*Journal of the International Neuropsychological Society* (1998), **4**, 265–278.


# The effects of focal anterior and posterior brain lesions on verbal fluency

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(RECEIVED May 2, 1997; REVISED August 27, 1997; ACCEPTED September 18, 1997)

**Abstract**

Seventy-four patients with focal brain lesions were compared to a neurologically normal control group on tasks of letter-based and category-based list generation. When patients were divided only by right frontal, left frontal, or nonfrontal lesion sites, the pattern of fluency impairments confirmed prior claims. When more precise lesion sites within the frontal lobes were compared between groups classified based on their fluency performance, much more specific brain–behavior relations were uncovered. Damage to the right dorsolateral cortical or connecting striatal regions, the right posterior area, or the medial inferior frontal lobe of either hemisphere did not significantly affect letter-based fluency performance. Superior medial frontal damage, right *or* left, resulted in moderate impairment. Patients with left dorsolateral and/or striatal lesions were most impaired. Left parietal damage led to performance relatively equivalent to the superior medial and left dorsolateral groups. The same lesion sites produced impairments in category based fluency, but so did lesions of right dorsolateral and inferior medial regions. Task analysis and correlations with other measures revealed that different cognitive processes related to different brain regions underlie performance on verbal fluency tests. (*JINS*, 1998, *4*, 265–278.)

**Keywords:** Verbal fluency, Frontal lobes, Hemispheric asymmetry, Brain function localization

## INTRODUCTION

Verbal fluency tasks have been used to test the effects of focal brain lesions on various cognitive processes. In one task, letter-based fluency, performance is assessed by requesting oral or written generation of words beginning with a defined letter (e.g., *F*, *A*, or *S*) over a limited period of time (usually 1 min). In a second task, category or semantic fluency, the participant produces as many words as possible from an identified category (e.g., animals, fruits), within a defined time period.

Most neuropsychological studies have demonstrated that left frontal lesions produce the greatest impairments on letter-based fluency tasks (Hécaen & Ruel, 1981; Janowsky et al., 1989; Milner, 1964; Perret, 1974; Ramier & Hécaen, 1970). Even studies that have not found a significant deficit after left frontal pathology have shown trends in that direction (Bornstein, 1986; Butler et al.,1993; Pendleton et al., 1982; Vilkki & Holst, 1994). This brain–behavior (left-frontal-lobe–fluency–activation) relation found in patient populations is supported by convergent evidence from fluency activation studies in normal individuals (Cantor-Graae et al., 1993; Cuenod et al., 1995; Frith et al., 1991a,b; Petersen et al., 1988; Warkentin & Passant, 1993; Wise et al., 1991).

The literature does not, however, unequivocally support the specificity of a left frontal basis for letter-based fluency. In several neuropsychological studies, fluency performance in patients with right frontal pathology has also been at least somewhat diminished (Benton, 1968; Bruyer & Tuyumbu, 1980; Butler et al., 1993; Miceli et al., 1981; Ramier & Hécaen, 1970). If the frontal lobes are essential for fluency

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(perhaps left greater than right), there is no agreement as to what subregions within the frontal lobes are most critical. Walsh (1985) emphasized the importance of the medial frontal regions. Milner (1964) suggested that the left inferior lateral frontal region, anterior to Broca's area, is most critical. Stuss et al. (1986) reported normal verbal fluency performance in patients with prefrontal leucotomies indicating that frontal polar systems, at least, are probably not essential.

There are other neuropsychological studies that have not found lesions of the frontal lobes to be particularly critical for fluency performance. Some studies suggested impaired fluency only with diffuse brain impairment (Boller, 1968; Borkowski et al., 1967; Pendleton et al., 1982; Vilkki & Holst, 1994). Others demonstrated hemispheric asymmetries for fluency without specific frontal significance; some emphasizing the relative importance of the left hemisphere (Bornstein, 1986; Hécaen & Ruel, 1981; Miceli et al., 1981; Newcombe, 1969), others the right (Joanette & Goulet, 1986). Thus, different investigators have proposed that fluency performance depends on either focal or diffuse regions and, if focal, either frontal or nonfrontal and if frontal, either lateral or medial, but if diffuse, either right or left predominant. Not surprisingly, therefore, other investigators have proposed a distributed systems approach (Cuenod et al., 1995; Frith et al., 1991b; Hermann & Wyler, 1988; Martin et al., 1990; Parks et al., 1988).

There are several factors that may be confounding the specificity of the relationship of the frontal lobes to letter-based fluency: (1) the absence of appropriate comparison groups (e.g., many neuropsychological studies did not use participants with posterior lesions); (2) the chronicity of the disorder (see Loring et al., 1994); (3) the precise localization of the lesions; (4) differences in etiology; (5) use of different dependent measures; (6) differences in several moderator variables such as age, education, stage of recovery; and (7) the presence of any aphasic disturbance (Bolla et al., 1990; Ramier & Hécaen, 1970; Reitan & Wolfson, 1994).

Semantic or category fluency has not been extensively studied in patients with focal lesions, but the literature suggests a slight difference in critical brain regions compared to letter-based fluency. This implies that different processes might be required for the semantic task. Laine and Niemi (1988) found that patients with left frontal pathology were significantly worse than those with right frontal lesions on semantic fluency. Grossman (1981) reported that left-hemisphere-damaged lesion patients, fluent or nonfluent aphasics, had significantly fewer semantic clusters than those with right hemisphere lesions. Very few lesion studies have directly compared letter-based and semantic fluency, and none provide specific lesion-location–performance comparisons. There is some evidence that letter-based fluency is more impaired after frontal lesions than is semantic fluency (Coslett et al., 1991; Milner, 1964; Perret, 1974) and that semantic fluency is more sensitive to temporal pathology (Newcombe, 1969), but Owen et al. (1990) found that patients with frontal lesions were impaired on both types of fluency tasks. Joanette and Goulet (1986), comparing right and left hemisphere CVA patients, found that right hemisphere lesions caused impaired semantic fluency compared to a control group, perhaps reflecting an additional contribution of the right hemisphere to lexical–semantic processing. They did not find a rostral–caudal effect for either letter-based or semantic fluency tasks.

Whatever the evidence from focal lesion research, there is other evidence of a considerable functional dissociation between letter-based and semantic fluency tasks. Greater impairment on semantic fluency compared to letter-based fluency tasks was observed in patients with Alzheimer's disease (Monsch et al., 1994; Patterson et al., 1996, for reviews). M. Alexander (1997) demonstrated profound loss of semantic fluency despite preserved letter-based fluency in a patient with hypoxic brain disease with SPECT evidence for bilateral (left $>$ right) temporal lobe impairments. Moscovitch (1994) found that letter-based but not semantic fluency was reduced by concurrent sequential finger tapping in normal individuals. This finding suggests that the letter-based fluency task demands more effort, perhaps requiring more frontal lobe modulation of attention and strategy development, than semantic fluency. Category-based fluency, on the other hand, may be more sensitive to nonfrontal regions (particularly in the left temporal lobe), because of greater linguistic demands for semantic retrieval.

