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Clinical Utility Of The Smell Identification Test In Differentiating Persons With Dementia Of The Alzheimer'S Type From Depressed Elderly And Elderly Controls

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CLINICAL UTILITY OF THE SMELL IDENTIFICATION TEST IN DIFFERENTIATING PERSONS WITH DEMENTIA OF THE ALZHEIMER'S TYPE FROM DEPRESSED ELDERLY AND ELDERLY CONTROLS

A Dissertation

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Theodore Lynn Moretz

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ABSTRACT

Accurate differential diagnosis between Dementia of the Alzheimer's Type (DAT) and depression is important in providing appropriate treatment to persons suffering from each of these disorders; however, accurately differentiating between these disorders is often problematic. The purpose of this study was to determine whether the Smell Identification Test (SIT) could accurately distinguish between persons with DAT; depressed, non-demented elderly; and elderly controls.

The sample consisted of three groups of 30 white subjects matched for age, gender, and smoking behavior. Group I consisted of persons with early DAT. Group II consisted of persons diagnosed as suffering from depression and Group III consisted of non-depressed, non-demented controls.

The null hypothesis was tested by a one way analysis of variance (ANOVA) and Duncan's Multiple Range Test. Results suggested that persons with DAT scored significantly lower on the SIT than did either the depressed or control groups. Depressed subjects did not differ significantly from control subjects on the SIT. The DAT group also gave a higher rate of "don't know" responses and made more intrusion errors than did subjects in the other groups. While the depressed group gave more "don't know" responses than the control group, over half of these responses were given by a single

subject.

Current results suggest that the SIT may have clinical utility in differentiating person with DAT from those suffering from depression. While additional research is needed in this area, it would appear that both a high number of "don't know" responses and intrusion errors on the SIT may be pathognomic for DAT.

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Chapter 1

INTRODUCTION

Counseling psychology has traditionally dealt with helping people deal with developmental issues that occur across the lifespan (Woody, Hansen, & Rossberg, 1989). The past several decades have seen a steady increase in lifespan in industrialized countries (Cote, 1985). This increase has been accompanied by an increase in numerous conditions associated with aging, especially the various dementing disorders. It is estimated that from 11% (Cote, 1985) to 50% (Lamy, 1992) of all persons over age 65 exhibit some type of dementia.

Degenerative Dementia of the Alzheimer's Type (DAT) is the most prevalent type of dementia seen in industrialized societies (Alzheimer's Association, 1987; and Lezak, 1995), with estimates ranging from 55.6% (Selkoe, 1992) to 75% (Gurland & Cross, 1986) of all cases of dementia. Cote (1985) noted that approximately 25% of the population will develop symptoms of DAT by age 80, while Lamy (1992) suggested that over 50% of those age 85 and over will develop this disorder. Approximately 4 million people in the United States are currently diagnosed with DAT, and as

the number of elderly in this population increases, this figure is expected to reach 14 million by 2050. The prevalence of this disorder suggests that it is a developmental issue that many elderly persons and their families will face.

Neuropsychology, the branch of applied psychology dealing with the behavioral aspects of brain dysfunction (Heilman & Valenstein, 1993; Lezak, 1995), evolved from a need for psychometric methods to discriminate between psychiatric and neurological disorders (Benton, 1988; Egel & Hughes, 1989; Meier, 1992; Reitan, 1989). This discrimination remains one of the major reasons for client referral for neuropsychological evaluation.

Purpose

One of the diagnostic distinctions often required is the differentiation of clients with depressive disorders from those suffering some type of dementing process, including DAT. This is not surprising, given that depression is the most prevalent mental disorder in the elderly (Blazer, 1990; Solomon & Patch, 1974), and that depression in this population often presents with a picture of cognitive deficit (Alzheimer's Association, 1987; King et al., 1995; McHugh, 1975). When depression mimics the features of dementia, without involvement of the higher cortical centers, a state of "pseudodementia" is said to exist (Caine, 1982; Crevel, 1986; Madden, Luban, Kaplan, & Manfredi, 1952).

In addition to the spurious cognitive decline seen in many depressed elderly, depression is often one of the first symptoms seen in dementia (Bieliauskas, 1993b; Lezak, 1995). Research findings have varied, with incidence rates of depression ranging from 30% to 50% for persons with DAT (Cummings et al., 1994; Lezak, 1995; Teri & Reifler, 1987).

Because of the overlap of depressive symptomatology and impaired performance on measures of cognitive ability, the differential diagnosis between depression and dementia can be problematic (Bieliauskas, 1993b; Caine, 1982; Crevel, 1986; Lezak, 1995; Strub & Black, 1977), with the diagnostician being forced to rely primarily upon historical data and symptom progression to make the differential diagnosis (Janowsky, 1982; McAllister, 1983). Erroneous diagnosis of either depression or dementia has numerous negative consequences (Gurland & Cross, 1986). In addition to under- or over-estimating the prevalence of the condition, persons with remediable disorders may not receive the necessary care, leading to unnecessary morbidity and/or mortality. Misdiagnosis also leads to excessive use of the health care system. Inappropriate diagnosis of depression may lead to prescription of antidepressant medication. Unfortunately, the anticholinergic properties of some of these drugs may worsen the symptom presentation in an individual with dementia (Dysken, Merry, & David, 1978; Paddison, 1984).

Until recently, little was available other than

supportive techniques for the management of DAT. Currently tacrin is being used with many persons who have DAT to slow the early symptom progression of the disorder (Manning, 1994; Warner-Lambert, 1993). Due to the hepatotoxicity and gastrointestinal effects of this drug, accurate diagnosis is needed to prevent its use on persons without DAT (Manning, 1994). Accurate diagnosis and feedback are also important to provide appropriate support services and future planning for the victim and family (Gass & Brown, 1992; Gurland & Cross, 1986).

Problems with the accurate early diagnosis of DAT have continued to lead researchers to search for more effective methods of accurately identifying the disorder. Research has shown that the neurofibrillary tangles and senile (amyloid) plaques characteristic of DAT occur in numerous regions of the brain, including the olfactory nucleus (Averback, 1983) and the olfactory bulb (Brizzee, 1984). Not surprisingly, olfactory deficits have been noted early in the course of DAT (Doty & Reyes, 1987; Peabody & Tinkenberg, 1985; Serby, Corwin, Conrad, & Rotrosen, 1985).

While olfactory deficits may be related to depression, the results are less clear (Harrison & Pearson, 1989). Lesions to the olfactory bulbs have been found to cause depressive behavior in rats (Richardson, 1991) and depressive symptomatology in two humans (Levenson, 1985). Zenter and Zenter (1985) reported that depressed persons report decreased vividness of all sensory qualities,

including olfaction. Controlled studies have failed, however, to support the idea of olfactory deficits in depressed persons (Amsterdam, Settle, Doty, & Abelman, 1987; Warner, Peabody, and Csemansky, 1990).

While olfactory assessment is a routine part of the standard neurological examination, the assessment is brief and is done to insure that the first cranial nerve is intact (Deymer, 1980; Mechner, 1975). The lack of extensive olfactory assessment by neurology and neuropsychology has been largely due to the fact that, until recently, olfactory assessment was a cumbersome task, necessitating maintaining several bottles of aromatic compounds at precise intensities (Harrison & Pearson, 1989). Development of the Smell Identification Test (SIT) has simplified this task by providing a standardized and maintenance free means of olfactory assessment that may lead to increased use of olfactory testing in the differential diagnosis of various disorders.

Statement of the Problem

Current research suggests that olfactory deficits occur early in the course of DAT. The research is mixed, however, regarding the extent to which such deficits occur as a result of depression, with controlled studies suggesting no olfactory decline. If this is the case, then standardized olfactory assessment should be able to accurately distinguish between these groups. This study examined the ability of the Smell Identification Test (SIT) to accurately

differentiate persons with DAT; non-demented, depressed elderly; and elderly controls.

Delimitations

Due to the complexity of cross matching subjects on several variables, and only limited availability of a multiethnic population, all subjects were white. The subject groups were restricted to persons age 65 and older. Subjects were limited to persons in the earlier stages of Alzheimer's disease. All subjects were residents of Indiana or Illinois at the time of the study.

Definition of Terms

To ensure a clear understanding of the various terms used in this study, operational definitions are presented below.

Dementia: The presence of dementia was operationally defined as a score of below 24 on the Mini Mental State Examination.

Dementia of the Alzheimer's Type: Person's were considered to have DAT if they had been previously diagnosed with this disorder by a physician.

Early Dementia of the Alzheimer's Type: Early DAT was operationally defined to include persons at stages 3, 4, or 5, as measured by the Global Deterioration Scale rating assigned by health care providers.

Depressed Subjects: Classification of a subject as depressed was based upon a history of depressive disorder,

accompanied by a score of 11 or greater on the Geriatric Depression Scale.

Intrusion Error: Intrusion errors consist of responses that are unrelated to a particular question or test item. Common intrusion errors include perseverative and confabulatory responses.

Microsmia: Mild to moderate impairment of olfactory functioning.

Normosmia: Unimpaired olfactory functioning.

Assumptions

Basic assumptions relevant to the study are discussed below:

1. The participants in the DAT group were accurately diagnosed by a physician.

2. DAT participants were accurately rated according to stage of dementia by health care professionals.

3. All participants put forth their best effort on both screening instruments for dementia and the measure of olfactory functioning.

4. All participants responded candidly to the Geriatric Depression Scale and background history questions.

Organization of the Remainder of the Dissertation

Chapter 2 is a review of related research concerning DAT, its underlying physiological and behavioral manifestations, how these pertain to current diagnostic strategies, and the relative effectiveness and shortcomings

of these strategies. A discussion of the physiological underpinnings of olfaction and how these are related to both depression and DAT is also presented. A description of the research methods, instruments used, data collection, and statistical analysis used is presented in Chapter 3. Chapter 4 presents and discusses the results of the study. Conclusions drawn from this study, implications, and recommendations for future research are found in Chapter 5.

Chapter 2

RELATED RESEARCH

The symptoms of Dementia of the Alzheimer's Type (DAT) have been recognized for over 2000 years; however, attempts to distinguish between dementia and other mental disorders are a relatively recent development (Gurland & Cross, 1986). While DAT was first defined clinically by Alois Alzheimer in 1907 (Lamy, 1992), it was initially believed to be a rare disorder occurring in middle life (Rue, 1992). It was not until the 1970s that this disorder was first recognized as a common disorder in later life and began to attract both public and professional interest (Gurland & Cross, 1986; Rue, 1992).

