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USE OF EXECUTIVE CONTROL IN ACCESSING EPISODIC AND SEMANTIC MEMORY IN PATIENTS WITH ALZHEIMER*S DEMENTIA

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Daniel Malcolm Spica

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USE OF EXECUTIVE CONTROL IN ACCESSING EPISODIC AND SEMANTIC MEMORY IN PATIENTS WITH ALZHEIMER'S DEMENTIA

Ву

Daniel Malcolm Spica

A DISSERTATION

Submitted to Michigan State University in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

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ABSTRACT

USE OF EXECUTIVE CONTROL IN ACCESSING EPISODIC AND SEMANTIC MEMORY IN PATIENTS WITH ALZHEIMER'S DEMENTIA

By

Daniel Malcolm Spica

Executive control functions are believed to mediate, among other processes, the organization of material to be stored into or retrieved from declarative memory stores. The construct of declarative memory typically divides the memory stores into two subsystems, episodic (memory of autobiographical information and events), and semantic memory (generalized knowledge including meanings of words).

Both executive control and memory deficits have been documented in Alzheimer's disease (AD) dementia; however, it has not been clear to what extent executive control dysfunction may differentially affect episodic and semantic memory in AD patients. Similarly, while it has been hypothesized that normal elderly males exhibit more executive dyscontrol than elderly females, it is not known if these relative weaknesses are more prominent in the episodic or semantic memory systems.

Executive control deficits in 26 Alzheimer's disease (AD) patients were examined in episodic and semantic memory performances through comparisons with performances of 26 normal control subjects. The two declarative memory subsystems were tested by the administration of the California Verbal Learning Test to examine episodic memory, and Category and Letter Fluency tasks to examine semantic memory. Executive control functions during the memory performances were evaluated through the performance characteristics of a) semantic clustering (grouping words by meaning), b) phonemic clustering (grouping words by sound), c) Perseveration errors, and d) Intrusion errors.

While the AD patients exhibited significant numbers of Intrusion and Perseveration errors compared to normal controls, these deficits in executive control were not specific to a single memory system (semantic or episodic). No differences in semantic and phonemic clustering were significant. In regards to memory impairments, the AD patients demonstrated the greatest memory deficits on the Category Fluency Test, a task believed to maximally tax the semantic network, providing support for semantic network degradation in AD. Finally, analysis of the normal control sample performances did not provide statistical support for the prediction that elderly males would exhibit greater decline in executive controls than females; male and female normal control subjects demonstrated general equality in levels of performance. Possible future directions for research are discussed.

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TABLE OF CONTENTS

Page
List of Tablesv
List of Figuresvi
Introduction1
Memory Deficits in Alzheimer's Disease
Hypotheses17
Method
Results
Hypothesis 1 Analyses
Discussion
List of References

LIST OF TABLES

Tal	ble Page
1	Subject Characteristics21
2	Summary of Correlation Coefficients from Independent Raters
3	Summary of Raw Scores on Memory tasks24
4	Summary of Multivariate Test Statistics26
5	Summary of Univariate F-Tests26
6	Summary of T-Test Comparisons of AD Patient and Normal Control Performance Characteristics
7	Summary of Standardized AD Patient Performances (Based on Normal Control Levels of Performance)30
8	Normal Subject Characteristics
9	Summary of Raw Scores of Normal Control Subjects on Memory Tasks
10	Summary of Multivariate Test Statistics Comparing Normal Male and Normal Female Performance34
11	Summary of Univariate F-Tests Comparing Normal Male and Normal Female Performance
12	Summary of Significant Findings

LIST OF FIGURES

Fi	gure Page
1	Performance Characteristics on Episodic and Semantic Memory Tasks25
2	Performance Characteristics of Alzheimer's Patients and Normal Controls (Standard Scores)28
3	Mean Performance Characteristic Levels of Normal Controls on Episodic and Semantic Memory Tasks (Standard Scores)
4	Performance Characteristics of Normal Controls on Episodic Memory Tasks (Standard Scores)35
5	Performance Characteristics of Normal Controls on Semantic Memory Tasks (Standard Scores)36
6	Sample Semantic Network "Vehicles"42

INTRODUCTION

In recent years there has been a surge of interest in Alzheimer's disease (AD) both in the medical community and the general public. The prevalence of AD in this country is typically estimated around 6 percent in persons over 65 (Schneck, Reisberg, & Ferris, 1982), and the tragic nature of AD's symptoms and prognosis has surely helped in making it so prominent. At present, AD is incurable and its symptoms untreatable. However, major advances have been made in the study of AD, primarily in diagnostic techniques differentiating it from other dementing disorders, some of which have a greater likelihood of remission than AD (Wells, 1984). Memory loss, reputed to be among the best early indicators of dementia (Lezak, 1983), has served as a valuable area of study for the differentiation of AD victims both from people with other dementing conditions, and from otherwise healthy forgetful elderly persons.

Memory Deficits in Alzheimer's Disease

Diagnostic techniques involving memory functions have helped to provide the greatest diagnostic gains in discriminating between AD victims and normal aged persons.

While decline in memory functions is a major component of both normal aging and, to a greater extent, the pathological process of AD (Poon, 1985), evidence is mounting that the specific nature of the memory decline is quite different in these two aged conditions. While routinized, "overlearned" tasks and skills have been found to be well preserved in normal aging as well as in at least the early and middle stages of the AD process (Wilson, Kaszniak, & Fox, 1981), new acquisition of factual information has been found by various researchers to be particularly difficult for AD victims (Joynt & Shoulson, 1985; Mesulam, 1985).

It is not yet clear if AD victims are deficient in learning all types of new information. On tasks which require recall and recognition of novel verbal or visual spatial information, such as learning a list of words or set of drawings, AD patients are consistently found to be impaired beyond the decline associated with normal aging (Flicker, Ferris, Crook, Bartus, & Reisberg, 1986). However, only inconsistent evidence is available showing AD patients as impaired on tasks requiring acquisition of new cognitive-motor processes, such as reading words or images in a mirror (Eslinger and Damasio, 1985; Gordon, 1984).

The possible dissociation of such "types" of memory functions has led researchers to devise multi-system memory theories (see Tulving, 1987, for discussion). Certainly both types of learning tasks mentioned above (list learning and motor process learning) require access to long-term

memory stores for good performance, but the nature of the information needed is clearly different; indeed, the technical distinction between these types of cognitive functions is that of "Procedural" and "Declarative" memory.

Divisions of Long-Term Memory; Procedural and Declarative Memory

The necessity of dividing memory into general realms of "knowing how" and "knowing what" has been recognized both in psychology (e.g., Bergson, 1911; Bruner, 1969) and in philosophy (Ryle, 1949). The direct distinction between procedural and declarative memory was first made in the field of artificial intelligence to delineate the knowledge of skills and procedures from the knowledge about which we (or computers) are able to make declarations (Winograd, This particular terminology has held fast in the 1975). neurosciences, helping to accommodate experimental and clinical findings that some amnesic conditions can result in individuals with preserved abilities in learning, while at the same time the subject does not have access to the conscious experience of acquiring the particular skill. For example, the now famous case of H.M. illustrates such a dissociation; H.M. suffered a severe amnesic syndrome following bilateral medial temporal lobe resection intended to curtail his frequent epileptic seizures. Subsequent to the temporal lobotomy H.M. was able to show improvement on a mirror-tracing task (new skill learning) after repeated

daily testing, but had no recollection from one session to the next of prior exposure to the task (Milner, 1962). H.M. similarly showed improved performances on other perceptual-motor tasks, such as bimanual tracking and rotary pursuit tests, but was unable to recollect ever having seen the tasks before (Corkin, 1968).

Other amnesic conditions have also been shown to differentially affect skill performances from the memory of acquiring the skill, such as amnesia caused by electroconvulsive shock therapy. Squire, Cohen, and Zouzounis (1984) taught a mirror-reading skill to depressed psychiatric patients in anticipation of each patient's course of electroconvulsive shock treatments. Despite marked retrograde amnesia following the treatments, including an inability to remember being taught the skill, the patients' post-therapy mirror-reading performances remained at normal levels. That is, their knowledge of the procedure survived the amnesic process while the conscious knowledge of acquiring the skill was lost (Squire, Cohen, & Zouzounis, 1984).

