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Neuropsychological performance of right- and left-frontotemporal dementia compared to Alzheimer's disease

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Abstract

The performance of 16 patients with Alzheimer's disease (AD) was compared to 11 patients with right-frontotemporal dementia (FTD) and 11 patients with left-FTD on a comprehensive neuropsychological battery. Standardized scores (i.e., *z* scores based on normal control data) were analyzed for 5 cognitive domains. The results revealed that the AD group displayed significant impairment in visual–constructional ability relative to the two FTD groups; however, no significant difference was found between the groups on memory scores (verbal and nonverbal). Patients with left-FTD scored significantly below patients with AD on the language measures (e.g., word retrieval, verbal semantic memory), and verbal executive ability (phonemic fluency); AD patients did not differ from patients with right-FTD on these measures. Patients with right-FTD exhibited significantly more perseverative behavior than AD patients; AD patients did not differ from left-FTD patients on this parameter. These results indicate that the pattern of neuropsychological performance of AD patients is distinguishable from patients with left and right frontal frontotemporal dementia. (*JINS*, 2001, *7*, 468–480)

Keywords: Alzheimer's disease, Left and right frontotemporal dementia, Neuropsychological scores, Executive function

INTRODUCTION

Alzheimer's disease (AD) and frontotemporal dementia (FTD) are among the most prevalent neurodegenerative disorders (Cherrier et al., 1997; Pasquier & Petit, 1997). A large number of studies have emerged within the past two decades on the neuropsychological profile of AD, demonstrating that the disorder is characterized by deficits in episodic memory, anomia, and visual–spatial and constructional skills (see Heindel et al., 1993, for review). In contrast, there has been less investigation regarding the cognitive deficits of patients with frontotemporal deficits, and findings from these studies suggest that FTD patients represent a heterogeneous group. The few, relatively recent neuropsychological studies suggest that behavioral problems and personality changes, combined with deficits in executive skills are among the first domains to be compromised in patients with FTD (Cummings & Benson, 1992; Johansen & Hagberg, 1989; Neary et al., 1986). Other investigators have found conflicting results regarding deficits in memory, language, attention, and intellectual functioning (Frisoni et al., 1995; Jagust et al., 1989; Johansen & Hagberg, 1989; Miller et al., 1991; Neary et al., 1986).

Even less research examining the cognitive patterns of AD and FTD patients has been conducted. An initial inquiry, on a small sample size (i.e., 4 FTD patients) demonstrated profound executive skills deficits relative to memory functioning in FTD patients, depressed memory functioning relative to executive skills in AD, and poor performance in naming and constructional skills in both groups (Jagust et al., 1989). In a more recent study, involving a

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larger sample size of FTD and AD patients matched on disease severity, we found that while the FTD patients outperformed the AD patients on nonverbal memory tasks, the two groups did not differ on other cognitive domains (Pachana et al., 1996). However, when relative performance was examined, AD patients displayed greater deficits in memory functioning as compared to executive tasks, while FTD patients displayed the opposite pattern of performance.

Failure to find more statistically significant differences between groups may have been due to the heterogeneity of the FTD group. Two recent investigations lend support to this hypothesis. In a study by Hodges et al. (1999), FTD patients were divided into two groups based on frontal *versus* temporal lobe variant presentation of the disease and their performance was compared with AD patients on a neuropsychological battery. These authors found that the AD patients displayed severe deficits in episodic memory, with subtle impairments in semantic memory and visual–spatial skills. In contrast, the temporal lobe variant FTD patients (referred to as semantic dementia) were found to display severe impairments in semantic memory as well as surface dyslexia, with less impaired performance on verbal and nonverbal episodic memory relative to the AD patients. The frontal lobe variant FTD patients were found to be the least impaired, showing only mild deficits in episodic memory and verbal fluency, and relatively preserved semantic memory. This study was the first to raise the possibility that FTD is not a unitary disorder, and to show that when FTD patients are subdivided based on region of pathology, distinct neuropsychological patterns emerge.

In a recently completed study, we examined the impact of disease asymmetry on FTD neuropsychological performance (Boone et al., 1999). Comparison of patients with asymmetrical left- or right-sided anterior hypoperfusion revealed that right-FTD patients exhibited relatively worse performance on PIQ than VIQ, and in general performed worse on nonverbal executive tasks compared to their verbal analogs, with the left-FTD patients showing the opposite pattern. Specifically, the right-FTD group performed more poorly on picture sequencing relative to word sequencing, and on design generation relative to word generation, with the left-FTD showing the reverse profile. In addition, the right-FTD patients committed more errors, a larger number of perseverative responses, and had poorer percent conceptual level responses on the Wisconsin Card Sorting Test. The left-FTD patients performed worse on object naming, as well as on rapid word reading and color naming. The results of this study provided further support that FTD is not a homogeneous disorder and that differential neuropsychological patterns can be detected based on lateralization of pathology.

While the Boone et al. (1999) study was able to identify distinct cognitive profiles in FTD based on disease asymmetry, how the two groups contrast with AD patients was not examined. Thus, the purpose of the present study was to compare the neuropsychological performance of left- and right-FTD patients with that of AD patients.

METHODS

Research Participants

Twenty-seven patients who were diagnosed with FTD according to criteria set forth by the Lund-Manchester Group (Brun et al., 1994) participated. All patients underwent single photon emission computed tomography (SPECT) brain studies on both ^{133}Xenon and ^{99m}Tc-HMPAO scans, and were determined to have frontal–temporal hypoperfusion with sparing of parietal and occipital regions.

The determination of symmetry, described in detail in Edwards-Lee et al. (1997) and Boone et al. (1999), was based on two clinicians' blind ratings of the SPECT scans. Of the 27 cases, 11 displayed hypoperfusion primarily of the left-sided frontotemporal region and 11 displayed hypoperfusion primarily of the right-sided frontotemporal region. Five patients displayed bifrontal hypoperfusion, and due to the small subgroup size, were excluded from subsequent analyses.

Sixteen patients with the diagnosis of AD as determined by criteria set forth by the National Institute of Neurological and Communicative Diseases and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA; McKhann et al., 1984) also participated. SPECT scans documented bilateral temporal–parietal hypoperfusion with sparing of anterior regions.

Magnetic resonance imaging (MRI) scans of FTD and AD patients ruled out dementia due to strokes and other lesions.

Healthy, normal elderly control participants were selected from two larger pools of archival data for comparison with the demented groups. Control participants had no history of head injuries, major affective or psychotic disorder, seizures, or substance abuse within the past 5 years. The demographic information for all groups including gender, age, and education is presented in Table 1. The AD group was significantly older than the control and FTD groups, which did not differ from each other. Groups did not differ in education level. The superscript of "1" and "2" denotes which control group was used for comparison with the patient groups and for *z*-score transformation for each test. Normative data from Hall et al. (1996) were used to obtain *z*-scores for the Beery Developmental Test of Visual Motor Integration.

Neuropsychological Battery

The following is a list of the cognitive domains assessed and the specific tests used to measure each domain:

Intelligence

Satz-Mogel format of the Wechsler Adult Intelligence Scale–Revised (WAIS–R[2]; Adams et al., 1984; Wechsler, 1981), with the exception of Picture Arrangement, which was administered in its entirety.

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Table 1. Demographic information, mean (±*SD*) raw scores for all participants, and group comparisons.

