

## NOTE

### INTACT IMPLICIT MEMORY IN PATIENTS WITH FRONTAL LOBE LESIONS

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**Abstract**—Patients with frontal lobe lesions and control subjects were administered tests of word-stem completion priming. In this implicit memory test, subjects are first presented words (e.g. MOTEL, PARADE) in an incidental learning paradigm. Following word presentation, subjects are shown word stems (e.g. MOT, PAR) and asked to produce the first word that comes to mind. Patients with frontal lobe lesions exhibited normal levels of word-stem completion. These findings indicate that implicit memory can operate normally despite damage to the prefrontal cortex. The present results substantiate previous neuropsychological and positron emission tomography findings which indicate that word priming depends critically on posterior cortical areas.

### INTRODUCTION

THE DISTINCTION between explicit and implicit memory has provided a useful framework for neuropsychological analyses of memory function (for review, see Refs [14]–[16], [19] and [21]). In particular, patients with organic amnesia resulting from damage to the medial temporal region or the diencephalic midline are impaired on tests of explicit memory (e.g. recall, recognition), yet they can perform in an entirely normal fashion on tests of implicit memory (e.g. skill learning, priming effects). Based on these findings, it has been suggested that the areas damaged in amnesia contribute to a particular form of memory processing [10, 19, 24]—one that involves declarative or explicit memory. In contrast, implicit memory can operate fully in amnesic patients and thus does not appear to involve medial temporal or diencephalic areas.

Recent neuropsychological findings suggest that implicit memory is not tied to any single neural system or structure. That is, the underlying neural substrates associated with various forms of implicit memory (e.g. skill learning, word priming, classical conditioning) appear to be related to the specific information processing operations that are involved in performance [19]. For example, Huntington's disease, a basal ganglia disorder which impairs motor functions, also impairs motor skill learning, as measured by impaired performance on the pursuit-motor task [3, 4]. Yet, patients with Huntington's disease are not impaired on implicit memory tests involving lexical information, as measured by intact performance on the word-stem completion test [4, 13, 18]. In this lexical priming test, words are presented incidentally (MOTEL, PARADE), and later subjects are asked to complete three-letter word beginnings (i.e. word stems; MOT, PAR) with the first word that comes to mind [2, 22, 23]. Several studies have shown that both amnesic patients and patients with Huntington's disease perform normally on the word-stem completion task [2, 4, 13, 18].

Unlike amnesic patients or patients with Huntington's disease, patients with Alzheimer's disease are impaired on the word-stem completion test [8, 13, 18]. Although Alzheimer's disease affects many neocortical areas, it has been suggested that the deficit in word priming is attributed to damage in posterior associational areas, which are presumed to be the storehouse of lexical and semantic representations [13, 18]. Some support for this view is provided by the finding that circumscribed lesions of the medial temporal area—the area most affected by Alzheimer's disease—do not impair performance on this test [2]. Also, positron emission tomography (PET) studies

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have suggested that metabolic activity in posterior cortical areas may be related to performance on the word-stem completion test [20]. Interestingly, patients with Alzheimer's disease were not impaired on a test of perceptual identification priming [8]. It has been suggested that perceptual identification priming is mediated by visual processing in occipital cortex, an area which is relatively spared in early stages of Alzheimer's disease (for further discussion, see Refs [8], [16] and [21]).

One brain region that has not been evaluated in terms of implicit memory functions is the frontal lobes. Previous studies have indicated that many aspects of *explicit* memory are not affected in patients with frontal lobe lesions. Specifically, patients with lesions involving the dorsolateral prefrontal cortex exhibit normal performance on many standard tests of new learning capacity, such as word recognition, cued recall and paired-associate learning [5]. However, certain explicit memory functions are reliably affected by frontal lobe lesions, including free recall [5], memory for temporal order [9, 17], source memory [7] and metamemory [6]. To our knowledge, there are no published reports of the status of implicit memory in patients with circumscribed frontal lobe lesions. In the present study, we tested word-stem completion priming in patients with lesions involving the dorsolateral prefrontal cortex. The assessment of these patients was conducted to determine whether impairment of word priming is restricted to cases in which posterior cortical damage occurs (e.g. Alzheimer's disease) or if impaired priming can also occur as a result of damage to prefrontal cortex.

