This is to certify that the

dissertation entitled

An Investigation of the Prefrontal Cortex Function Theory Of Cognitive Aging

presented by

Julie Daugherty Simensky

has been accepted towards fulfillment of the requirements for

Ph.D. degree in Clinical Psychology

Norma Abela
Major professor

Date April 27, 2001

AN INVESTIGATION OF THE PREFRONTAL CORTEX FUNCTION THEORY OF COGNITIVE AGING

By

Julie Daugherty Simensky

A DISSERTATION

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

DOCTOR OF PHILOSOPHY

Department of Psychology

2001

ABSTRACT

AN INVESTIGATION OF THE PREFRONTAL CORTEX FUNCTION THEORY OF COGNITIVE AGING

By

Julie Daugherty Simensky

The particular vulnerability of the prefrontal cortex to age-related deterioration has been frequently posited as an explanation for functional decline in aging. West's (1996) prefrontal cortex function theory of cognitive aging maintains that age-related decline in cognitive processes supported by the prefrontal cortex emerge at an earlier age and are of greater magnitude than age-related declines observed in cognitive processes supported by nonfrontal regions. In this study, four specific processes underlying prefrontal cortex function (prospective memory, retrospective memory, interference control, and inhibitory control) were theorized to account for age-related declines in a number of cognitive functions, including verbal memory. This study investigated to what extent these four prefrontal cortex processes were discernable and the mediating role they played between age and verbal memory. One hundred nine healthy older adults, aged 55-88 years, completed multiple performance measures thought to evaluate prefrontal cortex function, verbal memory, and depression. Exploratory factor analyses indicated a two-factor model of prefrontal cortex function that was only marginally consistent with West's proposed model. These two factors were: 1) a factor containing measures of interference control, sustained attention, processing speed, and inhibitory control; and 2) a working memory factor. Structural

equation modeling analyses indicated that this two-factor measurement model strongly mediated the relationship between age and verbal memory performance. Verbal memory performance decreased as a result of poorer prefrontal cortex function performance with older age. Results suggested that despite difficulties in the specific and selective measurement of prefrontal cortex function, there is strong support for the hypothesis that cognitive aging is highly dependent on the integrity of prefrontal cortex functions.

In memory of my father, Richard A. Daugherty

ACKNOWLEDGEMENTS

The assistance and support of many people contributed to my ability to successfully finish this project. I want to first thank members of my committee for their unique contributions and support. In particular, I want to sincerely thank my committee chairperson and advisor, Norman Abeles, Ph.D., for his guidance, wisdom, and unwavering support throughout my graduate studies. I consider it an honor to have had the privilege to work with him. I would also like to thank Alex VonEye, Ph.D. for his particular expertise and guidance in completing my statistical analyses. I want to especially thank Mindy Firland-Whitsett, Ph.D. for her empathetic support, technical knowledge, and friendship – because of her assistance structural equation modeling is no longer a mystery to me. I must also extend my sincere gratitude to the participants who made this study possible.

Most importantly, I want to thank my family. You have loved, supported, and encouraged me throughout all of my accomplishments and hardships. Because of you, I am proud of who I am today. To my husband, Steve - there are no words strong or beautiful enough to convey how much your support, patience, humor, and love have meant to me throughout the years and during the completion of this project. Thanks to you and to my family for helping me to

keep my focus on the fact that the true joy of life is the trip, rather than the final destination.

TABLE OF CONTENTS

LIST OF TABLES..ix

LIST OF FIGURES..x

INTRODUCTION..1
Neurobiology of the Aging Prefrontal Cortex........................1
Structural Changes in the Aging Brain........................1
Functional Changes in the Aging Brain........................3
Cognitive Functions of the Prefrontal Cortex........................7
The Role of Prefrontal Cortex Function in Memory.........10
Hierarchical Model of Prefrontal Cortex Function...........11
Specialization of Function Within the Prefrontal Cortex....13
The Prefrontal Cortex Function Theory of Cognitive Aging.........16
Prospective Memory and Frequency Estimation..............19
Interference Control and Sustained Attention.................23
Inhibition of Prepotent Response..............................25
Working Memory..26
Measurement and Alternative Theoretical Considerations...........30

HYPOTHESES..32

METHOD..35
Participants..35
Procedure..36
Measures..36
Wisconsin Card Sorting Test..................................36
Stroop Color and Word Test..................................37
Paced Auditory Serial Addition Test..........................38
Ruff Figural Fluency Test......................................39
Trailmaking Test A & B..40
Symbol-Digit Modalities Test..................................40
Controlled Oral Word Association Test........................40
Wechsler Memory Scale-Revised Digit Span..................41
Wechsler Memory Scale-Revised Visual Memory Span.....41
California Verbal Learning Test..............................42
Wechsler Memory Scale-Revised Logical Memory...........43
Measure of Mental Status......................................43

Measures of Depression..44

RESULTS..44
Missing Data..44
Preliminary Data Examination..45
Hypothesis 1..47
Correlations of Manifest Variables to Latent Variable.......48
Exploratory Analysis of 3-Factor Model..49
Identification of a New Measurement Mode.l................52
Selection of Additional Variables..53
Results of Exploratory Factor Analyses..54
Hypothesis 2 – Structural Equation Modeling..58
Model 1..59
Model 2..60
Model 3..61

DISCUSSION..63
The Model of Prefrontal Cortex Function..64
Alternative Models..67
Measurement Issues..72
Relationship Between Measurement and Neuroanatomy....74
Sample Characteristics..77
Prefrontal Cortex Function as a Mediator..80
Theoretical Considerations and Future Directions..86

APPENDIX A..89

APPENDIX B..91

APPENDIX C..93

APPENDIX D..95

APPENDIX E..97

REFERENCES..99

LIST OF TABLES

Table 1 – Four Secondary Processes of West's (1996) Prefrontal Cortex Function Theory of Cognitive Aging

Table 2 – Correlations of Manifest Variables to each Latent Variable

Table 3 – Communalities of the 12 Original Prefrontal Cortex Function Variables

Table 4 – Varimax 3 – Factor Structure of Retained Original Variables

Table 5 – Communalities of Retained Original Prefrontal Cortex Function Variables and Added Relevant Variables

Table 6 – Varimax 3 – Factor Structure of Final Variables

Table 7 – Varimax 2 – Factor Structure of Final Variables

LIST OF FIGURES

Figure 1 – Three Factor Model of Prefrontal Cortex Function

Figure 2 – Two Factor Model of Prefrontal Cortex Function

Figure 3 – Causal Model of Prefrontal Cortex Function as a Mediator

Figure 4 – Model 1 Standardized Path Coefficients – Direct Effects Model

Figure 5 – Model 2 Standardized Path Coefficients – Indirect Effects Model

Figure 6 – Model 3 Standardized Path Coefficients – Mediating Model

INTRODUCTION

A substantial body of research has identified measurable declines in some cognitive abilities with normal aging. There is growing evidence that the process of normal aging may be linked to a selective decline in cognitive functioning associated with the frontal lobes, particularly the prefrontal cortex. Substantial neural changes occur with advancing age and evidence demonstrates that the prefrontal cortex is more sensitive to the effects of aging than other cortical regions (Haug & Eggers, 1991). Furthermore, persons with age-associated memory impairment demonstrate disproportionate decline in frontal lobe functioning as assessed by both neuropsycholgoical tests and neuroimaging studies (Hanninen et al., 1997). West (1996) proposed a prefrontal cortex function theory of cognitive aging which incorporated existing theory and research. This theory states that the prefrontal cortex is responsible for the integration, formation, and execution of complex, novel behavioral structures or temporal gestalts, which support the direction of behavior in an orderly, purposeful manner. The normal aging process interferes with the secondary processes which contribute to this integrative function. The overall purpose of this study is to investigate the applicability of this prefrontal cortex function theory of cognitive aging to a sample of healthy older adults. The specific questions were: 1) to what extent do the data fit the model of prefrontal cortex function decline with age; and 2) are the secondary processes which contribute to the overall integrative function of the prefrontal cortex discernible in older adults?

