EFFECTIVENESS OF THE NEUROBEHAVIORAL COGNITIVE STATUS EXAMINATION IN ASSESSING ALZHEIMER'S DISEASE

DISSERTATION

Presented to the Graduate Council of the University of North Texas in Partial Fulfillment of the Requirements

For the Degree of

DOCTOR OF PHILOSOPHY

By

Normand B. Begnoche, M.S.
Denton, Texas
December, 1996
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Accurate, early diagnosis of Alzheimer's Disease is becoming increasingly important in light of its growing prevalence among the expanding older-aged adult population. Due to its ability to assess multiple domains of cognitive functioning and provide a profile of impairment rather than a simple global score, the Neurobehavioral Cognitive Status Examination (NCSE) is suggested to better assess such patterns of cognitive deficit for the purpose of diagnosis. The performance of the NCSE was compared with that of the Mini-Mental State Examination (MMSE) for diagnostic sensitivity in a sample of patients diagnosed as having probable Alzheimer's Disease. The strength of correlation between severity of cognitive impairment on these tests and report of behavior problems on the Memory and Behavior Problems Checklist (MBPC) was also explored, as was performance on the NCSE and report of behavior problems using the MBPC in predicting Single Photon Emission Computed Tomography (SPECT) scan results.
The NCSE was found to exhibit greater sensitivity to physician diagnosis of probable Alzheimer’s Disease relative to two versions (Serial 7’s or WORLD) of the MMSE (.90, .77 and .68, respectively). While both measures were found to correlate significantly with the report of behavior problems, only a moderate proportion (NCSE = .22 and MMSE = .33) of the explained variance was accounted for by either test. Severity of cognitive impairment on the NCSE was found to be significant, though small in estimate of its effect size, for predicting the absence/presence of pathognomonic findings on SPECT scans. In contrast, the report of behavior problems on the MBPC did not significantly predict SPECT scan outcomes.

The NCSE would appear to be a sensitive tool for the identification of the extent and severity of cognitive impairment found among demented individuals; however, it may be "over"-sensitive to such diagnosis. Although relationships between cognitive impairment and behavior problems and/or neuroradiological findings are observed, their meaningfulness remains with the need for further, more detailed, study using standardized criteria for comparison purposes.
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Overview

The trends observed in the aging of the general population and the associated increase in dementia prevalence create significant issues for the public as a whole. Morris (1994) described dementia as a "public health problem of enormous proportions, both in monetary terms... and in the emotional and physical toll it exacts from families and caregivers" (p.71). The economic costs for the medical treatment and care of individuals diagnosed with dementia are burgeoning. Estimates in the United States alone suggest that the cost of dementia care is rapidly approaching 100 billion dollars annually (Berg, 1994; Morris, 1994). In addition to the personal difficulties endured by those individuals diagnosed with dementia are those burdens experienced by their caregivers, as it is estimated that approximately 80% of dementia patients are cared for by others in the community, primarily female relatives (Hart & Semple, 1990). The impact on caregivers can include poorer health, increased, stress, a higher incidence of depression, and an overall lower satisfaction with life (Hart & Semple, 1990). Particularly problematic
for dementia patients and their caregivers during the progression of the disease is the presentation of a variety of cognitive, emotional, and behavioral disturbances.

**Epidemiology of Dementia**

With the expanding growth of the older aged adult population, particularly in the latter half of this century, the prevalence of many illnesses commonly associated with this population is growing as well. Albert (1988) observed that "half of the people who have lived past the age of sixty-five since the beginning of recorded history are alive today" (p.3). It is expected that in the next twenty-five years the overall population of the sixty-five years and older age group will expand to two and a half times their number of fifteen years ago (Mortimer & Hutton, 1985), and three times their number for those eighty and older (Henderson, 1987).

Among such illnesses afflicting the older aged adult population is dementia, estimated to directly affect approximately ten to twenty percent of the population of older aged adults over sixty-five (Mortimer, Schuman, & French, 1981). These estimates suggest that approximately two and a half million individuals in this age group in the United States alone are affected by dementing disease (Morris, 1994). The incidence of dementia in the older aged adult population has been observed to increase with advancing age (Treves, 1991), to the point of affecting
twenty to forty percent of individuals over eighty years old (Cummings & Benson, 1992). However, it is the increasing longevity of the older adult population as a whole that also contributes to the growing number of individuals being diagnosed with dementia. The observation that the prevalence and risk for developing dementia increases exponentially with age (Jorm, Korten, & Henderson, 1987) predicts that an even greater number of individuals will be afflicted with this disease over the next century as the older aged population grows and survives longer (Mortimer & Hutton, 1985).

**Diagnosis of Dementia**

Dementia is rather universally defined as an acquired and sustained syndrome that is marked by a deterioration in two or more areas of intellectual functioning (Moss & Albert, 1988; Cummings & Benson, 1992; Morris, 1994). These areas include: language, memory, visuospatial skills, emotion or personality, abstraction, calculation, judgement, and executive functions, among others (Cummings, Benson, & LoVerme, 1980). Dementia is distinguished from congenital syndromes such as mental retardation in that the latter is not acquired; single, focal, neuropsychological disorders such as aphasia and amnesia; and delerium states, which typically occur with a reduction of consciousness (Cummings & Benson, 1992).
Diagnostic criteria for the diagnosis of dementia was first introduced in the Diagnostic and Statistical Manual of Mental Disorders, Third Edition (DSM III) (American Psychiatric Association [APA], 1980), setting a standard upon which physicians could uniformly rely for diagnosis. Now in its fourth edition (American Psychiatric Association [APA], 1994), the DSM IV stipulates that:

The essential feature of a dementia is the development of multiple cognitive deficits that include memory impairment and at least one of the following cognitive disturbances: aphasia, apraxia, agnosia, or a disturbance in executive functioning. The cognitive deficits must be sufficiently severe to cause impairment in occupational or social functioning and must represent a decline from a previously higher level of functioning. (p. 134)

The development of multiple cognitive deficits and resulting occupational and/or social impairments are required criteria for diagnosis of all but a few rare dementia-like conditions. Most dementia disorders share a common symptom presentation, but are typically differentiated on the basis of etiology (APA, 1994).

Of the major types of dementing disorders Alzheimer's Disease (AD) is recognized as the major cause of dementia (Berg, 1994), representing fifty to sixty-five percent of dementia cases. Also the most common of primary
degenerative dementias, AD shares with these forms of dementia a pattern of insidious onset and progressive decline. A far second in its incidence among the dementias is vascular dementia, of which Multi-Infarct Dementia (MID) is most prevalent, comprising eleven to twenty percent of all dementia cases (Katzman, 1982; Tomlinson, Blessed, & Roth, 1970). As with the other vascular dementias, MID is the result of cerebrovascular disease, either in the form of focal strokes, multiple embolic infarcts, or multiple lacunar infarcts (Funkenstein, 1988). Multi-Infarct Dementia presents suddenly, with a rather focal pattern of cognitive deficits, and is observed to progress with a step-wise pattern of deterioration. This pattern of onset and progression is considered to be the result of cognitive deterioration due to multiple cerebral infarctions and hemorrhages over time (Hachinski, Lassen, & Marshall, 1974). The clinical diagnosis of dementia relies upon several resources, including a thorough gathering of history, medical and neurological examination, laboratory tests, and neuropsychological evaluation.