Variable	Controls[1]	Controls[2]	Alzheimer's	Right-FTD	Left-FTD	*df*	*F*
Age	60.87 (±9.09)	60.36 (±9.64)	73.31 (±9.40)	59.07 (±11.10)	63.0 (±8.87)	3,45	4.45*
Male/Female	5/6	33/71	7/9	5/6	7/4		
Education	14.73 (±2.52)	14.82 (±3.31)	14.80 (±3.00)	15.27 (±1.85)	15.27 (±3.80)	3,44	0.09
Full-Scale IQ[a]	n/a	116.81 (±14.06)	89.88 (±18.79)	83.00 (±21.05)	79.00 (±11.78)	3,135	38.52***
Verbal IQ	n/a	115.76 (±13.26)	87.75 (±18.86)	79.27 (±14.27)	88.80 (±12.51)	3,135	32.57***
Performance IQ	n/a	114.50 (±15.14)	94.69 (±21.98)	86.82 (±24.35)	73.11 (±13.92)	3,136	33.04***
Language Processing							
Boston Naming	n/a	56.16 (±3.31)	46.50 (±12.92)	49.73 (±6.17)	14.91 (±21.42)	3,96	61.71***
FAS	44.45 (±10.17)	n/a	20.56 (±11.17)	16.18 (±15.80)	6.00 (±6.96)	3,45	22.33***
Category	19.09 (±6.70)	n/a	9.70 (±5.12)	6.55 (±5.32)	2.72 (±3.41)	3,44	19.48***
Stroop A	n/a	43.32 (±7.28)	68.50 (±19.61)	52.50 (±9.77)	87.25 (±29.07)	3,127	51.03***
Stroop B	n/a	59.25 (±10.14)	118.23 (±46.96)	86.50 (±25.69)	143.60 (±31.57)	3,123	64.30***
Executive Function							
Wisconsin Card Sorting Test							
Category	n/a	4.99 (±1.54)	3.28 (±1.55)	1.20 (±1.93)	3.80 (±2.74)	3,132	15.61***
Set Failure	n/a	0.81 (±1.08)	1.33 (±2.24)	0.00 (±0.00)	1.43 (±3.00)	3,118	1.39
Persv.	n/a	18.25 (±14.76)	54.00 (±42.73)	102.29 (±31.51)	32.00 (±21.43)	3,123	47.32***
Tot. Err	n/a	30.64 (±20.84)	68.20 (±31.03)	82.00 (±21.32)	42.00 (±16.14)	3,122	18.82***
%Concept.	n/a	64.33 (±18.55)	37.39 (±20.56)	19.53 (±22.43)	59.89 (±17.96)	3,126	15.81***
Desig. Generation	29.63 (±20.11)	n/a	12.23 (±9.85)	6.45 (±9.70)	7.45 (±6.55)	3,42	8.15***
Sentence sequ. error	0.00 (±0)	n/a	5.00 (±3.21)	4.00 (±3.56)	5.00 (±3.39)	3,26	7.25***
Visual–Spatial/Construction Skills							
Beery	n/a	n/a	19.75 (±9.40)	31.20 (±10.36)	29.82 (±11.91)		
Rey-O Copy	34.82 (±2.09)	n/a	20.34 (±12.02)	24.73 (±8.81)	29.55 (±6.53)	3,45	6.61***
Memory							
Rey-O 3-min delay	18.23 (±6.80)	n/a	6.81 (±7.10)	6.05 (±7.35)	7.59 (±7.55)	3,45	7.24***
Shop List delay	9.30 (±1.25)	n/a	2.75 (±3.42)	3.27 (±3.29)	1.90 (±3.10)	3,44	15.38***
Logical Mem I	n/a	12.58 (±9.26)	9.44 (±8.32)	10.45 (±8.58)	7.73 (±7.48)	3,137	7.03***
LM % retention	n/a	80.24 (±16.57)	14.48 (±27.79)	37.48 (±30.25)	41.39 (±39.57)	3,129	43.58***
Difference Scores							
VIQ − PIQ	n/a	1.14 (±15.12)	6.94 (±17.23)	7.55 (±13.24)	−16.67 (±12.53)	3,135	5.62**
FAS-Des. Flu.	14.82 (±25.38)	n/a	9.92 (±8.20)	9.73 (±7.40)	−1.45 (±6.76)	3,42	2.66***
Sent Seq. − Pict Seq.	1.36 (±15.12)	n/a	.64 (±2.11)	1.38 (±3.11)	−3.90 (±2.92)	3,29	7.77**
Verbal Mem. − Nonverbal Mem.	−9.55 (±6.72)	n/a	−4.94 (±6.41)	−2.77 (±5.50)	−5.68 (±5.19)	3,44	2.55**

[a]No significant differences between patient groups [$F(2,33) = 1.14$, $p = .33$].
*$p < .01$, **$p < .001$, ***$p < .0001$.

Language processing

Boston Naming Test[2] (BNT; Kaplan et al., 1983; Lezak, 1995); Controlled Oral Word Association Test of verbal fluency[1] (FAS; Benton & Hamsher, 1976); category fluency[1] (animals); and the Comalli Stroop Test[2], Parts A and B (Mitrushina et al., 1999).

Executive function

Wisconsin Card Sorting Test[2] (WCST; Heaton et al., 1993); 5-min unstructured design generation task[1] (Design Fluency; Jones-Gotman & Milner, 1977); and a sentence sequencing task[1] (Boone et al., 1999).

Visual–spatial/constructional skills

Rey-Osterrieth (Rey-O) Complex Figure copy[1] (Lezak, 1995; Mitrushina et al., 1999); and Beery Developmental Test of Visual Motor Integration (Hall et al., 1996).

Memory

Logical Memory[2] subscale of the Wechsler Memory Scale–Revised (WMS–R; Wechsler, 1987; Lezak, 1995); 10-item Shopping List test[1] (Boone et al., 1999); Rey-Osterrieth Complex Figure 3-min delay[1] (Rey-O; Boone et al., 1993; Lezak, 1995).

The following test scores were used for statistical analyses: Verbal, Performance, and Full Scale IQ scores; individual scaled scores for the 11 WAIS–R subtests; immediate recall and percentage of retention on 30-delay for Logical Memory subtest of the WMS–R; time in seconds to complete Stroop A (color reading) and Stoop B (color naming); total words generated in 3 min for the letters *f*, *a*, and *s*; total number of animals generated in 1 min; total score on the Beery; copy and 3-min delayed recall scores on the Rey-O Complex Figure; five WCST measures (number of categories completed, failures to maintain set, total errors, perseverative responses, and percent conceptual understanding); total number of correctly sequenced sentences out of a possible 10 (Boone et al., 1999); total number correct out of 60 objects on the BNT; total items generated in the design fluency task; and number of shopping list items recalled on 15-min delay. Because many patients across all groups were unable to complete Stroop C, data from this test could not be analyzed. Additionally, all patient scores on the WCST except for percent conceptual understanding were doubled, because the single deck (64 cards) version of the test was administered to these participants, while the full test (128 cards) was administered to normal controls.

To render performance metrics across tests comparable, scores were converted to standardized scores. That is, mean test scores for the patients were converted into standard equivalents using the score means and standard deviations from the control groups. *Z*-scores were then used as dependent variables for comparison of the performance of the three patient groups (AD, left-FTD, right-FTD) on each test. It should be noted that *z*-scores were adapted so that the greater the value the better the performance. Raw test scores are, however, presented in Table 1.

