The Relationship Between Daily Stress and Neuropsychological Test Performance.

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THE RELATIONSHIP BETWEEN DAILY STRESS AND NEUROPSYCHOLOGICAL TEST PERFORMANCE

A Dissertation

Submitted to the Graduate Faculty of the Louisiana State University and Agricultural and Mechanical College in partial fulfillment of the requirements for the degree of Doctor of Philosophy

in

The Department of Psychology

by

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ABSTRACT

Much research has focused on identifying the causes and risk factors associated with Alzheimer's disease (AD). Surprisingly, stress, which has been implicated in the course of a variety of other diseases, has been generally ignored in research on AD despite the fact that several different areas lend indirect support for a relationship between stress and the progression of AD. In this study, the effect of daily stress on the clinical course of AD was examined. Also, given that no study has examined the effects of daily stress on neuropsychological test performance, this relationship was examined as well.

Forty-five out-patients with AD and 45 normal elderly controls participated in the study. All subjects were administered a battery of neuropsychological tests assessing general intelligence, attention, academic skills, language, memory, graphomotor skills, personality, and daily stress. Results suggested that daily stress was inversely related to WRAT-R arithmetic performance of the normal elderly controls, and was inversely related to immediate visual reproduction scores and attention scores of both groups. Within the AD group, subjects responded with greater distress to their daily stress events, but they did not report any difference in the frequency of stressful events in their lives.
The results indicated that AD patients relative to controls reported significantly greater distress to stressful events. The results also suggested that daily stress should be considered when interpreting certain neuropsychological tests of memory and attention given to elderly individuals. Moreover, results suggested that daily stress needs to be accounted for when examining the data obtained from memory and attention tests.
INTRODUCTION

Dementia is a process involving deterioration in intellectual performance, problem solving, abstract thinking, and memory (Davies, 1988). A short list of known causes of dementia might include Down's syndrome, Multi-infarct dementia (MID), metabolic deficiency (i.e., vitamin B₁₂), hypothyroidism, neurosyphilis, Huntington's disease, Parkinson's disease, cerebral tumors and subdural hematomas (Haase, 1977). However, the most common cause of dementia is Alzheimer's Disease (AD; McKhann et al., 1984; Katzman, 1986; Becker, 1990; Kolb & Whishaw, 1990; Fratiglioni, et al. 1991), which will be the main focus of this study.

By the 1800's, it was commonly held that the brain underwent age related changes (Kolb & Whishaw, 1990). The first formal report of these changes was published in 1907 by a German physician named Alois Alzheimer (Katzman, 1986, 1987). The case report involved the autopsy findings of a woman who died at the age of 55 of presenile dementia. With the use of newly available silver stains, Alzheimer was able to identify abnormal brain structures in the cerebral cortex including tangles of nerve fibers and clusters of degenerating nerve endings. These pathological findings combined with the behavioral manifestations of progressive dementia became known as
Alzheimer's Disease. In the 1960's researchers recognized that the symptoms and pathology of both presenile and senile patients were alike (Terry, Gonatas, & Weiss, 1964), so the disease is now viewed to be a single entity affecting all ages (Katzman, 1986).

Alzheimer's Disease is currently considered a major health care problem (Becker, 1990; Lipkowitz, 1988). More hospitalizations in the United States involve neurological and mental disorders than any other major disease group, including heart disease and cancer (NFBR, 1990). Compounding the problem, the most rapidly growing segment in our population is the over 85 age group, which currently represents 9% of the population, and is currently estimated to grow to 19% of the population in 50 years (Von Dras & Blumenthal, 1992). This increasing percentage of elderly individuals, with concomitant increased prevalence of age-related diseases like AD may have contributed to President Bush's signing of a declaration passed by Congress to establish the 1990's as the Decade of the Brain (NFBR, 1990). Following this action, the National Institute of Neurological Disorders and Stroke published an implementation plan for the decade of the brain designating as much as 20 million dollars per year to support grants for studies examining AD (NINDS, 1990).
These programs have led to an enormous increase in research on AD. Although many different aspects of the disease have been examined, a great deal of the AD research has focused on identifying its specific etiology. Various etiological theories have been proposed for AD. Additionally, a variety of risk factors, such as age of onset, family history, smoking, duration of illness, etc., have been studied in an attempt to determine the variables which influence the onset and progression of AD. Although stress has been implicated as a risk factor in numerous diseases including coronary heart disease, cancer, infectious disease, diabetes mellitus, arthritis, and others, at the present time no studies have attempted to look at the effects of stress on the onset or course of AD. The present study attempted to determine if daily stress affected the test performance of AD subjects differently during the clinical course of AD.

Before the relationship between stress and AD can be investigated, one must first examine the effects of daily stress on neuropsychological tests in non-impaired individuals. Considerable research has examined the effects of imposed stress (e.g., heat, physical work, carbon monoxide exposure, etc.) on neuropsychological test performance, but no study has addressed the effects of ecologically relevant daily "hassles" on
neuropsychological test performance. In the present study, the influence of daily stress on neuropsychological test performance among nonclinical samples was also examined. Jointly, the main goal of this research was to examine the effects of daily stress on the neuropsychological test performance of normal and neurologically impaired (i.e., AD) elderly subjects.

The following sections will present brief reviews of the literature relevant to this study: 1) description of AD, 2) proposed etiology of AD, 3) risk factors for AD, 4) stress and AD, and 5) stress and neuropsychological test performance.
REVIEW OF LITERATURE

Description of the Disease

Alzheimer's disease is a form of dementia essentially characterized by pronounced cognitive and intellectual deterioration relative to the patient's previous level of functioning (Katzman, 1986, 1987; McKhann et al., 1984). The deficits in cognitive functioning must be severe enough to interfere with occupational or social performance (Katzman, 1986, 1987). Memory difficulties, especially for recent events, are the hallmark complaint in AD (APA, 1987). Cognitive deficits may also include language problems, perceptual difficulties, poor learning, and decreased abstract reasoning. In order to provide a fuller description of AD, the physical and psychological manifestations of AD will be delineated, followed by brief accounts of the prevalence and diagnosis of the disease.

Pathophysiological Changes

There are three pathophysiological changes which typify AD: neurofibrillary tangles, neuritic plaques, and amyloid bodies in and around cerebral blood vessels (Katzman & Jackson, 1991; Kolb & Whishaw, 1990).

Neurofibrillary tangles, also known as paired helical filaments (PHFs) because of their double helical configuration (Von Dras & Blumenthal, 1992), contain tau
proteins thought to be derived from abnormal phosphorylation (Joachim, Morris, Selkoe, & Kosik, 1987).

AD is also characterized by neuritic plaques, also known as senile plaques, which consist of a central core of protein material called amyloid, surrounded by degenerated axonal and dendritic processes. Glenner and Wong (1984) identified the precursor protein which they named, appropriately enough, amyloid precursor protein (APP). Subsequently, it has been demonstrated that the gene that codes for APP is located on chromosome 21 (Goldgaber, Lerman, McBride, Saffiotti, & Gajdusec, 1987); however, unequivocal confirmation of this specific gene locus has yet to be provided (Von Dras & Blumenthal, 1992).

Similar to the senile plaques, the third typical change seen in AD are the amyloid collections in and around cerebral blood vessels (Von Dras & Blumenthal, 1992; Katzman, 1986). It appears that these protein collections are composed of the same protein observed in senile plaques (Von Dras & Blumenthal, 1992).

Other Characteristics

In addition to the pathophysiological changes, psychological manifestations of AD have been noted. It is commonly held that patients with AD tend to lose insight into their deteriorating condition (Katzman, 1986, 1987;
Weiner, 1991). Alzheimer patients also appear to experience periods of depression which can occur throughout the course of AD (Shuttleworth, Huber, & Paulson, 1986). Wragg and Jeste (1989) suggest that 40-50% of AD patients suffer from depressed mood, with a diagnosis of major depression in 10-20% of the patients. Whether depression is a symptom of AD or occurs as a psychological reaction to receiving the diagnosis of AD is difficult to determine (Cummings & Benson, 1992).

In addition, other psychiatric manifestations are sometimes noted as well (Katzman, 1986, 1987; Weiner, 1991; Davies, 1988). Patients may be socially avoidant and fearful. Paranoid symptoms and delusions can also be seen. Other patients may appear more irritable, agitated, and physically aggressive. In the final stages of the disease, the patients are often so impaired that they can no longer manage without assistance (Aronson, 1988), requiring help with eating, dressing, grooming, and toileting. The individual may become incontinent, and often will wander and fall down, necessitating environmental changes to make it safer (Jarvik & Trader, 1988; Chafetz, 1991).

Throughout the course of this disorder, major life changes are noted. The afflicted individual is likely to experience many of the problems described above (e.g.,
cognitive deterioration, personality changes, psychiatric complications, etc.), which leads to changes in the way they perceive themselves and are perceived by others (Aronson, 1988). As problems worsen, patients and caregivers are forced to make changes in the patient's everyday routine, and these alterations in life style may be an additional source of stress, supporting the need for an examination of the effects of stress on the course of AD.

**Prevalence**

Bachman and colleagues (Bachman et al., 1992) reported probable AD constituted 56% of all dementia cases with 11.7/1000 males and 30.1/1000 females manifesting the disorder. They noted that rates tended to increase with advancing age, with 0.5% of individuals between 65 and 74, 4.1% of those between 75 and 84, and 13.1% of those over 84 diagnosed as probable AD. While the sex difference is not always observed (Becker, 1990), several other research groups have reported similar overall prevalence rates and age differences for AD (Fratiglioni et al., 1991; Becker, 1990).

Some researchers have reported even higher rates of AD in people over 60. The East Boston Study (Evans et al., 1989) as well as Rocca and his colleagues (Rocca et al., 1990) reported that 6% of people over 60 and almost
half of all people over 80 suffer from AD. The differences in prevalence are attributable to methodological differences in that Bachman and his colleagues included only those individuals with moderate to severe AD. Less severe (and therefore less certain) cases were included in the East Boston Study. Nonetheless, it appears that AD is quite prevalent in the population.

**Diagnosis**

A confirmed diagnosis of AD requires histopathological evidence obtained from biopsy or autopsy (McKhann et al., 1984). However, the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) and the Alzheimer's Disease and Related Disorders Association (ADRDA) formed a work group to establish premortality clinical criteria for the diagnosis of AD (McKhann et al., 1984). Appendix A shows the criteria that were put forth by this group.

The essential features of AD include impairment in short- and long-term memory, abstract reasoning, judgment, and other higher cortical functions. Personality change may also be noted. The disturbance must significantly interfere with work or usual social activities. Also, other causes of dementia must be excluded by history, physical exam, and laboratory tests before AD is
diagnosed. Katzman (1986) recommended that several tests should be conducted in order to rule out other causes of dementia and improve diagnostic accuracy, including a CT scan, chest film, comprehensive biochemical screening, determination of the vitamin B₁₂ level, thyroid-function tests, serologic test for syphilis, cerebrospinal fluid (CSF) exam, and electroencephalogram. The NINCDS-ADRDA criteria provide a reliable premortality diagnostic tool, with correct classification confirmed at autopsy in over 90% of the cases (Katzman, 1986; Katzman & Jackson, 1991) up to 100% in some studies (Martin et al., 1987; Morris, McKeel, Falling, Torach, & Berg, 1988).

**Etiology of AD**

While the specific etiology of AD remains unknown (Nalbantoglu, Lacoste-Royal, & Gauvreau, 1990), several theoretical possibilities have been suggested and will be addressed briefly.

**Genetic Basis**

The basic premise of this theory is that the disease is inherited as part of one's genetic endowment. The genetic theory is strengthened by the finding that nearly all people with Down's syndrome, a known genetic disorder, develop the neuropathological lesions of AD (Brugge et al., 1994). It has been estimated that only 30% of individuals with Down's syndrome manifest clinically
significant dementia as inferred by progressive deterioration of functioning (Wisniewski, Wisniewski, & Wen, 1985). However, individuals with Down's syndrome have (1) lower levels of premorbid functioning against which to measure cognitive changes, and (2) a shorter life expectancy relative to normal individuals due to cardiovascular and other medical problems and may not live long enough to display the progressive deterioration characteristic of Alzheimer's Disease. Also, by age 40, nearly all individuals with Down's syndrome will have the typical AD neuropathology with most experiencing cognitive deficits similar to AD (Brugge et al., 1994).