We had two general objectives in extending the study of these two verbal fluency tasks. The first was to reassess the specificity of the letter-based and semantic fluency measures as indicative of involvement of specific brain regions by studying a relatively large number of patients with circumscribed single lesions. Our hypothesis: Letter-based fluency would be reduced with lesions of either right or left frontal lobe damage and semantic fluency would be reduced with lesions of the left nonfrontal regions, perhaps with the greatest impairment secondary to lesions in the left temporal lobe. Within this general objective of defining more explicitly the brain–behavior relations of verbal fluency in individuals with focal lesions, we anticipated clarifying the role of the right hemisphere in letter-based fluency. We also wished to reexamine the possibility that the right hemisphere impairment in semantic fluency postulated by Joanette and Goulet (1986) was restricted to the right frontal or posterior regions. As a method for defining brain–behavior relations, we planned to follow our previous approach and use test performance as the independent variable, to determine if more specific anatomical regions or systems were related to performance differences (Stuss et al., 1994a).

Our second general objective was to examine potential mental processes underlying overall fluency measures of performance. Verbal fluency tasks, as with many neuropsychological measures, are coarse instruments and do not address the component processes required to complete the task. Individuals may obtain the same final score, but do so for different reasons. Task analysis suggested that four different processes may be required, and potentially may be related to distinct brain regions. First, language functioning clearly

is involved; as such, left frontal and left nonfrontal pathology would result in impairment. We were uncertain as to the role of less semantic based language capabilities, although the literature did imply that the right hemisphere was relevant. Capacity to initiate word production is clearly necessary in a timed task. The most salient region for this initiation function was hypothesized to be the left medial frontal region. There were no *a priori* reasons to indicate a dissociation within the superior and inferior medial structures. Second, because of the need to produce words for 1 min, sustained effort in production is necessary. One possible brain region would be the right frontal area, implicated in sustained attention (see Stuss et al., 1994b, for review). Third, since participants have to keep a running account of what they produced and what they are supposed to produce, we expected some role of a basic working memory function. Finally, retrieval strategies would affect results. Our hypothesis here was that impairment, if present, would occur after frontal but not nonfrontal brain damage.

## METHODS

### Research Participants

A total of 74 patients with focal lesions in frontal and nonfrontal brain regions were recruited from neurosurgery, neurology, and rehabilitation centers in Ontario and Massachusetts, and control participants from the Rotman Research Institute participant pool. The project was approved by a University of Toronto Scientific and Ethics Review Committee at Baycrest Centre, and signed consent forms to participate were obtained from all participants. All patients had CT or MRI scans available for review. To be included each patient's scan had to demonstrate a single lesion limited to frontal, striatal, or nonfrontal structures. In a few patients a very minor overlap of frontal and nonfrontal structures or a minor secondary lesion were observed but allowed. As would be expected by the lesions, the study included patients with language disturbance. This is evidenced by the results on the Boston Naming Test (Kaplan et al., 1983). All patients had fluent, grammatical language output, with some having mild word-finding problems. None had significant communication problems. None had any speech production deficits (dysarthria, apraxia, etc.) Patients with severe aphasia were excluded. The Token Test (Boller & Vignolo, 1966; maximum score = 44) results indicate that all had adequate comprehension. This patient selection enabled us to investigate the effects of mild linguistic deficits such as naming problems on verbal fluency.

All scans were analyzed by two raters (C.P. and M.P.A.), who were blind to experimental results. Lesions were localized with standard atlases and transferred to template according to the method of Damasio and Damasio (1989). Assembling patient groups that adequately represent all frontal structures cannot be accomplished if only patients with single infarctions are used. The use of nonstroke patients or patients with more than one stroke may create pathophysiological differences among subgroups of frontal cases. Despite these problems, in our prior work we were able to demonstrate specific effects of brain regions on memory and to demonstrate that etiology was not a significant factor in the results (Stuss et al., 1994a). Patients with paramedian lesions had more mixed etiologies, with a higher proportion of patients with bilateral lesions and a broader range of lesion sites. Patients with resected meningiomas or low-grade gliomas were scattered in all groups. For all patients with frontal lesions, involvement of various subregions was noted according to the model of Stuss et al. (1995). The same raters decided by consensus if the frontal lesion involved dorsolateral frontal or striatal, superior medial or inferior medial structures. These specific brain regions were used for the differentiation of the participants by performance.

All patients were tested at least 3 months postonset to be certain that all transient pathophysiologic disturbances such as edema and hemorrhage had cleared. A group of control participants ($N = 37$) without neurological or psychiatric disorder, matched as closely as possible in mean age and education to the other groups, were tested for comparison. The demographic data (with occasional missing values) for all groups are presented in Table 1. Ninety-three percent of the participants were right-handed or ambidextrous. Removing the left handers did not alter the results. For demographic purposes, patients were originally classified into *right frontal* (19), *left frontal* (20), *bilateral* (15), *right nonfrontal* (9), and *left nonfrontal* (11) groups. There was no significant group effect of age. There was a significant group effect of education [$F(5, 105) = 4.04$, $p < .01$], with the control group having significantly more education than the bifrontal and right frontal groups, and the left frontal group more than the bifrontal group. The Digit Span forward and the National Adult Reading Test (NART; Nelson & O'Connell, 1978) presented information on basic abilities of each group. There was no significant difference for Digit Span forward. There was a significant group difference on the NART [$F(5, 101) = 8.6$, $p < .01$], with the control group being significantly greater than all groups except the right nonfrontal group, and this group having a significantly higher NART than the bifrontal group. Basic language processes, independent of fluency, were measured with the Boston Naming Test and the Token Test. Working memory was measured by Digit Span backwards. These last three tests were used to investigate potential differences in processes underlying performance on the fluency tests. The lesion location and etiology of the patient participants are detailed in Table 2.

### Tasks

Two verbal fluency tasks were administered to all the participants. The *letter-based* fluency task was that described by Benton and Hamsher (1976). Participants were required to generate orally as many words as possible that begin with the letters *F*, *A*, or *S* (1 min each). They were instructed not to give names of people or places, and not just to add pre-

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**Table 1.** Demographic data for the participant groups

| | Right frontal | | Left frontal | | Bifrontal | | Right nonfrontal | | Left nonfrontal | | Control | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Variable | *M* | *SD* | *M* | *SD* | *M* | *SD* | *M* | *SD* | *M* | *SD* | *M* | *SD* |
| Age | 52.7 | 12.4 | 57.8 | 10.2 | 50.4 | 12.7 | 49.3 | 14.4 | 50.4 | 15.0 | 54.4 | 14.4 |
| Education | 11.8 | 2.7 | 13.5 | 3.0 | 10.7 | 2.9 | 13.2 | 3.4 | 12.7 | 1.1 | 13.9 | 2.3 |
| Boston Naming | 51.4 | 7.6 | 50.3 | 7.8 | 49.7 | 8.3 | 56.9 | 2.7 | 47.9 | 8.4 | 55.5 | 4.1 |
| Digit Span forward | 5.7 | 1.3 | 6.2 | 1.1 | 6.4 | 1.2 | 7.2 | 1.0 | 6.2 | 1.5 | 6.9 | 1.4 |
| Digit Span backward | 4.8 | 1.5 | 4.1 | 1.3 | 4.1 | 0.9 | 5.9 | 1.8 | 4.4 | 1.7 | 5.7 | 1.4 |
| Digit Span total | 10.7 | 2.6 | 10.4 | 2.1 | 10.7 | 1.7 | 13.1 | 2.4 | 10.6 | 2.7 | 12.8 | 2.2 |
| NART | 104.2 | 9.8 | 104.5 | 9.2 | 100.0 | 9.6 | 110.4 | 7.8 | 102.8 | 7.9 | 113.8 | 6.1 |
| Token | 41.9 | 3.0 | 41.4 | 3.7 | 41.1 | 4.3 | 44.0 | 0.0 | 41.0 | 2.4 | 42.8 | 1.5 |
| Number male | 10 | | 14 | | 10 | | 6 | | 3 | | 19 | |
| Number female | 9 | | 6 | | 5 | | 3 | | 8 | | 18 | |

fixes or suffixes to create a different word (e.g., *fool*; *fools*). In the *semantic* fluency task, participants were asked to generate as many names of animals as possible over a 1-min period.

