

# Suppression of false recognition in Alzheimer's disease and in patients with frontal lobe lesions

A. E. Budson,<sup>1,3</sup> A. L. Sullivan,<sup>1</sup> E. Mayer,<sup>4</sup> K. R. Daffner,<sup>1,3</sup> P. M. Black<sup>2,3</sup> and D. L. Schacter<sup>5</sup>

<sup>1</sup>Division of Cognitive and Behavioral Neurology, Department of Neurology and <sup>2</sup>Department of Neurosurgery, Brigham and Women's Hospital, <sup>3</sup>Harvard Medical School, Boston, <sup>4</sup>Smith College, Northampton and <sup>5</sup>Department of Psychology, Harvard University, Cambridge, MA, USA

Correspondence to: Andrew E. Budson, MD, Division of Cognitive and Behavioral Neurology, Department of Neurology, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, USA  
E-mail: abudson@partners.org

## Summary

Previous research has shown that patients with Alzheimer's disease show increasing levels of false recognition across five repeated study–test trials of semantic associates. The present study tested the hypotheses that (i) the increasing false recognition was partly due to the frontal lobe dysfunction of patients with Alzheimer's disease, and (ii) a failure of source monitoring was the central mechanism by which frontal lobe dysfunction led to increasing false recognition across trials. In Experiment 1, patients with frontal lobe lesions and controls were examined in the same repeated trials paradigm as that used previously in patients with Alzheimer's disease. Although controls were able to reduce their false recognition across trials, the patients with frontal lobe lesions were not, and instead showed a constant level of elevated false recognition across the study–test trials. In Experiment 2, two groups of patients with Alzheimer's disease and healthy

older adult controls were studied: the first group was given a single study session followed by a recognition test, the second group was given five study sessions followed by a single recognition test. Older adults who were exposed to five study lists demonstrated lower levels of false relative to true recognition, whereas patients with Alzheimer's disease in this condition exhibited levels of false recognition elevated to that of their true recognition, even with the source memory confusion of intervening tests eliminated. The authors suggest that impairment in aspects of frontal lobe function, such as verification–inhibition mechanisms, probably contributes to the inability of patients with Alzheimer's disease to suppress their false recognition across repeated trials. Lastly, it is speculated that one way in which the frontal lobes enable normal episodic memory function is by facilitating the suppression of false recognition and other distortions of memory.

**Keywords:** Alzheimer's disease; frontal lobes; source monitoring; false recognition; memory

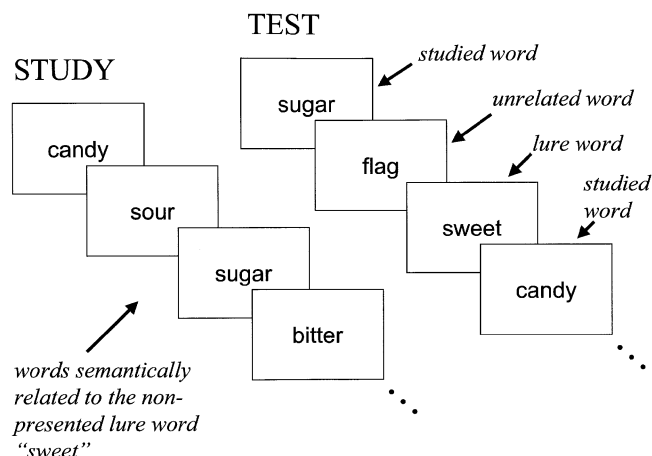
**Abbreviations:** CERAD = Consortium to Establish a Registry for Alzheimer's Disease; DRM = Deese/Roediger–McDermott; MMSE = Mini-mental Status Examination

## Introduction

Increasing attention has been focused on memory distortions in patients with various kinds of brain damage. Research in this area has contributed to our understanding of normal memory function (e.g. Schacter *et al.*, 1998a), memory failure in specific brain diseases (e.g. Balota *et al.*, 1999) and the occurrence of clinically relevant memory distortions in certain patient populations (e.g. Budson *et al.*, 2000). Memory distortions in patients with amnesia and those with probable Alzheimer's disease have recently been explored using experimental false recall and recognition paradigms. False recognition occurs when people incorrectly claim to have previously encountered a novel item that is in some way

related to a previously studied item. Roediger and McDermott (1995), modifying a paradigm initially developed by Deese (1959), have demonstrated robust levels of false recognition in healthy adults. After studying lists of semantic associates (e.g. candy, sour, sugar, bitter, good, taste, and so forth) that all converge on a non-presented theme word or related lure (e.g. sweet), participants frequently intruded the related lure on free recall tests (Deese, 1959) and made very high levels of false alarms to these words on recognition tests (Roediger and McDermott, 1995) (Fig. 1).

Schacter and colleagues studied patients with amnesia using a modified version of the Deese/Roediger–McDermott



**Fig. 1** Schematic representation of the Deese/Roediger-McDermott (DRM) paradigm.

(DRM) paradigm in which there were five study–test trials (Schacter *et al.*, 1998b). They found that, on the first trial, patients with amnesia made fewer false alarms to related lures than did control participants, consistent with other studies (Schacter *et al.*, 1996a, 1997a; Koutstaal *et al.*, 1999, 2001; Melo *et al.*, 1999). With repeated study–test trials, control participants exhibited increasing levels of true recognition together with decreasing levels of false recognition. Patients with amnesia also demonstrated increased true recognition but, in contrast to controls, showed no evidence of decreasing false recognition across trials. Interestingly, patients with Korsakoff amnesia exhibited increased false recognition across trials, whereas patients with non-Korsakoff amnesia (e.g. those who suffered anoxia, encephalitis or other types of damage to their medial temporal structures) showed fluctuating levels of false recognition across trials.

Schacter and colleagues interpreted their results on the basis of the idea that true and false recognition depend on memory for two different kinds of information: specific details of a prior encounter with a particular item (item-specific recollection), and the general meaning, idea or gist conveyed by a collection of items (Schacter *et al.*, 1998b) (gist information) (Reyna and Brainerd, 1995; Schacter *et al.*, 1998a). As the items are presented in the DRM paradigm, a gist representation is developed, which may result in an experience of recollection or familiarity when either a studied item or a related lure is presented on a later recognition test. Thus, in the DRM paradigm, accurate recognition of previously studied items probably depends on both item-specific and gist information, whereas false recognition of related lure words depends on remembering gist but not item-specific information (cf. Payne *et al.*, 1996; Schacter *et al.*, 1996a; Brainerd and Reyna, 1998).

Budson and colleagues studied false recognition in patients with Alzheimer's disease, older adults, and younger adults using a paradigm similar to that used previously by Schacter and colleagues (Budson *et al.*, 2000; Schacter *et al.*, 1998b).

Budson and colleagues found that patients with Alzheimer's disease, compared with older adults, showed lower levels of false recognition after a single exposure to a list of semantic associates (consistent with Balota *et al.*, 1999) but higher levels of false recognition after five study–test trials. In older adults, false recognition showed a fluctuating pattern, ultimately yielding a lower level of false recognition on the fifth trial compared with that of the first trial. Thus, false recognition increased in patients with Alzheimer's disease over the five trials, as it did also in patients with Korsakoff amnesia.

Budson and colleagues argued that for patients with Alzheimer's disease, as for patients with Korsakoff amnesia, the repeated study and testing of the semantic associates created an increasingly robust representation of semantic gist that, when unchecked by item-specific recollection, produced increasingly elevated levels of false recognition (Budson *et al.*, 2000). Healthy older adults, like the controls in the study of Schacter and colleagues, made use of explicit recollection which allowed them to use increasingly conservative response criteria and greater sensitivity to item-specific recollection that served to counteract or suppress the strengthening gist representation (Schacter *et al.*, 1998b; but see also Kensinger and Schacter, 1999, who found that healthy older adults were less able than younger adults to suppress false recognition across trials).