Alzheimer’s Dementia (AD)

The most common of all forms of dementia, AD is now recognized as the fourth leading killer among Americans over the age of sixty-five (Chawluk & Alavi, 1995). Alone, it is estimated to affect ten percent of all individuals in this age group, suggesting that as many as four million
individuals are afflicted with the disease. Established risk factors for AD include advancement of age, a positive family history of the disease, and concommitent diagnosis of Down’s Syndrome (Berg, 1994). Other possible genetic and environmental causes remain hypothetical and continue to be investigated.

The establishment of specific diagnostic criteria for Alzheimer’s Disease by the National Institute of Neurological and Communicative Disorders, and Stroke (NINCDS)/Alzheimer’s Disease and Related Disorders Association (ADRDSD) work group (McKhann, Drachman, Folstein, Katzman, Price, & Stadlin, 1984) has aided in the differential diagnosis of the disorder from other forms of dementia. Relatively similar to NINCDS/ADRDSD criteria in its standards for diagnosis (Graves & Kukul, 1994), The DSM IV (APA, 1994) characterizes "Dementia of the Alzheimer’s Type" as having a "...gradual onset and continuing cognitive decline", and that the "...cognitive deficits..." cannot be attributed to "...other central nervous system conditions that cause progressive deficits in memory and cognition" (p. 142). Berg (1994) stipulated that "AD is strictly defined as the combination of clinical dementia and characteristic histological abnormalities detected upon examination of brain tissue" (p.229). Essentially, assumptions are made regarding the diagnosis of AD based upon medical, laboratory, and neuropsychogical findings; whereas, actual
accurate diagnosis to date can only be confirmed post-mortem upon examination of the brain tissue. The neuropathological markers for definitive diagnosis of Alzheimer’s Disease include the abundant presence of neurofibrillary tangles and neuritic plaques under microscopic examination of the brain tissue at the time of autopsy (Berg, 1984; Moss & Albert, 1988). Many contend that it is the combination of clinical and histological evidence that provides for definitive diagnosis of AD (Moss & Albert, 1988). The possibility that other characteristic changes in the brain, such as neuronal loss, neurotransmitter and peptide depletion, and deposits in the cerebral vasculature, remains under investigation through ongoing post-mortem research (Hollander, Mohs, & Davis, 1986).

As with most other forms of dementia, clinical evaluation of AD must be relied upon for the initial diagnosis and subsequent treatment and care of those individuals presenting with established symptoms. Cummings & Benson (1992) suggested that the timing and sequence of cognitive deficits and behavioral problems are important guidelines for clinical diagnosis. Standard in the presentation of patients and their families is the retrospective report of a gradual decline in memory functioning or overall productivity (Berg, 1994). Indeed, complaint of a memory disturbance is typically the initial
cognitive deficit to mark the onset of AD (Cummings & Benson, 1992). Though not nearly as common as a first symptom, evidence of visuospatial problems and language dysfunction often follow reports of forgetfulness and the inability to learn new information. As the disease progresses to moderate stages a broader range of other cognitive deficits follow and independent day-to-day functions begin to more noticeably decline. Behavioral difficulties also become more prominent, in the form of pacing and disturbed gait, possible hallucinations and paranoid thinking, and increasing aggressive and assaultive behaviors (Swearer, 1994). As the decline progresses to advanced stages, individuals begin showing significant drops in their expression of remote memory and intellectual functioning, confusion and incontinence develops, they may become mute, unable to feed themselves, and their range of consciousness narrows.

Clinical diagnosis of AD is typically aided through the use of various neuropsychological measures such as the Mini-Mental Status Examination (MMSE) (Folstein, Folstein, & McHugh, 1975), which can indicate an average of 3-4 points on the MMSE lost annually over the course of a typical 8-10 year decline (APA, 1994). Serum laboratory tests are not as helpful in confirming diagnosis of AD but help in ruling out other possible origins for the symptom presentation.

Neuroradiological imaging techniques (i.e., CT, MRI, PET,
SPECT) have also become increasingly helpful in the differential diagnosis of dementia.

Assessment of Cognitive Impairment in Dementia

It is often the complaint of memory problems, or some other form of cognitive difficulty that is known to accompany the onset of dementia, that brings the patient or their family to seek medical evaluation for the individual. Recall that the DSM IV (APA, 1994) diagnostic criteria requires the observation of "multiple cognitive deficits" (p. 142) for the diagnosis of dementia to be made. The acquisition of a thorough cognitive history, including information regarding the types of problems exhibited by the patient, symptom onset, and the progression of behavioral change, are helpful in determining diagnosis (Albert, 1988). The assessment of cognition for the absence or presence of impairment is necessary not only for diagnosis, but is also helpful in monitoring the progression of dementing disease. It is for these reasons that formal tests of cognitive functioning are also necessary for proper evaluation and diagnosis of the demented patient. A comprehensive battery of neuropsychological tests should be expected to include measures that assess attention, memory, language, visuospatial ability, and conceptualization (Albert, 1988; Zec, 1993). Despite the availability of lengthy and thorough neuropsychological evaluations for the assessment of cognitive impairment, a number of brief screening tests
are more commonly used in medical clinic settings. This is in response to the need of rather quick, easy to administer, and simple to understand measures that can still provide an accurate and reliable indication of the absence or presence and severity of dementia. It is for these same reasons that brief cognitive screening measures are commonly used in the research literature in that they quickly and easily assess cognitive decline in patients and its progression over repeated measurements.

Among the most widely used mental status exams is the MMSE (Folstein, Folstein, & McHugh, 1975). Relatively quick and easy to administer, the MMSE is comprised of several short items that assess orientation, registration, attention, calculation, recall, language, and praxis (Folstein et al., 1975). Successful completion of these items produces a total score that ranges from 0 to 30, with 30 being an errorless score. An MMSE score of 23 or lower is considered indicative of dementia (Kluger & Ferris, 1991). Folstein et al.’s (1975) original reliability and validity studies utilizing the MMSE indicated the instrument to be an effective tool in the diagnosis of dementia. Subsequent research has also supported the validity of the MMSE with a variety of populations (Feher et al., 1992; Uhlmann & Larson, 1991). However, concerns have also been expressed regarding the MMSE’s susceptibility to the confounding effects of education (Anthony et al., 1982) and
questionable sensitivity for detecting subtle forms of dementia or focal deficits, the latter being responsible for findings of higher false-negative rates (Nelson, Fogle, & Faust, 1986). The fact that the MMSE and similar screening tests provide a single score for determination of the absence or presence of cognitive impairment and its severity has been cited as one of the reasons for their difficulties with sensitivity (Schwamm et al., 1987). The problem with tests that provide a single global cutoff score is that they can often overlook specific deficits that may be indicative of impairment even when the total score falls within the non-impaired range.

