Verbal fluency in dementia of frontal lobe type and dementia of Alzheimer type

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Abstract
This study compares semantic (category) and letter-initial verbal fluency performance in dementia of frontal lobe type, dementia of Alzheimer type, and control subjects matched for age, sex, and level of education. As well as demographic characteristics, patients were matched for severity of dementia as estimated by the mini mental scale (23-2 (SD 4-9)). All patients with dementia of frontal lobe type had a frontal hypoperfusion on single photon emission computed tomography whereas patients with dementia of Alzheimer type showed mainly posterior deficits. Patients had significantly lower verbal fluency than controls but those with dementia of frontal lobe type did not differ from those with dementia of Alzheimer type in the number of words generated, intrusions, or perseverations. Category fluency was more impaired than letter fluency in both dementias. No correlation between frontal index, frontal/parietal index, and fluency was found. Verbal fluency tests are sensitive tools for detecting dementia but do not seem useful in distinguishing between patients with dementia of Alzheimer type and those with dementia of frontal lobe type in early disease.

(J Neurol Neurosurg Psychiatry 1995;58:81-84)

Keywords: Alzheimer’s disease; verbal fluency; dementia of frontal lobe type

Verbal fluency tasks are useful cognitive measures for detecting dementia of Alzheimer type.\(^1\) Performance decrements in fluency tasks are correlated with activities of daily living and behaviour impairment measured by geriatric rating scales.\(^6\) Category fluency tasks have been found superior to letter fluency tasks in distinguishing patients with dementia of Alzheimer type from healthy elderly control subjects.\(^7\) This superiority may indicate deterioration of semantic knowledge even in early dementia of Alzheimer type.\(^8\) This test is, however, more sensitive than specific. Diminution of word fluency is supposed to be one feature of prefrontal dysfunction, especially of the left, dominant, hemisphere.\(^8\) No particular region of the frontal lobe seems responsible for the verbal fluency deficit, but the volume of impaired tissue may be important.\(^9\) Subcortical lesions give rise to predominantly frontal dysfunction, due to the corticosubcortical loops linking the prefrontal cortex to the basal ganglia.\(^10\) Patients with Parkinson’s disease,\(^11\) progressive supranuclear palsy,\(^12\) and Huntington’s disease\(^13\) have specific difficulties in lexical fluency compared with patients with dementia of Alzheimer type matched for level of intellectual deterioration.

Dementia of frontal lobe type differs from dementia of Alzheimer type in several respects: the behavioural disorder (disinhibition, oral hyperactivity, restlessness, or social withdrawal) may precede the cognitive disorder; memory impairment, spatial disorientation, and an abnormal EEG are less common in the early stages.\(^14\) Early dementia of frontal lobe type is dominated by emotional and personality changes that may cause differential diagnostic problems with affective disorders. Patients with dementia of frontal lobe type show bilateral reduced regional cerebral blood flow in frontal, and especially prefrontal areas, by contrast with dementia of Alzheimer type, which shows a consistent reduction in the temporoparietal cortex.\(^15,16\) It is important to distinguish dementia of frontal lobe type from Alzheimer’s disease in terms not only of clinical diagnosis but also of treatment and research.\(^14\) The verbal fluency test seemed of potential value in this respect.\(^17\)

The main purpose of this study was to compare category fluency and letter fluency performance in patients with dementia of frontal lobe type, patients with dementia of Alzheimer type matched for severity of dementia, and normal demographically matched elderly controls. The ancillary purpose was to look for a link between fluency task performance and the single photon emission computed tomography (SPECT) frontal uptake index.

Patients and methods

PATIENTS
Outpatients with cognitive difficulties were recruited from the University Memory Disorders Unit. All fulfilled the diagnostic and statistical manual of mental disorders, third edition, revised criteria for “primary degenerative dementia” after evaluation by one senior staff neurologist and one senior staff psychiatrist. Dementia of frontal lobe type was diagnosed clinically, from the history, neuropsychological testing, and indications provided by Gustafson,\(^18\) Neary et al,\(^20\) and Cole.\(^17\)

Patients with dementia of frontal lobe type
had a history of behavioural disturbance pre-dating dementia, with early personality change, loss of social skills, disinhibition, and apathy. The family considered memory impairment of secondary importance compared with the behavioural disorder. Affect was flat or bland. Two had hypochondriacal delusions. None had visuospatial impairment and especially no spatial disorientation. The EEG was normal in all cases.

