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Functional Ability in Executive Variant Alzheimer's Disease and Typical Alzheimer's Disease

Carla Back-Madruga[1,2], Kyle Brauer Boone[3], John Briere[1], Jeffrey Cummings[2], Susan McPherson[2], Lynn Fairbanks[2], and Elizabeth Thompson[4]

[1]University of Southern California, Keck School of Medicine, Los Angeles, CA, USA, [2]UCLA Alzheimer's Disease Center, Los Angeles, CA, USA, [3]Harbor UCLA Medical Center, Torrance, CA, USA, and [4]Fuller Theological Seminary, Pasadena, CA, USA

ABSTRACT

A frontal, or executive, variant of Alzheimer's disease (EAD) has been described in the literature in which frontal dysfunction accompanies temporal and parietal changes in the early stages of the illness. However, no study has empirically investigated associated aspects, such as neuropsychiatric symptoms, instrumental activities of daily living, or caregiver burden in this EAD subgroup. We compared the performance of two subgroups of mild Alzheimer's disease patients (e.g., EAD and typical Alzheimer's disease; TAD) on neuropsychological and associated measures. Results revealed that the EAD group, selected based on poor executive scores, did not significantly differ from the TAD group on nonexecutive neuropsychological tests of intelligence, language, verbal and nonverbal memory, or visual-spatial abilities. However, the EAD group evidenced more severe neuropsychiatric symptoms, impaired activities of daily living, and greater caregiver distress than the TAD group. Thus, the EAD subgroup is characterized by executive dysfunction, neuropsychiatric symptoms, and functional disability in excess of that seen in TAD. Whether our EAD subgroup represents an actual frontal variant of Alzheimer's disease awaits replication in a larger sample including neuroimaging and pathological confirmation, as well as longitudinal assessment of cognition and neuropsychiatric symptoms.

The literature on Alzheimer's disease supports the existence of heterogeneous subtypes. A frontal, or executive, variant of Alzheimer's disease (EAD) has been described in which frontal changes coexist with bitemporal/parietal dysfunction. Specifically, numerous neuroimaging studies have documented decreased blood flow (O'Brien, Eagger, Syed, Sahakian, & Levy, 1992; Perani et al., 1998; Waldemar et al., 1994; Weiner et al., 1993) and metabolism (Chase, Burrows, & Mohr, 1987; Grady et al., 1988; Grady et al., 1990; Haxby et al., 1988; Mann, Mohr, Gearing, & Chase, 1992) in the frontal, temporal and parietal lobes in a subgroup of Alzheimer's disease patients, and some have noted accompanying executive neuropsychological deficits (Chase et al., 1987; Mann et al., 1992), and psychiatric and behavioral abnormalities (Chase et al., 1987; Grady et al., 1990). In most cases, these findings were unrelated to disease severity or duration (Grady et al., 1988; Grady et al., 1990; Haxby et al., 1988; Mann et al., 1992; O'Brien et al., 1992; Perani et al., 1998; Waldemar et al., 1994).

A pathological and clinical study on a sample of six subjects (Johnson, Head, Kim, Starr, & Cotman, 1999) identified a subgroup of patients with pathologically confirmed Alzheimer's disease who presented in the early stages of dementia

Address correspondence to: Carla Back-Madruga, Ph.D., Assistant Professor of Psychiatry and Behavioral Sciences, University of Southern California, Keck School of Medicine, 1300 North Mission Road, Los Angeles, CA 90033, USA. Tel.: +1 323 343 8259. E-mail: cback@hsc.usc.edu
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with disproportionate impairment on tests of executive functioning (e.g., FAS and Trails A) and evidenced a greater than expected degree of neurofibrillary tangle pathology in the frontal lobes. Regarding studies employing specifically neuropsychological methods, Binetti et al. (1996) found that a subgroup of mild Alzheimer's disease patients performed poorly on at least two out of four executive neuropsychological measures, whereas the rest of the sample did not evidence such frontal dysfunction. Several other neuropsychological investigations have documented executive deficits in mild Alzheimer's disease patient groups in general (Bhutani, Montaldi, Brooks, & McCulloch, 1992; Lafleche & Albert, 1995; Reid et al., 1996), however, these studies did not investigate whether subgroups might be present based on neuropsychological patterns in the early stages of the illness.