Data collected with H.M. and with numerous other patients has repeatedly demonstrated preserved learning capacity during amnesia in skills as varied as perceptual-motor (working jigsaw puzzles; Brooks & Baddeley, 1976), conceptual reasoning (tower of Hanoi task; N. Cohen, 1984), application of numerical rules (Wood, Ebert, & Kinsbourne. 1982), and learning through priming effects

(Graf, Squire, & Mandler, 1984). Priming refers to the facilitation of performance by prior exposure to material, such as target words. For example in the Graf et al. (1984) study, the amnesic subjects were shown a number of words (they were thus "primed"). Then the subjects were provided with a stimulus of three-letter word stems, and asked to complete the word. The findings revealed a priming effect of biasing the subject to complete the stimuli stems using words to which they had just been exposed, rather than other words sharing the same first three letters. Further, the amnesics exhibited the priming effect to the same extent as normal controls, despite the amnesics' marked deficiencies in recalling or even recognizing the target priming words (Graf, Squire, & Mandler, 1984).

Work investigating priming effects for AD patients has not shown the same facilitation evidenced by other types of amnesics. So called "implicit" memory for verbal material, as measured by lexical priming tasks has been found to be severely impaired in AD victims compared to age-matched controls (Butters, Heindel, & Salmon, 1990; Salmon, Shimamura, Butters, & Smith, 1988). Likewise, implicit memory for pictorial information, as measured by picture priming, has also been demonstrated to decline rapidly in AD samples (Heindel, Salmon, & Butters, 1990).

Subsystems in Declarative Memory

In further distinguishing long-term memory functions,

Tulving (1972) proposed that there exists two subsystems within "propositional" (declarative) memory which he called "episodic" and "semantic" memory. In his 1983 book "Elements of Episodic Memory" which reviews the fund of research generated after his 1972 proposal, Tulving describes episodic memory as essentially the autobiographical and subjectively experienced information (memory of an event or episode), and semantic memory as roughly the generalized knowledge we possess and draw upon (including our mastery of concepts such as semantic meanings of words). Some researchers have suggested that the episodic/semantic dichotomy does not fully describe human memory due to overlap in the systems (see McKoon, 1985, 1986; Ratcliff, 1986); however, Tulving (1983) stated: "Episodic memory is concerned with unique, concrete, personal experiences dated in the rememberer's past; semantic memory refers to a person's abstract, timeless knowledge of the world that he shares with others" (p. v).

While research into these memory systems has spanned into animal models and experiments, for the purposes of this study we will concentrate on the assessment of memory abilities in humans. Over the years, human episodic memory tasks have been developed in various forms, such as recall of pictures (Nebes, Martin & Horn, 1984), picture recognition (Damasio, Eslinger, Damasio, Van Hoesen, & Cornell, 1985; Tulving, Schacter, McLachlin, & Moscovitch, 1988), story recall (Butters et al., 1987; Ostergaard,

1987), and numerous tests of list learning (e.g., Bushke & Fuld, 1974; Delis, Kramer, Kaplan, & Ober, 1987; Ostergaard, 1987). Similarly, various versions of fluency tasks have been developed to tap semantic memory, as discussed below. In addition, there have been some semantic memory investigations using measures requiring the recognition of celebrity faces (Damasio et al., 1985), memory for historical events (Cermak & O'Connor, 1983), and even knowledge of the rules, jargon, and etiquette of golf (Schacter, 1983).

A Measure of Episodic Memory

The recent advent of the California Verbal Learning Test seems especially promising since the measure's design was theory-driven, and it may be the only test to date that quantifies (and provides normative data based on 273 subjects) the multifactorial ways in which an examinee attempts to organize, encode, consolidate, and retrieve verbal material processed through the episodic memory system (Delis et al., 1987). The routine scoring procedures also include indices of semantic clustering, serial clustering, primacy-middle-recency effects, perseverations and intrusions, discriminability, response bias, free and cued recall, and many other dimensions pertinent to the concept of executive control in memory processing (Delis et al., 1987; Lezak, 1983).

8

Verbal Fluency Tasks as a Measure of Semantic Memory

Tests of verbal fluency, which require subjects to generate a list of words belonging to some prescribed group, have been used in clinical neuropsychology since the mid-1960s when they were found to be sensitive to cerebral dysfunction, particularly of the left frontal and left temporal cortical regions. Of the methods researched to assess verbal fluency, the two most commonly employed are (a) asking the subject to produce as many words as possible in one minute beginning with a certain letter (letter fluency), and (b) requiring as many words as possible within a certain category, such as animals, fruits, or vegetables, within a one minute time limit (category fluency). The most popular representative procedure for letter fluency testing is probably that of the Controlled Oral Word Association Test, a component of the Multilingual Aphasia Examination (Benton & Hamsher, 1976), which uses the letters "C", "F" or "L". Likewise, procedures for category fluency tests are found as part of the Boston Diagnostic Aphasia Exam (Goodglass & Kaplan, 1983), the Western Aphasia Battery (Kertez, 1980) and the Mattis Dementia Rating Scale (Mattis, 1976).

Role of Executive Control; An Overview

The concept of some controlling mechanism that mediates and modulates our attention to stimuli and dictates the process through which we are to receive, decode, and/or respond to that stimuli has taken on many related forms over the years in the scientific literature (see Pylyshyn, 1990). Ashcraft's (1989) description states: "This component has the responsibility of parcelling out the mental resources of attention in reaction to the three memory components' [sensory, long-term, and short-term/working] changing demands for processing resources" (p.66).

Among the most detailed conceptions of executive control is that from Gordon D. Logan, who has demonstrated that four major executive functions can be distinguished (Logan, 1985):

- <u>Choice</u> among alternative strategies to approach a particular task.
- <u>Construction</u> or instantiation of the strategy chosen to enable performance of the task.
- <u>Execution</u> and maintenance of the strategy to perform the task in real-time.
- 4) <u>Inhibition</u> or disablement of the strategy in response to changes in the goals or environment that make the strategy irrelevant or inappropriate.

Through a series of experiments, Logan showed that each of his proposed functions have empirical consequences in tasks employing common cognitive psychology techniques. For instance, he presented the words ABOVE and BELOW to subjects on a screen either above or below a fixation point (i.e.,

spatial Stroop task). The subjects were asked to identify each presented word by pressing specified keys, and their performances were evaluated by latencies and error rates. In addition, Logan varied the tasks by manipulating the frequencies at which the words identities and positions were compatible or conflicting; e.g., the word ABOVE positioned above the fixation point = compatible, ABOVE presented below the fixation point = conflicting. As Logan describes (1985), numerous strategies are possible for good performance as the relative frequencies of compatible/ conflicting word positions vary, and his experiments were interpreted as demonstrating that subjects will actively choose the strategies enabling them to best achieve their performance goals (Logan, 1980; Logan & Zbrodoff, 1979).

Similarly, using the same spatial Stroop task, Logan added the dimension of cuing; before the presentation of the word, an X would appear on the screen signalling where the word will appear (above or below fixation). By varying the delay intervals between the appearance of the cue X and presentation of the target word, Logan and Zbrodoff found that the subjects' response times began to decrease when a 400 to 600 msec delay was provided. That is, the subjects decreased reaction times indicate that they were able to construct a response strategy if given 400 to 600 msec to do so (Logan & Zbrodoff, 1982).

Logan's work was less definitive on the nature of strategy *execution* and maintenance function, except to say

that the procedures do occur. He presented two potential scenarios and provided research evidence for each: a) a strategy may be engaged reflexively and ballistically to similar stimuli with very little modification or intervention (Logan 1978), or b) a strategy may require continual monitoring and executive control for its maintenance (Schneider & Shiffrin, 1977). Logan resolved these competing scenarios and lines of evidence by suggesting that different cognitive tasks and strategies will require different levels of monitoring throughout their execution.

Finally, in discussing inhibition or abandonment of strategies as the environment changes, Logan (1985) recounted evidence from stop-signal studies which require a subject to cease an activity as soon as possible once a "stop" signal has been given. For instance, Ladefoged and colleagues (1973) found that subjects required only 200 msec to stop speaking when signalled, and Logan (1982) demonstrated that subjects stopped typing only 300 msec after the stop signal. Further, Logan and Cowan (1984) pointed out that the response to a stop signal appears to take very similar amounts of time irrespective of task complexity. For example, in comparing performances for simple reaction times (responding to a light display) and choice reaction times (responding only to a specified color of light display), a choice reaction time response took on average only 17 msec longer to stop than a simple reaction

time response (Logan, 1984).