Calls for greater emphasis on assessing a comprehensive range of independent areas of cognitive functioning (Albert, 1988; Lezak, 1983) have led to the introduction of screening measures such as the Neurobehavioral Cognitive Status Examination (NCSE) (Kiernan, Mueller, Langston, & Van Dyke, 1987). The NCSE assesses several cognitive domains independent of each other, including four measures of language (fluency, comprehension, repetition, and naming), constructional ability, memory, calculation, and verbal reasoning in the form of a similarities task and a judgement measure. The test begins with separate orientation and attention items in order to provide a quick assessment of the patient's level of consciousness. Through the use of a "screen and metric approach" for all but the orientation and
memory subtests (Kiernan et al., 1987), which requires initial completion of particularly difficult item before moving on to the next subtest, testing time is shortened considerably for the cognitively intact person. In contrast, failure of the difficult screen item results in the required completion of a graded series of test items within the subtest to provide a more quantitative and qualitative evaluation. In addition to the original standardization group of sixty adult volunteers (ages 20 to 39 and 40 to 66) with no history of medical, neurological, or substance use problems, data were collected on a group of fifty-nine geriatric volunteers (ages 70 to 92) who were also screened for medical problems. These standardization samples produced a normative profile range, which is visually displayed on the front of the test protocol for scoring and review. Slight corrections are provided on the Constructions, Memory, and Similarities subtests to accommodate the broader "normal" performance range of the geriatric group (Kiernan et al., 1987).

To determine the sensitivity of the NCSE in detecting the absence or presence of cognitive impairment, Schwamm, Van Dyke, Kiernan, Merrin, and Mueller (1987) found the measure to be highly sensitive to even minor deficits in twenty-eight of thirty neurosurgical patients with confirmed lesions for a false-negative rate of seven percent. The additional administration of the MMSE and CCSE (Jacobs,
Bernhard, Delgado, & Strain, 1977) in the Schwann et al.
study (1987) revealed these latter screening tests to have
false-negative rates of forty-seven and fifty-seven percent,
respectively. The greater sensitivity of the NCSE was
attributed to the advantages described above. Subsequent
studies have found favor with the utilization of the NCSE
over the MMSE in screening for cognitive impairment in
geriatric patients (Fields, Fulop, Sachs, Strain, & Fillit,
1992; McBride-Houtz, 1993), and in predicting functional
status change in stroke patients (Mysiw, Beegan, & Gatens,
1989).

Behavior Problems in Dementia

Behavioral disturbances are also a common and expected
component of the dementia symptom picture. It has become
readily understood that patients with dementing disorders
will exhibit behavior problems during the course of the
disease, and they are often among the initial presenting
complaints for patients and their families seeking medical
evaluation (Gilley, 1993). Little attention has been paid
to the issue of problem behaviors in dementia. More
recently, investigators have made a concerted effort to
better understand, classify, and measure the variety of
behavioral disturbances that individuals diagnosed with
dementia present. Doing so is particularly important in
light of the positive relationship recognized between the
frequency and severity of behavior problems and both
caregiver burden and the decision to institutionalize dementia patients (Zarit & Zarit, 1983). Swearer (1994) provided a comprehensive review of the efforts that have been made to determine the various types of behavior problems exhibited by patients with dementing disease and reported by their caregivers, their prevalence, and their impact upon the caregivers. The various types of behavior problems reported among dementing disorders are grouped by many into four categories: aggressive and assaultive behaviors, disordered thinking and personality changes, mechanical and motor abnormalities, and vegetative disorders (Drachman, Swearer, O'Donnell, Maloon, & Mitchell, 1992). The highest prevalence within each of these categories, respectively, are verbal attack and rage reactions, hallucinations and delusional thoughts, pacing and hyperkinesia, sleep and appetite changes and incontinence (Swearer, 1994).

Research in the area of behavioral disturbances has tended to focus primarily on their relationship to several other features associated with dementia such as demographic factors, previous history, diagnosis, and disease severity (Swearer, 1994). Of the over one hundred various geriatric rating scales that assess behavior problems in various capacities (Isreal, Lozarevic, & Sartorious, 1984), many are not designed to measure dementia related behavior problems. Others, including the Memory and Behavior Problems Checklist
(MBPC) (Zarit & Zarit, 1983), the Caretaker Obstreperous Behavior Rating Assessment (COBRA) Scale (Drachman et. al., 1992), and the Behavior Problems Checklist (BPC) (Teri, Borson, Kiyak, & Yamgishi, 1989) are specific to the geriatric population diagnosed with dementia and their caregiver's perception of burden. Much of the recent literature in this area has focused on the prevalence of various behavior problems within and across the several forms of dementia (Gilley, 1993). However, few specific behavior problems have been found to be consistently related to dementia type (Swearer, 1994). Attempts to link the severity of cognitive impairment with behavior problems has also produced mixed results. In his review of the literature in this area, Gilley (1993) observed that "the overall level of cognitive impairment provides limited prediction of the presence and severity..." (p. 129) of selected behavioral disturbances.

Some of the relationships found between the frequency and severity of behavior problems and cognitive impairment include Folstein, Folstein and McHugh's (1975) finding of an association between MMSE scores and physician ratings of behavior problems. However, earlier studies such as this lacked more operationally defined and standardized assessment of behavior problems and for the recording of problem frequency and severity. Kurita, Blass, Nolan, Black, and Thaler (1993) obtained data on patient
performance on the MMSE and two dementia rating scales, the latter from which derived behavior scales were extrapolated. These authors reported respectable and significant correlations between decreasing MMSE scores and various indices of behavior ranging from -0.52 (negative personality changes) to -0.82 (decreased social interaction). In contrast, Cooper, Mungas, and Weiler (1990) reported "relatively low" (p. 868) correlations between the number of abnormal behaviors exhibited by Alzheimer’s patients and declining MMSE scores, adding that "other as yet unproven factors may play an as large or greater role than MMSE score in predicting such behaviors" (p. 867). More specific with regard to problem behaviors, Swearer, Drachman, O’ Donnell, and Mitchell (1988) found a significant relationship between dementia severity and the presence and severity of various types of disruptive behaviors. Performance on a mental status test was found to have a significant negative correlation with assaultive and violent behaviors. Consistent with these findings was Cohen-Mansfield, Marx, and Rosenthal’s (1990) report of a strong relationship between agitated behavior and both overall cognitive impairment and activities of daily living. In contrast, Teri, Borson, Kiyak, and Yamagishi (1989) found no relationship of significance between behavior problems and overall level of cognitive impairment.
Neuroimaging in Dementia

With the introduction of Computed Tomography (CT) in the 1970's it has become possible to noninvasively view the brain for the purposes of diagnosis and research (Wippold II, 1994). Today, CT remains the preferential choice for viewing anatomical structures within the brain. Its ability to differentiate tissues of varying densities within the cerebrum from cerebrospinal fluid provides an effective means of assessing ventricular size and volume (Charletta, Bennett, & Wilson, 1993). Unaffected by many of the imaging artifacts that hamper CT scans, Magnetic Resonance Imaging (MRI) offers several advantages, including its greater sensitivity to tissue composition and the resulting ability to distinguish between areas of similar density on the image produced (Charletta, Bennett, & Wilson, 1993). Its sensitivity to identifying even subtle white matter disease changes makes it a common choice for evaluation of vascular diseases such as MID. A "second revolution" (Parks, Haxby, & Grady, 1993, p. 460), in neuroimaging has created the ability to view various physiological and biochemical processes in the brain via nuclear imaging techniques. The introduction of Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT) provides functional information regarding metabolism in the brain that is not obtainable from the structural images produced by older scanning techniques such as CT and MRI. Through
the observation of metabolism for indices such as cerebral blood flow, oxygen consumption, and glucose consumption, researchers have been able to isolate areas of dysfunction or disease by noting the reduction in, or absence of, normal flow or consumption rates in focal areas of the brain. Indeed, it is argued that functional brain imaging, such as that provided by PET and SPECT, should become part of the diagnostic evaluation for dementia, replacing CT and MRI (Griffeth & Royal, 1994).