Thus, evidence is emerging that an EAD subgroup exists. However, there is a dearth of research on related abnormalities in EAD, such as accompanying neuropsychiatric symptoms, instrumental activities of daily living, and caregiver burden. This is a critical issue given the economic and societal ramifications of disturbance in these areas (e.g., institutionalization, elder abuse, etc.). Delineation of the specific functional features associated with EAD would add support to the concept of EAD as a specific subtype of Alzheimer's disease and could have both diagnostic and treatment implications.

Two of the studies mentioned above (Chase et al., 1987; Grady et al., 1990) examined the presence of psychiatric abnormalities in EAD based on symptoms reported in a clinical history. Specifically, Chase et al. (1987) observed changes in personality and social behavior in those patients with frontal, temporal, and parietal involvement, while Grady et al. (1990) noted an increased incidence of anxiety, agitation, inappropriate behavior, personality change, depression, and psychosis in Alzheimer's disease patients with hypometabolism in the frontal, as well as temporal and parietal regions. However, neither study employed quantitative measurement of both the presence and severity of a wide range of neuropsychiatric symptoms in this subgroup.

No study has investigated instrumental or higher level activities of daily living in EAD. Activities of daily living in Alzheimer's disease patients in general have been shown to relate to psychiatric symptomatology, with poorer functional capacity noted in patients who exhibit hallucinations, delusions, and/or uncooperative behavior (Mayeau, Stern, & Spanton, 1985). In a study of mixed etiology neurological patients, Burgess, Alderman, Evans, Emslie, and Wilson (1998) found that performance on executive tests (e.g., Trails B, FAS, Wisconsin Card Sorting Test, Cognitive Estimates, and/or Simplified Six Element Test) was related to observer's ratings of patients' dysexecutive problems in every day life (e.g., temporal sequencing problems, impulsivity, planning difficulties, poor decision making). In addition, several publications have suggested that competence in activities of daily living, especially "higher level" activities of daily living, is dependent on intact executive abilities (Almkvist, Wahlund, Andersson-Lundman, Basun, & Backman, 1992; Boone, Miller, & Lesser, 1993; Duncan, 1986; Miller et al., 1991; Nadler, Richardson, Malloy, Marran, & Hostetler-Brinson, 1993). These reports hypothesize that executive functions (e.g., higher level problem-solving skills thought to be associated with frontal lobe integrity) are critical for the planning, organization, and initiation of functional activities in the elderly, and that performance of everyday tasks of living is dependent on intact functioning in these areas (Boone et al., 1993).

The relationship between caregiver burden and the EAD subtype has also not been formally investigated. Neuropsychiatric symptoms of depression, psychosis, and agitation are among the most common abnormalities in Alzheimer's disease (Levy et al., 1996) and are associated with greater caregiver burden (Ryden, 1988) and earlier institutionalization of patients (Deutsch, Bylsma, Rovner, Steele, & Folstein, 1991; Martinson, Muwaswes, Gilliss, Doyle, & Zimmerman, 1995; Morriss, Rovner, Chase, & Folstein, 1990; Steele, Rovner, Chase, & Folstein, 1990). Patients with EAD and higher levels of psychiatric symptoms would be expected to be associated with greater caregiver burden.

The purpose of the present study was to determine whether significant executive involvement in Alzheimer's disease (EAD) is associated with increased functional disability, relative to those subjects with less significant executive deficits (typical Alzheimer's disease; TAD). It was hypothesized that the EAD group, selected based on poor executive scores, would not differ from TAD patients on nonexecutive cognitive scores. Secondly, it was hypothesized that the EAD group would be associated with increased neuropsychiatric symptoms, more impaired activities of daily living, and greater caregiver stress, compared to the TAD group.