That patients with Alzheimer's disease showed a pattern of false recognition similar to that seen in patients with Korsakoff amnesia and different from that seen in patients with non-Korsakoff amnesia may be attributable to the fact that patients with mild to moderate Alzheimer's disease show dysfunction of frontal networks, as do also patients with Korsakoff amnesia (Moscovitch, 1982; Squire, 1982; Schacter, 1987; Shimamura, 1995). Patients with Alzheimer's disease demonstrate pathological changes in the frontal lobes at autopsy (Lidstrom *et al.*, 1998) and neuropsychological and neuroimaging studies of patients with Alzheimer's disease have demonstrated frontal lobe dysfunction (Mountjoy *et al.*, 1983; Haxby *et al.*, 1988; Baddeley *et al.*, 1991; Dalla Barba *et al.*, 1999). Damage to the frontal lobes has been associated with high levels of false recognition (Parkin *et al.*, 1996; Schacter *et al.*, 1996c). Additionally, a number of neuroimaging studies have strongly implicated various regions within the frontal lobes in episodic memory (Shallice *et al.*, 1994; Tulving *et al.*, 1994; Buckner *et al.*, 1995; Nyberg *et al.*, 1995; Schacter *et al.*, 1996b). Moreover, anterior prefrontal regions may be specifically related to post-retrieval monitoring and verification processes (Rugg *et al.*, 1996; Schacter *et al.*, 1996d, 1997b; Wilding and Rugg, 1996). Such processes, which may be related to the inhibitory functions of the frontal lobes (Shimamura, 1995), would presumably be required in order to use item-specific information to suppress false recognition and may be impaired in patients with Alzheimer's disease compared with older adults.

Another possible explanation for the results of the patients with Korsakoff amnesia in studies by Schacter and colleagues and the results of the patients with Alzheimer's disease in studies by Budson and colleagues is that deficits in frontal lobe function linked to source memory confusion could be implicated in these patients' inability to suppress false recognition (Schacter *et al.*, 1998b; Budson *et al.*, 2000). Source memory confusion is frequently reported in individuals with frontal lobe dysfunction (Schacter *et al.*, 1984; Janowsky *et al.*, 1989). Patients with Alzheimer's disease are known to show deficits in source memory (Dalla Barba *et al.*, 1999). Because the paradigm used consists of repeated presentations and tests across trials, the ability to discriminate studied items from related lures necessitates identification of their source. Both studied items and related lures would have been encountered on previous trials; related lures would only have been present on earlier test lists, whereas studied items would have been present on both study and test lists. Patients with Alzheimer's disease and those with Korsakoff amnesia may have had particular difficulty in remembering whether an item had been presented on a study or test list.

In brief, we hypothesize that frontal lobe deficits in both patients with Alzheimer's disease and those with Korsakoff amnesia are responsible for their increasing level of false recognition across repeated study–test trials. Furthermore, source memory confusion between study and test items may be one important means by which frontal lobe dysfunction increases the level of false recognition in these patient groups. In the present paper, we attempt to shed light on both of these hypotheses.

## Investigations of false recognition in frontal lobe lesion patients (Experiment 1)

### *Background to Experiment 1*

A number of studies have demonstrated elevated false recognition in patients with lesions of the frontal cortex (Delbecq-Derouesné *et al.*, 1990; Parkin *et al.*, 1996, 1999; Schacter *et al.*, 1996c; Rapsak *et al.*, 1999, 2001; Ward *et al.*, 1999). Here we present data from 13 patients with anatomical lesions in the frontal cortex who underwent repeated trials using the DRM paradigm. The study closest to our experiment is that of Melo and colleagues, who studied false recognition in patients with frontal lobe lesions using the standard DRM paradigm (Melo *et al.*, 1999). These patients showed greater false alarms to related lure words than their controls. However, because these patients also showed greater false alarms to the unrelated distracter words, patients and controls did not differ significantly in their false recognition after correction for these unrelated words.

Given these previous studies, we predicted that our patients with frontal lesions, like those of Melo and colleagues (Melo *et al.*, 1999), would show an increase in their false alarms to related lure items on the initial study test trial compared with controls. Across all five study–test trials, we presumed that

controls would be able to reduce their false alarms to lure items and their corrected false recognition with increasing item-specific recollection, as in previous studies (Schacter *et al.*, 1998b; Budson *et al.*, 2000). Because patients with frontal lobe lesions show impaired item-specific recollection (Schacter *et al.*, 1996c; Melo *et al.*, 1999; Parkin *et al.*, 1999; Rapsak *et al.*, 1999, 2001), we suspected that our patients would be unable to reduce either their false alarms to lure items or their corrected false recognition over the five study–test trials.

## Investigation of false recognition in Alzheimer's disease patients (Experiment 2)

### *Background to Experiment 2*

Source memory has been examined previously in patients with Alzheimer's disease; most studies have found that source memory is impaired in this patient population (Schacter *et al.*, 1984; Mitchell *et al.*, 1986; Dick *et al.*, 1989; Bartlett *et al.*, 1995; Multhaup and Balota, 1997; Fleischman *et al.*, 1998; Dalla Barba *et al.*, 1999; Tendolkar *et al.*, 1999). (For an alternative view, see Goldman *et al.*, 1994.) Furthermore, the study of Budson and colleagues required differentiation of items from two different sources, both experienced in the laboratory (Budson *et al.*, 2000); all studies of this type have demonstrated impairments in patients with Alzheimer's disease (Mitchell *et al.*, 1986; Dick *et al.*, 1989; Multhaup and Balota, 1997; Dalla Barba *et al.*, 1999; Tendolkar *et al.*, 1999).

We therefore thought it likely that source memory errors between items encountered on study lists and lure items encountered on test lists contributed to the increasing levels of false recognition seen in patients with Alzheimer's disease in the studies by Budson and colleagues, in which there were five study–test trials (Budson *et al.*, 2000). Thus, we expected that in the present paradigm of five study sessions followed by a single test, false recognition in patients with Alzheimer's disease would not increase up to the level of true recognition as it did in the study by Budson and colleagues (Budson *et al.*, 2000).

## Patients and methods

### *Frontal lobe lesion patients (Experiment 1)*

Thirteen right-handed patients with anatomical lesions in the frontal cortex participated in the experiment. Patients were recruited from the neurology and neurosurgery services at Brigham and Women's Hospital, Boston, Massachusetts, USA. The patients were specifically recruited for the study because they had lesions in the dorsolateral prefrontal cortex (primarily Brodmann areas 9 and 46; see Table 1 for specific lesion localizations). Nine patients had had brain tumours resected and the remaining four patients had had strokes. All participants had stable lesions for at least 1 year prior to testing. Seventeen control participants were matched to the

patients on the basis of age (patient mean = 47.8 years, range = 25–81 years; control mean = 48.0 years, range = 19–83 years) and education (patient mean = 15.8 years, range = 12–23 years; control mean = 16.5 years, range = 12–21 years); gender was not significantly different between groups (eight male and five female patients; eight male and nine female controls). Control participants were recruited from spouses and friends of the patients by the use of flyers and posters placed in and around Boston, and by word of mouth. Written informed consent was obtained from all participants. The study was approved by the Human Subjects Committee of Brigham and Women's Hospital. Participants received US\$10/h for their participation. Participants were excluded if they were characterized by clinically significant depression, alcohol or drug use, or if English was not their primary language. Controls were also excluded if they had suffered brain damage (such as that due to stroke, tumour or traumatic brain injury). To obtain measures of the characteristics of participants, standard neuropsychological tests were performed (Table 2). One control participant who performed more than 3 SD below the mean of the other 16 controls was excluded as an outlier.

