.55(-0.14)
		right	0.26	9468(767)	9628(1106)	9971(1083)	0.14(-0.54)	0.83(-0.17)	0.22(-0.31)
	surface area	left	0.61	3634(361)	3758(371)	3725(412)	0.34(-0.24)	0.47(-0.34)	0.95(0.08)
		right	0.62	3778(455)	3788(409)	3855(469)	0.41(-0.17)	0.99(-0.02)	0.45(0.15)
	thickness	left	0.67	2.40(0.10)	2.39(0.14)	2.42(0.12)	0.76(-0.16)	0.58(0.07)	0.37(-0.20)
		right	0.27	2.31(0.13)	2.34(0.11)	2.38(0.10)	0.11(-0.55)	0.56(-0.22)	0.39(-0.34)
Supra-marginal	volume	left	0.44	10746(1699)	10532(1533)	10779(1531)	0.68(-0.02)	0.46(0.13)	0.67(-0.16)
		right	0.44	9949(1246)	10094(1111)	10336(1431)	0.34(-0.29)	0.83(-0.12)	0.25(-0.19)
	surface area	left	0.54	3695(507)	3607(460)	3636(473)	0.79(0.12)	0.29(0.18)	0.36(-0.06)
		right	0.43	3481(373)	3498(339)	3574(507)	0.27(-0.21)	0.98(-0.05)	0.31(-0.18)
	thickness	left	0.49	2.58(0.11)	2.60(0.14)	2.62(0.16)	0.34(-0.32)	0.92(-0.18)	0.31(-0.13)
		right	0.99	2.58(0.13)	2.61(0.17)	2.59(0.16)	0.96(-0.06)	0.96(-0.16)	0.99(0.10)

Supplementary Table ST4.1. (cont.) Statistical results for cortical measurements (i.e. volume, surface area and thickness) of the individual parcel within each superparcel

Cortical parcel	Measure	Side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Cohen's d effect size)		
				DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Isthmus cingulate	volume	left	0.40	2515(390)	2394(374)	2501(468)	0.51(0.03)	0.17(0.32)	0.38(-0.25)
		right	0.88	2208(371)	2260(363)	2291(467)	0.65(-0.20)	0.97(-0.14)	0.69(-0.07)
	surface area	left	0.36	965(140)	908(133)	913(155)	0.25(0.35)	0.19(0.42)	0.67(-0.04)
		right	0.96	878(135)	878(143)	862(162)	0.79(0.11)	0.94(0.00)	0.87(0.11)
	thickness	left	0.11	2.45(0.17)	2.49(0.21)	2.56(0.20)	0.063(-0.56)	0.87(-0.18)	0.11(-0.34)
		right	0.29	2.38(0.16)	2.45(0.25)	2.47(0.21)	0.12(-0.49)	0.47(-0.32)	0.49(-0.11)
Posterior cingulate	volume	left	0.093	3000(620)	3144(530)	3351(527)	0.034* (-0.61)	0.43(-0.25)	0.21(-0.39)
		right	0.78	3101(632)	3059(605)	3209(314)	0.85(-0.23)	0.63(0.07)	0.48(-0.33)
	surface area	left	0.10	1126(196)	1148(133)	1211(171)	0.070(-0.46)	0.98(-0.13)	0.095(-0.41)
		right	0.71	1202(221)	1131(184)	1172(132)	0.53(0.17)	0.43(0.35)	0.76(-0.26)
	thickness	left	0.10	2.43(0.16)	2.52(0.18)	2.53(0.16)	0.034* (-0.60)	0.19(-0.51)	0.56(-0.05)
		right	0.087	2.35(0.14)	2.46(0.20)	2.48(0.17)	0.031* (-0.77)	0.12(-0.62)	0.73(-0.08)
Temporal Superparcel									
Superior temporal	volume	left	0.082	11627(1373)	11442(1393)	12051(1184)	0.54(-0.33)	0.13(0.13)	0.027* (-0.47)
		right	0.72	11014(1302)	11493(1355)	11446(1129)	0.43(-0.36)	0.56(-0.36)	0.89(0.04)
	surface area	left	0.22	3639(306)	3533(367)	3698(421)	0.67(-0.16)	0.22(0.31)	0.082(-0.42)
		right	0.61	3452(284)	3471(332)	3482(321)	0.50(-0.10)	0.78(-0.06)	0.36(-0.03)
	thickness	left	0.19	2.76(0.14)	2.81(0.12)	2.84(0.15)	0.087(-0.48)	0.70(-0.36)	0.23(-0.18)
		right	0.17	2.78(0.16)	2.89(0.12)	2.86(0.16)	0.083(-0.51)	0.12(-0.76)	0.95(0.18)

