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NEUROCOGNITIVE DIFFERENTIAL DIAGNOSIS OF DEMENTING DISEASES: ALZHEIMER'S DEMENTIA, VASCULAR DEMENTIA, FRONTOTEMPORAL DEMENTIA, AND MAJOR DEPRESSIVE DISORDER

ALYSSA J. BRAATEN

Nova Southeastern University
Center for Psychological Studies
Fort Lauderdale, Florida, USA

THOMAS D. PARSONS

Department of Neurology, School of Medicine
University of North Carolina at Chapel Hill
Chapel Hill, North Carolina, USA.

ROBERT McCUE

South Florida Neurology Associates, P.A.
Delray Beach, Florida, USA

ALFRED SELLERS
WILLIAM J. BURNS

Nova Southeastern University
Center for Psychological Studies
Fort Lauderdale, Florida, USA

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Address correspondence to Thomas D. Parsons, Ph.D., Department of Neurology, CB # 7025, University of North Carolina School of Medicine, 3114 Bioinformatics Building, Chapel Hill, NC 27599-7025, USA. E-mail: tparsons@neurology.unc.edu

Similarities in presentation of Dementia of Alzheimer's Type, Vascular Dementia, Frontotemporal Dementia, and Major Depressive Disorder, pose differential diagnosis challenges. The current study identifies specific neuropsychological patterns of scores for Dementia of Alzheimer's Type, Vascular Dementia, Frontotemporal Dementia, and Major Depressive Disorder. Neuropsychological domains directly assessed in the study included: immediate memory, delayed memory, confrontational naming, verbal fluency, attention, concentration, and executive functioning. The results reveal specific neuropsychological comparative profiles for Dementia of Alzheimer's Type, Vascular Dementia, Frontotemporal Dementia, and Major Depressive Disorder. The identification of these profiles will assist in the differential diagnosis of these disorders and aid in patient treatment.

Keywords cognition, dementia, differential diagnosis, neuropsychological tests

Clinical overlap in the presentation of Dementia of the Alzheimer's Type, Vascular Dementia, Fronto-Temporal Dementia, and Major Depressive Disorder, poses significant challenges in differential diagnosis. Although numerous studies have compared the neuropsychological profile of patients with Dementia of the Alzheimer's Type, Vascular Dementia, and depression, findings have been inconsistent. Due to these inconsistencies, unique neuropsychological profiles for each disorder, when present, are not firmly established. As such, it has been difficult for clinicians confidently to discern which neuropsychological variables provide relevant information for differential diagnoses. Although less research has been done comparing Fronto-Temporal Dementia to that of Dementia of the Alzheimer's Type, Vascular Dementia, and depression, similar inconsistencies exist in the few studies currently available. Inconsistencies across studies may be attributable to several factors, primarily related to methodological considerations. These include: (1) differences in selection of participants for study inclusion, (2) failure to control for dementia severity, and (3) over-reliance on tests of statistical significance.

The neuropathological process behind Dementia of the Alzheimer's Type involves a preferential destruction of the parieto-temporal regions, including the hippocampus and surrounding cortical structures, thus deficits in memory and learning are thought to be hallmark features of the disease (Bondi et al., 1996; Storey et al., 2002). Previous studies have shown that the most prominent feature of Dementia of the Alzheimer's Type, and most frequently noticed distinguishing feature of the disorder, is a disproportionate decline in memory function relative to other cognitive domains. Patients with Dementia of the Alzheimer's Type may also display a clearly progressive anomic aphasia, or difficulty in naming in the context of relatively intact

speech fluency, auditory comprehension, articulation, prosody, and repetition (e.g., Cummings & Benson, 1992). Studies have shown that the first language abnormality to become apparent in Dementia of the Alzheimer's Type is impaired word finding; this anomia leads to circumlocution that is evidenced in poor word-list generation, particularly for words in a given semantic category (Mendez & Cummings, 2003). Literature has also shown that patients with Dementia of the Alzheimer's Type have difficulty accessing semantic information intentionally which manifests itself in a manner that appears to reflect a general semantic deterioration (Bondi et al., 1996).

Fronto-Temporal Dementia is a degenerative condition of the frontal and anterior temporal lobes, which control reasoning, personality, movement, speech, social graces, language and some aspects of memory. Fronto-Temporal Dementia is characterized by rigid and inflexible thinking and impaired judgment. Because the neuropathological process involved in Fronto-Temporal Dementia differs from that of Dementia of the Alzheimer's Type, and affects primarily the frontal lobes, deficits in memory are not a prominent feature of Fronto-Temporal Dementia (Neary et al., 1998; Brun et al., 1994; Rosen et al., 2002).

Major Depressive Disorder most commonly affects attention, concentration, and memory abilities. The extent of cognitive deficits has been shown to correlate with depression severity. Memory failure in these patients may reflect impairment in retrieval processes, which in turn depend on ability to attend to stimuli. These results may be useful in the differential diagnosis between Major Depressive Disorder and early Dementia of the Alzheimer's Type (Baudic et al., 2004; Lezak, 1995; Levy et al., 1998).

The nature of the neuropsychological profile associated with Vascular Dementia is highly variable and dependent on the distribution of cerebrovascular disease and related factors (Cummings & Benson, 1992). Consequently, Vascular Dementia can be primarily cortical, primarily subcortical, or a combination of cortical and subcortical. The location and nature of the lesion substantially determines the nature of deficits observed. In general, deficits will conform to known neuroanatomical correlates of behavior (Roman et al., 2004).