While initially conceptualized as a separate entity from senile dementia (Caine, 1992; Gurland & Cross, 1986; Strub & Black, 1977; World Health Organization, 1978), the clinical picture for each of the disorders, other than age of onset, is identical (Lezak, 1995). Consequently, these categories are now conceptualized as a single diagnostic entity (Lezak, 1995; Paddison, 1984). As noted earlier, in rare cases, persons may develop this disorder in their 40s, however most cases occur after age 65 (American Psychiatric

Association, 1994).

The extent to which DAT represents a homogenous disorder remains open to debate. Lezak (1995) reviewed the current literature in the field and noted that differences in symptom presentation, possibly suggestive of distinct subtypes of DAT, have been found in two areas. The first is age of onset, with persons developing symptoms before the age of 65 exhibiting a greater degree of language impairment, more rapid symptom progression, a greater prevalence in left-handers, and having a greater familial history of DAT. Lezak noted, however, that research on these differences has produced mixed, and often conflicting results. Lezak cited Naugle and Bigler (1989) who argued that these age-related differences may be the artifactual result of more comprehensive assessments and better baseline data obtained for younger persons presenting with a cognitive decline, as opposed to constituting a distinct subgroup of the disorder.

Research also raises the possibility of different subtypes of DAT based upon which cerebral hemisphere is more severely impaired (Lezak, 1995). From 20 - 40% of the persons presenting with DAT appear to show greater involvement of one cerebral hemisphere, with left hemisphere deficits showing more rapid deterioration than right hemisphere deficits. It should be noted, however, that Walker, Hom, Bonte, Tintner, and Weiner (1989), using measures of neuropsychological functioning and cerebral

blood flow, failed to support the idea of clinically distinct subgroups of DAT based upon localization or lateralization of cognitive impairment.

Rue (1992) argued that current evidence is insufficient to support the idea of clinically distinct subgroups of DAT. The differences in clinical course often cited as evidence of distinct subtypes of the disorder may be better explained as a result of differing levels of premorbid cognitive abilities. Undiagnosed, but coexisting, medical conditions may also influence the course of the disorder, leading researchers to inaccurately attribute differences to subtypes of DAT.

While the debate continues, Parasuraman and Haxby (1993) have noted that the heterogeneity of the clinical course of DAT may support the idea of distinct subgroups of this disorder. The full clinical picture, however, remains poorly defined until the later stages of the illness. As a result, this factor cannot be controlled for in research studies focusing on the early stages of the disorder.

Diagnostic Criteria

DAT is a progressive, degenerative dementia involving the multiple loss of intellectual abilities, including memory, abstract thinking, and judgement (American Psychiatric Association, 1994; Caine, 1982). Other cortical functions are also impaired, with the victim experiencing deficits in constructional ability (Caine, 1982; Strub & Black, 1977), and changes in personality and behavior

(Caine, 1982; Rubin, Kinscherf, & Morris, 1993; Strub & Black, 1977). Eventually the person enters a persistent vegetative state until death from pneumonia or other physical illness (Lezak, 1995).

The American Psychiatric Association (1994, pp. 142-143) gives the following diagnostic criteria for DAT:

A. The development of multiple cognitive deficits manifested by both
   (1) memory impairment (inability to learn new information or to recall previously learned information)
   (2) one (or more) of the following cognitive disturbances:
      (a) aphasia (language disturbance)
      (b) apraxia (impaired ability to carry out motor activities despite intact motor function)
      (c) agnosia (failure to recognize or identify objects despite intact sensory function)
      (d) disturbance in executive functioning (i.e., planning, organizing, sequencing, abstracting)

B. The cognitive deficits in Criteria A1 and A2 each cause significant impairment in social or occupational functioning and represent a significant decline from a previous level of functioning.

C. The course is characterized by gradual onset and

continuing cognitive decline.

D. The cognitive deficits in Criteria A1 and A2 are not due to any of the following:

(1) other central nervous system conditions that cause progressive deficits in memory and cognition (e.g., cerebrovascular disease, Parkinson's disease, Huntington's disease, subdural hematoma, normal pressure hydrocephalus, brain tumor)

(2) systemic conditions that are known to cause dementia (e.g., hypothyroidism, vitamin B_{12} or folic acid deficiency, niacin deficiency, hypercalcemia, neurosyphilis, HIV infection)

(3) substance-induced conditions

E. The deficits do not occur exclusively during the course of a delirium.

F. The disturbance is not better accounted for by another Axis I disorder (e.g., Major Depressive Disorder, Schizophrenia).

Medical diagnosis may differentiate between possible DAT and probable DAT, based upon symptom duration, symptom severity, and the presence of other conditions that may be influencing the symptom picture (McKhann et al., 1984; Lamy, 1992). However, research has failed to find a significant difference in diagnostic accuracy using the possible versus probable differentiation of DAT (Hom & Brewer, 1991).

Stages of DAT

Since DAT is by definition a progressive disease, various stage models have been developed to track the progress of the disorder. It should be noted that, while all persons with DAT will pass through the proposed stages, there is considerable individual variability with regard to the amount of time each stage lasts and the order with which symptoms develop (Lezak, 1995).

Parke-Davis (1993) outlined three stages of DAT. Stage 1 lasts from 2 - 4 years and is characterized by the victim exhibiting confusion about names or places, decreased recall, difficulty managing money, loss of initiative, and anxiety about the symptoms. Stage 2, which can last from 2 - 10 years, is characterized by increasing memory loss and confusion, restlessness, difficulty recognizing close friends and family members, perceptual and motor problems, loss of language, problems with logical thinking, and loss of social skills. The final stage lasts from 1 - 3 years, during which time the victim is unable to recognize self or family, unable to care for self, experiences weight loss, becomes incontinent, loses the ability to use or understand language, exhibits delusional behavior and mood changes, has difficulty swallowing, and may develop seizures.

While the three stage model developed by Parke-Davis (1993) covers the entire range of the disorder, two problems exist. First, these stages do not allow the fine discrimination needed at times between normal age-associated

memory loss and DAT. Second, Stage 2 covers a lengthy span of symptom progression, bridging the mild dementia seen in Stage 1 and the very severe dementia seen in Stage 3. The model is therefore not suitable for studies requiring a finer differentiation between symptoms seen in the moderate stages of dementia.

While not specifically stage models of dementia, two assessment instruments have been frequently used to gauge the progression of DAT. The Clinical Dementia Rating Scale (CDRS) (Berg, 1988) is designed to assign one of five impairment ratings (none, questionable, mild, moderate, or severe) on six areas of functioning (memory, orientation, judgement and problem-solving, community affairs, home and hobbies, and personal care). Impairment ratings are made in comparison with the person's premorbid level of functioning as opposed to norms established for the general population. In addition, this rating scale is time consuming, requiring a 90 minute interview, followed by the administration of several brief neuropsychological instruments.

Rosen, Mohs, and Davis (1984) have developed the Alzheimer's Disease Assessment Scale (ADAS) to rate persons with regard to memory, orientation, language, constructional ability, ideational praxis, and general level of impairment. The ADAS takes from 45 minutes to one hour to administer. While an overall impairment rating is given, this instrument does not define specific stages of the illness (Rue, 1992).

A more suitable model for research where finer

distinctions are necessary and little time is available, is the Seven Stages of Global Deterioration Scale, developed by Reisberg (1983). Stage 1 represents normal functioning in the elderly, with no deterioration present.

Stage 2 is associated with normal aging changes. While not demented, the person exhibits age-associated memory impairment (AAMI), which is common in 50 - 80% of the elderly (Lamy, 1992; Reisberg, 1983). AAMI is characterized by diminished recall and concentration. It should be noted that AAMI is not characterized as a disease state, but is seen as a natural product of aging.

Stage 3 is associated with mild confusion, impaired concentration, and mild neuropsychological impairment. Family members and coworkers begin to notice memory problems. Cognitive and affective changes (especially anxiety and depression) may be present.

Stage 4 is characterized by a mild-moderate cognitive decline, including decreased knowledge of current events, problems managing finances, difficulty traveling to unfamiliar places, and inability to accurately recall aspects of one's personal history. The individual obviously denies memory problems and withdraws from situations they may be unable to manage. Flattening of affect may also occur.

Stage 5 is typical of moderate DAT. The victim can no longer function independently and may begin to exhibit symptoms of paranoia or delusions. The victim is easily

confused and unable to remember relevant personal information such as their address or names of family members. They are disoriented regarding time and need increased assistance for meeting basic living needs.

Symptoms of stage 6, or moderately severe DAT include urinary and fecal incontinence, disorientation to place, and increased disorientation to time. Severe personality changes, including delusions are typical. The person becomes totally dependent upon others to meet all basic living needs.

The individual at stage 7, or very severe DAT, has lost all verbal abilities and basic motor skills. Most persons at this stage are institutionalized and completely dependent on others. This stage progresses to stupor, coma, and eventually death.

Etiological Factors

While no single etiological factor has been noted in DAT, a genetic predisposition to the disorder is noted, especially in cases where the age of onset is under 70 (Amaducci, Falcini, & Lippi, 1992; Lezak, 1995; Rue, 1992). St. Georgy-Hyslop (1987) has implicated a gene on chromosome 21 as related to DAT. Pericak-Vance and Associates (cited in Whitehouse, Lerner, and Hedera, 1993) have found a gene on chromosome 19 that also appears to play a role in DAT.

While some research suggests an autosomal dominant pattern, with approximately 50% of the first degree relatives of victims of DAT developing the disorder by age

90 (Mohs et al., 1987), most studies have found a familial incidence rate of 35% to 40% (Lezak, 1995). Heston and associates (1981) reported that, for approximately 60% of their sample, the index case was the only family member to develop DAT. Finally, Nee and associates (1987) found only a 40% concordance rate with regard to DAT in monozygotic twins. These findings suggest that factors other than genetics also play an etiological role for DAT.

Although Crapper, Krishnan, and Dalton (1973) implicated aluminum as a causative factor, this remains a subject of debate. Whitehouse, Lerner, and Hedera (1993) reviewed the literature and concluded that subsequent studies have failed to support aluminum as a causative factor in DAT. Lamy (1992) conducted a similar review and concluded that the current evidence (specifically the presence of high levels of aluminum in the brains of person's with DAT) continues to implicate this substance in the development of Alzheimer's disease. Rue (1992) suggested, however, that a breakdown of the blood-brain barrier may accompany Alzheimer's disease and lead to the high levels of aluminum, implying that the presence of this mineral could be a byproduct of the disorder, as opposed to a causative agent.