Supplementary Table ST4.1. (cont.) Statistical results for cortical measurements (i.e. volume, surface area and thickness) of the individual parcel within each superparcel

Cortical parcel	Measure	Side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Cohen's d effect size)		
				DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Middle temporal	volume	left	0.089	10438(1613)	9960(932)	10823(1402)	0.59(-0.26)	0.13(0.38)	0.030* (-0.74)
		right	0.28	11628(1583)	11329(908)	11755(1424)	0.91(-0.08)	0.16(0.24)	0.14(-0.37)
	surface area	left	0.23	3110(450)	2965(298)	3101(330)	0.93(0.02)	0.13(0.39)	0.11(-0.43)
		right	0.18	3409(400)	3269(270)	3389(353)	0.84(0.05)	0.14(0.42)	0.071(-0.38)
	thickness	left	0.12	2.79(0.17)	2.77(0.14)	2.85(0.15)	0.11(-0.39)	0.78(0.08)	0.074(-0.52)
		right	0.89	2.86(0.16)	2.90(0.14)	2.89(0.18)	0.63(-0.16)	0.78(-0.26)	0.88(0.08)
Inferior temporal	volume	left	0.54	9533(1124)	9834(1225)	10013(1381)	0.27(-0.38)	0.66(-0.26)	0.56(-0.14)
		right	0.041*	9482(1213)	9772(1301)	10446(1201)	0.016* (-0.80)	0.49(-0.23)	0.10(-0.54)
	surface area	left	0.73	3236(405)	3260(420)	3254(444)	0.75(-0.04)	0.66(-0.06)	0.43(0.02)
		right	0.076	3052(411)	3068(448)	3227(400)	0.14(-0.43)	0.48(-0.04)	0.035* (-0.37)
	thickness	left	0.22	2.55(0.11)	2.58(0.11)	2.61(0.12)	0.089(-0.47)	0.56(-0.26)	0.34(-0.22)
		right	0.29	2.72(0.12)	2.77(0.12)	2.78(0.13)	0.12(-0.50)	0.31(-0.45)	0.73(-0.06)
Temporal pole	volume	left	0.17	2257(258)	2355(355)	2472(383)	0.087(-0.67)	0.75(-0.32)	0.18(-0.32)
		right	0.63	2084(226)	2175(254)	2170(298)	0.47(-0.33)	0.35(-0.38)	0.72(0.02)
	surface area	left	0.65	443(52)	460(80)	457(68)	0.48(-0.24)	0.88(-0.27)	0.42(0.05)
		right	0.74	405(70)	410(59)	415(53)	0.67(-0.16)	0.75(-0.06)	0.46(-0.10)
	thickness	left	0.23	3.68(0.11)	3.71(0.25)	3.78(0.25)	0.10(-0.58)	0.63(-0.19)	0.31(-0.29)
		right	0.69	3.70(0.33)	3.75(0.28)	3.77(0.31)	0.39(-0.22)	0.66(-0.15)	0.75(-0.08)

Supplementary Table ST4.1. (cont.) Statistical results for cortical measurements (i.e. volume, surface area and thickness) of the individual parcel within each superparcel