Implementing neuroimaging as a required part of the evaluation process, though desirable, remains a significant cost-benefit issue, particularly in the use of the newer and more expensive technologies. Though less costly and more readily available, CT and MRI scans may provide only limited diagnostic information; whereas, the location of relatively few PET scanners in this country places the cost and availability of such imaging out of reach for most physicians and their patients. The observation that scanning newly diagnosed dementia patients has resulted in the finding of treatable causes in up to 10% of cases led Wippold II (1994) to conclude that the imaging of individuals with atypical presentations of dementia is a reasonable benefit which outweighs its cost. Despite their considerably greater expense, lower spatial resolution, and poorer specificity, the use of PET scans continues to grow in both dementia research and evaluation settings as the
equipment becomes more available. Not nearly as hampered by cost and availability, the use of SPECT also continues to grow, though it shares with PET many of the same problems with regard to resolution and specificity.

There appears to be a general consensus that functional brain imaging can reliably differentiate between normal individuals and those suffering from moderate to severe dementia (Tikofsky, Hellman, & Parks, 1993), and particularly so from the diagnosis of AD (Parks, Haxby & Grady, 1993). Common to analyses of PET scans of AD patients is the finding of hypometabolism in the temporoparietal region, with subsequent deterioration typically observed in the frontal areas (Griffeth & Royal, 1994). Holman, Johnson, Gerada, Carvalho, and Satlin (1992) reported similar findings for SPECT scans, noting an approximate eighty percent sensitivity to AD diagnosis when posterior temporal lobe or parietal lobe defects are considered. Although many physicians still rely primarily on the MRI for differential diagnosis of MID, AD and MID are typically differentiated on PET and SPECT scans by the more general and symmetrical areas of reduced metabolism characteristic of AD and the rather asymmetrical, scattered patterns of multiple deficits common to MID (Bartolini, Gasparetto, & Loeb, 1990). Though not as reliably, attempts have been made to determine consistent patterns of absent or reduced metabolism in other forms of dementia, including
Pick's Disease, Huntington's disease (Parks, Haxby, & Grady, 1993), Parkinson's disease, and Creutzfeldt-Jakob disease (Griffeth & Royal, 1994).

Correlational studies reviewing the relationships between the regional effects of dementia on functional brain scans with patient performance on large batteries of neuropsychological tests have yielded interesting results. DeLeon et al. (1983) correlated the severity of deficits observed on PET scans with a rating of the overall severity of dementia and with the severity of specific cognitive deficits. Other correlations have been found for patients diagnosed with AD between left-sided temporoparietal region deficits and verbal test scores (Riege, Metter, & Kuhl, 1985) and with left-frontal lobe hypoperfusion and verbal I. Q. scores (Friedland et al., 1983). More recently, various cognitive activation studies, which assess brain metabolism during completion of a cognitive task, have been of primary interest, in the hope that relationships can become understood within and between particular focal regions of the brain and specific cognitive skills.

Rationale for the Present Study

Several investigations have been reported in the literature (cited earlier in this review) regarding the sensitivity, specificity, and predictive value of the MMSE with a variety of dementia outcome measures (i.e., diagnosis, severity, behavior problems, functional ability,
neuroimaging results). Relatively new to the arena of screening assessment in dementia, early investigations utilizing the NCSE have provided some indication that it may be more accurate and clinically useful than the MMSE in predicting diagnosis and possibly even outcomes. However, the current literature lacks such information in several areas (i.e., diagnosis and severity, behavior problems, neuroimaging), particularly with regard to dementia diagnosis. In order to become an even more useful tool as part of the initial dementia work-up, and in the measurement of dementia progression, an investigation of the NCSE's ability to detect impairment consistent with diagnosis of dementia, particularly in comparison to the widely used MMSE appears indicated.

With the ability to provide more than a simple global measure of impairment, the NCSE offers the opportunity to assess and observe dementia from the perspective of multiple cognitive domains. This provides the investigator with the ability to search for and observe the possibility of relationships between independent areas of cognitive functioning and the outcome measures described above without resorting to the lengthy and often costly task of administering a comprehensive neuropsychological test battery. The importance of this is found in the calls for greater understanding and predictability in the relationship between patterns of cognitive deficit and patterns of
reported behavior problems (Swearer et al, 1988; Teri et al, 1989). Patients, caregivers, and medical professionals may benefit greatly in the understanding of such relationships by being able to have a better expectation of behavior problems and subsequent functional ability based on the observation of specific patterns of cognitive deficits. Developing a greater understanding of similar relationships between laboratory findings on neuroimaging scans and patterns of cognitive impairment may provide similar information.

Hypotheses for the Present Study

1. It is hypothesized that the NCSE will identify as diagnostically impaired (scores in the impaired range on the memory subtest and one other subtest) a greater number of patients diagnosed by their physician as having probable Alzheimer’s Disease than the MMSE (score of 23 or less).

2. There will be a significant positive correlation between the total number of NCSE subtests falling in the impaired range and the number of reported behavior problems on the MBPC; whereas a significant negative correlation is expected between MMSE summary scores and the number of reported behavior problems on the MBPC. Furthermore, there will be significant negative correlations between the 10 NCSE subtest scores and the number of reported problem behaviors (items checked as occurring once or more) on the MBPC.
3. There will be a statistically significant difference in the number of subtests on the NCSE falling in the impaired range when comparing patients with normal SPECT scans versus those with abnormal SPECT scans. There will also be a statistically significant difference in the number of reported behavior problems on the MBPC when comparing patients with normal SPECT scans versus those with abnormal SPECT scans.
CHAPTER II

METHOD

Subjects

Subjects for the present study were obtained from the patient files of the Division on Aging Geriatrics Clinic at the University of Arkansas Center for Medical Sciences (UAMS). Typically referred by primary care physicians or family, patients present to the Geriatrics Clinic on an outpatient basis for evaluation of a variety of medical problems associated with the older aged adult population, including suspected dementia and/or related conditions. Thorough review of the Geriatrics Clinic files revealed 120 subjects who had been given a primary diagnosis of probable Alzheimer’s Dementia by the attending physician. Physician diagnosis was determined upon review of dementia work-up findings (patient history and report of symptoms, serum laboratory results, neuropsychological test scores, and MRI and SPECT scans) according to NINCDS/ADRDA (McKhann et al, 1984) and DSMIV (APA, 1994) diagnostic criteria. Prospective subjects were not selected for inclusion in the present study if they had been given additional diagnosis of other forms of dementia, psychiatric condition, or other severe neurological condition. Of the obtained sample of
120 subjects, 36 were male and 84 were female, with ages ranging from 43 to 89 and a mean age of 73.72 years. Ninety-two percent of the sample ranged in age from 60 to 85. Ninety-three percent of the sample were Caucasian, six percent were African-American, and one subject reported an Hispanic background.