## METHOD

### *Subjects*

*Patient with frontal lobe lesions.* Nine patients with unilateral frontal lobe lesions were identified by review of medical records and CT or MR scans. All patients had infarctions in the region of the dorsolateral prefrontal cortex due to occlusion of the precentral branch of the middle cerebral artery (see Fig. 1). Based on quantitative analyses of neuroimaging data, average lesion volume was estimated to be 43.1 cc. Patients were included if medical records indicated a history of a single cerebral infarction and no history of other significant medical disease, such as psychiatric disorder, dementia, substance abuse, or additional neurological events (e.g. head injury). Of the nine patients (seven men and two women), five had right hemisphere lesions and four had left hemisphere lesions. They averaged 62.0 years of age and 13.0 years of education.

On neuropsychological tests (see Table 1), the patients scored within the normal range on the Full-Scale Wechsler Adult Intelligence Scale—Revised (WAIS—R) (mean = 99.1). Their mean scores on the five scales of the Wechsler Memory Scale—Revised (WMS—R) were as follows: Attention = 92.2, General Memory = 98.6, Delayed Memory = 86.9, Verbal Memory = 99.0, Visual Memory = 98.3. The patients were variably impaired on the Wisconsin Card Sorting Test, achieving an average of 3.4 correct categories out of a total of six categories and an average of 36.3 perseverative errors. The patients were impaired on the FAS Verbal Fluency Test [1], averaging 17.9 words produced. The four patients with left hemisphere lesions and one of the patients with a right hemisphere lesion (patient R.K.) were mildly dysfluent or anomia. However, none of the patients had moderate or severe aphasia.

*Control subjects.* Nine healthy, normal individuals (seven men and two women) participated as control subjects. These individuals were volunteers at the Martinez VA Medical Center and were matched to the patients with frontal lobe lesions with respect to age (65.7 years) and education (13.6 years). The control subjects scored comparably to the patients with frontal lobe lesions on the Information (control subjects = 23.2; frontal patients = 22.3) and Digit Symbol (control subjects = 43.3; frontal patients = 34.6) subtests of the WAIS—R. However, the control subjects performed marginally better than the frontal patients on the Vocabulary subtest (control subjects = 51.6; frontal patients = 35.8,  $t$  [15] = 2.0,  $P$  = 0.06).

### *Stimuli and procedure*

The words and stems were the same as those used by SALMON *et al.* [13] in a study of word-stem completion in patients with either Korsakoff's syndrome, Alzheimer's disease, or Huntington's disease. Subjects were shown 10 words (e.g. MOTEL, PARADE) sequentially and asked to rate how much they liked each word on a 5-point scale (1 = dislike very much, 5 = like very much). Words were printed on 5 × 8 in. index cards (Helvetica type, 18 PT). Subjects were given enough time to produce a rating for each word (approximately 3–5 sec), and the liking scale was displayed at all times. After all words were presented in the rating task, they were presented again using a different random order. For each presentation, two filler words were placed at the beginning of the list, and three were placed at the end to reduce primacy and recency effects, respectively. Following the two presentations of the words, subjects were instructed that a different task would be done. Twenty word stems (e.g. MOT, PAR) were printed on a sheet in a random order, and subjects were asked to say the first word that came to mind for each stem. Ten of the stems could be completed using presented words, and the other 10 stems could be completed with non-presented words and were used to assess baseline guessing rates. Words and word stems used to assess priming performance for one subject were used to assess baseline guessing rates for another subject. Subjects were instructed to use English words; proper nouns were not accepted as correct responses. This entire rating and stem-completion procedure was then repeated for each subject using a different set of word stimuli and stems.