Neurobiology of the Aging Prefrontal Cortex

Structural Changes in the Aging Brain

The aging brain loses weight, volume, and neurons. Morphological changes in the aging brain have been examined by a wide range of techniques, from measurement of the gross anatomical volume of various regions to evaluation of synaptic density and integrity and neurochemistry (West, 1996). Morphological study evidence of a general decrease in gross brain volume reaching significance in the 7th decade of life has been well documented (Haug & Eggers, 1991; Raz, 1996). The greatest regional differences in the degree of volume reduction, estimated to be 10-17%, are found in the prefrontal cortex. This is compared to volume reductions in the temporal, parietal, and occipital cortices, all estimated at 1% (Giaquinto, 1988; Guttman et al., 1998; Haug et al., 1983; Haug & Eggers, 1991; Raz et al., 1997). These volume reductions are the result of a reduction in neuron size rather than from an actual loss of neurons (Haug & Eggers, 1991). With advancing age, all areas of the cortex evidence reduced neuronal size; however, earlier and more severe reductions in neuron size are observed in the frontal cortex, when compared to the parietal, temporal, or primary visual cortex.

Scheibel et al. (1975) have described how neurons proceed through a series of degenerative changes with advancing age which may explain the origin of reductions in neural size with advancing age. Neurons appear to undergo subtle alterations with progressive loss of horizontally oriented dendritic systems in areas that are known to receive specific synaptic terminals. At the same time, this loss is accompanied or preceded by the irregular swelling of the soma and major dendrites (Scheibel et al., 1975). This loss of dendritic arborization and the cellular decrease are believed to impair the communication capabilities of the nervous tissue. Reviewing studies on neural depletion in aging, Squire (1987) suggested that "losses from the prefrontal cortex may be sizable, even in terms of a daily estimate" (p.119). West (1996) concluded that the reduction in neuronal size with advancing age could result from the loss of connective processes of the neuron.

With advancing age, an increased number of pathological structures in the brain accompanies the reduction in cortical volume. Senile plaques and tangles increase in number throughout the life span in both humans and non-human primates (West, 1996).

In post-mortum studies, Struble et al. (1985) measured the origin and regional distribution of senile plaques in non-human primates revealing greater numbers in the prefrontal and temporal cortices compared with the posterior, frontal-parietal, or hippocampal regions. Furthermore, these researchers suggested that the most mature plaques were located within the prefrontal and temporal regions. Similar results were reported by Heilbroner and Kemper (1990) who noted that highest concentrations of senile plaques were observed in the frontal areas in non-human primates. Thus, in contrast to Alzheimer's disease where plaques are predominantly found in the hippocampus, locus coeruleus, nucleus basalis, and association cortex, healthy non-human primates demonstrate greater concentrations in the frontal and temporal cortices (Giaquinto, 1988; West, 1996).

Other white matter changes in normal aging have been documented. Studying MRI findings of periventricular high-signal intensity patterns in a sample of healthy, older adults over age 60, Gerard and Weisberg (1986) found that 10% had periventricular lesions. These lesions were localized to the anterior frontal regions in all cases. This percentage increased to 31% when patients having risk factors but no cerebrovascular symptoms were included. Furthermore, neuroimaging has indicated demyelination in the periventricular white matter connected to the anterior frontal horns (Gerard & Weisberg, 1986; Giaquinto, 1988; Guttman et al., 1998).

A number of region-specific declines in the synthesis, concentration, and number of receptor sites for some neurotransmitters associated with cognitive functioning occur with advancing age. Some have demonstrated greater changes in neurotransmitter systems with advancing age within the frontal cortex in both humans and non-human primates (DeKosky et al., 1985; Fuster, 1998; Goldman-Rakic & Brown, 1981; Marcusson et al., 1984; Suhara, 1990; Wong, et al., 1984). However, others have failed to confirm such effects (Giaquinto, 1988).

<u>Functional Changes in the Aging Brain</u>

Two neuroimaging methods have been primarily used to study the functional integrity of the aging brain. The Xenon[133] inhalation (Xe) method measures the rate of regional cerebral blood flow (rCBF) or oxygen use in the cortex. A newer and less utilized method, positron emission tomography (PET) measures both cerebral blood flow and glucose metabolism. Utilizing Xe and the PET oxygen monitoring methods, consistent declines in rCBF with advancing age have been documented (Gur et al., 1987; Meyer et al., 1994; Shaw et al., 1984; Warren, Butler, Katholi, & Halsey, 1985). This age-related reduction in rCBF during a resting state has been estimated to exceed 27% in some cortical regions (Shaw et al., 1984). Specifically, in young and early middle-aged participants (under age 45), a pattern of hyperfrontality, characterized by greater blood flow in the anterior versus the posterior cortical regions is frequently observed. However, in older participants, this pattern is reversed, referred to as hypofrontality. This finding has been demonstrated in both cross-sectional and longitudinal studies (Gur et al., 1987; Shaw et al., 1984). The greatest reduction in rCBF has been observed in the prefrontal and temporal cortices, or selectively in the left-anterior cortex in cross-sectional studies (Gur et al, 1987; Warren, Butler, Katholi, & Halsey, 1985). Shaw et al.'s (1984) longitudinal study demonstrated that over a 4-year period, during which time participants remained healthy, significant reductions in rCBF were observed only in the prefrontal cortex. Furthermore, this study also showed an interaction between the effects of normal aging and the degree of cerebrovascular disease in relation to rCBF. For participants younger than 70 years, the presence of increasingly severe cerebrovascular disease resulted in increased declines in rCBF. For participants older than 70 years, this interaction was not observed, suggesting that the effect of cerebrovascular disease may be more deleterious during the middle and early-late adult years (West, 1996). Together, these results demonstrate that with advancing age, rCBF at rest is selectively reduced, especially in the frontal cortex.

Changes in rCBF with age have also been documented during the performance of cognitive tasks. For all participants, an increase in rCBF is evidenced while performing cognitive tasks such as mathematical calculations, verbal analogies, and verbal memory tasks (Gur et al., 1987; Raglund et al., 1997; Warren et al., 1985). Age-related differences in the magnitude or pattern of activation have not been observed in response to cognitive demands, despite consistent declines in resting rate of rCBF (Gur et al., 1987; Warren et al., 1985). However, neither of these studies considered the impact of behavioral performance. Raglund et al. (1997) examined PET rCBF change during working and declarative memory in relation to task performance and found that activational patterns diverged when performance was considered. High performers on tasks of working memory activated frontal dorsolateral and inferior regions whereas high performers on the declarative memory task activated only the occipitotemporal region. Notably, older adults were not included in this study; however, based on previously reviewed findings, it could be hypothesized that different activational patterns may be evidenced by older adults. Specifically, because of the well-documented prefrontal neural decline, less divergence in activational patterns according to task performance would be expected. Grady et al. (1995) obtained results from their rCBF study of young and old adults during encoding and recognition of faces which partially supported this hypothesis. Young adults (M = 29 years) showed increased rCBF in the right hippocampus and left prefrontal and temporal cortices during encoding and in the right prefrontal and parietal cortex during recognition. Older adults (M = 69 years) demonstrated no significant activation in areas activated during encoding in young adults but did show right prefrontal activation during recognition.