As seen above, subjects can disengage from tasks very rapidly, even when the tasks are relatively ballistic, such as talking or typing. Therefore, Logan reasoned that some functional entity that serves as an executive controller is monitoring and, when necessary, discontinuing responses. That is, an executive process may determine the significance of the incoming stimuli, then either respond to it quickly if the goals of the task have changed or an error is detected, or place them in a line with the other responses if they require the conventional response (Logan, 1985).

Inhibition probably constitutes the single most widely-recognized function of executive control. For instance, Martin, Caplan, and Hier (1984) associated verbal perseverations with a lack of inhibition of inappropriate response by executive control. Santo Pietro and Rigrodsky (1986) later focused on a combination on what corresponds to Logan's first (choice) and fourth (inhibition) executive functions to interpret oral-verbal errors in adult aphasics. They attempted to account for errors of perseveration by looking to an inability to <u>release</u> information from working memory, thereby causing the subject, during a list learning task, to draw on a limited pool of words "trapped" in a cycle between working and short-term memory (Santo Pietro & They suggested that once a word had been Rigrodsky, 1986). retrieved from the long-term memory store, it was retained in working memory through non-volitional rehearsal, which in

turn reduced the capacity of working memory and impaired its ability to add new words or resume the search of long-term memory. Considering Logan's proposed executive functions, it is the responsibility of the executive control system to release the information from working memory (choose to or choose not to rehearse specific information in working memory), as well as to inhibit uttering the wrong response.

Other putative errors made by the executive control system include failure to "chunk" or cluster information in meaningful arrays to facilitate retrieval or manipulation (Delis et al., 1987; Lezak, 1983). Whereas it has been demonstrated that the use of contextual cues for organization of material to be memorized varies with age, socioeconomic class, and other organismic dimensions (Craik, Byrd, & Swanson, 1987), profound impairment of such functioning is the hallmark of AD. As Moscovitch and Umilta (1990) state, "A malfunctioning central executive [in working memory] is typically an early symptom of dementia" (p. 33).

As noted above, one view of executive control is that of "...parcelling out the mental resources of attention..." (Ashcraft, 1989, p. 66). A recent review of attentional processes in older individuals reports advances in measuring attention in a multitude of categories: divided attention, attention switching, sustained attention, and selective attention (McDowd & Birren, 1990). The equipment required to test attention performances involve technology such as

electroencephalograms (Thompson & Marsh, 1973), visual tracking equipment (Hartley, Kieley, & McKenzie, 1987) and other tests of chemical and electrical activity of the brain, and, although such methods are beyond the scope of this study, they may prove useful in the future for determining to what extent general arousal is necessary for utilization of executive control functions. Lowered general levels of central nervous system arousal has been noted in older as compared to younger normal adults (e.g., Woodruff, 1975); conversely, over-arousal has also been postulated to explain attentional performance differences in older adults. As noted by McDowd and Birren (1990), further investigation is needed to determine the role arousal may play in the various cognitive performances of older individuals.

For the present purposes, the analysis of intrusion errors (lack of inhibition), perseveration errors (lack of inhibition and possible lack of release from working memory cycle), and inefficient production or recall grouping (lack of clustering) will be used in this study to assess the relative use of executive control in accessing episodic and semantic memory stores.

Executive Control Deficits in Alzheimer's Disease

James Becker (1987, 1988) has proposed a multiple factor hypothesis of cognitive decline in Alzheimer's dementia. After analyzing data from 71 AD patients in his 1988 study, Becker discovered a two-component pattern of

dissociable impairments, comprising functions in (a) secondary memory and (b) the central executive system as described by Baddeley (Baddeley, 1986; Baddeley, Bressi, Della Sala, Logie, & Spinnler, 1986).

Secondary memory refers to the episodic long-term memory operations discussed above. The central executive system oversees the actions of short-term memory processes by parcelling out attentional resources to the memory stores, also discussed above. Becker found these two components to be dissociable in his sample even to extent that two of his subjects demonstrated unique deficits for one of each component. That is, one patient was impaired on secondary memory tasks while scoring within normal limits on executive system tasks, and the other patient had the reverse pattern of normal secondary memory scores and impaired executive system performances (Becker, 1988). This two-component hypothesis may prove useful in adding to our conception of the previously observed inconsistent dissociation between the two declarative memory systems in AD patients.

Dissociation of Semantic and Episodic Memory in Alzheimer's Disease

While comparing performances of demented, Huntington disease, and alcoholic-Korsakoff patients on tasks of semantic and episodic memory, Butters and his colleagues found the three groups to demonstrate different patterns of

impairment (Butters, Granholm, Salmon, Grant, & Wolfe, To investigate the subdivisions of long-term memory, 1987). they used recall of narrative passages to test episodic memory, and both category and letter fluency to test semantic retrieval. While all three patient groups were profoundly impaired on memory for passages, their performances on fluency tasks differentiated the AD group from the Huntington disease and alcoholic-Korsokoff Specifically, on both the letter and category patients. fluency tasks, the Huntington disease patients exhibited moderate impairment, and the alcoholic-Korsokoff patients were found to be severely impaired. Conversely, the AD patients were found to have deficits only in category naming fluency, while showing preserved abilities in letter fluency (Butters et al., 1987).

These findings are in partial conflict with earlier studies of AD performances on letter fluency tasks (e.g. Ober, Dronkers, Koss, Delis, & Friedland, 1986; Rosen, 1980). Because of this inconsistency in the literature pertaining to fluency performances in AD samples, it was of interest to replicate the procedures with additional analysis of the strategies used (phonemic and semantic clustering) and errors made by the patients. Perhaps as Becker (1988) suggested a differentiating factor between AD subjects and their age peers is their faulty use of executive control when attempting to recall information from their long-term memory store.

<u>Hypotheses</u>

The purpose of this study was to investigate similarities and differences in how AD patients access their two declarative (episodic and semantic) long-term memory stores. To that end, this study compared the utilization of specific executive control functions by AD subjects on an episodic memory test relative to their utilization of such functions during tests of semantic memory. To determine the relative sufficiency of the AD access strategies, patterns of performance of the AD group were compared to those exhibited by age matched normal controls on the same tasks.

In light of the preceding discussion, executive control access strategies were examined by analyzing performances during a list-learning task (episodic memory) and two verbal fluency tasks (semantic memory). Four parameters of executive control during information access were identified. These parameters are performance characteristics of a) the response errors made, and b) the extent and types of clustering used.

Analyzable errors were of two classes, comprising:

1. Perseveration of response within a task trial

2. Intrusion errors of inappropriate responses As noted above, efficiency of executive strategy during retrieval of information from long-term memory stores can be assessed by examining the use of clustering of information retrieved. A lack of clustering is believed indicative of compromised executive control. Clustering of responses was

operationally defined by two related parameters, comprising:

1. Extent of semantic clustering (word meanings)

2. Extent of phonemic clustering (word sounds)

As described above, these performance characteristics reflect the quality and extent of executive control exercised by both participant groups during episodic and semantic tasks. A number of contrasts were examined within and between groups, and were intended to help elucidate the nature of executive processing in memory access through a variety of comparisons; normals vs. AD, females vs. males, semantic vs. episodic functions, perseverative errors vs. intrusion errors, semantic vs. phonemic clustering, etc. Although the existing literature did not lend itself to hypotheses about all of these contrasts, a number of predictions were possible, discussed below.

Hypothesis 1:

In light of the above discussion, executive control of AD patients was expected to be more compromised during tasks of episodic memory as opposed to semantic memory tasks. Therefore, the AD group was expected to exhibit greater impairment of performance on each of the parameters (errors made, and extent and type of clustering used) during an episodic memory task (California Verbal Learning Test) than during semantic memory tasks (verbal fluency). The levels of impairment on these parameters were determined relative to the age-matched controls. That is, it was predicted that

the AD subjects would utilize less semantic and phonemic clustering and to exhibit more perseveration and intrusion errors during the episodic task than during the semantic tasks.