In addition, epidemiological studies have shown that first-degree relatives of AD patients have an increased risk of developing the disease themselves (Nalbantoglu et al., 1990). Reports on the magnitude of this risk range from 15% (Heyman et al., 1984) to 50% (Breitner & Folstein, 1984; Chase, Folstein, Breitner, Beaty, & Self, 1983). Chase et al. (1983) stated that the discrepancy stemmed from limits on the length of the risk period, which extends into the ninth decade according to Chase. Also, in some studies, rates may be lower because of premature mortality in relatives from unrelated causes.

The results of twin studies also provide some support for a genetic theory. Rapoport, Pettigrew, and Schapiro
(1991) found 50% concordance rate among 28 MZ twin pairs. However, Nee et al. (1987) found similar concordance rates between dizygotic and MZ twin pairs (both about 42%). Thus, the lack of 100% concordance in MZ twins and the similar concordance rates for MZ and DZ twin pairs weakens the argument that AD is entirely a genetic disorder.

Most recently, researchers have provided evidence from genetic studies to suggest that the Apolipoprotein E4 (APOE E4) allele is an important risk factor for AD (Katzman, 1994). The role of APOE E4 was first suggested when researchers demonstrated a genetic linkage site in affected members of families with apparent autosomal dominant inheritance and onset after the age of 60 (Pericak-Vance, Bebout, & Gaskell, 1991). This site was located on chromosome 19 at locus 19q13.2, close to genes for APOC11 and APOE. Subsequent research has demonstrated that the APOE gene, and more specifically the APOE E4 allele, appears to be the responsible gene for a large number of individuals who develop AD (Brousseau et al., 1994; Rebeck et al., 1994; Peacock & Fink, 1994). Overall, current estimates suggest that between 25 and 40 percent of the cases with AD can be attributed to APOE E4 (Katzman, 1994; Brousseau et al., 1994).
Transmissible Agents

The theory that transmissible agents could cause AD was developed in response to the similarity between AD and Creutzfeldt-Jakob disease (CJD). CJD is an infectious disease that results in progressive dementia, impaired movement and posture, and death. It was originally thought that CJD was transmitted by virus (Roos, 1981). Because of the similarity between CJD and AD, it was proposed that AD might have a similar etiology.

Since the original speculations of a relationship between AD and CJD, it has been suggested that the agent for CJD may be not be a virus. Rather, it may be a protein particle called a prion (Prusiner, 1984). Moreover, Prusiner has suggested that the amyloid bodies observed in AD may be collections of prions. However, Glenner and Wong (1984) identified differences in the amino acid structure of the amyloid bodies in AD and CJD. Overall, Glenner (1989) states that until the relationship between the development of AD and a specific causal agent can be elucidated, such theorizing is strictly conjectural. If and when an agent is identified, this still will not rule out genetic influences. In other disorders, incubation time and range of infectivity can be dictated by the genetic makeup of the host organism (Nalbantoglu et al., 1990). Therefore, if an infectious
agent is implicated in the development of AD, the genetic makeup of the "infected" individual will still be a likely component in determining susceptibility to the agent.

Environmental Toxins

Perl and Brody (1980) presented data showing accumulation of aluminum in the neurofibrillary tangles and aluminum silicate in the amyloid plaques of AD patients. It could be the case that high amounts of aluminum had been ingested presumably by using aluminum utensils and containers, deodorants containing aluminum, and a variety of other mechanisms. However, Glenner (1989) points out that there is not a higher incidence of AD in workers for aluminum factories. Glenner suggests that the correlation is purely a secondary phenomenon rather than a primary causative factor. It is now generally accepted that aluminum is not a viable factor in the development of AD (Katzman, 1986, 1987; Glenner, 1989; Nalbantoglu et al., 1990).

Cerebral Blood Flow

Several investigators have suggested that decreased cerebral blood flow accounts for the development of AD (Foster et al., 1984). These authors have demonstrated that the pathophysiological changes of the cerebral cortex are mirrored by changes in relative metabolic rates of glucose as measured by the PET scan. More specifically,
several researchers have reported that the temporal and parietal lobes show particular decreases (Foster et al., 1984). Others have also implicated the frontal lobe as well (Farkas et al., 1982). Additionally, Parks et al. (1990) have suggested that it is possible to use PET to differentiate between normals and people with AD.

The cerebral blood flow hypothesis is rather incomplete in accounting for the development of AD. It is not known, and it would be difficult to determine, whether the changes in glucose metabolism and cerebral blood flow are secondary to pathophysiological changes or whether decreased cerebral blood flow causes them. Until this relationship is specified, the cerebral blood flow theory will remain unsubstantiated as a causal hypothesis (Katzman, 1986, 1987).

Abnormal Proteins

The major changes in AD involve the accumulation of abnormal fibrous proteins leading several researchers to suggest that people with AD suffer from cerebral amyloidosis (Glenner, 1989). Such a suggestion seems logical given the changes consistently observed in individuals with AD. Researchers have proposed that the affected neurons produce the abnormal protein and then release it into synaptic clefts. However, there are substantial differences between amyloid protein and
proteins in the paired helical filaments, and even if a common peptide unit exists, the factor associated with the change from one protein form to the other has yet to be identified (Katzman, 1986). Also, the production of abnormal proteins may simply be secondary to some other unidentified factor (e.g., genetic disorder; Glenner, 1989).

**Acetylcholine Theory**

AD patients typically have less acetylcholine (ACh), a neurotransmitter associated with memory functioning (Katzman, 1986, 1987). A variety of possibilities could account for lower ACh activity including: (1) an excess of the enzyme that degrades ACh (i.e., acetylcholinesterase; AChE); (2) a deficit in the number of cells that produce ACh; (3) metabolic errors in ACh synthesis or degradation; (4) precursor deficits; or (5) re-uptake problems. However, there are numerous problems with this theory including: (1) treatment with lecithin, an ACh precursor, is ineffective (Cooper, 1991); (2) treatment with AChE inhibitors is similarly ineffective (Cooper, 1991); and (3) one cannot determine whether decreases in ACh cause AD or are the result of the disease. As a result, the ACh theory alone has not been viewed to be an adequate explanation of development of AD (Cummings & Benson, 1992).
Summary

As stated originally, no theory accounts for all data regarding AD. Several authors have attempted to account for the data by proposing two different forms of AD, a genetically based one and a non-familial form (Breitner & Folstein, 1984). Some support for this theory comes from the work of Rapoport et al. (1991), who reported that in 28 MZ twin pairs the concordant pairs had significantly higher frequency of positive family history of AD than the discordant MZ twin pairs. These authors suggested that the concordant twins had a heritable form of AD whereas the AD patient of the discordant MZ twins may have resulted from some other factor (e.g., environmental toxin, chromosomal aberration during cell proliferation, etc.). At this point, given the recent advances in the understanding of the genetic basis of AD, a genetic theory may be the most promising in accounting for the observed data.

Risk Factors and Clinical Course of AD

Having discussed many of the proposed etiological theories of AD, it is probably no surprise that none of them adequately accounts for the development of AD. Given the strength of the genetic findings, one would think that at the very least there must be a genetic predisposition for AD in some patients. However, given that concordance
rates of AD in identical twins is not 100%, one would expect an environmental, metabolic, or other non-genetic factor to play a significant role in the development of AD.

The question that arises is what risk factors might influence the development and course of the disease. Because of problems with premortality, diagnosis, and obtaining large numbers of disease-free elderly normals, the identification of risk factors for AD has been extremely difficult especially when compared to similar work on cerebral vascular disease and cancer (Katzman & Jackson, 1991). Many risk factors have been investigated including: age, family history, sex, duration, history of head injury, smoking, and other psychiatric or physical disorders among others (Katzman & Jackson, 1991; Von Dras & Blumenthal, 1992; Williams, Annegers, Kokmen, O'Brien, & Kurland, 1991; Apple, 1981; Grossberg, Nakra, Woodward, & Russell, 1989; Kokmen et al., 1991; Mendez et al., 1992; Stern, Mayeux, Sano, Hauser, & Bush, 1987; Mortimer, French, Hutton, & Schuman, 1985; Thal & Grundman, 1986; Huff, Growdon, Corkin, & Rosen, 1987; Ortof & Crystal, 1989; Burns, Jacoby, & Levy, 1991; Teri, Hughes, & Larson, 1990). Each of these risk factors will be discussed in terms of their effect on the development and course of AD.
Age of Onset

In several prevalence studies, greater numbers of senile-onset patients have been observed, leading authors to question whether age of onset affects progression (Fratiglioni et al., 1991; Bachman et al., 1992; Rocca et al., 1990). Huff et al. (1987) reported more rapid deterioration in senile-onset cases. However, these authors stated that while the correlations were significant, the observed relationship was a weak one, and therefore age of onset would not be a good predictor of rate of progression. Additionally, Burns et al. (1991), using NINCDS/ADRDA criteria to diagnose 110 patients, found no relationship between the course of the disease and age of onset. Similarly, most authors have failed to show a relationship between age of onset and pace of cognitive decline (Ortof & Crystal, 1989; Thal & Grundman, 1986) or morbidity (Beard, Kokmen, O'Brien, & Kurland, 1994). Recently, Jacobs and colleagues (Jacobs et al., 1994) reported that early onset of symptoms was correlated with more rapid cognitive deterioration. At this point, it is uncertain how age of onset influences the rate of progression.

Family History of AD

As previously stated, epidemiological studies have shown that first-degree relatives of AD patients have an
increased risk of developing the disease themselves (Nalbantoglu et al., 1990; Prince, Cullen, & Mann, 1994). The magnitude of this risk has varied in different studies from 15% (Heyman et al., 1984) to 50% (Breitner & Folstein, 1984; Chase et al., 1983). Thus, it appears that a positive family history to some degree predisposes first-degree relatives to developing AD. The next question concerns the rate of progression of AD.

Burns et al. (1991) showed a positive relationship between family history and cognitive decline, but only on the Mini-Mental Status Exam (MMSE; Folstein et al., 1975) and not on the abbreviated mental test score (AMTS; Thompson & Blessed, 1987). Also, Burns et al. (1991) further qualify the relationship by adding that the family history-MMSE relationship was no longer significant when the Bonferroni correction of alpha levels was applied. Likewise, Thal & Grundman (1986) did not find the relationship between family history of AD and rate of progression to be significant. Therefore, while family history is related to AD onset, this factor appears, at most, to have a mild effect on AD progression.

**Sex**

Teri et al. (1990) failed to find a differential rate of decline between males and females. Burns et al. (1991) reported similar results. As with age, the primary
sex effect appears to be on prevalence. Many studies show more females with AD than males (Bachman et al., 1992; Rocca et al., 1990; Thal & Grundman, 1986). Yet, just as many reveal non-significant differences (Fragiglioni et al., 1991; Schoenberg, Anderson, & Haerer, 1985). Longer life span in woman may account for some of the variation (Mendez et al., 1992). Yet even when controlling for this factor, some studies find more women than men (Breitner, Silverman, Mohs, & Davis, 1988) and some reveal non-significant differences (Schoenberg, et al., 1985). The fact that no study has reported more males than females may suggest that females may be more prone to have AD, but there is no data to suggest that sex differentially affects rate of progression.

Duration of illness

Thal & Grundman (1986) found a negative correlation between duration of illness and rate of decline. That is, individuals who had been diagnosed with the disorder longer showed slower rates of decline. The results of Teri et al. (1990) confirmed this finding. However, Huff et al. (1987) found no relationship. A closer inspection of these three studies reveals a striking difference: the first two groups of researchers extended their repeat evaluations over several years, whereas all evaluations in Huff's study were conducted within one year. This
difference alone could account for the discrepancy. One must then conclude that the longer one lives following a diagnosis of AD, the slower the rate of decline.