Materials, design and procedure have been described elsewhere (Budson *et al.*, 2000). See Figure 1 for an illustration of the basic DRM paradigm.

### ***Alzheimer's disease patients (Experiment 2)***

Twenty-three patients with a clinical diagnosis of probable Alzheimer's disease (National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer's Disease and Related Disorders Association criteria; McKhann *et al.*, 1984) and 20 healthy older adults were recruited for the experiment. Patients with Alzheimer's disease were recruited from the clinical population at the Memory Disorders Unit, Brigham and Women's Hospital, Boston, Massachusetts, USA. Older adults were recruited from participants in a longitudinal study of normal ageing at Brigham and Women's Hospital, from spouses and friends of the patients, and by the use of flyers and posters placed in senior centres in and around Boston. Written informed consent was obtained from all participants and their care-givers (where appropriate). The study was approved by the Human Subjects Committee of Brigham and Women's Hospital. Participants were paid US\$10/h for their participation. Older adults were all community-dwelling and were excluded if they scored below 27 on the Mini-mental Status Examination (MMSE; Folstein *et al.*, 1975). Most patients with Alzheimer's disease showed mild to moderate impairment on the MMSE, though one scored in the normal range (mean = 22.7, range 17–30). Seventeen of the patients with Alzheimer's disease performed in the impaired range on measures of frontal lobe function as part of their clinical evaluation; two patients performed normally on these measures and the results were not available for four patients. [These measures of frontal lobe function included Graphic Pattern Generation (Glosser and Goodglass,

1990), a motor go/no-go task (Weintraub and Mesulam, 1985), Luria's hand motor sequences (Christensen, 1979), The Trailmaking Test Part B (Adjutant General's Office, 1944), digit span backwards (Wechsler, 1981), the short category test (Wetzel and Boll, 1987), letter word fluency (Monsch *et al.*, 1992), serial subtraction (Folstein *et al.*, 1975), backwards spelling (Folstein *et al.*, 1975), the conceptualization subtest of the Dementia Rating Scale (Mattis, 1988), months of the year backwards (Blessed *et al.*, 1968), the Wisconsin Card Sorting Test (Berg, 1948) and the Stroop Interference Test (Trenerry, 1989).] Participants were excluded if they were characterized by clinically significant depression, alcohol or drug use, cerebrovascular disease or traumatic brain damage, or if English was not their primary language. All participants had normal or corrected to normal vision and hearing. The patients were matched to the older adults on the basis of gender (six male and 17 female patients, six male and 14 female older adults), age (patient mean = 75.5 years, range = 55–89 years; older adult mean 71.8 years, range 53–83 years) and education (patient mean = 15.6 years, range = 9–20 years; older adult mean = 16.2 years, range = 12–20 years).

### ***Study design***

The paradigm used in this experiment was similar to that used in the frontal lobe lesion experiment (Experiment 1). The differences between the paradigms are described here.

In order to be able to compare false recognition after one study session with false recognition after five study sessions, patients with Alzheimer's disease and controls were assigned to either the one study session condition (12 patients, 10 controls) or the five study sessions condition (11 patients, 10 controls). Participants in the two types of session condition were matched with respect to gender, age, education and, for the patients, MMSE score.

Analyses of false alarm rates to unrelated lures and unrelated targets indicated no significant differences between them [ $t(42) = 0.43$ ,  $P = 0.665$ ], so the two types of unrelated items were treated as a single category in all experimental analyses.

In the one-study session condition, participants were told that there would be a single study list followed immediately by a recognition test. In the five study sessions condition, participants were told that there would be five study sessions with the same materials, followed by a single recognition test. Pilot studies showed that, for older adults in particular, simply reading the same 90 words five times was tedious. Thus, to facilitate engagement with the materials, a slightly different task was given to the participants for each study session. For session 1, participants were instructed to 'read the words out loud and try to remember them'. For the next four sessions, these initial instructions were given, followed by an additional instruction. In session 2, this was 'pay attention to the way the words sound when you say them out loud'; in session 3 it was 'this time think about whether you like or dislike each

**Table 1** Patients with frontal lobe lesions

Patient	Gender/Age	Lesion site	
CD1	F/34	L	
		4	
		6	
		8	
		9	
		10	
SM	M/35	L	
		6	
		8	
		9	
		10	
		24	
RH	M/45	L	
		9	
		24	
		32	
		45	
		46	
CD2	F/49	L	
		9	
		10	
		24	
		44	
		45	
JB	M/58	L	
		8	
		9	
		10	
		32	
		45	
ET	M/25	R	
		6	
		9	
		10	
		11	
		24	

word'; in session 4 it was 'this time try to pay attention to the way the words look on the computer screen'; and in session 5 it was 'this time try to visualize each word'. Debriefing indicated that these different instructions helped participants to remain engaged with the study lists.

## Results

### Frontal lobe lesion experiment (Experiment 1)

#### Neuropsychological measures





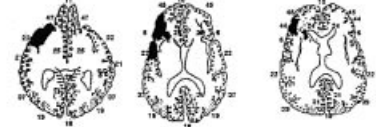


Although they did not perform in the impaired range according to published norms (Morris *et al.*, 1989; Monsch *et al.*, 1992; Lezak, 1995), the patients performed significantly worse than controls on word fluency to letters and categories as well as on all three parts of the CERAD (Consortium to Establish a Registry for Alzheimer's Disease) word list memory test. Results of the other neuropsychological tests did not differ between groups (Table 2).

#### Initial trial

*True and false recognition.* A 2 (Group: patients versus controls)  $\times$  2 (Item Type: true versus false recognition) analysis of variance (ANOVA) yielded a Group  $\times$  Item Type interaction [ $F(1,27) = 6.36, P = 0.018$ ] and no main effects [Group,  $F(1,27) = 2.70, P = 0.121$ ; Item Type,  $F(1,27) = 2.82, P = 0.104$ ] (Table 3). *Post hoc* tests explain that this interaction is present because while controls showed higher levels of true compared with false recognition [ $t(15) = 3.04, P = 0.008$ ], the patients showed no difference between these measures [ $t(12) = 0.59, P = 0.565$ ]. Furthermore, while these groups made nearly identical numbers of 'old' responses to studied items [true recognition:  $F(1,27) < 0.1$ ], the patients made more 'old' responses to related lure items than did controls [false recognition:  $F(1,27) = 5.13, P = 0.032$ ].

*Unrelated items.* Unrelated target and unrelated lure items provide an index of baseline false alarms for the studied and

Table 1 Continued

LB	F/28	R			
		6			
		9			
TG	M/40	R	45		
		4			
		6			
		8			
		9			
		44			
PM	F/45	R	46		
		9			
		10			
		11			
		24			
JM	M/48	R	45		
		6			
		8	46		
		9			
		10			
		44			
SS	M/73	R			
		6			
		22			
		44			
		45			
		47			
DC2	F/82	R			
		6			
		9			
		44			
		45			
		46			
DC1	M/67	R	L		
		6	6		
		45	46		
		46			

Schematic diagrams of lesion locations are drawn on standardized templates (Damasio and Damasio, 1989). Images follow radiological convention with the right hemisphere on the left side of the template. Black areas represent regions where brain tissue has been replaced by CSF. Grey areas represent regions where brain tissue has been severely damaged, as indicated by increased signal on T<sub>2</sub>-weighted MRI. Grey areas are outlined in black for clarity. Lesion site numbers correspond to Brodmann areas. The table is ordered first by lesion laterality (left, right, bilateral) and then by patient age.