In a previous study (Boone et al., 1999) we found that difference scores were most useful in differentiating between left- *versus* right-FTD groups. In the current study we were again interested in finding whether these same difference scores differentiated AD from the two FTD groups. Thus, the following difference scores were calculated: (1) VIQ minus PIQ, (2) FAS minus design fluency (*z*-score differences), (3) word sequencing minus picture sequencing (*z*-score differences), (4) shopping list 15-min delayed recall minus Rey-Osterrieth 3-min delayed recall (*z*-score differences).

Due to the multiple comparisons, the *p* value required for statistical significance was lowered to .01 rather than the standard .05 value. Significance values for the follow-up analyses were set at the standard .05 level. While we recognize that this may not entirely protect against Type I error, a more stringent criteria would increase Type II error due to the small sample size.

RESULTS

As shown in Table 1, groups did not differ in education, but did differ in age; AD patients were significantly older than all other groups, which did not differ from each other. Groups also differed in Full Scale IQ, with the controls scoring significantly higher than the patients. The patient groups did not differ from each other in overall IQ, indicating that patient groups were comparable in disease severity.

Multivariate analysis of variances (MANOVA) were computed comparing the three patient groups on the *z*-scores for each cognitive domain. As mentioned above, the relative performance of the three patient groups to the normal controls was captured in the *z*-score analyses. However, comparison of all four groups (including the controls) were also performed and are presented in Table 1.

Intellectual Functioning

Because we were interested in identifying unique patterns of group performance across all Verbal and Performance subtests, we computed two MANOVAs. One was designed to assess group differences for the Verbal subtests (i.e., Group × Verbal Subtests), and a second analysis was designed to assess group differences for the Performance subtests (i.e., Group × Performance Subtests). The mean scaled scores for the Verbal subtests are depicted in Figure 1 and the mean scaled scores for the Performance subtests are presented in Figure 2. When examining the Verbal subtests, no main effect of group was found [$F(2,32) = 2.26$, $p = .121$]; however, significant main effects of Verbal subtests, Wilks's Lambda [$F(4,29) = 4.96$, $p = .004$], and a trend toward a significant interaction of Group × Verbal Subtest, Wilks's Lambda [$F(10,58) = 2.46$, $p = .016$], were documented. Follow-up analyses, using one-way ANOVAs were

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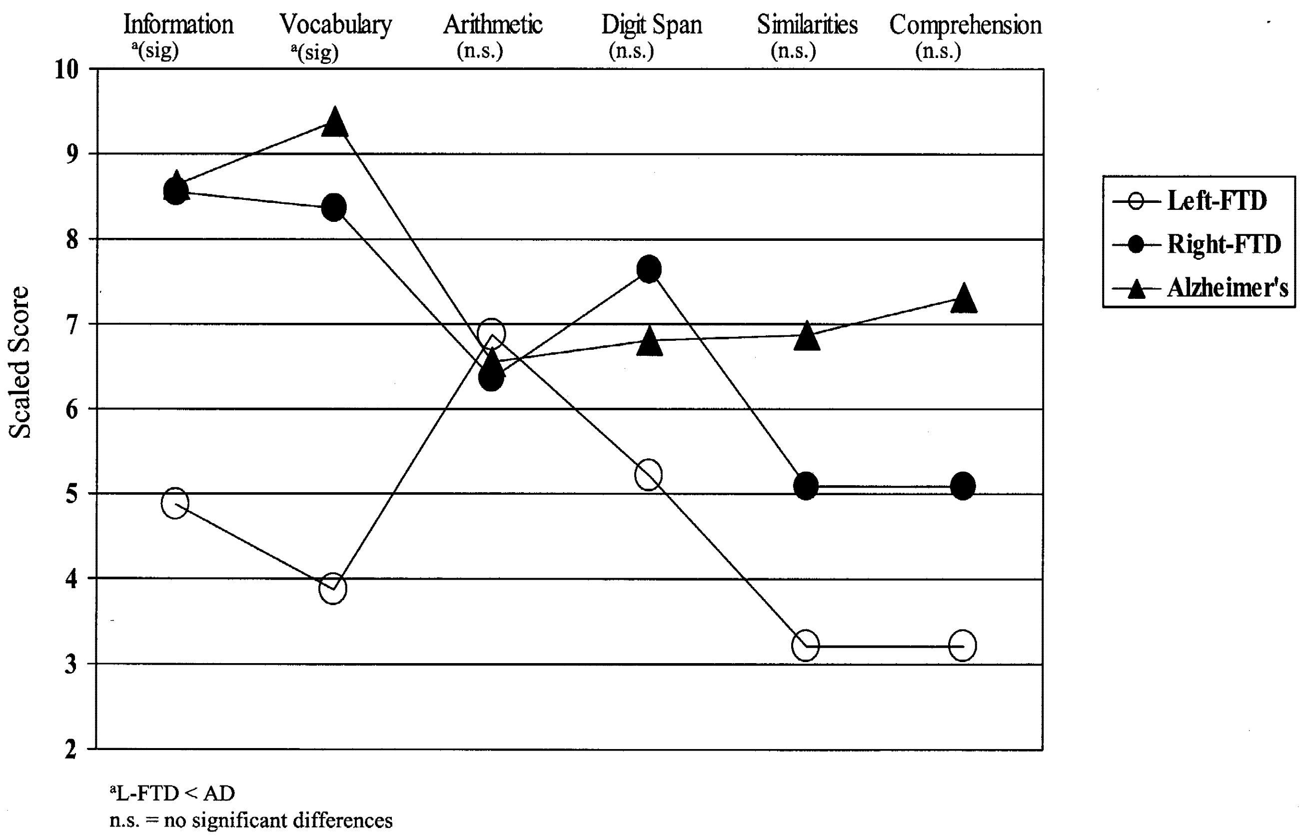

Fig. 1. Mean scaled scores of the Verbal IQ subtests for each group.