Issues of differences in selection of participants for study inclusion and failure to control for dementia severity have led to considerable inconsistencies in currently published studies. Standardized criteria are not commonly used in the selection of participants for investigation. This leniency in participant inclusion creates confounds in between group comparisons, as patient groups

may not be correctly defined and varying stages of illness severity may be included. This issue is particularly noteworthy in light of the fact that certain characteristics of a given disorder are absent at some stages and quite evident at others. Fortunately, the development of consensus statements for the diagnosis of Dementia of the Alzheimer's Type, Vascular Dementia, and Fronto-Temporal Dementia (NINCDS-ADRDA, NINDS-AIREN, Hackinski Ischemia Scale, DSM-IV-TR, Neary Consensus Criteria), and making use of instruments such as the Folstein Mini-Mental Status Exam (MMSE; Folstein et al., 1975) make defining dementia type and severity possible.

A further issue is that null hypothesis significance testing does not quantify the size of effects. Null hypothesis tests yield binary results that offer limited clinical utility. Furthermore, null hypothesis significance testing is greatly influenced by sample size (Cohen, 1990). A remedy for this over reliance on null hypothesis statistical significance is the use of the Cohen's d statistic to calculate an effect size. It is calculated by computing the difference between means and dividing this difference by their pooled standard deviations (i.e., $[u_1\text{-}u_2\ ]/SD_{p)}$. It provides a standard unit of measure that allows compilation of findings across studies as well as comparison of variables otherwise calibrated on dissimilar scales. Further, it offers an index of the degree to which groups overlap on a given variable (Zakzanis, 2001). Cohen (1988) suggested that $d = 0.2$ represents a small effect size, $d = 0.5$ reflects a medium effect size, and $d = 0.8$ is considered a large effect size. A more conservative view, however, proposes an effect size of $d = 1.0$, which corresponds to a 45% overlap, and offers improved possibility of discriminating. An ideal effect size is one of $d = 3.0$ or greater which suggests a degree of overlap of 5% or less allowing optimum separation of groups on a given variable (Zakzanis, 1998a). Overall, the use of effect sizes in addition to tests of null hypothesis offers important information regarding which variables are most appropriate for use in the differential diagnosis of dementia.

Ambiguity regarding the nature of neuropsychological differences among dementia groups and those with depression has served to obscure the ability to make a distinction among these diagnoses. The neuropsychological differential diagnosis of dementia is further complicated by the fact that little research has been conducted comparing the performance of patient's with Fronto-Temporal Dementia to patients with Vascular Dementia. This presents a significant problem due to the fact that patients with Vascular Dementia tend to display "frontal" deficits upon neuropsychological evaluation (e.g., Cummings, 1990; Perez et al., 1975; Villardita, 1993). Hence, identifying a neuropsychological profile of patients with Fronto-Temporal Dementia in comparison to those

with Dementia of the Alzheimer's Type and Vascular Dementia would be advantageous.

In summary, there is a growing need for research that will aid the clinician in early and accurate differential diagnosis of the dementias. Although decades of research have provided a wealth of data concerning the neuropsychological characteristics of Dementia of the Alzheimer's Type, Vascular Dementia, Fronto-Temporal Dementia, and Major Depressive Disorder, inconsistencies in findings raise concerns, and very little research has been done to assist in the ease of differential diagnosis. The problem addressed by the current research study was to identify specific neuropsychological comparative profiles, or a typical pattern of scores, for Dementia of the Alzheimer's Type, Vascular Dementia, Fronto-Temporal Dementia, and Major Depressive Disorder. The identification of these profiles will assist in the differential diagnosis of these disorders and aid in patient treatment. Based upon the current literature (drawing heavily from Zakzanis et al., 1999), the following hypotheses are made:

1. Dementia of the Alzheimer's Type patients perform significantly lower than patients with Vascular Dementia, Fronto-Temporal Dementia, or Major Depressive Disorder on measures of delayed memory, confrontational naming, and semantic fluency.
2. Vascular Dementia patients perform significantly lower than patients diagnosed with Dementia of the Alzheimer's Type, Fronto-Temporal Dementia, or Major Depressive Disorder on measures of phonemic fluency, immediate recall.
3. Fronto-Temporal Dementia patients perform significantly lower than patients diagnosed with Dementia of the Alzheimer's Type, Vascular Dementia, or Major Depressive Disorder on the color/word portion of the Stroop test. In addition to the Stroop, it is hypothesized that patients with Fronto-Temporal Dementia perform significantly lower on Trail Making Test Part B.
4. Major Depressive Disorder patients perform significantly lower than patients diagnosed with Dementia of the Alzheimer's Type, Vascular Dementia, or Fronto-Temporal Dementia on measures of attention and concentration, as well as delayed recall portion.

METHOD

Design

Archival data of 120 community-dwelling individuals examined in a neurology clinic were analyzed in this study. Each participant was administered a

neuropsychological battery including tests of verbal fluency, expressive language, memory, and executive functioning. Participants were divided into four groups according to diagnosis. The four groups are described in detail in what follows, and include patients diagnosed with Dementia of the Alzheimer's Type, Vascular Dementia, Fronto-Temporal Dementia, and Major Depressive Disorder. Patients included in dementia categories were also divided into subgroups according to disease severity. Mild and moderate subgroups were included in the study, whereas those within the severe range were eliminated.

Participants

Participants were referred by a neurologist for neuropsychological assessment to assist in clarifying the absence or presence of, extent, and nature of cognitive impairment. The sample consisted of 111 participants, 56 male and 55 female, with a mean age of 76.55 years ($SD = 5.54$; range = 47 to 88). All participants in the study were Caucasian (Table 1). Premorbid intelligence estimates were calculated using the Wechsler Test of Adult Reading (WTAR; Psychological Corporation, 2001) and the regression equation of Barona and colleagues (1984) for the prediction of premorbid intellectual functioning. The mean premorbid intelligence estimate for the group was 109.62 ($SD = 9.53$; range = 89 to 130).