Dementia of Alzheimer type was diagnosed according to National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer’s Disease and Related Disorder Association criteria. Ten patients with probable Alzheimer’s disease were selected from the memory disorders unit data file to be matched with the first 10 consecutive patients with dementia of frontal lobe type able to achieve the verbal fluency task. The selection criteria were sex, level of education (six to seven years of schooling, n = 6, 11–15 years of schooling, n = 4), age (± 5 years), typical Alzheimer syndrome (insidious onset, progressive memory loss, language and visuospatial disorders, often accompanied by minor behavioural disturbance such as suspiciousness) and mini mental state examination scores (± 2 points). Patients with severe cognitive impairment were excluded, as they could not perform the task and as both frontal lobe dysfunction and pronounced behavioural disturbance have been reported in advanced Alzheimer’s disease. None received psychotropic medication in the month before the study. Patients had no previous neurological or psychiatric history. Clinical examination and laboratory investigations were normal. The Ischaemic score was < 4 and no abnormality other than atrophy was found on CT or MRI.

Patients were assessed with a comprehensive neuropsychological test battery including the Mattis dementia rating scale, digit span, logical memory subtest (Wechsler memory scale), selective reminding test (Bushke), delayed visual recognition, assessment of aphasia, agnosia, gestual, and constructive apraxia, and semistructured interview with the patient and family conducted by a psychogeriatrician. The memory deficit, and especially Grober and Buschke enhanced cued recall was compatible with an organic mental disorder in all cases.

A SPECT study with Tc–HM–PAO (Tomomatic 564, Medimatic, Copenhagen) was performed on 14 patients (seven with dementia of Alzheimer type and seven with dementia of frontal lobe type). Cerebral uptake indices were calculated bilaterally with the cerebellum as reference in frontal and parietal cortical regions. All patients with dementia of frontal lobe type showed the characteristic frontal hyperfusion pattern whereas patients with dementia of Alzheimer type showed mainly posterior metabolic deficits.

Ten voluntary control subjects were matched for sex, level of education, and age. Their mini mental state examination score was ≥ 29 and they had no neurological or psychiatric history. They did not undergo SPECT.

All patients and controls were native French speakers.

**PROCEDURE**

Subjects were asked to provide as many animal words as they could for the category fluency task (excluding proper nouns and variants) and as many words beginning with P as they could for the letter fluency task, in two minutes. The verbal fluency tasks were given by the same speech therapist, blinded to the final diagnosis of dementia (dementia of Alzheimer type or dementia of frontal lobe type).

The scores analysed (by analysis of variance (ANOVA)), were the total number of correct answers for each fluency task, the number of intrusions (non-animal words in the category task, words not beginning with P in the fluency task), and the number of perseverations for each fluency task.

**Results**

The table gives the demographic characteristics.

**VERBAL FLUENCY (FIGURE)**

Repeated measures ANOVA showed a significant group effect (F(2, 27) = 3.39, p = 0.04). Controls produced more words than dementia of Alzheimer type + dementia of frontal lobe type (F(1, 27) = 6.74, p = 0.01). Type of fluency task was also significant (category v letter P, F(1, 27) = 97.43, p < 0.0001): both controls and patients generated more animal
names than words beginning with P. There was a significant interaction between group (controls vs. dementia of Alzheimer type vs. dementia of frontal lobe type) and type of fluency (F(2,27) = 4.05, p = 0.02). The difference between controls and patients was larger for animal than for letter fluency (interaction between type of fluency and the contrast (F(1,27) = 7.85, p = 0.009)). There were no significant differences between dementia of Alzheimer type and dementia of frontal lobe type in the number of words generated (25.5 (SD 10.7) vs. 26.7 (14.5), F(1,18) = 0.04, p > 0.83), intrusions (0.10 (0.3) vs. 0.20 (0.6), F(1,18) = 0.2, p = 0.66), or perseverations (1.2 (1.9) vs. 1.3 (1.8), F(1,18) = 0.01, p = 0.90). There was no interaction between type of dementia (dementia of Alzheimer type vs. dementia of frontal lobe type) and type of fluency (F(1,18) = 0.21, p = 0.65).