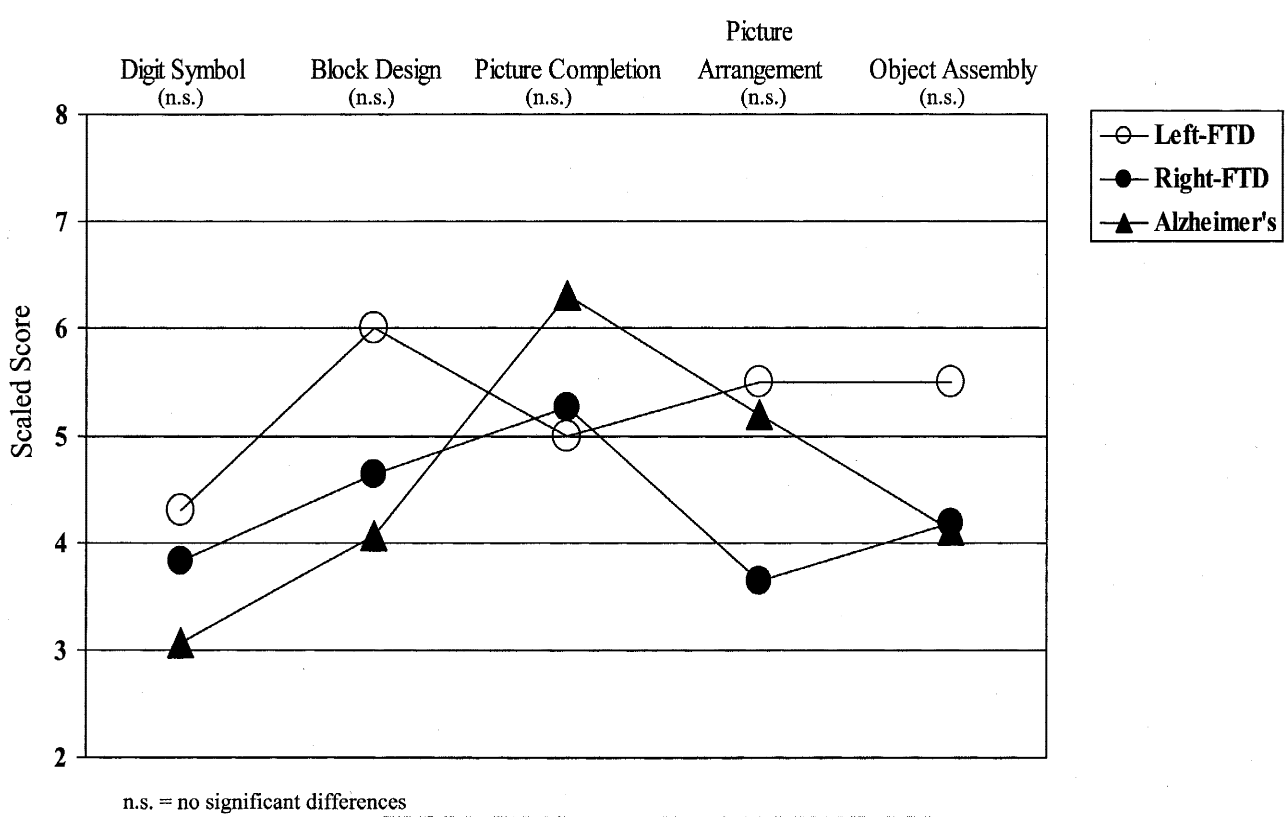

Fig. 2. Mean scaled scores of the Performance IQ subtests for each group.

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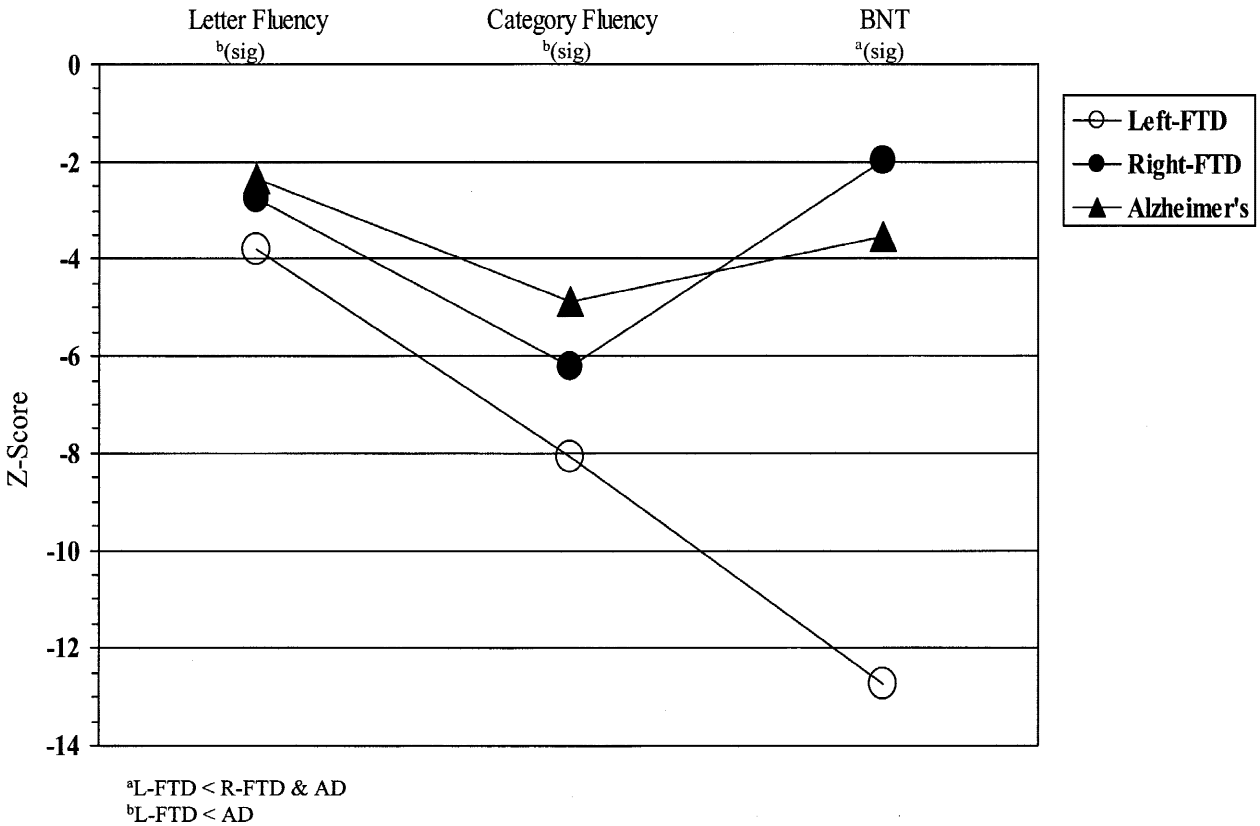

Fig. 3. Mean *z*-score values for groups as a function of language task performance.

performed in order to assess the interaction effect. Results revealed a trend toward a significant group difference for the Information subtest [$F(2,32) = 4.07$, $p = .027$], and a Tukey's *post-hoc* comparison revealed that the left-FTD patients performed poorer than the AD patients ($p < .05$). Additionally, group differences were found for the Vocabulary subtest [$F(2,33) = 4.75$, $p = .01$], with the left-FTD patients performing poorer than the AD ($p < .05$).

The Group × Performance subtest MANOVA revealed a statistically significant main effect of subtest [$F(4,31) = 4.22$, $p = .008$]. Follow-up analyses revealed that for all patient groups, digit symbol performance was lower relative to the other subtests ($p < .05$). No significant main effect of group [$F(2,34) = .79$, $p = .46$] was observed. Additionally, the interaction effect of Group × Performance subtest failed to reach statistical significance, Wilks's Lambda [$F(8,64) = 2.25$, $p = .036$].

Patients did not differ in VIQ [$F(2,33) = 3.00$, $p = .06$] or PIQ [$F(2,34) = 1.10$, $p = .34$].

Language Processing

A MANOVA designed to assess group differences on three specific tests of language (letter fluency, category fluency, and BNT) was used. Mean *z*-score values for each group are presented in Figure 3. The results revealed a significant main effect of group, [$F(2,33) = 18.17$, $p = .0001$], a significant main effect of language test, Wilks's Lambda [$F(2,32) = 63.38$, $p < .0001$], and a significant interaction of Group × Language test, Wilk's Lambda [$F(4,66) = 7.01$, $p = .0001$].

Follow-up one-way ANOVAs were performed to further assess the interaction effect. Analysis of the BNT revealed a significant effect of group [$F(2,34) = 17.54$, $p = .0001$], with Tukey *post-hoc* analyses revealing poorer naming ability by the left-FTD group relative to the right-FTD and AD groups (both p values $< .05$). An ANOVA designed to assess letter fluency performance revealed a significant effect of group [$F(2,35) = 5.05$, $p = .01$], with Tukey's *post-hoc* analyses exhibiting fewer word production by the left-FTD group relative to the AD group ($p < .05$). Analyses of category fluency again revealed significant group differences [$F(2,34) = 5.91$, $p = .006$], with Tukey's *post-hoc* analyses displaying fewer animal exemplars produced by the left-FTD group relative to the AD group ($p < .05$).