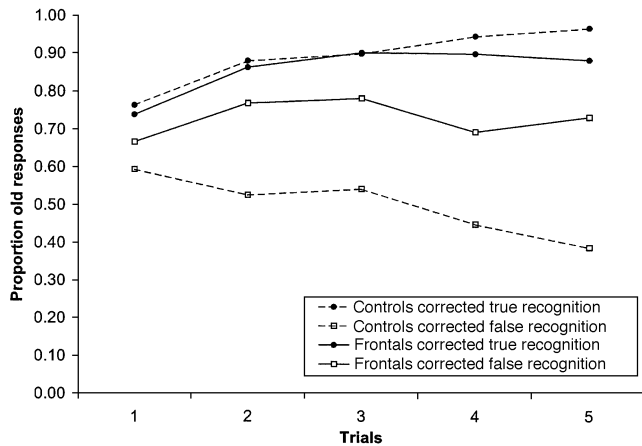
related lure items, respectively. Frontal patients showed a near-significant trend towards making more 'old' responses to non-studied, unrelated targets and unrelated lures compared with controls. A 2 (Group: patients versus controls)  $\times$  2 (Item Type: unrelated targets versus unrelated lures) ANOVA yielded the near-significant effect of Group [ $F(1,27) = 3.69, P = 0.066$ ], a trend towards an effect of Item Type [ $F(1,27) = 3.24, P = 0.083$ ] and no interaction [ $F(1,27) = 1.41, P = 0.245$ ]. The trend towards an effect of Item Type was present because frontal patients showed some tendency towards making more false alarms to unrelated lures than to unrelated targets.

*Corrected true and false recognition.* Corrected true recognition was obtained by subtracting the proportion of 'old' responses to unrelated targets from the proportion of 'old' responses to studied words; similarly, corrected false recognition was obtained by subtracting the proportion of 'old' responses to unrelated lures from the proportion of 'old' responses to related lures. An ANOVA on the corrected data yielded an effect of Item Type [ $F(1,27) = 5.99, P = 0.021$ ], no effect of Group and no interaction [ $F(1,27) < 1$ ]. The effect of Item Type was present because, overall, participants showed lower levels of corrected false recognition than corrected true recognition (Fig. 2).

**Table 2** Results of standard neuropsychological measures in patients with frontal lobe lesions and controls

Test	Patient													Patient mean (SD)	Control mean (SD)	df	F	FT2>P	
	CD1	SM	RH	CD2	JB	ET	LB	TG	PM	JM	SS	DC2	DC1						
Global cognitive score																			
MMSE (Folstein <i>et al.</i> , 1975)	29	26	29	30	29	27	30	28	30	30	29	29	29	28.85 (1.21)	29.56 (0.73)	(1,20)	2.44	ns	
Intelligence																			
ANART (Blair and Spreen, 1989)	115	108	108	124	114	118	109	103	111	120	116	125	127	115.23 (7.38)	119.44 (5.43)	(1,20)	2.12	ns	
Attention/executive function																			
Trail Making B (Adjutant General's Office, 1944)	105	161	97	60	89	75	–	144	66	61	–	–	59	91.70 (36.06)	70.56 (21.42)	(1,17)	2.34	ns	
Maze planning (Wechsler, 1991)	0	5	0	0	4	0	–	0	0	3	–	–	4	1.60 (2.12)	2.22 (1.72)	(1,17)	<1	ns	
Rey figure (Organization) (Hamby <i>et al.</i> , 1993)	3	1	1	1	1	2	–	1	3	1	–	–	2	1.60 (0.84)	1.67 (0.71)	(1,17)	<1	ns	
Short Category (Wetzel and Boll, 1987)	48	15	24	25	36	28	–	29	34	21	–	–	14	27.4 (10.20)	30.00 (17.43)	(1,17)	<1	ns	
Verbal fluency (Monsch <i>et al.</i> , 1992)																			
Letters (FAS)	32	31	24	45	23	44	42	23	43	41	41	31	43	35.62 (8.54)	52.75 (15.17)	(1,27)	13.14	<0.01	
Categories (animals, fruits, vegetables)	45	41	32	56	21	52	42	34	58	43	34	35	54	42.08 (10.90)	56.31 (11.17)	(1,27)	11.91	<0.01	
Naming																			
Boston naming test (Kaplan <i>et al.</i> , 1983)	58	49	52	60	59	55	–	58	60	57	–	–	60	56.55 (3.73)	58.33 (1.52)	(1,17)	1.78	ns	
Memory (CERAD; Morris <i>et al.</i> , 1989)																			
Word List Memory	28	22	15	–	14	23	21	16	18	19	18	20	21	19.58 (3.85)	22.56 (3.18)	(1,26)	5.03	0.03	
Word List Recall	6	6	0	–	5	9	9	5	4	9	5	3	3	5.33 (2.74)	8.38 (1.50)	(1,26)	14.17	<0.01	
Word List Recognition	10	10	9	–	8	10	10	8	9	9	6	10	8	8.92 (1.24)	9.88 (0.34)	(1,26)	8.77	0.01	
Visuospatial ability (Spreen and Strauss, 1991)																			
Rey figure (Accuracy)	35	32	36	36	36	36	–	36	33	36	–	–	36	35.15 (1.60)	34.67 (3.04)	(1,17)	<1	ns	

Missing values in the frontal data are indicated with a dash (–). The results for the MMSE, ANART, Trail Making B, Maze Planning, Rey figure, Short Category and Boston Naming Test were not available for seven control participants. Values for df, F and P are from one-way ANOVAs between frontal patients and controls. ns = non-significant,  $P > 0.10$ . ANART = American National Adult Reading Test.



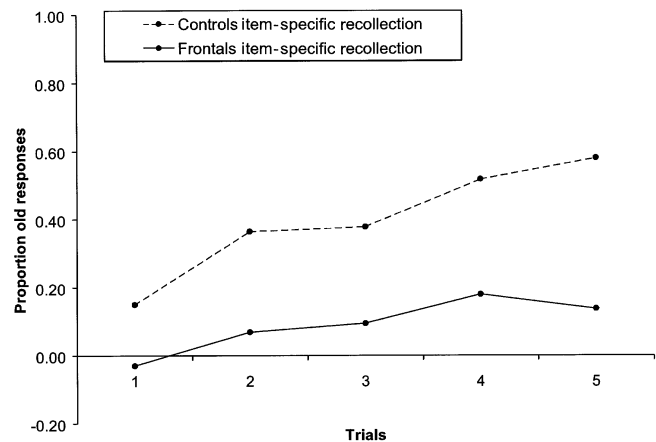
**Fig. 2** Corrected true recognition obtained by subtracting the proportion of 'old' responses to unrelated targets from the proportion of 'old' responses to studied words, and corrected false recognition obtained by subtracting the proportion of 'old' responses to unrelated lures from the proportion of 'old' responses to related lures in patients with frontal lobe lesions and controls as a function of study-test trial.

*Item-specific recollection.* True recognition ('old' responses to studied items) can be thought of as a combination of gist memory plus item-specific recollection. In contrast, false recognition ('old' responses to related lure items) is probably a measure of gist memory minus any item-specific recollection that is available to counteract the effect of gist. Thus, subtracting false recognition from true recognition should provide a measure of the item-specific recollection used by the groups. As suggested by the Group  $\times$  Item Type interaction above, control participants showed more item-specific recollection than the patients [ $F(1,27) = 6.36, P = 0.018$ ] (Fig. 3).

