California Verbal Learning Test: performance by patients with focal frontal and non-frontal lesions

M. P. Alexander,1,3 D. T. Stuss1,2 and N. Fansabedian1

1Rotman Research Institute of Baycrest Centre for Geriatric Care, 2Departments of Psychology and Medicine (Neurology, Rehabilitation Science), University of Toronto, Toronto, ON, Canada and 3Department of Neurology, Harvard University, Beth Israel Deaconess Medical Center, Boston and Boston University School of Medicine

Correspondence to: Dr Michael P. Alexander, Behavioral Neurology Unit, KS2, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Boston, MA 00215, USA
E-mail: malexand@bidmc.harvard.edu

Summary
Although frontal lobe lesions do not cause classic amnesia, they may disrupt learning and memory in a number of ways. To investigate in finer detail the regions of frontal injury that are associated with impaired learning and to define the cognitive processing deficits specific to each region that disrupt memory, we compared 33 patients with focal frontal injury with patients with non-frontal injury and with normal controls on a standard neuropsychological instrument, the California Verbal Learning Test (CVLT). Subgroups of patients with distinct lesion site profiles were compared in a number of learning measures. All of the subgroups of patients with frontal lesions (with one exception) had inefficient learning due to poor implementation of a strategy of subjective organization. Despite this organizational deficiency, the performance of patients with frontopolar lesions normalized across trials. Only the subgroups with lesions centred either on the left posterior dorsolateral frontal region or the posterior medial frontal region had overall impaired learning and recall. The left posterior dorsolateral frontal group was most significantly impaired on all measures. This recall impairment was secondary to a mild lexical–semantic deficit. A recognition memory deficit in the same group was due to an abnormal response bias. Several groups had a modest increase in perseverative recalls; the underlying mechanisms differed. Disruption of different cognitive processes associated with specific frontal regions underlies the varied patterns of memory impairment. This study has demonstrated even finer differentiations within the frontal region than previously known.

Keywords: list learning; memory; frontal lobe; recognition memory; strategic deficits

Abbreviations: AMF = anterior medial frontal; ant. LDF = anterior left dorsolateral frontal; ant. RDF = anterior right dorsolateral frontal; CART = Classification and Regression Tree; CVLT = California Verbal Learning Test; LNF = left non-frontal; NART-R = National Adult Reading Test—Revised; PMF = posterior medial frontal; post. LDF = posterior left dorsolateral frontal; post. RDF = posterior right dorsolateral frontal; RNF = right non-frontal

Introduction
Patients with purely frontal lesions do not have classic amnesia. Damage in the frontal lobes in humans may, however, result in a variety of memory impairments, such as loss of source memory (Janowsky et al., 1989b; Johnson et al., 1993), disturbed memory for temporal order (Butters et al., 1994) and other complex aspects of memory that are sometimes considered metamemory or the ‘use’ of memories (Moscovitch, 1992). These deficits are secondary to defects in one or more executive functions, such as attention, working memory, strategy formulation, inhibition of competing recollections, and monitoring ongoing mental activity.

There is controversy about the extent of impairments that patients with frontal lobe lesions show in straightforward learning tasks that call for an uncertain amount of executive function. Group studies are required to determine possible regional differences in the effects of frontal damage. Of the few group studies reported, most have amalgamated lesions in all frontal regions into a single frontal group to be compared with a non-frontal group. Others have been assembled from patients of convenience in a particular clinic and have poorly represented the range of frontal regional injury. Most investigations of this question have used...
list-learning tasks, an appropriate approach, but with rare
exceptions (Janowsky et al., 1989a; Eslinger and Grattan,
1994) the lists were idiosyncratically crafted to explore
particular hypotheses about frontal lesions and memory. The
traditional neuropsychological instrument that has been most
studied is the Rey Auditory Verbal Learning Test, which
consists of 15 unrelated words. Eslinger and Grattan (1994)
and Janowsky et al. (1989a) found poor performance on the
Rey test in heterogeneous groups of patients with frontal
injuries. Both groups attributed poor performance primarily
to poor subjective organization during encoding of the lists.
In a previous report, we analysed the performance of patients
with frontal lesions, grouped a priori by coarse regional
differences, on an experimental list that was categorized and
unblocked (Stuss et al., 1994), i.e. the items are from a small
group of semantic categories but the words are presented
pseudorandomly so that items from the same category are not
presented sequentially. There were regional differences in
recall, recognition and error types. Poor subjective organ-
ization accounted for only a portion of the impairment.
Failure to take advantage of the potential for semantic
categorization did not contribute to poor performance.