Of interest was the pattern of language performance (i.e., letter *vs.* category *vs.* BNT) within each group.[1] A repeated-measures ANOVA revealed significant differences between

[1] It should be noted that 3 min were allotted for the letter fluency (F, A, S) *versus* 1 min for the category fluency (animal) tasks. However, *z*-score conversions adjusted for this difference in difficulty level.

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language tasks for the left-FTD group, Wilks's Lambda [$F(2,9) = 66.11$, $p = .0001$], with significantly worse performance on object naming relative to category and letter fluency (p values $< .05$), as well as poorer performance on category compared to letter fluency ($p < .05$). A second repeated-measures ANOVA revealed differences between language performance for the AD group, Wilks's Lambda [$F(2,12) = 9.38$, $p = .004$], with pairwise comparisons revealing poorer category relative to letter fluency ($p < .05$). A final repeated-measures ANOVA again revealed significant differences among the language tests for the right-FTD group, Wilks's Lambda [$F(2,9) = 24.52$, $p = .0001$], with *post-hoc* analyses indicating greater naming ability relative to category fluency ($p < .05$), and greater letter relative to category fluency ($p < .05$).

A MANOVA comparing group differences on the verbal processing speed tasks (Stroop A and Stroop B) was computed. Mean *z*-score values for each group are presented in Figure 4. The results revealed a significant main effect of task [$F(1,23) = 5.63$, $p = .026$]. Comparison of group means revealed that the performance of all groups was poorer for color naming relative to color reading. The MANOVA also revealed a significant main effect of group [$F(2,23) = 6.22$, $p = .007$], with Tukey's *post-hoc* comparison revealing an overall worst performance by the left-FTD relative to the right-FTD patients ($p < .05$).

Executive Functioning

A MANOVA designed to assess group differences on five specific variables of the Wisconsin Card Sorting Test was computed. Mean *z*-score values for each group are presented in Figure 5. The analysis revealed a significant main effect of group [$F(2,16) = 29.74$, $p = .0001$], a main within-group effect of WCST variables, Wilks's Lambda [$F(4,13) = 13.67$, $p = .0001$], as well as a significant interaction effect of WCST Variables × Group [$F(4,14) = 4.79$, $p = .01$]. Follow-up analyses of the interaction effect, using one-way ANOVAs, were performed. Significant differences between the groups were found in the level of conceptual understanding of the task [$F(2,21) = .03$, $p = .005$], with Tukey's *post-hoc* comparison revealing that the right-FTD group had a significantly lower conceptual task understanding than the left-FTD group ($p < .05$). A second one-way ANOVA revealed group differences for the number of perseverative responses made [$F(2,21) = 8.22$, $p = .002$], with Tukey's *post-hoc* analysis revealing that the right-FTD group made greater perseverative responses than both the left-FTD and the AD groups (p values $< .05$). A trend toward a difference among groups was found for the total number of errors [$F(2,21) = 4.90$, $p = .02$], with Tukey's analysis indicating greater number of errors for the right-FTD relative to the left-FTD group ($p < .05$). While the number of

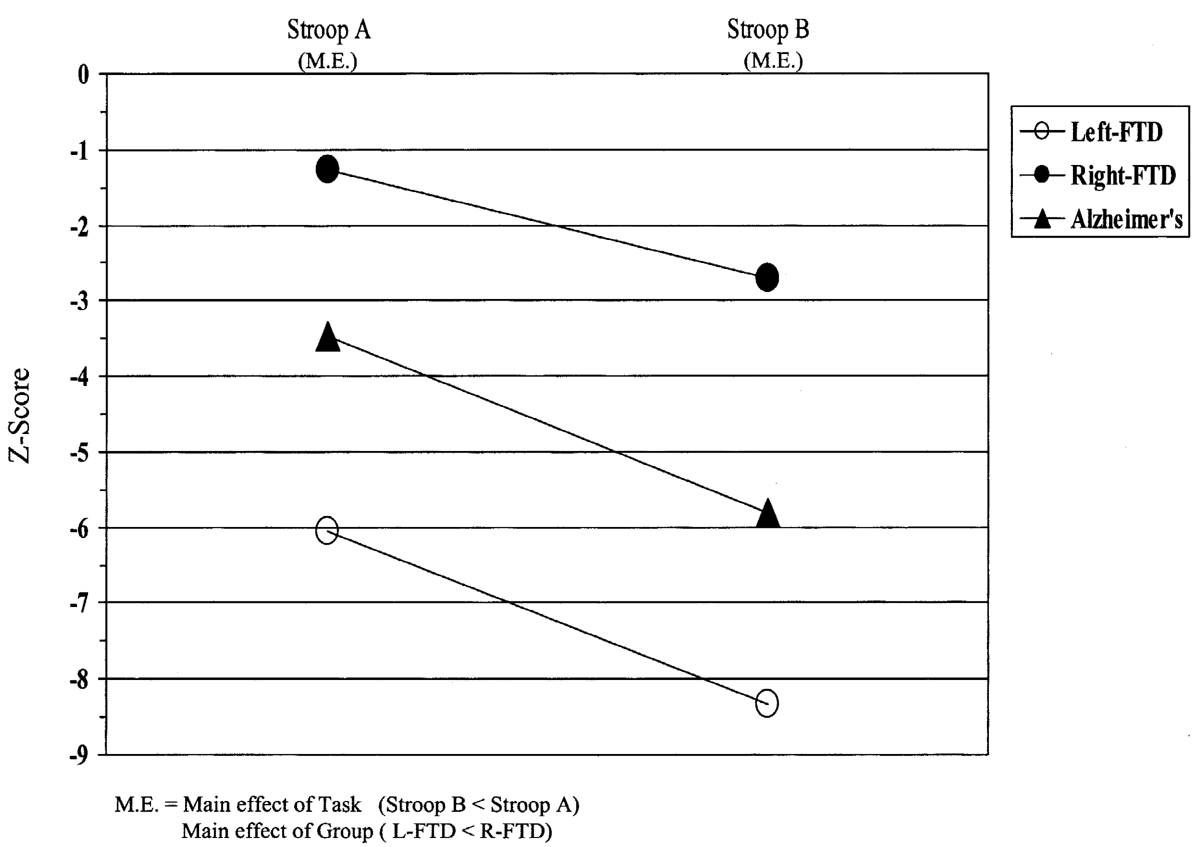

Fig. 4. Mean *z*-score values for groups as a function of verbal processing speed performance.