Hypothesis 2:

Consonant with existing AD literature, the AD subjects were expected to show inferior performances on all tasks in comparison with normal controls. Further, based on the previous studies noted above, the rank order of task performance discrepancy from normal levels was expected to be as follows, beginning with the task predicted to yield the lowest performance:

- 1. List-learning task (California Verbal Learning Test)
- 2. Category fluency task
- 3. Letter fluency task

Hypothesis 3:

In light of the fact that normal aged males have been found to exhibit more signs of frontal lobe pathology than aged normal females (Albert & Kaplan, 1980; Veroff, 1980) and one such system is involved in executive control (Lezak, 1983; Milner, 1964; Ramier & Hecaen, 1970; Walsh, 1978), the same indicators of faulty executive control discussed in hypotheses 1 and 2 were expected to be more prevalent in the normal male subjects than the normal female subjects.

METHOD

<u>Participants</u>

Twenty-six individuals who were involved in the ongoing Michigan State University (MSU) Psychological Clinic Aging Research Project volunteered to participate in the current study. The MSU Psychology Clinic project participants ranged in age from 61 to 83 years old. They had been deemed through history and interview to be relatively healthy and free from significant problems of mood state, and were participating with informed consent in a longitudinal study of cognition. Twenty-six individuals diagnosed with AD involved in a similar ongoing study in the MSU Department of Psychiatry Neurobehavioral Clinic and Research Center also volunteered to take part in the current study. For those participants deemed to be too cognitively impaired to appreciate all aspects of his or her research consent, consent was also obtained from the appropriate guardians. Each of the 26 participants in the AD sample were outpatients who had been previously diagnosed with AD by their attending neurologist and met the criteria for "primary degenerative dementia" outlined in the Diagnostic and Statistical Manual of Mental Disorders, Third Edition (American Psychiatric Association, 1987) and met the criteria for "possible Alzheimer's disease" developed by the National Institute of Neurological and Communicative Disorders and Stroke and The Alzheimer's Disease and Related Disorder Association (McKhann, Drachman, Folstein, Katzman,

Price, & Stadlan, 1984).

Descriptive data for the two groups of participants are shown in Table 1. Matching was successful in that the age of the normal control group (Mean [M] = 71.27, standard deviation [SD] = 6.40) did not differ significantly from that of the AD group (M = 71.65, SD = 5.62): t(50) = 0.230, p = .819. The groups did differ significantly in years of education, as the healthy normal control group averaged 13.19 years (SD = 2.89) and the AD grouped averaged 11.54 years (SD = 1.68): t(50) = -2.527, p = .015. Each group consisted of 10 males and 16 females, combining to a total sample of 52 participants.

TABLE 1

Normal Controls N = 26	Alzheimer's Patients N = 26	Total	prob
	······		
71.27 ± 6.40	71.65 ± 5.62	71.46 ± 5.97	ns
61 - 83	60 - 81	60 - 83	
ion			
13.19 ± 2.89	11.54 ± 1.68	12.37 ± 2.48	.015
8 - 20	8 - 16	8 - 20	
cy)			
10	10	20	ns
16	16	32	ns
	Controls N = 26 71.27 \pm 6.40 61 - 83 ion 13.19 \pm 2.89 8 - 20 Cy) 10	Controls N = 26 71.27 \pm 6.40 61 - 83 13.19 \pm 2.89 8 - 20 10 Patients N = 26 71.65 \pm 5.62 60 - 81 11.54 \pm 1.68 8 - 16 10	Controls N = 26Patients N = 26Total 71.27 ± 6.40 $61 - 83$ 71.65 ± 5.62 $60 - 81$ 71.46 ± 5.97 $60 - 83$ ion 13.19 ± 2.89 $8 - 20$ 11.54 ± 1.68 $8 - 16$ 12.37 ± 2.48 $8 - 20$ cy) 10 10 20

SUBJECT CHARACTERISTICS

<u>Procedure</u>

Participants volunteering for either of the two MSU projects were tested with a battery of cognitive tests and interviewed as part of the ongoing studies. Each participant was tested individually in a single session. Included in the comprehensive battery were the following measures: The Category Fluency task (Goodglass & Kaplan, 1983), the Letter Fluency Task (Benton & Hamsher, 1976), and the California Verbal Learning Test (Delis et al., 1987). The Category Fluency task requires the participant to name as many animals as possible in one minute. The Letter Fluency task requires the participant to provide as many words as possible that begin with the letters "C", "F", and "L" (separate trials of 60 seconds each). The California Verbal Learning Test (CVLT) is a word-list learning task in which the participant is aurally presented a list of 16 shopping items and required to recall as many as possible, in any order (repeated for five trials total). All participants were administered each measure according to the exact instructions provided in the respective manuals.

Scoring the four parameters of performance characteristics (Semantic clustering, Phonemic clustering, Perseveration errors, Intrusions errors) was carried out on the three measures according to the procedure prescribed in the CVLT manual (Delis et al., 1987). The CVLT scoring procedures were well suited for the fluency tasks as they involved simply tallying either the raw number of perseverations, intrusions, or the occurrence of consecutive correct responses from the same category (semantic or phonemic) depending on the dimension being scored (Delis et al., 1987). The tallied raw scores for the four parameters were divided by the total production of words for that test

to control for varying number of words produced.

Because the fluency tasks (Category and Letter) do not involve finite constrained sets of words from which the subjects may respond, a standard method was devised to determine which responses were semantically and phonemically related during these tasks. This was accomplished through three independent raters who, blind to the subjects' group membership and the hypotheses, tallied the occurrences of semantic and phonemic clustering for every protocol. [Each rater was a licensed practicing neuropsychologist. Rater disagreements were resolved by majority ratings. Inter-rater reliabilities, as measured by Pearson correlation coefficients between the three raters, ranged from 0.701 to 0.942. Specific correlations of semantic and phonemic clustering ratings are listed in Table 2.

TABLE 2

SUMMARY OF CORRELATION COEFFICIENTS FROM INDEPENDENT RATERS

Ratings	of	Performance	Cha	racteristics	During	Category	Fluency:	
		Semar	ntic	Clustering		Phonem	ic Clustering	
		RATEF	R 1	RATER 2		RATER 2	I RATER 2	
RATER	2	0.924	ł			0.701		
RATER	3	0.926	ò	0.929		0.818	0.712	
Ratings	of	Performance	Cha	racteristics	During	Letter F	luency:	
Ratings	of			racteristics Clustering	During		luency: ic Clustering	
Ratings	of		tic		During		ic Clustering	
Ratings		Semar	tic 1	Clustering	During	Phonemi	ic Clustering	

RESULTS

Table 3 lists the means and standard deviations for each of the three memory tasks, including indices of performance characteristics.

TABLE 3

SUMMARY OF RAW SCORES ON MEMORY TASKS

	Alzheimer's Patients		Normal Controls		
	Mean St	andard Deviation	Mean	Standard Deviation	
California Verbal Lea	rning Te	st:			
(Total Trials 1-5)	18.35	9.60	46.39	12.75	
Semantic Clustering	0.243	0.324	0.372	0.162	
Phonemic Clustering	0.071	0.093	0.050	0.031	
Perseveration Errors	0.166	0.384	0.106	0.080	
Intrusion Errors	0.697	0.993	0.069	0.108	
Category Fluency Test	9.23	5.00	18.69	4.07	
Semantic Clustering	0.579	0.319	0.551	0.127	
Phonemic Clustering	0.075	0.185	0.008	0.020	
Perseveration Errors	0.209	0.297	0.016	0.030	
Intrusion Errors	0.083	0.317	0.000	0.000	
Letter Fluency Test	22.39	11.51	39.31	12.56	
Semantic Clustering	0.104	0.133	0.084	0.066	
Phonemic Clustering	0.189	0.123	0.231	0.128	
Perseveration Errors	0.096	0.153	0.033	0.051	
Intrusion Errors	0.059	0.122	0.003	0.011	

To make the various tests statistically comparable, all performance data were transformed to Z-scores based on the entire sample. A MANOVA was performed with one betweensubject factor (Diagnosis: AD or Normal Control) and two within-subject factors: a) task type (Episodic memory task [CVLT], and semantic memory tasks [Category Fluency and Letter Fluency]) and b) Performance Characteristics [Semantic clustering, Phonemic clustering, Perseveration

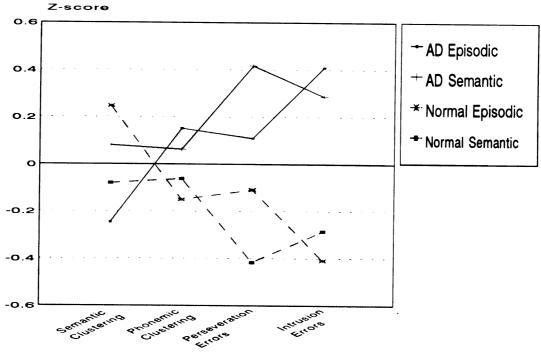
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errors, and Intrusion errors]. In this analysis, the Category Fluency and Letter Fluency tests were averaged to provide overall scores of semantic memory functioning for each performance characteristic. Mean Z-score values for the Episodic (CVLT) and Semantic (Category and Letter Fluency tests) memory performance characteristics are depicted in Figure 1.