Of the 116 subjects who reported an acquired educational level, 18% did not progress further than grade school, 49% attended or completed high school, and 33% went on to obtain some form of post-secondary education. For those 70 subjects who reported an actual number of completed years of education, the mean number of years completed was 11.243 and the mode was that of a high school graduate (12 years). With regard to occupation, 16.2% of those reporting an occupation (71 subjects) fell within the professional category, 30.5% were described as semi-skilled, and 21% were unskilled; whereas, 32.4% reported being a housewife or unemployed, and no information was given for 15 subjects. While the majority of subjects (65.8%) were reported as being married, 33% were widowed, two were single, one was separated from her spouse, and the remaining two were divorced. The majority of subjects were reported as living with their spouse (55%), 22.5% of the sample were living alone, 19.2% lived with someone other than a spouse, 2.5% resided in a nursing home or low income housing for the elderly, and a single subject had no response given.
Measures

**Mini-Mental Status Examination (MMSE).** The MMSE (Folstein et al., 1975) is comprised of several short items that assess orientation, registration, attention/calculation, recall, language, and constructional ability. The Attention/Calculation item affords the option of requiring the examinee to count backwards by seven’s from one hundred or alternatively to spell the word "WORLD" backwards. In most cases, patients to which to MMSE was administered were asked to complete both items, resulting in two scores, and subsequently two total scores here-to-fore referred to as MMSE(7) and MMSE(W). Completion of all items produces a total score that ranges from an errorless score of 30 and declining with increasing impairment to 0. A MMSE score of 23 or lower is considered indicative of dementia (Kluger & Ferris, 1991).

**Neurobehavioral Cognitive Status Examination (NCSE).** The NCSE (Kiernan et al., 1987) assesses several cognitive domains independent of each other, beginning with orientation and attention items, followed by four measures of language (fluency, comprehension, repetition, and naming), then constructional ability, memory, calculation, and verbal reasoning in the form of a similarities task and a judgement measure. A "screen and metric approach" is utilized for all but the orientation and memory subtests, which requires initial completion of a particularly difficult
item before moving on to the next subtest. If the "screen" item is failed, a series of items of graduated difficulty referred to as the "metric" is administered. Performance in any individual test that falls below the normative average range is considered indicative of impairment in that particular area of cognitive functioning. As such, no actual summary score is obtained; rather, a cognitive profile results. To determine the sensitivity of the NCSE with regard to dementia diagnosis, criteria consistent with the DSM IV (APA, 1994) will be utilized in which impairment on the memory subtest and one other area of cognitive functioning must be indicated for positive diagnosis.

Memory and Behavior Problems Checklist (MBPC). The MBPC (Zarit & Zarit, 1983) consists of 29 specific items and concludes with an open ended "other problem" item, to which a caregiver responds based on their current experience. The frequency of behavior problem occurrence is scored categorically on an ordinal scale as follows: 0 indicates the problem "does not occur"; 1 indicates the problem "has occurred but not in the past week"; 2 indicates the problem "has occurred one or two times in the past week"; 3 indicates the problem "has occurred a few times "in the past week"; and 4 indicates the problem "occurs daily". The scale then switches to a nominal scale where the number 5 indicates the problem "has occurred, but not in the past six months" and 7 indicates the problem "would occur if not
supervised." The total number of behavior problems identified as occurring at least once was tabulated for each patient for the purposes of the present study.

**Single Photon Emmission Computed Tomography (SPECT).** One of the most recent forms of brain imaging, SPECT "is the process by which cerebral blood flow is demonstrated with tomographic single-photon scintigraphic techniques (Holman, Nagel, Johnson, & Hill, 1991; p.165). SPECT imaging of regional perfusion relies on the introduction, typically intravenously, of selected radiopharmaceuticals (radionuclides) into the blood stream, where it is eventually distributed in the brain in proportion to regional cerebral blood flow. The radiopharmaceutical utilized for scans reviewed in the present study was Tc-99m HMPAO. Imaging typically begins ten to twenty minutes after introduction of the radiopharmaceutical. Over the course of a thirty to forty minute period, with the patient lying completely still, the emission of single photons in the brain by radionuclide decay is collected through the use of detectors in a single or multi-head gamma camera system that is moved or rotates around the head. Using computers, this information is collected for eventual algorithmic reconstruction of a three-dimensional data set into various viewing planes of clinical interest. Typically, some combination of trans-axial, coronal, and sagittal images are reproduced for radiological and clinical analysis.
Radiological reports of SPECT scans completed on subjects by the radiology department at UAMS were reviewed by the attending radiologist for report of the absence/presence of cerebral blood flow abnormalities and a subsequent diagnostic impression. These reports were recorded as indicative of such perfusion abnormalities or the absence of the same.

Procedure

Prior to the patient’s presentation for the initial appointment, patients or their caregivers were sent an extensive questionnaire that included items regarding personal and family information as well as functional and behavioral checklists. Upon presentation for their initial appointment a complete diagnostic work-up (review of history, medical exam, serum lab work, and/or neuroradiological scans) was conducted or scheduled by nursing and physician staff relevant to the patient’s presenting complaints. In cases of suspected dementia, neuropsychological testing (MMSE, NCSE) was completed with the patient by a trained psychometric technician or in rare cases the staff neuropsychological consultant. A presumptive diagnosis was typically given on the day of the initial visit; however, a return visit in approximately one month was scheduled for a review of all test results with the patient and family, at which time a probable diagnosis was given.
Information was obtained through review of patient files by the primary investigator for compilation of a database under the supervision and direction of Michael G. Hazelwood, Ph.D., an Assistant Clinical Professor with the Division on Aging at UAMS. Data recorded from the patient files were transcribed to a separate recording summary sheet, identified by the patient file number. The data collection summary sheets subsequently remained in the possession of Dr. Hazelwood and his staff for entry into a computer database, at which time a three digit number was assigned to each data set. A key, listing the patient file number with its corresponding three digit number remained in the possession of the Center on Aging staff. An isolated database was then created by Dr. Hazelwood for use by the primary investigator for the purposes of this study.

Obtained information for the purposes of this study included confirmation of probable Alzheimer's Disease diagnosis, made upon review of the most recent physician note, concurrent to the patient's last visit, and was subsequently used as the criterion for diagnostic comparisons in the present study. Additional obtained data included demographic information; summary scores for both versions of the MMSE; NCSE subtest scores; The total number of NCSE subtests scores falling in the impaired range; the absence or presence of impairment on the NCSE Memory subtest and at least one other subtest; the total number of problems
indicated on the Memory and Behavior Problem Checklist; and the absence or presence of abnormalities reported in the results of SPECT scans.

