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Neural correlates of enhanced working-memory performance in dissociative disorder: a functional MRI study

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ABSTRACT

Background. Memory functioning has been highlighted as a central issue in pathological dissociation. In non-pathological dissociation, evidence for enhanced working memory has been found, together with greater task-load related activity. So far, no imaging studies have investigated working memory in dissociative patients.

Method. To assess working memory in dissociative patients functional magnetic resonance imaging was used during performance of a parametric, verbal working-memory task in patients with a dissociative disorder ($n=16$) and healthy controls ($n=16$).

Results. Imaging data showed that both groups activated brain regions typically involved in working memory, i.e. anterior, dorsolateral and ventrolateral prefrontal cortex (PFC), and parietal cortex. Dissociative patients showed more activation in these areas, particularly in the left anterior PFC, dorsolateral PFC and parietal cortex. In line with these findings, patients made fewer errors with increasing task load compared to controls, despite the fact that they felt more anxious and less concentrated during task performance.

Conclusions. These results extend findings in non-pathological high dissociative individuals, suggesting that trait dissociation is associated with enhanced working-memory capacities. This may distinguish dissociative patients from patients with post-traumatic stress disorder, who are generally characterized by impaired working memory.

INTRODUCTION

Dissociative disorders are believed to be post-traumatic developmental psychiatric disorders, characterized by a disruption in the usually integrated functions of consciousness, memory, identity, or perception of the environment (APA, 1994). Several studies have reported a relation between childhood sexual abuse, physical abuse, and emotional neglect and adult dissociation (Chu & Dill, 1990; Mulder *et al.* 1998; Kisiel & Lyons, 2001; Draijer & Langeland, 1999). Memory anomalies, particularly dissociative amnesia (defined as an inability to recall important personal information that is too extensive to be explained by ordinary forgetfulness (APA, 1994), are considered to be key symptoms of pathological dissociation. Accordingly, the role of disordered attention and memory has been highlighted as a central issue in understanding the phenomenology of

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dissociative disorders. Dorahy (2001), for example, hypothesized that dissociative patients are characterized by working-memory impairments, owing to a failure to keep working memory free from irrelevant burdensome stimuli. Studies on memory functioning in dissociative disorders are scarce, however, and have primarily focused on anomalies in autobiographical recall and information transfer across symmetric and asymmetric amnesic states (Eich *et al*. 1997; Elzinga *et al*. 2003; Huntjens *et al*. 2003). To date, little is known about potential deficits in working memory in these disorders.

Working memory as defined by Baddeley (1996) refers to a limited capacity system that provides temporary maintenance and manipulation of information necessary to execute complex tasks. Cognitive inhibitory processes are believed to keep working memory relatively free of irrelevant stimuli. Evidence from lesion, pharmacological, and pre-clinical studies indicates that the prefrontal cortex (PFC) is a key brain structure in working memory (Fuster, 1997) This is supported by neuroimaging studies showing a significant linear relationship between the increase in working memory load and the degree of activation observed in the dorsolateral prefrontal cortex (DLPFC), ventrolateral PFC (VLPFC), anterior cingulate cortex (ACC), as well as in the parietal cortex (Braver *et al*. 1997; Rijpma *et al*. 1999; Jansma *et al*. 2000; Veltman *et al*. 2003).

Several studies have shown that working memory is particularly sensitive to exposure to (acute and chronic) stress (Arnsten, 1998). Working-memory impairments have been found, for example, after exposure to psychosocial stress in non-clinical participants (Elzinga & Roelofs, 2005). Post-traumatic stress disorder (PTSD) is similarly characterized by working-memory deficits (McFarlane *et al*. 1993; Bremner *et al*. 1993; Uddo *et al*. 1993; Semple *et al*. 1996). Moreover, impaired working memory in PTSD is associated with reduced activation of the PFC (Galletly *et al*. 2001; Clark *et al*. 2003). Given the overlap with respect to trauma history and symptomatology between dissociative patients and patients with PTSD, working-memory impairments have been hypothesized to be a key cognitive deficit of dissociative patients as well (Dorahy, 2001).