Other risk factors for DAT include a familial history of Down's syndrome, female gender (Rocca, Amaducci, & Schoenberg, 1986), history of head injury, increased mother's age at the time of the person's birth, history of

thyroid disease, and later position in the family birth order (Whitehouse, Lerner, & Hedera, 1993). Efforts to find infectious agents as a causative factor in DAT have thus far been futile (Lezak, 1995; Prusiner, 1987; Rue, 1992).

Anatomy and Physiology of DAT and Depression

Before beginning a discussion of the biological factors in DAT, it should be noted that the effects of brain lesions, regardless of cause, are rarely limited to one narrow area, but are rather regional in nature (Luria, 1969). It should also be noted that cognitive and psychological functions, such as memory, are not confined to one narrow area, but rather result from the simultaneous and successive participation of various areas of the brain (Luria, 1969; Goldman-Rakic, 1992). Lesions to any of these zones can result in disruption of the functional system, however the disorganization will vary according to the zone damaged (Luria, 1969). For example, impairment of recent memory has consistently been linked to lesions in the limbic system, especially the hippocampus, thalamic nuclei, and mammillary bodies (Luria, 1971; Selkoe, 1992).

Affective changes seen in DAT may be attributable to degeneration of the amygdaloid area, as well as to frontal lobe degeneration (Brizee, 1984). Current biological explanations for affective changes in persons without brain lesions focus on the role of decreased neurotransmitter activity in either the noradrenergic or serotonergic systems (Grilly, 1989).

Recent research has demonstrated significant overlap between the brain localization of both affective and memory disorders. Bench and associates (1992), analyzing cerebral blood flow, have demonstrated marked abnormalities in the pre-frontal and limbic regions of persons with major depression. Rats with experimentally induced learned helplessness exhibit alteration of glucocorticoid RNA in the limbic system, especially the hippocampus (Lachman et al., 1993). Dubrosky (1993) commented on alterations in the adrenal hormones in the hippocampus of depressed individuals. The incidence of depression in persons with Huntington's chorea has led to speculation that degeneration of the pathways connecting the paralimbic system and basal ganglia may be involved in depression (Mayberg et al., 1992). Finally, Fu and associates (1993) observed that the affective changes (including depression) seen in persons with Borna disease appear to be related to loss of neurons and astrocytes at the limbic level.

Neuropathology in DAT is characterized by cortical atrophy and the presence of neurofibrillary tangles and amyloid (Senile) plaques (Lamy, 1992; Lezak, 1995; Rue, 1992). Neurofibrillary tangles consist of neurofibrils of paired helical filaments of tau protein at the dendrites and axon terminals, resulting in abnormal intraneural configurations (Brizzee, 1984; Selkoe, 1993). While found in the frontal and temporal cortex, these tangles are more densely located within the olfactory bulb (Brizzee, 1984),

limbic system, and entorhinal cortex (Cottman, Geddes, & Kahle, 1990). Within these structures, neurofibrillary tangles tend to be located at area CA1 of the hippocampus (Cottman, Geddes, & Kahle, 1990; Flood & Coleman, 1990; Van Hoesen & Hyman, 1990), anterior olfactory nucleus (Averbach, 1983), layers II and IV of the entorhinal cortex (Van Hoesen & Hyman, 1990), and layers III and IV of the parahippocampal cortex (Flood & Coleman, 1990; Van Hoesen & Hyman, 1990). Cottman, Geddes, and Kahle (1990) and Flood and Coleman (1990) have speculated that neurofibrillary tangles may be the result of attempts by the brain to compensate for the neuronal loss that accompanies DAT.

Amyloid plaques consist of altered axons and dendrites, as well as beta-amyloid, and may be found in the cerebral cortex, cerebellum, meninges, olfactory nucleus (Averback, 1983), thalamus, and hippocampus (Lamy, 1992; Selkoe, 1993). Glial cells, which normally provide structure and support for the neurons, are altered, with microglial cells (scavenger cells) found inside the plaque, and astrocytes along the outside.

These plaques, which form slowly and may take years to develop, are characterized by extracellular deposits of protein fragments folded in an identifiable three dimensional pattern called a beta-pleated sheet (Selkoe, 1993). Like neurofibrillary tangles, amyloid plaques are found in both normal brains and the brains of persons with DAT, but with significantly greater numbers for the latter.

Beta-amyloid is formed from beta amyloid precursor protein (beta-APP) (Lamy, 1992; Selkoe, 1993). While once believed to be the result of neural stress, beta-amyloid has been found in the blood vessels of unimpaired individuals, and is now considered to precede, rather than to follow, neural degeneration (Selkoe, 1993). Beta-amyloid is believed to be the primary causative factor in DAT (Lamy, 1992; Selkoe, 1993). The amino acid structure for beta-APP is located on chromosome 21, with amyloid plaques being seen in Down's syndrome (which is caused by a trisomy of chromosome 21) as well as in DAT. While there are several types of beta-APP, current thinking holds that erroneous splitting of beta-APP 695 (Selkoe, 1993) or beta-APP 751 (Lamy, 1992) is responsible for the development of beta-amyloid.

It should be noted that beta-amyloid may result from neurotoxic exposure (Selkoe, 1993). Consequently, mutation of beta-APP without a genetic component may also lead to DAT. Much research is currently focusing on the enzyme responsible for this splitting. It is currently believed that a substitution of glutamine for glutamic acid at position 22 of beta-APP is the most likely mechanism of mutation (Lamy, 1992; Selkoe, 1993).

Changes have also been identified in the neurochemical substrate of persons with DAT (Lamy, 1992). Choline acetyltransferase levels are 40% - 90% lower in victims of Alzheimer's disease. As a result, these persons experience

a decrease in the synthesis of acetylcholine, especially in the posterior paratemporal cortex.

Research is also investigating the role of N-acetyle-Daspartate (NDMA) receptors in DAT (Lamy, 1992). These receptors are densely located in the hippocampus and are responsive to glutamate. Glutamate is an excitatory neurotransmitter that is primarily involved in neural degeneration secondary to ischemia or hypoxia. As oxygen levels decrease, the level of glutamate rises, causing a massive influx of calcium ions, which overloads the neuron, killing it. Results remain inconclusive as to the role this mechanism may play in the neural loss seen in this disorder.

A decrease in the levels of somatostantin has also been found in the brains of persons with DAT, however the relationship of this decrease to the overall disease process remains unclear (Rue, 1992). Gracon, Grossberg, and Jurkowski (1993) suggested that the neurochemical basis for DAT appears rather complex, and noted that future research is likely to implicate other neurotransmitters in the disease process.

Prevalence Estimates and Diagnostic Issues

Because of problems accurately diagnosing DAT prior to autopsy, prevalence estimates for this disorder remain crude (Gurland & Cross, 1986; Schoenberg, 1981), ranging from 2% - 10% of the population over age 65 (American Psychiatric Association, 1994; Rocca, Amaducci, & Schoenberg, 1986). The incidence appears to increase with age and may be as

high as 50% for persons over age 85 (Evans, 1989; Lamy, 1992).

The earliest symptoms of DAT are often unrecognized or mistakenly attributed to fatigue, boredom, or depression by both health care personnel and family members (McHugh, 1975). Impairment of recent memory is typically the first cognitive symptom seen (Lezak, 1995; Rue, 1992; Strub & Black, 1977). The condition may begin insidiously, with symptoms not being apparent until a disruption in normal routine leaves the victim disoriented, confused, and unable to cope with the unfamiliar situation. Early in the course of the disorder other symptoms such as inattention, cognitive dulling, social withdrawal, emotional blunting, and mild agitation may lead to the erroneous diagnosis of depression.

Kay, Beamish, and Roth (1964) noted that diagnostic errors are common in the early stages of dementia, with both physicians and psychologists having to rely heavily upon clinical judgement for differential diagnosis (Parasuraman & Haxby, 1993). Lezak (1995) reviewed the literature and noted that the diagnostic accuracy of DAT may run as high as 86%. Unfortunately, this still leaves at least 14% of the cases as being misdiagnosed. The incidence of misdiagnosis is not surprising, given that the only accurate methods of diagnosis are autopsy and brain biopsy, to evaluate for the presence of neurofibrillary tangles and amyloid plaques (Gurland & Cross, 1986). Unfortunately, autopsy comes too

late to be of value in the treatment of the individual, and brain biopsy is considered inappropriate because of the mortality risk entailed by the procedure. Victoroff, Mack, Grafton, Schreiber, and Chui (1994) noted that the advent of both approved and experimental treatments for this disorder have increased the need for accurate antemortem diagnosis.

Differential diagnosis is especially difficult between dementia and depression (American Psychological Association, 1994; Bieliauskas, 1993a; Bieliauskas, 1993b; Caine, 1982; Crevel, 1986; Strub & Black, 1977). This is partially attributable to the fact that depression is among the most prevalent mental disorders in the elderly (Blazer, 1990; Solomon & Patch, 1974), often with symptoms that mimic cognitive deficit (Alzheimer's Association, 1987; McHugh, 1975). When such a symptom picture occurs, without structural damage to the brain, a state of pseudodementia is said to exist (Caine, 1982; Crevel, 1986; Madden et al., 1952).

To further complicate matters, depression may be one of the earliest symptoms of dementia (Bieliauskas, 1993b), with perhaps 30% of the victims of DAT also meeting the criteria for clinical depression (Teri & Reifler, 1987). Teri and Wagner (1992) reported that the depressive symptoms may decrease as the disorder progresses. This depression may be secondary to an inability to cope with situational stressors (Caine, 1982). It is also possible that degeneration of the amygdaloid and frontal areas may also provide a biological

explanation for the depressive symptoms (Brizee, 1984). Lezak (1995) noted that a combination of situational and organic factors may best explain these symptoms. In any event, merely evaluating for depression may fail to distinguish between those suffering solely from depression and those in the early stages of DAT. Since the changes associated with normal aging are quantitatively rather than qualitatively different from those seen in early DAT, differential diagnosis of age-associated memory impairment (AAMI) and DAT is also problematic (Lamy, 1992; Selkoe, 1992).

