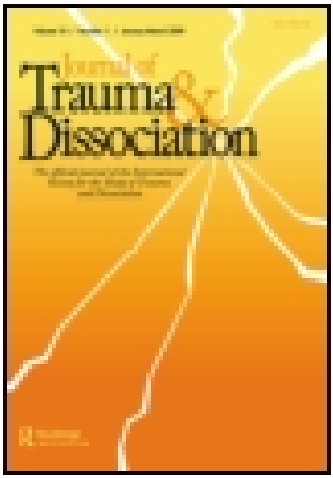

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HMPAO SPECT Study of Regional Cerebral Blood Flow in Dissociative Identity Disorder

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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. Fifteen patients with dissociative identity disorder and eight healthy volunteers participated in the study. The clinical diagnosis of dissociative identity disorder was confirmed using the Structured Clinical Interview for DSM-IV Dissociative Disorders. The Structured Clinical Interview for DSM-III-R was also administered to all patients in

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or der to screen comorbid psy chi at ric con di tions. Re gional ce re bral blood flow was studied using a SPECT system with Tc99m-hexamethyl - propylenamine (HMPAO) as a tracer. The rCBF ra tio was de creased in orbito-fron tal re gion bi lat er ally and in creased in left (dom i nant hemi- sphere) lat eral tem po ral re gion among pa tients with dissociative iden tity dis or der when com pared to the con trol group. The struc tured in ter view di ag no ses of con cur rent or life time ma jor de pres sion, PTSD, psy chotic dis or der, or on go ing drug treat ment were not sig nif i cantly re lated to per- fu sion in these re gions. There was no sta tis ti cally mean ing ful dif fer ence in rCBF ra tios be tween host and al ter per son al ity states. Our find ings sug gest that orbito-fron tal and left (dom i nant hemi sphere) lat eral tem po- ral re gions are af fected in dissociative iden tity dis or der. A rep li ca tion of this study on a larger group of drug-free dissociative pa tients and var i ous psy chi at ric con trol groups would lead to more de fin i tive find ings.*[Ar ti- cle cop ies avail able for a fee from The Haworth Doc u ment De liv ery Ser vice: 1-800-342-9678. E-mail ad dress: <getinfo@haworthpressinc.com> Website: <http://www.HaworthPress.com> © 2001 by The Haworth Press, Inc. All rights re served.]*

KEYWORDS. SPECT, dissociative iden tity dis or der, im ag ing, re gional ce re bral blood flow

INTRODUCTION

Dissociative identity disorder is a chronic dissociative condition char ac ter ized by the pres ence of two or more dis tinct per son al ity states or iden ti ties within a sin gle per son which take con trol of be hav ior re cur- rently (Amer i can Psy chi at ric As so ci a tion, 1994). Each per son al ity state can have dif fer ent ac cess into mem ory re sult ing in a state-de pend ent in- abil ity to re call im por tant per sonal in for ma tion. These al ter per son al i- ties can be char ac ter ized by dif fer ent emo tional re sponses, cognitions, moods, and perceived self-images. Dissociative identity disorder is con sid ered as a post-trau matic de vel op men tal psychopathology closely re lated to child abuse and ne glect (Putnam, 1997).

Brain im ag ing stud ies on se ries of pa tients with dissociative iden tity disorder are still lack ing. One sin gle case SPECT study (Saxe, Vasile, Hill, Bloomingsdale, & Van der Kolk, 1992) yielded a mean per fu sion in crease of 10.7% in the left tem po ral lobe when as sessed dur ing ac ti va- tions of four al ter per son al ity states. One pre vi ous sin gle case SPECT study (Mathew, Jack, & West, 1985) uti liz ing lower res o lu tion tech-

nique reported increase of perfusion in right temporal lobe. A recent single case functional magnetic resonance imaging (MRI) study (Tsai, 1999) on a woman with dissociative identity disorder and PTSD demonstrated bilateral hippocampal inhibition (with inhibition stronger on the right side) while the patient was switching from host to alter personal ity. 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. The hippocampal volume was significantly smaller than reported values for normal female adults obtained with the same technique.

The aim of our study was to investigate if there were any characteristics of regional cerebral blood flow (rCBF) in dissociative identity disorder. We compared the brain SPECT images of dissociative identity disorder cases with those of non-traumatized healthy volunteers. In a subgroup of dissociative patients, we also documented rCBF in host and alter personal ity states using repeated measurements and tried to test the consistency of the findings.