**Smoking**

Apple (1981) presented a rather extensive review of neurotransmitter and receptor site changes in various age related diseases. According to this author's data, tobacco smokers were at a decreased risk of developing AD. The rationale given by this author was that smoking somehow changed cholinergic nicotinic receptors. Grossberg and colleagues (Grossberg et al., 1989) reported similar findings with a larger group of 144 Alzheimer's patients. Neither author was able to specify exactly why this relationship was observed. Perhaps the nicotine induces the types of changes Apple discusses. Alternatively, one's susceptibility to smoke (if there is one) and the protective mechanism against AD may be co-inherited or co-acquired. Also, the smokers who would have acquired AD may die of smoking related illness before they manifest AD. Therefore, a variety of possibilities to explain this relationship exist, but given the data regarding the nicotine-AD relationship, more study is warranted.
History of Head Injury

Several groups of researchers have reported that having suffered a previous head injury puts one at risk for AD (Heyman, et al., 1984; Mortimer et al., 1985; Paschalis, Polychronopoulus, Lekka, & Harrison, 1990; French et al., 1985). However, Mendez et al. (1992) reported no significant differences in the prevalence of a previous head injury among three groups: AD, non-AD dementias (non-AD dem), and normal elderly controls (NEC). Similarly, several other research groups revealed no relationship (Chandra, Philipose, Bell, Lazaroff, & Schoenberg, 1987; Shalat, Seltzer, Pidcock, and Baker, 1987; Williams et al., 1991). The reason for the discrepancy between these two sets of results is difficult to determine. It may well be that the patients from the studies showing a positive relationship were misdiagnosed. In addition, some other factor may be affecting the relationship. For instance, none of the studies have used a good measure to gauge the severity of head injury. If only the more severe head injuries lead to increased incidence of AD, this might then account for the discrepancy. At this point, given the data that has been collected, one must conclude that the relationship between head injury and AD is tenuous, and there is no evidence of a relationship between head injury and course of AD.
Other Physical and Psychiatric Problems

Mendez et al. (1992) failed to find significant differences among the AD, non-AD dem, and NEC groups in regard to heart disease, thyroid disease, cerebrovascular disease, hypertension, previous psychiatric illness, or alcoholism. Stern et al. (1987) reported that a concurrent diagnosis of psychosis or extrapyramidal signs was correlated with greater rate of decline in AD patients. Kokmen et al. (1991) compared 415 diagnosed AD patients with 415 community controls, matched for age, sex, and duration of community medical record. As with Mendez et al. (1992), they found no group differences for many factors including coronary heart disease, alcoholism, a variety of general systemic diseases such as diabetes, thyroid disease, or liver disease, and neurological disorders such as meningitis, epilepsy, Parkinson's disease, or narcolepsy. On the other hand, Kokmen et al. (1991) reported that history of episodic depression, personality disorder, or hypertension may be risk factors for AD. However, these findings remain suspect in that their psychiatric diagnoses were not independently confirmed, and given their large number of post-hoc comparisons, it would have been appropriate to correct for possible type I error. Also, this finding has not been replicated.
Stress and Alzheimer's Disease

A great deal of research has been conducted on the relationship of AD and caregiver stress (Katzman & Jackson, 1991). The majority of the work demonstrates that as a result of the increased burden brought on by the management of a family member with AD, a higher incidence of stress, depression, burnout, and other physical and psychiatric disorders are noted among caregivers (Zarit, Orr, & Zarit, 1985; Brody, 1985; Aronson, 1988). However, very little work has examined the relationship of stress in the etiology and course of AD. In fact, no published research has examined the effects of stress on the onset or rate of progression of AD. Despite this, several researchers have proposed theories on this stress-AD relationship.

Theories Regarding Stress and AD

Hall's theory. Hall (1988) proposed a theory for the decline observed in AD which was based on Lawton's (1982) ecological model of behavioral adaptation. According to Lawton's model, optimal behavioral adaptation occurs when the person's competence (P) "fits" with the level of environmental demand (E). In Hall's application of this theory to AD, the progressive impairment of the person's intellectual integrity is (P) and various stressors (fatigue, novelty, complex stimuli, and physical insult)
represent (E). Although he does not specify the cause, Hall proposes that as stress tolerance thresholds decline (P) over the course of the disorder, and environmental stressors increase (E), dysfunctional behaviors become increasingly more prominent as the P to E "fit" becomes increasingly imbalanced. By reducing these stressors, Hall proposes that an individual's overall well being will improve as the P to E "fit" returns to a more balanced state. Overall, while Hall's theory certainly seems to be plausible, no one has yet provided an empirical test and confirmation of this model.

**Henry's theory.** Henry (1986) also proposed a relationship between psychosocial stress and Alzheimer's. According to his theory, hormone-induced (e.g., corticoids) failure of the hippocampal cells leads to hippocampal degeneration, but he does not specify the mechanism of cell death. A diagram of Henry's theory of the progression of the disease is presented in Figure 1. The entire theory rests on several preexisting relationships: (1) plaques and tangles are observed in the hippocampal pathophysiology; (2) the hippocampus functioning as the helplessness center; (3) the hippocampus may be involved in activation of the pituitary adrenal cortical system; and (4) hippocampal cells are very sensitive to the effects of corticoid hormones.
Figure 1. Henry's (1986) proposed relationship between stress and aging
There are at least three major flaws in this model. Several researchers have demonstrated that individuals with dementia may manifest increased helplessness (Solomon & Szwabo, 1992). However, a consistent relationship between normal aging and the development of helplessness has not been established, weakening the basic premise of Henry's theory. Second, this author is unaware of any data which suggests psychic trauma can lead to brain damage. Finally, many of the original premises upon which the theory is based have not been firmly established (i.e., helplessness is localized to the hippocampus). As a result, it is unlikely that this theory will be helpful in guiding research to elucidate the stress-AD relationship.

Glucocorticoid cascade. Sapolsky (1992) has recently summarized a rather extensive literature examining the effects of stress on the nervous systems of rats. It has been demonstrated that the ability to regulate and limit glucocorticoid secretion becomes increasingly impaired during aging. As the impairment increases, the cumulative effect of excessive exposure to glucocorticoids over the lifetime can accelerate aspects of brain aging, especially in the cells of the hippocampus. The changing levels of secretion of glucocorticoids is called the glucocorticoid cascade.
Now in the context of stress and its relationship to neuronal death, Sapolsky maintains that the glucocorticoids are not intrinsically toxic, but rather they impair the neurons ability to survive insult (e.g., hypoxia, seizure, hypoglycemia, etc.). More importantly, Sapolsky reports that glucocorticoid secretion varies according to several conditions including psychological stress. He reports that lifelong glucocorticoid secretion can be decreased under less stressful conditions, which may decelerate neuronal death. Overall, while this theory has received empirical support from animal studies, it is has yet to be examined with humans.

Summary. As discussed, several individuals have proposed a relationship between stress and dementia, but none of these individuals have empirically tested their theories in human populations. Despite this fact, there are several reasons why stress would be expected to impact AD. Each of these will be discussed in turn.

Stress and Disease

The general relationship between stress and disease has been studied in great detail. Following an extensive review of the literature, several authors have suggested that stress had been demonstrated to affect coronary heart disease (i.e., hypertension and ischemic heart disease), infectious diseases, diabetes mellitus, arthritis, pain
disorders, asthma, and cancer (Newberry, Jaikins-Madden, & Gerstenberger, 1991). Newberry and colleagues (Newberry et al., 1991) also point out that different diseases can respond differently to the physiological processes that stress influences, and that the relationship between stress and a disease state can be quite variable. Nevertheless, given that stress has been demonstrated to impact many disease, one must consider the possibility that stress, whether chronic or acute, might also affect the progression of AD.

**Head Injury, Stress, and AD**

As discussed previously, there is some support for the relationship between head injury and AD. Also, repeated head trauma has been shown to cause another form of dementia (e.g., dementia pugilistica) which is characterized by neurofibrillary tangles only (Corsellis, 1978). Both sets of findings suggest a correlation between head injury and AD. Moreover, if one assumes that suffering a head injury leads to increased physical and psychological stress, then having an increased likelihood of AD following a head injury at the very least indirectly supports the hypothesized stress-AD relationship.

**Personality**

Several studies have demonstrated personality differences between AD patients and normals. Kokmen et
al. (1991) reported that individuals with premorbid personality disorders, especially obsessive-compulsive (O/C) personality disorder, were at a greater risk of developing AD. Kay, Beamish, & Roth (1964) suggested that trait differences existed between AD patients and normal elderly persons including tendency to moodiness, prone to anxiety or to concern about their own health, and low sociability. Additionally, Mears & McClure (1990) found that AD patients were more career oriented and less family oriented than normal controls.

It is important to note that all three of these studies involved correlational analyses limiting cause and effect statements. However, one suggestion from these studies is that there may be personality differences between Alzheimer's patients and normals. Moreover, traits like obsessive/compulsive, career oriented, moody, and anxious suggests a person who is more stressed than relaxed. Once again, although this is only speculation, it supports the position that the stress-AD relationship needs to be studied in more detail.

Animal Research

Animal research has provided evidence that chronic stress leads to changes in brain anatomy and physiology. In a series of tests examining the effects of chronic stress on "young" and "old" rats (Allison, 1991), stress
was shown to disrupt neural transmission in the hippocampus of young animals without any apparent cell loss. Older rats, on the other hand, showed decreases in hippocampal neurons following chronic stress, but no change in neural transmission (Allison, 1991). These findings suggest that stress may well be an important factor in changes in brain functions, and may be related to accelerated atrophy in older subjects.

A similar line of animal research lends support to the importance of stress. The behavior of rats "recovered" from lateral hypothalamic damage deteriorates under stressful situations that "normal" rats tolerate quite well. For example, in a slightly cold environment, recovered rats will increase their food intake to compensate for heat loss. However, in extremely cold conditions, recovered rats stop eating. Normal rats will increase food intake in both conditions (Strickler, Friedman, & Zigmond, 1975). Results of these studies suggest that environmental factors may exacerbate preexisting brain dysfunction. Moreover, the general conclusion from a review of animals studies is that environmental factors, particularly stress, may lead to brain changes and may cause further deterioration in previously compromised central nervous systems.
Summary of Rationale

Throughout the preceding discussion, a rationale was presented to suggest a relationship between stress and AD. In this study, the relationship between daily stress and neuropsychological test performance of AD subjects was examined in the hopes shedding some light on the relationship between stress and the course of AD.

Neuropsychological Testing and Stress

Another question to be addressed in this study is the effects of stress on neuropsychological tests. The discussion of this area is best divided into three areas: 1) test anxiety, 2) imposed stress, and 3) daily stress.

Test anxiety

Test anxiety is typically defined as a situation specific (i.e., under the stress of a test) personality trait with cognitive, behavioral, and affective components (Spielberger & Vagg, 1987). A vast literature has accumulated examining the relationship between test anxiety and test performance, typically resulting in the finding that test anxiety interferes with test performance (Zeidner, 1991; Gross, 1990; Calvo & Alamo, 1987; Sarason, 1986; Burchfield, Stein, & Hamilton, 1985). Several studies (Chavez, Trautt, Brandon, & Steyaert, 1983; King, Hannay, Masek & Burns, 1978) have also specifically
addressed the effects of anxiety on neuropsychological tests, finding the same negative relationship.

Given the rather extensive study of test anxiety, it will not be included among the primary points of interest in this study. Rather, any differential effects associated with test anxiety was controlled for statistically, if necessary.

**Imposed Stress and Test Performance**

A large number of researchers have examined how test performance is affected by imposed stress [i.e., heat, physical work, and CO exposure (i.e., carboxyhemoglobin; Bunnell & Horvath, 1988, 1989); stressful instructions (Malhotra & Hasija, 1990); shock (Keinan, 1987); etc.]. With the exception of heat, these studies have demonstrated that experimenter imposed stress is consistently associated with deterioration in subject performance.