As previously mentioned, evidence from PET glucose metabolism studies is less definitive. Some studies demonstrate trends towards reduced rates of cerebral metabolism with age when young and old participants are compared, with increased reduction being evidenced in the frontal regions (de Leon et al., 1983; Kuhl, Metler, Rieger, & Hawkins, 1984). Other research has shown preserved glucose metabolism with advancing age in healthy adults (de Leon et al., 1984).

In summary, studies utilizing both Xe and PET methods have generally found age-related decreases in oxygen use; however, PET studies have not typically demonstrated significant age-related changes in glucose metabolism (West, 1996). Both theoretical and methodological reasons have been offered to explain this inconsistency. Roland (1984) proposed that although oxygen utilization and glucose metabolism are closely related in young- and middle-age, they become "decoupled" in older adults. Methodologically, differences in sample characteristics could explain differences in study findings. West (1996) suggests that participants in the Xe studies may not have been screened as strictly as those in the PET glucose metabolism studies. Furthermore, because of the economic and ethical costs of PET studies, smaller numbers of participants are used, which may result in insufficient power to detect meaningful differences between young and old participants.

There has been a recent proliferation of functional magnetic resonance imaging (fMRI) studies that have demonstrated strong support for the frontal aging hypothesis. Grady et al. (1994) have demonstrated that older adults show greater cortical activation outside of the prefrontal cortex when compared to younger adults during a spatial working memory task. Greater left prefrontal activity during a verbal encoding task and greater right prefrontal activity during a retrieval task demonstrated by younger adults was not seen in a sample of older adults (Cabeza et al., 1997; Tulving, et al, 1994). Comparitively, older adults demonstrated little prefrontal activity during encoding but engaged bilateral prefrontal activity during retrieval. Madden et al. (1999) found that during a recognition verbal memory task, younger adults demonstrated primarily right prefrontal activation when compared to a more bilateral pattern of prefrontal activation demonstrated by older adults. Reuter-Lorenz (2000) studied PET activation patterns of younger and older adults during both letter identity and spatial location memory tasks.

Younger adults showed left-sided frontal activation for the letter identity task and right-sided frontal activation for the spatial location task, whereas older adults showed bilateral frontal activation during both tasks. A possible explanation for these findings is that prefrontal cortex functioning is selectively impaired in older adults and that the effort to recruit all available prefrontal resources results in increased activation of prefrontal and some non-prefrontal areas in older but not younger adults.

Taken together, these data suggest substantial structural and probable functional changes in the cerebral cortex of healthy older adults. This provides considerable morphological and functional support for a prefrontal cortex theory of cognitive aging.

Cognitive Functions of the Prefrontal Cortex

Harlow (1868) was one of the first to describe the changes in behavior and personality resulting from prefrontal damage in reports of his patient, Phineas Gage. The nature of function(s) of the prefrontal cortex have been the center of much focus and debate. Some have suggested that few if any cognitive functions are controlled by the prefrontal cortex, based on frequent observations that little or no change occurs in some humans and animals after prefrontal insult (Stuss & Benson, 1986). Others, such as Luria (1980), have theorized that the prefrontal cortex supports the highest level of cognitive organization, serving as the central executive of the brain. Early theory and description of prefrontal cortex function was based on observations of survivors of frontal lobe damage or animal studies. More recent advances such as neuroimaging have allowed for more precise examination and subsequent elaboration of knowledge of the prefrontal cortex.

Clinically, descriptions of changes as a result of prefrontal damage include disruption of: initiation, planning and goal selection, attention, memory, anticipation, abstraction, use of feedback, and self-awareness (Fuster, 1998; Luria, 1980; Stuss & Benson, 1984; Perecman, 1987; Shimamura, Janowsky, & Squire, 1991; West, 1996). Luria (1973) described one of the more prevalent deficits related to prefrontal damage as the fragmentation of complex behavior and action sequences. While individual units that comprise an action sequence are able to be performed perfectly, there is a lack of structure and goal directedness. Furthermore, complex behavior is fragmented by a disruption of the temporal gestalt (Fuster, 1998); a temporal guideline cannot be formed to direct individual behavioral units required for task completion. For example, a person with a prefrontal injury may be able to complete any individual house cleaning task in isolation but when given a list of house cleaning tasks to perform, would have great difficulty doing so because of an inability to organize the requirements of the list efficiently.

When behavior is not guided by temporal gestalts, a number of behavioral deficits that are commonly observed in persons with prefrontal injury may occur. Stuss and Benson (1987) have described a dissociation between self-consciousness and self-knowledge; when a person is fully aware of making performance errors based on some external criteria but is unable to utilize this knowledge to change her/his behavior. This dissociation has been clearly demonstrated in studies of persons with prefrontal damage on two common neuropsychological tests purported to measure frontal lobe functioning. The Wisconsin Card Sorting Task (WCST; Heaton, 1981) requires an individual to sort a series of cards based on a continually changing rule. When a category shift occurs, persons with prefrontal damage frequently continue to sort the cards to the now incorrect category, despite being able to express that their behavior is incorrect (Heaton, 1981; Stuss & Benson, 1986). In the Stroop Color-Word Naming Task (Stroop; 1935), one trial requires the naming of the color of ink in which a word is printed rather than reading the word. Persons with prefrontal damage will frequently continue to read the word rather than naming the color despite being able to explain the rule they are to follow (Duncan, 1995; West, 1996). Taken together, these performances suggest a type of goal neglect; inability to utilize knowledge of "what to do" to guide behavior. West (1996) theorizes that this goal neglect can lead to two other types of behavior that are often observed in persons with prefrontal damage: perseveration and distractibility.

Perseveration is the tendency to persist in elements of some previous task or behavior after that response has become inappropriate. In other words, an action sequence gets "captured" by one of its constituent parts. Distractibility is the tendency to respond to external stimuli that are not related to achieving a goal. When this occurs, an action sequence is "captured" by an irrelevant element in the external environment. Both result from the disturbance and breakdown of a temporal gestalt or sequence of actions (Fuster, 1998). Perseveration is a particularly common and noticeable consequence of prefrontal pathology (Goldberg & Bilder, 1987; Luria, 1980; Stuss & Benson, 1984).

The Role of the Prefrontal Cortex in Inhibition

An inhibitory control model of prefrontal cortex function suggests that prefrontal function is represented by processes which inhibit prepotent responses and sustain attention. Inhibition of prepotent responses keeps highly salient but unsuited responses from gaining control of a behavior or action sequence (Dempster, 1991). Inhibitory processes also allow attention to be sustained, even while there is the risk of distraction from external/environmental sources. Stuss and Benson (1986) highlighted the importance of the prefrontal cortex in maintaining attention over time and preventing distraction, both of which allow information to be organized into workable chunks. Furthermore, inhibitory control allows attention to be focused and sustained upon novelty within the environment. Detection of novelty permits the ability to encode other behaviorally relevant aspects of an event, contributing to the formation of a temporal gestalt (West, 1996). A deficit in novelty detection not only hampers the ability to code the beginning and end of discrete events and tag them with appropriate temporal-spatial information (Knight & Grabowecky, 1995), it creates an experience of the environment in which even common events and actions are unpredictable and unforeseen (Fuster, 1998).