We report the results of a new group of patients with frontal
lesions, who had well-defined and limited focal injury in a
wide range of discrete regions. These patients were compared
with patients with non-frontal lesions and with normal
controls on a standard presentation of the California Verbal
Learning Test (CVLT), another neuropsychological test of
learning and memory that is widely used in clinical neurol-
ogy. The CVLT differs from the Rey Auditory Verbal
Learning Test in that it is a categorized, unblocked list.

There were two goals for this research: to confirm the
distinctive profiles of memory impairment associated with
different regions of frontal injury using a previously
unexamined test (CVLT), and, if confirmed, to extend our
previous analysis of the effects of regional frontal injury on
verbal learning. If performance on the CVLT is comparable
to performance on the other list-learning tasks, combining
results reported on standard instruments (e.g. Eslinger and
Grattan, 1994) and experimental ones (e.g. Stuss et al., 1999),
four predictions can be made: (i) only lesions in a subset of
frontal regions will impair recognition; (ii) patients with
frontal lesions of all locations will have poor recall due to
deficits in secondary memory and subjective organization;
(iii) failure to demonstrate semantic clustering during recall
will not account for these impairments; and (iv) patients with
right dorsolateral lesions will have increased intra-list
repetitions of recall.

Methods
Patients were selected according to the following inclusion
criteria: (i) the aetiology was an acute event—infarction,
haemorrhage, traumatic contusion or resection of a benign
tumour; (ii) they were at least 2 months after onset (one
exception was 1.8 months) and had completely recovered
from any acute-phase complications; and (iii) CT or MRI
scans were available showing lesions entirely in frontal
structures or entirely in non-frontal structures. Patients were
all fluent English speakers. By report, some of the patients
had been mildly aphasic in the acute phase of injury, but none
of the patients were overtly aphasic at the time of testing. All
had fluent grammatical output without paraphasias, with
normal word and sentence repetition and normal auditory
comprehension. Some had mild deficits in confrontation
naming. They were excluded for uncorrected hearing loss,
recent seizures, untreated hydrocephalus, history of alcohol-
ism, symptomatic depression or prior unrelated neurological
illness. A total of 33 patients with frontal and 11 with non-
frontal patients fitted our criteria for study inclusion (see
below for lesion groupings).

A control group of 14 normal volunteers with no history of
neurological disease, psychiatric disorder or alcoholism were
recruited as controls. They were matched to the patient group
for gender, age and education. The study was approved by
The University of Toronto/Baycrest Centre research ethics
committee. Each participant was fully informed of the project
and signed consent was obtained.

Experimental measures
The CVLT was administered by the standard method (Delis
et al., 1987). Performance was measured as prescribed in the
standard clinical manner, and additional probes were imple-
mented to measure various specific memory processes not
routinely assessed by clinical scoring.

Immediate free recall
The CVLT consists of two different lists of words (A and B),
each list composed of 16 words, four words from four
different categories presented in a pseudo random manner.
List A is presented five times, List B once immediately after
List A fifth presentation recall.

For list A, the following measures were obtained: number
correct for each of the five trials and total correct for all five
trials summed. For list B, the total correct was noted for the
single presentation. The direct comparison of list A, first trial,
with list B assesses proactive interference.

Primacy and recency for recall were scored according to
the CVLT standards: primacy (first four items); middle
(interior eight items); recency (last four items). Primary
memory is the total recall of words for which the intra-trial
retention interval was seven words or fewer. Secondary
memory is the total recall of all words with intra-trial
intervals greater than seven (Tulving and Colotla, 1970). The
intra-trial retention interval is the total number of words
interpolated between presentation of a word and recall,
including words presented after the word or recalled before
the word.
Recognition performance
Recognition was assessed by performance on the target/distractor items at 20 min delayed recall. The CVLT discriminability and response biases were calculated. Hits, false alarms, and hits minus false alarms were also measured.