**Daily stress and test performance**

Imposed stress is different than daily stress, defined as "irritating, frustrating, and distressing occurrences" that occur during the course of a normal day (Lazarus & Folkman, 1984). Daily stress has been demonstrated to impact a variety of physical disorders, including Crohn's disease (Garrett, Brantley, Jones, & McKnight, 1991), postconcussion symptoms (Gouvier, Cubic,
Jones, Brantley, & Cutlip, 1992), arthritis (Thomason, Brantley, Jones, Dyer, & Morris, 1992), and flu symptoms (Delongis, Folkman, & Lazarus, 1988).

Affective changes in normal control subjects may occur as a result of daily stress. Bogler, Delongis, Kessler, and Schilling (1989) demonstrated daily stressors accounted for 20% of the variance in mood. Also, Holahan, Holahan, and Belk (1984) showed that daily "hassles" were related to psychological distress in elderly adults (ages 65-75).

However, the effects of daily stress or stressful environmental events on neuropsychological testing has not been elucidated. Indeed, no study has examined its effects on test performance. In this study, the effects of daily stress on test performance were examined.

Summary of Research Questions

The following research questions were addressed in this study:

(1) What is the relationship between daily stress and neuropsychological test performance? It was expected that daily stress would account for a significant amount of variance in the test performance of the subjects.

(2) Which areas of cognitive functioning are affected most by daily stress? It was expected that memory and attention would be the most adversely affected
by daily stress as these areas are more "fluid," and that general intelligence and academic functioning would be affected least as they are more "crystallized."

(3) Does daily stress differentially affect the test performance of AD patients? Daily stress was expected to account for more variance in the performance of AD patients than normal controls, lending support for a conclusion that daily stress may exacerbate the cognitive difficulties of AD patients. Possible differences between the AD and normal control subjects on the set of "fluid" and "crystalized" tests was also examined.

(4) Does the amount of daily stress reported by AD patients differ according to disease severity? Given that AD results in numerous life changes, especially physical and mental limitations, it was expected that the frequency of stressful life events would be greater in more advanced stages of the disease within a range restricted to those whose self report of stressors can be trusted.

(5) Accounting for disease severity, what is the relationship between daily stress and neuropsychological test performance of AD patients? The cognitive functioning in the AD patients experiencing higher levels of daily stress would be more greatly impaired than those experiencing lower levels of stress, even after controlling for the relative severity of their disease.
If demonstrated, additional support would be given to the conclusion that daily stress exacerbates the cognitive difficulties of AD patients.
METHODS
Subjects

Forty-seven outpatients with AD and 47 normal elderly control subjects agreed to participate in this study. Each of the out-patients was initially screened for cognitive dysfunction using the Folstein Mini-Mental State Exam (MMSE; Folstein et al., 1975), the clock drawing test (Spreen & Strauss, 1991), and a basic apraxia exam. If the patient's scores on the screening test were not within normal limits, a more comprehensive examination was recommended, including neurologic, psychiatric, and neuropsychologic evaluations. At this point, the patient was referred by a neurologist for neuropsychological testing.

Prior to participation in this study, a letter of consent was read, agreed to, and signed by each participant (Appendix B). Also, in order to be included in this study, each individual was provisionally diagnosed with senile dementia of the Alzheimer's type (SDAT) according to NINCDS-ADRDA criteria (Appendix A). All patients received physical, neurological, visual, and hearing exams, CSF serology (VDRL) and blood tests (for thyroid screen, CBC, SMAC, B-12, Folate, etc.), and MRI scan to assess the contribution of other possible causes of dementia. Several individuals (N=10) were diagnosed
with mixed dementia involving SDAT and dementia related to cerebrovascular disease (N=7), alcohol abuse (N=1), metabolic disorder (N=1), or Parkinson's disease (N=1). Because of the severity of their illness, two of the AD patients were excluded because they completed less than half of the tests administered. As a result, a total of 45 AD patients (N=45) participated in this study.

The control group consisted of an equal number of normal elderly controls (N=47). These individuals were recruited from the community through solicitation of church and volunteer groups. All individuals were screened using the Mattis Dementia Rating Scale (DRS; Mattis, 1973) to ensure generally intact cognitive functioning. The inclusion criterion was that all subtest scores of the DRS were within normal limits (i.e., above standard cutoffs for normal versus demented functioning). Also, individuals with a diagnosed neurological disorder (e.g., Parkinson's Disease, cerebral vascular accident, encephalitis, etc.) were excluded from consideration. Two individuals was excluded because their DRS scores were below the standard cutoff on the memory subtest. This yielded a total of 45 normal elderly control subjects (N=45).
Measures of Cognitive Functioning

Various factors influenced the decision of which tests were to be included in this study. The areas of cognitive functioning assessed in this study represented the areas typically assessed in evaluations of dementia (Lezak, 1983). Moreover, the specific measures used to assess each of the areas were tests which are commonly used in neuropsychological assessments (Lezak, 1983). Additionally, test selection required specific consideration of the patient group used in this study. In an attempt to minimize the mental and physical fatigue of the research participants, the battery of tests selected attempted to maximize the amount of information obtained from each test. Also, short forms of tests, when available, were utilized in order to shorten the total test time.

General Intelligence

Several subtests of the Wechsler Adult Intelligence Test-Revised (Wechsler, 1981; WAIS-R) were administered: Information, Vocabulary, Digit Span, Similarities, Picture Completion, Block Design, and Digit Symbol. These subtests were selected because they provide the most information in the shortest amount of time. The exception to this rule is Vocabulary, which was included because it
is the subtest which is most highly correlated with the full scale intelligence quotient.

These scores were prorated to yield a full scale intelligence quotient (FSIQ), verbal intelligence quotient (VIQ) and performance intelligence quotient (PIQ). Prorated sums of scaled scores for the Verbal and Performance subscales were derived by multiplying the total of subtest scores for tests administered for a particular subscale by the number of subtests on the scale (e.g., 6 for the Verbal subscale and 5 for the Performance subscale) divided by the number of tests administered from a particular subscale. The Full Scale sum of scaled scores was derived by adding the two prorated subscale scores. IQ scores were computed directly from the prorated sums of scaled scores for VIQ, PIQ, and FSIQ.

The split-half reliability of the WAIS-R FSIQ, VIQ, and PIQ scores is very high (above .93; Wechsler, 1981). Subtest split-half reliabilities are somewhat lower, but generally above .80 (Wechsler, 1981). The test-retest reliability of these IQ scores is also high (above .89) with somewhat lower scores noted for subtest scores (generally above .80; Wechsler, 1981). Banken and Banken (1987) suggested that the reliability of the WAIS-R FSIQ, VIQ, and PIQ scores were relatively similar when using abbreviated versions of the WAIS-R. Also, several authors
suggest that prorated IQs are acceptable "quick" estimates of intelligence (Lezak, 1983; Groth-Marnat, 1990).

WAIS-R IQ scores have been demonstrated to correlate highly with other measures of intelligence (Spreen & Strauss, 1991). Banken and Banken (1987) reported that while the validity of the WAIS-R may be slightly compromised when using abbreviated versions, shortened versions should be used when testing individuals with impaired mental status (e.g., dementia patients).

**Attention**

Factor analyses of the WAIS-R consistently have yielded 3 factors (Sattler, 1982): Verbal Comprehension, Perceptual Organization, and Freedom from Distractibility. The Freedom from Distractibility (FFD) factor, which includes scores from the Arithmetic, Digit Span, and Digit Symbol subtests, measures attention, concentration, and memory (Spreen & Strauss, 1991). Using the FFD factor as a guideline, the Digit Span and Digit Symbol subtests were averaged to yield a rough estimate of attention/concentration and short-term memory.

**Achievement Testing**

The reading and arithmetic subtests of the Wide Range Achievement Test-Revised (Jastak & Jastak, 1965; WRAT-R) were administered to measure basic academic functioning. The spelling subtest was excluded in order to shorten
total test time. The reading subtest required subjects to read single words from a printed card and measures letter and word recognition. The arithmetic subtest required that subjects complete as many problems as possible in a 10 minute period yielding a measure of basic arithmetic skills. The reading and arithmetic raw scores were used in the analyses.

According to the test manual (Jastak & Jastak, 1965), measures of internal consistency range from .90 to .99. The test authors also present data which suggests that the WRAT-R correlates highly with other measures of achievement (usually above .70). However, other authors suggest that correlations with other measures of academic achievement may be modest (Spreen & Strauss, 1991). Their criticisms notwithstanding, Spreen and Strauss also point out that the WRAT-R is a good quick screening measure of academic skills, particularly with subjects who have impaired mental status (e.g. dementia patients). For this reason, the WRAT-R was viewed to address the specific needs of this study, thereby justifying its use.

Language

The Controlled Oral Word Association (COWA) was used to test word fluency in this experiment. This test required patients to self-generate as many words as possible beginning with each of the three letters. The
letters T, F, and L, which are part of Benton and Hamsher's Multilingual Aphasia Examination (Benton & Hamsher, 1978), were used in this study.

Additionally, the psychometrics of word fluency tests are generally good. DesRosiers & Kavanagh (1987) found the test-retest reliability to be high (.88). Also, several authors have reported that word fluency test scores are highly related to locus and laterality of lesion, with greater impairment seen in left frontal relative to right frontal lobe injuries (Parks, et al., 1988; Perrett, 1974).

The Boston Naming Test (BNT; Kaplan, Goodglass, & Weintraub, 1978) was used as a measure of confrontational naming. The test consists of 60 large ink drawings ranging in degree of familiarity which the subject is required to identify. The total score was the total number of correct responses. The split-half reliability of the BNT has been reported to be high (above .80; Huff, Collins, Corkin, & Rosen, 1986). Additionally, the test adequately discriminates between normal elderly subjects and patients with AD or other dementias (Williams, Mack, & Henderson, 1989).

**Memory**

Three subtests of the Wechsler Memory Scale-Form I (WMS; Wechsler & Stone, 1973) which comprise the Russell
Memory test (Russell, 1975, 1988) were used to test for short term memory: Logical Memory (LM), Visual Reproduction (VR), and Associate Learning (AL). LM examined the subjects ability to recall information presented in two passages presented to them. VR required subjects to reproduce simple geometric designs from memory following only a brief exposure. AL required the patient to listen to paired associations of words and then recall the correct response to stimulus words over three trials. Raw scores for each of the three areas (LM, VR, and AL) were used in the analyses.

Following a 30 minute delay, subjects were tested for delayed recall of information from these subtests. This latter step produced a measure of long term memory. The raw scores for each of these tests was used in the analyses.

Russell's version of the WMS (1975, 1988) represented a significant improvement in the reliability and validity of the original WMS. Reliability was improved by utilizing more specific and stringent scoring criteria. Russell (1988) also reported that scores discriminated between normal and demented individuals as well as between patients with left- and right-hemisphere damage.
Tests of Graphomotor Functioning

The Rey-Osterrieth complex figure (Rey-O; Rey, 1941) provided a measure of gross graphomotor functioning. Administration of the test involved presenting the examinee with a drawing of the complex figure, a blank piece of paper, and a pencil. The examinee was then required to reproduce the complex drawing without tracing it.

The scoring procedure used to rate each of the drawings was obtained from Denman's Memory Scale, an eight part test of which memory of the Rey-O figure is one component (Denman, 1989). The raw scores obtained using Denman's system were used in the analyses of this study. Denman (1989) reported obtaining an inter-scorer reliability of .95 for his Rey-O scoring procedure. Denman did not report validity studies involving the copy score of the Rey-O. However, the copy score of the Rey-O has been demonstrated to reliably discriminate between normal and right-hemisphere damaged adults (Binder, 1982).