METHOD

Subjects

Subjects included 20 patients referred for neuropsychological testing at the UCLA Alzheimer's Disease Center as part of an initial diagnostic evaluation. All patients were community dwelling and met the National Institute of Neurological and Communicative Diseases and Stroke-Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria for probable or possible AD (McKhann et al., 1984). Patients with medical, substance abuse, neurologic or psychiatric disorders other than AD which could account for their cognitive compromise were excluded. Magnetic resonance imaging (MRI) was performed on all patients to rule out stroke or other conditions that could cause dementia. Routine laboratory studies were also performed to rule out other etiologies for dementia. In order to evaluate patients in the mild stages of dementia, a Mini Mental State Examination (MMSE: Folstein, Folstein, & McHugh, 1975) score of 20 or higher was required for study entry. Because of the documented impact of depression on cognitive function in the elderly, subjects were excluded if they met the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (1994) criteria for major depression. EAD was identified by significant impairment on executive neuropsychological tests requiring scores falling at least 1.5 *SD* below normative age and/or educational means on at least three out of four executive tests (Trail Making Test, Part B, FAS, Stroop C, and/or WAIS–R Similarities). The EAD subjects were matched to 10 TAD subjects with similar MMSE scores, age, education, and gender, who did not evidence executive impairment as defined above. The following subjects were taking psychotropic medications at the time of testing: 1 TAD patient (on Trazadone), and 4 EAD patients (1 on Xanax, 2 on Haldol, 1 on Paxil, and 1 on Sertraline; 1 patient was on two medications). Approximately 70 AD patients were screened from the UCLA Alzheimer's Disease Center to identify the 10 EAD subjects.

Procedure

Subjects were administered a 2.5-hr battery of neuropsychological tests as described below. The functional tests (also detailed below) were administered to the patients' caregiver in a 1-hr session by a research nurse.

Measures

Neuropsychological Tests

The specific cognitive domains assessed and the tests used to evaluate these were:

General Intellectual Functioning Wechsler Adult Intelligence Scale–Revised (WAIS–R; Wechsler, 1981). An abbreviated version of this test was employed to limit time demands and patient fatigue (Satz-Mogel; Satz & Mogel, 1962). Verbal, Performance, and Full Scale IQ scores were obtained.

Attention WAIS–R Digit Span subtest (Lezak, 1983; Wechsler, 1981).

Information Processing Speed Kaplan revision of the Stroop Test (Parts A & B; Stroop, 1935) and Trail Making Test (Part A; Reitan, 1958).

Language Boston Naming Test (Kaplan, Goodglass, & Ober, 1983) and WAIS–R Vocabulary subtest (Wechsler, 1981).

Visuoconstructional Rey–Osterrieth Complex Figure (R–O; Rey, 1941) and WAIS–R Block Design subtest (Wechsler, 1981).

Verbal Memory Logical Memory (LM) subtest of the Wechsler Memory Scale – Revised (WMS–R; Wechsler, 1987).

Nonverbal (Visual) Memory Visual Reproduction (VR) subtest of the WMS–R (Wechsler, 1987).

Executive Functioning Trail Making Test (Part B; Reitan, 1958; Segalowitz, Unsal, & Dywan, 1992), Stroop Test (Part C; Bench et al., 1993; Liddle, Friston, Frith, & Frackowiak, 1992; Pardo, Pardo, Janer, & Raichle, 1990; Perret, 1974; Stroop, 1935), Controlled Oral Word Association Test of verbal fluency (FAS;

Benton & Hamsher, 1976; Elfgren, Ryding, & Pleasant, 1996; Frith et al., 1995; Liddle et al., 1992; Miceli, Caltagierone, Gainotti, Musullo, & Silveri, 1981; Miller, 1984; Milner, 1964, 1971; Perret, 1974; Pujol et al., 1996), and WAIS–R Similarities subtest (Chase et al., 1984; Rao, 1990; Sheer, 1956; Wechsler, 1981).