Statistical Analysis

Statistical frequencies, means, and ranges were calculated for all demographic information obtained (noted above), as well as for all recorded test scores and indices. Additional statistical analysis necessary to test each of the present study's hypotheses are described below.

Hypothesis 1. To determine test sensitivity for the NCSE and both versions of the MMSE, the number of patients identified as cognitively impaired by each test (TruePositives) were divided by the total number of subjects to whom the test was administered, thus creating a proportion and subsequent percentage. For the purpose of exploratory comparison, SPECT scan findings were also included in this and subsequent analyses relevant to the testing of the first hypothesis. The number of patients not identified as cognitively impaired by these same tests (False Negatives) were determined by subtracting their respective test sensitivity percentages from 100. Differences in sensitivity for the four tests were evaluated for statistical significance, followed by discordant pair analyses of all possible pairings of the same four measures.

Hypothesis 2. Pearson correlation coefficients were calculated to determine the strength of relationships
between the total number of NCSE subtest scores falling in
the impaired range, both MMSE total scores, the number of
reported behavior problems on the MBPC, and performance on
each of the subtests.

**Hypothesis 3.** A t-test was calculated to determine
the significance of difference between the number of NCSE
subtests found to be in the impaired range among patients
with normal SPECT scans and the number of NCSE subtests
found to be in the impaired range among patients with
abnormal SPECT scans. A t-test was also calculated to
determine the significance of difference between the number
of reported behavior problems on the MBPC among patients
with normal SPECT scans and the number of reported behavior
problems on the MBPC among patients with abnormal SPECT
scans. A finding of significant difference between SPECT
groups on each dependent variable was followed by an
additional analysis for an estimate of effect size.
CHAPTER III

RESULTS

Test sensitivity was calculated for the NCSE, both versions of the MMSE, and SPECT. Table 1 shows the proportion of subjects found to be impaired by each test to the total number of subjects tested, as well as the subsequently calculated percentages of True Positives and False Negatives. Of the 120 subjects obtained for this study, all were tested with the NCSE. The total number of impaired scales on the NCSE for each subject ranged from the minimum of 0 to the maximum of 10 (mean = 5.31, mode = 5, S.D. = 2.71), with 108 subjects accurately identified by the test as impaired (impairment on the Memory subtest and at least one other subtest). Twelve subjects, two of whom did not show impairment on any scale of the NCSE, were inaccurately identified as non-impaired, inconsistent with physician diagnosis of Probable Alzheimer's Disease. As a result, the NCSE was calculated to have a sensitivity of 90% with a corresponding False Negative rate of 10%.

Of the 117 subjects who were administered the MMSE(7), in which the total scores for each subject ranged from 3 to 28 (mean = 18.85, mode = 21, S.D. = 5.61), 90 were
Table 1

Comparison of the Test Sensitivity and False Negatives for the NCSE, MMSE, and SPECT

<table>
<thead>
<tr>
<th></th>
<th>True Positives</th>
<th>Test Sensitivity</th>
<th>False Negatives</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Sample Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCSE</td>
<td>120</td>
<td>.900</td>
<td>.100</td>
</tr>
<tr>
<td>MMSE</td>
<td>117</td>
<td>.769</td>
<td>.231</td>
</tr>
<tr>
<td>Serial 7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMSE</td>
<td>118</td>
<td>.678</td>
<td>.322</td>
</tr>
<tr>
<td>World</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPECT</td>
<td>101</td>
<td>.782</td>
<td>.218</td>
</tr>
</tbody>
</table>

accurately identified as cognitively impaired (total score ≤ 23); whereas, 27 were inaccurately identified as non-impaired, inconsistent with physician diagnosis. This indicated sensitivity for the MMSE(7) of 77% with a corresponding False Negative rate of 23%. Of the 118 subjects who were administered the MMSE(W), in which the total scores for each subject ranged from 3 to 29 (mean = 20.01, mode = 23, S.D. = 5.595), 80 were accurately identified as cognitively impaired (total score ≤ 23); whereas, 38 were inaccurately identified as non-impaired,
inconsistent with physician diagnosis. This indicated sensitivity for the MMSE(W) of 68% with a corresponding False Negative rate of 32%.

Of the 101 subjects given a SPECT scan, the radiological reports of 79 patients (78%) were identified by the attending neurologist as having a scan that indicated a pathognomonic or "abnormal" finding, consistent with physician diagnosis of dementia; whereas, 22 patients (22%) were identified by the attending radiologist as "normal", inconsistent with physician diagnosis. As a result, the SPECT scan was calculated to have a sensitivity of 78% with a corresponding False Negative rate of 22%. Statistical comparison of the obtained proportions of subjects diagnosed with dementia across the four measures revealed a significant difference between the proportions (Cochran's Q = (3,101) = 58.32, p < .001). As such, a series of discordant pair analyses (See Figure 1) were conducted to determine the significance of differences between pairings of each of the test measures. These comparisons consistently revealed the NCSE to accurately identify significantly larger numbers of impaired subjects when the MMSE(7) (McNemar (1, 117) = Binomial 2-tailed, p < .0026) and the MMSE(W) (McNemar (1,118) = 19.53, p < .0000) did not. Between the two versions of the MMSE, the MMSE(7) indentified a significantly larger number of impaired subjects when the MMSE(W) did not (McNemar (1,117) =
Binomial 2-tailed, \( p < .0074 \). Analysis of the discordant pairs between the SPECT scan and the NCSE (McNemar (1, 101) = Binomial 2-tailed, \( p < .0525 \), the MMSE(7) (McNemar (1, 100) = .3214, \( p < .5708 \)), and the MMSE(W) (Mcnemar (1, 100) = Binomial 2-tailed, \( p < .0216 \)) failed to reveal one test as significantly different in its ability to detect impairment from the other.

**Figure 1.** Discordant pair analyses of test sensitivity. Scores in the impaired range (+) and unimpaired range (−) are given. Cells marked with Asterisks denote discordant pairs. \( p \) values were calculated by McNemar’s Test for Paired Categorical Data.