Performance Characteristic

Figure 1: Performance Characteristics on Episodic and Semantic Memory Tasks

The 3-way interaction of the MANOVA was not significant, as seen on Table 4. Table 5 lists the related univariate F-tests for the three factors.

TABLE 4

SUMMARY OF MULTIVARIATE TEST STATISTICS

Source	Multivariate F	df	P
Performance Characteristics* [Perf (C] 0.000	3, 48	1.000
Diagnosis x Perf C	7.992	3, 48	<0.001
Task Type x Perf C	0.000	3, 48	1.000
Diagnosis x Task Type x Perf C	2.388	3, 48	0.080

*Performance Characteristics [Perf C] include a) Semantic clustering, b) Phonemic clustering, c) Perseveration errors, and d) Intrusion errors.

TABLE 5

Source	SS	df	MS	F	р
Between Subjects: Diagnosis Error	10.421 152.955	1 50	10.421 3.059	3.407	0.071
Within Subjects: Task Type	0.000	1	0.000	0.000	1.000
Diagnosis x Task Type Error	1.157 50.833	1 50	1.157 1.017	1.138	0.291
Perf C* Diagnosis x Perf C Error	0.000 11.167 92.035	3 3 150	0.000 3.722 0.614	0.000 6.067	1.000 0.001
Task Type x Perf C	0.000	3	0.000	0.000	1.000
Diagnosis x Task Type x Perf C Error	4.665 84.767	3 150	1.555 0.565	2.752	0.045

SUMMARY OF UNIVARIATE F-TESTS

*Performance Characteristics [Perf C] include a) Semantic clustering, b) Phonemic clustering, c) Perseveration errors, and d) Intrusion errors.

<u>Hypothesis 1</u>

With regard to the three hypotheses stated above, Hypothesis 1 predicted that Alzheimer's patients would exhibit more prominent executive dysfunction on the episodic memory task (CVLT) than on the semantic memory tasks

(Category Fluency and Letter Fluency). That is, the AD patients would exhibit greater differences from the normal controls (strictly in terms of executive control performance characteristics) while performing the CVLT than when performing the Fluency tasks; these differences would be evidenced as utilizing semantic clustering and phonemic clustering less frequently, and providing more perseveration and intrusion errors. While the data in Table 3 demonstrate the overall performance superiority of the normal controls over the AD subjects on the three memory tasks, Hypothesis 1 is restricted to executive controls alone, and to only the AD subjects; the AD subjects did not show a significant differential in their use of executive control relative to the type of memory task. That is, the results pertaining to executive function variables alone indicate no significant Diagnosis x Task Type interaction (Table 5). Consequently, Hypothesis 1 was not supported; AD subjects did not consistently perform significantly lower on the CVLT than on Fluency measures. However, a significant Diagnosis x Performance Characteristic interaction was noted and explored further. Mean Z-score values for the four performance characteristics (collapsed across task type) are depicted in Figure 2.

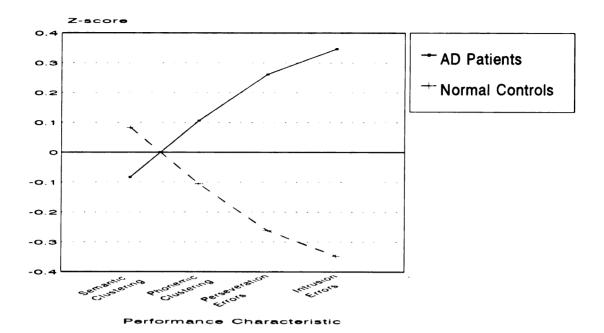


Figure 2: Performance Characteristics of Alzheimer's Patients and Normal Controls (Standard Scores)

To further elucidate the nature of the interaction, comparisons between AD patients and normal controls on the individual Performance Characteristics were conducted, revealing significant differences in AD vs. normal control performances in Perseveration error rates and Intrusion error rates across task types, as tabulated below (Table 6).

TABLE 6

SUMMARY OF T-TEST COMPARISONS OF AD PATIENT AND NORMAL CONTROL PERFORMANCE CHARACTERISTICS

	Т	df	р
Semantic Clustering	-0.706	50	0.484
Phonemic Clustering	1.019	50	0.313
Perseveration Errors	2.327	50	0.028
Intrusion Errors	3.515	50	0.001

In light of the fact that the AD and normal control groups differed significantly in years of education (11.54 years and 13.19 years, respectively), the MANOVA was repeated entering years of education as a covariate. The results revealed that the education variable did not significantly contribute to the Diagnosis x Performance Characteristic interaction: Multivariate F(3,47) = 0.088, p = 0.966.

<u>Hypothesis 2</u>

The first level of Hypothesis 2, which predicted that the AD participants in this study would show inferior performances on all tasks in comparison to normal controls, was supported as suggested by the means and standard deviations in Table 3. All AD vs. Normal comparisons were significant: CVLT t(50) = -8.96, p = <.001; Category Fluency t(50) = -7.49, p = <.001; Letter Fluency t(50) = -5.06, p = <.001.

To address the second level of Hypothesis 2 (predicting that the AD patient's performance discrepancy from normal levels would be greatest for the CVLT, and least for the Letter fluency task), additional analyses were conducted. Standard scores were computed for the AD patients on all three tasks (2-scores based on the performances of the normal controls). The resultant means and standard deviations for the three tasks are listed in Table 7.

TABLE 7

	Mean Standard Deviatio		on Range	
California Verbal Learning (Total Trials 1-5) Category Fluency Test	Test -2.20 -2.32	0.75 1.23	-3.560.66 -3.86 - 0.08	
Letter Fluency Test	-1.35	0.92	-2.73 - 0.77	

SUMMARY OF STANDARDIZED AD PATIENT PERFORMANCES (BASED ON NORMAL CONTROL LEVELS OF PERFORMANCE)

Comparisons of the scores in Table 7 revealed that while the AD patients' CVLT performances were not significantly more impaired than their Category Fluency performances (t[25] = 0.614, p = .545), their Category Fluency performances were significantly more impaired than their Letter Fluency performances (t[25] = -4.295, p =<.001). The CVLT performances were also significantly more impaired than the Letter Fluency performances (t[25] =-4.691, p = <.001). That is, Hypothesis 2 predicted the rank ordering of the tasks, progressing from yielding the greatest impairment to least impairment in AD patient performance, would be as follows:

- 1. List-learning task (California Verbal Learning Test)
- 2. Category Fluency task
- 3. Letter Fluency task

The actual results found the following order:

- 1. Category Fluency task
- 2. List-learning task (California Verbal Learning Test)
- 3. Letter Fluency task

Hypothesis 3

Hypothesis 3 predicted that the normal male participants would exhibit more executive dysfunction on the three tasks than the normal female participants. That is, the normal males would utilize semantic clustering and phonemic clustering less frequently and make more perseveration and intrusion errors than the normal females in the sample. Demographics for the normal controls are listed in Table 8. The normal male and female participants did not differ significantly in age (t[24] = 0.760, p =0.449) or levels of education (t[24] = 0.562, p = 0.579). The means and standard deviations for the male and female performances are provided in Table 9.