*Initial trial summary.* On the first trial, patients with frontal lesions made more 'old' responses to related lure items than controls, giving the patients a higher level of uncorrected false recognition compared with controls (Table 3), consistent with the findings of Melo and colleagues (Melo *et al.*, 1999). However, because the patients showed some tendency towards making more false alarms to unrelated lures than controls (Table 3), patients and controls showed similar levels of corrected false recognition (Fig. 2), also consistent with the findings of Melo and colleagues (Melo *et al.*, 1999). The analysis of item-specific recollection suggests that the patients experienced more difficulty than controls in distinguishing between studied and related lure items (Fig. 3).

### All five trials

*True and false recognition.* Consideration of all five trials shows that the patients were more likely than controls to respond 'old' to either studied or related lure items, and both groups of participants were more likely to respond 'old' to studied compared with related lure items (Table 3). A



**Fig. 3** Proportion of 'old' responses to studied words minus related lures (item-specific recollection) in patients with frontal lobe lesions and controls as a function of study-test trial.

repeated-measures ANOVA on all five trials with Group (patients versus controls) as a between-subjects variable and Item Type (true versus false recognition) and Trial as within-subject variables yielded overall effects of Group [ $F(1,27) = 5.47, P = 0.027$ ] and Item Type [ $F(1,27) = 72.59, P < 0.0005$ ] and significant Group  $\times$  Item Type [ $F(1,27) = 28.98, P < 0.0005$ ] and Trial  $\times$  Item Type [ $F(4,108) = 13.79, P < 0.0005$ ] interactions. There was a trend towards the three-way interaction of Group  $\times$  Trial  $\times$  Item Type [ $F(4,108) = 2.14, P = 0.081$ ], no effect of Trial [ $F(4,108) = 1.52, P = 0.202$ ] and no Group  $\times$  Trial interaction [ $F(4,108) < 1$ ].

The Group  $\times$  Item Type interaction was present because while both patients [ $F(1,12) = 6.50, P = 0.026$ ] and controls [ $F(1,15) = 86.18, P < 0.0005$ ] showed significant differences between true and false recognition, this difference was more prominent in the control group (see analysis of item-specific recollection below). The Trial  $\times$  Item Type interaction is present because overall, levels of true recognition increased across trials while levels of false recognition decreased. An ANOVA on true recognition alone showed a significant effect of Trial [ $F(4,108) = 18.56, P < 0.0005$ ], no effect of Group [ $F(1,27) = 2.40, P = 0.133$ ] and no interaction [ $F(4,108) = 1.78, P = 0.137$ ], while an ANOVA on false recognition alone showed significant effects of Trial [ $F(4,108) = 4.83, P = 0.001$ ] and Group [ $F(1,27) = 13.53, P = 0.001$ ] and no interaction [ $F(4,108) < 1$ ]. Thus, across all five trials the patients showed higher levels of false recognition than controls. The trend towards the three-way interaction of Group  $\times$  Trial  $\times$  Item Type was present because while both patients [ $F(4,48) = 4.77, P = 0.003$ ] and controls [ $F(4,60) = 16.70, P < 0.0005$ ] showed increases in true recognition across trials, only controls showed significant decreases in their false recognition across trials [controls,  $F(4,60) = 5.66, P = 0.001$ ; patients,  $F(4,48) < 1$ ].

*Unrelated items.* Overall, participants made fewer false alarms to non-studied, unrelated items across trials. A



**Table 3** True recognition of studied words, false recognition of related lures and false alarms to unrelated targets and unrelated lures in patients with frontal lobe lesions and controls (proportion 'old' responses)

Trials	Patients with frontal lobe lesions (SD)	Controls (SD)
True recognition of studied words		
1	0.80 (0.13)	0.80 (0.17)
2	0.88 (0.13)	0.92 (0.09)
3	0.91 (0.10)	0.95 (0.06)
4	0.91 (0.11)	0.98 (0.04)
5	0.89 (0.11)	0.99 (0.03)
False recognition of related lures		
1	0.83 (0.22)	0.65 (0.23)
2	0.81 (0.21)	0.55 (0.31)
3	0.82 (0.20)	0.57 (0.22)
4	0.73 (0.30)	0.46 (0.26)
5	0.76 (0.22)	0.41 (0.22)
False alarms to unrelated targets		
1	0.06 (0.11)	0.03 (0.09)
2	0.01 (0.05)	0.04 (0.07)
3	0.01 (0.05)	0.05 (0.10)
4	0.01 (0.05)	0.03 (0.07)
5	0.01 (0.05)	0.02 (0.06)
False alarms to unrelated lures		
1	0.17 (0.24)	0.05 (0.08)
2	0.04 (0.07)	0.02 (0.06)
3	0.04 (0.07)	0.03 (0.09)
4	0.04 (0.10)	0.01 (0.04)
5	0.03 (0.06)	0.02 (0.07)

repeated-measures ANOVA with Group (patients versus controls) as a between-subjects variable and Item Type (unrelated targets versus unrelated lures) and Trial as within-subject variables yielded an effect of Trial [ $F(4,108) = 5.09, P = 0.001$ ] and Group  $\times$  Trial [ $F(4,108) = 2.86, P = 0.027$ ] and Group  $\times$  Item Type [ $F(1,27) = 6.29, P = 0.018$ ] interactions, and no other effects or interactions [Group,  $F(1,27) < 1$ ; Item Type,  $F(1,27) = 2.60, P = 0.119$ ; Trial  $\times$  Item Type,  $F(4,108) = 1.53, P = 0.199$ ; Group  $\times$  Trial  $\times$  Item Type,  $F(4,108) < 1$ ]. The Group  $\times$  Trial interaction was present because the patients showed a significant reduction in these false alarms over the five trials [ $F(4,48) = 4.07, P = 0.006$ ], while controls did not [ $F(4,60) = 1.16, P = 0.339$ ]. The Group  $\times$  Item Type interaction was present because the patients made somewhat more false alarms to unrelated lure items than unrelated target items [ $F(1,12) = 4.18, P = 0.063$ ] while controls made numerically (though not significantly) more false alarms to the unrelated target items than the unrelated lure items [ $F(1,15) = 1.36, P = 0.261$ ].

**Corrected true and false recognition.** The corrected data demonstrated that the patients showed overall higher corrected recognition levels (true and false combined) relative to the controls. Both groups showed higher levels of corrected true versus false recognition (Fig. 2). An ANOVA on the data after correction for baseline false alarms yielded effects of

Group [ $F(1,27) = 4.44, P = 0.045$ ], Item Type [ $F(1,27) = 85.50, P < 0.0005$ ] and Trial [ $F(4,108) = 3.24, P = 0.015$ ] as well as significant Group  $\times$  Item Type [ $F(1,27) = 21.80, P < 0.0005$ ] and Item Type  $\times$  Trial [ $F(4,108) = 6.64, P < 0.0005$ ] interactions. The three-way interaction of Group  $\times$  Item Type  $\times$  Trial was nearly significant [ $F(4,108) = 2.33, P = 0.061$ ] and there was no Group  $\times$  Trial interaction [ $F(4,108) = 1.32, P = 0.270$ ].