Participants included in the study were selected on the basis of meeting criteria for dementia or depression according to published standards. Participants with dementia were then classified into three levels of disease severity (mild, moderate, and severe) according to scores on the Folstein Mini-Mental Status Exam (MMSE; Folstein et al., 2001). Participants with MMSE scores

Table 1. Demographic data: Means (Standard deviations)

Group	*n*	Gender M/F	Age (years) M(SD)	Barona/WTAR IQ M(SD)	MMSE M(SD)
DAT	30	17/13	77.67(3.67)	110.47(7.76)	26.70(1.85)
VaD	31	17/14	78.26(4.48)	107.65(5.40)	27.48(2.00)
FTD	20	8/12	74.00(5.63)	109.95(14.15)	27.70(2.74)
MDD	30	14/16	76.27(8.39)	110.4(10.81)	28.67(1.15)
TOTAL	111	56/55	76.55(5.54)	109.62(9.53)	27.64(1.94)

DAT = Dementia of the Alzheimer's Type; VaD = Vascular Dementia; FTD = Fronto-Temporal Dementia; MDD = Major Depressive Disorder; MMSE = Folstein Mini-Mental Status Exam; WTAR = Wechsler Test of Adult Reading.

of 27–30 were classified as within the mild range, participants with scores of 21–26 were defined as moderately impaired, and patients with scores of 20 and below were classified as severe. Patients with severe dementia classification were not included in the study.

Group 1, identified as the Dementia of the Alzheimer's Type Group, consisted of 30 patients diagnosed with probable Alzheimer's Disease according to the criteria developed by the National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association Work Group criteria (NINCDS-ADRDA; McKhann et al., 1984). Dementia of the Alzheimer's Type group participants had a mean age of 77.67 years ($SD = 3.67$; range = 70 to 88). There were 17 males and 13 females in Group 1. The mean premorbid intelligence estimate for the Dementia of the Alzheimer's Type group was 110.47 ($SD = 7.76$; range = 99 to 130).

Group 2 consisted of 31 patients diagnosed with Vascular Dementia according to the National Institutes of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences (NINDS-AIREN) criteria for Vascular Dementia (Roman et al., 1993) and the Hachinski Ischemia Scale (Hachinski et al., 1975). Vascular Dementia group participants had a mean age of 78.26 years ($SD = 4.48$; range = 69 to 89). There were 17 males and 14 females in the Vascular Dementia group. The mean premorbid intelligence estimate for the Vascular Dementia group was 107.65 ($SD = 5.40$; range = 98 to 123).

Group 3 consisted of 20 patients diagnosed with Fronto-Temporal Dementia according to the consensus criteria postulated by Neary et al. (1998). As listed previously, these criteria include the presence of five core diagnostic features including insidious onset, early decline in social interpersonal conduct, and early impairment in the regulation of personal conduct, early emotional blunting, and early loss of insight. The criteria also require the presence of behavioral disorder, speech and language deficits, physical signs, and neuropsychological, brain imaging, or EEG verification for diagnosis.

Those participants included in the Fronto-Temporal Dementia group had a mean age of 74.00 years ($SD = 5.63$; range = 47 to 83). There were 8 males and 12 females in the Fronto-Temporal Dementia group. The mean premorbid intelligence estimate for the Fronto-Temporal Dementia group was 109.95 ($SD = 14.15$; range = 95 to 124).

Group 4 consisted of 30 patients diagnosed with Major Depressive Disorder according to Beck Depression Inventory-Second Edition (BDI-II) score and criteria as listed in the Diagnostic and Statistical Manual-Fourth Edition, Text

Revision (DSM-IV-TR; American Psychiatric Association, 2000). Depression group participants had a mean age of 76.27 years ($SD = 8.39$; range = 60 to 80). There were 14 males and 16 females in the Depression group. The mean premorbid intelligence estimate for the Depression group was 110.4 ($SD = 10.81$; range = 83 to 127).

Group Classification

The independent variable in this study was the diagnostic group (Dementia of the Alzheimer's Type, Vascular Dementia, Fronto-Temporal Dementia, and Major Depressive Disorder). In each case, the diagnostic categorization was made according to relevant criteria as described earlier (e.g., NINCDS-ADRDA, NINDS-AIREN, Hackinski Ischemia Scale, DSM-IV-TR, Neary Consensus Criteria). In diagnosing the clinical groups (i.e., groups 1 through 4), emphasis was placed on non-neuropsychological variables, to the degree possible, which included emphasis on such variables as clinical history, neurological factors, and neuroimaging data. Specifically, clinical histories and neurological factors were used for the diagnosis of each of the 111 study participants. However, of the 111 participants, only 104 were classified into diagnostic category with the assistance of neuroimaging data (e.g., Computed Tomography (CT) Scan/Magnetic Resonance Imaging (MRI) data). Twenty-nine of the 30 Dementia of the Alzheimer's Type group participants, 31/31 Vascular Dementia patients, 20/20 Fronto-Temporal Dementia patients, and 24/30 Major Depressive Disorder patients were classified with the assistance of neuroimaging data. This was done in order to avoid problems of circularity when subsequently comparing the groups on neuropsychological variables. Premorbid intelligence levels were estimated with the use of the Wechsler Test of Adult Reading.