## Dependent Measurements

The following measurements were taken for each subject for each of the two tasks.

1. *Generation*: Number of correct words generated in each 15-s period, as well as over the total 60 s. For the letter-based fluency task, these were summed across all three letters.
2. *Errors*: Total number of errors: Although several error measures were recorded (e.g., perseverations, use of proper names, nonwords, and alternate forms), the number within each error type was limited, and therefore all errors were combined for analyses.
3. *Clustering*: The procedure used for scoring the number of semantic and letter-based clusters was adapted from Laine and Niemi (1988). Within each task, both semantic and letter-based word clusters were defined. In the letter-based fluency task, letter-based word clusters were defined as two or more words beginning with at least the same first two letters (e.g., *fa*t, *fa*st). The semantic clusters within the letter-based fluency task were broadly defined as related to each other by meaning, as described by one of the following categories: synonyms (e.g., *fabulous*, *fantastic*); associative (e.g., *sun*, *sky*); semantic category (e.g., *skirt*, *slacks*). In the semantic fluency task, letter-based clusters were defined as words beginning with the same letter or letters (e.g., *pig*, *panda*). Semantic clusters in the animal generation task were defined as two or more successive words belonging to one of the following subcategories: pets, farm animals, forest animals, desert animals (including African *or* Australian), exotic animals, birds, reptiles–lizards–frogs, insects, rodents, aquatic animals–fish. Different terms for the same animal (e.g., *hog*, *pig*), and specific examples (e.g., *bird*, *bluebird*) were not classified as semantic clusters. Two judges scored the clusters, and only those clusters mutually agreed upon were counted. For each task, the mean semantic–letter-based cluster size, and the percentage of clustered words to the total number of words produced, were analyzed.

# RESULTS

Normative data for three age groups (21–39; 40–64; 65–81 years) for both tests, broken down by gender, are provided in the Appendix for basic clinical purposes. There were no consistent correlations of performance with education, or the NART, across the different experimental groups. Further analyses involving education and NART are therefore not presented in the results.

## Patients Grouped by Standard Lesion Site Analyses

These data are schematically illustrated (see Figure 1) and described for comparison to previous research and to establish a framework for our more specific anatomical analyses. When lesion location is defined according to coarsely defined standard regional definitions such as the right or left frontal or nonfrontal regions, significant group differences are observed. Damage to the left hemisphere, frontal or nonfrontal, affects both letter-based and semantic fluency. Patients with right frontal damage are mildly impaired in letter-based fluency tasks and more impaired in the semantic fluency task, even though letter-based fluency is more difficult. Damage to right nonfrontal regions does not affect performance on either fluency task. Damage involving the left frontal area resulted in the greatest number of errors in comparison to total production. These errors could not be differentiated according to type because of the

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**Table 2.** Lesion location and etiology within patient groups

| Participant no. | Etiology | Lesion location |
|---|---|---|
| | Right frontal lobe | |
| 1041 | Lobectomy | Dorsolateral, inferior medial |
| 1054 | Tumor | Dorsolateral, inferior medial |
| 1067 | Stroke | Dorsolateral |
| 1068 | Stroke | Dorsolateral, striatal |
| 2001 | Stroke | Dorsolateral, striatal |
| 2018 | Stroke | Dorsolateral, striatal |
| 2024 | Stroke | Dorsolateral, striatal |
| 2027 | Stroke | Dorsolateral, striatal |
| 1064 | Stroke | Striatal |
| 2052 | Stroke | Striatal |
| 2006 | Stroke | Striatal, inferior medial, septal |
| 2005 | Tumor | Medial, dorsolateral |
| 2019 | Trauma | Medial, dorsolateral, temporal |
| 2011 | Stroke | Superior medial |
| 2044 | Tumor | Superior medial |
| 2048 | Infarct | Superior medial |
| 2059 | Stroke | Superior medial |
| 1055 | Infarct | Superior medial, dorsolateral |
| 2047 | Stroke | Inferior medial |
| | Left frontal lobe | |
| 1053 | Trauma | Dorsolateral |
| 1071 | Stroke | Dorsolateral, parietal |
| 1081 | Hemorrhage | Dorsolateral |
| 2023 | Stroke | Dorsolateral, occipital |
| 2046 | Stroke | Dorsolateral |
| 2056 | Tumor | Dorsolateral |
| 2071 | Stroke | Dorsolateral, striatal |
| 1079 | Stroke | Striatal |
| 2012 | Tumor | Striatal, superior medial |
| 2050 | Stroke | Striatal |
| 2063 | Stroke | Striatal, superior medial, parietooccipital |
| 2067 | Stroke | Striatal |
| 2075 | Stroke | Striatal |
| 2079 | Hemorrhage | Striatal |
| 2058 | Tumor | Medial, dorsolateral |
| 2073 | Hemorrhage | Medial |
| 2100 | Stroke | Medial, septal |
| 1056 | Stroke | Inferior medial |
| 2049 | Hemorrhage | Inferior medial |
| 2102 | Trauma | Inferior medial, dorsolateral |
| | Bilateral frontal lobe | |
| 1059 | Trauma | Medial |
| 1060 | Stroke | Medial |
| 1073 | Trauma | Medial, dorsolateral (right) |
| 1075 | Hemorrhage | Medial |
| 2002 | Infarct | Medial, dorsolateral |
| 2045 | Stroke | Medial, septal |
| 2069 | Stroke | Superior medial, dorsolateral (right) |
| 1065 | Trauma | Inferior medial |
| 1069 | Tumor | Inferior medial |
| 1070 | Stroke | Inferior medial |
| 1077 | Trauma | Inferior medial |
| 2013 | Stroke | Inferior medial, septal |
| 2014 | Stroke | Inferior medial |
| 2042 | Trauma | Inferior medial |
| 2053 | Trauma | Inferior medial (right), dorsolateral (left) |
| | Right nonfrontal regions | |
| 2008 | Tumor | Temporal, parietal |
| 2021 | Stroke | Temporal, occipital |
| 2040 | Lobectomy | Temporal |
| 2055 | Hemorrhage | Temporal |
| 2057 | Lobectomy | Temporal |
| 2025 | Stroke | Parietal |
| 2065 | Stroke | Parietal |
| 2103 | Stroke | Parietal |
| 2043 | Stroke | Occipital |
| | Left nonfrontal regions | |
| 1058 | Stroke | Parietal |
| 2010 | Stroke | Parietal |
| 2016 | Stroke | Parietal |
| 2031 | Stroke | Parietal |
| 2061 | Stroke | Parietal, occipital |
| 2077 | Stroke | Parietal |
| 2028 | Stroke | Temporal, occipital |
| 2032 | Lobectomy | Temporal |
| 2036 | Lobectomy | Temporal |
| 2038 | Lobectomy | Temporal |
| 2054 | Lobectomy | Temporal |

relatively small numbers. An analysis of the logged data in the pattern of production of words over time indicated that the control and right nonfrontal groups were equivalent for both tasks (see Figure 2). The bifrontal and left frontal groups produced less over time in the letter-based fluency task; the bifrontal and right frontal groups dropped more in output over time in the semantic fluency task. There was no indication in our strategy analyses of group differences when the proportion of clusters to total output was analyzed. These data essentially replicate previous findings.