<table>
<thead>
<tr>
<th>MMSE(7)</th>
<th>MMSE(W)</th>
<th>SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>N(+)</td>
<td>86</td>
<td>N(+)</td>
</tr>
<tr>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>S(-)</td>
<td>*4</td>
<td>S(-)</td>
</tr>
<tr>
<td>E(-)</td>
<td>*4</td>
<td>E(-)</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(( p &lt; .0026 ))</td>
<td>(( p &lt; .0000 ))</td>
<td>(( p &lt; .525 ))</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MMSE(7)</th>
<th>MMSE(W)</th>
<th>MMSE(W)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+)</td>
<td>(+)</td>
<td>(+)</td>
</tr>
<tr>
<td>(-)</td>
<td>(-)</td>
<td>(-)</td>
</tr>
<tr>
<td>S(+)</td>
<td>63</td>
<td>S(+)</td>
</tr>
<tr>
<td>P</td>
<td>P</td>
<td>M</td>
</tr>
<tr>
<td>E</td>
<td>E</td>
<td>S</td>
</tr>
<tr>
<td>C</td>
<td>C</td>
<td>E</td>
</tr>
<tr>
<td>T(-)</td>
<td>*12</td>
<td>T(-)</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(( p &lt; .5708 ))</td>
<td>(( p &lt; .0216 ))</td>
<td>(( p &lt; .0074 ))</td>
</tr>
</tbody>
</table>
Statistical relationships between the number of NCSE subtests falling in the impaired range for each subject, total scores for each subject on both versions of the MMSE, and the total number of behavior problems reported for each subject were calculated for the Pearson correlation coefficients presented in Table 2. The obtained correlations of .48, -.58, and -.57 between the total scores on the NCSE, MMSE(7), and MMSE(W), respectively, with the total number of reported behavior problems on the MBPC were all significant (p < .01, two-tailed), yet each relationship accounted for only a moderate amount of the variance between the measures (approximately 23%, 33%, and 33%, respectively). As an aside, observation of the obtained correlations between the NCSE with both versions of the MMSE (-.81 and -.82, respectively) were not only significant (p < .01, two-tailed), but they also accounted for approximately two-thirds (65% and 67%, respectively) of the explained variance. As might be expected, the strength of relationship between the two versions of the MMSE (.94) was also not only statistically significant (p < .01, two-tailed), but also accounted for 88% of the explained variance.

Pearson r correlation coefficients calculated to determine the strength of relationship between the individual subtest scores of the NCSE with the total number
Table 2

Pearson r Intercorrelation Matrix for NCSE, MMSE, and MBPC total scores

<table>
<thead>
<tr>
<th></th>
<th>NCSE</th>
<th>MMSE(7)</th>
<th>MMSE(W)</th>
<th>MBPC</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCSE</td>
<td>----</td>
<td>-.8061**</td>
<td>-.8191**</td>
<td>.4751**</td>
</tr>
<tr>
<td>MMSE(7)</td>
<td>-.8061**</td>
<td>-----</td>
<td>.9398**</td>
<td>-.5784**</td>
</tr>
<tr>
<td>MMSE(W)</td>
<td>-.8191**</td>
<td>.9398**</td>
<td>-----</td>
<td>-.5718**</td>
</tr>
<tr>
<td>MBPC</td>
<td>.4751**</td>
<td>-.5784**</td>
<td>-.5718**</td>
<td>-----</td>
</tr>
</tbody>
</table>

Note. NCSE = total number of subtests on the NCSE scoring in the impaired range; MMSE(7) = total score on the Serial Seven version of the MMSE; MMSE(W) = total score on the World version of the MMSE; MBPC = total number of reported behavior problems on the MBPC.

*p < .05, two tailed.

**p < .01, two tailed.

of behavior problems reported on the MBPC are presented in Table 3. As can be observed, all subtests of the NCSE correlated significantly with the report of behavior problems (p < .01, two-tailed); however, an exception to the strength of these relationships is noted with the smaller and less significant correlation (p < .05, two-tailed) between the Memory subtest of the NCSE and the report of behavior problems on the MBPC.
Table 3

**Pearson r Correlation Coefficients for MBPC and NCSE Subtest Scores**

<table>
<thead>
<tr>
<th>MBPC</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Orientation</td>
<td>-.5074**</td>
</tr>
<tr>
<td>Attention</td>
<td>-.2872**</td>
</tr>
<tr>
<td>Comprehension</td>
<td>-.3785**</td>
</tr>
<tr>
<td>Repetition</td>
<td>-.3405**</td>
</tr>
<tr>
<td>Naming</td>
<td>-.3568**</td>
</tr>
<tr>
<td>Construction</td>
<td>-.4088**</td>
</tr>
<tr>
<td>Memory</td>
<td>-.2374*</td>
</tr>
<tr>
<td>Calculation</td>
<td>-.4118**</td>
</tr>
<tr>
<td>Similarities</td>
<td>-.3619**</td>
</tr>
<tr>
<td>Judgement</td>
<td>-.3536**</td>
</tr>
</tbody>
</table>

*Note.* MBPC = total number of reported behavior problems on the MBPC.

*P* < .05, two tailed.

**P** < .01, two tailed.

Finally, the break down of abnormal versus normal subjects on the SPECT scans is reported previously in this chapter. When these two groups were compared on the number of subtests on the NCSE that were found to be impaired for each subject, those individuals who had been identified as
having an "abnormal" SPECT scan were found to be impaired on a significantly greater number of NCSE subtests (mean = 5.42, S.D. = 2.65) than those individuals who were identified as having "normal" SPECT scans (mean = 3.27, S.D. 3.42, = 2.41), \( \bar{t}(99,101) = p < .001 \). Based on Eta squared = .105, estimate of the effect size reveals only ten percent of the variance is explained by the NCSE scores.

Of those subjects who were given a SPECT scan and had a MBPC completed on their behalf, 20 (23%) were identified by the attending radiologist as "normal"; whereas, 68 patients (77%) were identified by the attending neurologist as having a scan that indicated a pathognomonic or "abnormal" finding. When these two groups were compared on the total number of reported behavior problems on the MBPC for each subject, the difference between "normals" (mean = 11.15, S.D. = 5.815) and "abnormals" (mean = 11.93, S.D. = 6.56), was not statistically significant \( \bar{t}(86,88) = .48, p < .635 \).
CHAPTER IV

DISCUSSION

Crucial to the effectiveness of a cognitive screening tool is its ability to accurately identify the presence of impairment specific to a diagnostic group. Taken further, it would seem reasonable to expect that such an instrument would bear some relationship to other factors relevant to the severity and progression of impairment observed within such a diagnostic group. Indeed, the fact that conclusive diagnosis in disorders such as Alzheimer's Disease cannot be made until the condition has completed its course, in this case upon autopsy, noninvasive indicators of the disease must be that much more consistently accurate.

The focus of the present study was to explore the diagnostic accuracy of the NCSE, through its sensitivity to physician diagnosis of probable Alzheimer's Disease relative to that of the MMSE, the latter being one of the most commonly used screening tools for the assessment of cognitive impairment. The utility of the NCSE was also explored through determination of the extent of its relationship to behavior problems typically reported by caregivers of individuals diagnosed as having suspected Alzheimer's Disease. Also explored was the extent to which
the severity of cognitive impairment on the NCSE and the number of reported behavior problems corresponded to identification of neuroradiological markers on SPECT scans thought to be consistent with dementia diagnosis.