Instrumentation

The dependent variables in the present study consisted of measures that reflect the neuropsychological domains identified for analysis: verbal fluency (phonemic and semantic), confrontational naming, immediate recall, delayed recall, working memory (attention and concentration), and executive functioning. These measures include the Controlled Oral Word Association Test (COWAT-FAS), Category Naming (Animals), Boston Naming Test (BNT), selected subtests from the Wechsler Memory Scale-Third Edition (WMS-III), the Stroop Test, and the Trail Making Test-Parts A and B. Additional

measures utilized in the study include the Folstein Mini-Mental Status Exam (MMSE; Folstein et al., 1975), the Beck Depression Inventory-Second Edition (BDI-II; Beck, 1987), and the Wechsler Test of Adult Reading (WTAR; The Psychological Corporation, 2001).

Analyses

Multiple planned comparisons were performed to test the hypotheses detailed previously. The critical level for tests of statistical significance was set at $\alpha \leq .01$ to provide protection against Type I error while attempting to avoid the susceptibility to Type II error that may occur with the introduction of a more stringent procedure. The magnitude of effect size (d statistic; Cohen, 1998) for each planned comparison was also examined. Twenty-seven planned comparisons were performed and effect sizes were calculated for each. Specifically, planned comparisons were conducted for each of the 11 neuropsychological variables in order to compare performances between the groups. Effect sizes were calculated between each of the four groups. Statistical findings are presented later in the article for each hypothesis in turn. Bonferroni corrections were applied to adjust the critical alphas for these effect sizes, using an alpha of .05 divided by 12 neuropsychological test variables, compared to yield a critical alpha of .0042.

RESULTS

Group Demographic Data

Demographic data, including means and standard deviations, are included in Table 1. Means and standard deviations of all neuropsychological variables are in Table 2. There were no significant differences among the participant groups on sex (F (3,107) = .484, p = .694), or estimated premorbid intelligence level (F (3, 107) = .591, p = .622). However, there was a significant difference among the participant groups for age (F (3, 107) = 6.010, p = .001) and MMSE scores (F (3, 107) = 4.933, p = .003). Post-hoc Tukey indicated that patients in the Vascular Dementia participant group were slightly older overall as compared to patients belonging to the Major Depressive Disorder and Fronto-Temporal Dementia groups. This age difference likely had little effect on subsequent analyses, as patient performance has been found to be independent of age. The Tukey also indicated that patients within the Dementia of the Alzheimer's Type group performed significantly lower overall as compared to patients within

the Major Depressive Disorder group. These significant differences occurred despite attempts to limit differences by including only participants with MMSE scores of 21 and greater.

Dementia of the Alzheimer's Type

Of the planned comparisons between groups with regard to delayed memory, two were significant. Specifically, the Dementia of the Alzheimer's Type group performed significantly below the Major Depressive Disorder ($p < .001$) and Fronto-Temporal Dementia ($p < .001$) groups. Calculated effect sizes revealed a small to moderate difference in performance between patients diagnosed with Dementia of the Alzheimer's Type and those diagnosed with Vascular Dementia (i.e., $d = -.32$). However, large differences in performance were identified between patients with Dementia of the Alzheimer's Type and Fronto-Temporal Dementia (i.e., $d = -1.21$), and Dementia of the Alzheimer's Type and Major Depressive Disorder (i.e., $d = -.90$). Effect sizes for delayed memory are listed in Table 3. Of the planned comparisons between groups with regard to delayed memory, all three were significant. Specifically, the Dementia of the Alzheimer's Type group performed significantly below the Vascular Dementia group ($p = .007$), the Fronto-Temporal Dementia group ($p = .005$), and Major Depressive Disorder group ($p < .001$). Effect sizes for confrontational naming in the Dementia of the Alzheimer's Type group are listed in Table 3. Of the planned comparisons between groups with regard to category fluency, two were significant. Specifically, the Dementia of the Alzheimer's Type group performed significantly below the Vascular Dementia group ($p < .001$), and Fronto-Temporal Dementia group ($p < .001$). Effect sizes for category fluency for the Dementia of the Alzheimer's Type group are listed in Table 3.

Vascular Dementia

Of the planned comparisons between groups with regard to phonemic fluency, two were significant. Specifically, the Vascular Dementia group performed significantly below the Major Depressive Disorder ($p < .001$) and Fronto-Temporal Dementia ($p < .001$) groups. Effect sizes for phonemic fluency are listed in Table 3. Of the planned comparisons between groups with regard to immediate recall, two were significant. Specifically, the Vascular Dementia group performed significantly below the Major Depressive Disorder ($p < .001$) and Fronto-Temporal Dementia ($p < .001$) groups. Immediate recall effect sizes are listed in Table 3.

Table 2. Means and SDs of neuropsychological variables

	DAT			VAD			FTD			MDD		
	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*	Mean	SD	*n*
WMS IMI	80.5	9.2	27	86.9	8.1	31	101.5	20.9	19	99.8	13.9	29
WMS WMI	108.6	13.6	30	93.9	14.6	27	105.4	15.3	20	111.4	9.9	29
WMS GMI	84.2	8.4	27	89.1	9.7	27	102.4	16.9	19	102.6	17.3	29
BNT	88.0	12.8	30	102.7	6.8	24	104.0	17.0	20	108.2	21.3	30
Phonemic fluency	86.1	26.1	30	86.9	12.0	31	106.0	15.1	20	103.0	16.0	30
Semantic fluency	83.1	11.5	30	101.6	5.1	31	99.5	17.4	20	88.7	19.1	30
Stroop color/word	102.3	9.6	29	103.6	6.9	31	83.9	15.1	20	110.3	7.2	24
Trails B	93.5	13.4	30	100.0	5.9	26	86.3	12.4	20	104.0	18.5	30
MMSE	26.8	1.9	30	27.5	2.0	31	27.7	2.7	20	28.7	1.2	30
BDI	1.9	1.8	30	5.6	4.0	31	1.2	1.1	20	19.0	4.9	30
WTAR	110.5	7.8	30	107.6	5.4	31	110.0	14.2	20	110.4	10.8	30