TABLE 8

	$\begin{array}{l} \text{MALES} \\ \text{N} = 10 \end{array}$	FEMALES $N = 26$	prob
	N = 10	N = 28	
Age (Mean±SD)	72.50 ± 5.97	70.54 ± 6.72	ns
Range	62 - 80	61 - 83	
Years of Education (Mean±SD)	13.6 ± 2.37	12.94 ± 3.21	ns
Range	9 - 20	8 - 16	

NORMAL SUBJECT CHARACTERISTICS

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TABLE 9

SUMMARY OF RAW SCORES OF NORMAL CONTROL SUBJECTS ON MEMORY TASKS

	MALES			FEMALES		
	Mean St	tandard Deviation	Mean	Standard Deviation		
California Verbal Lea	arning Te	est				
(Total Trials 1-5)	42.00	14.13	49.13	11.42		
Semantic Clustering	0.355	0.164	0.383	0.052		
Phonemic Clustering	0.047	0.038	0.052	0.028		
Perseveration Errors	0.071	0.062	0.128	0.084		
Intrusion Errors	0.065	0.139	0.072	0.087		
Category Fluency Test	9.23	5.00	18.69	4.07		
Semantic Clustering	0.585	0.124	0.530	0.128		
Phonemic Clustering	0.000	0.000	0.013	0.024		
Perseveration Errors	0.021	0.035	0.013	0.028		
Intrusion Errors	0.000	0.000	0.000	0.000		
Letter Fluency Test	22.39	11.51	39.31	12.56		
Semantic Clustering	0.089	0.058	0.081	0.073		
Phonemic Clustering	0.283	0.149	0.198	0.105		
Perseveration Errors	0.070	0.065	0.010	0.019		
Intrusion Errors	0.000	0.000	0.005	0.015		

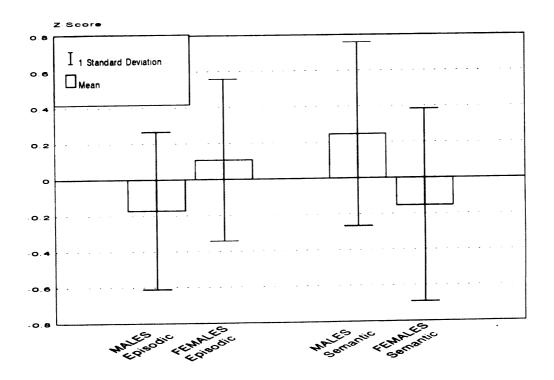


Figure 3: Mean Performance Characteristic Levels of Normal Controls on Episodic and Semantic Memory Tasks (Standard Scores)

Mean Z-score values for the four performance characteristics are depicted in Figure 3.

Examination of Table 8 reveals that the performance superiority of the normal female subjects over the normal males was inconsistent. Statistical analyses were conducted, and as data on only 10 male and 16 female normal control participants were obtained for the study, caution was warranted in interpreting the following results.

All performance data were transformed to Z-scores based on the normal control sample. A MANOVA was again performed with one between-subject factor (Sex) and two within-subject factors: a) task type (Episodic memory task [CVLT], and semantic memory tasks [Category Fluency and Letter Fluency]) and b) Performance Characteristics [Semantic clustering, Phonemic clustering, Perseveration errors, and Intrusion errors]. As in the previous MANOVA (investigating Hypothesis 1), the Category Fluency and Letter Fluency tests were averaged to provide overall scores of semantic memory functioning. Whereas this combining of the two semantic memory tasks was required by Hypothesis 1 in the previous analysis, it was necessary to combine the scores in the current analysis due to the lack of variation on the Category Fluency Intrusion Errors variable (no normal control subjects of either sex made an intrusion error during the Category Fluency test). The MANOVA results indicated the 3-way interaction was not significant, as seen on Table 10. Table 12 lists the related univariate F-tests

TABLE 10

SUMMARY OF MULTIVARIATE TEST STATISTICS COMPARING NORMAL MALE AND NORMAL FEMALE PERFORMANCE

Source	Multivariate F	df	р
Performance Characteristics* [Perf C Sex x Perf C) 0.025 0.464	3, 22 3, 22	0.995 0.711
Task Type x Perf C	0.133	3, 22	0.939
Sex x Task Type x Perf C	2.495	3, 22	0.086

*Performance Characteristics [Perf C] include a) Semantic clustering, b) Phonemic clustering, c) Perseveration errors, and d) Intrusion errors.

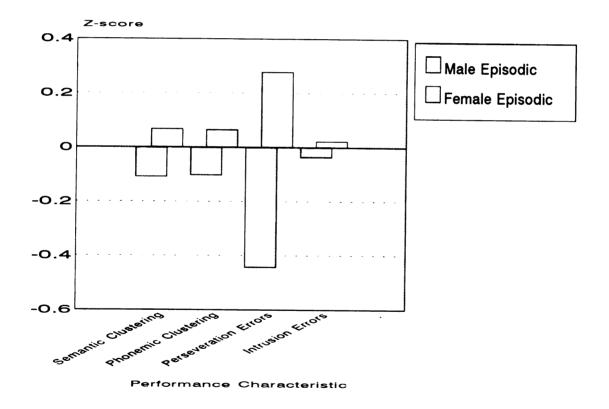
TABLE 11

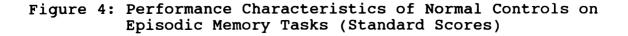
SUMMARY OF UNIVARIATE F-TESTS COMPARING NORMAL MALE AND NORMAL FEMALE PERFORMANCE

Source	SS	df	MS	F	P
Between Subjects Sex Error	0.178 28.444	1 24	0.178 1.185	0.150	0.702
Within Subjects Task Type	0.303	1	0.303	0.418	0.524
Sex x Task Type Error	5.694 17.410	1 24	5.694 0.725	7.850	0.010
Perf C *	0.079	3	0.026	0.026	0.994
Sex x Perf C Error	1.490 72.689	3 72	0. 4 97 1.010	0.492	0.689
Task Type x Perf C	0.375	3	0.125	0.134	0.939
Sex x Task Type x Perf C Error	7.040 67.055	3 72	2.347 0.931	2.520	0.065

*Performance Characteristics [Perf C] include a) Semantic clustering, b) Phonemic clustering, c) Perseveration errors, and d) Intrusion errors.

A significant main effect for Sex was not found, nor was a Sex x Performance Characteristic interaction (Table 11). Hypothesis 3 was not supported as males did not yield 11). Hypothesis 3 was not supported as males did not yield significantly different Performances Characteristics than the females. However, a significant Sex x Task Type interaction was evident (Table 11). Mean Z-score performance characteristics values for the Episodic (CVLT) and Semantic (Category and Letter Fluency tests) tasks of the male and female normal control subjects are depicted in Figure 4 and Figure 5.





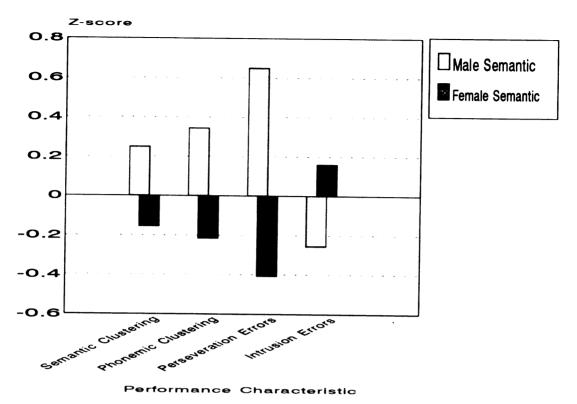


Figure 5: Performance Characteristics of Normal Controls on Semantic Memory Tasks (Standard Scores)

Examination of the raw data (Table 9) and of the Z-scores (Figures 4 and 5) suggests males made more errors on the semantic memory tasks (Fluency Tests) than the females. In fact, 9 of the 10 normal control males made at least one perseveration error, while 5 of the 16 females made such errors. Conversely, only two control subjects (both women) made intrusion errors (both on the Letter Fluency test). However, post hoc comparisons of the individual Task Types were conducted, revealing no clear significant differences between normal male and female participant performances on either their episodic (F[1, 24]= 2.428, p = 0.132) or semantic task performances (F[1, 24] = 2.428, p = 0.132) or semantic task performances (F[1, 24] = 3.533, p = .072). Although Hypothesis 3 was not fully supported, a trend for males to make more perseverative errors on the semantic memory tasks was noted, particularly the Letter Fluency Test. DISCUSSION

The significant results of the analyses are summarized in Table 12.