Delayed recall
For both immediate and long delay, correct words were measured in both free and cued recall conditions.

Errors and efficiencies
(i) Intrusions are ‘recalled’ words that were not actually on the list. They were measured for free and cued recall, and divided into semantic intrusions (words that were semantically related to a target word) and non-semantic intrusions. (ii) Intra-list repetitions are repetitions of a word within the same recall trial. They can be immediate perseverations or double recalls, i.e. words separated by other items. This analysis was corrected for the total number of words recalled on a trial. (iii) Inconsistency is the failure to recall a word on a later trial when it had been recalled on an earlier trial. This analysis also controlled for the total number of words recalled. This measure is the converse of the standard CVLT consistency score.

Organization in free recall
(i) Serial order recall is the number of words recalled in the same order as presented. A proportional measure was obtained by dividing the number of serial order clusters by the theoretically maximal number of order clusters, which in turn depends on the total number of words recalled. (ii) Semantic organization is measured as the number of consecutively recalled words from the same semantic category. The control for the number of words presented was completed by calculating a ratio of repetition measures (Frender and Doubilet, 1974). In the CVLT, this measure is calculated using the total number of words recalled, including intrusions and perseverations. We also calculated the semantic organization score as proposed by Stricker et al. (2002) for comparison. (iii) Subjective organization was measured by Pair Frequency Analysis (Sternberg and Tulving, 1977). This measure, which adjusts for the number of words recalled, tabulates the number of word pairs recalled together from one trial to the next.

Imaging
All scans (CT or MRI) were converted to standard templates (Damasio and Damasio, 1989). For patients with frontal lesions, individual subregions were identified as involved or not according to templates and methods described and implemented previously (Stuss et al., 1995). All patients with non-frontal lesions were classified simply as ‘left’ or ‘right’. Our goal was to isolate specific effects of lesions in different frontal regions on CVLT performance. Within the frontal lesion group, patients had various combinations of multiple regional damage. For each patient, imaging templates were examined for lesions in each area defined by Stuss et al. (1995), regardless of what other areas might also be involved.

Standard anatomical groupings can obscure more specific brain–behaviour relations. Our approach has been to use a modified case study group approach (Shallice, 1988; Stuss et al., 1994) in which patients are grouped by performance on a defined process, and the relation to lesion site is then sought. Using the architectonic divisions defined by Petrides and Pandya (1994) and superimposed on an adult human brain template, each architectonic region is identified for each patient as damaged or not. We then used a regression procedure, the Classification and Regression Tree (CART; Breiman et al., 1984), to identify the most precise and logical subgroups of lesions that had maximally separable performance on the primary measure. The total number of words recalled on all five trials of immediate free recall of list A of the CVLT was defined as the primary measure of memory. If a reasonable number of patients have pathology in regions of interest, then the relationship between a defined performance measure and each specific region can be calculated. This procedure splits a large heterogeneous lesion group into smaller discrete lesion groups that are homogeneous on the primary measure, avoiding ad hoc creation of regions of interest.

The CART analysis separated the frontal patients into five groups with distinct performances on the primary measure of list A total recall. There were 10 patients with left lateral lesions. The CART procedure separated them into two groups. The posterior left dorsolateral frontal (post. LDF) group (n = 5) was very homogeneous; one patient had only a large capsular–striatal lesion. In the group labelled ‘anterior left dorsolateral frontal’ (ant. LDF; n = 5) there was some involvement of medial polar areas, but all five patients had dorsolateral involvement generally centred a few centimetres anterior to the position in the post. LDF patients. The eight right dorsolateral frontal patients had lesions in dorsolateral structures, although four of the other eight had some involvement of medial structures. Each patient was assigned to a group based solely on the CART.