Cortical parcel	Measure	Side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Cohen's d effect size)		
				DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Transverse temporal	volume	left	0.16	1079(211)	1073(175)	1184(202)	0.22(-0.51)	0.56(0.03)	0.071(-0.59)
		right	0.72	849(172)	841(154)	877(155)	0.83(-0.17)	0.59(0.05)	0.42(-0.23)
	surface area	left	0.81	433(70)	444(89)	447(86)	0.66(-0.17)	0.86(-0.14)	0.55(-0.03)
		right	0.43	326(51)	325(62)	338(56)	0.561(-0.23)	0.48(0.02)	0.20(-0.23)
	thickness	left	0.10	2.24(0.24)	2.21(0.24)	2.38(0.27)	0.10(-0.52)	0.76(0.11)	0.062(-0.62)
		right	0.96	2.28(0.33)	2.29(0.24)	2.32(0.28)	0.80(-0.12)	0.89(-0.04)	0.94(-0.10)
STS banks	volume	left	0.016*	2356(339)	2493(470)	2700(403)	0.006* (-0.93)	0.40(-0.34)	0.071(-0.47)
		right	0.93	2374(309)	2463(349)	2450(386)	0.78(-0.22)	0.71(-0.27)	0.89(0.04)
	surface area	left	0.079	942(123)	997(148)	1040(168)	0.026* (-0.67)	0.37(-0.41)	0.29(-0.27)
		right	0.30	942(93)	939(97)	952(118)	0.84(-0.10)	0.23(0.20)	0.13(-0.12)
	thickness	left	0.014*	2.50(0.11)	2.47(0.17)	2.58(0.17)	0.074(-0.53)	0.27(0.21)	0.005* (-0.62)
		right	0.61	2.58(0.18)	2.68(0.21)	2.62(0.19)	0.67(-0.23)	0.32(-0.51)	0.49(0.28)
Para-hippocampal	volume	left	0.35	2207(287)	2129(305)	2294(401)	0.39(-0.25)	0.59(0.26)	0.16(-0.47)
		right	0.79	2128(370)	2165(430)	2208(390)	0.49(-0.21)	0.74(-0.09)	0.75(-0.10)
	surface area	left	0.29	735(105)	694(104)	721(110)	0.61(0.12)	0.12(0.39)	0.22(-0.26)
		right	0.81	687(140)	697(147)	690(120)	0.87(-0.02)	0.54(-0.07)	0.59(0.06)
	thickness	left	0.82	2.68(0.19)	2.70(0.29)	2.75(0.36)	0.54(-0.25)	0.83(-0.08)	0.73(-0.15)
		right	0.68	2.74(0.19)	2.76(0.23)	2.82(0.27)	0.39(-0.34)	0.70(-0.09)	0.69(-0.25)

Supplementary Table ST4.1. (cont.) Statistical results for cortical measurements (i.e. volume, surface area and thickness) of the individual parcel within each superparcel