DAT = Dementia of the Alzheimer's Type; VaD = Vascular Dementia; FTD = Fronto-Temporal Dementia; MDD = Major Depressive Disorder; MMSE = Folstein Mini-Mental Status Exam; WTAR = Wechsler Test of Adult Reading; BDI = Beck Depression Inventory; WMS IMI = Wechsler Memory Scale-Third Edition (WMS-III) Immediate Memory Index; WMS WMI = Wechsler Memory Scale-Third Edition (WMS-III) Working Memory Index; WMS GMI = Wechsler Memory Scale-Third Edition (WMS-III) General Memory Index; BNT = Boston Naming Test; Trails B = Trailmaking Test B.

Table 3. Results of tests of the hypotheses

	Hypothesis	Test	*F*	*p*	*d*
1	DAT<VAD	WMS Delayed Memory	25.95	<.001	.32
	DAT<FTD	WMS Delayed Memory	14.03	<.001	1.21
	DAT<MDD	WMS Delayed Memory	<.001	.970	.90
	DAT<VAD	Boston Naming	11.07	<.001	.98
	DAT<FTD	Boston Naming	11.86	<.001	1.07
	DAT<MDD	Boston Naming	23.40	<.001	1.35
	DAT<VAD	Animal Fluency	26.53	<.001	1.23
	DAT<FTD	Animal Fluency	16.40	<.001	1.09
	DAT<MDD	Animal Fluency	2.34	.129	.37
2	VAD<DAT	COWAT	.03	.870	.05
	VAD<FTD	COWAT	13.04	<.001	1.26
	VAD<MDD	COWAT	11.70	<.001	1.07
	VAD<DAT	WMS Immediate Mem.	3.42	.067	
	VAD<FTD	WMS Immediate Mem.	14.68	<.001	
	VAD<MDD	WMS Immediate Mem.	14.43	<.001	
3	FTD<DAT	Stroop Test	43.72	<.001	1.23
	FTD<VAD	Stroop Test	51.29	<.001	1.32
	FTD<MDD	Stroop Test	82.40	<.001	1.76
	FTD<DAT	TrailMaking Test B	3.44	.066	.49
	FTD<VAD	TrailMaking Test B	11.50	<.001	.91
	FTD<MDD	TrailMaking Test B	19.55	<.001	1.16
4	MDD>DAT	WMS Working Memory	0.64	.424	.19
	MDD<VAD	WMS Working Memory	24.27	<.001	1.17
	MDD<FTD	WMS Working Memory	2.39	.125	.40
	MDD<VAD	WMS Delayed Memory	1.75	.188	.90
	MDD<FTD	WMS Delayed Memory	20.40	<.001	.01
	MDD>DAT	WMS Delayed Memory	25.95	<.001	1.22

DAT = Dementia of the Alzheimer's Type; VaD = Vascular Dementia; FTD = Fronto-Temporal Dementia; MDD = Major Depressive Disorder; MMSE = Folstein Mini-Mental Status Exam; WTAR = Wechsler Test of Adult Reading; WMS = Wechsler Memory Scale—Third Edition (WMS—III); COWAT = Controlled Oral Word Association Test.

Fronto-Temporal Dementia

Of the planned comparisons between groups with regard to executive functioning as measured by the Stroop Test (color/word), all three were significant. Specifically, the Fronto-Temporal Dementia group performed significantly below the Dementia of the Alzheimer's Type ($p < .001$), Vascular Dementia ($p < .001$), and Major Depressive Disorder ($p < .001$) groups. Effect sizes for delayed memory are listed in Table 3. Of the planned comparisons between

groups with regard to executive functioning, as measured by the Trail-Making Test Part B, two were significant. Specifically, the Fronto-Temporal Dementia group performed significantly below the Vascular Dementia ($p < .001$) and Major Depressive Disorder ($p < .001$) groups. Effect sizes for delayed memory are listed in Table 3.

Major Depressive Disorder

Of the planned comparisons between groups with regard to Major Depressive Disorder and attention and concentration, one was significant. Specifically, the Major Depressive Disorder group performed significantly below the Vascular Dementia group ($p < .001$). Effect sizes for delayed memory are listed in Table 3. Of the planned comparisons between groups with regard to delayed memory, two were significant. Specifically, the Major Depressive Disorder group performed significantly *above* the Dementia of the Alzheimer's Type group ($p < .001$) and significantly *below* the Fronto-Temporal Dementia group ($p < .001$). There was no significant difference in delayed memory abilities between the Major Depressive Disorder and Vascular Dementia groups. Effect sizes for delayed memory are listed in Table 3.

DISCUSSION

The primary goals of the present study were to: (1) evaluate the neuropsychological differences between dementia types and (2) to assess directly the presence, if any, of differences in neuropsychological performance between patients with Dementia of the Alzheimer's Type, Vascular Dementia, Fronto-Temporal Dementia, and Major Depressive Disorder. Neuropsychological domains directly assessed in the study included: immediate memory, delayed memory, confrontational naming, verbal fluency, attention, concentration, and executive functioning. Four hypotheses were generated based on a review of the literature comparing the patient groups across various neuropsychological domains.