Although the original CART procedure did not distinguish two right frontal groups with distinctive performances on the criterion recall task, we divided the right dorsolateral frontal group into a posterior subgroup (post. RDF; n = 5) and an anterior subgroup (ant. RDF; n = 3) to create a parallel with the other frontal lesion groups. The anatomical parallels of the right and left dorsolateral groups are clear in Fig. 1. The majority of the 15 patients with medial lesions had bilateral lesions, which were symmetrical except as indicated in Table 1. One of the groups created by the CART analysis had lesions entirely restricted to the orbital and polar regions. None had septal lesions, any cingulate damage was very...
anterior, and only two had modest dorsolateral damage. Thus, we consider this group to be anterior, medial and polar frontal, left, right or bilateral (anterior medial frontal, AMF; \( n = 8 \)). The last group had a lesion distribution similar to that of the previous group, but the lesions were bigger, extending further in two directions. There was much more damage posteriorly along superior, medial structures. All seven had considerable cingulate damage. There was also septal damage in four of the seven. Thus, we consider this group to be anterior and posterior inferior medial and polar frontal, left, right or bilateral (posterior medial frontal, PMF; \( n = 7 \)).

The lesion overlaps in each patient group are displayed in Fig. 1 and the individual lesions are described in Table 1. We have labelled them by the dominant region involved. Not all patients had lesions in the cortex, so the cortical maps may under-represent the actual lesion extent. These groups have the maximally distinct profiles of performance on immediate free recall, but they are obviously less than perfectly distinct anatomically. The lesions of the groups do have different central foci, but there are individual patients within some of the groups with divergent lesions. Nevertheless, the groups constructed by performance on a cognitive test have reasonable anatomical coherence.

In summary, there were patients with right or left dorsolateral or with medial (unilateral or bilateral) frontal lesions, and each of these patient groups was further subdivided into those with more posterior or anterior lesions. That an independent statistical analysis of performance on a cognitive task generated five of these six groups and that the groups are generally coherent anatomically suggests that there are real differences in function within these groups. These six frontal subgroups were compared with two posterior lesioned control groups [right non-frontal (RNF; \( n = 5 \)); left non-frontal (LNF; \( n = 6 \)] and one normal control group (note that the posteriors were not entered into the CART) in all subsequent analyses.

Lesion size was computed by superimposing the lesion from templates to a constant pixel diagram and counting the pixels. The lesion total was divided by the total pixel count for all axial slices, giving a measure of the percentage of the brain involved. The lesion location, lesion size and time after onset for each patient are listed in Table 1.

**Results**

For all analyses, only results exceeding \( P < 0.01 \) will be reported.

**Neuropsychological measures**

There were no significant group differences for the National Adult Reading Test—Revised (NART-R) or forward digit span. The effect on the Boston Naming Test approached significance \([F(7,49) = 2.5, P < 0.03]\), the post. LDF group (\( \bar{x} = 39.4 \)) being significantly worse than the control group (\( \bar{x} = 55.5 \)). There was also a significant group effect on letter fluency (FAS) \([F(8,46) = 4.97, P < 0.001]\). The PMF (\( \bar{x} = 28.5 \)), ant. LDF (\( \bar{x} = 23.0 \)), post. LDF (\( \bar{x} = 16.5 \)) and RDF...
CVLT measures

Immediate free recall

List A, total five trials (Fig. 2). Recall that this effect was used to define the study groups and is a creation of the CART procedure. There was a significant group effect \(F(8,48) = 5.62, P < 0.001\). The post. LDF group performed the worst, all but the PMF, ant. LDF and post. RDF groups being significantly better. The CTL and RNF groups were also significantly better than the PMF and post. RDF groups.

List A, first trial. There was a significant group difference in the number of words recalled in the first trial \(F(8,48) = 5.62, P < 0.001\). The post. LDF and PMF groups were impaired compared with the RNF and CTL groups; the ant. LDF and post. RDF groups were impaired compared with the RNF group only.