## Patients Grouped by Fluency Performance

Compared to other studies of this type, the sample size of our groups is relatively large, increasing the stability of the group comparisons. Such group analyses, however, could

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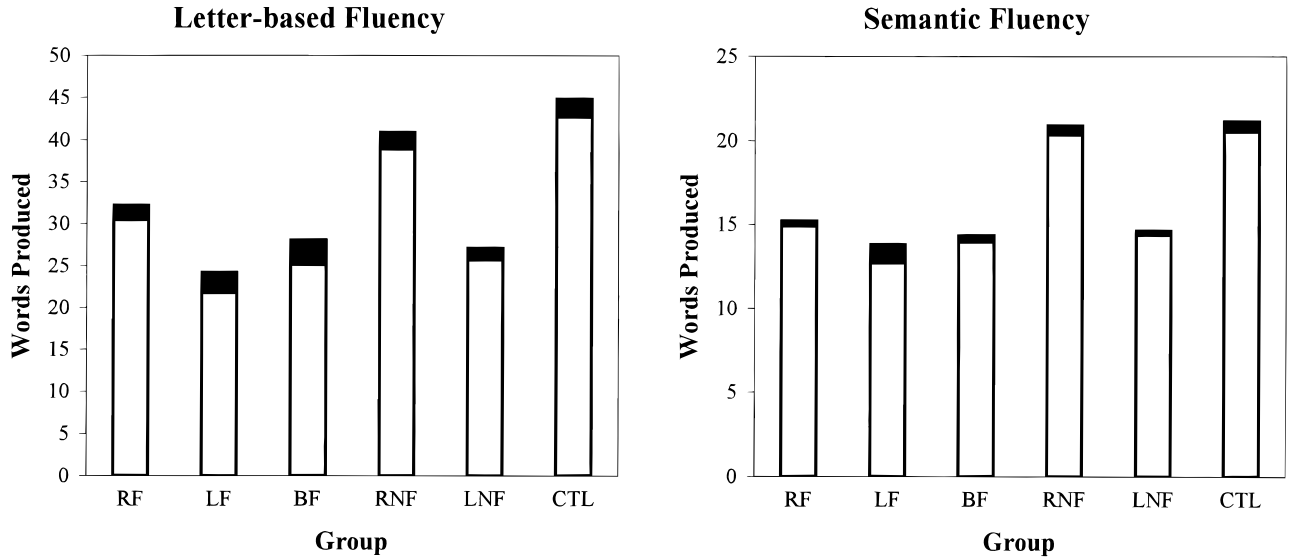


**Fig. 1.** The total number of words produced for all three letters (*F-A-S*, left) and for a specific category (animals, right) are presented for each of the groups studied. Each total production score is divided into the number of acceptable words produced (clear) and nonacceptable words or errors (stippled). Error types are defined in the text.

obscure more specific brain–behavior relations. Standard deviations indicated significant variability, particularly in the patient groups. In each patient group, some patients were significantly impaired, while others performed as well as or better than many control participants. We (Stuss et al., 1994a) have advocated a modified case-study–group approach in which patients are grouped by their performance on the experimental task without regard to lesion site. Determinants of that performance are then sought. Potential determinants are based on current research. In order to discover the most precise and logical anatomical groupings that would maximize performance differences among groups, for each patient each frontal brain area as defined earlier was coded as 1 (*damaged*) or 0 (*not damaged*). We then used a regression technique to classify patients into new anatomical groupings that would provide the most separable performance-based categories possible on the particular fluency test [classification and regression trees (CART); Brieman et al., 1984]. There were two limiting factors in the use of this method of regrouping the patients: the sample size, and the presence of multiple regions of pathology in several patients. For example, it was possible that, if a group of patients with a similar performance level had had inferior medial damage, a patient with additional small right dorsolateral damage might have been classified in a right dorsolateral group. To maintain some logical consistency in these cases, we reclassified a small percentage of patients (11%) into the groups representing their maximum area of pathology. The overall process was repeated for the patients with posterior lesions, using the brain localization classification of left or right temporal or parietal regions. The new final groupings were then tested to see if brain–behavior relations were improved. The new groups (2 patients' scans, 1 frontal and 1 posterior, could not be found for this detailed anatomical analysis, and were subsequently omitted) formed by this CART method were (1) left or right frontal dorsolateral and/or lenticular striate regions (*LDL*, $N = 14$; *RDL*, $N = 11$); (2) superior medial frontal involvement from either left frontal, right frontal, or bifrontal damage (*SM*, $N = 17$); (3) inferior medial involvement from either left frontal, right frontal, or bifrontal damage (*IM*, $N = 11$); (4) left temporal damage (*LT*, $N = 5$); (5) left parietal involvement (*LP*, $N = 5$); and (6) right nonfrontal involvement (*RNF*, $N = 9$; see Figure 3).

## *Letter-based fluency*

Using the new groupings, there was a significant group effect for letter-based fluency [$F(7,101) = 14.18$, $p < .001$] but the brain–behavior relationships were now more specific than in the previous analyses (see Figure 4). *Post-hoc* analyses revealed that the control and RNF groups had a significantly better score than the SM, LP, and LDL groups (in that order). The RDL and IM frontal patients were also significantly different from the lowest group, the LDL group. There were no significant differences involving the LT group (recall that these are mostly patients who have had lobectomies, not patients with posterior lateral temporal damage.) Their score was better than the LP group, and this was significant on direct comparison.

The error profile with this new classification was similar to the original analysis, with the LDL group making significantly more errors as a proportion of output than the control group [$F(7,101) = 2.46$, $p < .03$]. Sex showed no significant effect in our 40–64-year-old normative group (see Appendix), but was added in the CART analysis because of