Both inhibitory control and sustained attention have been demonstrated to be related to the functioning of the anterior cingulate within the midprefrontal region (Posner & Raichle, 1996). The anterior cingulate functions to assist in preparing an individual for some anticipated event. Specifically, it allows for inhibition of an automatic response so that a less automatic or less compatible response can be reported, such as in the Stroop color-word naming trial. Additionally, human neuropsychological studies have shown that damage to the right dorsolateral region has been shown to impair performance on tasks of sustained attention (Vendrell et al., 1995) and inhibition of prepotent responses (Wilkins, Shallice, & McCarthy, 1987). Incisa della Rocchetta and Milner (1993) demonstrated that left dorsal prefrontal incisions impaired the ability to suppress potentially interfering items during a verbal memory task. However, some have questioned the frontal-lobe specificity of these processes because of the interconnections the frontal lobes have to midbrain and brain stem attention and arousal systems (Stuss & Benson, 1986).

The Role of Prefrontal Cortex Function in Memory

The significance of the frontal lobes in memory function has been subject to much research and debate. Some have emphasized the primary role of the frontal cortex on memory tests such as delayed response, conditioned associative learning, and memory for temporal order (Levine, Stuss, & Milberg, 1997; Mangels, 1997; Parkin, Walter, & Hunkin, 1995; Petrides, 1985; Schacter, 1987). Others, however, have suggested that memory functions per se are not impaired in patients with frontal damage and that decrements in performance on memory tests are secondary to disorders of attention, problem-solving, and inhibitory control (Hecaen & Albert, 1978; Luria, 1973). Stuss and Benson (1986) have suggested that the accumulated evidence on the role of the frontal lobes in memory implies that lesions and neuronal loss do not cause a primary disturbance of memory, but that they do interfere with mnestic activity. In contrast, Shimamura, Janowsky, and Squire (1991) have concluded that specific memory disorders are the result of frontal lobe lesions, including impaired short-term memory, free recall, metamemory, memory for temporal order, and source memory.

A memory-based model of prefrontal function has been proposed largely on the basis of evidence from non-human primate studies utilizing variations of the delayed-response task (West, 1996). A typical delayed-response task would involve a monkey watching while a reward was hidden at one of a number of locations. After a delay, the monkey is allowed to retrieve the reward. Successful performance requires the maintenance of an internal representation of the hidden location of the reward over a delay. This representational memory, also referred to as working memory, allows the animal to bridge the temporal gap between hiding and responding (Goldman-Rakic, 1987). Disruption of representational memory can contribute to secondary deficits, including perseveration and distractibility (West, 1996). If an animal cannot maintain on-line, context-specific information to guide behavior, then its behavior is influenced by habitual, prepotent responses (perseveration) and/or external cues (distractibility).

In addition to the non-human primate literature supporting a representational memory deficit of prefrontal dysfunction, a computational model has been designed (Kimberg & Farah, 1993) which has been shown to simulate performance accurately on a number of tasks sensitive of the effects of prefrontal injury, including representational memory. In this mathematical model, the strength of various associations in representational memory is affected by prefrontal insult, resulting in a decreased ability to determine the relevance of specific goals and declarative and environmental information for task performance. Using this model, the authors successfully simulated performance on the Stroop Color-Word Task, WCST, and a motor sequencing task which suggested that the weakening of associations as a result of prefrontal damage provides an accurate explanation of many of the performance deficits observed following prefrontal injury, including representational memory.

A number of findings question the adequacy of the representational memory model of prefrontal function. Delayed-response deficits are not observed in the absence of external distracting stimuli or competing response alternatives (Fuster, 1998). West (1996) suggests that if the simple passage of time and loss of access to representational memory were sufficient to elicit the delayed-response deficit, then it should be observed under all conditions. Thus, a deficit in representational memory does not sufficiently account for all of the behavioral deficits which arise after prefrontal insult. Some have suggested that it an additional function of the prefrontal cortex which was previously discussed, inhibition of prepotent responses, accounts for these additional performance deficits (Posner & Rothbart, 1991; Stuss & Benson, 1987).

Hierarchical Model of Prefrontal Cortex Function

Fuster (1998) suggested that the most characteristic function of the prefrontal cortex is temporal structuring of behavior. Accordingly, the prefrontal cortex forms a temporal framework for any behavior that has a unifying goal or purpose in novel situations. The most critical factor demanding the function of the prefrontal cortex is time; to bridge temporal gaps. This temporal structuring of behavior is subserved by three subordinate functions: provisional memory, prospective memory, and interference control (Fuster, 1998). The two memory processes within this model represent a division of Goldman-Rakic's (1987) representational memory aspect of prefrontal cortex function. The first, provisional memory, is similar to the idea of short-term or primary memory (West, 1996). Provisional memory allows referencing of some event/action to past experiences or to some future goal/action sequence. Information, which may be either newly acquired or a reactivation of some existing memory trace, is held until a goal is attained, providing a foundation on which the action sequence is constructed.

Prospective memory includes anticipation, foresight, or preparatory set. It functions to operate on information derived from the provisional process to prepare the individual for some impending response (West, 1996). The prefrontal cortex, using data from the provisional memory process, prepares for anticipated events on the way to achievement of goals.

These two types of prefrontal memory processes are distinguishable in reports of the frequently observed dissociation of self-consciousness and self-knowledge with prefrontal damage. The ability to verbalize the requirements of a task is preserved (provisional memory), however the task-relevant knowledge cannot be applied in the direction of behavior (prospective memory) (Fuster, 1998). The prefrontal cortex is not assumed to store the actual representation used to guide behavior (the outcome of the provisional memory process) but rather supports the maintenance of this representation stored in temporal and parietal cortices through an interaction with subcortical structures (West, 1996). However, prospective memory is theorized to be highly dependent on the prefrontal cortex, making it more susceptible to prefrontal insult.

The final component of prefrontal functioning according to this model is interference control. Fuster (1998) described this as the suppression of influence of potentially interfering stimuli existing in the external environment or arising from internal sources. Impaired interference control leads to a distortion of the temporal gestalt. Notably, he theorized that this process was localized within the orbitomedial prefrontal cortex.

In summary, Fuster's model suggests that temporal structuring of behavior is the primary role of the prefrontal cortex. It is supported by three subordinate functions which allow for the formation and execution of temporal gestalts or complex behavioral sequences that are novel to the organism. This theory was one of the first to address the issue of unity and diversity of the prefrontal cortex and to stress the importance of the temporal integration of behavior (Stuss & Benson, 1986).

Specialization of Function Within the Prefrontal Cortex

The prefrontal cortex is generally divided into three distinct areas: dorsolateral, orbitomedial, and anterior cingulate. Many have speculated that various functions are localizable to these given regions. For instance, Goldman-Rakic's (1987) work with non-human primates has suggested that representational memory is localized to the principle sulcus and inferior convexity. Much debate exists about the localization of inhibitory control processes. Some have suggested that inhibitory control, as a memory-related process, is localizable within the dorsolateral region (Diamond, 1990) whereas others have suggested it is a function of the orbitomedial area (Fuster, 1998). Goldman-Rakic (1987) has proposed that both inhibitory control and memory processes are distributed across the substructures within both of the divisions of the prefrontal cortex. Most recently, the anterior cingulate has been shown to be involved in preparation for an anticipated event by inhibiting automatic responses to allow for less automatic responses to be selected (Cabeza and Nyberg, 1997; Posner & Raichle, 1996). This effect was demonstrated most strongly in reviewed studies that employed the Stroop task.

