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Frontal and occipital perfusion changes in dissociative identity disorder

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Abstract

The aim of the study was to investigate if there were any characteristics of regional cerebral blood flow (rCBF) in dissociative identity disorder. Twenty-one drug-free patients with dissociative identity disorder and nine healthy volunteers participated in the study. In addition to a clinical evaluation, dissociative psychopathology was assessed using the Structured Clinical Interview for DSM-IV Dissociative Disorders, the Dissociative Experiences Scale and the Clinician-Administered Dissociative States Scale. A semi-structured interview for borderline personality disorder, the Hamilton Depression Rating Scale, and the Childhood Trauma Questionnaire were also administered to all patients. Normal controls had to be without a history of childhood trauma and without any depressive or dissociative disorder. Regional cerebral blood flow (rCBF) was studied with single photon emission computed tomography (SPECT) with Tc99m-hexamethylpropylenamine (HMPAO) as a tracer. Compared with findings in the control group, the rCBF ratio was decreased among patients with dissociative identity disorder in the orbitofrontal region bilaterally. It was increased in median and superior frontal regions and occipital regions bilaterally. There was no significant correlation between rCBF ratios of the regions of interest and any of the psychopathology scale scores. An explanation for the neurophysiology of dissociative psychopathology has to invoke a comprehensive model of interaction between anterior and posterior brain regions.

Keywords: Dissociative disorder; Borderline personality disorder; Neurophysiology; Orbitofrontal lobe; Occipital lobe; Childhood trauma

1. Introduction

The essential feature of dissociative disorders is a disruption in the usually integrated functions of consciousness, memory, identity, and perception of the environment. The disturbance may be sudden or gradual, transient or chronic (American Psychiatric Association, 1994). Dissociative identity disorder is characterized by the presence of two or more distinct personality states or identities within a single person that take control of his or her behavior recurrently. Each personality state may have different access into memory resulting in a state-dependent inability to recall important personal information. These alter personalities are characterized by different emotional responses, cognitions, moods, and perceived self-images. Dissociative identity disorder is considered as a post-traumatic developmental

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psychopathology closely related to child abuse and neglect (Putnam, 1997).

Although the DSM-IV (American Psychiatric Association, 1994) defines other types of dissociative disorders as well (i.e. dissociative amnesia, dissociative fugue, depersonalization disorder, and dissociative disorder not otherwise specified), we chose to limit the study group to patients with dissociative identity disorder, because it is the most complex, chronic, and severe of these diagnostic categories, and it is usually superposed to other dissociative disorders on a symptomatological level. In fact, dissociative symptoms and disorders may accompany other psychiatric disorders as well (Sar and Ross, 2006). Substance abuse (Karadag et al., 2005), borderline personality disorder (Sar et al., 2003, 2006), obsessive-compulsive disorder (Lochner et al., 2004), post-traumatic stress disorder (Briere et al., 2005), acute stress disorder (Spiegel et al., 2000), eating disorders (Farrington et al., 2002), pathological gambling (Grant and Kim, 2003), kleptomania (Grant, 2004) and even schizophrenia (Ross and Keyes, 2004) are among them. A somatoform type of dissociation is also described which is proposed to be the underlying mechanism in conditions characterized by medically unexplained symptoms; i.e. conversion symptoms (e.g. pseudoseizures), psychogenic pain, and somatization disorder (Nijenhuis et al., 1996; Sar et al., 2004). Thus, beyond constituting a group of disorder on its own, dissociation as a mental mechanism may play a role in various psychiatric disturbances or it may confound them. Its relationship to childhood adverse events increases its importance as a mental mechanism further.

Brain imaging studies on series of patients with dissociative identity disorder are rather scarce. One study using single photon emission computed tomography (SPECT) demonstrated bilateral orbitofrontal hypoperfusion and left (dominant hemisphere) lateral temporal hyperperfusion (Sar et al., 2001). A positron emission tomography study using scripts for symptom provocation in 11 women with dissociative identity disorder revealed the existence of different patterns of regional cerebral blood flow (rCBF) for different senses of self (Reinders et al., 2003). The authors presented evidence for the medial prefrontal cortex and the posterior associative cortices to have an integral role in conscious experience.

In a single case, functional magnetic resonance imaging demonstrated bilateral hippocampal inhibition (with inhibition stronger on the right side) while the patient was switching from host to alter personality (Tsai et al., 1999). The right parahippocampal and medial temporal regions were also inhibited, as were small regions of the substantia nigra and globus pallidus. In contrast, switching back toward the host personality involved only right hippocampal activation. One of two previous single case SPECT studies yielded a mean perfusion increase of 10.7% in the left temporal lobe when assessed during activations of four alter personality states (Saxe et al., 1992) and the other yielded an increase of perfusion in right temporal lobe (Mathew et al., 1985). In a recent volumetric study on patients with dissociative identity disorder and healthy controls, the sizes of the amygdala and the hippocampus were diminished in a dissociative group (Vermetten et al., 2006).