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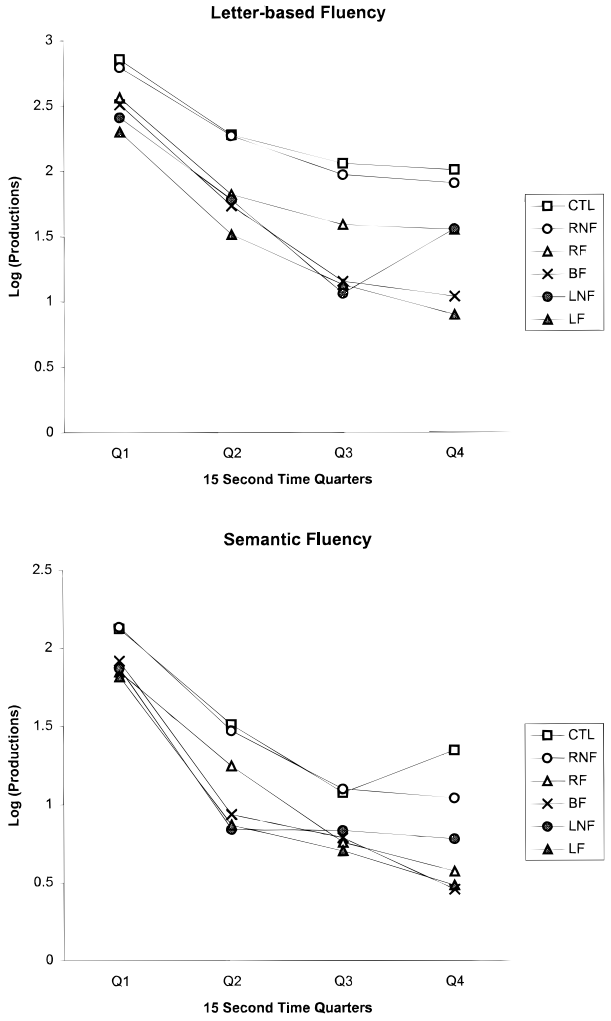


**Fig. 2.** The productions over the 1-min test period, divided into 15-s segments, are presented for the letter-based (top) and semantic (bottom) fluency tasks. The mean number of words produced within each 15-s interval was the dependent measurement. These data were logged to allow comparison of output over the four 15-s intervals.

previous research (Shaywitz et al., 1995). The inclusion of sex produced a single effect. In the RDL group only (who had normal performance overall), the male patients performed significantly worse ($M = 32.8$) than female patients [$M = 39.9$; $t(9) = 2.3$, $p < .05$]. Lexical–semantic retrieval and auditory verbal working memory were assessed to evaluate the possibility that basic language deficits or working memory might account for some of the fluency performance. Correlation coefficients between fluency scores and the Token Test, BNT, and Digit Span backward scores were calculated in each subregion grouping. There were no significant correlations with the Token Test. In the control group, naming and correct productions were correlated ($r = .54$, $p = .001$). There were no significant naming–fluency correlations within any patient group, although the LDL group correlation approached significance ($r = .54$, $p = .06$). The lack of a detectable association between confrontation and generative (fluency) naming for the patient groups was most evident in the left nonfrontal patient group for letter-based fluency. For the left temporal patients, the BNT score was 42, and the FAS total score was 29.2. For left parietal patients, on the other hand, the BNT was 54 and the FAS score was 19.8. There were significant correlations with digit span backward score for the LDL ($r = .71$, $p = .02$) and IM groups ($r = .68$, $p = .03$). As in the original patient groupings, there were no group effects on mean cluster size or proportion of clusters in the letter-based fluency task.

The new group classifications were reanalyzed for their logged fluency production over time (see Figure 5). In the initial 15-s interval, the LDL, LP, SM, and RDL groups produced significantly fewer words than the control group. The LDL ($p < .05$) and SM ($p < .001$) groups had proportionately greater reduced production over time. The major differences in this analysis from the initial lesion grouping was the refinement in patients with medial lesions, the majority who were previously classified together in the BF group.

### *Semantic fluency*

A significant group difference was obtained for the total correct output [$F(7,101) = 8.8$, $p < .001$] (see Figure 4). *Post-hoc* analyses revealed that the control and RNF groups were significantly better than all other groups except LT, which was borderline ($p < .07$). While there was variation among the other groups (LDL and LP groups were the worst), no significant differences among these groups were observed. There were no significant differences in the number or proportion of clusters or errors produced.

There were no significant correlations between the Token Test and the semantic fluency score within any of the groups. Significant correlations between the Boston Naming Test and semantic fluency were observed only for the IM ($r = .74$, $p < .01$), RNF ($r = .70$, $p < .04$) and the control ($r = .52$, $p < .001$) groups. There was a significant correlation of digit span backward and semantic fluency in the LDL ($r = .73$, $p = .02$) group only.

The new groupings altered the analyses of output over time (see Figure 5). The LP and LDL group produced significantly fewer words in the first 15 s than the control group ($p < .05$), this new analysis separating the effect of LT and LP lesions. The notable comparison was the inability of the RDL group to sustain performance in the semantic fluency task compared to the performance of this group on letter-based fluency. This group had the largest proportional drop in semantic word production over time.

### *Summary*

By revising the lesion groupings we were able to supplement the original coarse anatomical classification with a finer-grained analysis of lesion location. Damage to the right dorsolateral cortical or striatal areas, the right posterior region, or the medial inferior frontal lobe of either hemisphere did not result in significantly diminished performance

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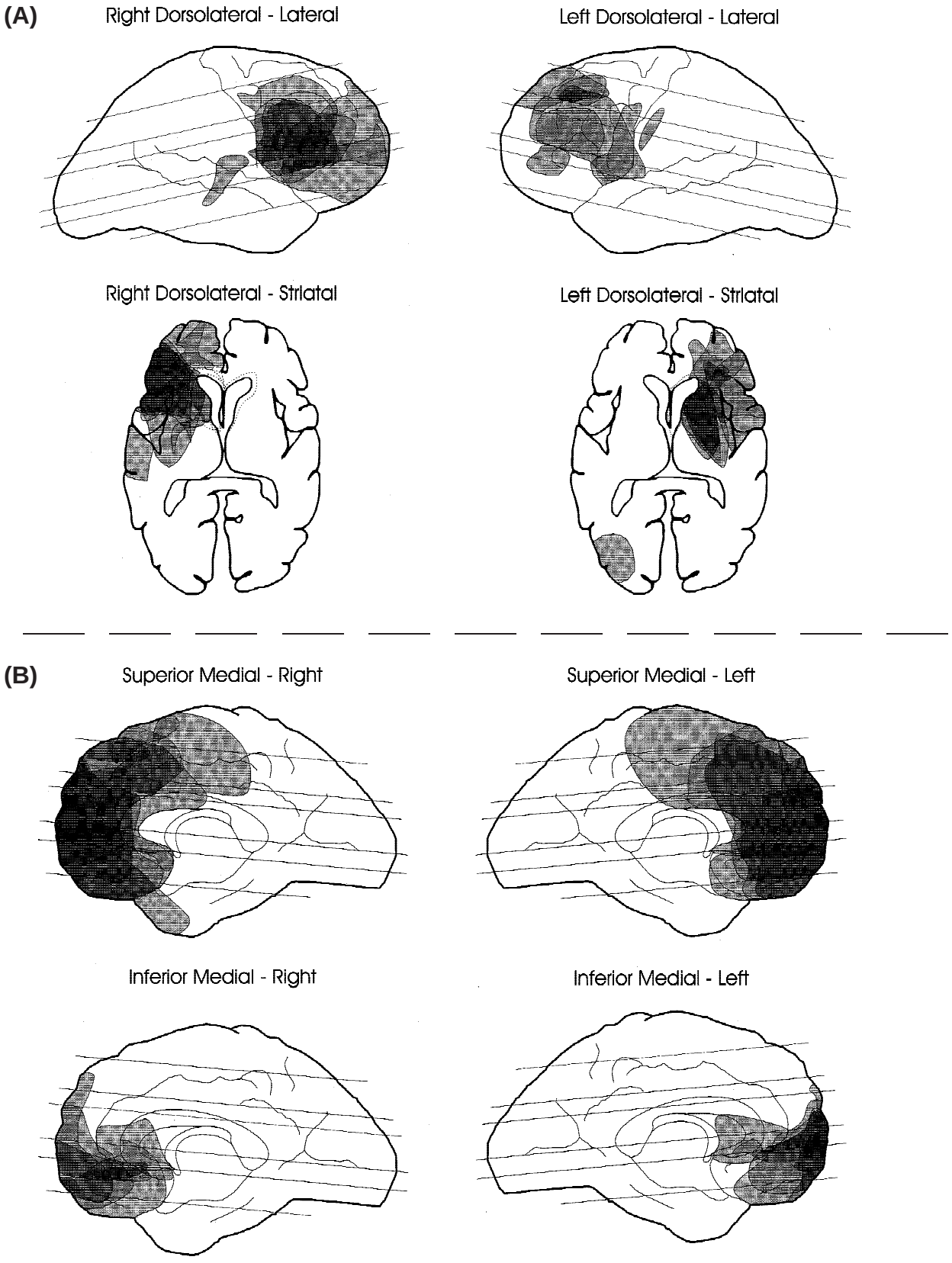