The scores used for analysis included Full Scale IQ (FSIQ); Digit Span, Vocabulary, Block Design, and Similarities non-age-corrected scaled scores of the WAIS–R; time (in seconds) to complete Parts A, B, and C of the Stroop Test; time (in seconds) to complete Parts A and B of the Trail Making Test; total words generated in 3 min for the letters *f*, *a*, and *s* (1 min for each letter); total score for the copy for the R–O Complex Figure; immediate and 30-min delay recall for the LM and VR subtests of the WMS–R; total correct out of 60 on the Boston Naming Test (spontaneously and semantically cued responses).

Functional Measures

Neuropsychiatric Assessment Neuropsychiatric Inventory (NPI; Cummings et al., 1994). The NPI is a caregiver-based instrument designed to assess 12 behavioral disturbances occurring in dementia patients: delusions, hallucinations, dysphoria, anxiety, agitation, euphoria, disinhibition, irritability, apathy, aberrant motor behavior, night-time behavior disturbances, and appetite and eating abnormalities. To serve as an informant, the caregiver must have at least daily contact with the patient. The questions pertain to changes in the patients' behaviors that have appeared since the onset of the illness and were present in the past 4 weeks. A frequency rating (1–4) multiplied by a severity rating (1–3) produces a subscale score for each behavior, and the summation of subscale scores produces a total NPI score. Higher scores suggest greater frequency and severity of psychiatric symptoms. The NPI has been shown to be valid when compared with a variety of other diagnostic approaches and to have high interrater and test-retest reliability (Cummings et al., 1994). The test variables used for analysis included the NPI total score and 12 subscale scores.

Functional Assessment Instrumental Activities of Daily Living (IADL; Lawton & Brody, 1969). The IADL assesses a patient's ability to perform activities in eight domains of functioning: ability to use a telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility for own medications, and ability to handle finances. The measure is administered to the patient's caregiver and each domain is scored 0 or 1. Higher scores suggest better adaptive functioning. The IADL has been reported to have moderate reliability and validity (Lawton & Brody, 1969). The test variable used for analysis was the total score (0–8).

Caregiver Burden Assessment Domain of Caregiver Appraisal (DCA; Lawton et al., 1989). The DCA is 47-item, caregiver administered instrument designed to assess five domains related to caregiving experience: subjective caregiving burden, impact of caregiving, caregiving mastery, caregiving satisfaction, and cognitive reappraisal. Each question is scored on a 5-point Likert scale. The subjective caregiving burden subscale consists of 13 questions which assess the degree of caregiver distress related to caring for an elderly person with dementia. The impact of caregiving subscale consists of nine items which evaluate the effect of caring for an elderly demented individual on the caregiver's social and daily life functions. Higher scores on the subjective caregiver burden and impact of caregiving scales suggest greater caregiver stress, while higher scores on the remaining scales suggest greater caregiver satisfaction and mastery. Reliability and validity of the measure has been reported (Lawton et al., 1989). The test variables used for analysis included the total score on the Caregiver Burden subscale and the Impact of Caregiving subscale.

RESULTS

Ten patients with EAD (age range 54–87) and 10 TAD patients (age range 66–88) were included in the study; the groups were matched for key demographic and illness severity measures. Descriptive characteristics of the two groups are shown in Table 1.

t-Test comparisons of the two groups revealed no significant group differences in age [$t(18) = 1.74$, $p = .099$], MMSE score [$t(18) = 1.00$, $p = .330$], duration of illness [$t(18) = 1.04$, $p = .309$], or age of onset [$t(18) = 1.38$, $p = .184$]. A trend was observed for education, with TAD patients slightly less educated [$t(18) = -2.04$, $p = .057$], however, the education discrepancy was judged not to be clinically significant. *t*-Test comparisons of the two groups on the executive tests revealed significant group differences for three of the four executive measures (Trails B, [$t(13) = -2.42$, $p = .031$]; FAS [$t(18) = 2.39$, $p = .027$]; and Stroop C, [$t(17) = -2.09$, $p = .051$]), with the EAD group performing more poorly. (Note: Higher scores on Trails B and Stroop C represent poorer performance, while

Table 1. Descriptive Characteristics for the TAD and EAD Groups.