These findings are supported by neuroimaging studies conducted with healthy adults. Specifically, performance on tests of working memory has been associated with disproportionately increased activity (as measures by rCBF, MRI, and PET methods) in the dorsolateral prefrontal cortex (Smith, Jonides, Marshuetz, & Koeppe, 1998; Barch et al., 1997; Cabeza & Nyberg, 1997; Raglund et al., 1997; Posner & Raichle, 1996; Schumacher et al., 1996). Increased activity in the orbitomedial prefrontal cortex has been associated with performance on measures of sustained attention and interference control (Cabeza & Nyberg, 1997; Malloy, Bihrle, Duffy, & Cimino, 1993). Performance on tasks of selective attention and ability to inhibit prepotent responses has been associated with increased activity in the anterior cingulate (Cabeza & Nyberg, 1997; Posner & Raichle, 1996). However, much of the research investigating specialization of function within the prefrontal cortex has been conducted with individuals and animals that have focal lesions or with healthy, young adults. Are these same functional declines evidenced in more common cases of global or generalized prefrontal damage, such as in the case of head injury or aging processes?

<u>The Relationship Between Prefrontal and Non-Prefrontal Brain Regions</u>

Because of the interconnectedness of the prefrontal region to other brain regions, it is important to ask how prefrontal regions interact with the rest of the brain in accomplishing the task of guiding purposeful behavior. Any theory of prefrontal function must address the separation of function between prefrontal and other brain regions. This is a daunting task, as the frontal lobes are one of the most highly interconnected areas of the brain to both cortical and subcortical brain regions. However, evidence exists which suggests a dissociation of some types of memory functions that are ascribed to damage of the prefrontal cortex versus damage to other brain regions, primarily the medial temporal cortex and hippocampus (West, 1996). The pattern of errors made on memory tasks following prefrontal and hippocampal lesions is markedly different in both humans and non-human primates (Diamond, 1990). Those with prefrontal lesions demonstrate a characteristic pattern of returning to a previously rewarded, prepotent response. In contrast, those with hippocampal lesions make errors that are unrelated to previous rewarded responses. A number of studies have demonstrated that persons with prefrontal damage outperform those with medial temporal damage on tasks of paired associate learning, story recall, and diagram recall. In contrast, on memory tasks in which structure is not inherent in the material and must be supplied by the person, such as the California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1984), individuals with prefrontal damage performed significantly worse (Schacter, 1987; Shimamura, 1995; Stuss, 1991). Moscovitch (1994) investigated cognitive resources and dual-task interference effects at retrieval in healthy older adults, concluding that strategic memory functions which are more resource demanding were mediated by the prefrontal cortex and dissociated from episodic memory functions involving the medial temporal lobes and hippocampus. More recently, Winocur, Moscovitch, and Stuss (1996) demonstrated that explicit memory was reliant upon medial temporal functioning and was dissociated from implicit memory, which was reliant on prefrontal cortex functioning.

Although evidence exists which supports the notion that clear dissociations can be made between prefrontal cortex functioning and cognitive process supported by other brain regions, a number of findings suggest that localization may not be as clearly defined. Work with both animals and humans suggests that damage to the medial temporal area can result in functional impairments similar to those arising from prefrontal insult (West, 1996). Incisa della Rocchetta and Milner (1993) demonstrated that persons with hippocampal excisions demonstrated similar impairment of free recall in unstructured situations to individuals with left-frontal excisions. Similarly, Corcoran and Upton (1993) demonstrated that patients with hippocampal damage performed more poorly on the WCST than those with frontal damage. Winocur (1988) suggested that removal of the hippocampus can result in an increased susceptibility to interference in learning paradigms. Kopelman and Stanhope (1997) found that patients with temporal lobe or diencephalic lesions demonstrated major deficits initially acquiring information and had faster long-term forgetting rates when compared to those with frontal lobe lesions. Finally, West's (1996) review of the literature on source memory led him to conclude that medial temporal insult also results in disruptions of memory for context.

Furthermore, the three major divisions of the prefrontal cortex are highly connected with subcortical regions; thus executive function is supported by an integrated and synergistic system arising from parallel prefrontal-subcortical circuits. These three parallel frontostriatal circuits underlie executive function and emotion (Denckla & Reiss, 1997). Particularly, lesions in the dorsolateral - dorsolateral caudate - globus pallidus - thalamic circuit result in executive dysfunction as evidenced by impaired working memory. Lesions in the orbitofrontal - ventromedial caudate - globus pallidus - thalamic circuit result in irritability and disinhibition. Finally, lesions to the anterior cingulate - nucleus accumbens - globus pallidus - thalamic circuit result in inertia and apathy. As such, it is difficult to specifically ascribe any differential neuropsychological functions specifically to neuroanatomical substrates.

The Prefrontal Cortex Theory of Cognitive Aging

As previously described, a distinct set of cognitive deficits is associated with prefrontal cortex damage. These deficits must be accounted for by any theory of prefrontal cortex function. Although previously reviewed theories accounted for portions of the deficits observed after damage to the prefrontal cortex, none were able to account for all of the following: fragmentation of complex sequential behavior, increased distractibility and perseveration, and insensitivity to external stimuli which leads to an inability to modify behavior based on verbal instructions, to differentiate novelty from familiar, and to detect temporal characteristics of information retained in the environment. West (1996) proposed an integrative model of prefrontal cortex function, incorporating ideas from previously reviewed theories. His theory states that the function of the prefrontal cortex is organized in to a hierarchy of interactive processes. Based upon Fuster's work (1998), this theory describes that at a general level, the prefrontal cortex supports the integration, formation, and execution of complex, novel behavioral structures or temporal gestalts. This allows behavior to be directed in an orderly, purposeful manner (West, 1996). This integrative function is supported by four secondary processes as outlined in Table 1: provisional/retrospective memory, prospective memory, interference control, and inhibition of prepotent responses (Diamond, 1990; Fuster, 1989; Goldman-Rakic, 1987). The retrospective memory process maintains on-line, task-relevant information on which the temporal gestalt is constructed. The prospective memory process serves to prepare the person for the execution of the temporal gestalt in response to appropriate external or internal cues. The interference control process serves to clear current task inappropriate information from the retrospective memory store. The inhibition of prepotent responses process keeps behavior from being captured by dominant internal response patterns or highly salient environmental stimuli. The action and interaction of these four processes support a wide range of cognitive activities, including the selection of task-relevant information, the integration of semantic and contextual

Table 1

Four Secondary Processes of West's (1996) Prefrontal Cortex Theory of Cognitive Aging

Term	Definition	Example
Retrospective memory	maintains on-line, task relevant information on which a time-line for action is constructed	Recalling ingredients and steps for a recipe.
Prospective memory	prepares person to execute time-line action sequence in response to some internal/external cue	Remembering what ingredients to add when the timer you previously set goes off.
Interference control	clears action-irrelevant information from the retrospective memory store	"Clearing" the steps in the recipe you have completed from your mind, as well as information not related to the task (i.e., ingredients/steps from the previous recipe you completed).
Inhibition of prepotent responses	prevents behavior from being "captured" by a dominant internal response pattern or a highly salient environmental stimuli	Not becoming distracted by the television or thoughts about work that might lead to adding the same ingredient twice or adding the wrong ingredient.

information into discrete memory traces, and the planning and execution of complex, purposeful behavior (West, 1996).

In order for a model or theory to be of value, it must accurately depict findings from a wide range of empirical work. It should accurately predict when age-related deficits should be observed both at general and specific levels. A theory of cognitive aging should be able to account for the types of tasks that should and should not demonstrate evidence of age-related decline, as well as be able to distinguish those task conditions that do and do not produce age-related deficits (West, 1996). Furthermore, it should be able to differentiate age-related declines which are the result of functional impairment of the prefrontal cortex versus other brain structures or some general process, such as age-related reduced processing speed (Salthouse, Fristoe, & Rhee, 1996).