A final complicating factor in the diagnosis of DAT is that numerous anti-cholinergic medications may produce a delirium which may be confused with dementia in the elderly (Dysken, Merry, and David, 1978; Paddison, 1984). Drug categories capable of producing these symptoms include various anxiolytics, antidepressants, antipsychotics, belladonna agents, cold medications, allergy medications, antacids, cough suppressants, sleep aids, anti-motion sickness agents, laxatives, and analgesics.

Neuropsychological Evaluation in Early DAT

Neuropsychological evaluation is helpful in documenting the presence of memory impairment and other cognitive deficits seen in DAT, and in charting the progression of these deficits over time (Altman, 1983; Crook, 1983). Such evaluation is also useful in determining if the pattern of deficits seen is consistent with DAT as opposed to another

dementing disorder such as multi-infarct dementia (Altman, 1983).

Neuropsychological assessment of the individual with a suspected dementia, regardless of the assessment battery used, involves the assessment of orientation to time, person and place; language skills; fund of knowledge; recent memory; attention span; abstract reasoning; and constructional ability (Strub & Black, 1977; Lezak, 1995; McHugh, 1975).

Hom (1992) and Whitehouse, Lerner, and Hedera (1993) have noted that neuropsychological assessment is sensitive to deficits of higher cognitive functioning attributable to DAT. Early in the course of the disorder the person tends to have relatively stable intellect, language skills, verbal memory, and visuospatial skills (Jones et al., 1992; Lezak, 1995). Measures of temporal orientation, visuoconstructional ability, and visual memory are more likely to be diagnostically useful at this point (Jones et al., 1992).

It should be noted, however, that test performance often overlaps for normal elderly, depressed, elderly, and those in the early stages of DAT (Rue, 1992). Consequently, the final diagnostic impression will be based upon test results, behavior observation, and the victim's history (Altman, 1983). While adding significant information to assist in the diagnostic process, neuropsychological testing has not solved the problem of the accurate early

identification of DAT (Rue, 1992). It should also be noted that neuropsychological testing may be quite stressful for both normal elderly and DAT sufferers, and it is therefore recommended that such assessment be as brief as possible (Volana, 1989).

Medical Assessment of DAT

Like neuropsychological assessment, medical assessment is also prone to diagnostic errors in the differentiation of DAT from depression, with the differential diagnosis based heavily upon clinical judgment (Caine, 1982). Perry and Cella (1986) reported that physicians are prone to underdiagnose dementia, opting instead for a psychiatric diagnosis such as depression or noncompliance with treatment.

Medical assessment of the person with a suspected dementia may include x-ray computed tomography (CT scan), lumbar puncture, serum B_{12} level, tests of thyroid function, chest and skull x-rays, electroencephalograph (EEG), and syphilis screening (Caine, 1982). Walkin and Blennow (1992) recommended including an electrocardiogram and cerebrospinal fluid test as part of the assessment device. This variety of tests is recommended to rule out other disorders such as tumors, endocrine disturbances, and infections, and with the possible exception of the CT scan and EEG, contribute little to the definitive diagnosis of dementia.

Medical technology has produced numerous diagnostic devices, including the CT scan, positron emission tomography

(PET scan), magnetic resonance imaging (MRI), neuromagnetic imaging (NMI), pneumoencephalography (PEG), radioscope cisternography, EEG, and brain electrical activity mapping (BEAM), which have been evaluated as potential tools for improving the reliability and validity of the differential diagnosis of DAT.

The CT scan is widely used in the evaluation of demented persons (National Institute of Mental Health, 1989; Powell & Benson, 1990). It is especially useful in the diagnosis of multi-infarct dementia, as well as for ruling out neoplasms, subdural hematomas, cysts, etc. (Jacobson & Farmer, 1979; Powell & Benson, 1990). While decreased cortical mass will result in ventricular enlargement in about half the persons diagnosed with DAT (Lezak, 1995; Powell & Benson, 1990), a 50% false negative rate still exists. In addition, numerous other conditions, including Binswanger's disease (Rosenberg et al., 1979), nutritional deficits (Powell & Benson, 1990), and normal aging (Ford & White, 1981; Morris & McManus, 1991) may produce CT patterns similar to those seen in DAT. These findings led Powell and Benson (1990) and Rue (1992) to conclude that, while possibly helpful, the CT scan is not diagnostically specific for DAT.

PET scanning is a technique whereby an isotope (oxygen-15 or fluorine-18) is injected into the patient either intra-veneously or intra-arterially, and the emitted radioactivity is measured and imaged (Powell & Benson,

1990). This technique makes possible the in vivo study of the physiological and biochemical processes of the brain. Regional hypometabolism has been noted in several areas of the brain affected by DAT (Rue, 1992). While PET scanning has shown promise in the differential diagnosis of DAT (National Institute of Mental health, 1988; Powell & Benson, 1990), there is still considerable overlap between the patterns detected in persons with DAT and normal elderly, leading Rue (1992) to conclude that this technique must still be considered experimental in nature. In addition, the short half-lives of the isotopes used (two minutes to 1.7 hours) necessitate immediate access to a cyclotron, which puts this technology out of the reach of all but the most heavily research oriented institutions (National Institute of Mental Health, 1989; Powell & Benson, 1990).

Benson and Powell (1990) noted that MRI is based upon the manipulation of protons via a magnetic field and a radiofrequency pulse that causes realignment of the protons, producing an image. While these images can be produced by different techniques, including inversion, saturation recovery, and spin echo, the latter is most commonly used. Advantages of the MRI include the production of images that can be constructed along any three dimensional plane, no artifact from bone interference, and no exposure of the patient to radiation. MRI poses no known harm to subjects (National Institute of Mental Health, 1989) and produces a clearer image than CT scans (National Institute of Mental

Health, 1989; Powell & Benson, 199). While these advantages give the MRI more clinical utility than the CT scan, no standard method to interprete MRI scans for DAT exists, and studies have demonstrated only low to modest interrater reliability with regard to dementia (Victoroff et al., 1994). Finally, like the CT scan, the ventricular dilation seen on MRI may be attributable to numerous conditions other than dementia, including normal aging (Morris & McManus, 1991).

NMI maps the brain by non-invasively recording the magnetic signals produced by the electrical activity of the cerebral cortex (National Institute of mental Health, 1989). While this technique has shown promise in localizing lesions related to epilepsy, insufficient research exists to determine it's utility in detecting DAT.

PEG is one of the older brain imaging techniques, involving the introduction of air into the cerebrospinal circulation pathway and taking x-rays of the air containing cranial contents (Powell & Benson, 1990). While PEG demarcates the ventricular system more clearly than the CT scan, suggesting some utility in the diagnosis of DAT, this is a highly invasive technique that is rarely performed because of an unacceptable mortality rate.

Radioisotope cisternography involves the injection of radioactive compounds into the subarachnoid space (Powell & Benson, 1990). While an older technique, this may still be used to rule out communicating hydrocephalus as a cause of

the dementia. Communicating hydrocephalus occurs when the arachnoid villi fail to absorb cerebrospinal fluid (CSF), causing CSF to build up at the foramens of Mengendie and Luschke (Ganong, 1979). The resulting pressure produces a dementia with a non-specific symptom pattern (Whitehouse, Lerner, & Hedera, 1993). Differential diagnosis is important because this disorder may be reversible by surgically introducing a shunt to increase flow of the CSF.

EEG is a technique by which electrodes are placed along the scalp to monitor the electrical activity of the brain (Schnieder & Tarshis, 1980). While EEG slowing is noted in the later stages of DAT (Cummings & Jarvik, 1989; Rue, 1992), the EEG may be normal early in the course of the disorder (Cummings & Jarvik, 1989). Also, EEG slowing may be caused by a number of disorders, (Rue, 1992), as well as seen in normal elderly (Morris & McManus, 1991). While the EEG may have some utility in differentiating dementia and depression (Tym, 1989), it lacks the diagnostic specificity needed for a definitive diagnosis of DAT.

Traditional EEG technology has been limited by the slow recording capabilities of the EEG pens (Schneider & Tarshis, 1980). BEAM is a diagnostic technique where the EEG results are transmitted directly to a computer for analysis (Walker & Patoon, 1988). While advocates of this technology argue that BEAM is superior to EEG, CT scans, and neuropsychological testing in making various differential diagnoses, including cerebrovascular disease, mass lesions,

and the residual effects of head trauma, the research base for these claims is limited. The existing BEAM equipment is poorly standardized from one manufacturer to another, and there are no set criteria defining the qualifications for technicians using this equipment (Binnie & MacGillivray, 1992). Rue (1992) noted that this technique must still be considered experimental.

The popular press continually reports on new diagnostic procedures for DAT (including blood tests, skin tests, and eye examinations). Unfortunately, these tests remain highly experimental and are not seen as being ready for clinical use for several years (Gracon, Grossberg, & Jurkowski, 1993).

Olfaction in Dementia and Depression

Olfactory assessment has traditionally played a minor role in the neurological examination (Demyer, 1980; Mechner, 1975) and has been virtually non-existent as part of the neuropsychological evaluation. Harrison and Pearson (1989) attributed this neglect to the fact that, until recently, precise olfactory assessment was a rather cumbersome task, necessitating maintaining several bottles of aromatic compounds at precise intensities. Engen (1982) noted that the anecdotal nature of olfactory testing has also contributed to the lack of research in this field. Development of a standardized olfactory assessment device, the Smell Identification Test (SIT) (Doty, 1983) has simplified this task and may lead to increased use of

olfactory assessment in the differential diagnosis of various disorders (Harrison & Pearson, 1989).

While complete lack of olfactory sensitivity without some type of precipitating trauma is rare (.2% of the United States population) (Engen, 1982), decreased olfactory sensitivity in the elderly is well documented (Colavita, 1978; Corso, 1981). This decreased sensitivity is believed to result from depletion of the olfactory receptors in the epithelium secondary to repeated exposure to infectious and toxic agents, as opposed to impairment of the brain regions associated with olfaction (Corso, 1981).

Both anosmia (complete loss of smell) and dysnosmia (impaired ability to smell) have been documented in victims of closed head injury (Costanzo & Zasler, 1992). In both cases the dysfunction may occur through injury to the first cranial nerve, structural damage to the nasal passages, or damage to the regions of the brain involved in olfaction.