METHODS

Subjects

Fifteen patients (11 women and 4 men) who fully met the DSM-IV (American Psychiatric Association, 1994) criteria for dissociative identity disorder and 8 healthy volunteers (6 women and 2 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 University Istanbul Medical Faculty Hospital. Informed consent was obtained from all subjects after the procedures had been fully explained.

All patients were evaluated with the Dissociative Experiences Scale (Bernstein & Putnam, 1986; Carlson, & Putnam, 1993) and the Structured Clinical Interview for DSM-IV Dissociative Disorders (Steinberg, 1994). The Turkish versions of these instruments have excellent validity and reliability (Yargic, Tutkun, & Sar, 1995; Sar et al., 1997; Kundakci, Sar, Kiziltan, Yargic, & Tutkun, 1998). Childhood trauma histories were obtained using the Childhood Abuse and Neglect Questionnaire (Yargic, Tutkun, & Sar, 1994). All probands were clinically evaluated by two psychiatrists who had extensive experience in evaluation, treat-

ment, and research on dissociative disorders. In all patients switching of personality states and amnesias were observed several times during interviews. In order to evaluate comorbid conditions, we administered the Structured Clinical Interview for DSM-III-R including the module for PTSD and the section for borderline personality disorder to all patients with dissociative identity disorder (Spitzer, 1987).

All patients were right handed. They all underwent a structural brain imaging examination with either CT or MRI to exclude the presence of a cerebral disease or focal lesions except one male subject who refused the CT or MRI scan being afraid of the conditions of the procedure. The existence of epileptic disorder was ruled out using EEG in all patients. None of the subjects had any structural lesions in the central nervous system except one male subject who had bilateral optical atrophy in neurological examination. The etiology of this finding could not be illuminated despite inpatient and outpatient neurological follow-up. Another male subject had been diagnosed as having Behçet's disease, however, he had no neurological complications. None of the remaining subjects had any physical disorder. Ten patients were under either an antidepressant or anxiolytic medication, five patients were drug-free. We did not impose a drug cessation or wash-out periods for the probands under medication except on the study day as we did not want the study to interfere with the ongoing treatment of these difficult patients.

Eight non-traumatized, right-handed healthy volunteers (6 women and 2 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 traumas and/or neglect. They had to have scores less than 10 on the Dissociative Experiences Scale and Beck Depression Inventory (Beck, Wrad, Mendelson, Mock, & Erbaugh, 1961) and negative responses to all items of the Childhood Abuse and Neglect Questionnaire. They all had to be right-handed.

Procedure

The study consisted of two phases. In the first phase, three cerebral perfusion SPECT studies were performed sequentially on six patients. The first SPECT scintigraphies were done on patients when they were in the host state. After at least one week, scintigraphies on the patients were performed when in an alter personality state. The alter personality states were activated by the patient's therapist stating "I would like to speak with (name of the personality state) for the assessment." After the

personality state appeared, 555 MBq Tc99m-hexamethylpropylenamine (HMPAO, Ceretec, Amersham) was injected intravenously. The therapist did not continue to speak during scanning. After a further period of at least one week, the patients had their third scintigraphies in the same alterpersonality state as when they had been previously scanned. The alterpersonality states were elicited for the third scintigraphy using the same procedure. The purpose was to see whether there was any difference between host and alterpersonality states, and to look for any similarity between second and third scintigraphies as they were obtained during the same alterpersonality state. In the second phase of the study, one scintigraphy was performed on each of nine other patients in the host personality state without activating any alterpersonality. A total of 27 scintigraphies were performed.

According to the guidelines by Juni and colleagues (1998), the scanning was performed 60 minutes after the injection. The patient's head was immobilized on a headrest 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 degrees rotations) in 64 3 64 matrix, for 30 seconds per projection. The acquisition time was approximately 16 minutes.

Data Analysis

SPECT reconstruction was performed on the ADAC Pegasys workstation. Transaxial images were obtained by the filtered backprojection method using Butterworth filter with a frequency cut-off 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 analyzed both visually and by semiquantitative analysis. The visual analysis of SPECT images was done independently by two investigators both of whom were a specialist and faculty member in nuclear medicine. When reading the images, one of the investigators was aware of the group membership of the participants whereas the second investigator was blind to all data including the group membership of the participants. An area was defined hypoperfused if the amount of tracer uptake appeared substantially lower than that in adjacent and/or contralateral area of the brain.