Descriptive variable	Group		*p* value
	TAD Mean (*SD*)	EAD Mean (*SD*)	
n	10	10	
Gender (males/females)	5/5	5/5	
Age	79.9 (6.1)	73.6 (9.6)	.099
Education	13.7 (2.3)	15.9 (2.5)	.057
MMSE	23.7 (3.1)	22.2 (3.6)	.330
Duration of illness (years)	3.1 (2.60)	2.2 (.78)	.309
Age of onset	76.8 (7.39)	71.4 (9.9)	.184
Trails B	217.7 (79.0)	284.2 (36.2)	.031
Stroop C	240.5 (99.9)	401.2 (208.8)	.051
Similarities	7.3 (2.8)	5.5 (2.80)	.185
FAS	28.3 (9.9)	19.9 (4.9)	.027

Table 2. Frequency of Impaired Performance on the Executive Neuropsychological Measures for TAD and EAD Groups.

Executive measure	Group		*p* value
	TAD	EAD	
Trails B	6 (60%)	10 (100%)	.087
FAS	2 (20%)	8 (80%)	.023
Stroop C	5 (50%)	10 (100%)	.033
Similarities	1 (10%)	6 (60%)	.057

lower scores on FAS and Similarities represent poorer performance.)

Table 2 shows the frequency of impaired performance on the executive measures (e.g., scores falling at least 1.5 *SD* below normative age and/or educational means) for the TAD and EAD groups using Chi-square analyses.

Significantly more EAD patients evidenced impaired scores on FAS and Stroop C measures. Trends were observed for Trails B and Similarities, again with a greater number of EAD subjects performing more poorly than the TAD subjects.

Table 3 shows the group means and standard deviations for the various nonexecutive neuropsychological measures for the TAD and EAD groups.

A significant group difference was documented on only one of the neuropsychological measures (Stroop A), with the EAD group performing more poorly. The groups did not significantly differ on FSIQ, Digit Span, Stroop B, Trails A, Boston Naming Test, Vocabulary, Block Design, Rey–Osterrieth Figure, Logical Memory I, Logical Memory II, Visual Reproductions I, and Visual Reproductions II.

Table 4 shows the group means and standard deviations for the various behavioral and caregiver measures for the TAD and EAD groups.

Significant group differences were found for all three measures, with more disturbance documented in the EAD group. Specifically, significant group differences were documented on the NPI, IADL, and Caregiver Appraisal Burden subscale. A trend was observed for the Impact of Caregiving subscale.

Table 5 shows the contributing frequency of the various neuropsychiatric symptoms in the two groups as measured by the NPI using Chi-square analyses.

A significant group difference was documented for agitation, with the EAD group evidencing a higher score on the subscale measuring this symptom. Trends were observed for greater disinhibition and eating abnormalities in the EAD group.

To examine the relationship between the four executive measures and three functional tests, exploratory correlational analyses were performed for the 20 TAD and EAD subjects

Table 3. Mean Neuropsychological Test Scores for the TAD and EAD Groups.

Neuropsychological tests	Group		*p* value
	TAD Mean (*SD*)	EAD Mean (*SD*)	
Intelligence FSIQ	95.7 (8.5)	89.7 (9.5)	.163
Attention			
Digit Span	8.5 (2.0)	7.6 (2.1)	.343
Information Processing Speed			
Stroop A	85.6 (16.6)	117.1 (25.0)	.005
Stroop B	58.4 (14.1)	68.3 (18.3)	.210
Trails A	73.6 (25.1)	92.7 (31.3)	.149
Language			
Boston Naming Test	40.1 (12.1)	44.3 (7.7)	.369
Vocabulary	9.4 (2.4)	9.4 (1.8)	1.000
Visual/spatial			
Block Design	4.4 (1.2)	3.5 (1.6)	.130
Rey–Osterrieth Figure	23.4 (8.9)	20.8 (8.1)	.508
Verbal Memory			
Logical Memory I	9.1 (5.6)	6.8 (4.3)	.319
Logical Memory II	3.6 (4.8)	1.6 (2.0)	.243
Nonverbal Memory			
Visual Reprod I	13.7 (6.7)	14.3 (6.7)	.844
Visual Reprod II	3.9 (6.0)	1.0 (2.8)	.189