List A, trial by group (see Figure 3). There was a significant group effect \(F(9,48) = 7.85, P < 0.001\), a significant effect for trials \(F(3,3,192) = 57.31, P < 0.001\) and a significant group \(\times\) trial interaction \(F(3,3,29.7) = 2.1, P = 0.002\). Post hoc analysis revealed that PMF and post. LDF were impaired compared with other groups. The RNF and CTL groups performed significantly better than the PMF and post. LDF groups on all five trials. AMF and ant. RDF had significantly higher scores than post. LDF on trials 2–5. The ant. RDF group was also significantly better the PMF group on trial 4. LNF was significantly better than post. LDF on trials 3–5. The LNF group primarily had problems on trial 1, having a significantly worse score than the RNF and CTL groups. Similarly, the ant. LDF group was significantly impaired compared with the RNF group on trial 1 only. AMF was better than PMF on trial 4. Post. RDF was impaired compared with RNF on trials 1, 2, and 4, the control group on trials 3 and 4, and the AMF group on trial 4. In addition to the deficits on individual trials, the post. LDF group had poor improvement over trials. There was a significant group difference in the learning slopes \(F(8, 48) = 2.9, P = 0.011\), the post. LDF group having the flattest curve \((\bar{x} = 0.42)\).

Primacy/recency and primary/secondary memory. There were no group differences in the standard CVLT measures for the serial position effect (primacy, middle or recency) when controlled for the number of words. There was also no group effect for primary memory (Sternberg and Tulving, 1977), but for secondary memory the group effect was significant \(F(8,48) = 7.73, P < 0.001\). Post hoc analyses revealed essentially the same group differences as the overall free recall scores on list A.

List B. There was a trend to a significant group effect \(F(8,48) = 2.71, P = 0.015\), the control group \((\bar{x} = 8.2)\) performing better than the post. LDF group \((\bar{x} = 3.4)\). Performance on list B was compared with the first trial of list A. There was a non-significant group \(\times\) list interaction, implying that a proactive interference effect was not present in any group.

Recognition memory

There was a significant hits minus false alarms group effect, indicating a recognition deficit in one or more groups \(F(8,48) = 4.81, P < 0.001\). Post hoc analysis indicated that the post. LDF group had a significantly lower score than all other groups except the post. RDF group. Since there was no significant group difference on recognition hits, this recognition deficit appears primarily to be secondary to the number of false alarms \(F(8,48) = 3.39, P = 0.004\). The post. LDF group had more than double the false positives of the second highest group (Fig. 4).

Both the CVLT discriminability and response bias scores were also analysed. There was a significant group discriminability difference \(F(8,48) = 4.81, P < 0.001\). The post. LDF group \((\bar{x} = 70.0)\) performed significantly worse than all other groups except the post. RDF group \((\bar{x} = 85.9)\).

Delayed free recall

Short delay. A significant group difference on short-delay free recall \(F(8,48) = 5.39, P < 0.001\) was similar to the immediate free-recall findings. The post. LDF \((\bar{x} = 2.8)\) group was significantly worse than the control \((\bar{x} = 11.5)\), RNF \((\bar{x} = 11.4)\) and ant. RDF \((\bar{x} = 11.7)\) groups, and the PMF \((\bar{x} = 5.1)\) group was significantly different from the control group. The significant group difference in short-delay cued recall \(F(8,48) = 4.59, P = 0.001\) also showed the same pattern, the PMF group \((\bar{x} = 6.7)\) being significantly different from the RNF group \((\bar{x} = 13.4)\).

Long delay. A highly significant group effect was obtained for long-delay free recall \(F(8,48) = 6.16, P < 0.001\), and the post hoc analysis of group differences was similar to that obtained for the immediate total free-recall analysis. The post. LDF group \((\bar{x} = 2.8)\) was significantly inferior to all groups except the PMF \((\bar{x} = 5.0)\) and ant. LDF \((\bar{x} = 8.6)\) groups, and the PMF group was worse than the AMF \((\bar{x} = 11.0)\), RNF \((\bar{x} = 12.4)\), ant. RDF \((\bar{x} = 12.7)\) and control \((\bar{x} = 11.5)\) groups. The long-delay cued recall was also similar \(F(8,48) = 5.08, P < 0.001\), with the post. LDF \((\bar{x} = 3.8)\) and PMF \((\bar{x} = 6.3)\) groups worse than the control \((\bar{x} = 11.6)\) and RNF \((\bar{x} = 13.4)\) groups and the post. RDF group worse than the AMF \((\bar{x} = 11.8)\) and ant. RDF \((\bar{x} = 12.3)\) groups.