With this in mind, under which conditions would age-related deficits be expected to arise? With respect to provisional or retrospective memory, deficits would be expected when performance on a task becomes dependent on the retrieval of contextual information about an event and less related to the semantic content of memory. Prospective memory deficits would be expected to occur when task performance cannot be supported by external cues or reminders. Finally, as interference control and inhibition of prepotent response processes are compromised by advancing age, this model suggests that observed behavior will become increasingly characterized by a tendency to respond to current task-inappropriate information or based on a dominant behavioral pattern (West, 1996). In the following sections, evidence from the following paradigms is reviewed in light of the proposed model of prefrontal cortex function: prospective memory, frequency estimation, source memory, interference control and sustained attention, inhibition of prepotent responses, and working memory.

Prospective Memory and Frequency Estimation

The effects of advancing age on memory for activities to perform, or prospective memory, are somewhat limited (West, 1996). Prospective memory differs from the kind of memory that is dependent on the integrity of the medial temporal lobe or diencephalic structures in that the former is needed to manipulate and organize memory, whereas the latter is needed to store and consolidate new memories (Shimamura, Janowsky, & Squire, 1991). Cues to elicit a prospective action can be either event- or time-based. The prefrontal cortex model of aging predicts that time-based memory tasks should demonstrate greater age-related decline than event-based tasks because time-based tasks are presumably devoid of external cues that support prospective action. McDaniel and Einstein (1992) found that older adults were less accurate than younger adults on tasks involving time- but not event-based cues to elicit the prospective action. However, in a study examining the effects of increasing the delay between receiving the prospective instructions and the cue to perform the prospective actions, Einstein Holland, McDaniel, and Guynn (1992) found that performance was not affected and that this increase in delay did not interact with age.

The complexity of the prospective cue or action has also been investigated. Older adults demonstrated impaired performance relative to younger adults when a task required monitoring of four prospective cues, which was in contrast to the similar performance of both groups when a task required the monitoring of only one cue (Einstein et al., 1992).

A final way in which prospective memory performance has been examined is in studies of the use of external memory aids. Overall, these studies have demonstrated that performance on a variety of memory tasks, including prospective tasks, is enhanced by the use of an external memory aid (West, 1996). What has yet to be determined is the role that advancing age plays in the use and effects of external aids during prospective memory tasks. Older adults may rely more on memory aids as task difficulty increases or it may be that older adults would not use memory aids as effectively as task demands increase. The prefrontal cortex theory of cognitive aging would predict that prospective memory performance would be enhanced by using external aids because part of the role of the prefrontal cortex would be replaced by the external aid.

Frequency estimation has received considerable attention in field of cognitive aging. A typical frequency estimation task requires the studying of a list of items over a period of time and then providing a judgment about the frequency of the studied stimuli during a test phase. Hasher and Zacks (1979) proposed that encoding of frequency information was an automatic process and thus would not be influenced by the effects of advancing age. Aging research has both supported and questioned the age insensitivity of the encoding of frequency information. Older and younger adults have been found to make comparable estimates at low frequencies of occurrence; however at high frequencies of occurrence, the performance of older adults was impaired (Kausler, Salthouse, &

Saults, 1987; Hasher & Zacks, 1979). The current model of prefrontal function would suggest that this deficit results from an inability to form discrete context-dependent memory traces of the study stimuli with increasing frequency of occurrence or to update existing representations (West, 1996).

Target familiarity has also been shown to differentially effect frequency estimation performance in younger and older adults. Wiggs (1993) found that the performance of younger and older adults was comparable in their accuracy of estimation for English words but that older adults were significantly impaired in estimation when Japanese ideograms were used as stimuli. This finding is in agreement with existing ideas of prefrontal function, as older adults, like persons with frontal lobe lesions, may experience difficulty when novel stimuli must be incorporated into memory. Overall, West's (1996) review of the frequency estimation literature led him to conclude that existing instances of age invariance in frequency estimation appear either to be predicted by the prefrontal cortex model or to have resulted from methodological problems.

Source Memory

Numerous studies of episodic memory and source amnesia have suggested that older adults are impaired relative to younger adults in their ability to remember the source of newly acquired information. Reduced source memory has been attributable to decreased effectiveness in the ability to integrate events with their temporal context in memory (McIntyre & Craik, 1987). Evaluating source memory requires an individual to recall the context in which some fact was learned or action performed. Variables that appear to influence performance on source memory tasks include the length of time between initial exposure to the material and recall of source information and the discriminable salience of informational sources (West, 1996).

McIntyre and Craik (1987) demonstrated that older adults (M = 69.2 years old) performed more poorly on a source memory task which required learning of both real and fictitious facts about famous, non-famous, and fictitious people when compared to younger adults (M = 19.4 years old). This effect was demonstrated after 10 minutes and even more strongly after one week. Notably, the decrease in source memory with increasing delay was accompanied by a decrease in item recognition memory for older adults at the one-week follow-up; thus, poor performance of the older adults at this time point may have been partly attributable to reduced memory overall. Craik et al. (1990) found that the degree of source amnesia in a sample of healthy adults was significantly related to age, verbal fluency, and performance on the WCST, leading to the conclusion that impairments resulting from the normal aging process are related to functioning of the prefrontal cortex. Janowsky, Shimamura, and Squire (1989) found that the frequency of source errors committed by healthy older adults (M = 63.9 years old) and patients with frontal lobe lesions were similar and exceeded the number committed by healthy younger adults (M = 43.9 years old). In these latter two studies, decreased source memory was not accompanied by or related to reduced item recognition. Parkin and Walter (1992) found that explicit verbal recognition, defined by having participants indicate that their answer was based on "remembering" the source of the information, declined with age and familiarity-based recognition, defined by having participants indicate that their answer was based on information that they "knew", increased. Furthermore, the extent to which older participants relied on familiarity-based recognition correlated with reduced performance on neuropsychological indices of frontal dysfunction.

Evidence for the effect of increasing delay on source memory appears to be mixed. While some studies have demonstrated greater source amnesia with increased delays (Spencer & Raz, 1994; McIntyre & Craik, 1987), other have found no such effects (Schacter et al., 1991). West (1996) concluded that the effect of increasing delay on source memory appears to be tied to a concurrent reduction in overall recall but that source memory difference between younger and older adults persist even when no item recall deficit is observed.

Another factor proposed to influence the effect of advancing age on source memory is the focus of attention within the encoding phase of the task. Schacter et al. (1994) found that directing attention to the source or fact information during the encoding phase of an experiment did not produce difference in source memory for younger or older adults. Thus, age-related differences in source memory do not appear to be the result of differences in the ability of younger and older adults to attend to information.

In conclusion, the current model of prefrontal function would suggest that the source memory deficits observed in older adults result from the impoverished integration of content and context information at encoding and possibly recall (West, 1996). Thus, it could be hypothesized that on tasks of verbal memory recall and recognition, which involves the presentation of two separate lists of related items to remember, such as the CVLT, advancing age should result in decreased recognition discriminability and increased incidence of intrusion errors specific to the related lists (i.e., items presented on the first list being reported during recall of the second list and items from the second list being reported during a delayed recall of the first list).

Interference Control and Sustained Attention

The study of interference control has most commonly employed the Brown-Peterson Consonant Trigram Task or tasks on which performance involves release from proactive interference. Researchers examining age-related performance declines on the Brown-Peterson task have generally indicated that older adults tend to demonstrate poorer recall than younger adults and that this age-related deficit does not interact with the length of the retention interval (West, 1996). This is consistent with findings from the study of the effects of advancing age on working memory, which suggest that increasing age is associated with a decline in the number of items maintained on-line but that this information is relatively stable across time (Salthouse, 1994).