Table 4. Mean Functional Test Scores for TAD and EAD Groups.

Functional tests	Group		*p* value
	TAD Mean (*SD*)	EAD Mean (*SD*)	
NPI total score	7.8 (5.6)	24.0 (14.2)	.006
IADL	6.0 (2.1)	3.7 (1.1)	.014
Caregiver Appraisal			
Burden	18.4 (4.3)	28.8 (9.4)	.012
Impact Caregiving	14.0 (5.5)	20.8 (9.4)	.069

Table 5. Frequency of Neuropsychiatric Symptoms as Measured on the NPI for TAD and EAD Groups.

NPI neuropsychiatric symptom	Group		*p* value
	TAD	EAD	
Delusions	0 (0%)	2 (20%)	.474
Hallucinations	0 (0%)	0 (0%)	–
Agitation	2 (20%)	8 (80%)	.023
Dysphoria	4 (40%)	5 (50%)	1.00
Euphoria	1 (10%)	3 (30%)	.582
Apathy	6 (60%)	8 (80%)	.628
Disinhibition	0 (0%)	4 (40%)	.087
Irritability	3 (30%)	7 (70%)	.179
Anxiety	2 (20%)	6 (60%)	.170
Aberrant motor behavior	2 (20%)	6 (60%)	.170
Night-time behavioral disturbances	2 (20%)	3 (30%)	1.00
Appetite and eating abnormalities	0 (0%)	4 (40%)	.087

combined. Given that the scores were not normally distributed, Spearman correlations were conducted. Of interest, significant correlations were found between the WAIS–R Similarities raw score and IADL total score ($r = .48$, $p = .05$), Stroop C and NPI total score ($r = .47$, $p = .04$), Trails B and the Impact of Caregiving

subscale ($r = .45$, $p = .05$), Stroop C and NPI aggression ($r = .62$. $p = .004$), WAIS–R Similarities raw score and NPI apathy ($r = –.51$, $p = .02$), WAIS–R Similarities scaled score and NPI apathy ($r = –.49$, $p = .03$), Trails B and NPI irritability ($r = .48$, $p = .03$), Trails B and NPI abnormal motor behavior ($r = .51$, $p = .02$), WAIS–R Similarities raw score and NPI appetite and eating abnormalities ($r = –.66$, $p = .002$), and WAIS–R Similarities scaled score and NPI appetite and eating abnormalities ($r = –.61$, $p = .004$). These preliminary findings suggest that there may be a link between executive performance and these behavioral characteristics, and these potential relationships should be explored in future studies.

CONCLUSIONS

The present study was an initial attempt to examine neuropsychiatric symptoms, instrumental activities of daily living, and caregiver burden in subgroups of mild Alzheimer's disease patients with and without prominent executive impairment (e.g., EAD and TAD). We are not aware of any other study which has empirically investigated both neuropsychological functioning and associated aspects in a priori-grouped EAD and TAD.

The results of the present study revealed that, as hypothesized, the TAD and EAD groups performed similarly on nonexecutive neuropsychological tests of intelligence, language, verbal and nonverbal memory, and visual-spatial ability, with no significant group differences documented. The EAD group was significantly more impaired than the TAD group on one measure of cognitive speed (Stroop A), however, this observation was not corroborated on two additional measures of information processing speed (Trails A, Stroop B). In contrast, the EAD group exhibited significantly poorer performance on three of the four executive neuropsychological measures (e.g., Trails B, Stroop C, and FAS) compared to the TAD group, and a significantly greater frequency of EAD patients than TAD patients evidenced impaired scores on two out of four executive tasks (Stroop C and FAS).