Dissociation as a trait in non-clinical individuals, in contrast, has been associated with *enhanced* working-memory capacities. One study comparing 119 students with high and low trait-dissociation scores found that high-dissociative students performed better on a verbal working-memory task than low-dissociative students (De Ruiter *et al*. 2004). This was further substantiated in a functional imaging study using two parametric working-memory tasks showing that high-dissociators performed slightly better than low-dissociators during both working-memory tasks and also had increased task load-related activity in the left DLPFC and left parietal cortex (Veltman *et al*. 2004). Apparently, non-pathological dissociative tendencies correspond with enhanced attentional and working-memory abilities. Given the high level of genetic influences in both pathological and non-pathological dissociation and the substantial shared genetic variance (Jang *et al*. 1998), a fundamental cognitive mechanism may be involved in both clinical and non-clinical dissociation. When confronted with adverse life events, eminent dissociative abilities, including an enhanced capacity to focus attention ('absorption') may be invoked to cope with these situations by attending to neutral elements, therewith detaching from the aversive emotions (Cloitre, 1992, De Ruiter *et al*. 2006).

In sum, identification of the neural underpinnings of working-memory processes in dissociative patients is very relevant to increase our understanding of dissociative phenomenology and symptomatology. This study aims to contribute to the characterization of working-memory functioning in terms of cognitive and neural information processing in a group of female dissociative patients.

METHOD AND MATERIALS

Subject recruitment and assessment

Thirty-two women participated in the study, 16 patients diagnosed with dissociative identity disorder (DID) or dissociative disorder – not otherwise specified (DD-NOS) and 16 healthy control subjects.

Patients were recruited by Parnassia Psychomedical Center, Center of Intensive Treatment, Den Haag, The Netherlands. Information regarding the study was sent to patients eligible

for participation. Patients returned an informed consent form with name and phone number if they were willing to participate, upon which they were contacted by the main investigator (B.M.E.). Healthy subjects were recruited via advertisements, and were matched for age and education level.

In patients the diagnosis DID or DD-NOS was established using the Structured Clinical Interview for DSM-IV Dissociative Disorders (SCID-D; Steinberg, 1993, Dutch translation Boon & Draijer, 1994) conducted by a trained psychologist (A.A.). Axis I disorders (current and past depression, dysthymia, current and past alcohol and drug abuse, and PTSD) were established using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I; First *et al*. 1997, Dutch translation Groenestijn *et al*. 1998).

Healthy control subjects were screened for the absence of any psychiatric disorder using the Mini-International Neuropsychiatric Interview (M.I.N.I., Sheehan *et al*. 1998) by a master's-level psychologist (M.K.H.).

All subjects were screened to determine if they were free of major internal or neurological illnesses. Other exclusion criteria were pregnancy, repeated psychotic episodes, and drug and alcohol addiction or abuse. All subjects were free of medication, except for two patients (one patient had a steady dose of 30 mg/day mirtazapine and 75 mg/day venlafaxine, one patient 70 mg/day citalopram). Participants' medication was not discontinued for the purpose of participating in the study.

On the basis of the SCID-D interview, seven patients were diagnosed with DID and six with DD-NOS†. (For co-morbid diagnoses see Table 1.) As expected, patients had higher dissociation scores as measured with the Dissociative Experiences Scale (DES; Bernstein & Putnam, 1986). Patients also reported more post-traumatic stress symptoms as measured with the Davidson Trauma Scale (DTS; Davidson, 1996), and higher levels of state anxiety, as measured with the state section of the Dutch version of the State-Trait Anxiety Inventory (STAI-DY I; Spielberger *et al*. 1983, Dutch translation Van der Ploeg *et al*. 1980). Patients reported more adverse experiences in childhood, including emotional neglect, emotional abuse, physical abuse, sexual harassment, and sexual abuse as measured with the Traumatic Experiences Checklist (TEC; Nijenhuis *et al*. 2002). Dissociative patients did not differ in age or years of education from controls (see Table 1).

Table 1. *Subject characteristics*

	Dissociative patients ($n=13$) Mean ± S.D.	Controls ($n=14$) Mean ± S.D.
Mean age	40·8 ± 10·7	34·6 ± 10·9
Education (yr)	13·3 ± 2·3	13·7 ± 2·8
Co-morbid diagnoses		
PTSD	12	0
MDD	2	0
Dysthymia	4	0
History		
MDD	10	0
Alcohol abuse	6	0
Substance abuse	3	0
Traumatic Experiences Checklist	42·6 ± 14·3	7·6 ± 8·8****
Emotional neglect	10·0 ± 2·9	3·5 ± 4·8****
Emotional abuse	10·3 ± 2·8	1·9 ± 4·0****
Physical abuse	8·2 ± 4·4	1·1 ± 2·2****
Sexual harassment	5·7 ± 4·1	1·0 ± 2·2****
Sexual abuse	8·5 ± 5·0	0·1 ± 0·3****
Dissociative Experiences Scale	45·5 ± 17·1	6·2 ± 8·6****
Davidson Trauma Scale	68·3 ± 33·8	4·4 ± 4·9****
State Anxiety Inventory	48·4 ± 12·6	32·5 ± 7·4****

PTSD, Post-traumatic stress disorder; MDD, major depressive disorder.
**** $p<0·0001$.