Older adults generally demonstrate greater buildup of interference over trials (Dobbs, Aubrey, & Rule, 1989) which can be attributable to a decreased ability to clear information from working memory, a deficit of the interference control process. Shimamura and Jurica (1994) demonstrated that advancing age was associated with heightened proactive interference due to previously presented stimuli during an investigation using a self-ordered pointing task of prefrontal cortex function. Detection and control of buildup of interference during an implicit stem completion task was found to be related to performance on tasks of prefrontal cortex function and declined with advancing age (Nyberg, Winocur, & Moscovitch, 1997). Dobbs et al.'s (1989) review of existing literature in the area of release from proactive interference led to the conclusion that when an appropriate measure of release (the Wickens ratio) is used, older adults demonstrated reduced release from proactive interference in each of the five studies reviewed.

Investigation of the evidence of declines in sustained attentional ability or vigilance with age yields mixed results. Chao and Knight (1997) used event-related potentials and behavioral measures to compare the performance of healthy young and old adults on two different auditory delayed match-to-sample tasks. Older adults had reduced attention-related activity over frontal regions and distracting stimuli elicited an enhanced primary auditory evoked response in older adults. The authors concluded that increased distractibility and impaired sustained atttention in older adults may be due to altered prefrontal cortex functioning. Optimal performance on a sustained attention task is a function of the ability to focus over time, discriminate between target and nontarget stimuli, maintain preparatory set, and respond quickly and accurately (West, 1996). The prefrontal cortex has been implicated in the support of each of these skills (Fuster, 1980; Posner & Rothbart, 1991).

Age-related decline in target hit rate was observed by Parasuraman and Giambra (1991), who concluded that older adults demonstrated faster rates of attention decrease than younger adults while completing assessed tasks. This age-related decline was not attenuated with extensive practice and was exacerbated by increased event rate. Age-related decline on the Paced Auditory Serial Addition Test (PASAT; Gronwell & Sampson, 1974; Gronwell & Wrightson, 1974), a task assessing sustained attention and rate of information processing, has been consistently reported (O'Donnell et al., 1994; Brittain et al., 1991; Stuss, Stethem, & Poirier, 1987). On auditory delayed match-to-sample tasks, older adults were significantly more impaired than younger adults by distractors during long delays (Chao & Knight, 1997). Furthermore, during this task, older adults demonstrated significantly reduced attention-related activity over frontal regions, as measured by event-related potentials. However, preserved sustained attention capacity in older adults has been reported in studies using tasks that place fewer demands on a potentially limited capacity attentional mechanism (West, 1996). Overall, the data seem to suggest that age-related deficits in sustained attention will arise under task conditions which place a high demand on a limited capacity attentional system.

In conclusion, the effects of age on the performance on tasks sensitive to the effects of interference in the short-term retention of material and the ability to sustain attention over time can all be interpreted within the current theoretical framework of prefrontal cortex function (West, 1996). Age-related decline on measures of interference control and sustained attention represent difficulties with controlling the interfering effects of internal and external stimuli, contributing to difficulties in the formation of a temporal gestalt and action sequence.

Inhibition of Prepotent Response

Research utilizing the Stroop Color-Word Naming Task has provided numerous findings related to the effects of advancing age on the ability to suppress a prepotent response. Older adults consistently demonstrate slowed performance during the color-word trial and increased interference scores (Wecker et al., 2000; Hanninen et al., 1997; Uttl & Graf, 1997; West, 1996; Uchiyama et al., 1994; LaRue, 1992; Stuss & Benson, 1986). Houx et al.'s (1993) cross-sectional lifespan study indicated that age-related increases in these effects begin to appear in the 6th and 7th decades of life and continue to increase with age. Additionally, health status has been shown to interact with the effects of advancing age, demonstrating an accelerated increase with age in the Stroop effect for persons with even relatively minor health problems (West, 1996).

A number of explanations have been offered to explain the Stroop effect with advancing age. Dulaney and Rogers (1994) have suggested that the inability on the part of older adults to use a reading suppression response is the reason for age-related increases in the Stroop effect. Panek, Rush, and Slade (1983) theorized that older adults demonstrate greater Stroop effects due to an increase in response dominance for word reading over color naming with advancing age. Notably, age-related differences in the Stroop effect persist after controlling for the effect of decreased processing speed (Spieler, Balota, & Faust, 1996). West (1996) concluded that none of these theories has been able to provide a full account of age-related increased in the Stroop effect, leaving open the possibility that at least part of this effect is attributable to a reduced efficiency of the inhibition of prepotent response processes supported by the prefrontal cortex.

The ability to inhibit a prepotent response keeps highly salient but unsuited responses from gaining control of a behavior or action sequence (Dempster, 1991). As such, perseverative errors can be thought of as a break down in this inhibitory process. Perseverative errors represent an action sequence which is "captured" by one of its constituent parts which may have been previously rewarded, as is the case with perseverative errors on the WCST. Thus, measures of perseverative errors provide another way of analyzing the effects of increasing age on the ability to suppress a prepotent response. It could be hypothesized that advancing age would be associated with increased frequency of perseverative errors on tasks requiring the production of responses to various task demands such as free and cued recall, design fluency, and the WCST, due to decreased ability to suppress prepotent responses.

Working Memory

West (1996) used the term retrospective memory to describe the process which serves to maintain on-line, task-relevant information on which the temporal gestalt is constructed. When combined with his definition of prospective memory, these two constructs are more commonly known as working memory. Working memory has been described as knowing what to do, when to do, and how to do it (Pribram, 1997). These three factors are heavily dependent on the integrity of prefrontal cortex function. The "what" is related to familiarity, a particular kind of memory. The "when" is a result of sustained attention and the ability to discern when automatic processes become ineffective. The "how" involves determining what is appropriate; when something works and does not work. Thus, decreased working memory performance as a result of prefrontal disturbance means that under certain conditions intentional and attentional processes needed for the completion of learning tasks are disrupted (Pribram, 1997).

Decline in working memory performance with advancing age has been consistently demonstrated. Libon et al. (1994) demonstrated that working memory performance, as measured by overall performance on the WCST, as well as performance on other tasks of executive functioning, declined with advancing age, with an old-old (75 years and older) group of healthy volunteers demonstrating poorest performance. Hanninen et al. (1997) demonstrated that even when adjusting for the effects of education, older adults with age-associated memory impairment demonstrated signficantly worse performance on the WCST and Trail Making Tests when compared to age-matched healthy controls. In a study of short-term memory and frontal dysfunction, Parkin and Walter (1991) found that performance on a working memory task (WCST) declined with age and was related to performance on the Brown-Peterson task. WCST performance by a group of healthy 80 to 87 year old adults versus a group of healthy 64 to 69 year old adults revealed significant differences for the number of categories attained and total number of errors committed. Hultsch et al. (1992) examined changes in mean performance on working memory, information processing, and intellectual ability tasks over a three year period in a sample of healthy community-dwelling older adults. Results showed significant average decline on working memory, verbal fluency, and world knowledge. A step-down analysis revealed that covarying decline in speed of information processing did not eliminate these significant declines. Similarly, age-related declines in WCST performance, described as being reminiscent of frontal lobe and/or basal ganglia damage, were demonstrated in a sample of healthy volunteers even after the effects of speed of information processing were controlled for (Robbins et al., 1998). In contrast, Salthouse (1994) summarized a number of his collaborative studies conducted on age effects of working memory. Results consistently demonstrated that age was associated with significant amounts of the variance in computation and reading span performance. However, many of the age-related influences were mediated by slower speed of information processing. More recent studies reviewed demonstrated that slower processing primarily influenced the time required to achieve a stable encoding of the material rather than the rate at which material was lost across time or subsequent processing. Similarly, Fristoe, Salthouse, and Woodard (1997) demonstrated that age-related reductions in processing speed mediated age differences in working memory performance and feedback-usage on the WCST. Hartley et al. (2001) compared the performances of younger and older (mean age = 72.9 years) on a series of working memory tests. They concluded that there is generalized decline in working memory systems with advancing age, with the age differences being mediated, to a moderate extent, by age-related differences in processing speed. Thus, age-related decline in working memory performance has been strongly demonstrated. However, evidence is mixed as to the role of speed of information processing in this decline. The current model of prefrontal cortex function would suggest that the working memory deficits observed in older adults result from difficulty maintaining on-line, task-relevant information and impaired ability to prepare for execution of the temporal gestalt in response to appropriate cues, all of which are influenced the integrity of interference control mechanisms. It could be that decreased processing speed is a result of ineffective, inefficient interference control mechanisms; if inhibitory control processes cannot serve to limit the access of currently task-irrelevant information to current processing efforts, new behavioral sequences cannot be planned and executed as quickly. Since inhibitory control functions serve a dual purpose of preparing an individual to respond to current task demands based on event-specific information and to separate events into distinct temporal units, break down of these functions can be expected to result in decreased speed of information processing, as well as an increased frequency of errors in information processing.