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 OML (Damasio & 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 (Figure 1). For this template, the hippocampal line was used which was parallel to the longitudinal axis of the temporal lobe. Determination of the regions of interest (ROI) is shown in Figure 1. ROIs were drawn manually over one hemisphere and mirrored to the contralateral side. Regional cerebral blood flow (rCBF) ratio was calculated for each ROI using the mean number of counts divided by the mean cerebellar counts (Catafau et al., 1996). The scintigraphies obtained during the hosts personality state were used for this analysis.

RESULTS

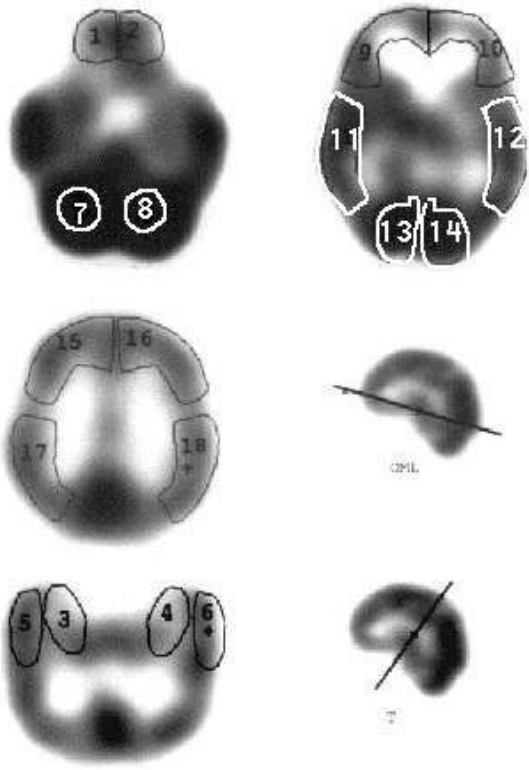
Characteristics of the Subjects

There was no significant difference ($t = 0.32$, $df = 21$, $p > 0.05$) on age between dissociative patients (mean = 25.5, SD = 4.6) and healthy volunteers (mean = 24.9, SD = 4.8). The difference in years of education between dissociative patients (mean = 9.5, SD = 3.3) and healthy volunteers (mean = 11.6, SD = 3.2) was also not significant ($t = 1.47$, $df = 21$, $p > 0.05$). Eleven dissociative patients (73.3%) and 6 healthy volunteers (75.0%) were women; there were no significant gender differences between the groups (Fisher exact test, $p > 0.05$).

The mean Dissociative Experiences Scale score in the dissociative disorders group was 48.0 (SD = 18.9, median = 48.2, range = 16.4-81.1). All probands reported at least one type of childhood trauma. Thirteen patients (86.7%) reported childhood sexual abuse; 7 (46.7%) of them were incest victims. Eleven patients (73.3%) reported physical abuse, 11 (73.3%) emotional abuse, and 12 (80.0%) neglect in childhood. None of the subjects in the control group reported any type of childhood abuse or neglect.

According to the Structured Clinical Interview for DSM-III-R, the patients with dissociative identity disorder fit diagnostic criteria of several psychiatric disorders at the same time (Table 1). Seven (46.7%) patients had concurrent major depression. An additional 3 patients reported past episodes of major depression yielding a lifetime major depression

FIGURE 1. Regions of interest used for semi-quantitative analysis of rCBF ratios. 1-2: Right and left orbito-frontal regions; 3-4: Right and left mesial temporal regions involving hypocampus; 5-6: Right and left lateral temporal regions; 7-8: Right and left cerebellar regions; 9-10: Right and left median 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



rate of 66.7% (N = 10). Six patients (40.0%) met the criteria for PTSD and eight patients (53.3%) met the criteria for some type of somatoform disorder. Although none of the patients had any psychotic or schizophrenic disorder in clinical evaluation, 10 patients (66.7%) of them had a false positive diagnosis of psychotic disorder on structured interview based mainly on hallucinations of dissociative type. Eleven (73.3%) of the patients met the criteria for borderline personality disorder according to the DSM-III-R.

TABLE 1. Co-di ag no ses of pa tients with dissociative iden tity dis or der (N = 15) accordingto the Struc tured Clin i cal Inteview for DSM-III-R.