The first hypothesis of this study was that there would be rCBF differences among patients with dissociative identity disorder compared with normal controls. The second hypothesis was that there would be diminished perfusion rates in orbitofrontal regions bilaterally. Findings of a previous study (Sar et al., 2001) and theoretical considerations concerning neurodevelopmental consequences of childhood traumatization (Shore, 1996; Forrest, 2001) led us to these hypotheses.

2. Methods

2.1. Participants

Twenty-one patients (14 women and 7 men) who fully met the DSM-IV (American Psychiatric Association, 1994) criteria for dissociative identity disorder and nine healthy volunteers (6 women and 3 men) who did not have any childhood trauma history participated in the study. All cases were patients in the Dissociative Disorders Program at the Department of Psychiatry, Istanbul Medical Faculty Hospital, Istanbul University. Written informed consent was obtained from all subjects after the procedures had been fully explained. All patients were right handed. None of the participants had any physical disorder. All patients were drug-free for at least 1 month.

In all patients, intra-interview switching of personality states and dissociative amnesia had been observed clinically several times. Beside clinical examinations by a senior psychiatrist (V.S.) with extensive clinical and research experience in general psychiatry and in dissociative disorders specifically, all patients were evaluated using the Structured Clinical Interview for Dissociative Disorders (SCID-D) (Steinberg, 1994) and the Dissociative Experiences Scale (Bernstein and Putnam, 1986). Fifteen patients were assessed using the Clinician-Administered Dissociative State Scale (CADSS) (Bremner et al., 1998) and the Hamilton Depression Scale (Williams, 1978) as well. Childhood trauma histories were obtained using the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 1994). In consideration of the high comorbidity between borderline personality disorder and dissociative identity disorder (Sar et al., 2003), all patients were also evaluated using the Borderline Personality Disorder section of the Structured Clinical Interview for DSM-IV Personality Disorders (Spitzer et al., 1987).

Nine non-traumatized, right-handed healthy volunteers (6 women and 3 men) constituted the comparison group. Inclusion criteria were the absence of medical or neurological illness and a negative personal and family history of psychiatric disturbances, alcoholism, drug abuse, and childhood abuse and/or neglect. They had to have scores below 10 on the Dissociative Experiences Scale and the Beck Depression Inventory (Beck et al., 1961).

2.2. Procedure

The SPECT scintigraphies were done on patients when they were in the host state. A dose of 555 MBq Tc99m-hexamethylpropylenamine (HMPAO, Ceretec, Amersham) was injected intravenously. The therapist did not continue to speak during scanning. According to the guidelines by Juni and colleagues (1998), the scanning was performed 60 min after the injection. The patient's head was immobilized on a head rest and secured with Velcro straps. The scanning was performed with a dual headed ADAC Vertex gamma camera. Each detector was equipped with a low-energy high resolution collimator. Data were collected for 64 projections (360° rotations) in a 64×64 matrix, for 30 s per projection. The acquisition time was approximately 16 min.

All patients were instructed to maintain the host personality state during the study evaluation beginning from the injection until the end of the SPECT evaluation. Thus, an instruction to switch to an alter personality state was not given during the study procedure; on the contrary, the patients knew that 'switching' was not desired during the procedure. Host personality has been defined as the personality state that is present for the longest time during an ordinary day (Putnam, 1997).

2.3. Data analysis

SPECT reconstruction was performed on an ADAC Pegasys workstation. Transaxial images were obtained by the filtered back-projection method using a Butterworth filter with a frequency cut-off of 0.225 cycles per centimeter (power order: 6). Attenuation correction of the transaxial images was performed using the Chang algorithm.

Images were obliquely reconstructed parallel to and sequentially above the orbito-meatal line (OML). The reconstructed images were subjected to semiquantitative analysis. For semi-quantitative analysis, four templates were used. Three of them were delineating anatomic structures 3.5, 5.5, and 7.5 cm above and parallel to the orbitomeatal line (Damasio and Damasio, 1989). Temporal slices were taken parallel to the long axis of the temporal lobe. The fourth template was used to place the lateral and mesial temporal regions involving the hippocampus. This template used the hippocampal line, which was parallel to the longitudinal axis of the temporal lobe. Regions of interest (ROIs) were drawn manually over one hemisphere and mirrored to the contralateral side. The rCBF ratio was calculated for each ROI using the mean number of counts divided by the mean cerebellar counts (Catafau et al., 1996).