**Fig. 3.** This figure depicts overlap of the lesions of the patients, providing examples of those who have impaired or spared performance. On the left of (A), patients in the right dorsolateral group (top–dorsolateral; bottom–striatal) are presented, and on the right side the left dorsolateral group. Patients with superior and inferior medial lesions are presented on (B). Note that many of the SM patients have both superior medial and inferior medial pathology but the maximum involvement is more superior than the pure IM group.

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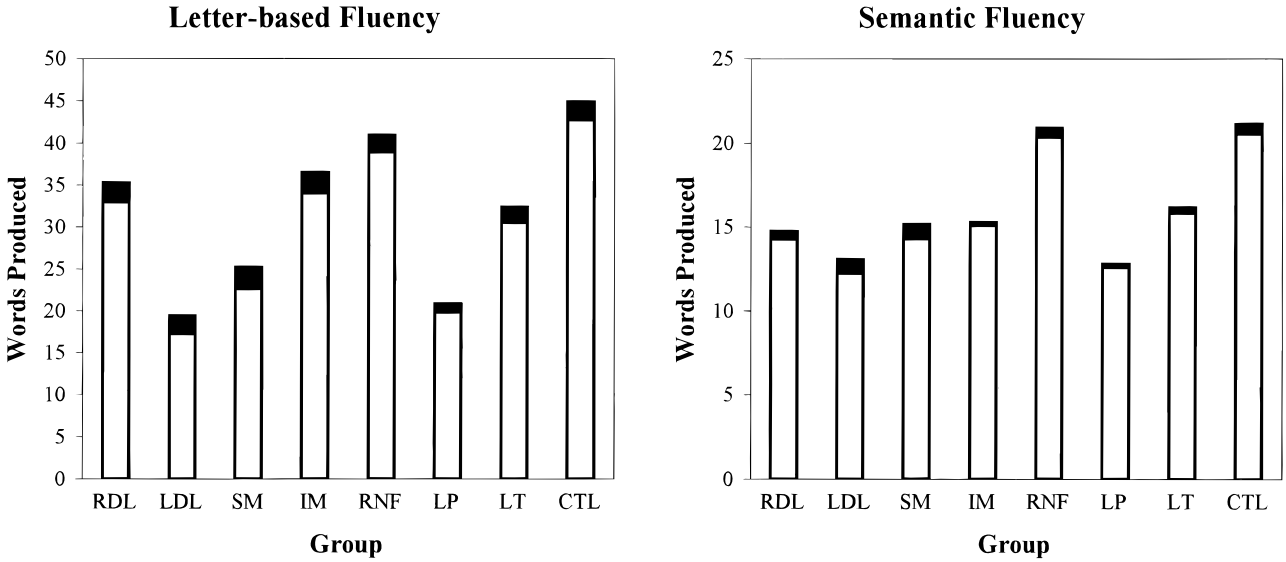


**Fig. 4.** Letter-based and semantic fluency scores for both correct words produced (clear) or errors (stippled) are presented for the new lesion groupings. The score is the total of the three letters *F-A-S*, or the number of animal words presented, averaged across participants within each group. RDL = right frontal dorsolateral and/or lenticular striate; LDL = left frontal dorsolateral and/or lenticular striate; SM = superior medial frontal involvement from LF, RF, or BF patients, either in isolation or in combination with inferior medial lesions; IM = inferior medial frontal lobe involvement from either RF, LF or BF lesions; RNF = right nonfrontal involvement; LP = left parietal damage; LT = left temporal damage.

in letter-based fluency compared to the control group. If either right *or* left superior medial frontal lobe areas were involved, moderate impairment resulted. The patients with left dorsolateral and/or striatal lesions were the most significantly impaired group. The important factor for the left nonfrontal group was the location of the lesion. If damage was limited to the left anterior temporal region, there was no significant deterioration in performance. If left parietal regions were involved, however, the results approximated the performance of those frontal patients with left dorsolateral and superior medial (of either hemisphere) lesions. The differences in the semantic fluency task compared to the letter-based fluency task were the additional poorer performances of the RDL and IM groups (and almost the LT group) compared to the control group.

## DISCUSSION

We have two general sets of conclusions; the first regarding lesion–behavior relations, and the second regarding methodology:

### Lesion–Behavior Relations

The results using standard coarse lesion groupings provide a link with previous research and set the context for the more specific findings, but they are superseded by the results of the new methodology. We are claiming greater specificity for lesions in specific regions of the frontal lobes in disruption of verbal fluency than previous reports. The considerable variability among other reports may be due to the classification of lesions by coarse standards. As a group effect left frontal lesions impair letter-based fluency but not all patients with left frontal pathology are impaired. If the lesion is restricted to the inferior medial area, there is no significant impairment. This is compatible with the neuroimaging activation studies (Warburton et al., 1996) and research in patients with orbitofrontal leucotomies (Stuss et al., 1986). Involvement of the left superior medial area (as well as the right) or the left DL region (including striatum) did affect letter-based fluency.

Involvement of the superior medial region in verbal fluency has been documented in activation studies in normals, but there is uncertainty about the precise region of the superior medial area. Frith et al. (1991a) observed activation foci in the anterior cingulate cortex. Warburton et al. (1996) reported medial activation in the anterior cingulate and supplementary motor areas. Petersen et al. (1988) found anterior cingulate cortex activation in a semantic generation task in a region similar to our lesion locations. We were unable to isolate a role for the anterior cingulate cortex, because there were no selective lesions in the cingulate area in our patients. Our findings do suggest a possible functional differentiation within the anterior cingulate area. Some of the patients with inferior medial lesions had anterior cingulate cortex (areas 24 and 32) involvement, yet they were not significantly different from the control group. The anterior cingulate cortex is a relatively large region, and there are likely to be very important functional differences within area 24