Research has also demonstrated olfactory impairment in several dementing conditions. Olfactory impairment has been reported early in the course of DAT (Doty & Reyes, 1987; Peabody & Tinkenberg, 1985; Serby et al., 1985) and Down's syndrome (Warner, Peabody, & Berger, 1988). Olfactory deficits may be seen in Parkinson's disease (Serby et al., 1985), Parkinsonism-dementia complex of Guam (Doty et al., 1991), and dementia secondary to infection with the human immunodeficiency virus (HIV) (Brody, Serby, Etienne, & Kalkstein, 1991). Similar deficits have also been reported

in persons with Korsakoff's dementia, schizophrenia, and Huntington's disease (Harrison & Pearson, 1989).

Olfactory deficits may be related to depression, however the results are less clear (Harrison & Pearson, 1989). Lesions to the olfactory bulbs have been found to cause depressive behavior in rats (Richardson, 1991) and depressive symptomatology in two humans (Levinson, 1985). Zenter and Zenter (1985) reported that depressed persons report decreased vividness of all sensory qualities, including smell. Controlled studies have failed, however, to support the idea of olfactory deficits in depressed persons. Warner, Peabody, and Csemansky (1990) were unable to differentiate six male subjects suffering from major depression from control subjects on the basis of olfaction. Amsterdam and associates (1987) reported no olfactory differences between 80 adult subjects with depression and non-depressed controls.

Other factors are also related to depression and should be controlled for in any well designed study related to the field. Gender differences in olfaction have been well documented, with females being more sensitive to most odors (Doty, Shaman, & Dann, 1984; Engen, 1982). Racial differences have also been documented with regard to odor acuity, suggesting a need to match subjects with regard to ethnic background. Finally, smokers have been found to be less sensitive to smell, regardless of the amount smoked (Doty, Shaman, & Dann, 1984).

Anatomy and Physiology of Olfaction

The sense of smell is initiated via chemical stimulation of the olfactory-receptor cells of the olfactory neuroepithelium (Smith & Shipley, 1992). These cells are located along the top of the nasal vault, as well as at the upper section of the nasal septum, the medial wall of the superior turbinate, and in the cribriform plate region. Olfactory receptors are primitive bipolar sensory neurons, and are accompanied within the epithelium by supporting cells, basal cells, and microvillar cells (Smith & Shipley, 1992; Tamar, 1972).

The olfactory receptor cells must continually regenerate themselves due to injury from viral infection, toxic exposure, and other environmental hazards (Smith & Shipley, 1992). The basal cells are the site of this regenerative process, serving as stems for the new receptor cells. While this theoretically suggests that complete recovery is possible from damage to the olfactory nerve, a number of conditions, including gliosis, edema, and impaired structural integrity at the cribriform plate may prevent the newly sprouting axons from reaching the olfactory bulb (Costanzo & Zasler, 1992).

Bowman's glands lie within the lamina propria and help produce the mucus layer that covers the olfactory epithelium (Price, 1987). This aqueous mucus aids in protecting the olfactory neurons. Olfactory stimuli must pass through the aqueous mucus in order to reach the receptor cells. This

makes it difficult to predict how much of any given stimulus actually reaches the receptor cells. This difficulty is increased by the fact that the olfactory epithelium rapidly metabolizes the various stimuli via cytochrome P-450 dependent oxygenase at the level of the aqueous mucosa. While this process serves to protect the olfactory receptors, it also makes it impossible for researchers to guarantee the purity or intensity of a stimulus as it reaches the receptor cells.

The olfactory neurons swell slightly at their peripheral endings, forming the olfactory knob, at which point a layer of cilia extends into the mucus layer (Smith & Shipley, 1992). While the role of the cilia remains unclear, it is believed that they aid in the chemical transduction process (Adamek, Gesteland, Mair, & Oakly, 1984; Nakamura & Gold, 1987). It should be noted, however, that destruction of these cilia do not alter olfactory potential (Tamar, 1971).

Current thinking holds that odorants bind to specific receptor proteins in the olfactory cilia (Smith & Shipley, 1992). This binding activates a G-protein within the cell, which begins a chemical process whereby adenylate cyclase increases the production of cyclic adenosine monophosphate (cAMP). The increased level of cAMP leads to depolarization of the cell, triggering a neural pulse. It should be noted that this model is believed to be rather simplistic, and that future research is expected to identify a number of

specific olfactory receptor proteins. Secondary messengers, such as inositol triphosphate may also play a significant role.

The non-myelinated axons of the olfactory receptor cells become ensheathed by Schwann cells in the basal lamina, at which point bundles of these cells join to form the 15 to 20 fascicles of the first cranial nerve (Mechner, 1975; Smith & Shipley, 1992). This nerve passes through the cribriform plate ipsilaterally to the olfactory bulb (Smith & Shipley, 1992; Tamar, 1972).

Before moving into a discussion of the subcortical components of olfaction, it should be noted that some chemical stimuli can also result in stimulation via the trigeminal or fifth cranial nerve (Mechner, 1975; and Moulton & Beidler, 1967). The trigeminal system carries information about intranasal and intraoral irritation as opposed to specific odor identification. Sensations via this tract will remain intact despite damage to the olfactory system. As a result, trigeminal functioning has been used in the detection of persons feigning olfactory dysfunction (Smith & Shipley, 1992). Unfortunately, stimulation of the fifth cranial nerve also leads to increased nasal secretions, decreasing the amount of subsequent odorants reaching the receptor cells (Tucker, 1963). Since this leads to a decrease in the acuity of subsequent stimuli, an alternative method of detecting dissimulation would be desirable.

The first cranial nerve extends to the glomerular layer of the olfactory bulb, where synaptic contact is made with the dendrites of the mitral and tufted cells (Smith & Shipley, 1992). While no strict organization of the olfactory bulb's output to the olfactory cortex has been identified, the projections are not random (Scott, 1987). The complexity of this neural organization is not surprising given that each neuron may connect to over 50,000 synapses from adjacent neurons (Gazzaniga, 1992).

Areas of the olfactory cortex include the anterior olfactory nucleus, piriform cortex, olfactory tubercle, lateral entorhinal cortex, and corticomedial amygdala (Smith & Shipley, 1992). These areas are then closely connected to numerous cortical and subcortical areas, including the orbitofrontal cortex, insular cortex, mediodorsal and submedial thalamus, hippocampus, and anterior and medial hypothalamus.

Tamar (1972) noted that the olfactory system is unique in having neural pathways projecting directly into these systems rather than first being routed through the thalamus. Wenzel (1974) noted the direct link that the olfactory tract has to the limbic structures associated with memory. Riss, Halpern, and Scalia (1969) and Stoddart (1988) have proposed that the limbic and olfactory systems evolved in conjunction with each other, accounting for the close tie between the two systems.

The significant overlap between the brain structures

related to olfaction and areas subject to degeneration early in the clinical course of DAT provides a biological basis for the olfactory deficits seen early in the course of DAT. Significant overlap is also noted between the brain structures related to olfaction and emotional arousal. However, as noted earlier the relationship between depression and olfaction is less clear. Given the decrease in olfactory functioning seen in DAT, it is possible that olfactory deficits would provide one means of differentiating between persons with depression and Alzheimer's disease.

Chapter 3

METHODOLOGY

The review of the literature suggests that olfactory deficits occur early in the course of dementia of the Alzheimer's type (DAT), and may precede both cognitive impairment and personality change (Gracon, Grossberg, & Jurkowski, 1993; Harrison & Pearson, 1989). While the literature is mixed, controlled studies have failed to detect olfactory deficits in depressed individuals (Amsterdam et al., 1987; Warner, Peabody, & Csemansky, 1990). This suggests that differences in olfactory functioning may help distinguish between these groups.

Description of the Sample

Sample size is a function of several variables, including subject availability, cost of equipment, time limitations, and the statistical procedures to be used (Ferguson & Takane, 1989). Typically, as large a sample as is feasible is desired, because increasing the sample size is the only way to simultaneously decrease the likelihood of both Type I and Type II error. Ferguson and Takane have recommended a minimum sample size of 30 for most statistical tests, including analysis of variance.

Because olfactory differences have been found with regard to gender (Doty, Shaman, & Dann, 1984; Engen, 1982) and smoking behavior (Doty, Shaman, & Dann, 1984), participants were cross-matched according to these variables. Research has also documented that olfactory functioning declines steadily with age (Colavita, 1978; Corso, 1981). For this reason, participants were also cross-matched by age, using the age categories upon which the Smell Identification Test was normed (Doty, 1983). Given that most cases of DAT develop after age 65 (Whitehouse, Lerner, & Hedera, 1993), the participant pool was restricted to those age 65 and older.

While differences in olfactory acuity have also been demonstrated across different racial groups (Engen, 1982), limited access to a large multiracial population posed problems with cross-matching along the other variables. Consequently, the current sample consisted of all White participants.

Costanzo and Zasler (1992) reported a higher incidence of olfactory dysfunction in persons suffering from closed head injury. For this reason, persons reporting any type of head injury resulting in inpatient hospital treatment were excluded from the study. Harrison and Pearson (1989) reported that persons with a variety of dementing disorders, including Parkinson's dementia, Huntington's dementia, and schizophrenia exhibited impaired olfactory functioning. Consequently, individuals with a history of any type of

dementia other than DAT were also excluded from the study.

Because of the difficulty cross-matching each participant across groups with regard to age, gender, and smoking behavior, as well as the cost of test materials, the sample was limited to 30 subjects per group. A comprehensive breakdown of participants after cross-matching is found in Table 1.

Table 1. Participant Pool Following Cross-Matching for Age, Gender, and Smoking Behavior.

Age	Male		Female	
Grouping	Smoker	Nonsmoker	Smoker	Nonsmoker
61-65	1	2	0	0
66-70	4	3	0	1
71-75	2	2	0	1
76-80	2	3	0	1
81-85	1	1	0	2
86-90	0	2	0	2

Instrumentation

Global Deterioration Scale (GlDS) (Reisberg, Ferris, DeLeon, & Crook, 1982) is a rating scale designed for assessing the clinical course of DAT. It offers an objective system for health care professionals to chart the victim's progression through the course of the disorder along seven stages. The clinician incorporates information from the individual's daily activities, cognitive abilities, and behavioral symptomatology to make this rating (Eisdorfer et al., 1992; Reisberg et al., 1982). The GlDS also allows

for the rater to incorporate the victim's previous level of educational attainment, cultural factors, and socioeconomic status into the rating (Reisberg et al., 1982).