The overall effect of Trial probably indicates that the first trial yielded somewhat lower levels of corrected recognition overall compared with the later trials. As was the case for the uncorrected data, the Group  $\times$  Item Type interaction was present because while both patients [ $F(1,12) = 13.44, P = 0.003$ ] and controls [ $F(1,15) = 87.45, P < 0.0005$ ] showed significant differences between their corrected true and false recognition, this difference was more prominent in the control group (see analysis of item-specific recollection below). The Trial  $\times$  Item Type interaction was present because overall levels of corrected true recognition increased across trials while levels of corrected false recognition showed a fluctuating pattern. An ANOVA on corrected true recognition alone showed a significant effect of Trial [ $F(4,108) = 16.29, P < 0.0005$ ], no effect of Group [ $F(1,27) = 1.10, P = 0.304$ ] and no interaction [ $F(4,108) < 1$ ], while an ANOVA on corrected false recognition alone showed a significant effect of Group [ $F(1,27) = 10.72, P = 0.003$ ], no effect of Trial [ $F(4,108) = 1.95, P = 0.107$ ] and a trend towards an interaction [ $F(4,108) = 2.10, P = 0.086$ ]. Thus, as with the uncorrected data, the patients showed higher levels of corrected false recognition than controls across the five trials (Fig. 2). The near-significant three-way interaction of Group  $\times$  Trial  $\times$  Item Type was present because while both patients [ $F(4,48) = 8.25, P < 0.0005$ ] and controls [ $F(4,60) = 9.56, P < 0.0005$ ] showed increases in the levels of their corrected true recognition across trials, only controls showed significant decreases in their corrected false recognition across trials [controls,  $F(4,60) = 3.69, P = 0.009$ ; patients,  $F(4,48) < 1$ ].

**Item-specific recollection.** As with the initial trial results, we subtracted 'old' responses to related lure items from 'old' responses to studied items to obtain a measure of the item-specific recollection used by the groups. While both groups showed increasing item-specific recollection across trials, controls demonstrated higher levels of this measure (Fig. 3). An ANOVA showed effects of Group [ $F(1,27) = 29.00, P < 0.0005$ ] and Trial [ $F(4,108) = 13.19, P < 0.0005$ ] and a trend towards an interaction [ $F(4,108) = 2.14, P = 0.081$ ]. The trend towards an interaction was present because while controls showed a robust increase in item-specific recollection across trials [ $F(4,60) = 15.34, P < 0.0005$ ], the patients showed a somewhat weaker increase [ $F(4,48) = 2.49, P = 0.055$ ].

**All five trials summary.** Consideration of all five trials revealed similar patterns of uncorrected true recognition but different patterns of uncorrected false recognition for patients and controls (Table 3). Across trials, both groups increased

**Table 4** Pearson correlations between neuropsychological measures and corrected true recognition, corrected false recognition and item-specific recollection for trials 1 and 5 in patients with frontal lesions and controls

Test	n	Trial 1			Trial 5		
		Corrected true recognition	Corrected false recognition	Item-specific recollection	Corrected true recognition	Corrected false recognition	Item-specific recollection
Global cognitive score							
MMSE	22	–	–	–	–	–	–
Intelligence							
ANART	22	–	–	–	–	–	–
Attention/Executive Function							
Trail Making B	19	–	–	–	–	–	–
Maze Planning	19	–	–	–	–	–	–
Rey figure	19	–0.50*	–	–	–	–	–
(Organization)							
Short Category	19	–	–	–	–	–	–
Verbal Fluency							
Letters (FAS)	29	–	–	–	–	–0.56*	0.59*
Categories (animals, fruits, vegetables)	29	–	–	–	–	–0.67**	0.71**
Naming							
Boston Naming Test	19	–	–	–	–	–	–
Memory (CERAD)							
Word List Memory	28	–	0.42*	–	0.50*	–0.42*	0.62**
Word List Recall	28	–	–	–	0.48*	–0.43*	0.57*
Word List Recognition	28	–	–	–	–	–0.45*	0.52*
Visuospatial Ability							
Rey figure (Accuracy)	19	–	–	–	–	–	–

– =  $P > 0.05$ ; \* $P < 0.05$ ; \*\* $P < 0.00064$ . See Table 2 for references. ANART = American National Adult Reading Test.

**Table 5** True recognition of studied words, false recognition of related lures and false alarms to unrelated items as a function of the number of study sessions in patients with Alzheimer's disease and older adults (proportion 'old' responses)

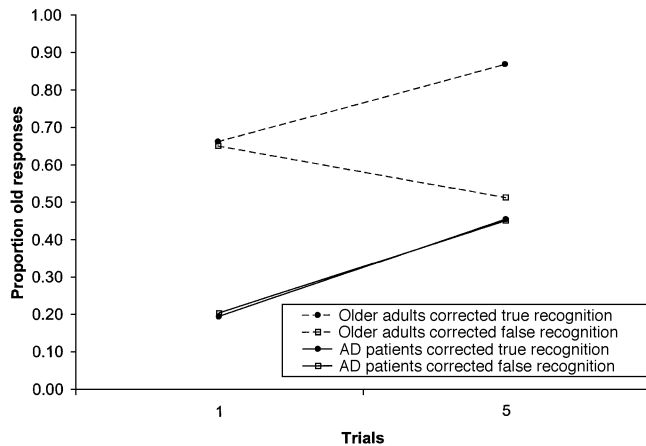
Item type	Number of study sessions			
	Alzheimer's disease patients		Older adults	
	1 (SD)	5 (SD)	1 (SD)	5 (SD)
True recognition of studied words	0.62 (0.24)	0.81 (0.17)	0.71 (0.16)	0.87 (0.11)
False recognition of related lures	0.62 (0.33)	0.80 (0.29)	0.70 (0.25)	0.52 (0.32)
False alarms to unrelated items	0.42 (0.27)	0.36 (0.26)	0.05 (0.04)	0.01 (0.03)

the level of their uncorrected true recognition while only controls showed a significant reduction in the level of their uncorrected false recognition. Additionally, the patients exhibited higher levels of uncorrected false recognition than controls overall (Table 3). This same pattern of results was also seen for corrected true and false recognition (Fig. 2). The analysis of item-specific recollection showed that the patients had more difficulty distinguishing between studied and related lure items than controls. Furthermore, although both groups showed increases in their item-specific recollection over the trials, there was a trend for controls to increase their item-specific recollection more powerfully compared with the patients (Fig. 3), as we suspected based upon previous research (Schacter *et al.*, 1996c; Melo *et al.*, 1999; Parkin

*et al.*, 1999; Rapcsak *et al.*, 1999, 2001). (Additional analyses were performed to determine if lesion laterality, lesion size, or specific lesion site affected the patients' true and false recognition. These analyses revealed no effect of lesion laterality, lesion size, or lesion site on true and false recognition.)

### Correlation analyses

Table 4 shows the Pearson correlations between the standard neuropsychological tests and corrected true recognition, corrected false recognition and item-specific recollection for trials 1 and 5. Although a number of correlations are significant with an  $\alpha$  value of 0.05, only three correlations



**Fig. 4** Corrected true and false recognition obtained by subtracting the proportion of 'old' responses to unrelated items from the proportion of 'old' responses to studied words and related lures, respectively, in patients with Alzheimer's disease and older adults as a function of one versus five study sessions.

remained significant, with an  $\alpha$  value of 0.00064 (after Bonferroni correction for 78 comparisons). These significant correlations are between (i) category fluency and trial 5 corrected false recognition; (ii) category fluency and trial 5 item-specific recollection; and (iii) CERAD word list memory and trial 5 item-specific recollection.