After complete description of the study to the subjects, written informed consent was obtained from all subjects. The study was approved by the scientific committee of Parnassia, Den Haag and the medical ethical committee in Arnhem ('Toetsingscommissie Patiëntgebonden Wetenschappelijk Onderzoek', Arnhem), The Netherlands.

Working-memory task

Stimuli were generated by a Pentium PC and projected onto a screen at the end of the scanner table. A mirror above the head enabled the subject to see the stimuli on the screen. Subjects' performance and reaction times were recorded through a MRI compatible response box, which they used with their right hand.

† Diagnostic assessment is reported over the 23 participants (13 dissociative patients and 14 control subjects) who were included in the behavioural and fMRI analyses.

n-letter back

A four-step parametric version of the verbal *n*-back task after a standard paradigm of Braver and colleagues (1997) was used in this study [see Fig. A1 (in online Appendix)]. Participants viewed single capital letters projected onto a screen with an interstimulus interval (ISI) of 2·92 s and were requested to press a (right hand) response key when (i) the letter 'x' appeared (baseline), (ii) the projected letter was the same as the last shown letter (1-back), (iii) the projected letter was the same as the letter preceding the last shown letter (2-back), (iv) the projected letter was the same as the letter preceding the last two shown letters (3-back). Each time a new condition started a condition-specific instruction was shown for 6 s [e.g. condition 1-back: 'Press button when letter is equal to preceding letter (e.g. AA)']. Each condition consisted of 20 stimuli, with six targets. Each condition was presented three times, in a pseudo-randomized order, resulting in a total of 12 blocks of each 20 stimuli. There were four different versions of the task, which were randomly distributed among participants. The total duration of the task was 10 min. Prior to scanning, all participants practised the task outside the scanner on a personal computer.

Scanning details

Functional MRI was performed at the Department of Radiology of the out-patient clinic of the VU University Medical Centre, using a 1.5 T Sonata whole-body system (Siemens AG, Erlangen, Germany) equipped with a head volume coil. Axial multislice T_2*-weighted images were obtained with a gradient-echo planar sequence (TE = 45 ms, TR = 2·92 s, 64 × 64 matrix, 32 slices, 3×3 mm in-plane resolution, slice thickness 2·5 mm with a 0·5 mm interslice gap), covering the entire brain. For each subject, 207 EPI volumes were acquired. In addition, a T_1-weighted structural 3D gradient-echo MR scan (1×1×1·5 mm voxel size) was performed for anatomical overlays of the functional data.

Emotional state

Current dissociative state was assessed by a trained psychologist (B.M.E.) with (a Dutch version of) the Clinician-Administered Dissociative State Scale (CADSS), a reliable and valid measure of the severity of dissociative states (Bremner *et al.* 1998). The CADSS was administered twice, once before the scanning procedure (baseline), and once (in an adapted version) immediately after the scanning procedure, to measure the dissociative symptom level while in the scanner. Subjects were also asked to rate their subjective anxiety, concentration and dissociation level on a 100-point scale (e.g. 0 = not at all anxious, 100 = extremely anxious) once outside the scanner (pre-baseline), once after entering the scanner (baseline), and immediately before the working-memory task (working memory).

Statistical analysis

Overall performance [percentage correct, i.e. the ratio (no. correct responses/total no. of presentations × 100 %), and reaction times for conditions × 1-, 2- and 3-back, and subjective scores of anxiety, dissociation and concentration] was assessed with repeated-measure ANOVAs with a mixed factorial design. Comparisons of the two groups on diagnostic variables were computed with *t* tests for independent groups. Imaging data were analysed with SPM2 [Wellcome Department of Cognitive Neurology (http://www.fil.ion.ucl.ac.uk)]. After discarding the first two scans of each time series to allow for a steady state to be induced, images were realigned, and spatially normalized into MNI space using each subject's co-registered structural T_1 scan. The data were smoothed spatially with an 8-mm isotropic Gaussian kernel. Subsequently, data were bandpass-filtered, and analysed in the context of the General Linear Model, using boxcar regressors convolved with the canonical haemodynamic response to model responses during each condition. For each task, linear contrasts were computed for main effects of task (baseline *versus* 1-, 2-, and 3-back together) and main effects of task load for each subject. The resulting contrast images were then fed into a second level (random effects) analysis and main effects for task and task load were assessed for each group, as well as group interactions. Main effects for each group are reported at $p < 0{\cdot}001$ corrected for multiple comparisons using the False Discovery Rate method (Genovese *et al.* 2002), with a cluster size restriction of 10 voxels. Interaction effects are reported at $p < 0{\cdot}001$