In a review of the literature, Eisdorfer and associates (1992) noted that numerous studies have found acceptable levels of interrater reliability for the GlDS (r= .82 to .92). With regard to validity, Reisberg and associates (1982) reported that the GlDS correlated significantly (r= .31 to .66, p<.05 to .001) with 13 of the 19 cognitive items on the Inventory of Psychic and Somatic Complaints in the Elderly. Significant correlations were also noted between the GlDS and the Buschke Verbal Learning Task (r= -.54 to -.63, p<.001), Design Memory (r= -.58 to -.61, p<.001), Facial Recognition Test (r= -.42 to -.52, p<.001), and Peterson and Peterson's Short Term Retention Test (r= -.48 to -.56, p<.001).

Both computerized axial tomography (CT) and positron emission tomography (PET) scans have documented changes in the structure and functioning of the brains of persons with DAT (Lezak, 1995; National Institute of Mental Health, 1989; Powell & Benson, 1989). The GlDS was also found to correlate significantly with CT scans of ventricular dilation (.61, p<.01) and sulcal enlargement (r= .53, p<.01) (Reisberg, et al., 1983). Finally, this measure was also found to correlate highly (r= .69 to .83, p< .05) with slowed glucose utilization in the caudate, thalamic, and temporal regions of the brain as measured by PET scan.

Geriatric Depression Scale (GDS) (Brink et al., 1982) is a self-report measure of depressive symptomatology designed to be less sensitive to confounding variables of depression in later life, such as physical complaints, decreased libido, and appetite changes (Hyer & Blount, 1984). 30 items follow a true - false format designed to yield a higher completion rate than measures using a multiple choice format, thereby leading to a more valid profile (Dunn & Sacco, 1989). Scores of 10 or less are interpreted as non-depressed. Scores of 11 - 20 are interpreted as mildly to moderately depressed, while scores greater than 20 suggest severe depression (Brink et al., 1982).

Brink (1985) demonstrated that the GDS has acceptable test-retest reliability (.86). Tomkin, Carson, Nixon, and Hyer (1985) reported that the GDS is not confounded by age. Studies have demonstrated the accuracy of this instrument in diagnosing depression in persons from their early 20s (Kongstvedt & Sime, 1991; Tomkin et al., 1985) to age 95 (Salamero & Marcus, 1992).

Regarding validity, no significant difference was found between the number of depressive symptoms reported on the GDS compared to the number of symptoms reported by three psychiatrists for 143 control subjects ($F= 0.14$, $p>.05$) and 51 depressed subjects ($F=.58$, $p>.05$) (Burke, Nitcher, Roccaforte, & Wengel, 1992). The GDS was able to accurately distinguish between these groups ($t=-5.9$, $p<.0001$). A study

by Hyer & Blount (1984) reported a high correlation between the GDS and Beck Depression Scale ($r=.73$, $p<.001$). This study also indicated that the GDS had both a lower false positive rate (16.6% versus 40%) and false negative rate (6.4% versus 12.9%) than the Beck Depression Scale. Other research has demonstrated a significant correlation between the GDS and both the Zung Depression Inventory ($r=.82$, $p<.001$) and Hamilton Rating Scale for Depression ($r=.82$, $p<.001$) (Brink et al., 1982). Furthermore, the GDS demonstrated both superior sensitivity (90% versus 86% and 88%) and specificity (80% versus 70% and 75%) to depression than either the Zung or Hamilton scales.

Mini Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) is a brief measure (11 questions, requiring 5 - 10 minutes to administer) designed to assess the cognitive status of patients. A maximum score of 30 is possible. Fewer than 24 items correct is suggestive of a dementing disorder. Nelson, Fogel, & Fogel (1986) reviewed the literature and noted that several studies suggest that the MMSE has a combined interrater/test-retest reliability of between .83 and .99. Research has consistently demonstrated a close relationship between the MMSE and the Wechsler Adult Intelligence Scale ($r= .83$, $p<.0001$) for identifying persons with cognitive impairment (Farber, Schmitt, & Lague, 1988). Gracon, Grossberg, and Jurkowski (1993) noted that the MMSE is the most useful brief screening instrument for differentiating persons on the

basis of cognitive impairment.

Smell Identification Test (SIT) (Doty, 1983) was developed to provide a standardized instrument for quickly and easily examining olfactory functioning. The test was developed over five separate studies, which were designed to identify a group of odorants easily identified by the majority of the population, develop a standardized administration format, determine extraneous factors which may affect test performance, and determine the reliability and validity of the instrument. The initial version of the test consisted of 50 different odorants (see Appendix A), however over the course of development, 10 of the odorants were eliminated. Nine of the odors (apple, black pepper, chili, musk, pumpkin pie, skunk, tomato, and whiskey) were eliminated because of a low correct response rate. Garlic was eliminated because of it's similarity to onion.

The current form of the SIT consists of 40 stimulus cards which utilize a "scratch and sniff" procedure to release the odorant (Doty, 1983; Doty, Shaman, & Dann, 1984). The subject identifies the odor from a four item multiple choice selection. Doty (personal communication, November 29, 1993) noted that each of the 40 current odorants has a low irritant value. At present, over 40,000 SIT protocols have been administered with no reported allergic reactions. Also, no incidents of traumatic memory recall have been reported from this instrument.

The reliability and validity of any sensory measure is

related to the extent to which the subject is able to perceive the stimulus being measured. Ghorbanian's staircase detection threshold provides a standardized approach to assess the intensity of an odorant necessary for it to be detected by a given population (Ghorbanian, Paradise, & Doty, 1983). Briefly, this task requires the subject to successively sniff two bottles, one with a neutral solution and the other with the neutral solution plus a given concentration of some aromatic compound that is relatively free of ability to elicit trigeminal stimulation. The subject is then asked which of the two bottles elicits the stronger sensation. The concentration is steadily increased by 1.0 log units until a specified number of consecutive correct responses is obtained. At this point, the concentration is consistently decreased by .5 log units until the subject has two consecutive errors. This alternating procedure yields one staircase being transversed. This procedure is continued until a specified number of staircases are covered, to insure a specific intensity of the given odorant.

To insure the intensity of odors on the SIT, they were compared to a standard solution obtained by using the Ghorbanian threshold procedure (Doty, 1983; Doty, Shaman, & Dann, 1984). The neutral odorant was propylene glycol and the stimulus odorant was perfume grade phenyl ethyl alcohol. The beginning intensity was 20 ml of each substance, and four staircases were traversed to obtain the comparison

odorant. The intensity of odors on the SIT was found to correlate highly ($r=.89$, $p< 0.001$). with the comparison solution.

Research on the SIT suggests good test-retest reliability at six months ($r=.918$, $p< 0.001$) (Doty, Shaman, & Dann, 1984). Validity studies have differentiated between person's with total bilateral anosmia, Korsakoff's syndrome, and normal controls (Doty, 1983; Doty, Shaman, & Dann, 1984). The SIT was also able to distinguish between control subjects, anosmic subjects, and persons instructed to fake an olfactory disorder. The criteria used for differentiating groups is found in Table 2.

Table 2. SIT Diagnostic Criteria

SIT Score	Olfactory Diagnosis
00 - 05	Probable malingering
06 - 19	Total anosmia
20 - 33	Microsmia (males)
20 - 34	Microsmia (females)
34 - 40	Normosmia (males)
35 - 40	Normosmia (females)

Doty (1983) provides age-related median scores for male and female subjects, however these norms are based upon relatively small sample sizes. Also, normative subjects were not screened for dementia, a history of closed head injury, or other factors which may have affected performance on the SIT. It is therefore possible that these scores are

lower than what would be seen in an unimpaired population. Median SIT scores for the age sample considered in Doty's normative study are found in Table 3.

Table 3. Age-Related Median Scores for the SIT

Age	Median Score (Males)	Median Score (Females)
61 - 65	34	35
66 - 70	29	34
71 - 75	27	32
76 - 80	17	24
81 - 85	20	23
86 - 90	26	25

Examiner Qualifications

Examiners used for data collection were doctoral candidates in counseling psychology, who had completed all doctoral course work, including neuropsychology and neuropsychological assessment. Each examiner had at least two years of professional experience related to psychological and neuropsychological assessment and counseling.

Procedure

All participants were informed of the purpose of the study before participation and were asked to sign an informed consent (see Appendix B). Participants indicated their understanding of the consent form by explaining the form in their own words, prior to signing it. In addition, consent to conduct research was obtained from all

institutions where participants were obtained. These included Deming Center, Terre Haute, Indiana; the Veteran's Administration Medical Center, Danville, Illinois; United Samaritan's Hospital, Danville, Illinois; and the Champaign County Nursing Home, Champaign, Illinois.

Issues of competency arise with any individual suffering from cognitive impairment (Lezak, 1995). For this reason, consent was not only required from the DAT participants, but from their legal guardians or next of kin as well.

Participants were also asked to complete a basic demographics sheet to obtain information related to age, gender, smoking behavior, and medical history (see Appendix C). Because persons with DAT may be poor historians (Schoenberg, 1981), demographic data for these individuals was obtained from interview with family members and medical records.

Three groups of 30 participants were run. Group 1 consisted of individuals previously diagnosed with DAT. These participants were obtained from area medical centers, day care programs for persons with DAT, and area nursing homes. They were administered the MMSE, with a score 23 or lower needed to confirm the existence of dementia. In addition, one of their primary health care providers, or a family member closed involved in their care, was asked to assign them a rating from the Global Deterioration Scale. Participants with a rating of stage 3, 4, or 5 on this scale

were considered to be in the earlier stages of the disorder, and were administered the SIT. No persons screened for the study fell below stage 5. One individual was dropped from this group prior to administration of the SIT, after family members indicated that he had experienced olfactory difficulties for several years following his career as a professional boxer.

All participants in groups 2 and 3 were administered the demographics sheet, GDS, MMSE, and SIT. A score of 24 or greater on the MMSE was used to indicate that participants included in these groups were cognitively intact.

Group 2 consisted of 30 individuals matched to group 1 with regard to age, gender, and smoking behavior. Each participant reported a history of treatment for depression. Participants were again obtained from area medical centers and day care programs, as well as being identified while screening for control subjects. All participants scored 11 or higher on the GDS, confirming the existence of depressive symptomatology at the time of testing. One individual was dropped from this group prior to administration of the SIT after indicating that he was left totally anosmic following a career as a professional boxer.

Group 3 served as a control group, and consisted of 30 persons also matched to group 1 with regard to age, gender, and smoking behavior. In addition to being obtained through area medical and retirement centers, part of the control

group was obtained through persons residing in the community. All participants obtained a score of 10 or below on the GDS, suggesting the absence of clinically significant depression.