Emotional/Self-Report

The Minnesota Multiphasic Personality Inventory is a self-administered test consisting of 566 True/False questions which measures basic personality functioning. Because of its length, many shorter versions of this test have been developed, including the Improved Readability
Form of the MMPI (MMPI-IRF; Ward & Selby, 1980). Scale scores from the MMPI-IRF have been demonstrated to correlate highly with scale scores for the full battery (Ward & Selby, 1980; Ward, 1986; Dillon & Ward, 1989). Also, the MMPI-IRF has been shown to be more readable and comprehendible than the MMPI (Ward, 1986; Dillon & Ward, 1989). The MMPI-IRF was administered to all subjects. The questions were read to participants as part of their neuropsychological assessment, and their answers were recorded. T-scores from the MMPI scales 2 (depression) and 7 (anxiety) were used as affective scores for depression and anxiety.

Measures of Stress

The Daily Stress Inventory (DSI; Brantley & Jones, 1989) was used to assess daily stress. The DSI is a 58-item inventory of daily stressful events or minor stressors. Respondents indicated which of the 58 events occurred over the previous 24 hours, yielding a "Frequency" score. Subjects also rated the perceived impact of the event on a 7 point Likert-type scale. The total of ratings of the endorsed stressful events provides the "Sum" score.

Overall, the DSI appears to be psychometrically sound (Brantley, Waggoner, Jones, & Rappaport, 1987). Brantley and colleagues (Brantley et al., 1987) reported that
Chronbach alpha coefficients were .83 and .87 for the frequency and sum scores respectively. Also, these authors reported that the Sum score correlated highly with measures of anxiety, but the Frequency score did not correlate with anxiety measures (Brantley et al., 1987). Brantley and colleagues (Brantley, Dietz, McKnight, Jones, & Tulley, 1988) also demonstrated that DSI scores were predictive of daily urinary measures of cortisol and vanillymandelic acid, providing additional support for the validity of the DSI. Also, the DSI has been demonstrated to remain relatively stable with repeated administration (Brantley, Cocke, Jones, & Goreczny, 1988).

Procedure

All subjects were administered each of the instruments described above during a single testing session, conducted between 9 a.m. and 4 p.m. The participants also completed the DSI for 3 consecutive days prior to, the day of, and the day after testing. They were instructed to complete the DSI sometime between 6 and 8 p.m. on each of the 5 specified days. Because AD patients have been demonstrated to have impaired insight primarily due to confabulation and anosognosia (Mangone et al., 1991), the primary caregiver was instructed to assist the patient in the completion of the DSI. Each caregiver was told not to complete the form for the patient.
Rather, they were instructed to assist the patient only by answering their questions about the questionnaire.

In order to control for reactivity to the completion of the DSI (Brantley et al., 1988), the scores for the first day were not included in the analyses. The numeric average of the Sum (SUM) and Frequency (FREQ) scores across the remaining 4 days was used in all subsequent analyses.

In this design, the independent variables (IV) included age, sex, years of education, group, affective scores (i.e., depression and anxiety), and DSI scores (i.e., Frequency and Sum). The dependent variables (DV) included FIQ, PIQ, VIQ, attention score, WRAT-R reading and arithmetic scores, COWA score, BNT score, Rey-O score, as well as immediate and delayed LM, VR, and AL scores.
RESULTS

Descriptive Statistics

Means and standard deviations of all independent variables as well as the frequencies of males and females, stratified by group, are presented in Table 1.

Group Comparisons on IVs

A series of t-tests was conducted in order to make group comparisons across the IVs. Only the variables that differed significantly between the two groups were used as covariates in subsequent analyses. The exception to this rule was the daily stress variables (i.e., SUM and FREQ) which were included irrespective of whether group differences existed because daily stress was the primary focus of this study. In evaluating each t-test, a probability value of $p<.05$ was corrected using Bonferoni's correction to control for possible Type I errors as a result of multiple comparisons. As 6 t-tests were conducted, the corrected $p$-value used was .008.

Results of the t-tests revealed that there was a significant difference between the two groups for age [$t(88)=4.42, p<.001$] as the AD group was older than the normal controls. There were not significant differences for years of education, depression, or anxiety (all $ps>.008$). Regarding the FREQ and SUM scores, the two groups did not differ on their FREQ scores.
Table 1

Means and standard deviations (in parentheses) for all independent variables, as well as gender frequencies, stratified by group.

<table>
<thead>
<tr>
<th>IVs</th>
<th>AD</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x</td>
<td>SD</td>
</tr>
<tr>
<td>Age (in years)</td>
<td>78.8 (4.8)</td>
<td>73.5 (6.5)</td>
</tr>
<tr>
<td>Years of Education</td>
<td>12.9 (2.8)</td>
<td>13.0 (2.7)</td>
</tr>
<tr>
<td>Depression¹</td>
<td>66.2 (11.6)</td>
<td>58.5 (14.1)</td>
</tr>
<tr>
<td>Anxiety¹</td>
<td>59.6 (10.6)</td>
<td>53.2 (10.7)</td>
</tr>
<tr>
<td>DSI-Frequency</td>
<td>10.2 (7.2)</td>
<td>9.4 (5.2)</td>
</tr>
<tr>
<td>DSI-Sum</td>
<td>30.4 (25.4)</td>
<td>18.2 (13.4)</td>
</tr>
<tr>
<td>Males/Females</td>
<td>21/24</td>
<td>11/34</td>
</tr>
</tbody>
</table>

¹ T-scores
However, the two groups differed significantly on SUM scores \( t(86) = 2.80, p < .006 \) with the AD group reporting significantly greater reactivity to a comparable number of stressors.

In addition, a chi-square analysis was used to test for group gender differences and failed to achieve statistical significance \( X^2 = 3.93, df = 1, NS \). In summary, only age was used as a covariate in subsequent analyses because age was the only demographic and affective variable which differed significantly between the groups.

Group Comparisons on the Neuropsychological Tests

The means and standard deviations for each of the neuropsychological measures are presented in Table 2. In order to assess for group differences on the various neuropsychological tests, one could conduct a series of t-tests. However, the concern was not whether specific test differences were noted; rather, one would expect that there would be a group difference on the neuropsychological measures as a whole. A Hotelling's \( T^2 \) was used to make a group comparison across the set of neuropsychological measures (FSIQ, PIQ, VIQ, WRAT-R reading and arithmetic, FAS score, BNT score, Rey-O score, immediate and delay LM scores, immediate and delay VR scores, and immediate and delay PA scores). A significant difference was demonstrated with the AD group performing
### Table 2

**Means and standard deviations (in parantheses) for the neuropsychological measures, stratified by group**

<table>
<thead>
<tr>
<th>Neuropsychological Measures</th>
<th>AD</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SD</td>
<td></td>
</tr>
<tr>
<td>FSIQ</td>
<td>83.3</td>
<td>105.8 (14.6)</td>
</tr>
<tr>
<td></td>
<td>(14.3)</td>
<td></td>
</tr>
<tr>
<td>VIQ</td>
<td>87.1</td>
<td>106.6 (12.8)</td>
</tr>
<tr>
<td></td>
<td>(14.1)</td>
<td></td>
</tr>
<tr>
<td>PIQ</td>
<td>79.4</td>
<td>103.0 (16.8)</td>
</tr>
<tr>
<td></td>
<td>(14.6)</td>
<td></td>
</tr>
<tr>
<td>Attention</td>
<td>4.9</td>
<td>8.0 (1.8)</td>
</tr>
<tr>
<td></td>
<td>(1.9 )</td>
<td></td>
</tr>
<tr>
<td>WRAT-R Reading</td>
<td>61.2</td>
<td>63.8 (13.9)</td>
</tr>
<tr>
<td></td>
<td>(16.1)</td>
<td></td>
</tr>
<tr>
<td>WRAT-R Arithmetic</td>
<td>21.4</td>
<td>29.0 (5.2)</td>
</tr>
<tr>
<td></td>
<td>(7.5 )</td>
<td></td>
</tr>
<tr>
<td>BNT</td>
<td>30.8</td>
<td>52.3 (5.1)</td>
</tr>
<tr>
<td></td>
<td>(15.3)</td>
<td></td>
</tr>
<tr>
<td>FAS</td>
<td>19.1</td>
<td>33.1 (11.4)</td>
</tr>
<tr>
<td></td>
<td>(12.3)</td>
<td></td>
</tr>
<tr>
<td>REY-O</td>
<td>35.1</td>
<td>66.4 (5.6)</td>
</tr>
<tr>
<td></td>
<td>(22.0)</td>
<td></td>
</tr>
<tr>
<td>LM</td>
<td>3.7</td>
<td>11.2 (3.1)</td>
</tr>
<tr>
<td></td>
<td>(3.8 )</td>
<td></td>
</tr>
<tr>
<td>LM-Delay</td>
<td>1.6</td>
<td>10.1 (3.0)</td>
</tr>
<tr>
<td></td>
<td>(3.3 )</td>
<td></td>
</tr>
<tr>
<td>PA</td>
<td>6.3</td>
<td>12.9 (3.7)</td>
</tr>
<tr>
<td></td>
<td>(3.0 )</td>
<td></td>
</tr>
<tr>
<td>PA-Delay</td>
<td>2.0</td>
<td>5.1 (1.5)</td>
</tr>
<tr>
<td></td>
<td>(1.1 )</td>
<td></td>
</tr>
<tr>
<td>VR</td>
<td>1.6</td>
<td>8.6 (3.0)</td>
</tr>
<tr>
<td></td>
<td>(1.7 )</td>
<td></td>
</tr>
<tr>
<td>VR-Delay</td>
<td>0.4</td>
<td>6.3 (4.2)</td>
</tr>
<tr>
<td></td>
<td>(1.1 )</td>
<td></td>
</tr>
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</table>
worse on the neuropsychological measures [Hotelling's $T^2(14,72) = 4.22, p<.05$]. In addition, post-hoc $t$-tests revealed significant group differences for each of the neuropsychological variables (all $p$s<.05) with the exception of the WRAT-R reading score which did not differ significantly between the groups [$F(1,85) = .38, NS$].

Zero Order Correlations

Correlations were computed between the average DSI Frequency (FREQ) and Sum (SUM) scores and each of the dependent variables stratified by group, providing an indication of the relationship between the two measures of daily stress and each of the neuropsychological measures. In addition, correlations were computed between the two stress measures and each of the WAIS-R subtests as well as the attention score. All of the correlations are presented in Tables 3 and 4, representing the AD and normal control groups, respectively. For the AD group, significant negative correlations were revealed between SUM and FSIQ ($r=-.32$), PIQ ($r=-.34$), attention ($r=-.40$), Digit Span ($r=-.34$), Picture Completion ($r=-.34$), Digit Symbol ($r=-.34$), VR-immediate ($r=-.44$), VR-delay ($r=-.30$) and Rey-O ($r=-.34$). Also, significant negative correlations were revealed between FREQ and VR-immediate ($r=-.37$) as well as VR-delay ($r=-.30$). However, in order to control for possible Type I errors as a result of
Table 3

Zero-order correlations between the neuropsychological variables and the DSI variables (i.e., FREQ and SUM) for the AD group