Diagnosis	N	%
Major depression (lifetime)	10	66.7
Disthymic dis or der	10	66.7
Major depression (current)	7	46.7
Bipolar II	0	0.0
Mania (past)	0	0.0
Mania (current)	0	0.0
Any affective disorder	12	80.0
Obsessive compulsive disorder	6	40.0
PTSD	6	40.0
Simple phobia	4	26.7
Social phobia	2	13.3
Agoraphobia without panic disorder	0	0.0
Panic disorder with agoraphobia	2	13.3
Generalized anxiety disorder	2	13.3
Panic disorder without agoraphobia	3	20.0
Any anxi ety dis or der (excl. PTSD)	12	80.0
Any anxi ety dis or der (incl. PTSD)	12	80.0
Psychotic dis or der NOS	8	53.3
Schizophrenic disorder	1	6.7
Schizoaffective disorder	1	6.7
Schizophreniform dis or der	2	13.3
Brief psychotic dis or der	0	0.0
Delusional disorder	0	0.0
Any psychotic dis or der	10	66.7
Somatization dis or der	6	40.0
Undifferentiated somatoform disorder	2	13.3
Hypochondriasis	0	0.0
Any somatoform dis or der	8	53.3
Alcohol abuse	0	0.0
Substance abuse	1	6.7
Anorexia nervosa	0	0.0
Bulimia nervosa	1	6.7
Borderline personality disorder	11	73.3

Perfusion Ratios

In visual analysis, all patients in the dissociative identity disorder group had hypoperfusion areas in orbito-frontal regions bilaterally. These hypoperfusion areas were recognized in visual assessment (Figures 2 and 3) and were reported by both investigators independently. The same perfusion pattern was also seen in repeated scintigraphies of the first six patients obtained during activation of alter personality states. None of the healthy control subjects had any perfusion defect in orbitofrontal regions in visual analysis.

This observation was confirmed by the semi-quantitative evaluation. Table 2 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 orbito-frontal regions and was increased in left lateral temporal region. However, only the latter finding remained significant after Bonferroni correction.

FIGURE 2. Orbito-frontal perfusion defect in a patient with dissociative identity disorder (sagittal section).

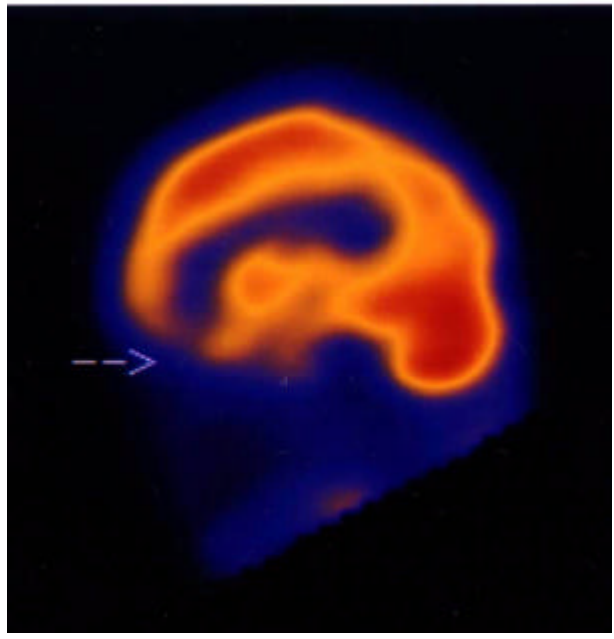


FIGURE 3. Orbito-frontal perfusion defect in a patient with dissociative identity disorder (transverse section).