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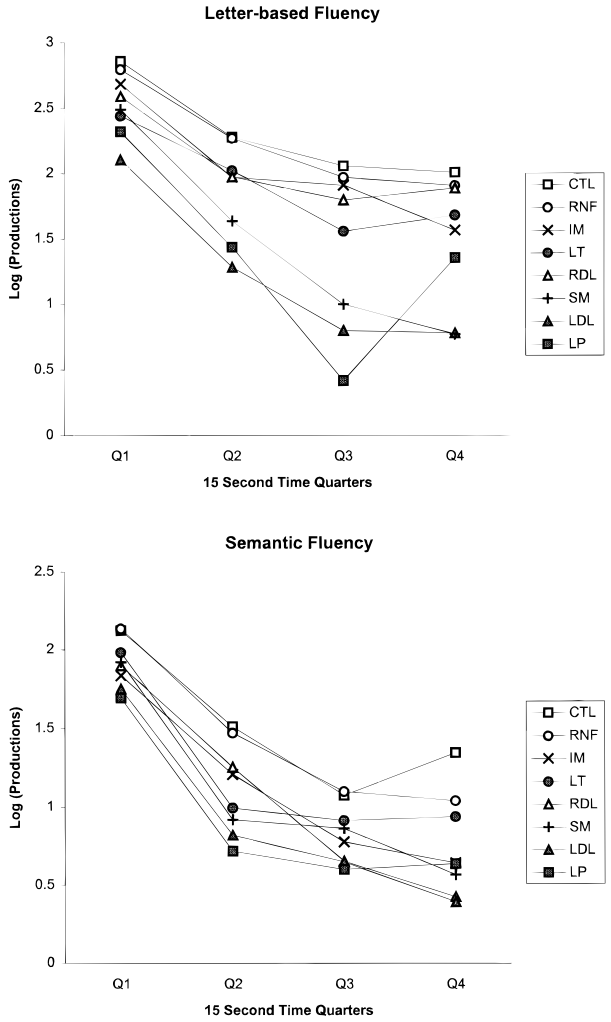


**Fig. 5.** The logged productions over the 1-min period, divided into 15-s quadrants, are presented for the new groupings.

(Devinsky et al., 1995). Thus, the anterior cingulate areas 24a and 24c narrow as they move ventrally around the corpus collosum but not area 24b. Both the anterior cingulate cortex (likely more superior) and the supplementary motor area are known to be critical for spontaneity and activation, and impoverished movement and diminished vocalization are maximal when both regions are damaged (MacLean, 1987). The left and right superior medial frontal regions are known to operate virtually as functional units (Jürgens, 1984). Lesions of either medial frontal region produce similar behavioral effects (reviewed in M. Alexander et al., 1989). Thus, it is not surprising that we found an effect of *both* superior medial regions. Frith et al. (1991a) also noted PET activation in both left and right cingulate areas on a fluency task in normals. This strongly suggests that general activation and mobilization is not hemisphere specific, and requires both medial regions. Akinetic mutism, the most severe expression of disturbed initiation, when secondary to medial frontal damage, requires bilateral medial pathology (Devinsky et al., 1995).

The most significant effect on letter-based fluency and the greatest tendency to make errors was produced by LDL frontal lesions. This brain region—approximately Brodmann's areas 46, 45, 44, 6, 8, and 9—is critical for a variety of functions that require activation and organization of basic language capacities. We are uncertain at present whether further anatomical differentiation can be identified within this region. PET activation suggests that the verbal articulatory rehearsal process is localized in the left inferior lateral frontal region (Broca's area; Paulesu et al., 1993; Salmon et al., 1996). Lesions in this area can produce transcortical motor aphasia, a disturbance in organization and retrieval of syntactic and narrative structures (Freedman et al., 1984). Damage to this region impairs activation of semantic encoding capacities and reduces verbal learning (Janowsky et al., 1989; Stuss et al., 1994a; Ween et al., 1996). Activation studies in normals that require any type of semantic generation capacity (associate naming, verb production from nouns, etc.) uniformly produce activation in some portion of LDL cortex with the suggestion that this region is involved with intrinsic generation rather than semantics (Frith et al., 1991a; Wise et al., 1991). That left striatal involvement produces deficits similar to LDL cortex should be anticipated based on the high interconnectivity between these regions. G. Alexander et al. (1986) described the existence of several discrete frontostriatal circuits in nonhuman primates, and Cummings (1993) has outlined the behavioral distinctions that exist between these discrete circuits in humans. Damage anywhere in a circuit—cortex to striatum—produces similar effects. Mega and M. Alexander (1994) described the striking similarity of the generative language deficits following striatal and DL convexity lesions.

Nonfrontal left hemisphere regions also have a role in letter-based fluency. Following Milner (1964), we found no significant impact of temporal lesions on FAS performance. There are three possible explanations for these results. First, our patients largely had lobectomies, and thus lesions were very anterior. A group with more posterolateral lesions might have very different results. Second, the chronicity of the lesion in these subjects may be a major factor in these negative data (Loring et al., 1994). Third, it is possible that the anterior temporal region is involved in semantic–lexical functions but not letter-based ones, and indeed the frontal lobes may inhibit superior temporal regions in letter-based fluency tasks (Frith et al., 1991a). Impairment after left parietal lesions was superficially not surprising. Frith et al. (1991a) reported activation in the left parietal area on fluency tasks in normals. Furthermore, we anticipated that anomic patients would have reduced fluency but we did not expect the dissociation that we observed: relatively preserved naming in the face of markedly impaired fluency. It is possible that the fluency defect in the left parietal patients reflects impairment in higher level semantic activation and search rather than direct semantic to lexical access that the Boston Naming Test demands (Goodglass & Stuss, 1979). This, however, is conjecture; it was not directly investigated. We are not claiming that the left temporal lobe

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plays no role in category-based fluency. The posterior temporal region is critical for lexical semantics, but lesions there disrupt direct confrontational naming. Patients with lesions in superior or inferior posterior temporal lobe had too much anomia for our tasks to be meaningful.

We found no major deficit in letter-based fluency after damage in the right dorsolateral, right inferior medial, or right nonfrontal regions. Damage to the right nonfrontal area does not impair letter-based fluency productions. Other studies (e.g., Joanette & Goulet, 1986) that found no rostral–caudal effect after right hemisphere damage used patients with MCA lesions wherein the pathology may not have been as restricted to frontal or nonfrontal regions. Within the right hemisphere, only the superior medial region is essential for letter-based fluency. We attempted to see if specific processes could be related to impaired performance, perhaps linked to these specific brain regions or systems. The strategic clustering measures we used were related to total output but did not differentiate among the groups. There appears to be a relatively strong relation of working memory to fluency performance in the LDL (for both tasks) and IM (for letter-based fluency) groups. The LDL group correlation is compatible with the suggested relationship of left dorsolateral frontal regions with the articulatory rehearsal process of verbal working memory (Coslett et al., 1991; Paulesu et al., 1993). The working memory impairment may account at least partially for the preponderance of errors in the LDL group (Laine, 1989). The correlation in the IM group is of uncertain significance. These data indicate that, in future studies of working memory, the inferior medial frontal region be considered. Pardo et al. (1990) had suggested that the anterior cingulate gyrus was related to an inner articulatory loop active during more complex tasks, and the letter-based fluency task was shown to be more difficult.

The sex differences were explored because of recent investigations of sex differences in performance after frontal lobe lesions (Goldberg et al., 1994; Shaywitz et al., 1995). We found only a modest effect in one lesion group (RDL), although it would be premature based on our limited sample to exclude other sex-based anatomical differences. Our data do support the importance of investigating sex differences in frontal lobe functioning.