<table>
<thead>
<tr>
<th>Neuropsychology Variables</th>
<th>FREQ</th>
<th>SUM</th>
</tr>
</thead>
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<tr>
<td><strong>Intelligence scores:</strong></td>
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<td></td>
</tr>
<tr>
<td>FSIQ</td>
<td>-.24</td>
<td>-.32*</td>
</tr>
<tr>
<td>PIQ</td>
<td>-.29</td>
<td>-.34*</td>
</tr>
<tr>
<td>VIQ</td>
<td>-.18</td>
<td>-.27</td>
</tr>
<tr>
<td>Attention Score</td>
<td>-.23</td>
<td>-.40*</td>
</tr>
<tr>
<td>WAIS-R Information</td>
<td>-.22</td>
<td>-.27</td>
</tr>
<tr>
<td>WAIS-R Vocabulary</td>
<td>-.05</td>
<td>-.04</td>
</tr>
<tr>
<td>WAIS-R Digit Span</td>
<td>-.17</td>
<td>-.34*</td>
</tr>
<tr>
<td>WAIS-R Similarities</td>
<td>-.15</td>
<td>-.23</td>
</tr>
<tr>
<td>WAIS-R Picture Completion</td>
<td>-.29</td>
<td>-.34*</td>
</tr>
<tr>
<td>WAIS-R Block Design</td>
<td>-.23</td>
<td>-.25</td>
</tr>
<tr>
<td>WAIS-R Digit Symbol</td>
<td>-.27</td>
<td>-.36*</td>
</tr>
<tr>
<td><strong>Achievement Scores:</strong></td>
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<td></td>
</tr>
<tr>
<td>WRAT-R Reading</td>
<td>-.00</td>
<td>-.08</td>
</tr>
<tr>
<td>WRAT-R Math</td>
<td>-.16</td>
<td>-.25</td>
</tr>
<tr>
<td><strong>Language Scores:</strong></td>
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</tr>
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<td>-.29</td>
</tr>
<tr>
<td>BNT</td>
<td>-.21</td>
<td>-.19</td>
</tr>
<tr>
<td><strong>Memory scores:</strong></td>
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<td></td>
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<tr>
<td>LM-immediate</td>
<td>-.12</td>
<td>-.10</td>
</tr>
<tr>
<td>LM-delay</td>
<td>-.09</td>
<td>-.02</td>
</tr>
<tr>
<td>VR-immediate</td>
<td>-.37*</td>
<td>-.44*</td>
</tr>
<tr>
<td>VR-delay</td>
<td>-.30*</td>
<td>-.30*</td>
</tr>
<tr>
<td>PA-immediate</td>
<td>-.11</td>
<td>-.18</td>
</tr>
<tr>
<td>PA-delay</td>
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<td>-.14</td>
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<tr>
<td><strong>Graphomotor score:</strong></td>
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<td></td>
</tr>
<tr>
<td>REY-O</td>
<td>-.25</td>
<td>-.34*</td>
</tr>
</tbody>
</table>

* denotes p<.05
Table 4

Zero-order correlations between the neuropsychological variables and the DSI variables (i.e., FREQ and SUM) for the normal control group

<table>
<thead>
<tr>
<th>Neuropsychology Variables</th>
<th>DSI Variables</th>
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<th></th>
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</thead>
<tbody>
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<td></td>
<td>FREQ</td>
<td>SUM</td>
<td></td>
</tr>
<tr>
<td>Intelligence scores:</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>FSIQ</td>
<td>-.09</td>
<td>.12</td>
<td></td>
</tr>
<tr>
<td>PIQ</td>
<td>-.02</td>
<td>.16</td>
<td></td>
</tr>
<tr>
<td>VIQ</td>
<td>-.15</td>
<td>.05</td>
<td></td>
</tr>
<tr>
<td>Attention Score</td>
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<td>-.04</td>
<td></td>
</tr>
<tr>
<td>WAIS-R Information</td>
<td>-.15</td>
<td>.03</td>
<td></td>
</tr>
<tr>
<td>WAIS-R Vocabulary</td>
<td>-.11</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td>WAIS-R Digit Span</td>
<td>-.19</td>
<td>-.04</td>
<td></td>
</tr>
<tr>
<td>WAIS-R Similarities</td>
<td>.11</td>
<td>.27</td>
<td></td>
</tr>
<tr>
<td>WAIS-R Picture Completion</td>
<td>-.07</td>
<td>.17</td>
<td></td>
</tr>
<tr>
<td>WAIS-R Block Design</td>
<td>-.04</td>
<td>.06</td>
<td></td>
</tr>
<tr>
<td>WAIS-R Digit Symbol</td>
<td>-.09</td>
<td>-.01</td>
<td></td>
</tr>
<tr>
<td>Achievement Scores:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WRAT-R Reading</td>
<td>-.08</td>
<td>.08</td>
<td></td>
</tr>
<tr>
<td>WRAT-R Math</td>
<td>-.36*</td>
<td>-.12</td>
<td></td>
</tr>
<tr>
<td>Language Scores:</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>FAS test</td>
<td>-.08</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td>BNT</td>
<td>-.14</td>
<td>-.03</td>
<td></td>
</tr>
<tr>
<td>Memory scores:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LM-immediate</td>
<td>.08</td>
<td>.11</td>
<td></td>
</tr>
<tr>
<td>LM-delay</td>
<td>.12</td>
<td>.15</td>
<td></td>
</tr>
<tr>
<td>VR-immediate</td>
<td>-.31*</td>
<td>-.17</td>
<td></td>
</tr>
<tr>
<td>VR-delay</td>
<td>-.30</td>
<td>-.14</td>
<td></td>
</tr>
<tr>
<td>PA-immediate</td>
<td>.10</td>
<td>.27</td>
<td></td>
</tr>
<tr>
<td>PA-delay</td>
<td>.12</td>
<td>.29</td>
<td></td>
</tr>
<tr>
<td>Graphomotor score:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>REY-O</td>
<td>-.06</td>
<td>-.04</td>
<td></td>
</tr>
</tbody>
</table>

* denotes p<.05
multiple comparisons, a Bonferoni's correction was applied to the p-value of .05. With 44 correlations computed, the corrected p-value used was .0011. Using this more conservative p-value, none of these correlations were statistically significant (all ps=n.s.).

For the normal control group, significant negative correlations were revealed between FREQ and WRAT-R arithmetic (r=-.36) as well as VR-immediate (r=-.31). However, when correcting for multiple comparisons yielding a corrected p-value of .0011 (i.e., a p-value of .05 corrected for 44 comparisons), no statistically significant correlations were revealed (all ps=n.s.).

In sum, a number of significant correlations were revealed, all of which were in the expected direction (i.e., higher daily stress was correlated with lower test scores). However, while a number of significant correlations were noted between the stress variables and the neuropsychological measures (particularly for the AD group), no significant correlations were noted when controlling for multiple comparisons.

Two additional analyses, Mann-Whitney U-tests, were conducted examining FREQ and SUM separately. The absolute zero-order correlations were ranked across groups for FREQ and SUM separately. Then, the sum of the rankings for the AD and normal control groups were compared to determine if
there was a reliable difference between the groups. The sum of the ranked correlations did not differ between the two groups when FREQ was used (p=n.s.). However, when the correlations of the neuropsychological measures with SUM were ranked, the sum of rankings for the AD group was significantly higher than the normal control group's summed rankings ($U = 9.33, p<.05$), suggesting that the AD group's set of correlations between the neuropsychological measures and SUM is reliably greater than the normal control's corresponding set of correlations.

What Effect Does Stress Have on Neuropsychological Test Performance?

In order to examine the relationship between daily stress and neuropsychological test performance, a series of hierarchical regression analyses was conducted, with separate analyses performed for each group so that the relative effects of daily stress could be identified. Also, separate analyses were conducted using either the FREQ or SUM scores as measures of daily stress. Because hierarchical regression examines the effects of each variable as it is entered into the model, while controlling for the previously entered variable, age was entered in the first step. In the next stage, either the FREQ or SUM scores were added to the model, which provided a measure of the amount of variance in neuropsychological
functioning accounted for by daily stress over and above the effect of age.

Tables 5 and 6 display a summary of the hierarchical regressions predicting neuropsychological test performance for the AD group using FREQ and SUM as measures of daily stress, respectively. The \( R^2 \) change score represents the variance accounted for in each of the neuropsychology measures by the variables entered into the model at that step. The F change statistic tests the significance of \( R^2 \) change. Of significance to this study is the F change statistic for the second step as it represents a significance test of the variance accounted for by daily stress after accounting for age.

As seen in Table 5, FREQ accounted for 8.2\% of the variance in immediate VR scores. Table 6 reveals that SUM accounted for 11.2\% of the variance in immediate VR scores and 11.8\% of attention scores. In addition, Table 6 shows that several other relationships approached significance, with SUM accounting for 7.4\% of the variance in PIQ scores \( [F \text{ change (2,42)} = 3.76, p=.059] \) and 7.6\% of the variance in REY-O scores \( [F \text{ change (2,41)} = 3.84, p=.057] \).

Tables 7 and 8 display a summary of the hierarchical regressions predicting neuropsychological test performance for the normal controls using FREQ and SUM as measures of daily stress, respectively.
Table 5

Summary of between subject hierarchical regressions predicting neuropsychological test performance for the AD group using FREO as the measure of daily stress

<table>
<thead>
<tr>
<th>DV</th>
<th>Predictor</th>
<th>$R^2$</th>
<th>$R^2$ Inc</th>
<th>F Change</th>
<th>df</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSIQ</td>
<td>1. AGE</td>
<td>.08</td>
<td>.08</td>
<td>3.81</td>
<td>1,43</td>
</tr>
<tr>
<td></td>
<td>2. FREQ</td>
<td>.12</td>
<td>.04</td>
<td>1.85</td>
<td>2,42</td>
</tr>
<tr>
<td>PIO</td>
<td>1. AGE</td>
<td>.10</td>
<td>.10</td>
<td>4.64*</td>
<td>1,43</td>
</tr>
<tr>
<td></td>
<td>2. FREQ</td>
<td>.16</td>
<td>.06</td>
<td>3.04</td>
<td>2,42</td>
</tr>
<tr>
<td>VIO</td>
<td>1. AGE</td>
<td>.07</td>
<td>.07</td>
<td>3.23</td>
<td>1,43</td>
</tr>
<tr>
<td></td>
<td>2. FREQ</td>
<td>.09</td>
<td>.02</td>
<td>.77</td>
<td>2,42</td>
</tr>
<tr>
<td>ATTN</td>
<td>1. AGE</td>
<td>.08</td>
<td>.08</td>
<td>3.45</td>
<td>1,42</td>
</tr>
<tr>
<td></td>
<td>2. FREQ</td>
<td>.12</td>
<td>.04</td>
<td>1.92</td>
<td>2,41</td>
</tr>
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<td>.00</td>
<td>.00</td>
<td>.01</td>
<td>1,43</td>
</tr>
<tr>
<td></td>
<td>2. FREQ</td>
<td>.00</td>
<td>.00</td>
<td>.00</td>
<td>2,42</td>
</tr>
<tr>
<td>MATH</td>
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<td>.00</td>
<td>.00</td>
<td>.11</td>
<td>1,43</td>
</tr>
<tr>
<td></td>
<td>2. FREQ</td>
<td>.03</td>
<td>.02</td>
<td>1.05</td>
<td>2,42</td>
</tr>
<tr>
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<td>.05</td>
<td>.05</td>
<td>2.32</td>
<td>1,43</td>
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<tr>
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<td>2. FREQ</td>
<td>.07</td>
<td>.02</td>
<td>.92</td>
<td>2,42</td>
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<tr>
<td>BNT</td>
<td>1. AGE</td>
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<td>.10</td>
<td>4.87*</td>
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<td>2. FREQ</td>
<td>.13</td>
<td>.03</td>
<td>1.43</td>
<td>2,42</td>
</tr>
<tr>
<td>LM-I</td>
<td>1. AGE</td>
<td>.13</td>
<td>.13</td>
<td>6.69*</td>
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</tr>
<tr>
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<td>.14</td>
<td>.01</td>
<td>.27</td>
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<tr>
<td>LM-D</td>
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<td>.07</td>
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<td>.00</td>
<td>.10</td>
<td>2,42</td>
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<td>.16</td>
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<td>.04</td>
<td>1.53</td>
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<td>.02</td>
<td>.96</td>
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<td>PA-D</td>
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<td>.06</td>
<td>2.69</td>
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<td>.11</td>
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<td>.04</td>
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</table>

* denotes $p<.05$
Table 6

**Summary of between subject hierarchical regressions predicting neuropsychological test performance for the AD group using SUM as the measure of daily stress**