Dementia of the Alzheimer's Type

With regard to delayed memory abilities, patients with Dementia of the Alzheimer's Type performed significantly worse than patients diagnosed with Fronto-Temporal Dementia or Major Depressive Disorder, according to demographically corrected standard scores. However, there was no significant

difference in performance between patients diagnosed with Dementia of the Alzheimer's Type and those diagnosed with Vascular Dementia. The neuropathological process behind Dementia of the Alzheimer's Type involves a preferential destruction of the parieto-temporal regions, including the hippocampus and surrounding cortical structures, thus deficits in memory and learning are thought to be hallmark features of the disease (Bondi et al., 1996). More specifically, previous literature has shown that the *most* prominent feature of Dementia of the Alzheimer's Type, and most frequently noticed distinguishing feature of the disorder, is a disproportionate decline in memory function relative to other cognitive domains. Thus, the significant deficits exhibited by Dementia of the Alzheimer's Type patients on a measure of delayed memory substantiate prior research. Because the neuropathological process involved in Fronto-Temporal Dementia differs from that of Dementia of the Alzheimer's Type, and affects primarily the frontal lobes, deficits in memory are not a prominent feature of Fronto-Temporal Dementia. Similarly, although patients suffering from Major Depressive Disorder exhibit decreased motivation and some delayed memory deficits, the deficits were not significant as compared to those of Dementia of the Alzheimer's Type (Lezak, 1995; Levy et al., 1998). However, because, as discussed previously, the nature of the neuropsychological profile associated with Vascular Dementia is highly variable and dependent on the distribution of cerebrovascular disease and related factors (Cummings & Benson, 1992), Vascular Dementia can be primarily cortical, primarily subcortical, or a combination of cortical and subcortical. The location and nature of the lesion substantially determines the nature of deficits observed. In general, deficits will conform to known neuroanatomical correlates of behavior. This variability in deficits likely explains the lack of significant difference between the performance of patients diagnosed with Dementia of the Alzheimer's Type and those diagnosed with Vascular Dementia.

Effect sizes revealed large differences in performance between patients with Dementia of the Alzheimer's Type when compared to those with Fronto-Temporal Dementia and Major Depressive Disorder. However, only a small to moderate effect size was found when comparing patients with Dementia of the Alzheimer's Type and those with Vascular Dementia. Clinically, these effect sizes indicate that patients with Dementia of the Alzheimer's Type can be expected to perform significantly worse on measures of delayed memory than patients diagnosed with Fronto-Temporal Dementia or Major Depressive Disorder. Thus, the use of measures of delayed memory can contribute considerably to the differential diagnosis of Dementia of the Alzheimer's

Type from that of Fronto-Temporal Dementia or Major Depressive Disorder. In contrast, only a small to moderate difference in performance on delayed memory measures between Dementia of the Alzheimer's Type and Vascular Dementia groups indicates minimal benefit in contributing to the differential diagnosis between these disorders.

With regard to the BNT, patients with Dementia of the Alzheimer's Type performed significantly worse than patients diagnosed with Vascular Dementia, Fronto-Temporal Dementia, or Major Depressive Disorder, according to demographically corrected standard scores.

Clinically, these findings suggest that confrontational naming is of limited benefit in contributing to the differentiation of Dementia of the Alzheimer's Type from Vascular Dementia. In contrast, Dementia of the Alzheimer's Type patients can be expected to perform significantly worse than patients with Fronto-Temporal Dementia, and Major Depressive Disorder. Therefore, consideration of this domain may offer great benefit in the differential diagnosis of Dementia of the Alzheimer's Type from that of Fronto-Temporal Dementia and Major Depressive Disorder. This finding is consistent with previous literature, which states that patients with Dementia of the Alzheimer's Type display a clearly progressive anomic aphasia, or difficulty in naming in the context of relatively intact speech fluency, auditory comprehension, articulation, prosody, and repetition (e.g., Cummings & Benson, 1992). Language changes are sensitive indicators of cortical dysfunction, and the difficulty with confrontational naming found in patients with Dementia of the Alzheimer's Type is indicative of the cortical destruction associated with the disease. Once again, the lack of significant difference in confrontational naming deficits between patients with Dementia of the Alzheimer's Type and those diagnosed with Vascular Dementia is likely due to the variability in lesion location and the associated unpredictability in deficits common to Vascular Dementia.

With regard to semantic word fluency as measured by the patients' ability to name as many animals as possible within a one minute period, patients diagnosed with Dementia of the Alzheimer's Type performed significantly worse than patients diagnosed with Vascular Dementia and those diagnosed with Fronto-Temporal Dementia. However, there was no significant difference between the performance of patients diagnosed with Dementia of the Alzheimer's Type and those diagnosed with Major Depressive Disorder.

The reduced performance of patients with Dementia of the Alzheimer's Type on measures of semantic word fluency is analogous to the language difficulties discussed previously. Specifically, studies have shown that the

first language abnormality to become apparent is the impaired word finding, this anomia leads to circumlocution, which is evidenced in poor word-list generation, particularly for words in a given semantic category (Mendez & Cummings, 2003). Literature has also shown that patients with Dementia of the Alzheimer's Type have a difficulty accessing semantic information intentionally, which manifests itself in a manner that appears to reflect a general semantic deterioration (Bondi et al., 1996). On the other hand, the decreased performance by patients diagnosed with Major Depressive Disorder is likely due to a lack of volition as presented in the recent literature (i.e., Mendez & Cummings, 2003).