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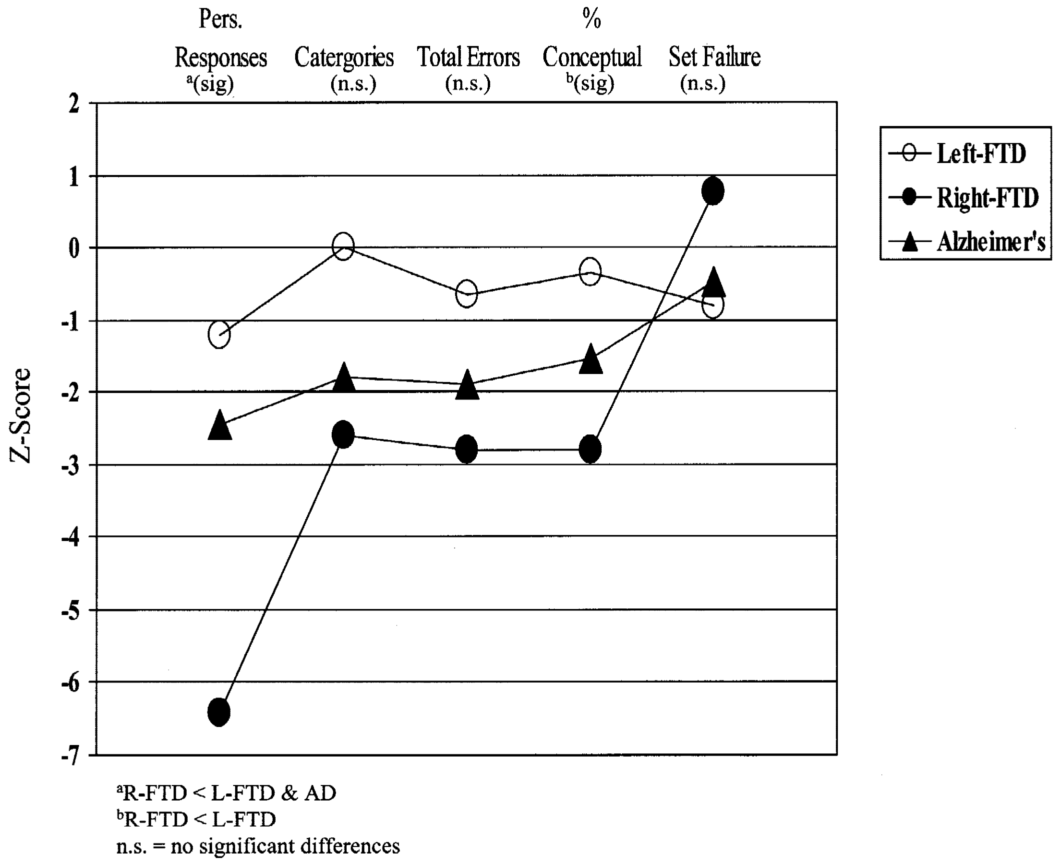

Fig. 5. Mean *z*-score values for groups as a function of WCST performance.

categorical sorts did not reach statistical significance, [$F(2,31) = 2.98$, $p = .065$], a trend for lower categorical sorts by the right-FTD group was present. No significant differences were found between the groups for the number of set failures [$F(2,17) = .55$, $p = .59$].

A one-way ANOVA was designed to assess group *z* scores for design generation performance revealed no significant effects [$F(2,32) = 1.47$, $p = .25$]. However, a second one-way ANOVA designed to examine group *z* scores for sentence sequencing revealed a nearly significant difference [$F(2,20) = 4.3$, $p = .03$]. While follow-up Tukey's analysis did not reach statistical significance, there was a trend for the right-FTD and AD groups to outperform the left-FTD group (*p* values were .06 and .07, respectively). No significant differences were present between the right-FTD and AD groups ($p = .91$).

Visual–Spatial/Constructional Skills

A MANOVA designed to assess group differences on two specific tests of visual–spatial functioning (Rey-O copy and Beery) was used. Mean *z*-score values are presented in Figure 6. The results revealed a significant main effect of group [$F(2,30) = 5.92$, $p = .007$], a significant main effect of visual–spatial tests, Wilks's Lambda [$F(2,32) = 32.84$, $p = .0001$], and a significant interaction of Group × Visual–Spatial Test, Wilks's Lambda [$F(2,30) = 4.92$, $p = .01$].

Follow-up one-way ANOVAs were performed in order to further assess the interaction effect. Analysis of the Beery revealed a nearly significant effect of group [$F(2,30) = 3.97$, $p = .03$], with Tukey *post-hoc* analyses exhibiting poorer constructional ability by the AD group relative to the right-FTD group ($p < .05$). Similarly, a trend towards a significant difference between the groups was observed for the Rey-O copy [$F(2,35) = 2.88$, $p = .07$], with *post-hoc* analyses indicating a significantly poorer copy ability by the AD relative to the left-FTD ($p = .005$).

Memory Function

Separate analyses, assessing group differences for verbal and nonverbal memory performances were carried out. The first MANOVA compared group performance on verbal memory measures (i.e., Shopping List Trial 5, delay recall, recognition memory, Logical Memory immediate recall, and retention over 30-min delay). This analysis revealed no significant main effect of groups [$F(2,29) = .35$, $p = .71$], or a significant interaction effect, Wilks's Lambda [$F(8,52) = .82$, $p = .74$]. However, a significant main effect of memory measure was found, Wilks's Lambda [$F(4,26) = 30.68$, $p =$

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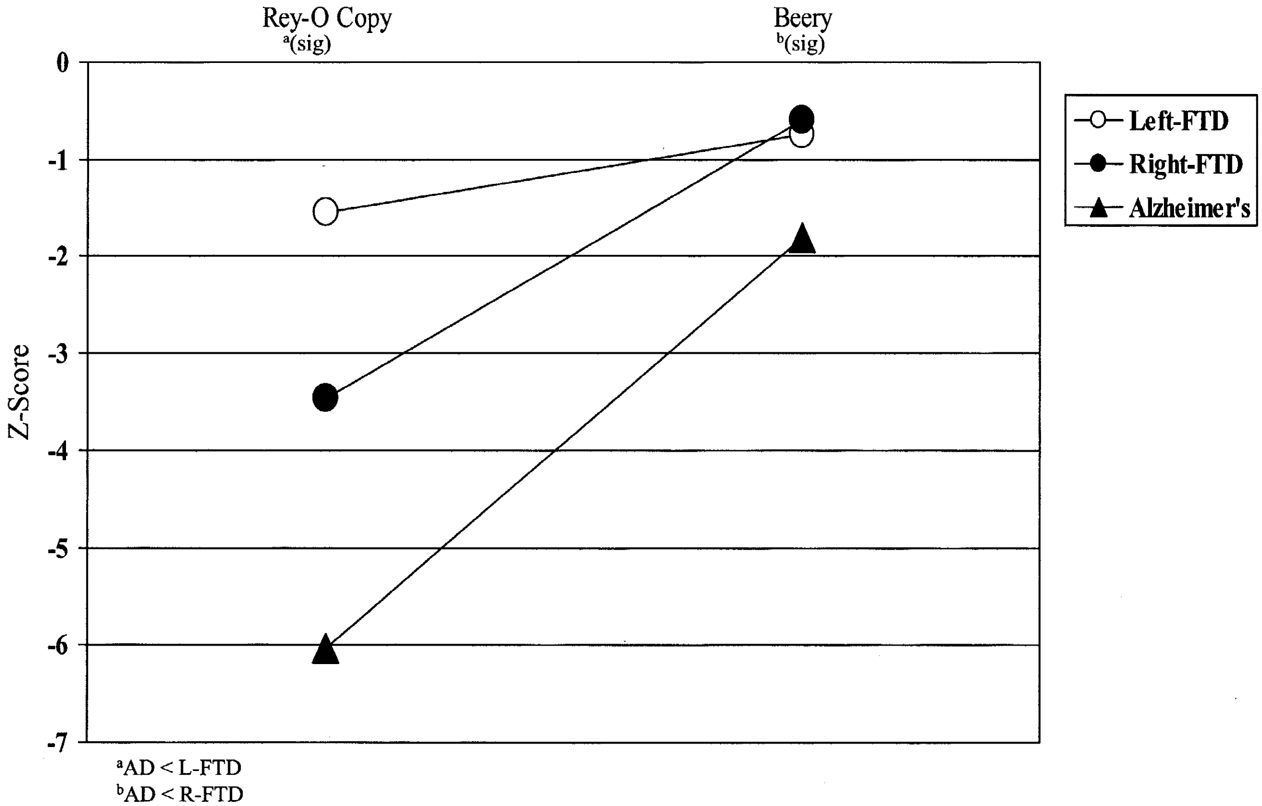

Fig. 6. Mean *z*-score values for groups as a function of visual–spatial/construction task performance.