Errors and efficiencies

Intrusions. There were no significant group differences.

Double recalls. There was no significant group effect using the CVLT measure of total perseverations across all trials \((P = 0.11)\).
<table>
<thead>
<tr>
<th>Patient group and subject number</th>
<th>Lesion location</th>
<th>Aetiology</th>
<th>Lesion size</th>
<th>Chronicity (months)</th>
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<tbody>
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<td>Anterior right dorsolateral frontal</td>
<td>Inferior medial, dorsolateral, ACG</td>
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<td>10.6 (12.2)</td>
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<td>3.4</td>
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<td>13.2 (13.4)</td>
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<td>Medial, septal, ACG</td>
<td>Stroke</td>
<td>7.43</td>
<td>59.8</td>
</tr>
<tr>
<td>2100</td>
<td>Medial, ACG, septal</td>
<td>Stroke</td>
<td>7.2</td>
<td>9.8</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td>4.3 (3.3)</td>
<td>15.8 (20.5)</td>
<td></td>
</tr>
<tr>
<td>Right non-frontal</td>
<td>Temporal</td>
<td>Lobectomy</td>
<td>2.06</td>
<td>89.3</td>
</tr>
<tr>
<td>2040</td>
<td>Occipital</td>
<td>Stroke</td>
<td>0.48</td>
<td>36.3</td>
</tr>
<tr>
<td>2055</td>
<td>Temporal</td>
<td>Haemorrhage</td>
<td>NA</td>
<td>55.3</td>
</tr>
<tr>
<td>2057</td>
<td>Temporal</td>
<td>Lobectomy</td>
<td>2.66</td>
<td>134.6</td>
</tr>
<tr>
<td>2103</td>
<td>Parietal, occipital (small)</td>
<td>Stroke</td>
<td>0.74</td>
<td>34.6</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td>1.5 (1.0)</td>
<td>70.0 (42.3)</td>
<td></td>
</tr>
<tr>
<td>Left non-frontal</td>
<td>Parietal</td>
<td>Stroke</td>
<td>NA</td>
<td>3.5</td>
</tr>
<tr>
<td>1058</td>
<td>Temporal, occipital</td>
<td>Stroke</td>
<td>0.95</td>
<td>28.5</td>
</tr>
<tr>
<td>2028</td>
<td>Temporal</td>
<td>Lobectomy</td>
<td>1.6</td>
<td>49.6</td>
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<tr>
<td>2032</td>
<td>Temporal</td>
<td>Lobectomy</td>
<td>NA</td>
<td>91.3</td>
</tr>
<tr>
<td>2036</td>
<td>Temporal</td>
<td>Lobectomy</td>
<td>1.17</td>
<td>144.7</td>
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<td>2038</td>
<td>Temporal</td>
<td>Lobectomy</td>
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<td>142.6</td>
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<tr>
<td>Mean (SD)</td>
<td></td>
<td>1.2 (0.3)</td>
<td>76.7 (59.3)</td>
<td></td>
</tr>
</tbody>
</table>

L = left; R = right; ACG = anterior cingulate gyrus; SM = superior medial.
Inconsistency. When the inconsistency score was taken as a proportion of the total correct words recalled, there was a significant group difference $[F(8,48) = 6.26, P < 0.001]$. The post. LDF group ($\bar{x} = 46.3$) had a significantly higher inconsistency score than all groups except the post. RDF ($\bar{x} = 36.0$) and PMF ($\bar{x} = 31.7$) groups, and the PMF group was significantly worse than the control group ($\bar{x} = 10.4$).

**Organization**

*Serial order recall.* The CVLT serial cluster ratio for number of words recalled in the same order as presented showed no significant group effects ($P = 0.278$).