Statistical Analysis

Because scores obtained from the SIT represent interval data, a one-way analysis of variance (ANOVA) was used to determine whether a significant difference existed between group scores (Ferguson & Takane, 1989; Nee et al., 1975). Since previous studies suggest that poorer performance would be found among persons with DAT and possibly with depression, a one-tailed test was employed. In addition to the ANOVA, Hartley's F_{max} test was used to insure homogeneity of variance between group scores. Duncan's multiple range test was used to determine what significant differences existed between groups. While less conservative than other post hoc comparison methods, such as Scheffe's method, Tukey's honestly significant difference, and Newman-Keuls method (Ferguson & Takane, 1989), the multiple range method was chosen to help counter-balance the level of error inherent in correctly diagnosing DAT prior to death.

The level of significance for a statistical test is determined to assess the likelihood of rejecting the null hypothesis, when it is in fact true (Ferguson & Takane, 1989). Research convention is to set the level of significance at the .05 level unless unusual circumstances dictate a more stringent set of criteria. Because no such

conditions were present in this study, the alpha level of all statistical tests was .05.

Research Question

The following was the research hypothesis for this study, stated in null form: No significant differences would be found between the SIT scores of a sample of participants with DAT, a matched sample of depressed participants without dementia, and a matched sample of controls without depression or dementia.

Chapter 4

RESULTS

The purpose of this study was to determine the differences between elderly persons with dementia of the Alzheimer's type (DAT); non-demented, depressed elderly; and non-demented, non-depressed elderly controls with regard to olfactory performance. The three groups under study were composed of 30 participants per group, matched with regard to age, gender, and smoking behavior.

In this chapter, the results of the study are reported with regard to the following null hypothesis:

Null Hypothesis. There is no significant difference between persons with DAT; non-demented, depressed elderly; and non-demented, non-depressed elderly controls with regard to performance on the Smell Identification Test (SIT).

Prior to testing the null hypothesis, group means, minimum scores, maximum scores, and standard deviations were obtained to provide a summary description of the data. This information is provided in Table 4. Homogeneity of variance for the data was demonstrated by use of Hartley's F_{max} test (F_{max}=1.36, $p>.05$).

Group comparisons were made using a one way analysis of variance. A summary of the ANOVA is found in Table 5. The

Table 4. Minimum Scores, Maximum Scores, Means, and Standard Deviations for the SIT Scores by Group.

Group	Min.	Max.	Mean	Standard Deviation
DAT	0	29	11.17	7.52
Depressed	7	38	27.37	7.38
Control	12	38	28.77	6.48

one way ANOVA shows a significant difference in performance on the SIT between groups, $F(2,87)=56.2458$, $p < .0000.$, leading to a rejection of the null hypothesis. Differences between groups were analyzed using Duncan's multiple range test. Results suggested that the DAT group scored significantly lower on the SIT ($p < .05$) than either the depressed or control groups. No significant difference was found between SIT scores for the depressed and control groups.

Table 5. ANOVA Summary Table.

Source	SS	df	MS	F	p
Between	5741.6	2	2870.8000	56.24	.0000
Within	4440.5	87	51.0402		
Total	10182.1	89			

In addition to the differences between groups demonstrated on the ANOVA, three unexpected findings were noted. First, the groups differed with regard to the number of "don't know" responses that participants gave. The forced choice format of the test suggests that the expected number of this type of response would be zero. It was noted, however, that the DAT group gave substantially more

"don't know" responses than either the depressed or control groups (see Table 6). While the depressed group also gave

Table 6. "Don't Know" Responses on the SIT by Group.

Group	Raw Score	Percent of Responses
DAT	311	25.92
Depressed	55	4.58
Control	3	0.25

more of this type of response than did the control group, 30 of the "don't know" responses were given by a single participant. If this subject is dropped from the sample, the percentage of these responses for the depressed group drops to 2.08%. The extreme score obtained on the Hartley's F_{max} test (F_{max}=1298.88) suggested that this set of data violated the assumption of homogeneity of variance to such a degree that no formal statistical analysis was conducted.

The second area in which the groups differed was with regard to the number of responses given, other than "don't know", which varied from the forced choice format. A summary of these intrusion responses is found in Table 7.

Table 7. Intrusion Responses on the SIT by Group.

Group	Raw Score	Percent of Responses
DAT	9	0.75
Depressed	1	0.08
Control	1	0.08

Intrusion responses were rare for both the depressed and control groups, but were more common for the DAT group.

Only participants in the DAT group gave more than one intrusive response per protocol. This data also violated the assumption of homogeneity of variance to such a degree (F_{max}=33.41) that formal statistical analysis was not performed.

While test performance was not timed, it was observed that persons with DAT took substantially longer to complete the SIT than did participants in either the depressed or control groups. While all non-demented persons completed the SIT in less than 30 minutes, DAT subjects frequently required over one hour to complete the test, with one individual requiring over two hours.

Discussion

The purpose of this study was to determine whether there were significant differences in performance on the SIT between persons diagnosed with DAT; non-demented, depressed elderly; and non-demented, non-depressed elderly controls who were matched with regard to age, gender, and smoking behavior. The null hypothesis, which assumed no differences between groups was rejected. Scores for the DAT group were significantly lower than those of either the depressed or control groups. No significant difference was found between depressed and control subjects.

A comparison between groups suggested that the SIT was able to distinguish the DAT group from both the depressed and control groups. This is consistent with previous research demonstrating poorer performance on measures of

olfactory functioning for persons with DAT (Doty & Reyes, 1987; Peabody & Tinkenberg, 1985; Serby et al., 1985).

Current literature suggests three possible hypotheses to explain these deficits. One possibility is that the olfactory deficits seen in DAT are directly related to degenerative changes in the peripheral olfactory system. Yamagishi and Ishizuka (1994) have suggested that the presence of tau protein in the olfactory mucosa may be related to olfactory loss. Given that tau protein is also one of the pathological changes associated with the neurofibrillary tangles present in DAT (Brizzee, 1984; Selkoe, 1993), its presence in the olfactory mucosa may implicate degeneration of the olfactory receptor cells and nerve bundles in the epithelium and lamina propria as one mechanism of olfactory loss. Additional research with persons diagnosed as having Down's syndrome, a disorder with similar neuro-degenerative pathology to DAT, has also implicated pathological changes in the olfactory epithelium as a possible mechanism for olfactory loss in persons with DAT (Zucco & Negrin, 1994).

The presence of neurofibrillary tangles and amyloid plaques have also been documented in areas of the brain related to olfactory processing, particularly the olfactory bulb (Brizzee, 1984), entorhinal cortex (Cottman, Geddes, & Kahle, 1990; Van Hoesen & Hyman, 1990) and anterior olfactory nucleus (Averbach, 1983). In addition to degeneration of the anterior olfactory nucleus secondary to

neurofibrillary tangles and amyloid plaques, ter Laak, Renkawek, and Van Workum (1994) have identified a large number of "very primitive plaques" throughout the olfactory bulbs of six persons with DAT. Together, these findings suggest that the pathology associated with olfactory loss in persons with DAT is primarily located in the brain structures related to processing smell.

The third possibility is that the poorer performance by persons with DAT on various olfactory tasks is due to the cognitive impairment accompanying DAT, as opposed to an actual olfactory deficit per se (Serby, Larson, & Kalkstein, 1991). Given that the SIT is a rather complex task, requiring individuals to remember specific directions throughout testing, to "scratch and sniff" the various odorants, read over possible choices, match the odorant to a specific choice, and correctly mark their response or inform the examiner of their response, it seems reasonable to assume that at least some lowering of scores would result from the other cognitive deficits accompanying DAT.

Recent research by Nordin and Murphy (1996) suggests, however, that cognitive deficits alone are not sufficient to explain the difficulty that persons with DAT have on measures of olfaction. Their study suggested that persons with DAT exhibit impaired ability to detect odors, but not tastes. In addition, Nordin and Murphy found that their participant's ability to recognize odors was more severely impaired than their ability to recognize faces or symbols.

They hypothesized that the deficits seen in olfactory functioning for persons with DAT may be due to impaired functioning of the hippocampal and temporal lobe structures directly related to olfactory memory.

No significant difference was found between the depressed and control groups. This finding lends support to previous studies which have failed to find olfactory deficits in persons diagnosed with depression (Amsterdam et al., 1987; Warner, Peabody, & Csemansky, 1990).

Individuals with DAT gave a greater number of "don't know" responses than either depressed elderly or control subjects. While unexpected, this may be related to the degree of olfactory deficits seen in DAT; a result of the decreased cooperation, loss of interest in tasks, and increased passivity seen in DAT (Lezak, 1995); or a combination of several factors.

The greater number of "don't know" responses given by the depressed subjects was also unexpected. It should be emphasized that more than half of the "don't know" responses given for the depressed group occurred on one protocol. It is possible that motivational factors could have resulted in the high number of this type of response for this individual. Another possibility is that this individual was experiencing some type of olfactory problem not identified during screening. A final possibility is that this individual may be in the early stages of some type of dementing process, with symptoms other than olfactory

deficits not having progressed to the point where the MMSE was able to identify them.

After correcting the high number of "don't know" responses given by the one participant, a substantial difference remains in the number of "don't know" responses given by the depressed and control groups. These responses may be due to the decreased motivation and inability to make decisions that often accompany depressive disorders (American Psychiatric Association, 1994).

The DAT group exhibited a higher number of intrusion errors than did either the non-demented, depressed group or the control group. Crosson and associates (1993) reported that intrusion errors are related to temporal lobe pathology. Degeneration of the temporal lobes is found early in the course of DAT (Brizzee, 1984; Selkoe, 1993), leading one to expect a higher incidence of these errors with this population. This is consistent with previous research documenting the increased incidence of intrusive errors seen across tasks for persons with DAT (Fuld, 1983; Fuld, Katzman, Davies, & Terry, 1982; Jacobs, Salmon, Troster, & Butters, 1990).

While standard administration of the SIT does not require timing, it was observed that persons with DAT took substantially longer to complete the test than subjects in the other groups. This appears to be a function of several factors. DAT subjects required frequent repetition of instructions and assistance with the task. This is

consistent with what would be expected given the memory impairments seen with DAT (American Psychiatric Association, 1994; Lezak, 1995; Rue, 1992; Strub & Black, 1977).