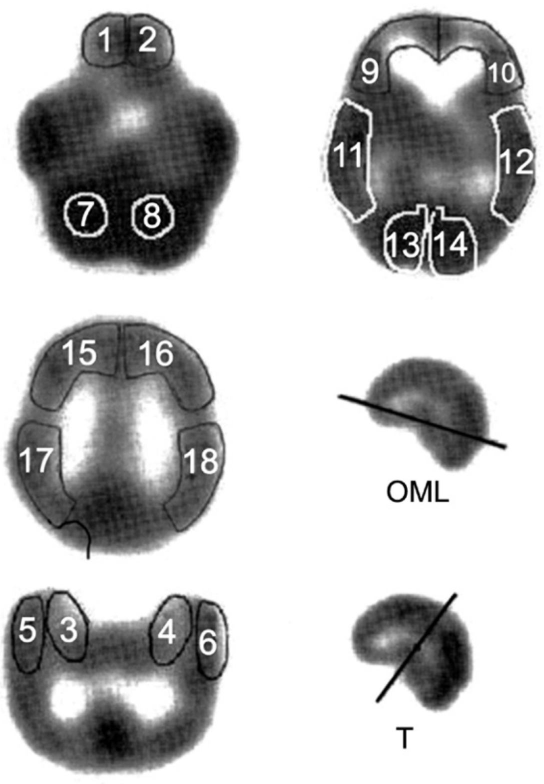

Fig. 1. Regions of interest used for analysis of rCBF ratios. 1–2: Right and left orbitofrontal regions. 3–4: Right and left mesial temporal regions involving hippocampus. 5–6: Right and left lateral temporal regions. 7–8: Right and left cerebellar regions. 9–10: Right and left medial frontal. 11–12: Right and left superior temporal regions. 13–14: Right and left occipital regions. 15–16: Right and left superior frontal regions. 17–18: Right and left parietal regions.

3. Results

3.1. Participants

There was no significant difference ($t=1.99$, $df=28$, $P>0.05$) on age between dissociative patients (mean = 21.9, S.D. = 3.6) and healthy volunteers (mean = 24.9, S.D. = 4.3). The difference in years of education between dissociative patients (mean = 11.6, S.D. = 2.7) and healthy volunteers (mean = 11.6, S.D. = 3.0) was also not significant ($t=0.06$, $df=28$, $P>0.05$). Women accounted for 66.7% of participants in both groups (14 dissociative patients and 6 healthy volunteers).

The mean Dissociative Experiences Scale score in the dissociative disorders group was 51.1 (S.D. = 15.7, median = 56.4, range = 16.4–71.1). The mean Hamilton Depression Scale score of 15 dissociative patients was 20.6 (S.D. = 8.6, range = 8–35); 9 (60.0%) of them had a score above 17. The mean CADSS score was 33.6 (S.D. = 17.6, range = 6–64). Fifteen (71.4%) of the patients had borderline personality disorder according to the DSM-IV; thus, they endorsed at least five of the nine diagnostic criteria. The mean number of borderline personality disorder criteria endorsed was 5.9 (S.D. = 2.49, range = 0–9). All patients reported at least one type of childhood abuse and/or neglect. The mean CTQ-53 score was 12.0 (S.D. = 3.9, range = 7.4–20.5).

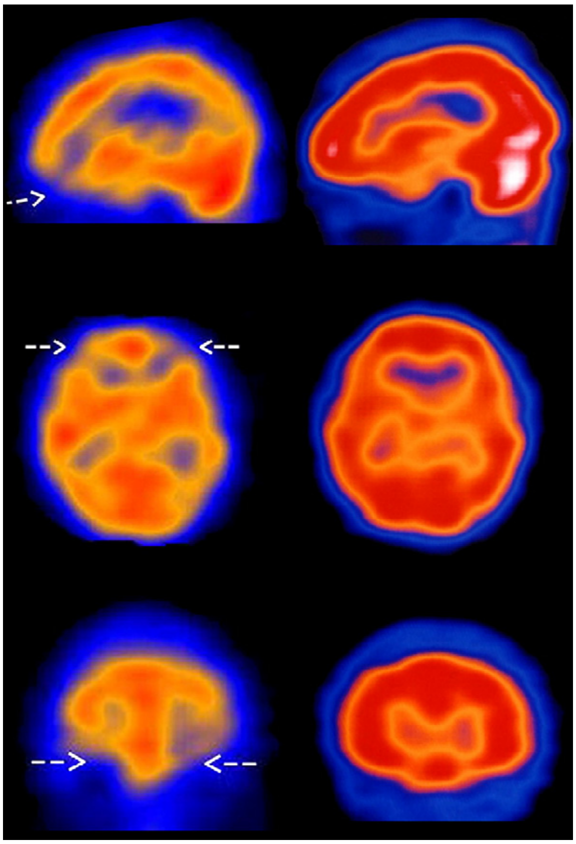

Fig. 2. Visually observed orbitofrontal perfusion defects in a patient with dissociative identity disorder (left) compared with the cerebral perfusion in a healthy volunteer (right).