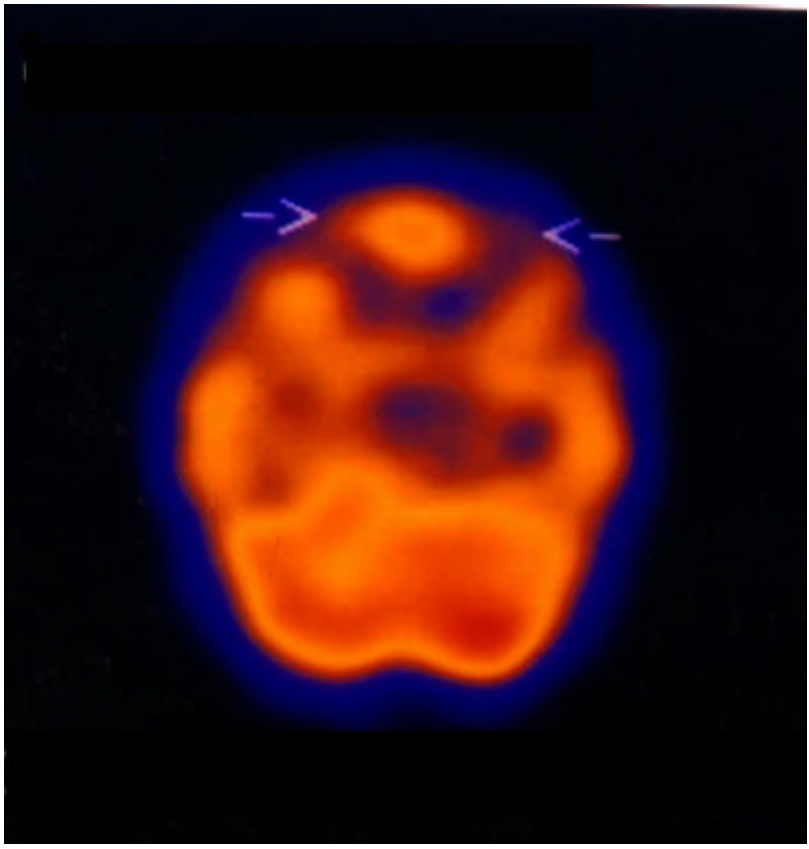


Table 3 shows the mean values of rCBF ratios in 6 patients with dissociative identity disorder obtained during host personality state, and alter personality state in two occasions. There was no significant difference between host and alter personality states concerning perfusion in any region.

rCBF ratios of the medicated and drug-free patients were compared (Table 4) in order to evaluate possible drug effect on perfusion. There was no significant difference between two groups in any region. Although the perfusion was slightly decreased in orbito-frontal region among dissociative patients who were medicated this difference was

TABLE 2. rCBT ratios of patients with dissociative identity disorder and healthy comparison subjects (applying Bonferroni method the adapted level of alpha is p = 0.003).

Region	Dissociative Patients (N = 15) Mean	SD	Healthy Comparison Subjects (N = 8) Mean	SD	t (df = 21)	p
Frontal						
Orbito						
Right	60.1	11.5	74.1	3.3	3.34	< 0.005
Left	58.1	13.2	73.9	3.8	3.27	< 0.005
Median						
Right	80.0	6.9	74.9	4.6	1.88	n.s.
Left	79.3	7.6	74.1	3.6	1.81	n.s.
Superior						
Right	83.3	5.4	78.1	6.8	2.01	n.s.
Left	81.5	5.4	78.6	6.6	1.14	n.s.
Parietal						
Right	77.1	6.2	79.0	4.0	0.76	n.s.
Left	77.9	5.5	80.4	2.7	1.17	n.s.
Temporal						
Mesial						
Right	76.2	10.2	75.0	5.9	0.30	n.s.
Left	75.5	6.5	71.9	2.2	1.54	n.s.
Lateral						
Right	81.0	8.0	76.8	4.7	1.38	n.s.
Left	83.1	4.0	74.0	2.6	5.72	< 0.001
Superior						
Right	86.5	4.9	83.0	4.0	1.72	n.s.
Left	85.9	6.8	84.3	3.5	0.63	n.s.
Occipital						
Right	93.5	5.7	88.9	5.0	1.92	n.s.
Left	94.0	5.7	89.4	3.9	2.04	n.s.

not statistically significant. The perfusion ratios in left lateral temporal region, a further area which seems to be affected in dissociative disorder group, were, however, very close in both medicated and drug-free groups.

Table 5 shows comparisons of the rCBF ratios in dissociative patients with various comorbid diagnoses. The orbito-frontal regions and left lateral temporal region which have been shown as related to the investigated condition in this study were selected for comparison. None of the comorbid diagnoses had statistically significant effect on rCBF ratios. Although not significant statistically, dissociative patients with comorbid major depression had lower rCBF ratios in orbito-frontal regions compared to dissociative patients who did not have major depres-

TABLE 3. rCBF ratios of patients with dissociative identity disorder in scintigraphies obtained in host and alter states (repeated measures analysis of variance, n = 6).