Cortical parcel	Measure	Side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Cohen's d effect size)		
				DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Entorhinal	volume	left	0.17	1777(347)	1717(259)	1925(371)	0.23(-0.41)	0.54(0.20)	0.071(-0.66)
		right	0.25	1570(275)	1726(286)	1802(435)	0.099(-0.65)	0.30(-0.56)	0.63(-0.21)
	surface area	left	0.14	410(78)	422(65)	451(87)	0.073(-0.49)	0.84(-0.17)	0.16(-0.37)
		right	0.39	347(87)	377(85)	396(107)	0.22(-0.50)	0.92(-0.36)	0.32(-0.19)
	thickness	left	0.10	3.44(0.29)	3.21(0.29)	3.29(0.28)	0.11(0.50)	0.040* (0.76)	0.42(-0.27)
		right	0.83	3.43(0.35)	3.50(0.25)	3.47(0.40)	0.63(-0.11)	0.56(-0.23)	0.85(0.08)
Fusiform	volume	left	0.89	9392(1462)	9656(1072)	9744(1127)	0.64(-0.27)	0.84(-0.21)	0.81(-0.08)
		right	0.29	8982(1246)	8986(1012)	9489(1114)	0.29(-0.43)	0.69(0.00)	0.14(-0.47)
	surface area	left	0.64	3208(409)	3219(400)	3237(314)	0.88(-0.08)	0.48(-0.03)	0.36(-0.05)
		right	0.13	3034(431)	3009(318)	3172(332)	0.20(-0.36)	0.47(0.07)	0.055(-0.50)
	thickness	left	0.43	2.62(0.13)	2.65(0.14)	2.67(0.13)	0.22(-0.35)	0.75(-0.20)	0.41(-0.14)
		right	0.65	2.67(0.14)	2.70(0.16)	2.70(0.12)	0.42(-0.22)	0.43(-0.19)	0.92(-0.01)
Occipital superparcel									
Lateral occipital	volume	left	0.54	11165(1475)	10959(1359)	11297(1455)	0.68(-0.09)	0.28(0.15)	0.41(-0.24)
		right	0.61	10635(1394)	10638(1587)	11013(1374)	0.66(-0.27)	0.61(0.00)	0.32(-0.25)
	surface area	left	0.67	4609(495)	4516(476)	4569(644)	0.88(0.07)	0.41(0.19)	0.44(-0.10)
		right	0.75	4421(519)	4360(576)	4420(644)	0.86(0.00)	0.60(0.11)	0.45(-0.10)
	thickness	left	0.38	2.17(0.13)	2.16(0.11)	2.21(0.12)	0.33(-0.31)	0.73(0.09)	0.20(-0.43)
		right	0.43	2.17(0.12)	2.18(0.16)	2.23(0.14)	0.26(-0.44)	0.95(-0.05)	0.32(-0.34)

Supplementary Table ST4.1. (cont.) Statistical results for cortical measurements (i.e. volume, surface area and thickness) of the individual parcel within each superparcel

Cortical parcel	Measure	Side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Cohen's d effect size)		
				DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Cuneus	volume	left	0.30	2907(666)	2752(236)	2930(355)	0.59(-0.04)	0.13(0.34)	0.24(-0.60)
		right	0.38	3017(441)	2904(272)	3109(501)	0.81(-0.20)	0.31(0.32)	0.17(-0.53)
	surface area	left	0.55	1477(289)	1416(112)	1452(192)	0.69(0.11)	0.29(0.30)	0.41(-0.23)
		right	0.52	1493(189)	1464(131)	1530(243)	0.56(-0.17)	0.59(0.18)	0.26(-0.35)
	thickness	left	0.12	1.83(0.13)	1.82(0.07)	1.89(0.10)	0.13(-0.47)	0.69(0.14)	0.065(-0.78)
		right	0.60	1.86(0.15)	1.83(0.11)	1.87(0.10)	0.93(-0.05)	0.42(0.28)	0.33(-0.39)
Lingual	volume	left	0.21	5895(869)	5928(904)	6331(961)	0.12(-0.48)	0.92(-0.04)	0.16(-0.43)
		right	0.79	6154(704)	6208(941)	6338(860)	0.49(-0.24)	0.74(-0.07)	0.72(-0.14)
	surface area	left	0.64	2876(351)	2841(423)	2951(396)	0.49(-0.20)	0.40(0.09)	0.49(-0.27)
		right	0.87	2913(348)	2886(378)	2920(400)	0.81(-0.02)	0.79(0.08)	0.60(-0.09)
	thickness	left	0.16	1.93(0.15)	1.95(0.09)	2.00(0.11)	0.11(-0.52)	0.93(-0.09)	0.11(-0.56)
		right	0.61	1.98(0.12)	2.01(0.12)	2.02(0.12)	0.35(-0.37)	0.85(-0.23)	0.50(-0.13)
Peri-calcarine	volume	left	0.90	1931(345)	1928(292)	1992(333)	0.65(-0.18)	0.83(0.01)	0.83(-0.21)
		right	0.46	2179(302)	2204(363)	2327(366)	0.23(-0.44)	0.73(-0.07)	0.43(-0.34)
	surface area	left	0.86	1335(213)	1337(204)	1340(220)	0.24(-0.02)	0.75(-0.01)	0.16(-0.01)
		right	0.28	1407(190)	1436(230)	1483(233)	0.34(-0.36)	0.47(-0.14)	0.95(-0.20)
	thickness	left	0.37	1.56(0.09)	1.58(0.09)	1.62(0.13)	0.16(-0.48)	0.41(-0.22)	0.67(-0.32)
		right	0.71	1.64(0.10)	1.63(0.11)	1.67(0.12)	0.49(-0.26)	0.98(0.08)	0.50(-0.32)