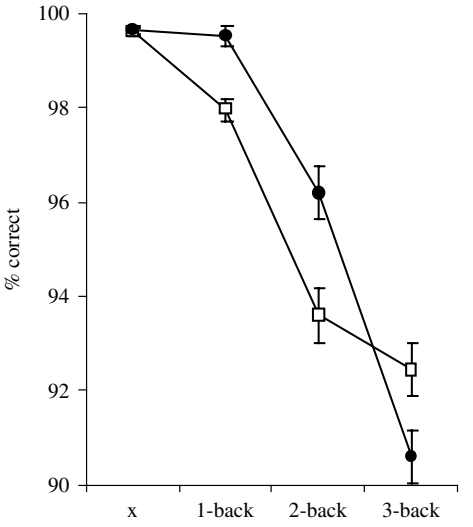

FIG. 1. Performance scores (% correct) (mean + S.E.M.) in dissociative patients (–□–; $n = 13$) and control subjects (–●–; $n = 14$) during performance of the *n*-back working-memory task.

uncorrected, masked with the appropriate main effect at $p < 0{\cdot}05$.

RESULTS

Working-memory performance

Three patients (out of the 16) were excluded from analysis (one scanning session was aborted due to intervening panic, one patient had not responded during the first half of the task due to dissociative symptoms, and one had to stop because of time constraints), as well as two control subjects (one due to technical problems of the scanner and one due to technical problems of the response box). Analysis of behavioural data (ANOVA) of the remaining 27 participants (13 patients and 14 control subjects) showed an overall decrease in performance with increasing working-memory load [main effect of task load: $F(3, 75) = 52{\cdot}47$, $p < 0{\cdot}0001$; see Fig. 1]. Patients did not differ from controls in their overall performance [no main effect of group: $F(1, 25) = 0{\cdot}56$, $p = 0{\cdot}46$]. In contrast, a quadratic within-subjects interaction effect was found for task load and group [$F(1, 25) = 16{\cdot}04$, $p < 0{\cdot}0001$]. *Post-hoc* analyses using Bonferroni correction for multiple comparisons indicated that this was due to the fact that patients showed a significantly smaller decline in performance from 2-back to 3-back (mean decrease $= 1{\cdot}2 \pm 2{\cdot}8\%$) compared to controls [mean decrease $= 5{\cdot}6 \pm 4{\cdot}4\%$, $t_{3\text{-}2\text{-back}}(25) = 3{\cdot}12$, $p < 0{\cdot}05$], and to a smaller extend from 1-back to 3-back [mean decrease patients $5{\cdot}5 \pm 3{\cdot}5\%$ *versus* controls $8{\cdot}9 \pm 4{\cdot}0\%$, $t_{3\text{-}1\text{-back}}(25) = 2{\cdot}35$, N.S.], but with correction this difference was not significant. Moreover, although the mean performance scores suggest that patients are better for the greatest load and worse for intermediate loads compared to controls, *post-hoc* independent *t* tests corrected for multiple comparisons showed that these group differences were not significant, either at baseline [$t(25) = 0{\cdot}1$, N.S.], 1-back [$t(25) = 2{\cdot}3$, N.S.], 2-back [$t(25) = 1{\cdot}6$, N.S.], or 3-back [$t(25) = 1{\cdot}2$, N.S.].