*Semantic categorization.* There was no significant semantic categorization effect when we controlled for the number of words presented ($P = 0.226$). Controlling for the total possible semantic clusters presented (Stricker et al., 2002), there was also no significant group effect ($P = 0.312$).

*Subjective organization.* For comparison with our earlier study (Stuss et al., 1994), we first evaluated all frontal patients relative to non-frontal and control groups. The frontal group was significantly impaired compared with controls (Fig. 5) $[F(2.53) = 7.98, P = 0.001]$. There was also a significant group effect in the nine-group analysis ($P = 0.007$), the post. RDF group having a significantly worse subjective organization score than the control group.

**Test correlations**

No correlational results met the level of significance established *a priori*. Several approximated significance, and are presented for future research and as a potential mechanism underlying memory problems in some of the patient groups. Total correct recall and recognition scores (hits minus false alarms) had very few correlations with any neuropsychological result. For the PMF ($r = 0.95, P = 0.011$) and ant. LDF groups ($r = 0.93, P = 0.02$) there was a correlation of recognition memory and digit span backwards. For the post. LDF group, total correct in recall correlated with letter fluency (FAS) ($r = 0.97, P = 0.035$), and recognition (hits only) correlated with the Boston Naming Test ($r = 0.93, P = 0.02$).

**Discussion**

Patients with frontal lesions may show difficulties with any aspect of an unstructured list-learning task, but there is no single frontal lobe syndrome of memory impairment. There are distinctions with lesions in different frontal subregions. This study has demonstrated important new frontal anatomical functional divisions. In addition to left–right differences, there are distinctions within the left lateral, right lateral and ventral medial regions.

Immediate free recall was impaired primarily in patients with post. LDF lesions, but also in those with PMF lesions, usually bilateral, involving the septal region, and to a lesser degree in those with post. RDF lesions. The demonstration that delayed free recall, both short and long, was also impaired after post. LDF and PMF lesions reinforces the conclusion that damage to these areas, uniquely among frontal lesions, impairs recall. Many patients with frontal lesions may show slow improvement in learning across trials, but performance is fairly normal by trial 5 and in delayed recall. This is not the case for those with post. LDF and PMF lesions.

For recognition memory, only the post. LDF group was impaired. The deficient performance was entirely due to false-positive endorsements of foils. The standard CVLT measure for recognition also isolated the post. LDF group. The post. LDF group demonstrated abnormal bias. If a criterion distinction is required, this group appeared to default to the posture that everything is a target. We documented a similar bias problem in left frontal patients using a reaction time task (Stuss et al., 2002). In the present study this bias may reflect defective semantic encoding, producing only a
general semantic sense to guide the construction of a criterion.

Where do the inefficiencies in learning and the defective overall learning in some groups arise? There are several reports on the performance of patients with frontal lesions on list-learning tasks, but they have limited power to account for specific regional effects of frontal injury. Some studies simply placed all patients with frontal lesions into a ‘frontal’ group and compared that group with a control group of normals or subjects with another type of non-frontal injury (Jetter et al., 1986; Janowsky et al., 1989a; Eslinger and Grattan, 1994; Gershberg and Shimamura, 1995; Kopelman and Stanhope, 1998). Within these ‘frontal’ groups, lesion locations were often limited to the primarily dorsolateral and superior and medial lesions (Incisa della Rocchetta, 1986; Incisa della Rocchetta and Milner, 1993). One explicitly rejects a role of semantic deficits (Vilkki et al., 1998). None of these studies used, however, a direct measure of semantic or lexical function. The studies that conclude that frontal lesions impair encoding (Janowsky et al., 1989a; Incisa della Rocchetta and Milner, 1993; Eslinger and Grattan, 1994; Gershberg and Shimamura, 1995) emphasize deficits in organization or categorization or clustering. If the distinctive effects of lesions in different frontal regions that we have demonstrated are correct, it is not surprising that studies that did not respect regional differences did not find them. In an earlier study by our group using an experimental test (Stuss et al., 1994), analysis of patients by regional lesion groups demonstrated that different regions were associated with different patterns of, and neural mechanisms for, impairment. Our investigation largely supports our original hypotheses, but also makes important new anatomical differentiations. Lesions in different regions of the frontal lobes affect list learning. Encoding, monitoring, discrimination and bias differ between groups. ‘Strategic’ deficits in learning are seen in most groups.