	Host State		Alter State		Alter State			
Region	Mean	SD	Mean	SD	Mean	SD	F (df = 2,5)	p
Frontal								
Orbito								
Right	64.8	9.4	63.0	20.2	53.2	22.4	1.96	n.s.
Left	61.2	9.0	61.8	21.1	51.2	23.3	2.00	n.s.
Median								
Right	79.7	6.5	82.7	7.4	78.7	11.2	0.40	n.s.
Left	78.3	8.7	82.2	11.3	75.2	12.8	0.77	n.s.
Superior								
Right	83.7	6.0	78.3	8.3	78.5	8.5	2.42	n.s.
Left	82.3	4.1	78.2	7.9	81.0	8.5	1.62	n.s.
Parietal								
Right	76.5	6.3	79.3	6.0	78.0	7.3	0.56	n.s.
Left	76.3	4.6	78.0	7.5	76.7	5.9	0.42	n.s.
Temporal								
Mesial								
Right	81.2	7.6	77.7	6.7	78.5	9.8	1.60	n.s.
Left	78.0	8.7	80.0	6.5	78.0	8.4	0.34	n.s.
Lateral								
Right	85.3	5.2	83.2	4.1	80.7	5.4	0.31	n.s.
Left	84.5	5.2	83.0	2.5	82.0	9.1	0.73	n.s.
Superior								
Right	85.2	5.5	88.3	4.8	85.8	4.9	0.08	n.s.
Left	86.5	6.6	88.3	3.9	86.7	4.5	0.48	n.s.
Occipital								
Right	95.7	4.2	94.5	6.6	92.5	8.8	1.33	n.s.
Left	95.7	4.2	94.5	6.6	95.0	5.3	0.34	n.s.

sion. Left lateral temporal region was, however, not affected by any comorbid condition among patients with dissociative identity disorder.

DISCUSSION

To our knowledge, this is the first multicase study of functional brain imaging in patients with dissociative identity disorder. Different cognitive and emotional characteristics of alter personalities observed among patients with dissociative identity disorder led us to obtain repeated scintigraphies in order to screen state-dependent perfusion changes. There was no significant difference in rCBF throughout repeated scinti-

TABLE 4. rCBF ratios of patients with dissociative identity disorder who were medicated or drug-free.

Region	Medicated Patients (N = 10) Mean	SD	Drug-Free Patients (N = 5) Mean	SD	t (df = 13)	p
Frontal						
Orbito						
Right	58.9	13.1	62.6	8.0	0.57	n.s.
Left	54.9	14.0	64.6	9.6	1.38	n.s.
Median						
Right	77.9	7.7	84.2	0.8	1.80	n.s.
Left	76.7	8.1	84.6	1.8	2.11	n.s.
Superior						
Right	82.4	5.7	85.2	4.9	0.94	n.s.
Left	80.5	6.0	83.6	3.7	1.05	n.s.
Parietal						
Right	78.9	4.2	73.6	8.6	1.64	n.s.
Left	79.1	4.5	75.6	7.1	1.17	n.s.
Temporal						
Mesial						
Right	75.5	12.1	77.6	5.9	0.36	n.s.
Left	76.1	7.2	74.4	5.2	0.47	n.s.
Lateral						
Right	81.6	9.2	79.8	5.7	0.40	n.s.
Left	83.9	4.7	81.4	1.5	1.15	n.s
Superior						
Right	85.3	4.9	88.8	4.5	1.34	n.s.
Left	84.8	7.7	88.0	4.4	0.86	n.s.
Occipital						
Right	94.8	4.4	90.8	7.4	1.32	n.s.
Left	95.7	3.5	90.6	8.0	1.75	n.s.

graphies obtained in different personality states suggesting that the observed perfusion pattern is a trait characteristic rather than a state-dependent one.

This study demonstrated perfusion differences in orbito-frontal regions bilaterally and in left lateral temporal region among patients with dissociative identity disorder compared with a group of non-traumatized healthy volunteers. Our results support findings of an earlier single case study on dissociative identity disorder which yielded increased perfusion in left temporal lobe during activation of alter personality states (Saxe et al., 1992). Hypoperfusion of the orbito-frontal regions have been, however, reported in dissociative identity disorder for the first time. Although only the finding concerning temporal region re-

TABLE 5. rCBF ratios in dissociative identity disorder patients with and without a comorbid diagnosis.