DAT subjects also required frequent breaks from the task and often became distracted, needing to be redirected to the task at hand. It is likely that these factors were related to the impaired attention and concentration seen with DAT (Lezak, 1995; Rue, 1992).

Interestingly, no persons with DAT requested stopping the testing, even though they were repeatedly told that they could do so if they desired. It was also common for the DAT participants to engage in storytelling or reminiscing about the past over the course of testing. This raises the possibility that the longer test sessions for this group were due in part to the individual attention given by the examiner.

Chapter 5

SUMMARY, CONCLUSIONS, IMPLICATIONS AND RECOMMENDATIONS

Summary

While clinicians have improved the accuracy of diagnosis for dementia of the Alzheimer's type (DAT), the differential diagnosis between persons in the early stages of DAT and non-demented elderly persons suffering from depression remains problematic, with many clinicians erroring by over diagnosing the latter disorder. With the advent of tacrine, an effective treatment became available for slowing the progression of DAT in some victims, however the multiple side effects of this drug make accurate diagnosis important. Given the progressive nature of DAT, it is also important for persons in the early stages of the disorder and their families to begin planning for long-term care and management of their estate while they remain competent to do so. Finally, depression is one of the more treatable mental disorders, and if accurately diagnosed, can be effectively managed by pharmacotherapy, psychotherapy, or a combination of the two.

Research suggests that olfactory deficits occur early

in the course of DAT, however the effect of depression on measures of olfaction is less well understood. The purpose of this study was to investigate whether the Smell Identification Test (SIT) could accurately differentiate between persons with DAT, depressed elderly, and elderly controls.

A review of the literature examined the historical background of DAT, current diagnostic criteria for this disorder, and various stage models for tracking the progression of DAT. The etiology of DAT, along with current knowledge regarding the anatomical and physiological characteristics of this disorder were covered. Prevalence and diagnostic issues relating to DAT were reviewed, especially regarding the effect that depression in the elderly may have in confounding accurate diagnosis. Olfactory studies on olfaction in both DAT and depression were examined, as well as the anatomical and physiological underpinnings of olfactory deficits as related to each of these disorders.

The review of the literature generated the following null hypothesis:

Null Hypothesis: There is no significant difference between persons with DAT; non-demented, depressed elderly; and non-demented, non-depressed controls with regard to performance on the Smell Identification Test (SIT).

The research sample was obtained from area hospitals,

nursing homes, and retirement communities, as well as from the general community. Three groups of 30 participants were cross matched for age, gender, and smoking behavior to control for the confounding effects that each of these variables may have on olfactory assessment. Given the limited availability of a multiethnic population, all participants were White. Persons with a history of any type of dementia other than DAT, or a history of serious closed head injury were excluded from the study. Participants were then assigned to one of three groups based upon the following criteria:

1. The DAT participant pool consisted of persons carrying a diagnosis of Alzheimer's disease. The presence of dementia was insured by a score of 23 or lower on the Mini Mental State Examination (MMSE)(Folstein, Folstein, & McHugh, 1975). Health care professionals or family members having close contact with the subjects rated all DAT participants at a dementia level of 3, 4, or 5 on the Global Deterioration Scale (GlDS)(Reisberg, Ferris, DeLeon, & Crook, 1982).

2. The depressed participant pool consisted of persons carrying a diagnosis of depression, which was confirmed by a score of 11 or greater on the Geriatric Depression Scale (GDS) (Brink et al., 1982). All persons in this group were considered cognitively intact on the basis of a score of 24 or greater on the MMSE.

3. The control participant pool consisted of persons with no previous history of depression. A score of 10 or lower on the GDS was used to confirm the absence of depression. These persons also scored 24 or greater on the MMSE, again demonstrating the absence of any dementing disorder.

Two participants were dropped because of multiple head traumas resulting in anosmia. Other participants were individually administered the (SIT) (Doty, 1983), a 40 item, forced choice, test of olfactory functioning.

Before discussing the conclusions and implications of the current study, it is important to remember that current results are based upon an all White sample with a limited number of female participants and no female smokers. Consequently, the current findings are most directly relevant to White males. Caution should be used in generalizing current findings to White females. Because of sampling limitations, results of this study may not be applicable to persons from different ethnic backgrounds or to female smokers.

Conclusions

The current study addressed whether significant differences existed with regard to performance on the SIT between persons with DAT, depressed elderly without dementia, and control subjects. Analysis of the results

obtained from this study suggest the following conclusions.

The SIT is able to differentiate elderly persons with DAT from depressed elderly and elderly controls. Lower overall scores on the SIT, a higher incidence of "don't know" responses, a higher number of intrusion errors, and a greater period of time to complete the test appear to be characteristic for the DAT subjects.

Results suggest that DAT subjects exhibit impaired olfactory functioning relatively early in the course of the disorder. The findings of this study also suggest that depressed elderly persons exhibit comparable olfactory functioning to their non-depressed agemates.

Implications

While a gradual decline in olfactory functioning is to be expected with increasing age, the development of extensive olfactory deficits in the absence of head trauma or some other type of neurological condition associated with decreased olfaction, such as Parkinson's disease, should alert the health care provider to the possibility of DAT. While neither persons with DAT nor normal elderly typically recognize their olfactory deficits (Nordin, Monsch, & Murphy, 1995), family reports of decreased olfactory functioning indicate a need for medical and cognitive screening to rule out early dementia.

The SIT shows promise as a relatively inexpensive,

standardized method to assess olfactory functioning, and may be a useful addition to either the neuropsychological or neurological examination. Formal olfactory assessment would provide collaborative evidence in cases of reported olfactory dysfunction. Current results also suggest that this instrument may be especially useful in differentiating persons in the early stages of DAT from those exhibiting pseudodementia secondary to depression.

The olfactory deficits exhibited by persons with DAT also present important considerations for their management. Olfaction contributes significantly to the quality of taste an individual experiences (Schneider & Tarshis, 1980). Consequently, persons experiencing any type of olfactory dysfunction may exhibit an increased preference for foods that are either sweet or salty (two of the four basic taste sensations). In such cases, careful monitoring is needed to insure that the individual maintains a balanced diet. Referral for dietary consultation may be helpful in assisting the primary caregivers to provide both nutritious and tasty food for the person with DAT.

Olfactory dysfunction also has implications for the individual's daily living. The sense of smell is important for identifying potential dangers, such as smoke or gas. While an individual who is cognitively intact should be able to compensate for impaired olfaction, the person with DAT will be unable to. Consequently, an individual with DAT

will require greater monitoring to ensure their safety.

In addition to the physical dangers presented by olfactory dysfunction, the person with DAT may fail to maintain adequate personal hygiene. Family members and primary caretakers may resort to blaming the individual by attributing lapses in hygiene to laziness or being uncooperative. It may be helpful to educate the caregivers about the individual's olfactory deficits and point out that the individual is not lazy or uncooperative. They are simply unable to smell the urine or other body odors that others are aware of.

Recommendations for Further Research

While the current study to has demonstrated the sensitivity of the SIT in differentiating persons with DAT from non-demented, depressed elderly and elderly controls, it does not address the utility of this instrument in differentiating subjects with various dementing conditions. Future studies are needed to address the sensitivity of the SIT in differentiating between DAT with other dementing conditions found within the elderly, such as Parkinson's dementia, multi-infarct dementia, and Pick's dementia.

Sampling limitations are also noted with regard to the current study. The current sample is confined to an all white population, suggesting that future research look at the utility of the SIT in differentiating similar subject

groups with a multiethnic population. The current sample was also limited with regard to the fact that no women smokers were included. Future research is needed to confirm the generalizability of current findings to this population.

The high number of "don't know" responses and intrusion responses given by the DAT group was unexpected given the forced choice nature of the test. The number of "don't know" responses given by the non-demented, depressed group also exceeded those given by the control group, which was also unexpected. Future research should address the potential utility of these responses in assisting differential diagnosis.

The current study made no attempt at developing relevant cut off scores for differentiating between DAT subjects from the depressed and control groups. Previous research has demonstrated that performance on the SIT declines with age (Doty, 1983). Appropriate cut off scores should therefore be age-related. Future research with a significantly larger sample size would be helpful in developing age appropriate norms to accurately differentiate persons with DAT from depressed and normal elderly.

The relationship between time to complete the SIT, especially with regard to the amount of assistance required to finish the test and the time spent off task, needs to be explored more fully. Additional research should address the utility of timed cut-off scores in accurately diagnosing

DAT.

Finally, the length of time required for some persons with DAT to complete the test may prohibit the use of the SIT in situations where rapid assessment is needed. The utility of abbreviated versions of this device in differential diagnosis needs to be explored.

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APPENDIXES

APPENDIX A

SIT ODORANTS

Peanut
Soap
Paint thinner
Motor oil
Smoke
Lemon
Menthol
Onion
Licorice
Wintergreen
Orange
Lilac
Grape
Gasoline
Bubble gum
Chocolate
Mint
Root beer
Cherry
Strawberry
Fruit punch
Rose
Turpentine
Pine
Pizza
(Doty, 1983)

Watermelon
Grass
Natural gas
Cinnamon
Pineapple
Coconut
Dill pickle
Clove
Banana
Garlic
Peach
Lime
Leather
Gingerbread
Cheddar cheese
Musk
Cedar
Apple
Black pepper
Chili
Tomato
Pumpkin pie
Skunk
Whiskey
Honey

APPENDIX B

CONSENT FORM

This study has been approved by the Counseling Department, Indiana State University, Terre Haute, Indiana. Questions may be directed to the Department of Counseling (812) 237-2870.

This is a research project being conducted by Theodore Lynn Moretz for his docotral dissertation. The purpose of this study is to evaluate the ability of the Smell Identification test to distinguish persons with neurological impairment from those without neurological impairment. Participation in this study requires completion of brief screening instruments often used in diagnosing such impairments. You will also be asked to complete a brief information sheet so that your responses can be compared to persons with a similar background.

Following completion of the screening instruments, you may be asked to take the Smell Identification test. This is a multiple choice test, asking you to identify 40 different odors. Current research suggests there is no risk of allergic reaction or other negative effects from this test.

Any questions that I may have regarding the purpose of this study or any of the instruments I have completed will be answered by the examiner.

I have read the consent form and understand that the confidentiality of my responses will be preserved throughout the study. I understand that I am free to withdraw from the study at any time, for any reason.

Subject_____ Date_____

Agency_____ Date_____

Guardian_____ Date_____