<table>
<thead>
<tr>
<th>DV</th>
<th>Predictor</th>
<th>$R^2$</th>
<th>$R^2$ Inc</th>
<th>F Change</th>
<th>df</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSIQ</td>
<td>1. AGE</td>
<td>.08</td>
<td>.08</td>
<td>3.81</td>
<td>1,43</td>
</tr>
<tr>
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<td>2. SUM</td>
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<td>2.98</td>
<td>2,42</td>
</tr>
<tr>
<td>PIQ</td>
<td>1. AGE</td>
<td>.10</td>
<td>.10</td>
<td>4.64*</td>
<td>1,43</td>
</tr>
<tr>
<td></td>
<td>2. SUM</td>
<td>.17</td>
<td>.07</td>
<td>3.04</td>
<td>2,42</td>
</tr>
<tr>
<td>VIQ</td>
<td>1. AGE</td>
<td>.07</td>
<td>.07</td>
<td>3.23</td>
<td>1,43</td>
</tr>
<tr>
<td></td>
<td>2. SUM</td>
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<td>.04</td>
<td>1.82</td>
<td>2,42</td>
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<tr>
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<td>.08</td>
<td>3.45</td>
<td>1,42</td>
</tr>
<tr>
<td></td>
<td>2. SUM</td>
<td>.19</td>
<td>.11</td>
<td>5.98*</td>
<td>2,41</td>
</tr>
<tr>
<td>READ</td>
<td>1. AGE</td>
<td>.00</td>
<td>.00</td>
<td>.01</td>
<td>1,43</td>
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<tr>
<td></td>
<td>2. SUM</td>
<td>.00</td>
<td>.00</td>
<td>.15</td>
<td>2,42</td>
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<tr>
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<td>.00</td>
<td>.11</td>
<td>1,43</td>
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<tr>
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<td>2. SUM</td>
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<td>.05</td>
<td>2.32</td>
<td>2,42</td>
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<td>.05</td>
<td>2.32</td>
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</tr>
<tr>
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<td>2. SUM</td>
<td>.10</td>
<td>.05</td>
<td>2.31</td>
<td>2,42</td>
</tr>
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* denotes $p<.05$
Table 7

Summary of between subject hierarchical regressions predicting neuropsychological test performance for the normal control group using FREQ as the measure of daily stress

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* denotes p<.05
Table 8

Summary of between subject hierarchical regressions predicting neuropsychological test performance for the normal control group using SUM as the measure of daily stress

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* denotes p<.05
From Table 7, it can be seen that daily stress, as measured by FREQ, accounts for significant variance in several areas for the normal controls. FREQ accounts for 13.8% of the variance in WRAT-R arithmetic scores, 9.9% of the variance in immediate VR scores, 9.0% of the variance in delayed VR scores, and 8.8% of the attention score. In addition, Table 8 shows that SUM accounted for 6.0% of the variance in immediate VR scores, which approached significance \([F \text{ change } (2,42) = 3.83, p=.057]\).

Overall, daily stress, as measured by FREQ or SUM, appears to account for significant variance in the test performance of all subjects, with FREQ appearing to account for more variance on a greater number of neuropsychological measures. However, the areas demonstrated to be related to stress differed among the groups. A more direct examination of the differential effects of daily stress was conducted in the next phase of the analyses.

Does Daily Stress Differentially Affect the Test Performance of AD Patients?

In order to determine whether or not stress differentially affected the overall test performance in the two groups, two separate factorial MANCOVAs were conducted, one using SUM and one with FREQ. Because the two groups differed significantly in age, age was used as a covariate. The AD and normal control groups were split
into three groups (i.e., high, medium, and low stress), roughly representing equal thirds. The upper and lower thirds were used in subsequent analyses, resulting in 4 different groups: high and low stress AD patients and high and low stress normal controls. While the two IV's (group and stress) were of some interest, the interaction between group and stress on the set of neuropsychological test scores directly addressed the question posed here (i.e., does daily stress differentially affect the test performance of AD patients?).

In assessing the significance of the MANCOVAs, Pillai's criterion was used as it has been demonstrated to be the most robust of the different criteria (Olson, 1979). The DVs for the first pair of MANCOVAs were the set of neuropsychological variables (i.e., FSIQ, PIQ, VIQ, WRAT-R reading and arithmetic, FAS score, BNT score, Rey-O score, immediate and delay LM scores, immediate and delay VR scores, and immediate and delay PA scores). Using the FREQ score as a measure of stress, the combined DVs were significantly affected by group membership only [F(1,54) = 18.5, p<.05], controlling for age. Stress and the interaction between stress and group membership did not appear to significantly affect the set of neuropsychology variables (both ps>.10). When using the SUM score as the measure of stress, the combined DVs were again
significantly affected by group membership only \[F (1,54) = 13.9, \ p<.05\], controlling for age. However, while SUM failed to significantly influence the set of DVs \(p>.10\), the interaction between SUM and group approached significance \[F (1,54) = 1.64, \ p=.10\].

Does Daily Stress Differentially Affect Performance on "Fluid" Versus "Crystallized" Tests?

As it was initially proposed that "fluid" (i.e., memory and attention) skills would be most affected by daily stress, two analyses were conducted looking at the effects of daily stress on the set of neuropsychological measures of memory and attention (i.e., ATTN, immediate and delay LM scores, immediate and delay VR scores, and immediate and delay PA scores). Separate MANCOVA analyses were conducted using the different stress measures. In addition, another pair of MANCOVA analyses assessed the effects of daily stress on the set of "crystallized" neuropsychological measures (i.e., FSIQ, PIQ, VIQ, and WRAT-R Reading), with separate MANOVAs for the two stress variables. These 4 MANOVAs utilized the same IVs and covariate: the IVs were high and low stress AD subjects and high and low stress normal controls. Age was again used as a covariate. The main question was whether daily stress differentially affects the test performance of AD patients on the set of "fluid" neuropsychological measures.
Using the FREQ scores as the stress variable and the "fluid" measures as the DV, the combined DVs were significantly affected by group \([F(1,54) = 34.6, p<.05]\), suggesting that the normal control group did significantly better than the AD group on the set of "fluid" measures. Also, stress significantly affected the set of "fluid" measures \([F(1,54) = 3.0, p<.05]\), revealing that the low stress group did significantly better than the high stress group, collapsing across all subjects. However, the interaction between stress and group membership failed to achieve significance \((p>10)\), failing to provide evidence that stress differentially affected the performance of the AD group on the set of "fluid" neuropsychological measures.

When using the SUM scores as the measure of stress and the "fluid" measures as the DV, the set of DVs was significantly affected by group \([F(1,54) = 27.1, p<.01]\), with the AD group performing significantly worse than the normal control group. Also, the set of "fluid" measures was significantly affected by stress \([F(1,54) = 3.8, p<.01]\), with high stress subjects performing worse than low stress subjects. However, as with FREQ, the interaction of SUM and group membership failed to achieve significance \((p>10)\).

In regard to the set of "crystallized" neuropsychological measures, the MANCOVA using SUM as the
measure of stress revealed a significant effect for group 
\(F (4,53) = 8.40, p<.05\), but not for stress or the 
interaction of group and stress (both ps>.10). Similarly, 
when using FREQ as the measure of stress, the groups 
differed significantly across the set of "crystallized" 
neuropsychological group measures \(F (4,53) = 8.40, 
p<.05\), but stress and the interaction of stress and group 
failed to achieve significance (both ps>.10).

Overall, these results suggest that high stress 
individuals, as measured by SUM or FREQ, perform 
significantly worse than low stress individuals on 
measures of "fluid" abilities but not measures of 
"crystallized" abilities.

Does Daily Stress Differ Across the Course of AD?

Two separate t-tests were used to test whether 
reported levels of daily stress differed across the course 
of the Alzheimer's disease. Using the MMSE scores as a 
measure of disease severity, three stages of illness were 
established (mild, moderate, and severe). Because there 
were no clear points of separation in the MMSE scores, 
groups were split with the criterion that each group would 
have an equal numbers subjects (N=15), with subgroup MMSE 
scores of 23 and above, 18 to 22, and below 18. FREQ and 
SUM scores were then compared between the high and low 
disease groups. Neither t-test revealed significant
differences between the high and low disease severity (both ps>.10), failing to provide support for the notion that daily stress differs across the course of disease severity.

Is Daily Stress Related to the Performance of the AD Group, Controlling for Disease Severity?

Another pair of one-way MANCOVAs, one with SUM and one with FREQ, were conducted to determine whether daily stress affected AD group performance on the entire set of neuropsychological measures even after accounting for disease severity. As before, the AD patients were split into high and low stress groups based on both the FREQ and SUM scores, and two separate MANCOVAs were conducted with each stress variable as an IV. The DV was the set of neuropsychological tests scores (FSIQ, PIQ, VIQ, WRAT-R reading and arithmetic, FAS score, BNT score, Rey-O score, immediate and delay LM scores, immediate and delay VR scores, and immediate and delay PA scores). Finally, the covariate was disease severity, represented by MMSE scores. The effect of stress, as measured by FREQ or SUM, failed to significantly effect the combined set of DVs, controlling for MMSE (both ps>.10).

In addition, 4 MANCOVAs were conducted in which the IV (i.e., FREQ or SUM) and covariate (i.e., MMSE) remained the same but the DVs differed. The DV was either the set of "fluid" neuropsychological measures (i.e., ATTN,
immediate and delay LM scores, immediate and delay VR scores, and immediate and delay PA scores) or the set of "crystallized" measures (i.e., FSIQ, PIQ, VIQ, and WRAT-R Reading). All 4 MANCOVAs failed to achieve significant differences for the stress variable (all ps>.10) suggesting that daily stress, as measured by either SUM or FREQ, does not significantly affect the "fluid" or the "crystallized" neuropsychological measures in AD subjects after accounting for disease severity.
DISCUSSION

The main goal of this research was to examine the relationship between daily stress and neuropsychological test performance of normal and neurologically impaired (i.e., AD) elderly subjects. In examining the results of the MANCOVAs (page 58), one must conclude that daily stress did not appear to significantly influence the neuropsychological test performance of all subjects. This finding is not surprising in that many of the areas assessed in this study represented more "crystallized" skills (e.g., general intelligence, verbal intelligence, basic reading skills, etc.). However, it was expected that memory and attention would be the most adversely affected by daily stress as these areas are more "fluid" measures. Examination of the results of the MANCOVA (page 59) in which memory and attention scores served as the DV suggested that daily stress, as represented by either SUM or FREQ, significantly affected the performance of the subjects. A significant effect of daily stress was not observed when the DV was the set of "crystallized" measures alone. These findings strongly support the conclusion that certain cognitive abilities (e.g., tests of memory and attention/concentration) are affected by daily stress.
In Which Areas Does Daily Stress Account for the Most Variance?

The zero-order correlations between the daily stress measures and each of the neurological measures revealed a number of significant negative relationships between the stress scores and specific neuropsychological measures. This was particularly the case for the AD groups where all correlations were negative, suggesting that higher daily stress was related with lower scores. However, when the p-value was corrected to account for the number of correlations computed, no significant correlations were revealed. Therefore, replication of this study is certainly warranted to determine whether the observed correlations were spurious findings or a replicable relationship.

This study also proposed to examine the relative effects of stress on the specific neuropsychological tests across the AD and normal control subjects. Because the AD group was significantly older than the normal controls (difference in means of about 5 years), the relative effects of age needed to be held constant. As a result a series of hierarchical regression analyses were conducted. In examining the findings from the hierarchical analyses, one notes that daily stress, as measured by FREQ, accounts for a significant amount of variance in the normal control group's WRAT-R arithmetic scores (13.8%), immediate VR
scores (9.9%), delayed VR scores (9.0%), and attention scores (8.8%). Additionally, FREQ accounted for 8.2% of the variance in immediate VR scores of the AD group. Also, SUM accounted for 11.2% of the variance in immediate VR scores and 11.8% of attention scores for the AD group.

The implication of these findings is that the amount of daily stress an individual experiences should be considered in interpretation of scores on some neuropsychological tests, particularly attention and memory scores. Clearly, if daily stress accounts for almost 14 percent of the variance in an individual's performance on the WRAT-R arithmetic test, one's reported daily stress must be considered when interpreting this score. Additionally, daily stress accounted for significant variance in the WMS Visual Reproduction and attention scores of both the AD and normal control groups. In essence, this is convergent validity that daily stress is related to performance on immediate VR and attention tasks. Given the data presented here, one should consider daily stress as part of interpretation of these neuropsychological tests.