Comorbid SCID-I DSM-III-R Diagnosis	rCBF Ratio Mean	SD	rCBF Ratio Mean	SD	t (df = 13)	p
Current major depression	Present (N = 7)		Absent (N = 8)			
Orbito-frontal (left)	52.6	16.3	63.0	7.9	1.61	n.s.
Orbito-frontal (right)	55.7	13.9	64.0	7.8	1.45	n.s.
Lateral temporal (left)	82.9	3.1	83.3	4.9	0.18	n.s.
Past or current major depression	Present (N = 10)		Absent (N = 5)			
Orbito-frontal (left)	54.3	14.2	65.8	6.9	1.69	n.s.
Orbito-frontal (right)	57.1	11.7	66.2	9.3	1.51	n.s.
Lateral temporal (left)	82.2	2.9	84.8	5.7	1.20	n.s.
PTSD	Present (N = 6)		Absent (N = 9)			
Orbito-frontal (left)	55.2	15.5	60.1	12.0	1.01	n.s.
Orbito-frontal (right)	58.3	9.3	61.3	13.2	0.70	n.s.
Lateral temporal (left)	81.7	2.4	84.0	4.7	1.11	n.s.
Any psychotic disorder	Present (N = 10)		Absent (N = 5)			
Orbito-frontal (left)	59.1	13.0	56.2	14.9	0.51	n.s.
Orbito-frontal (right)	62.9	9.6	54.6	14.0	1.90	n.s.
Lateral temporal (left)	83.0	4.4	83.2	3.5	0.09	n.s.

mained significant after Bonferroni correction, because of its potential importance, we did not simply omit the finding concerning orbito-frontal region from our discussions.

Some authors have claimed that there is an association between temporal lobe epilepsy and dissociative disorders (Mesulam, 1981). However, the conceptualization of dissociative disorders as a form of epilepsy has not gained wide acceptance (Devinsky, 1989). None of our patients in this study had epilepsy. Dissociative disorders have a different symptom profile than complex partial epilepsy and as such they can be differentiated from partial complex epilepsy even using structured interviews (Yargic, Sar, Tutkun, & Alyanak, 1998). Nevertheless, the limited popularity of the epilepsy model does not necessarily decrease the importance of temporal lobe for dissociative disorders, as there have been few studies about the subject as yet (Persinger, 1993). Although not consistent with the findings of the present study, using functional MRI, Tsai et al. (1999) demonstrated in a single case of dissociative identity disorder inhibition and activation on hippocampal area (medial temporal region) during switching. Our findings encourage further studies on temporal lobe in dissociative disorders.

A common feature of our patients is the presence of childhood

trauma histories. In a study with MRI (Stein et al., 1997), women who reported sexual victimization in childhood had significantly reduced (5% smaller) left-sided hippocampal volume compared to that of non-victimized women. Left-sided hippocampal volume correlated negatively with dissociative symptom severity, but not with indices of explicit memory functioning. Bremner and colleagues (1997) also found a decrease in left hippocampal volume with MRI in subjects with PTSD related to childhood abuse. Although these findings concerning hypofunction of medial temporal lobe are not in accordance with our observations about lateral temporal hyperperfusion, a direct comparison is not warranted because of the different methodologies, i.e., these studies were based on structural imaging.

Functional brain imaging studies also were conducted among subjects with childhood trauma histories. Shin and colleagues (1999) used positron emission tomography (PET) in women with histories of childhood sexual abuse during script driven imagery who either had or did not have concurrent PTSD. In the traumatic versus neutral control conditions, both groups exhibited rCBF increases in orbito-frontal and anteriortemporal lobes. These increases were greater in PTSD group than in the comparison group. Using a similar methodology, Bremner and colleagues (1999) demonstrated that memories of childhood sexual abuse were associated with alterations of rCBF in medial prefrontal cortex (subcallosal gyrus and anterior cingulated), hippocampus, and visual association cortex. These authors claim that brain perfusion changes in response to trauma scripts among subjects with childhood sexual abuse history are not specific to the pathological state of PTSD but are generalized neural responses to memories of upsetting childhood sexual abuse experiences. Although there are differences in the methodologies, the discrepancies between these observations and ours suggest that the findings of the present study cannot attributed solely to the traumatic childhood histories of our patients. The perfusion differences in our study also do not correspond to the Broca and Wernicke areas which are related to verbal communication abilities and have been mentioned as affected regions in brain imaging studies on PTSD (Shin et al.,1999; Rauch et al., 1996).

Frontal hypoperfusion has also been reported in SPECT studies conducted on depressive (Ito, 1996) and schizophrenic patients (Mozley et al., 1996; Andreasen, Swayze, Flaum, O'Leary, & Alliger, 1994), however, a general agreement on this finding has also not been achieved. Hypofrontality has been related to some disturbance in working memory rather than considered a feature specific to depressive or schizo-

phrenic disorders. Among schizophrenic patients, it is related mostly to negative symptoms of the disorder (Andreasen, 1994). Dissociation is a special form of consciousness in which events that would ordinarily be connected are divided from one another (Hilgard, 1977). Consequently, in the present study, we can expect to find abnormalities in the areas in central nervous system that are involved in the integration of ongoing experience. Our finding concerning orbito-frontal region is not at odds with the previous literature, because the frontal lobe is thought to function as a supervisory system for the integration of experience (Van der Kolk, Burbridge, & Suzuki, 1997).