Table 1
rCBF ratios of patients with dissociative identity disorder and healthy comparison subjects (Mann–Whitney *U* test, 2-tailed)

Region	Dissociative patients (N=21)		Healthy comparison subjects (N=9)			
	Mean	S.D.	Mean	S.D.	z	P
Frontal						
Orbito-						
Right	57.2	19.1	73.8	3.2	−2.79	0.005
Left	57.3	18.5	73.0	4.4	−2.88	0.004
Medial						
Right	80.2	5.0	74.8	4.4	−2.75	0.006
Left	80.2	5.6	74.2	3.3	−2.86	0.004
Superior						
Right	86.8	5.4	78.7	6.6	−2.73	0.006
Left	84.7	4.7	79.4	6.6	−2.45	0.014
Parietal						
Right	81.0	7.2	79.2	3.8	−1.48	0.138
Left	80.6	5.6	80.6	2.6	−0.59	0.554
Temporal						
Mesial						
Right	72.3	5.8	74.7	5.6	−0.95	0.341
Left	72.2	7.0	72.3	2.4	−0.36	0.716
Lateral						
Right	77.4	7.0	76.6	4.4	−0.50	0.618
Left	77.4	5.7	73.8	2.5	−1.95	0.051
Superior						
Right	85.9	4.9	83.0	4.0	−1.50	0.134
Left	85.1	4.6	84.3	3.5	−0.11	0.909
Occipital						
Right	93.5	5.3	88.9	4.7	−2.18	0.029
Left	94.4	6.1	89.3	3.7	−2.34	0.019

3.2. Perfusion ratios

In visual analysis, all patients in the dissociative identity disorder group had hypoperfusion areas in orbitofrontal regions bilaterally. These hypoperfusion areas were recognized in visual assessment (Figs. 1 and 2). None of the healthy control subjects had any perfusion defect in the orbitofrontal region in visual analysis. This observation was confirmed by the semi-quantitative evaluation. Table 1 shows the comparison of the rCBF ratios in dissociative patients with those of the healthy control group. Among patients with dissociative identity disorder, the perfusion was bilaterally decreased in orbitofrontal regions and was increased in median and

Table 2
Correlations (Pearson) between regional perfusion ratios and clinical measures

	HAM-D (N=15)		DES (N=21)		CADSS (N=15)		BPD (N=21)		CTQ (N=16)	
	r	P	r	P	r	P	r	P	r	P
Orbito-frontal										
Right	−0.50	0.060	0.07	0.776	−0.03	0.908	0.20	0.386	0.19	0.483
Left	−0.45	0.090	0.08	0.745	0.03	0.917	0.29	0.196	0.25	0.350
Medial frontal										
Right	−0.45	0.090	−0.39	0.081	−0.41	0.131	−0.00	0.993	−0.07	0.787
Left	−0.33	0.236	−0.41	0.065	−0.65	0.009	−0.06	0.797	−0.17	0.518
Superior frontal										
Right	−0.22	0.435	0.03	0.908	−0.27	0.340	−0.15	0.525	0.02	0.954
Left	0.06	0.832	−0.11	0.637	−0.29	0.296	−0.29	0.198	−0.29	0.272
Occipital										
Right	−0.25	0.363	0.40	0.075	−0.05	0.851	0.17	0.461	0.13	0.624
Left	−0.50	0.059	0.33	0.148	−0.15	0.592	0.17	0.463	0.12	0.649

HAM-D: Hamilton Depression Scale.
DES: Dissociative Experiences Scale.
CADSS: Clinician Administered Dissociative State Scale.
CTQ: Childhood Trauma Scale.
BPD: Number of DSM-IV Borderline Personality Disorder Criteria.

superior frontal lobes and occipital lobes (Table 1). However, there were not any significant correlations between regional perfusion changes and clinical assessment scores (Table 2).