Results on reaction times showed a significant increase of reaction times as the task load increased [baseline: $484{\cdot}5 \pm 11{\cdot}6$ ms, 1-back: $545{\cdot}5 \pm 14{\cdot}8$ ms, 2-back: $594{\cdot}4 \pm 15{\cdot}7$ ms, 3-back: $629{\cdot}5 \pm 16{\cdot}2$ ms; main effect of task load: $F(3, 75) = 40{\cdot}23$, $p < 0{\cdot}0001$]; see Fig. A2 (Appendix). Independent of the task-load level, patients did not differ in their reaction times from control subjects [no main effect of group: $F(1, 25) = 0{\cdot}07$, $p = 0{\cdot}40$]. Although mean reaction times showed greater delays with increasing task load for controls than for patients [controls (baseline: $483{\cdot}4 \pm 16{\cdot}1$ ms, 1-back: $541{\cdot}9 \pm 20{\cdot}5$ ms, 2-back: $615{\cdot}8 \pm 21{\cdot}8$ ms, 3-back: $653{\cdot}4 \pm 22{\cdot}4$ ms) *versus* patients (baseline: $485{\cdot}6 \pm 16{\cdot}7$ ms, 1-back: $549{\cdot}1 \pm 21{\cdot}3$ ms, 2-back: $572{\cdot}9 \pm 22{\cdot}6$ ms, 3-back: $605{\cdot}6 \pm 23{\cdot}3$ ms)], this load × group interaction was not significant [$F(3, 75) = 2{\cdot}14$, $p = 0{\cdot}10$].

Emotional state

Dissociative symptom levels as assessed with the CADSS were significantly higher in the dissociative patients at baseline (mean ± S.D. = $21{\cdot}3 \pm 10{\cdot}3$) compared to controls [$0{\cdot}2 \pm 0{\cdot}4$; $t(25) = 7{\cdot}65$, $p < 0{\cdot}0001$], and during the scanning session ($34{\cdot}2 \pm 19{\cdot}65$) compared to controls [$0{\cdot}4 \pm 0{\cdot}8$; $t(25) = 6{\cdot}43$, $p < 0{\cdot}0001$]. Table 2 shows the mean ratings of anxiety, concentration and dissociation at pre-baseline (outside the scanner), baseline (inside the scanner), and immediately before the working-memory task. Patients were more anxious, more dissociated, and less concentrated at all three time-points than control subjects. Regardless of group, all

Table 2. *Ratings of anxiety, concentration and dissociation at pre-baseline (outside the scanner), baseline (after entering the scanner), and immediately before the n-back working-memory task in dissociative patients (n = 13) and control subjects (n = 14)*

	Pre-baseline				Baseline				Working-memory task				Main effect group	
	Patients		Controls		Patients		Controls		Patients		Controls			
Variable[a]	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	F (df = 1, 25)	p
Anxiety	46·2	23·6	27·1	22·3	64·6	28·5	32·9	22·7	43·5	28·4	21·4	18·0	9·62	0·005
Dissociation[b]	39·2	28·6	11·4	20·4	31·9	28·4	16·1	26·2	44·6	29·9	8·9	17·5	9·98	0·005
Concentration	51·5	24·7	68·2	13·8	61·9	25·0	78·1	18·1	64·2	25·5	79·3	13·7	7·67	0·01

[a] The rating scale was 0–100.
[b] Significant interaction between time × group [$F(1, 25) = 6{\cdot}63$, $p < 0{\cdot}05$].

subjects reported more anxiety after entering the scanner compared to pre-baseline, which had decreased when performing the working-memory task [$F(2, 50) = 7{\cdot}69$, $p < 0{\cdot}001$]. For all subjects, concentration was increased during the working-memory task compared to baseline [$F(2, 50) = 5{\cdot}56$, $p < 0{\cdot}005$]. For dissociation, a group × time interaction [$F(1, 25) = 6{\cdot}63$, $p < 0{\cdot}05$] was found: compared to baseline, dissociative patients reported more dissociative symptoms in the scanner, both at baseline and before working-memory performance, whereas control subjects only showed a slight elevation when entering the scanner. No interaction between time and group was found for anxiety and concentration scores.

Imaging data

Task effects

For each group, working-memory performance was associated with activity in bilateral ventrolateral and dorsolateral prefrontal, parietal, R anterior prefrontal, and L premotor areas, as well as in dorsal ACC and right posterior temporal cortex (results are summarized in Table 3, see also Fig. 2). In addition, we found L anterior PFC, ACC, and R inferior temporal cortex in patients. Group × working-memory performance interaction effects were found in favour of the dissociative patients in left anterior PFC (x = −26, y = 54, z = 21; Z score 4·76, BA 10), DLPFC (x = −45, y = 42, z = 27; Z score 3·34, BA 46) and parietal lobe (x = −54, y = −48, z = 42; Z score 4·48, BA 40; and x = −51, y = −48, z = 51; Z score 3·19, BA 40) [see Fig. A3 (Appendix)]. In contrast, no group × task interaction effects were found in favour of the control group.