### *Alzheimer's disease experiment (Experiment 2)*

Table 5 shows the proportion of 'old' responses to words studied previously (true recognition) and related lures (false recognition) as a function of Group (patients with Alzheimer's disease versus older adults) and Condition (one versus five study sessions). Also shown are the 'old' responses to non-studied, unrelated items, which provide an index of baseline false alarms. Corrected true and false recognition was obtained by subtracting the proportion of 'old' responses to unrelated items from the proportion of 'old' responses to studied words and related lures, respectively (Fig. 4).

Because, compared with older adults, patients with Alzheimer's disease made significantly more false alarms to unrelated items [effect of Group,  $F(1,41) = 37.92$ ,  $P < 0.0005$ ], all analyses were performed on corrected true and false recognition data.

### *Corrected true and false recognition*

Overall, patients with Alzheimer's disease showed lower levels of corrected true and false recognition compared with older adults (Fig. 4). An ANOVA with Group (patients versus older adults) and Condition (one versus five study sessions) as between-subject variables and Item Type (corrected true versus false recognition) as a within-subject variable yielded main effects of Group [ $F(1,39) =$

$17.13$ ,  $P < 0.0005$ ] and Item Type [ $F(1,39) = 4.45$ ,  $P = 0.041$ ], as well as interactions of Group  $\times$  Item Type [ $F(1,39) = 4.69$ ,  $P = 0.036$ ] and Condition  $\times$  Item Type [ $F(1,39) = 4.38$ ,  $P = 0.043$ ], and a near-significant three-way interaction of Group  $\times$  Condition  $\times$  Item Type [ $F(1,39) = 3.78$ ,  $P = 0.059$ ]. There were no other effects or interactions [Condition,  $F(1,39) = 2.79$ ,  $P = 0.103$ ; Group  $\times$  Condition,  $F(1,39) = 1.70$ ,  $P = 0.200$ ].

The effect of Item Type indicates that participants overall showed higher levels of corrected true compared with false recognition. The Group  $\times$  Item Type interaction was present because levels of corrected true recognition were significantly higher than corrected false recognition in the older adults [ $t(19) = 2.66$ ,  $P = 0.015$ ] but not in the patients [ $t(22) = -0.05$ ,  $P = 0.964$ ]. The Condition  $\times$  Item Type interaction was present because, overall, participants in the one study session condition showed nearly identical levels of corrected true and false recognition [ $t(21) = -0.003$ ,  $P = 0.998$ ], while those in the five study sessions condition showed higher levels of corrected true versus false recognition [ $t(20) = 2.31$ ,  $P = 0.032$ ]. However, the near-significant three-way interaction demonstrates that the Condition  $\times$  Item Type interaction was being driven by the older adults (Fig. 4). Only the older adults showed differences between their corrected true and false recognition in the five study sessions condition [ $t(9) = 4.03$ ,  $P = 0.003$ ]; the patients with Alzheimer's disease showed nearly identical levels of corrected true and false recognition in this condition [ $t(10) = 0.04$ ,  $P = 0.968$ ].

### *Item-specific recollection*

As in Experiment 1, we subtracted false recognition from true recognition to provide a measure of item-specific recollection. An ANOVA with Group (patients versus older adults) and Condition (one versus five study sessions) as between-subjects variables yielded main effects of Group [ $F(1,39) = 4.45$ ,  $P = 0.041$ ] and Condition [ $F(1,36) = 4.38$ ,  $P = 0.043$ ], as well as a near significant Group  $\times$  Condition interaction [ $F(1,39) = 3.78$ ,  $P = 0.059$ ]. The effect of Group indicates that the older adults overall generated more item-specific recollection than the patients; the effect of Condition indicates that those participants who were exposed to five study sessions showed more item-specific recollection than those exposed to one study session. The near-significant interaction, however (mirroring the near-significant three-way interaction observed in the analysis of corrected true and false recognition above), suggests that those older adults in the five study session condition were driving both main effects. One-way ANOVAs showed that this near-significant interaction was present because older adults showed higher levels of item-specific recollection than patients with Alzheimer's disease for the five study sessions condition [ $F(1,19) = 7.39$ ,  $P = 0.014$ ] but not for the one study session condition [ $F(1,20) < 0.1$ ].

## Discussion

### *Frontal lobe lesion experiment (Experiment 1)*

Patients with lesions of their frontal lobes are unable to decrease their false recognition across trials in this repeated trials DRM paradigm, unlike matched controls. We argue that the inability of these patients to decrease or suppress false recognition across trials may help explain the increasing levels of false recognition observed in patients with Alzheimer's disease (Budson *et al.*, 2000) and Korsakoff amnesia (Schacter *et al.*, 1998b). We suggest that the reason that the level of false recognition in these latter groups increased (rather than remaining stable) across trials relates to the combination of the relatively low level of false recognition observed in the initial trial and their frontal lobe dysfunction. Budson and colleagues and Schacter and colleagues suggested that patients with Alzheimer's disease and Korsakoff amnesia showed lower levels of false recognition compared with their controls on the initial trial because their poor episodic memory resulted in diminished ability to extract and/or remember the semantic gist of the study lists (Schacter *et al.*, 1998b; Budson *et al.*, 2000). Across successive trials, the repeated presentations of study and test lists allowed these patient groups to build up the semantic gist of the lists. Neither of these groups, however, showed any ability to distinguish between studied and related lure items, i.e. they were unable to develop any item-specific recollection. We suggest that their inability to reduce false recognition across trials and acquire item-specific recollection is at least partly attributable to the frontal network dysfunction inherent in these patient groups. Supporting this hypothesis are the results of the patients with non-Korsakoff amnesia (Schacter *et al.*, 1998b). As expected, because these patients show episodic memory deficits without frontal network dysfunction, they exhibited low levels of false recognition on the initial trial and a fluctuating—not increasing—level of false recognition across trials.

A remaining question is why the false recognition of the patients with frontal lesions did not increase to their level of true recognition, as was observed in patients with Alzheimer's disease and Korsakoff amnesia (Schacter *et al.*, 1998b; Budson *et al.*, 2000). The answer is probably again due to the fact that these latter patient groups demonstrate medial temporal lobe and/or diencephalic dysfunction as well as frontal network dysfunction. In addition to impairments in extracting and/or remembering the semantic gist of the study lists, dysfunction of the medial temporal lobe system may also impair item-specific recollection. It may be that patients with Alzheimer's disease and Korsakoff amnesia demonstrated increasing levels of false recognition that matched the level of their true recognition because their item-specific recollection is impaired both by dysfunctional frontal networks and by a dysfunctional medial temporal lobe system.

Thus, Experiment 1 has shown that patients with frontal lobe lesions are unable to decrease false recognition across

repeated study–test trials. However, because such patients are known to be susceptible to source memory deficits, it is possible that the pattern observed by Budson and colleagues in patients with Alzheimer's disease—increasing false recognition across trials—is entirely attributable to source memory deficits produced by repeated testing of related lure items (Budson *et al.*, 2000). To test this idea, in Experiment 2 we used a paradigm in which study lists were repeated without any intervening tests. If source memory problems related to repeated testing are entirely responsible for the pattern previously observed in the patients with Alzheimer's disease, then study list repetition should affect patients and controls similarly, and patients with Alzheimer's disease should no longer show increased false recognition across trials. On the other hand, if the previous pattern is attributable, at least in part, to factors other than test-induced source confusions (e.g. reliance on gist information), then we would still expect a Group  $\times$  Trial (or in this case a Group  $\times$  Study Session Condition) interaction and patients with Alzheimer's disease should still show increasing false recognition across trials.