.0001]. Follow-up analyses revealed that all groups performed better on the logical memory measures (both immediate recall and retention) compared to the shopping list measures (p values $< .05$). Mean z scores are presented in Figure 7.

One-way ANOVA for Rey-Osterrieth 3-min delay comparing group z scores was performed and the mean values are presented in Figure 7. The results revealed no significant group differences [$F(1,35) = 0.12$, $p = .88$].

Difference Scores

Four one-way ANOVAs were performed in order to assess group performance on the difference scores. Mean group difference scores are presented in Table 1. Groups differed significantly for the VIQ *minus* PIQ measure [$F(2,33) = 8.50$, $p = .001$]; a Tukey pairwise comparison revealed a significantly poorer score for the left-FTD group relative to both the AD and the right-FTD groups (p values $< .05$). A significant difference between groups was also found for the FAS *minus* design fluency difference scores [$F(2,32) = 7.34$, $p = .002$], with a Tukey pairwise comparison again revealing a significantly poorer score for the left-FTD group relative to both the AD and the right-FTD groups (p values $< .05$). A significant effect of group was found for sentence sequencing *minus* picture sequencing [$F(2,19) = 5.72$, $p = .01$]; a Tukey pairwise comparison revealed a significantly poorer score left-FTD relative to the right-FTD group ($p < .05$), but not the AD group. The fourth ANOVA comparing groups on delayed verbal memory measure (10-item shopping test) *minus* the visual memory test (Rey-Osterrieth delay) did not reveal any significant differences, [$F(2,35) = 1.07$, $p = .36$]. Mean z-score values for the latter three difference scores are presented in Figure 8.

Analysis of Covariance

Given the significantly older age of the AD group, a series of analyses of covariance (ANCOVAs) were performed, with age as the covariate and groups and specific cognitive domains as independent variables. The results of the ANCOVA were nearly identical to the previous ANOVAs, with the exception of a lack of significant main effects in the following cognitive domains: information processing [$F(1,22) = 1.44$, $p = .24$], Wisconsin Card Sorting Test measures [$F(4,12) = 1.18$, $p = .37$], and verbal memory measures [$F(4,25) = 1.17$, $p = .35$]. The results of the ANCOVA suggest that age does not account for the group differences.

DISCUSSION

We have previously reported on differential neuropsychological profiles in FTD patients with primarily left-sided *versus* primarily right-sided anterior hypoperfusion (Boone et al., 1999). We found that patients with left-FTD dis-

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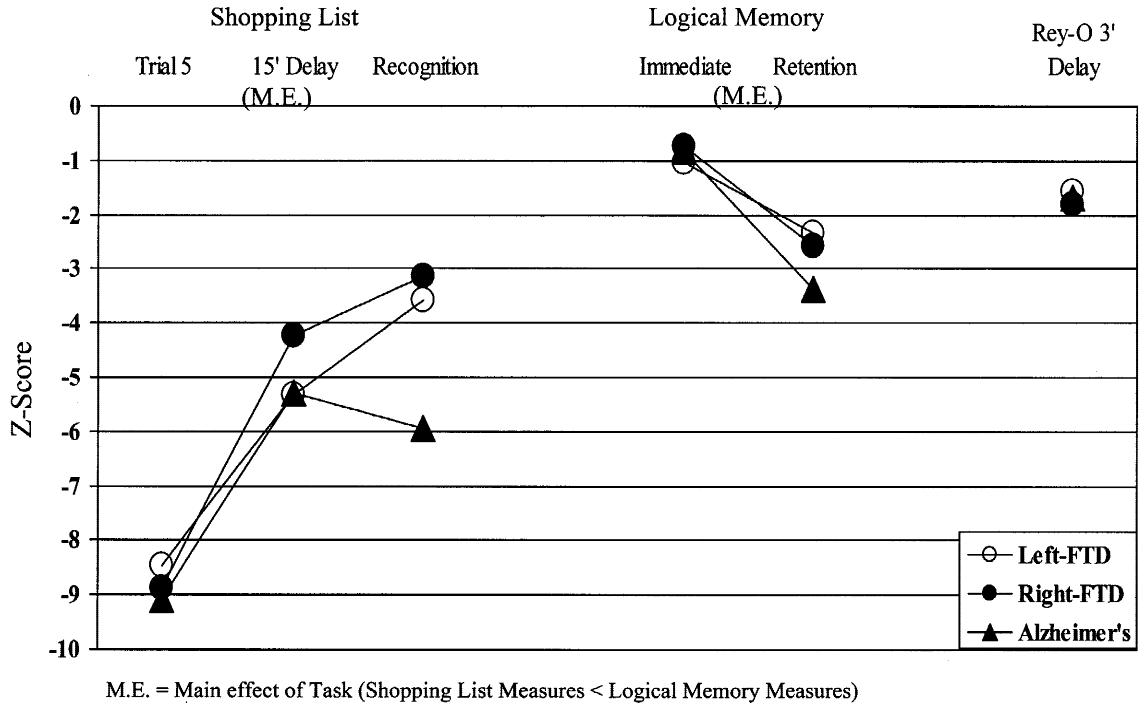

Fig. 7. Mean *z*-score values for groups as a function of memory performance.