Task load

For both groups, the task-load contrasts showed main effects in similar areas as the main task effects: bilateral parietal lobe, VLPFC and DLPFC, anterior PFC, premotor, precuneus, and posterior temporal cortex [see Table A1 (Appendix)]. In addition, we found bilateral striatal activity in the control group. In this comparison, group × task-load interaction effects were found in favour of the dissociative patients in the left parietal lobe (x = −57, y = −36, z = 51; Z score 3·11, BA 40). Again, no group × task-load interaction was found in favour of the control group.

DISCUSSION

In the present study, fMRI was used to investigate neural correlates of verbal working memory in dissociative patients. To this end, participants performed a parametric *n*-letter back task while being scanned. Dissociative patients showed more activation in the left anterior PFC, left DLPFC and left parietal lobe, brain areas that are normally activated in working-memory paradigms, whereas no additional activity was found for the control group. Consistent with the imaging data, behavioural data demonstrated that the decline in performance associated with increasing task load was smaller in dissociative patients compared to the healthy control group. Mean reaction times mirrored this pattern of results, with

Table 3. *Areas showing significant ($p<0{\cdot}001$ corrected extent threshold >10 voxels) increase in activity during performance of the n-back working-memory task in dissociative patients and control subjects (all conditions versus baseline)*

	Dissociative patients ($n=13$)					Control subjects ($n=14$)				
	Talairach coordinates					Talairach coordinates				
Region	x	y	z	*Z* score	BA	x	y	z	*Z* score	BA
L prefrontal										
Anterior	−36	54	21	5·90	10					
Dorsolateral	−45	33	33	5·18	9	−39	33	36	3·89	9
	−45	42	27	4·91	46					
Ventrolateral	−33	21	−6	4·87	47	−30	24	−3	3·36	47
						−45	27	0	3·20	47
						−51	6	15	3·85	44
						−24	9	24	3·56	44
R prefrontal										
Anterior	42	54	12	4·73	10	36	57	0	4·35	10
Dorsolateral	48	42	24	4·58	46					
	51	15	33	4·36	9					
	60	0	42	3·54	9	51	27	33	4·05	9
	27	6	51	4·12	6	51	9	45	3·85	6
Ventrolateral	30	27	−3	4·65	47	30	24	−3	4·63	47
	33	21	3	4·25	45	42	27	−3	3·38	47
						48	12	24	4·16	44
Dorsomedial	9	21	48	3·61	6	6	24	45	4·41	6
L parietal	−36	−51	42	4·98	40					
	−51	−48	42	5·71	40					
	−51	−48	51	5·48	40i	−39	−42	48	4·57	40i
R parietal	57	−42	51	3·95	40	42	−48	54	4·50	40
	33	−45	36	5·29	40i					
	45	−48	48	5·28	40i					
L premotor	−36	15	54	4·30	6	−33	9	39	3·78	6
	−21	3	54	4·54	6	−30	6	51	3·63	6
L precuneus	−12	−66	63	3·87	7					
	−6	−63	54	3·47	7					
	−9	−69	48	3·46	7					
R precuneus	18	−69	57	3·79	7					
	27	−69	54	3·33	7					
L ACC	−6	27	39	3·87	32					
R ACC	0	36	39	3·41	32					
L lateral temporal						−36	−54	5	3·97	37
						−45	−36	5	4·73	21
R lateral temporal	51	−57	−12	3·29	37	48	−63	−12	3·72	37
	45	−51	6	3·66	37	33	−60	5	4·07	37
						42	−45	5	4·99	21

ACC, Anterior cingulate cortex; i, inferior.

greater response delays with increasing task load in controls than in patients, although these differences were not statistically significant. These findings of enhanced working-memory performance in dissociative patients are remarkably consistent with two previous studies in non-clinical samples showing enhanced working-memory capacities in participants with dissociation scores approaching pathological ranges (Veltman *et al*. 2004; De Ruiter *et al*. 2004) and increased activity in the left DLPFC and left parietal cortex while performing the *n*-back task and the Sternberg working-memory task (Veltman *et al*. 2004). Taken together, these results are compatible with the conceptualization that dissociation as a trait reflects a constitutionally determined cognitive style, associated with enhanced attentional and memory capacities, especially when the task is sufficiently demanding (see Phaf & Wolters, 1997; Elzinga *et al*. 2000).