Two major process effects were observed in the analyses of productions over time. First, the left hemisphere, SM and RDL groups all had initial difficulty generating words beginning with the same letter, and the LDL and SM groups produced even less over time. Based on previous research, and in the absence of any other correlation suggesting a different process, it is likely that the SM deficit reflects initiation and continual activation processes. While this explanation cannot be excluded for the other groups, there is evidence for perhaps another problem in the LDL patients—a deficit in working memory, and potentially an impaired direct semantic access as suggested by the naming correlation.

The semantic fluency output results paralleled the letter-based fluency results with several additions. The RDL patients, a group that was only marginally deficient on letter-based fluency, were now significantly impaired in their performance. Moreover, it seems that their maximum impairment derived from their inability to sustain output for the last 30 s. The mental process contributed by the RDL region essential for semantic fluency but not letter-based fluency is unknown, but the lesion data are supported by activation studies in normals (Cardebat et al., 1996). Our data, and the studies of Joanette and colleagues (Joanette et al., 1988; Joanette & Goulet, 1986) also reporting that right hemisphere lesion patients had impaired semantic fluency but only in the last half of the task, seem to rule out a general "aspontaneity." A defect in sustained attention has been reported after right frontal lesions (Wilkins et al., 1987), but such a defect would have affected performance on both fluency tasks. The defects do not appear to be due to monitoring since there was no significant increase in this group in perseverative or unrelated errors. The right frontal lobe has been reported as relevant in semantic categorization (Incisa della Rochetta, 1986). A similar problem in strategy formation for list learning was observed with right frontal lesions in an earlier study (Stuss et al., 1994a). While there was no significant deficit in the RDL group in our semantic clustering measure, it is still possible that the right frontal deficit is related to lexical–semantic processing, but for a very specific reason—a deficit in strategic processing.

The absence of a significant left temporal deficit in semantic fluency does not allow us to confirm our hypothesis that the left temporal lobe is involved in verbal fluency but only, as suggested by Frith et al. (1991a) and M. Alexander (1997), in tasks that require semantic lexical functions but not letter-based ones. However, a borderline significant difference with our sample size makes us cautious in totally rejecting this hypothesis. The presence of a significant impairment in semantic fluency for the IM group, in juxtaposition to the better performance in letter-based fluency, could be due to deficient explicit memory performance which might have a greater effect in semantic fluency tasks. Many of these IM patients had involvement of septal memory regions.

## Methodology in Brain–Behavior Analyses

We propose a different approach in the methodology of study of brain–behavior relations. It is worthwhile to continue to group patients according to coarse lesion classifications such as *frontal–nonfrontal*, particularly for studies with smaller sample sizes, but grouping patients according to their performance level may be a more informative approach. We successfully used this method in previous studies (Stuss et al., 1994a). This approach is quite compatible with one described by Shallice (1988) that combines the best qualities of both group study and case study approaches.

A second methodological issue is the specificity of lesion location analyses. It is clear that the frontal lobes are not functionally homogeneous organs. Understanding the roles of frontal regions requires attention to specific lesion sites within the frontal lobes. M. Alexander (in Stuss et al., 1995)

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proposed a schematic approach to the anatomical analysis of the frontal lobes based on architectonic divisions and analyses of frontal connectivity (Pandya & Barnes, 1987; Petrides & Pandya 1994). Our current analysis is an extension of that approach.

In conclusion, there is an anatomical system and there are dissociable processes underlying performance on fluency tasks. Critical structures for letter-based fluency include *bilateral* superior medial regions (supplementary motor area and likely superior anterior cingulate—area 24), and several left hemisphere regions: left dorsolateral prefrontal, left striatal, and left parietal regions. According to Frith et al. (1991a), the left parahippocampus region is also relevant. The relevant processes include initiation and activation (SM; possibly LDL); direct semantic to lexical access (LDL); verbal articulatory rehearsal (LDL; IM) higher-level associative–semantic retrieval (LP); and sustained production (LDL; SM). While similar processes are required for semantic fluency, added processes and regions are necessary: lexical–semantic processing, potentially of different kinds [LT(?); RDL]; sustained production (RDL); and possibly memory [IM (septal)]. The cognitive architecture of the frontal lobes is anatomically and functionally discrete. In addition, the contribution of the other areas within the functional neural network must be considered. Processes related to other brain regions may also play a role in some if not all measures called "frontal lobe tests." The analyses of the processes rather than just the test scores provide insight into the contributory role of different brain regions within a neural network.

## ACKNOWLEDGMENTS

The study was funded by the Medical Research Council of Canada (MRC# MT-12853), the Ontario Mental Health Foundation, and a Rotman Research Institute Fellowship (B. Levine). Scoring and statistical assistance were provided by Ron Macdonald and Julia Hong. Antoinette Savas and Brigitte Boucher prepared the figures. Paula Mathews typed the manuscript. Drs. M. Schwartz and S. Black are thanked for referring patients. We are grateful to the patients and their families and the control participants for their efforts and good will in participating in the project.

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## APPENDIX

Normative data by age and sex

| | Age 21–39 years (10 M and 10 F) | | | Age 40–64 years (9 M and 16 F) | | | Age 65–81 years (9 M and 8 F) | | |
|---|---|---|---|---|---|---|---|---|---|
| Tasks | *M* | *SD* | Range | *M* | *SD* | Range | *M* | *SD* | Range |
| Letter-based fluency (score) | | | | | | | | | |
| Male | 53.2 | 13.1 | (28, 68) | 44.1 | 10.2 | (30, 58) | 37.1 | 10.1 | (23, 55) |
| Female | 48.4 | 10.3 | (29, 64) | 42.7 | 11.0 | (25, 63) | 47.5 | 14.8 | (29, 70) |
| Both | 50.8 | 11.7 | (28, 68) | 43.2 | 10.5 | (25, 63) | 42.0 | 13.2 | (23, 70) |
| Semantic fluency (score) | | | | | | | | | |
| Male | 26.3 | 2.6 | (23, 31) | 18.7 | 3.3 | (15, 25) | 16.7 | 1.7 | (14, 19) |
| Female | 23.0 | 3.9 | (16, 28) | 22.4 | 6.0 | (13, 36) | 18.1 | 5.9 | (8, 26) |
| Both | 24.7 | 3.5 | (16, 31) | 21.0 | 5.4 | (13, 36) | 17.4 | 4.1 | (8, 26) |
| Letter-based errors | | | | | | | | | |
| Male | 2.1 | 2.5 | (0, 7) | 2.3 | 2.0 | (0, 7) | 2.3 | 2.4 | (0, 7) |
| Female | 1.4 | 1.8 | (0, 6) | 2.2 | 1.6 | (0, 5) | 3.0 | 2.2 | (0, 7) |
| Both | 1.8 | 2.1 | (0, 7) | 2.2 | 1.7 | (0, 7) | 2.5 | 2.2 | (0, 7) |
| Semantic errors | | | | | | | | | |
| Male | 0.7 | 1.0 | (0, 3) | 0.7 | 0.9 | (0, 2) | 0.6 | 1.3 | (0, 4) |
| Female | 0.1 | 0.3 | (0, 1) | 1.1 | 1.4 | (0, 4) | 0.4 | 0.7 | (0, 2) |
| Both | 0.4 | 0.8 | (0, 3) | 0.9 | 1.3 | (0, 4) | 0.5 | 1.1 | (0, 4) |

https://doi.org/10.1017/S1355617798002653 Published online by Cambridge University Press