Effect sizes revealed large differences in performance between patients with Dementia of the Alzheimer's Type when compared to those with Vascular Dementia and Fronto-Temporal Dementia. However, only a small to moderate effect size was found when comparing patients with Dementia of the Alzheimer's Type and those with Major Depressive Disorder. Clinically, these effect sizes indicate that patients with Dementia of the Alzheimer's Type can be expected to perform significantly worse on measures of semantic fluency than patients diagnosed with Vascular Dementia or Fronto-Temporal Dementia. Thus, the use of measures of semantic fluency can contribute considerably to the differential diagnosis of Dementia of the Alzheimer's Type from that of Vascular Dementia and Fronto-Temporal Dementia. In contrast, only a small difference in performance on semantic fluency measures between Dementia of the Alzheimer's Type and Major Depressive Disorder groups indicates minimal benefit in contributing to differential diagnosis between Dementia of the Alzheimer's Type and Major Depressive Disorder patients, owing to a very substantial overlap in their performances.

Vascular Dementia

With regard to phonemic fluency, patients diagnosed with Vascular Dementia performed significantly worse than patients diagnosed with Major Depressive Disorder and Fronto-Temporal Dementia. However, there was no significant difference between the performance of patients diagnosed with Vascular Dementia and those diagnosed with Dementia of the Alzheimer's Type. These findings are consistent with literature that suggests that patients with a vascular component to their dementia are prone to slowed mental processing and disturbances in executive functioning (Lezak, 1995). Dementia of the Alzheimer's Type patient's significantly poorer performance on measures of phonemic fluency are likely explicated by the previously discussed language

difficulties associated with the disease, which include word-list generation. Effect sizes comparing Vascular Dementia to Dementia of the Alzheimer's Type revealed a small difference between groups. In contrast, a large effect size was found when comparing Vascular Dementia patient's performance with that of Fronto-Temporal Dementia patients. Similarly, a large effect size was discovered when comparing Vascular Dementia patients to Major Depressive Disorder patients. Clinically, this indicates that Vascular Dementia patients can be expected to perform significantly worse on measures of phonemic fluency when compared to patients with Vascular Dementia or Fronto-Temporal Dementia. In addition, this suggests that measures of phonemic fluency such as the Controlled Oral Word Association Test (COWAT) offer a great benefit in the differential diagnosis between these groups. In contrast, this domain is of minimal benefit in contributing to the differential diagnosis between Vascular Dementia and Dementia of the Alzheimer's Type patients, due to a very substantial overlap in their performances.

With regard to immediate memory, patients diagnosed with Vascular Dementia performed significantly worse than patients diagnosed with Major Depressive Disorder and Fronto-Temporal Dementia. However, there was no significant difference between the performance of patients diagnosed with Vascular Dementia and those diagnosed with Dementia of the Alzheimer's Type. According to current literature, patients diagnosed with Vascular Dementia display deficits in short-term, or immediate, memory abilities due to a dysfunction in memory retrieval in the context of relatively intact memory recognition (Lezak, 1995). This deficit has been attributed to impairment in the initiation of a systematic retrieval strategy when attempting to recall information, despite intact memory consolidation in subcortical dementias (e.g., Bondi et al., 1996). In contrast, patients diagnosed with a cortical dementia such as Dementia of the Alzheimer's Type experience difficulty in both the retrieval and recognition of information due to an inability to consolidate information for recall (Lezak, 1995).

Effect sizes comparing Vascular Dementia to Dementia of the Alzheimer's Type revealed a moderate difference between groups. Large effect sizes were found when comparing Vascular Dementia patients' performance with that of Fronto-Temporal Dementia patients and Major Depressive Disorder patients. Clinically, this indicates that Vascular Dementia patients can be expected to perform significantly worse on measures of immediate memory when compared to patients with Dementia of the Alzheimer's Type or Major Depressive Disorder. In addition, this suggests that measures of immediate memory such as those within the Wechsler Memory Scale—Third Edition are an asset to

the differential diagnosis between these groups. In contrast, this domain is of minimal benefit in contributing to the differential diagnosis between Vascular Dementia and Dementia of the Alzheimer's Type patients, due to substantial overlap in performance.

Fronto-Temporal Dementia

In regard to executive functioning as measured by the Trail-Making Test Part B, patients diagnosed with Fronto-Temporal Dementia received significantly lower scores than patients diagnosed with Vascular Dementia or Major Depressive Disorder. However, there was no statistically significant difference between patients diagnosed with Fronto-Temporal Dementia and those diagnosed with Dementia of the Alzheimer's Type. According to previous research, the neuropathological process involved in Fronto-Temporal Dementia affects, as the name implies, the frontal and temporal lobes. This degeneration of the frontal and temporal areas is the basis for deficits exhibited on the Trail-Making Test, including difficulty with shifting set and deficits in attention. Similarly, the disease process indicative of Dementia of the Alzheimer's Type, discussed earlier, also results in deficits of executive functioning, specifically in the early stages of the disease course. These deficits include lack of insight, difficulties with planning and goal-oriented behavior, and poor judgment and reasoning. Other abilities mediated by the frontal lobes and shown to be impaired in patients diagnosed with Dementia of the Alzheimer's Type including working memory, sustained and divided attention, set changing, response inhibition, and motor programming (Mendez & Cummings, 2003).

Effect sizes comparing Fronto-Temporal Dementia to Dementia of the Alzheimer's Type revealed a moderate difference between groups. Large effect sizes were found when comparing Fronto-Temporal Dementia patient performance with that of Vascular Dementia and Major Depressive Disorder patients. Clinically, this indicates that Fronto-Temporal Dementia patients can be expected to perform significantly worse on measures of executive functioning when compared to patients with Vascular Dementia or Major Depressive Disorder. In addition, this suggests that measures of executive functioning such as the Trail-Making Test Part B can offer a substantial benefit in the differential diagnosis between these groups. In contrast, the Trail-Making Test is of minimal benefit in contributing to the differential diagnosis between Fronto-Temporal Dementia and Dementia of the Alzheimer's Type patients, due to a sizeable overlap in performance.