SPECT pattern
Frontal index values were lower in patients with dementia of frontal lobe type than in those with dementia of Alzheimer type (78.52 (5.08) vs. 84.94 (5.07), F(1,12) = 5.59, p < 0.04). There was no significant asymmetry. Parietal values did not differ between the dementia of frontal lobe type and dementia of Alzheimer type groups (85.64 (2.81) vs. 83.57 (6.23), F(1,12) = 0.64, p = 0.45). The mean frontal/parietal ratio was 0.92 (0.07) in dementia of frontal lobe type and 1.02 (0.10) in dementia of Alzheimer type (F(1,12) = 4.42, p = 0.05).

No correlation was found between frontal index, frontal/parietal index, and fluency.

Discussion
These results confirm the sensitivity of verbal fluency tasks in early or mild dementia. They agree with most previous findings in showing that category fluency is more impaired than letter fluency in dementia of Alzheimer type. They disagree with Rosen who found greater impairment in letter than in semantic category fluency in early dementia of Alzheimer type. But our data fail to show greater impairment in patients with dementia of frontal lobe type than in patients with dementia of Alzheimer type matched for demographical characteristics and severity of dementia presenting with the typical parietal syndrome of dementia of Alzheimer type, based on clinical and SPECT features. Even at this early stage, SPECT showed lower frontal indices in dementia of frontal lobe type, in agreement with the clinical presentation and literature data. There was no interaction between type of fluency and type of dementia. In particular, the greater impairment in category than letter fluency was not significantly higher in dementia of Alzheimer type than in dementia of frontal lobe type, whereas frontally impaired patients were expected to perform poorly in any fluency task. This result emphasises the lack of specificity suspected by Monsch et al. Semantic impairment seems non-specific as semantic memory was not specifically impaired in dementia of Alzheimer type, as opposed to multi-infarct dementia of comparable severity. By contrast, category fluency correlates with the degree of dementia in both diseases. Furthermore, mildly demented Huntington’s disease shows the same pattern of “disruption in the structure of semantic knowledge” as dementia of Alzheimer type matched for severity of dementia in the supermarket fluency task on the Mattis dementia rating scale. The difference between category and letter fluency performance is thought to be more pronounced in early dementia of Alzheimer type where impairment of language tasks may be due more to a deterioration in semantic knowledge than to psychomotor slowing.

Impaired verbal fluency is a classic feature of frontal lobe dysfunction. Attempts to localise function within the prefrontal cortex in humans have not yet produced consistent results. Verbal fluency deficit has been consistently reported as impaired in both cortical and subcortical dementia, but performance in specific fluency tests follows a less consistent pattern, not only between studies but also within studies depending on the letter or category target. Diesfeld showed that low verbal fluency in dementia of Alzheimer type was probably not due to a loss of words and their meanings, but rather to a reduced accessibility of words. Successful retrieval depends on retrieval strategies as well as on the storage characteristics of the information to be retrieved. In dementia of Alzheimer type, loss of the specific features and associations of words reduces the availability of attributes necessary to arouse a concept—for example, of a specific kind of fruit or animal. The reduction in the availability of the set of attributes that determine word meanings leads to inadequate activation of the concept, which, in turn, may prevent retrieval of its name. In dementia of frontal lobe type, low category fluency performance could be due to impairment of the strategies needed to generate the maximum of items of a category in a limited time. Retrieval of words from a category is likely to depend on breaking the category down into subcategories and systematically searching each subcategory. A systematic strategy also reduces the resampling tendency (reretrieval of previously recalled items) that is almost inevitable during retrieval, even in normal subjects. A systematic search strategy necessarily implies a working memory that “temporarily holds the rules of the search procedure and keeps a tally of recalled category exemplars”. Reduced short term memory capacity in patients with dementia could partially explain impaired fluency performance.

Because reduced verbal fluency performance may be due to a dysfunction of one or several complex processes, verbal fluency tests are sensitive tools for detecting dementia but do not seem useful for distinguishing between dementia of Alzheimer type and dementia of frontal lobe type in early disease.
We are grateful to Alain Dubalme (Centre d'Etudes et de Recherche en Informatique Médicale, Lille) who revised the statistical analysis.