Patients recruited similar brain areas as the control group, consistent with brain areas that have been found in previous verbal

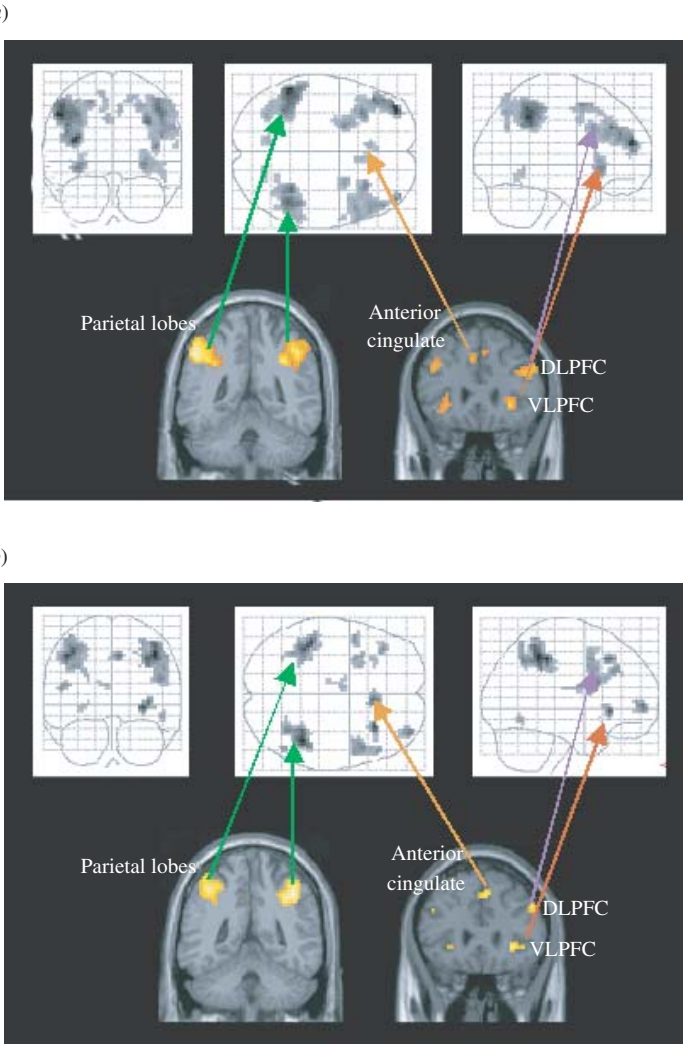

FIG. 2. Task-related activity during performance of the *n*-back working-memory task in (*a*) dissociative patients ($n=13$), and (*b*) control subjects ($n=14$).

working-memory studies using fMRI, including bilateral anterior PFC, DLPFC and VLPFC, parietal cortex, and the dorsal ACC and pre-motor areas. Dissociative patients recruited the left anterior PFC, left DLPFC, and left parietal cortex more than controls when comparing all active working-memory conditions (1-, 2-, and 3-back) with the baseline condition. In the task-load comparison more activation in favour of the dissociative patients was found in the left parietal cortex only. Thus, in dissociative patients PFC regions were more activated independent of task difficulty, while in the parietal cortex stronger activation was found with increasing task load. DLPFC activity during performance of the *n*-back task has been primarily associated with executive demands, such as manipulating working-memory contents (i.e. updating; Veltman *et al.* 2003). In addition, anterior PFC activity has been found at increasing task load, presumably reflecting higher-order cognitive control processes (Van den Heuvel *et al.* 2003). Left parietal cortex has previously been implicated in phonological storage (Paulesu *et al.* 1993), but has also been found in manipulation of working-memory

tasks, which has been interpreted as participation in executive functioning (Cohen *et al.* 1997; Collette *et al.* 1999), or due to increased attentional demands at higher task loads (Honey *et al.* 2000).