In regard to executive functioning as measured by the Stroop Test (specifically the color/word segment), patients diagnosed with Fronto-Temporal Dementia received significantly lower scores than patients diagnosed with Dementia of the Alzheimer's Type, Vascular Dementia, or Major Depressive Disorder. Previous research has suggested that performance on the Stroop Test, unlike the Trail-Making Test, is less often reduced by variables other than frontal deficits, and is less commonly found to be reduced in forms of dementia other than Fronto-Temporal Dementia. This clarifies the difference in significance between performances on the two, seemingly similar, tests.

Additionally, effect sizes revealed clinically important differences between groups. Specifically, large effect sizes were found when comparing the performance of patients diagnosed with Fronto-Temporal Dementia to those diagnosed with Dementia of the Alzheimer's Type, patients with Fronto-Temporal Dementia to those with Vascular Dementia, and patients with Fronto-Temporal Dementia compared to those with Major Depressive Disorder. These differences indicate that Fronto-Temporal Dementia patients can be expected to perform significantly worse on measures of executive functioning when compared to patients with Dementia of the Alzheimer's Type, Vascular Dementia, or Major Depressive Disorder. In addition, this suggests that measures of executive functioning such as the Stroop Test can offer an important advantage in the differential diagnosis among these groups.

Major Depressive Disorder

In regard to attention and concentration skills, as measured by the Wechsler Memory Scale—Third Edition, patients diagnosed with Major Depressive Disorder performed significantly lower than patients diagnosed with Vascular Dementia. However, there was no significant difference in attention and concentration skills among Major Depressive Disorder, Dementia of the Alzheimer's Type, and Fronto-Temporal Dementia patients. These findings are partially consistent with previous literature, which suggests that abnormalities in attention are a common finding in dementia with a subcortical component (Lezak, 1995; Paulsen et al., 1995). Additionally, although it was hypothesized that patients diagnosed with Major Depressive Disorder would perform significantly below patients diagnosed with Dementia of the Alzheimer's Type on tasks measuring attention and concentration, previous literature has shown that attention and concentration abilities are often impaired in Dementia of the Alzheimer's Type, specifically in the early stages of the disease. However, the finding that Major Depressive Disorder patients do not differ

in attention/concentration performance from patients with Fronto-Temporal Dementia is less consistent with previous literature.

Effect sizes indicate a small clinical difference between Major Depressive Disorder and Dementia of the Alzheimer's Type patient performance. Additionally, a small effect size was found when comparing the performance of Major Depressive Disorder patients and that of Fronto-Temporal Dementia patients. In contrast, a large effect size was found when comparing Major Depressive Disorder patient performance to that of Vascular Dementia patient performance. These differences indicate that Major Depressive Disorder patients can be expected to perform significantly better on measures of immediate memory when compared to patients with Vascular Dementia. In addition, this suggests that measures of immediate memory such as that the Wechsler Memory Scale—Third Edition, can offer slight assistance in the differential diagnosis between patients with Major Depressive Disorder and Vascular Dementia. However, the absence of significant differences between performance of patients with Major Depressive Disorder, Dementia of the Alzheimer's Type, and Fronto-Temporal Dementia indicate minimal contribution to the differential diagnosis of these disorders.

Regarding delayed recall, patients diagnosed with Major Depressive Disorder performed significantly better than patients with Dementia of the Alzheimer's Type. However, patients with Major Depressive Disorder performed worse on a measure of delayed recall than those diagnosed with Fronto-Temporal Dementia. Major Depressive Disorder patients' performance did not differ significantly from that of those diagnosed with Vascular Dementia. When considering effect sizes, a large effect size was found when comparing Major Depressive Disorder to Dementia of the Alzheimer's Type patient performance. Similarly, a large effect size was found when comparing patients diagnosed with Major Depressive Disorder to those diagnosed with Fronto-Temporal Dementia. However, a small effect size was found between Major Depressive Disorder and Vascular Dementia patient performance. These effect sizes suggest that when attempting to distinguish Major Depressive Disorder from Dementia of the Alzheimer's Type or Fronto-Temporal Dementia, a measure of delayed memory, such as that found within the Wechsler Memory Scale—Third Edition is of considerable assistance. However, when attempting to differentiate Major Depressive Disorder from Vascular Dementia, a measure of delayed memory is of little benefit.

The sample sizes for each diagnostic group consisted of approximately 20–30 patients each. This relatively small sample size warrants caution when an attempt is made to generalize study results to other patients with memory

complaints or objective neuropsychological impairment. The repetition of this study with the use of larger group sample sizes would strengthen and further define proposed diagnostic utility. Additionally, the current study does not include a control group. Future studies may benefit from utilizing a group of patients without complaints of memory disturbance. This may facilitate analyses of confounding factors and the identification and clarification of symptoms specific to each dementia type.

It should be noted that participants included in the present study were not administered measures of symptom validity or effort, as it was not considered likely that elderly, nonlitigating, patients with reported memory deficits were putting forth less than maximum effort. Nevertheless, although there was no clear evidence of insufficient effort in the cases included in the present study and it is unlikely that insufficient effort was operant, it cannot be stated with absolute certainty that insufficient effort was not a factor.

A suggested neuropsychological battery for use in the evaluation of dementia based on the results of the current study includes measures of executive functioning, memory, attention, concentration, intelligence, confrontational naming, phonemic fluency, and semantic fluency. Specific tests suggested for use include the Stroop Test, Wechsler Memory Scale—Third Edition, Wechsler Adult Intelligence Scale—Third Edition, Boston Naming Test, Controlled Oral Word Association Test, and Category Fluency (i.e., Animal Naming).

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