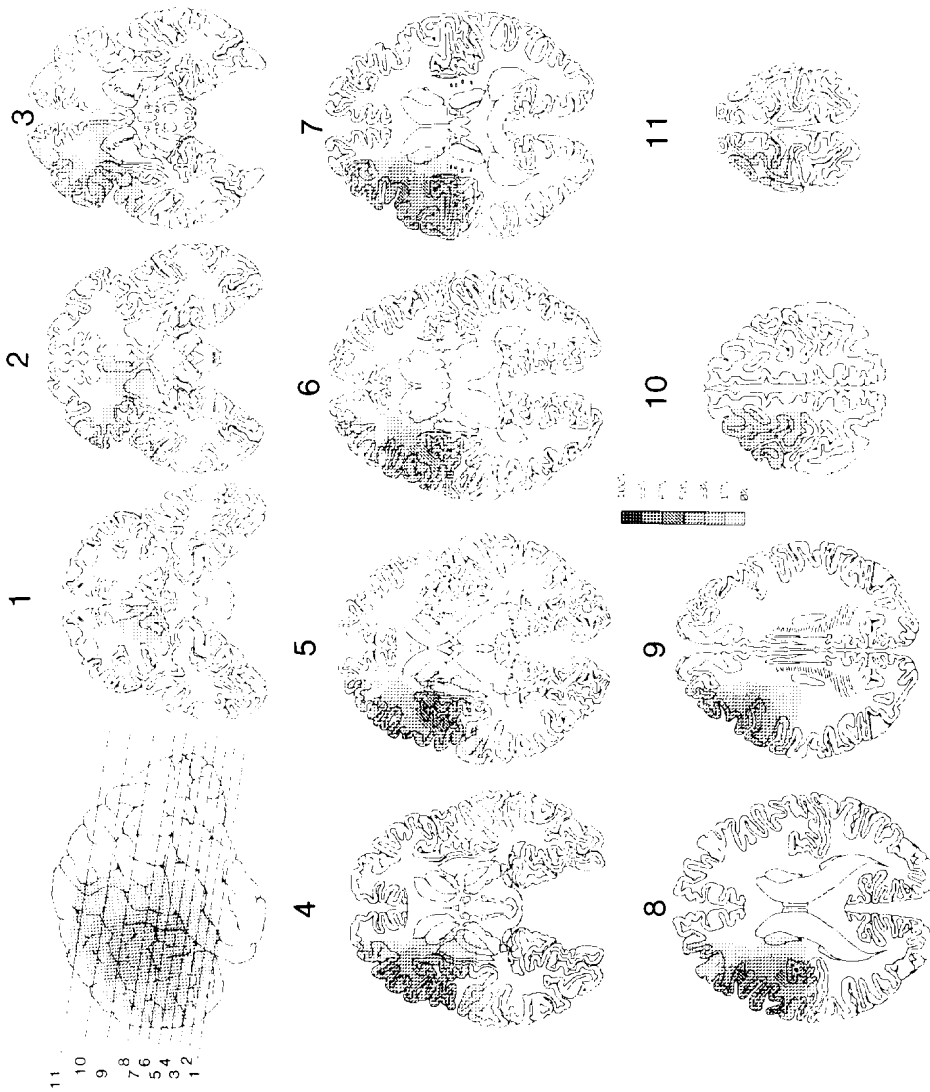


Fig. 1. Composite CT reconstructions of lesions in nine patients with frontal lobe lesions (average lesion volume = 43.1 cc). Both right and left hemisphere lesions are superimposed on the left side of each image template. The numbered lines on the lateral view indicate corresponding axial cuts from the most inferior cut (No. 1) to the most superior cut (No. 11). The grey scale refers to the percent of patients with lesions in that area.

Table 1. Patient characteristics and word-stem completion performance (%)\*

Patient	Lesion	Age	ED	IQ	MQ	WCST	PERS	FAS	Test 1	Test 2	Mean	BL
E.B.	Right	72	12	107	91	4	32	16	60	20	40	5
R.K.	Right	60	14	105	114	0	47	---	60	70	65	10
M.M.	Right	65	12	94	93	0	92	12	30	50	40	10
R.M.	Right	66	10	105	106	6	15	31	30	50	40	15
W.V.	Right	47	15	---	115	6	7	---	50	70	60	5
J.D.	Left	63	20	93	87	6	14	8	30	40	35	15
T.J.	Left	64	8	79	72	1	58	6	20	60	40	5
K.K.	Left	59	13	106	100	4	51	31	60	40	50	15
E.L.	Left	62	13	104	109	4	11	21	70	70	70	15
Frontal Mean		62.0	13.0	99.1	98.6	3.4	36.3	17.9	45.6	52.2	48.9	10.6
Control Mean		65.7	13.6	---	---	---	---	---	41.1	45.6	43.3	7.8

\*ED, years of education; IQ, WAIS—R Full Scale score; MQ, WMS—R General Memory Index; WCST, number of categories attained on the Wisconsin Card Sort Test; PERS, perseverative errors on the WCST; FAS, total number of words correct on the FAS Verbal Fluency Test; Test 1, first test of word-stem completion (%); Test 2, second test of word-stem completion (%); Mean, mean of Test 1 and Test 2; BL, baseline completion score (%); ---, score not available.

## RESULTS

Scores on the first and second tests of word-stem completion were not significantly different from each other for either control subjects or patients with frontal lobe lesions ( $t_s [8] < 0.8$ ; see Table 1). Thus, individual word completion scores were based on the mean score averaged across the two tests. There was no significant difference between patients with frontal lobe lesions and control subjects on the word completion test ( $t [16] = 0.3$ ,  $P = 0.75$ ). Patients with frontal lobe lesions averaged 48.9% words completed (10.6% baseline), and control subjects averaged 43.3% words completed (7.8% baseline). Thus, the "priming effect" (priming score minus baseline) for patients (38.3%) and control subjects (35.5%) differed by only 2.8%. In addition, the priming effect was similar for patients with right frontal (38.0%) and left frontal lesions (36.2%) (see Table 1).