Subjects with dissociative identity disorder or dissociative amnesia have a selective inability to retrieve memories from their personal past. Interestingly, similarities have been emphasized between amnesic patients with a clear organic (neurological) basis and psychogenic (dissociative) amnesic patients (Markowitsch, 1996a). It is proposed that common mechanisms underlie these two forms of retrograde amnesia. Case descriptions demonstrate that a selective type of retrograde amnesia may occur and it is proposed that a blockade, disruption, or disconnection mechanism affecting access to stored engrams is the basic mechanism of retrograde amnesia (Markowitsch, 1996b). Results from functional neuroimaging studies point out to the importance of the prefrontal cortex for the information recall (Markowitsch, 1999). Using functional MRI on normal probands, Markowitsch (personal communication, November 2000) observed that there were massive activations on orbito-frontal regions when emotional positive or negative memories were recalled. Positive memories led to medial and negative memories to lateral orbito-frontal activations. A combination of infero-lateral prefrontal and temporopolar regions is assumed to trigger the retrieval of stored old memories (Markowitsch, 2000b). The lateral temporal cortex seems not to be the principal storage site of episodic (autobiographical) memory, but the one which triggers cortical storage sites to provide memory output (Kroll, Markowitsch, Knight, & von Cramon, 1997). It is quite possible that there is a link between our findings concerning orbito-frontal hypofunction and lateral temporal hyperfunction (Markowitsch & Ewald, 1997; Kroll, Markowitsch, Knight, & von Cramon, 1997), e.g., reflecting an interactive balance between two regions. This point needs further inquiry.

On the other hand, orbitofrontal-region is not significant for memory research only. In a study on impulsive (particularly borderline) subjects, the orbito-frontal area (an inhibitory region of the cortex) had less response to agents that increase serotonergic activity (Siever et al.,

1999, cited in Koenigsberg et al., 2000). Genes related to the serotonergic system also appear to be related to impulsive aggression (Koenigsberg et al., 2000). It is well known that there is wide descriptive overlap between dissociative identity disorder and borderline personality disorder (Sar et al., 1999). Given the fact that 73.3% of the dissociative subjects in the present study had a comorbid diagnosis of borderline personality disorder according to the DSM-III-R criteria, Siever et al.'s findings might also have implications for dissociative disorders.

Our preliminary study has some limitations. First, some of our probands were receiving medication. However, there was also a subgroup of drug-free probands among our patients. Although the presence of the same perfusion pattern in both groups makes a difference created by medication highly improbable, this possibility should be ruled out with further studies using a larger group of drug-free patients. The second limitation is that all of our patients fit DSM-III-R diagnostic criteria of at least one additional psychiatric disorder besides the main diagnosis of dissociative identity disorder. However, this limitation cannot be eliminated in further studies, as high descriptive comorbidity is practically inevitable for subjects with dissociative identity disorder, and in fact, is even a characteristic feature of the disorder (Ellason, Ross, & Fuchs, 1996; Kiziltan, Sar, Kundakci, Yargic, & Tutkun, 1998). Although the comparison between rCBF ratios for various comorbid diagnoses in our patients does not reveal any significant difference, further studies should compare perfusion characteristics of dissociative patients with those of patient groups with various psychiatric disorders, e.g., major depression or schizophrenic disorder. As a third limitation, the Bonferroni correction for multiple comparisons put the statistical significance of our semi-quantitative findings concerning orbito-frontal region into question. However, the consistent observations in visual analysis (Figure 1) and the basic importance of the orbito-frontal region as a part of the limbic system (Markowitsch, 2000a,b) compels us to include this observation for further discussion.

CONCLUSIONS

The findings of this preliminary study suggest that left lateral temporal region and bilateral orbito-frontal regions are affected in dissociative identity disorder. In order to reach more definitive findings, this study should be replicated using larger groups of drug-free patients and vari-

ouspsychiatric control groups. On the other hand, brain imaging studies conducted on psychiatric disorders other than dissociative disorder should also include screening instruments for comorbid dissociative psychopathology.

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