TABLE 12

SUMMARY OF SIGNIFICANT FINDINGS

Hypothesis 1 Analyses: Diagnosis x Performance Characteristic Interaction - AD more Intrusions than controls - AD more Perseverations than controls Hypothesis 2 Analysis: Rank Order of AD Patients' Test Performances Greatest Impairment Category Fluency > Not Significant CVLT > Significant Letter Fluency Least Impairment Hypothesis 3 Analysis: Sex x Task Type Interaction - Males more errors on Fluency Tasks than females

The Hypothesis 1 analysis was intended to determine if executive control in the AD sample was more compromised during either the episodic or semantic memory tasks. The findings suggest no Diagnosis x Task interaction; although the AD patients did not perform as well as the normal controls on any of the memory tasks and they exhibited inferior executive control abilities, the AD subjects did not demonstrate a differential failure of executive controls (relative to the normal controls) on the episodic or

semantic tasks. Consistent with the findings of Becker (1988), the more general failure of executive control -across task types-- was found in the AD performances. Specifically, the AD patients made significantly more Intrusion and Perseveration errors than the normal control subjects across tasks.

Overall, the Hypothesis 1 analyses (i.e., no significant differences between execution function mediation in episodic and semantic systems) are consistent with Logan's and Cowan's (1984) suggestion that executive functions work with similar efficiency irrespective of task type. That is, the data presented here suggest that the executive control failure seen in AD is not system-specific, but that the executive functions, though compromised in AD, retain relative independence from the episodic and semantic memory systems. This independence is in further agreement with neuropsychological theories of attention developed by Pribram and McGuiness (1975), McGuinness and Pribram (1980), Tucker and Williamson (1984), and G. Goldberg (1987), which hold the executive controls as separate from, if not superordinate over, the other cognitive processes they mediate, such as memory.

Hypothesis 2 predicted the episodic memory task (CVLT) would reveal the greatest impairment for the AD sample. This was not supported. Category Fluency, one of the semantic memory tasks, revealed the greatest impairment in

the AD sample. This performance gradient is likely not due to executive control deficits, as Hypothesis 1 analyses indicated no significant differences in the use of executive control between episodic and semantic memory systems. Alternatively, the significant impairment on the Category Fluency task revealed in the Hypothesis 2 results may be more reflective of a deterioration in the underlying knowledge system in AD patients.

Although the Category and Letter Fluency tasks were grouped together in the analyses to form an index of semantic memory, hindsight suggests the two tasks may differ substantively. There is some evidence suggesting that the Category and Letter Fluency tasks both enlist frontal and temporal territories in the brain (Frith et al., 1991); however, evidence from brain-lesioned patients suggests a relatively greater reliance on left frontal regions during the Letter fluency task than the Category Fluency task (Benton, 1968; Milner, 1967; Perret, 1974). In addition, naming deficits for words within specific categories have been reported from temporal lobe damage (Hart, Berndt, & Caramazza, 1985; McKenna & Warrington, 1980).

Irrespective of mediating brain structures, the Category and Letter Fluency tasks share the requirements of initiation and maintenance of search and retrieval processes. The tasks differ behaviorally in the type of strategy used during the search and retrieval processes; reports suggest Letter Fluency is guided by phonemic and/or

lexical cues, while production in Category Fluency tasks is more dependent on the integrity of the underlying structure of semantic knowledge systems (Bayles, Salmon, Tomoeda, Jacobs, Kaszniak, & Troster, 1989)

It has recently been suggested that the structure of semantic knowledge --the 'semantic network'-- is maximally affected in the cognitive degeneration of AD (e.g., Ober & Shenaut, 1988; Schwartz, Marin, Saffran, 1979; Smith, Murdoch, & Chenery, 1989). The 'semantic network' refers to the knowledge base of an individual and is assumed to be organized hierarchically (Warrington, 1975). General concepts and attributes of information occupy superordinate positions, while more specific attributes and exemplars are positioned subordinately (see Figure 6). It has been proposed that access to a specific category member begins with accessing a superordinate category in the hierarchical network, with progressive activation downward, resulting in increasingly specific semantic representation (Smith et al., 1989), although at least one case study has been reported revealing exceptions to this general-to-specific rule (Rapp & Caramazza, 1989) .

One way in which the degradation of the semantic network in AD patients has been observed is in their decreased 'depth' of search; that is, when engaged in memory search for meaningful words (e.g., during a Letter Fluency task) normal subjects tend to produce specific exemplars of categories (Rosch, Mervis, Gray, Johnson, & Boyes-Bream,

1976), while AD patients have been found to provide more general classes of exemplars (Martin & Fedio, 1983). For example, whereas a normal control subject when asked to list words beginning with the letter 'F' may produce the words "flapjacks", "Fritos", and "frankfurters", AD patients tend to produce less specific exemplars such as "food." Such a pattern of semantic network degradation is described as 'bottom up' decay, as the lower end of the network (the most specific exemplar of a category) apparently becomes hardest to access first in AD.

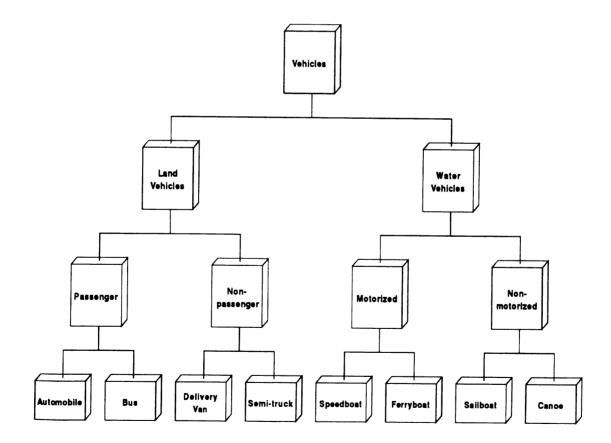


Figure 6: Sample Semantic Network "Vehicles" The rank ordering of the tasks on which the AD patients

differed from the controls in the Hypothesis 2 analyses (see Table 12) is consistent with the AD semantic network degradation hypothesis in that the Category Fluency test yielded the greatest impairment in overall word production relative to normal controls (Table 3). Moreover, the Letter Fluency task data suggest that in the AD group the use of phonemic cues remained relatively intact; for AD subjects Letter Fluency was least impaired of the three tasks administered, and in addition, the AD group's use of phonemic clustering on any of the three tasks was not significantly different from normal controls. The fact that the Category Fluency task in the present study yielded the greatest AD decrements of semantic and episodic memory measures is also consistent with a recent report by Monsch, Bondi, Butters, Paulsen, Salmon, Brugger and Swenson (1994) which yielded similar results.

The analysis of Hypothesis 3 did not provide statistical support for the prediction that normal elderly males would exhibit greater decline in executive controls (i.e., less clustering and more errors) than the normal elderly females. Male control subjects did produce more perseveration errors than female control subjects, although this difference was not statistically significant.

General equality of cognitive performance of male and female control subjects has been reported by Kaufman and colleagues, who found that while "fluid intelligence" (as

defined by Horn, 1978) declines as a function of age in late adulthood, males and females do not differ in their rates of decline (Kaufman, Kaufman-Packer, McLean, & Reynolds, 1991). Decline in fluid intelligence is presumably related to errors of perseveration in that perseveration demonstrates difficulty making appropriate transitions in mental set. Perseveration has been found to increase in later life; Ruff and colleagues reported significant increases in perseveration with age on a figural fluency test analogous to the verbal fluency tasks used in the present study (Ruff, Light & Evans, 1987). Similar findings were presented by Daigneault, Bruan, and Whitiaker (1992) who found significant increases in perseverative errors across a variety of neuropsychological tasks in 58 adults aged 45-65 years when compared to 70 adults aged 25-35 years. Those authors interpreted the results as suggesting significant, measurable deterioration in brain function in the prefrontal regions may occur in healthy normal persons prior to age 65.

Perseverative errors are routinely measured by the Wisconsin Card Sorting Test (Heaton, 1981). This task requires the subject to sort cards consistently to one of three conceptual categories (color, form, or number); once the subject demonstrates consistent set maintenance, the conceptual categorizing rule of the task is shifted (e.g., from color of design to number of design on the card), to which the subject must adapt through corrective feedback from the examiner. Perseveration errors occur when the

subject is unable to switch conceptual sets to meet the new categorizing rule.