Supplementary Table ST4.1. (cont.) Statistical results for cortical measurements (i.e. volume, surface area and thickness) of the individual parcel within each superparcel

Cortical parcel	Measure	Side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Cohen's d effect size)		
				DID	PTSD	HC	DID vs. HC	DID vs. PTSD	PTSD vs. HC
<i>Insula</i>									
Insula	volume	left	<0.001*	6373(579)	6376(523)	6999(446)	<0.001* (-1.22)	0.66(-0.01)	<0.001* (-1.29)
		right	0.31	6792(526)	6816(661)	7048(704)	0.51(-0.42)	0.41(-0.04)	0.12(-0.34)
	surface area	left	0.001*	2162(173)	2120(104)	2304(185)	0.005* (-0.79)	0.39(-0.30)	0.001* (-0.48)
		right	0.58	2279(131)	2286(214)	2288(230)	0.99(-0.05)	0.38(-0.04)	0.32(-0.01)
	thickness	left	0.29	2.90(0.14)	2.98(0.14)	3.00(0.19)	0.13(-0.55)	0.26(-0.53)	0.85(-0.08)
		right	0.22	2.93(0.17)	2.97(0.15)	3.02(0.17)	0.13(-0.50)	0.92(-0.21)	0.19(-0.32)

Abbreviations: DID = Dissociative Identity Disorder; PTSD = Post-Traumatic Stress Disorder; HC = Healthy Control.

* P-value ≤ 0.05 (uncorrected)

Supplementary Table ST4.2. Statistical results for dorsal striatal volumes (mm³) after excluding three DID patients with a history of typical antipsychotic use

Subcortical volume	Total/ side	Omnibus test	Mean(SD)			Group comparisons: P-Value (Cohen's d effect size)		
			DID (n=14)	PTSD (n=16)	HC (n=28)	DID vs. HC	DID vs. PTSD	PTSD vs. HC
Caudate	total	0.019*	7385 (849)	7037 (1005)	7071 (632)	0.006* (0.50)	0.024* (0.43)	0.79 (-0.04)
	left		3601 (406)	3441 (500)	3439 (323)	0.007* (0.49)	0.031* (0.39)	0.73 (0.00)
	right		3783 (462)	3596 (518)	3631 (328)	0.009* (0.48)	0.026* (0.46)	0.86 (-0.08)
Putamen	total	0.077	10891 (1120)	10408 (1379)	10764 (933)	0.25 (-0.03)	0.025* (0.25)	0.12 (-0.31)
	left		5542 (621)	5313 (702)	5513 (469)	0.41 (-0.14)	0.039* (0.18)	0.098 (-0.34)
	right		5349 (544)	5095 (694)	5251 (504)	0.17 (0.08)	0.029* (0.32)	0.21 (-0.26)
Pallidum	total	0.081	3247 (306)	3072 (408)	3128 (301)	0.068 (0.24)	0.32 (0.36)	0.50 (-0.16)
	left		1771 (189)	1704 (253)	1740 (181)	0.23 (0.07)	0.099 (0.22)	0.45 (-0.17)
	right		1475 (148)	1368 (161)	1387 (146)	0.019* (0.41)	0.016* (0.51)	0.67 (-0.12)

Abbreviations: DID = Dissociative Identity Disorder; PTSD = Post-Traumatic Stress Disorder; HC = Healthy Controls.

* P-value <= 0.05 (uncorrected)