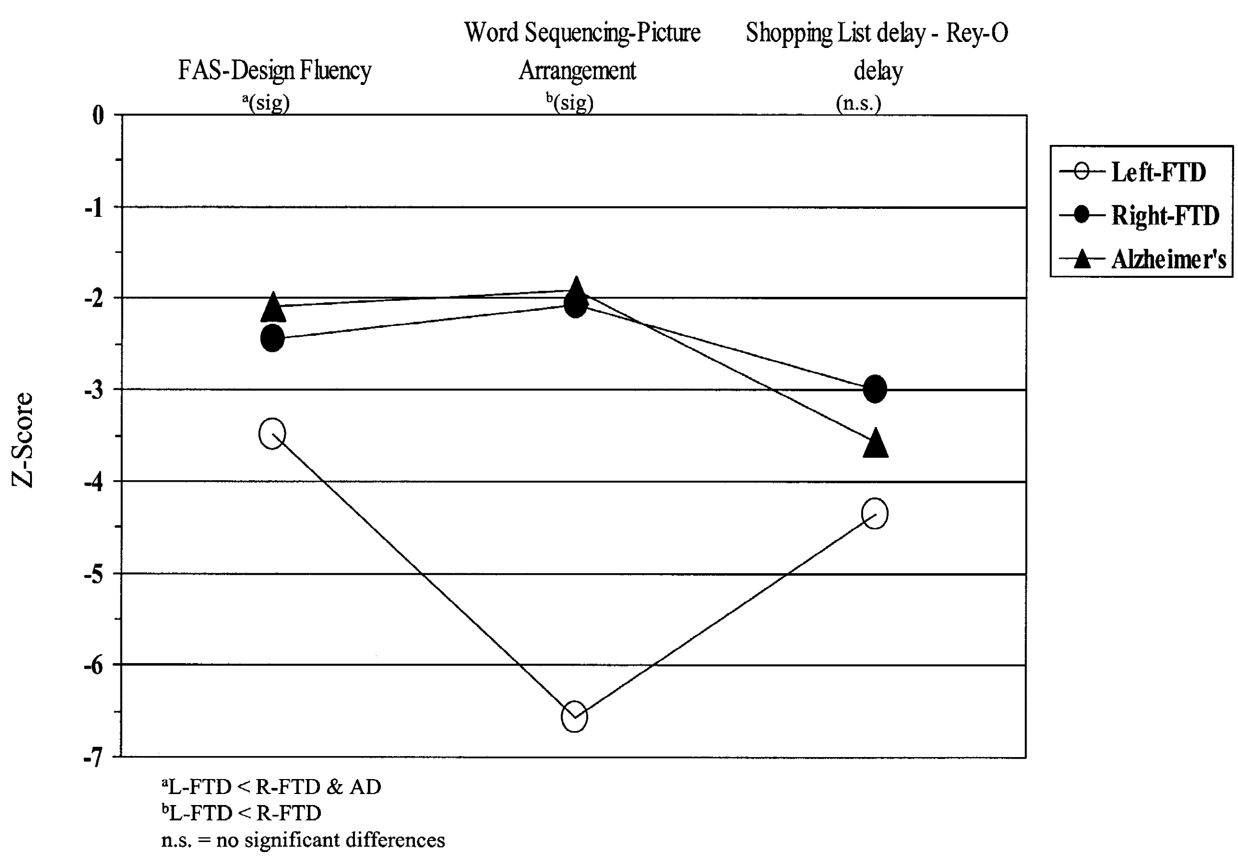

Fig. 8. Mean difference *z*-score values based on three comparisons: FAS *minus* Design Fluency, Word Sequencing *minus* Picture Arrangement, and Shopping List delay *minus* Rey-O delay.

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played verbal abnormalities, namely, VIQ less than PIQ, deficits in word-retrieval, and lowered verbal executive skills relatively to nonverbal executive skills (i.e., word generation less than design generation, word sequencing less than picture sequencing). In contrast, patients with right-FTD displayed a mirror opposite pattern of performance and also showed evidence of perseveration. Groups did not differ in memory (verbal and nonverbal) and spatial/constructional skills.

Left unaddressed in this study was whether the performances of the two FTD groups, while distinct from each other, also differ from that observed in Alzheimer's disease. Given that three groups display differential patterns of cerebral hypoperfusion, it was expected that the cognitive profiles across the three groups would also be unique. Specifically, it was anticipated that the bitemporal/parietal hypoperfusion and hippocampal atrophy found in AD would be associated with particular impairment in memory (both verbal and nonverbal) and visual perceptual/spatial deficits, with more minor abnormalities in word retrieval and executive tasks. In contrast, it was expected that the patients with left-FTD, who display marked hypoperfusion of left frontal/anterior temporal areas, would be characterized by pronounced deficits relative to the two other groups in verbal semantic knowledge, and verbal executive skills. Conversely, the patients with right-FTD, who show collateral hypoperfusion of right frontal/anterior temporal areas, were hypothesized to exhibit the worst performance of the three groups on nonverbal executive tasks (generation, sequencing) and to display the most perseverative behavior.

The findings from the current study generally confirmed these expectations. Patients with AD scored significantly below patients with right- or left-FTD on visual constructional tasks even after covarying for the older age of the AD patients; however, the AD group did not differ from the FTD groups on memory scores. On language tasks, patients with left-FTD scored significantly below patients with AD on measures of word-retrieval, verbal semantic memory (fund of general verbal information, vocabulary, and category fluency), and verbal executive ability (phonemic fluency); AD patients did not differ from patients with right-FTD on these measures. AD patients also exhibited significantly less perseverative behavior than right-FTD patients, and did not differ from left-FTD patients on this parameter. In addition, there was a trend toward the AD outperforming both FTD groups on design generation and the left-FTD group on verbal processing speed tasks.

We previously documented that difference scores can aid in the differentiation of cognitive profiles of left- *versus* right-FTD patients (Boone et al., 1999). In the current study we found that the AD group most closely resembled that of the right-FTD group when comparing VIQ minus PIQ scores and phonemic verbal fluency minus design fluency, with both groups outperforming the left-FTD group. However, the AD group did not differ from either group on the word sequencing minus picture sequencing difference scores, nor did any of the groups differ on the verbal memory minus visual memory difference scores. Taken together, these results suggest that the deficits in AD between the verbal and nonverbal analog tests are most similar to that of the right-FTD.

Additionally, we have previously reported that analysis of relative patterns of performance may actually be more effective in discriminating dementia groups than comparisons on absolute scores (Boone et al., 1999; Pachana et al., 1996). In addition to the differences in absolute scores described above, we found that on language tasks, patients with right-FTD displayed word-retrieval *z* scores that were uniformly higher than category fluency scores, while patients with left-FTD showed the opposite patterns. In contrast, most AD patients generally obtained word-retrieval scores that were comparable (i.e., within .5 *SD*) to category fluency.

In terms of verbal fluency performance, the present results are in agreement with previous findings indicating greater impairment in category fluency relative to letter fluency in patients with AD (Barr & Brandt, 1996; Butters et al., 1987; Crossley et al., 1997; Geffen et al., 1993; Hodges et al., 1999; Monsch et al., 1994). However, unexpectedly, the same pattern of performance (i.e., poorer category fluency relative to letter fluency) was also found for both left- and right-FTD patients. It has been previously reported that patients with frontal lobe disease and/or subcortical dementia (i.e., Huntington's disease, Parkinson's disease) demonstrate uniform compromise in both letter and category fluency (Butters et al., 1987; Hodges et al., 1990; Monsch et al., 1994; Tröster et al., 1989) or worse letter relative to category fluency (Matison et al., 1982). There have, however, been a few studies exhibiting poorer category compared to letter fluency performance in patients with Huntington's disease (Rosser & Hodges, 1994). Pasquier et al. (1995) found greater impairment in category relative to letter fluency in a group of patients with frontal lobe dementia, and speculated that this pattern of performance is due to impaired search strategies (i.e., inability to break a category into subcategories and carry out a thorough search). The present results would indicate that systematic search strategies are most impaired for left-FTD patients.

Interestingly, no significant differences were found between the groups on both absolute and difference scores for verbal and nonverbal memory tasks. Previous literature has suggested that AD patients demonstrate markedly poor recall and inability to retain information over short delays (Heindel et al., 1993), while FTD patients exhibit relatively spared memory (Neary & Snowden, 1996). Results from the current study indicate that any differences in free recall across groups are subtle at best, and less apparent than differences in performance on language, semantic memory, visual–spatial, and executive tasks.

In conclusion, results from the present study indicate that AD patients demonstrate a relatively distinct pattern of neuropsychological function compared to patients with right- *versus* left-FTD. However, given Hodges et al.'s (1999) recent discrimination of temporal lobe *versus* frontal lobe FTD, it is likely that there are further cognitive subtypes within right- and left-FTD, namely, left frontal, left temporal, right frontal, and right temporal. Future research is needed to determine whether AD patients continue to differ from these more discrete FTD subtypes. In addition, the frontal lobe variant of AD is only beginning to be understood. Johnson et al. (1999) identified a subgroup of pathologically confirmed AD patients (with large degree of neurofibrillary tangles on autopsy) who displayed impairment on frontal lobe tasks during the early stages of their illness. Future research is needed to ascertain how patients with the frontal variant of AD differ from FTD subgroups.

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