As hypothesized, significant group differences were found for the behavioral and caregiver measures; the EAD group scored significantly worse than the TAD group on all three measures. Specifically, the EAD group showed more severe neuropsychiatric symptoms, impaired activities of daily living, and greater caregiver burden than the TAD group. In addition, comparisons between the two groups on the percentage of the various neuropsychiatric symptoms assessed by the NPI suggest that EAD is associated with a greater frequency and severity of symptoms than found in TAD.

These data taken together indicate that, with the exception of degree of impairment in executive skills, EAD and TAD are neuropsychologically similar with declines in abilities mediated by both the temporal and parietal lobes. However, the two groups differ in terms of a variety of other aspects. The fact that the EAD group evidenced increased neuropsychiatric symptoms relative to the TAD group corroborates the limited anecdotal or qualitative research in this area (Chase et al., 1987; Grady et al., 1990). In addition, the finding of more impaired instrumental activities of daily living in the EAD group suggests that, as hypothesized by other investigators, executive functions play a role in the ability of elderly patients to perform everyday tasks of living (Almkvist et al., 1992; Boone et al., 1993; Duncan, 1986; Miller et al., 1991; Nadler et al., 1993).

A question could be raised as to whether diagnostically the EAD patients are indeed Alzheimer's disease patients, or instead suffer from fronto-temporal dementia given their notable psychiatric symptomatology and executive dysfunction (Lund and Manchester Groups, 1994; Neary et al., 1998). However, this would appear to be unlikely for two reasons. First, the average age of onset of the EAD patients (71 years) is older than what it typically seen in fronto-temporal dementia (e.g., age of onset before 65). Second, the EAD group evidenced significant visual-spatial dysfunction on neuropsychological tests; skills which are relatively preserved in fronto-temporal dementia until the later stages of the disease (Mendez et al., 1996).

Two conceptualizations of Alzheimer's disease have been proposed in the literature: the ''phase or stage model'' and the ''subgroup model.'' The phase or stage model of Alzheimer's disease

purports that for the most part, homogeneous deterioration of cognitive functioning occurs that increases as a function of disease progression (e.g., time); (Hom, 1992; Martin et al., 1986; Reisberg, Ferris, de Leon, Crook, 1982). In contrast, the ''subgroup model'' postulates the existence of distinct patterns of neuropsychological/psychiatric/neurological symptoms which define and differentiate patients, while accepting the idea of progressive deterioration over time (Jorm, 1985; Liston, 1979; Martin et al., 1986). Frontal lobe abnormalities occur in most patients in the late stages of Alzheimer's disease. Findings from preliminary neuroimaging and pathologic studies (Grady et al., 1988; Grady et al., 1990; Haxby et al., 1988; Johnson et al., 1999; Mann, Mohr, Gearing, & Chase, 1992; O'Brien et al., 1992; Perani et al., 1998; Waldemar et al., 1994), provide support for the existence of a separate frontal variant of Alzheimer's disease subgroup with early-onset executive dysfunction. Whether our EAD group identified with executive neuropsychological tests also represents a separate frontal variant of Alzheimer's disease awaits neuroimaging and pathological confirmation. Longitudinal assessment of cognition and neuropsychiatric symptoms in the EAD and TAD group is also needed to more definitively determine whether the EAD subjects represent a discrete subgroup.

In conclusion, the results from the current study have important clinical implications in that they indicate that the presence of prominent executive deficit, as determined by impairment on at least three of four brief neuropsychological tasks (FAS, Trails B, Stroop C, WAIS–R Similarities) identifies those early AD patients at substantial risk for decreased functional independence, more neuropsychiatric dysfunction, and greater caregiver burden. However, these preliminary findings, based on a small sample which included some patients on psychotropic medications, require additional replication.

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