Regarding the interpretation of these group differences in brain activation, we suggest that these greater areas of activation in patients reflect the neural correlates of relatively enhanced memory performance with increasing load in dissociative patients. This is consistent with several studies showing linear relations between increase in performance and increase in activation (Braver *et al.* 1997; Rypma *et al.* 1999; Jansma *et al.* 2000; Veltman *et al.* 2003). Moreover, similar results were found by Veltman *et al.* (2004) showing enhanced activation together with increased performance in high compared to low non-clinical dissociative participants. This pattern in dissociative patients is thus radically different from findings in, e.g. schizophrenia in which breakdown of DLPFC function at higher task loads has been observed coupled with increasingly poor performance (Jansma *et al.* 2004). It also differs, however, from observations in healthy elderly, in which increased activity in older *versus* younger subjects has been found together with similar performance (error rates), whereas reaction times were slower in the elderly group (Mattay *et al.* 2006). These authors explained their findings as the result of compensatory effort in elderly subjects to maintain adequate performance. In the present study, however, patients were found to *outperform* healthy controls with increasing task loads, whereas in the Mattay *et al.* study, performance deteriorated at higher task loads. Moreover, reaction times were similar between groups in our study, and reaction times were even faster for patients at the two highest loads. The hypothesis of greater effort in dissociative patients is also difficult to reconcile with the higher concentration scores in controls. However, another explanation may be that the enhanced activation in dissociative patients is not related to working-memory performance, but is rather an index of dissociative symptomatology. Although patients were indeed more dissociated than controls during task performance, it is not very likely that this increased with increasing task load, but rather this was a constant state during the entire working-memory task. Moreover, enhanced activation was solely found in brain regions typically associated with working-memory performance, contrary to what would have been expected if activation reflected dissociative symptoms.

Taken together, these findings of enhanced working-memory capacity may have important theoretical implications. Dissociative patients appear to be characterized by a different cognitive processing style than patients with PTSD as primary diagnosis, despite the fact that the dissociative patients in this study reported severe trauma histories and almost all fulfilled criteria for the diagnosis PTSD. Whereas PTSD is assumed to involve a breakdown in a number of executive functions, including working memory, probably due to insufficient inhibition of trauma-related thoughts and feelings (Bremner *et al.* 1993; McFarlane *et al.* 1993; Uddo *et al.* 1993; Semple *et al.* 1996; Galletly *et al.* 2001; Clark *et al.* 2003), dissociative patients may be characterized by strong executive control capacities, thereby inhibiting the processing of trauma-related memories. In dissociative patients, this may take place at the expense of other functions that require attention, however, such as a sense of personal identity and reality, inducing feelings of depersonalization and derealization, as is suggested by the enhanced state dissociation scores and the clinical observations of the dissociative patients when leaving the scanner [some patients, for example, were not able to recognize the experimenter, or assumed (incorrectly) that they had not been performing the task]. These findings are in line with those of Lanius and colleagues, who found that a subgroup of PTSD patients that reported dissociative symptoms while recalling a traumatic memory in the fMRI scanner had clearly distinct neuronal activation patterns compared to PTSD patients without dissociative symptoms (Lanius *et al.* 2002, 2005). These studies add to the emerging evidence of fundamental neurobiological differences in two subtypes of trauma responses, one primarily dissociative in nature and the other predominantly intrusive, that represent unique pathways to chronic stress-related psychopathology (Bremner, 1999).

This study has a number of strengths, including the relatively large sample of unmedicated dissociative patients, and the clear and consistent

pattern of results. Several aspects of the study deserve comment. First, the women with dissociative disorders in the current study present the typical dilemma of multiple co-morbidities, including PTSD, and to a lesser extent depression and a history of alcohol or substance abuse. Almost by nature of the disorder all patients met criteria for co-morbid PTSD, although in all cases the dissociative disorder was the primary diagnosis. We did not exclude women without PTSD as we felt that this selection of subjects (if possible) would not be representative of patients with dissociative disorders. We did exclude women with schizophrenia, psychotic symptoms, and bipolar disorders, however, and had extensive diagnostic assessment by a skilled interviewer. Second, we did not assess general intelligence. As a result, we do not know whether and how the enhanced working-memory capacities may relate to intelligence. We did match our groups on level of education, however, and a previous study in dissociative patients did not find any differences between dissociative patients and matched control subjects on a standard intelligence test (Rossini *et al.* 1996). Finally, the enhanced capacity of working memory involves only neutral material. An interesting question is what happens with working-memory capacity when emotional or trauma-related stimuli are involved, given the psychogenic amnesia for traumatic life events that dissociative patients may report. This is currently under study by our group.

In sum, to our knowledge this is the first study investigating neural correlates of working memory using fMRI in a sample of dissociative patients. Results show a clear picture of relative enhanced performance with increasing memory load and increased activation of left anterior PFC, DLPFC, and parietal cortex in dissociative patients, consistent with earlier findings in non-clinical high-dissociative subjects. These findings are highly relevant for our understanding of dissociative phenomenology and symptomatology.

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DECLARATION OF INTEREST

None.

NOTE

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