First, the NCSE was predicted to exhibit a significantly greater rate of diagnostic accuracy with respect to suspected Alzheimer's Disease, relative to the MMSE. This contention was supported by the findings of the present study, with the NCSE accurately identifying dementia in a physician diagnosed sample of Alzheimer's Disease patients a significantly greater proportion of the time (90%) than either the Serial Sevens (77%) or WORLD (68%) versions of the MMSE. These findings are consistent with those reported by Fields et al. (1992), in which the NCSE was found to be more sensitive to physician diagnosis of cognitive impairment in a geriatric sample (100%) when compared to the MMSE (83%), the exception being that no False Negatives were reported for the NCSE in the previous study. However, it is important to note that Fields et al., (1992) required impairment on only a single NCSE subtest to classify a patient as "cognitively impaired" (p. 98). The lack of a more stringent criteria for such diagnosis may have contributed to the authors' additional finding of a particularly low rate of specificity (the fraction of times a test makes a negative diagnosis, or True Negative, when
the disorder is absent) for the NCSE, the result of obtaining a number of False Positives.

McBride-Houtz (1993) reported significantly greater sensitivity for the NCSE (82%) over the MMSE (20%) and the CCSE (22%), utilizing neuropsychological test battery performance as the criterion measure for cognitive impairment in a geriatric sample. Although she also used the same, less stringent, criteria for diagnosis of impairment on the NCSE, her findings are strengthened by her use of the more objective criterion measure. McBride-Houtz' (1993) report of a remarkably low sensitivity for the MMSE was also attributed in part to the use of a "rigorous criterion standard" (p. 105). While McBride-Houtz' (1993) citation of Schwamm et al., (1987) findings do support the contention of characteristically low sensitivity for the MMSE in the form of high False Negative rate, there are few comparable findings of such a disparity between the NCSE and MMSE in the present investigation. Indeed, the present test findings for MMSE sensitivity are more consistent, though slightly lower, with that of several studies reflecting a sensitivity range between .81 to .87 (Anthony et al., 1982; Fields, 1992; Kafonek et al., 1984).

Relevant to the expected strength of association between the severity of cognitive impairment and report of behavior problems, both the NCSE and MMSE maintained correlations of moderate strength (.48, -.58, -.57,
respectively) with the total number of behavior problems indicated on the MBPC, consistent with some of the significant relationships identified by Kurita et al. (1993). These findings, and those of the above authors go beyond the smaller correlations reported by Cooper et al., (1990), suggesting that cognitive test scores may actually hold a greater value in predicting the frequency and severity of behavior problems among patients diagnosed with Alzheimer’s Disease and other dementing conditions than those authors suggest. A review of the correlations between specific areas of cognitive functioning and the report of behavior problems is as expected. The finding of the strongest relationship between the Orientation subtest and of the NCSE and reported behavior problems might be explained by the observation of increasing disorientation and subsequent confusion so common with the progression of moderate to severe Alzheimer’s dementia. In contrast, the relatively low correlation between the Memory subtest on the NCSE and reported behavior problems may not be as easily explained, as memory decline is the most common behavior problem reported by presenting patients. It may be possible that while Memory disturbance may correlate with forgetfulness, it bears only a mild relationship to overall report of behavior problems.

Indeed, the absence here of individual behavior problem frequency scores prevents a closer analysis of relationships
between specific types of cognitive impairment and either individual or clusters of problem behaviors. While such relationships have been previously explored, particularly with regard to agitated behavior (Cohen et al., 1990; Swearer et al., 1988), most studies have relied upon global scores of cognitive impairment. The NCSE affords an opportunity to explore cognitive-behavioral relationships more closely, hence potentially increasing the predictability between specific areas of cognitive dysfunction and observed individual disruptive behaviors or related behavior factors.

Finally, with the increasing growth of interest and subsequent implications for the utilization of neuroradiological techniques, particularly the recent advances with PET and SPECT, such techniques are rapidly becoming an integral part of the diagnostic process. The establishment of specific biological markers detected by these scanning techniques has moved from simple structural indicators (i.e., tumors, infarctions, ventricular enlargement, & atrophy) to biochemical indicators such as cerebral blood flow and glucose metabolism. The call for these newer scanning techniques to assist in the diagnosis of dementia (Griffeth & Royale, 1994) and the suggestion that neuropsychological testing and these scans combined improve the sensitivity to accurate diagnosis of probable Alzheimer’s Disease (Reige & Metter, 1988) lends to the need
for explorative relationships between these two forms of diagnostic assessment.

The finding of a modest relationship in the present study between the indication of pathology on SPECT scans and severity of impairment on the NCSE, particularly with regard to the need for the earliest possible detection techniques, suggests that dementia typically must reach the stage of moderate to severe impairment in order to be readily detected on SPECT scans. This suggestion is consistent with the general consensus that SPECT and similar forms of imaging can reliably differentiate between normal individuals and those suffering from moderate to severe dementia (Tikofsky, Hellman, & Parks, 1993). What remains, however is the question of how to best evaluate and confirm diagnosis of probable Alzheimer’s Dementia and other primary degenerative dementias.

These findings support the continued emphasis on neuropsychological assessment of cognitive functioning as a first indicator of dementia, and alternatively fails to support those who contend that the earliest of onset may be identified by biological markers before behavioral indices present. Although it is typically the complaint of behavior problems that bring an individual in for evaluation, the findings of the present study do not support a relationship with the types of biochemical markers identified by SPECT scans. Indeed, it would appear that behavior remains too
idiosyncratic to bear relationship to such markers. Rather, it would appear that cognitive deficits underlying such behavior problems (e.g., memory deficits contribute to forgetfulness) may provide the earliest indicator of potential dementia diagnosis.

Among those concerns identified during hypotheses testing was the lack of access to a non-diagnosed, or "normal" group for the purpose of evaluating test specificity, positive and negative predictive value, and various between group comparisons of the NCSE and MMSE performance. However, the consistent reports of low specificity using the NCSE would appear to be outweighed by the more crucial risk of missing potential cases of dementia due to poor sensitivity. The cost of requiring more intensive evaluation due to a false positive is seen as relatively small when compared to that of the implications of obtaining a false negative, particularly as treatments for the symptoms of Alzheimer's Disease further require accurate, early diagnosis. While not as readily a concern, access to the individual items of the MBPC would have been valuable for further analysis of the strength of relationships between specific areas of cognitive deficit found on the NCSE and either individual or combined behavior problems. Although the present study does confirm an overall relationship between these two areas of dementia presentation, the true potential for predictability between
them is more likely to be found through item and domain analysis.

Further investigation of the utility of short-form screening tools relative to more comprehensive assessment measures such as the NCSE with regard to test sensitivity, specificity, and both positive and negative predictive values may be better studied through the utilization of objective criteria upon which to substantiate independent variables such as cognitive impairment, behavior problems, and neuroradiological test findings. However, equally important will be the use of diagnostic cut-offs on such measures that are consistent with published criteria for the groups being investigated, in this case the establishment of cognitive deficits in memory and one other area of functioning. Future efforts to assess the relationship between the severity and types of cognitive impairment should rely upon objective forms of measurement for such factors as behavior problems, functional ability, and various biological markers.

The results of the present study support the contention that the NCSE is a very sensitive measure for the accurate identification of the patterns of cognitive impairment necessary for the diagnosis of dementia, in this case probable Alzheimer's Dementia. Significant, but modest, relationships were found between both global and specific indices of cognitive impairment and report of behavior
problems, and between the severity of cognitive impairment and neurobiological markers on radiological scans as well.
REFERENCES