The Wisconsin Card Sorting Test has repeatedly been found sensitive to frontal lobe function (Bornstein, 1986; Drewe, 1974; Hermann, Wyler, & Richey, 1988; Milner, 1963). However, Heaton (1981) found no sex differences on rates of perseverative errors for a sample of 150 adults aged below 65 years. When an older sample was studied (35 males and 56 females, aged 45-83 years), significant sex differences emerged for the Wisconsin Card Sorting Test, with males committing significantly more perseveration errors on the task than females, as well as scoring lower on four other standard indices from the same test believed reflective of frontal lobe efficiency: Number of Categories Achieved, Total Errors, Percent Conceptual Level Responses, and Number of Trials to First Category (Boone, Ghaffarian, Lesser, Hill-Gutierrez, & Berman, 1993).

Veroff (1980) also reported a significant positive correlation in a healthy normal aged sample between age and findings on neuropsychological tests suggestive of frontal lobe dysfunction. In that study men exhibited more signs of frontal dysfunction than women. Recent neuro-imaging studies have revealed cerebral blood flow changes in both sexes with advanced age, and that decreases in blood flow to the frontal regions is more pronounced in older men than women (Mathew, Wilson & Tant, 1986).

The normal control sample in the current study did not

е р е W f h 0 S S n W a T S Ve Fl C dj Wa tł f] fu hi Va af exhibit significant sex differences in executive function performances. The males did exhibit the more perseverative errors than females on the Fluency tasks, but the finding was not statistically significant. Perhaps this tendency for the normal males to commit more perseverative errors may have been more robust with a larger sample size, or a sample of more advanced age. Nevertheless, while it is tempting to speculate about frontal lobe dysfunction in the males of the sample, the remaining performance characteristic data did not show tendencies toward sex differences, and, consistent with Kaufman et al. (1991), provided no evidence of sex associated executive dyscontrol or frontal lobe dysfunction. The results do reveal, however, the importance of sex-specific normative data for clinical applications of the Verbal Fluency tasks.

Future Directions

The general findings of the three analyses are consistent with much of the existing literature: no differential use of executive controls across tasks types was evidenced in the AD patients; the AD patients showed their greatest memory performance decrements on semantic fluency tasks; normal control males exhibited more executive function errors than females on fluency tasks. However, hindsight suggests that the study could be modified in various ways to minimize potential confounds that may have affected the data. As in most experimental designs, two

general areas of potential confound could be addressed in future efforts to replicate the current study: a) difficulties in experimental samples or measures, and b) shortcomings in the related constructs.

Experimental Sample:

The primary concern with the experimental sampling in the current study is that the relatively small sample sizes (26 AD, 26 normal) may have led to Type II statistical errors. Larger cell sizes may have also benefitted this study by increasing the occurrence of intrusion errors, allowing more meaningful analysis of this behavior in both sample populations. The mean number of intrusion errors during either Fluency task was less than one error for both the AD patients and normal controls (with no normal control subjects making intrusion errors during Category Fluency). Such small numbers raise the potential for floor effects in the analyses.

It should be noted, however, that while more subjects is generally better than less, the logistics of clinical studies often make amassing a greater N size prohibitive to the completion of the work. On this point Kraemer (1981) has suggested that any experimental sample size be determined by the four principle factors of a) acceptability in the field of research, b) feasibility, c) power, and d) cost. In addition, she states that for most designs in the field of clinical psychiatry a sample size of 20 subjects

p f С d e r р i е E g 0 C g(Ug re Cų per cell frequently strikes the proper balance between these four factors (Kraemer, 1981).

Others aspects of amassing the sample could be improved. Specifically, the normal control subjects had significantly more years of education than the AD patients (13.19 and 11.54 years, respectively). Higher levels of education have been associated with greater efficiency in some executive control functions; e.g., the use of contextual cues for guiding memorization (Craik, Byrd, & Swanson, 1987). However, the influence this education disparity had on the present data appears insubstantial; the data pertaining to Hypothesis 1 was re-analyzed with education as a covariate and did not produce different results than without the covariate. Nevertheless, the possibility exists that the disparity in education has influenced the data in an unforeseen manner, and an education-matched sample is always more desirable.

Experimental Measures:

In addition to improving sampling procedures, it appears possible to refine the devices used to more optimally measure executive control in the samples. The CVLT, Category Fluency, and Letter Fluency tasks had the advantage of clinical relevance as these devices are widely used in patient evaluations of dementia. However, in retrospect, one of the experimental computer measures currently under development to measure executive controls

may be more suited to our analyses due to their greater precision, such as those presented by Bilder, Turkel, Lipschutz-Brock, and Lieberman (1993). These tasks have the advantage of collecting reaction time data, providing more subtle measures of executive processing. In addition, the tasks are designed to separate executive control processes from other mental operations, such as memory, when desired.

Revisions in Constructs:

A remaining possibility exists that the episodic-semantic dichotomy itself does not optimally describe human memory systems. In their 1994 chapter on this topic, neuropsychologists E. Goldberg and Barr questioned the sufficiency of the dichotomy based on cases of medial temporal lobe and diencephalic amnesia. Rather than conceiving knowledge as divided into procedural and declarative systems (with the declarative system further divided into semantic and episodic memory, as discussed above), E. Goldberg and Barr proposed a modified taxonomy dividing knowledge into Generic and Singular types. In this scheme, "Singular" knowledge describes knowledge of specific facts that pertains to single, unique entities (E. Goldberg & Barr, 1994). Singular knowledge can be void of temporal significance or association, e.g., "Rome is the capital of Italy", or can maintain an intrinsic temporal quality, such as knowledge for personal events or information: e.g., "I met my spouse in Rome in 1950." Singular knowledge also

includes finite sets of information intentionally encoded for later retrieval (i.e., episodic memory) such as shopping lists and specific scenes from one's experience. The processes used during the CVLT task correspond to the Singular-episodic system.

"Generic" knowledge, on the other hand, is void of intrinsic temporal quality, and pertains to entire classes of entities: e.g., "Mature frogs usually have four legs", "Both apples and bananas have peels." Linguistic (definitions, uses of words, grammatical rules, etc.) information is also within the Generic knowledge system. The Fluency tasks in the present study correspond to the Generic-semantic system. E. Goldberg and Barr make the additional point that Generic knowledge is not limited to lexical information, as it includes knowledge for proper procedures (e.g., sequence for cleaning a pipe), as well as peripheral aspects of meanings (e.g., "Camels do not have antlers"). E. Goldberg and Barr (1994) relate the original semantic-declarative taxonomy to their own by proposing, "Singular knowledge, by definition, includes all episodic and singular semantic knowledge. Generic knowledge includes all procedural and generic semantic knowledge" (p. 73). They use evidence from the amnesia syndromes to suggest impairment of Singular knowledge or impairment of Generic knowledge reflect two phenomenally and neuroanatomically dissociable conditions.

Applied to the Goldberg/Barr model, the current study

compares a portion of the Generic knowledge system, with a portion of the Singular knowledge system. As such, our findings suggest no clear disparity in use of executive controls in the two systems, but a more informative design would encompass all four components of the model, including the Singular-semantic and procedural aspects of knowledge. Future investigations may determine the utility of the Goldberg/Barr model in understanding degradation of memory systems in AD.

In summary, the current investigation suggests that patient's with Alzheimer's dementia exhibit significant executive function deficits in the form of intrusion and perseveration errors compared to normal controls, and that this decline in executive control is not specific to a single memory system (semantic or episodic). In addition, similar to recent findings pertaining to semantic network degradation in AD, the patients in this sample demonstrated the greatest memory deficits on a Category Fluency Test, a task believed to maximally tax the semantic network. Finally, analysis of the normal control sample performances did not provide statistical support for the prediction that elderly males would exhibit greater decline in executive controls, but the data instead demonstrated an equality of performance levels between the sexes.

It is a common hope among neuropsychology researchers to learn something new about the human brain through the

study of clinical conditions such as Alzheimer's disease. It is generally believed that executive controls operate in superordinate positions relative to other cognitive processes. Because the study presented here did not uncover a dimension of system-specificity in executive functions, it may provide further suggestion that the field is proceeding on the proper course.

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