Recall

Left dorsolateral lesions, centred on areas 44, 9 and 46, have the most potent effects on recall, and these effects are correlated with (and perhaps embedded in) the semantic/lexical residuals of these lesions (decreased naming and verbal fluency), even when the residuals are very mild. Non-frontal left lesions that impair semantic and lexical capacities also impair verbal learning (Ween et al., 1996). Medial lesions that include the septum may also impair recall. The cognitive process that underlies poor memory in this group is not clear, but the anatomical basis is likely to be loss of cholinergic projections to the hippocampus.

Double recalls are another form of defective recall. In this experiment, double recalls were not significantly increased in any group. The ant. LDF ($\bar{x} = 10.6$) and the post. RDF ($\bar{x} = 9.6$) groups showed a trend to significance ($P = 0.11$), with double recall rates approximately twice those of the controls and the next highest patient group. In our earlier study (Stuss et al., 1994) there was a significant increase in double recalls in the right frontal group, approximately equivalent to the post. RDF group of the present study, and a trend to an increase in the left frontal group. Although the two studies do not unequivocally demonstrate propensity to double recalls in any group, the trends are consistent and the lack of significance may be due to inadequate numbers of subjects. Deficient free recall was not due to proactive interference, at least as measured by the standard comparison of list B with list A, first trial. It could also not be attributed to an abnormal serial position effect or to defective primary memory capacity. The demonstration that impaired secondary memory profiles exactly parallel the free-recall results becomes, in this context, little more than a redundant statement that there is a free-recall defect.
The rate of false-positive endorsements is highly associated with the characteristics of the presented materials and the interactions of these factors, there can be considerable variability in false-positive endorsements. In the present experiment, some combination of a low proportion of items in each category in the total list (25%), unblocked presentation, highly associated targets, high foil frequency (50%) and instructions appears to have suppressed false recognition in the right frontal group and altered bias in the post. LDF group. Tasks with more manipulations and tighter distinctions of semantic foils might clarify this.

The use of empirically derived anatomical subgroups appears vindicated. The groups were reasonably homogeneous anatomically and they appeared to fit common regional distinctions of connectivity. Simple comparison of left, right and bilateral groups would have revealed none of these distinctive regional effects.

Future analyses of verbal memory in patients with frontal lesions must be driven by anatomical subgroups; simply assembling a group of ‘frontal’ lesions, even divided according to the hemisphere involved, does not address the functional heterogeneity of the frontal lobes. This conclusion is amply reinforced by similar findings of important regional effects on all standard neuropsychological tasks (Stuss et al., 1998, 2000, 2001a, b). It is also supported by recent imaging studies in normal subjects. The original demonstration of hemispheric asymmetries in memory only emphasized the left/encoding and right/retrieval differences. More recent studies have increasingly parsed the frontal lobes into smaller regions and demonstrated more specific relationships between discrete elements of memory (monitoring (Shallice, 1999), working memory (D’Esposito et al., 1995; Petrides 1995a), semantic activation (Petrides, 1995b), retrieval effort and retrieval success (Fletcher, 2001)) and very discrete regions of frontal activation. Lesion studies have not found the same elegant anatomical distinctions (Swick and Knight, 1996) as functional imaging, probably because lesion studies are hugely more difficult to control for many variables that affect the anatomical relationships of memory, such as the chronicity of damage and the exact site of injury. Many lesions affect multiple functional regions of the frontal lobes, and even two apparently equivalent lesions of the cortex may differ dramatically in their deep extent, producing very different patterns of regional disconnection and presumably of functional impairment. Nevertheless, this study demonstrates that careful attention to the regional anatomy of frontal lobe lesions can illuminate the processes that may be impaired in memory and learning.

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