### *Alzheimer's disease experiment (Experiment 2)*

Patients with Alzheimer's disease who were exposed to five study lists showed levels of corrected false recognition elevated to the level of corrected true recognition even with the source memory confound of the intervening tests and their lure words eliminated (Fig. 4). Healthy older adults who were exposed to five study lists, in contrast, showed lower levels of corrected false recognition relative to corrected true recognition, demonstrating the development of item-specific recollection with five study sessions. (For somewhat different results in older adults using a similar paradigm, see Benjamin, 2001.)

This finding suggests that source memory errors contributed relatively little to the pattern of false recognition seen for patients with Alzheimer's disease in the study by Budson and colleagues (Budson *et al.*, 2000). Thus, gist-based memory distortions and disruption of aspects of frontal lobe dysfunction, such as post-retrieval verification and monitoring processes and inhibition processes, were probably the most important factors in the false recognition of patients with Alzheimer's disease. Consistent with this view, studies have suggested that patients with Alzheimer's disease show impairments on a variety of tasks in which participants need to keep information in working memory, selectively direct their attention, divide their attention, and inhibit unwanted responses (Baddeley *et al.*, 1991, 2001; Greene *et al.*, 1996; Johnson *et al.*, 1997; Sebastian *et al.*, 2001; for reviews see Morris, 1996; Perry and Hodges, 1999). Moreover, the majority of our patients exhibited impairment on measures of frontal lobe functioning. Patients with Alzheimer's disease may therefore be particularly susceptible to gist-based false recognition because they are unable to use

fully their frontal lobes to evaluate critically the familiarity associated with the related lure item (see Conclusions).

Another possible explanation of our results is that, although we eliminated the explicit source memory confusion of intervening tests containing related lure items, patients with Alzheimer's disease may still have experienced source memory confusion related to implicit associative responses. Deese (1959) and others (e.g. Bousfield *et al.*, 1958; Underwood, 1965; Roediger and McDermott, 1995) have suggested that the high levels of recall intrusions seen with lists of semantic associates may be due to participants themselves spontaneously generating the related lure word during the study phase. Source memory confusion may thus still occur between these implicit associative responses and actually presented items when participants view related lures on the recognition test.

## Conclusions

Previous research has shown that patients with Alzheimer's disease and Korsakoff amnesia show increasing levels of false recognition across repeated study–test trials of DRM lists (Schacter *et al.*, 1998b; Budson *et al.*, 2000). We hypothesized that this increasing false recognition was in part attributable to the frontal lobe dysfunction inherent in these patient populations. Furthermore, we speculated that a failure in source monitoring might be the mechanism by which frontal lobe dysfunction in patients with Alzheimer's disease produced increasing levels of false recognition across repeated study–test trials.

Experiment 1 showed that patients with frontal lobe lesions were unable to decrease their false recognition across repeated study–test trials. This result confirmed our hypothesis that frontal lobe dysfunction may have contributed to the increasing levels of false recognition in patients with Alzheimer's disease and Korsakoff amnesia. Experiment 2 showed that patients with Alzheimer's disease, unlike healthy older adults, exhibited levels of false recognition as high as their true recognition after five exposures to the study list, without intervening tests. This latter result disputed our hypothesis that a failure of source monitoring was the specific mechanism by which frontal lobe dysfunction produced increasing levels of false recognition across repeated study–test trials in patients with Alzheimer's disease.

Together, these results suggest that aspects of frontal lobe dysfunction other than source monitoring between study and test items, such as verification–inhibition mechanisms, may be important in the increasing false recognition observed in patients with Alzheimer's disease across repeated study–test trials. (This suggestion may also be valid for patients with Korsakoff amnesia, but we have not demonstrated this since only patients with Alzheimer's disease were examined in Experiment 2.) This suggestion is consistent with previous studies which have found that patients with damage to the frontal lobes produced high levels of false recognition in paradigms which do not require source monitoring (Parkin

*et al.*, 1996; Schacter *et al.*, 1996c; see also Background to Experiment 1). Lastly, because increases in prefrontal blood flow have been correlated with category fluency performance (Audenaert *et al.*, 2000; Kitabayashi *et al.*, 2001) and successful encoding (Wagner *et al.*, 1998), the significant correlations we found in Experiment 1 between category fluency, word list memory (the encoding portion of the CERAD) and our trial 5 experimental measures also suggest the frontal lobes contribute to the suppression of false recognition and the development of item-specific recollection across repeated study–test trials.

There are several reasons why failure of verification–inhibition mechanisms in our patients may lead to increased false recognition in the DRM paradigm. For example, when participants develop a gist representation after viewing DRM lists, this representation may result in an experience of familiarity when a non-studied related lure word is seen at test. Healthy participants presumably engage at least two processes to reduce false alarms to these lure words. First participants need to inhibit the tendency to respond 'old' to lure words on the basis of this familiarity alone. Shimamura (1995) has suggested that enabling inhibitory controls may be a primary function of the prefrontal cortex; these inhibitory controls may be impaired in our patients with frontal lobe lesions and our patients with Alzheimer's disease. Once this initial inhibition has been accomplished, participants need to engage further in verification processes to correctly understand the basis of this familiarity. Schacter and colleagues hypothesized that the increases in frontal and cerebellar blood flow observed during false recognition were due to effortful monitoring processes reflecting the participants' attempt to retrieve specific perceptual and other contextual information (item-specific information) (Schacter *et al.*, 1996d). Retrieval of this specific information would suggest that the item in question was on the study list, while the absence of such information would suggest that the item is new, despite its familiarity based on gist.

The present research also has implications for understanding false recognition in older adults. Previous research has shown that, like our patients with frontal lesions in Experiment 1, older adults are also unable to suppress their false recognition in the repeated study–test trials DRM paradigm (Kensinger and Schacter, 1999; Budson *et al.*, 2000). Thus, one possible explanation of the inability of older adults to suppress false recognition in the repeated study–test trials paradigm may be their frontal lobe dysfunction (Levine *et al.*, 1997). Future studies, perhaps combining study–test trials as in Experiment 1 and study repetitions as in Experiment 2 in a single experiment, may be able to answer definitively whether the inability of older adults to suppress false recognition is due to a breakdown in source monitoring or to other aspects of frontal lobe functioning.

There is increasing evidence that the frontal lobes are important for episodic memory (Brewer *et al.*, 1998; Wagner *et al.*, 1998; Fletcher and Henson, 2001). We view the present

study as illustrative of one additional aspect of how the frontal lobes enable normal episodic memory: by facilitating the suppression of false recognition. In previous false recognition studies of patients with frontal lesions (see Background to Experiment 1), healthy controls showed lower levels of false recognition than the patients. There are many situations, however, in which healthy adults show quite high levels of false recognition (and other memory distortions) in the laboratory and in their daily lives (for reviews see Schacter, 1996, 2001). When high levels of false recognition are initially generated, healthy individuals are often able to reduce or suppress their false recognition using mechanisms such as the distinctiveness heuristic (Schacter *et al.*, 1999; Dodson and Schacter, 2001) and repeated exposure to materials, as in the current experiments (see also Schacter *et al.*, 1998b; Kensinger and Schacter, 1999; Budson *et al.*, 2000). The present study suggests that not only do the frontal lobes work to prevent high levels of false recognition from being generated, but they may also work towards reducing the elevated levels of false recognition that have already been produced.

Finally, from a clinical standpoint these results suggest that medications which enhance frontal lobe function may be useful in treating clinically relevant memory distortions in patients with Alzheimer's disease. Future studies of such medications in patients with Alzheimer's disease will determine whether improvement in frontal lobe function can reduce memory distortions both in the laboratory and in daily life.

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