Figure 2 displays word-stem completion performance by the patients with frontal lobe lesions and control subjects. Also displayed are the data from three patient groups tested by SALMON *et al.* [13]. As shown in Fig. 2, patients with frontal lobe lesions, patients with Korsakoff's syndrome and patients with Huntington's disease all demonstrated normal word-stem completion priming. Only patients with Alzheimer's disease were significantly impaired on this test.

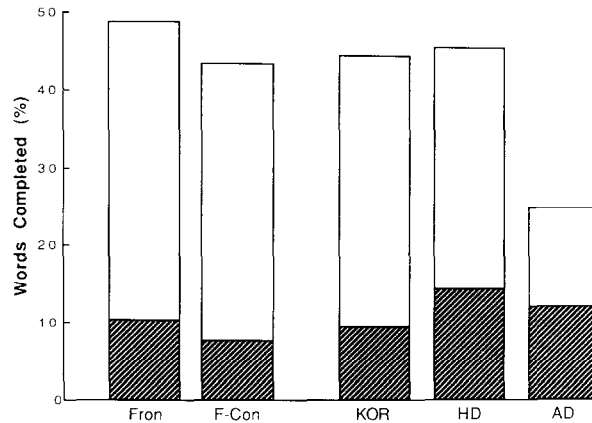


Fig. 2. Word-stem completion performance by patients with frontal lobe lesions (Fron) and control subjects (F-Con). Also shown are data from patients with Korsakoff's syndrome (KOR), patients with Huntington's disease (HD), and patients with Alzheimer's disease (AD) (data from SALMON *et al.* [13]). Only patients with Alzheimer's disease are impaired on the word-stem completion test. Shaded areas represent baseline word-stem completion for non-presented words.

## DISCUSSION

The present findings demonstrate that patients with frontal lobe lesions are not impaired on the word-stem completion test. Thus, patients with frontal lobe lesions, like patients with organic amnesia, exhibit intact implicit memory. Unlike amnesic patients, however, these patients exhibit intact performance on *explicit* memory tests, as indicated by WMS—R scores within the normal range and by findings from other studies (for review, see Ref. [17]). Despite their normal memory ability, patients with frontal lobe lesions are significantly impaired on tests of problem solving, perseveration and word fluency, as demonstrated by poor performance on the Wisconsin Card Sorting Test and on the Verbal Fluency Test.

These results extend the conditions under which preserved implicit memory can be observed. Previous findings have shown that word completion priming is not impaired in patients with possible frontal lobe dysfunction resulting from dementing disorders, such as Korsakoff's syndrome, Parkinson's disease and Huntington's disease [4, 12, 18]. The present findings indicate that word completion priming can operate fully despite large but circumscribed lesions in the prefrontal cortex. The findings are consistent with the view that lexical priming depends critically on *posterior* cortical areas (see also Refs [8] and [20]). Indeed, PET studies in normal subjects have suggested that posterior cortical areas may be particularly important for word-stem completion priming and the representation of the visual form of words [12, 20].

Several questions concerning implicit memory and the frontal lobes still remain unanswered. First, the patients

tested in the present study had lesions centered in the region of the dorsolateral prefrontal cortex. Thus, the findings may not generalize to patients with lesions in other areas of the frontal lobes, such as orbitofrontal lesions or mesial frontal lesions that occur as a result of rupture or repair of an anterior communicating artery aneurysm. Second, we assessed implicit memory in the domain of lexical processing. It is not known whether other implicit memory functions (see Refs [14] [16]), such as skill learning, nonverbal priming, or free-association priming (i.e. conceptual or semantic priming), are preserved in patients with frontal lobe lesions.

Finally, some aspects of stimulus activation or priming may be impaired in patients with frontal lobe lesions. For example, PERRET [11] found that patients with frontal lobe lesions exhibit impairment on the Stroop test, a test in which the presentation of color words interferes with ink color naming. This finding suggests that patients with frontal lobe lesions may be disproportionately affected under conditions in which stimulus activation or "priming" interferes with information processing. That is, the prefrontal cortex may be involved in monitoring or maintaining inhibitory control of cognitive activity [17]. Further analyses of implicit memory in patients with damage to various regions of the frontal lobes will be required to address these issues.

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