It is somewhat perplexing why the visual memory tasks appeared to be significantly related to reported daily stress, but the verbal memory tasks did not appear to be significantly related. While this question would be best
answered empirically, it may well be that the visual memory tasks involve a greater attentional component than the verbal memory tasks. Another logical question is the extent to which these specific results generalize and apply to neuropsychological tests other than the ones used in this study. Although research should address this issue, given the results of this study, one might expect to observe significant relationships between reported daily stress and many tests of attention/concentration and memory, particularly visual memory.

AD Versus Normal Controls

The results showed that the neuropsychological test performance of the two groups was statistically different, with the AD subjects obtaining significantly lower scores on the set of neuropsychological measures. Moreover, the AD group's performance was significantly worse than the normal controls on each of the neuropsychological test scores, with the exception of their WRAT-R reading scores. Notably, the WRAT-R reading score has been reported to be a good measure of premorbid intellectual functioning because of its relative stability across the course of dementing illnesses (Chehebar-Valdez, Mittenberg, & Levitt, 1992).

However, more specific comparisons were made between the AD and normal control group. The magnitude of the AD
group correlations was reliably greater than the normal control group correlations when using SUM as a measure of daily stress. Also, visual inspection of Tables 3 and 4 reveals that the correlations for the AD group are all in the predicted direction, whereas for the normal controls some variation is noted. Thus, the zero-order correlations provide some support for the hypothesis that the AD would be more greatly affected by daily stress.

Another important question was whether the magnitude of group differences would vary at greater or lesser degrees of reported daily stress. It was expected the performance of AD patients would be worse than normals at all levels of stress, with markedly worse performance noted at higher levels of reported stress among the AD but not the normal control group. Such a finding would have provided support for the notion that daily stress may exacerbate the cognitive difficulties of AD patients. While the results revealed that performance on the set of neuropsychological tests was different between groups, this performance differential did not vary as a systematic function of the high and low stress conditions. More importantly, the interaction between group membership and stress was nonsignificant, suggesting that the AD and normal controls did not perform differently when reporting high or low daily stress. However, the interaction
between group and stress scores approached a statistical
difference when using SUM as the stress measure. This
finding justifies further investigation of the hypothesis
that daily stress could differentially affect the test
performance of AD and normal control subjects. This
finding is also consistent with the previously discussed
result of greater zero-order correlations between SUM and
the neuropsychological test scores for the AD group
relative to the normal controls. Therefore, re-
examination of this potential relationship certainly seems
warranted.

A similar question was whether cognitive functioning
in the AD patients reporting higher levels of daily stress
would be more greatly impaired than those reporting lower
levels of stress, even after controlling for the relative
severity of their disease. The results failed to support
this conclusion for performance on the total set of test
scores or the subset of memory and attention scores.
Disease severity was strongly related to test performance
and removing the variance accounted for by MMSE left
little to be accounted for by daily stress.

Daily Stress Across the Course of AD

In regard to the amount of daily stress each group
reported, a nonsignificant difference for FREQ scores and
a significant difference for the SUM scores was noted.
This pair of findings suggests that the AD group reported significantly more distress to a relatively comparable number of daily stressors. Given that AD patients are generally considered to have poor insight and relative unawareness to life changes (Mangone et al., 1991), this is somewhat surprising finding. One implication of this finding is that AD patients may require assistance in coping with daily stressors, in the form of skills training or supportive psychotherapy.

Having demonstrated that AD subjects report significantly greater distress following daily stressors, the present study attempted to determine if AD subjects reported different amounts or different reactions to stressors across the clinical course of AD. Given that AD results in numerous life changes, especially physical and mental limitations, it was expected that the frequency of stressful life events would increase in more advanced stages of the disease. However, the results did not support the conclusion that the amount of daily stress varies across the course of the disorder. In comparing the most and least severe subjects with AD (as measured by MMSE), no difference was noted between them in FREQ or SUM scores.

There are several possibilities why a significant relationship between daily stress and the course of AD was
not observed. It may have been that the different levels of disease severity may not have been that different in regard to severity. However, given that MMSE has been demonstrated to correlate with disease severity (Burns et al., 1991) and the high and low severity groups represented the upper and lower thirds of the AD group, it is not likely that the two groups were more similar than different regarding disease severity. Alternatively, AD patients have been shown to be less cognizant of changes as the disease progresses (Mangone et al., 1991). It may well have been the case that the AD subjects did not report more stressors or greater response to the stressors because they were less aware of them. While assessing individuals longitudinally across several years may help to answer this question, longitudinal studies will not be able to control for the lack of insight or awareness that increases across the course of the disorder. Perhaps, independent observers (e.g., family members trained to complete the questionnaires for the AD subjects) would allow one to get an accurate indication of this relationship.

Directions for Future Research

Overall, the results of this study provide some support for the contention that daily stress affects neuropsychological test performance. Nonetheless,
replication of the results is necessary and several changes could be instituted to make conclusions more certain. In addition to the recommendations proposed already, future research should seek to make several improvements including:

(1) More sensitive measures of cognitive skills should be used in future research. The main purpose of this study was to assess how much variance was accounted for by daily stress in tests which are most commonly used in neuropsychological assessments. It would be interesting to assess the effects of daily stress on more sensitive measures of attention and memory. For instance, the Buschke-Fuld Selective Reminding Test is a much more sensitive measure of verbal memory than the semantic story of the WMS (Spreen & Strauss, 1991). Also, the Paced Auditory Serial Addition Task (Gronwall, 1977) is an extremely sensitive measure of attention and concentration skills (Gronwall & Wrightson, 1981). Given the findings with relatively gross measures of memory and attention, it would be interesting to assess the amount of variance accounted for in performance on more sensitive measures.

(2) A similar modification would be to use tests with a broader range of scores. Intuitively, daily stress may account for more variance in performance if there is a greater range of true variance in test scores.
(3) In order to make more firm conclusions regarding the effects of daily stress on the onset or course of AD, longitudinal studies will be necessary. While the relationship between daily stress and AD appeared to be a modest one, the findings support the need for additional examination of this relationship. Longitudinal studies would allow more firm conclusions regarding this relationship.

This study provided several strong indications that daily stress accounts for variance of scores on certain neuropsychological tests. There was also some weaker indications that daily stress had a relatively greater relationship to the performance of AD patients relative to normal controls. If the modifications in the research design suggested above are implemented, future studies are likely to replicate, and perhaps extend, the findings of this study.
REFERENCES


APPENDIX A

DIAGNOSTIC CRITERIA FOR DEMENTIA


1. The criteria for the clinical diagnosis of PROBABLE Alzheimer's disease include:
   a) dementia established by clinical examination and documented by neuropsychological examination;
   b) deficits in two or more areas of cognition;
   c) progressive worsening of memory and other cognitive functions;
   d) no disturbance of consciousness;
   e) onset between ages 40 and 90, most often after age 65; and
   f) absence of systemic disorders or other brain diseases that in and of themselves could account for the progressive deficits in memory and cognition.

2. The diagnosis of PROBABLE Alzheimer's disease is supported by:
   a) progressive deterioration of specific cognitive functions such as language, motor skills, and perception;
   b) impaired activities of daily living and altered patterns of behavior;
   c) family history of similar disorders, particularly in confirmed neuropathology; and
d) laboratory results of:
- normal lumbar puncture as evaluated by standard techniques,
- normal pattern or nonspecific changes in EEG, and
- evidence of cerebral atrophy on CT with progression documented by serial observation.

3. Other clinical features consistent with the diagnosis of PROBABLE Alzheimer's disease, after exclusion of causes of dementia other than Alzheimer's disease, include:
   a) plateaus in the course of progression of the illness;
   b) associated symptoms of depression, insomnia, incontinence, delusions, illusions, hallucinations, catastrophic verbal, emotional, or physical outbursts, sexual disorders, and weight loss;
   c) other neurologic abnormalities in some patients, especially with more advanced disease and including motor gaits such as increased muscle tone, myoclonus, or gait disorder;
   d) seizures in advanced disease; and
   e) CT normal for age.

4. Features that make the diagnosis of PROBABLE Alzheimer's disease uncertain or unlikely include:
   a) sudden, apoplectic onset;
b) focal neurological findings;
c) seizures or gait disturbances at the onset or very early in the course of the illness.

5. Clinical diagnosis of POSSIBLE Alzheimer's disease:
   a) may be made on the basis of the dementia syndrome, in the absence of other neurologic, psychiatric, or systemic disorders sufficient to cause dementia, and in the presence of variations in the onset, in the presentation, or in the clinical course;
   b) may be made in the presence of a second systemic or brain disorder sufficient to produce dementia, which is not considered to be the cause of the dementia; and
   c) should be used in research studies when a single, gradually progressive severe cognitive deficit is identified in the absence of other identifiable cause.

6. Criteria for diagnosis of DEFINITE Alzheimer's disease are:
   a) the clinical criteria for probable Alzheimer's disease and
   b) histopathologic evidence obtained from a biopsy or autopsy.

7. Classification of Alzheimer's disease for research purposes should specify features that may differentiate
subtypes of the disorder, such as:

a) familial occurrence;
b) onset before age of 65;
c) presence of trisomy-21; and
d) coexistence of other relevant conditions such as Parkinson's disease.
APPENDIX B

CONSENT FORMS

(1) Consent form for the patient group:

__________________________

Patient Name

__________________________

Subject number

NORTH BROWARD MEMORY DISORDER CENTER

201 E. SAMPLE ROAD

POMPANO BEACH, FLORIDA 33064

(305) 786-7392

We would like your permission to provide information collected by the North Broward Memory Disorder Center to be released to the Department of Psychology at Louisiana State University. This information will be used in conjunction with a research project being conducted at Louisiana State University.

Individuals who agree to participate in this project will not be treated in any way that is different from other patients at this clinic. Participation will not in any
way affect or otherwise alter medical care received at this clinic. You may refuse to participate or withdraw your consent at any time without jeopardizing, in any way, your medical treatment at this clinic in the present or future.

All medical information and test scores, names and addresses will be kept strictly confidential. The subject number listed above will be the only identifier listed on record forms.

__________________________     ____________
Signature                  Date

__________________________     ____________
Witness                    Date

(2) Consent form for the normal control group:

__________________________
Patient Name

__________________________
Subject number

We would like your permission to provide information collected during this testing session to be released to
the Department of Psychology at Louisiana State University. This information will be used in conjunction with a research project being conducted at Louisiana State University.

You may refuse to participate or withdraw your consent at any time.

All information and test scores, names and addresses will be kept strictly confidential. The subject number listed above will be the only identifier listed on record forms.

__________________________  ________________
Signature                        Date

__________________________  ________________
Witness                          Date
VITA

Mark Edward Todd was born on June 6, 1963 in Miami, Florida, the first child of three. He spent his formative years in South Florida before leaving to earn a Bachelor's Degree at Furman University in Greenville, South Carolina, with a major in biology. His interests then evolved towards psychology and he earned a Master's Degree from Wake Forest University located in Winston-Salem, North Carolina, with a major in general psychology. Following a year of specialized training with a neuropsychologist in Winston-Salem, Mark set off to the Bayou Country to finish training in clinical neuropsychology. He completed his doctorate at Louisiana State University in Baton Rouge, Louisiana. It was also at LSU that he met Angela Waguespack, a doctoral candidate in School Psychology. Mark and Angela married in August of 1993. He completed a clinical internship at Baylor College of Medicine in Houston, Texas, before returning to his childhood stomping grounds. He currently lives with his wife in South Florida and works as a neuropsychology resident.
Candidate: Mark E. Todd

Major Field: Psychology

Title of Dissertation: The Relationship Between Daily Stress and Neuropsychological Test Performance

Approved:

Wm. Drew Gower
Major Professor and Chairman

Dean of the Graduate School

EXAMINING COMMITTEE:

Date of Examination:

January 13, 1995