4. Discussion

Both hypotheses of this study were confirmed. First of all, this study demonstrated bilateral perfusion differences in frontal and occipital regions among patients with dissociative identity disorder compared with a group of non-traumatized healthy volunteers. Second, in relation to an orbitofrontal hypothesis for the etiology of dissociative identity disorder (Forrest, 2001), our results partially replicated the findings of an earlier study on dissociative identity disorder that also yielded decreased perfusion in orbitofrontal regions (Sar et al., 2001). Additionally, the present study documented increased perfusion in the medial and superior frontal and occipital regions bilaterally. Overall, anterior and posterior parts of the brain were affected by the disorder, and there was no evidence of lateralization. Lack of significant correlations between clinical measures and regional perfusion changes, however, underlines the necessity of a comprehensive explanation beyond possible associations of the psychopathology to the activities of certain brain regions.

Shore (1996) reported that there is a relationship between the development of the orbitofrontal cortex, emotion regulation, and attachment. Based on a neurodevelopmental approach, Forrest (2001) proposed an 'orbitofrontal model' for dissociative identity disorder which integrates and elaborates on theory and research from four domains: the neurobiology of the orbitofrontal cortex and its protective inhibitory role in the temporal organization of behavior, the development of emotion regulation, the development of the self, and experience-dependent maturation of the orbitofrontal cortex. This model hypothesizes that the orbitofrontal cortex plays a critical role in the development of 'distinct mental states' (Putnam, 1997) called dissociated identities due to its inhibitory functions. Although findings of the present and previous (Sar et al., 2001) studies support a role of the orbitofrontal lobe in dissociative psychopathology, they suggest that the neural isolation of 'Me-conceptual systems' is not arising through an 'active' inhibition from the orbitofrontal cortex, which Forrest (2001) proposed, but rather as a result of a lack of overall temporal organization as suggested by a weakened inhibition in the orbitofrontal cortex.

Also valid for the present study, there is wide descriptive overlap between dissociative identity disorder and borderline personality disorder (Sar et al., 2003; Sar et al., 2006). A recent study demonstrated that the orbitofrontal cortex may contribute to some core characteristics of borderline personality disorder, in particular impulsivity (Berlin et al., 2005). In accordance with these findings, we hypothesize that the increased perfusion rates in medial and superior frontal and occipital regions may be an inhibitory response to orbitofrontal perfusion change; i.e. they might have a role in overcoming the impulsivity due to orbitofrontal hypofunction. Anger, which may lead to self-destructive behavior such as suicide attempts and self-mutilation, is common both among patients with dissociative identity disorder and borderline personality disorder. These patients have continuously to deal with their unresolved past traumatic experiences and suffer emotional dysregulation (Sar et al., 2006). Thus, impulsive behavior among dissociative patients may be a final common pathway for diverse factors; e.g. anger, trauma-related flashbacks, switching from one personality state to the other, and affect dysregulation. The host personality state is an unstable condition characterized by internal struggles of various cognitive, psychosomatic, and emotional aspects represented by alter personality states; thus it represents a transient balance situation prone to experience dissociative amnesia and/or mental intrusion phenomena that may lead, in the most extreme form, to a switch to an alter personality state.

The documentation of no significant differences in rCBF between host and alter personality states in a previous SPECT study (Sar et al., 2001) led us to focus on diagnostic category rather than the dissociation mechanism (i.e. switching and/or presence of distinct mental states) itself. Thus, rather than investigating possible changes associated with the dissociation mechanism, we aimed to document the differences based on dissociative identity disorder as a diagnostic category. Accordingly, we limited our investigations to a single scintigraphy for each patient during the host personality state and we compared the brain SPECT images of dissociative identity disorder cases with those of non-traumatized healthy volunteers. The findings of the present study supported this notion; i.e. although there was no significant relationship between rCBF and any clinical measure, the rCBF differences between patients with dissociative identity disorder significantly differed from normal controls. Thus, although to a limited extent, the present study provides some contribution to the validity of dissociative identity disorder as a diagnostic category.

The main limitation of our study is that high psychiatric comorbidity is the rule rather than an exception among patients with dissociative identity disorder; i.e. eliminating comorbidity is practically impossible (Ellason et al., 1996). To dissect characteristics of dissociative disorders more specifically, future studies should benefit from control groups that consist of non-dissociative psychiatric patients. On the other hand, dissociative disorders may also confound other psychiatric disorders (Sar and Ross, 2006). Thus, brain imaging studies conducted on psychiatric disorders other than dissociative disorder should include screening instruments for comorbid dissociative psychopathology. Finally, SPECT is itself a limitation for this study; i.e. screening methods with higher resolution such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) would lead to more definitive results.

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