Many studies have examined the relationship between frontal lobe functioning and various aspects of verbal memory. A number of these studies provide further evidence demonstrating decline in working memory and other prefrontal abilities with advancing age. Parkin and Walter's (1992) investigation of recollective experience and age demonstrated that familiarity-based recognition increased with age (in contrast to source-based recognition, which declined with age) and was correlated with neuropsychological indices of frontal lobe dysfunction. These authors used the WCST and a verbal fluency test as two of their measures of frontal lobe dysfunction and found that performance on both declined with advancing age. In their investigation of changes in cerebral functioning with normal aging, Mittenberg et al. (1989) concluded that predominant age-related neuropsychological changes occur in frontal rather than right-hemisphere abilities. Neuropsychological measures of frontal function included verbal and design fluency, as well as verbal and visual recency discrimination. Levine, Stuss, and Milberg (1997) used conditional associative learning tasks to evaluate the hypothesis that age-related cognitive decline is related to frontal dysfunction. Results demonstrated that deficits in conditional associative learning were attributable to strategic rather than basic associative processes and error analysis revealed that past information failed to guide behavior in both persons with frontal lobe lesions and in a group of healthy, older adults ($\underline{M}$ = 71 years old). Furthermore, these authors concluded that congruence between older adults and the participants with dorsolateral prefrontal lesions on a measure of defective inhibitory control suggested that age-related decline in inhibitory processes is due to prefrontal dysfunction. A rCBF study examining the relationship between age and recognition memory ability revealed that older adults (M = 69.4 years old) showed no significant activation in areas (right hippocampus and left prefrontal and temporal cortices) activated during encoding in young adults (M = 25.2 years old) but did show right prefrontal activation similar to younger adults during recognition (Grady et al., 1995).

In summary, all of these studies suggest decline in working memory, as well as potentially other memory abilities, with advancing age. The prefrontal cortex theory of cognitive aging posits that advancing age results in a breakdown of many of the processes which support the integration, formation, and execution of complex, novel behavioral structures. These processes include those related to working memory, as well as to interference control. The former involves maintaining on-line, task-relevant information on which the temporal gestalt is constructed, as well as preparation for execution of the temporal gestalt in response to appropriate external or internal cues. The latter involves clearing current task inappropriate information from memory stores and keeping behavior from being captured by dominant internal response patterns or highly salient environmental stimuli. Data from this proposed investigation of the prefrontal cortex theory of cognitive aging are expected to demonstrate the existence of discernible neuropsychological functions which are associated with prefrontal cortex function. Performance on neuropsychological measures of prefrontal lobe functioning is expected to decline with advancing age. Furthermore, this decline performance on prefrontal cortex function measures with advancing age is expected to significantly influence the relationship between age and verbal memory performance.

Measurement and Alternative Theoretical Considerations

A number of methodological challenges exist when attempting to substantiate any theory of cognitive functioning, as few investigative procedures are available which allow for definitive localization of function and evaluation of specific cognitive processes underlying neuropsychological test performance. It is often assumed that levels of performance on different cognitive measures and the age-related effects on those measures are determined by separate and distinct mechanisms. With many neuropsychological tests, the discovery of selective impairments by individuals with damage in particular brain regions has led to the inference that various brain structures are specialized for different types of processing. When combined with results indicating age-related deficits on those measures, these findings have led to speculation that certain brain regions are more sensitive to age-related decline than others (Salthouse, Fristoe, & Rhee, 1996). Although certain measures may be sensitive to damage in particular brain regions, the measures may not be specific because damage to other regions could lead to similar patterns of impairment. Seidman et al. (1995) raised this issue in their investigation of experimental and clinical neuropsychological measures of prefrontal dysfunction in schizophrenia, stating that frontal deficits may be due to diffuse brain damage, circumscribed prefrontal damage, and/or damage in other brain regions having prefrontal connections. Furthermore, many of the neuroimaging studies used to identify what brain regions are activated during performance on various cognitive tasks contribute to these methodological concerns. Often times "activation" of a specific brain region is equated with excitatory activity, leading to the conclusion that the activated brain region is responsible for the a certain function. However, alternative explanations must be considered: 1) "activation" may represent inhibitory activity; and/or 2) "activation" may represent a system of excitatory or inhibitory processes in which the end result is activation of a specific brain region.

Additionally, neuropsychological measures used to associate cognitive performances with certain brain regions often represent more than one functional process. Salthouse, Fristoe, and Rhee (1996) investigated the localizability of age-related effects on neuropsychological measures and found that they were not independent. Across all variables examined, an average of 58% of the age-related variance in a given variable was shared with that in other variables. The authors concluded that only a portion of the age-related influences on many commonly used neuropsychological measures is specific and potentially localizable. Delis, Squire, Bihrele, and Massman (1992) performed a componential analysis of measures of problem-solving ability, determining that a wide spectrum of deficits in abstract thinking, cognitive flexibility, and use of knowledge contributed to problem-solving performance. This has been confirmed by a number of factor analytic studies of commonly used measures of frontal lobe functioning which have demonstrated similar results (Greve et al., 1996; Sullivan et al., 1993).

An alternative theoretical consideration to the decline of cognitive performance with advancing age is that decreased speed of information processing underlies the poorer frontal lobe and memory performance observed at older ages (Salthouse, 1985). Slower speed of processing has been shown to moderate the effects of decreased memory, reasoning, and spatial, and fluency performance with advancing age (Fristoe, Salthouse, & Woodard, 1997; Fisk & Warr, 1996; Salthouse, Fristoe, & Rhee, 1996; Salthouse, 1994; Lindenberger, Mayr, & Kliegl, 1993; Tun et al., 1992). However, Robbins et al. (1998) demonstrated more support for a frontal lobe functioning versus processing speed decline hypothesis of cognitive aging. Notably, measurement and "localization" of processing speed is plagued by many of the same difficulties as the measurement of prefrontal cortex functioning. Furthermore, although it has been assumed that processing speed indicates the underlying rate at which information is activated within areas of cognitive functioning, this interpretation is open to debate and may not constitute exclusive support of an account of cognitive age deficits in terms of information activation (Fisk & Warr, 1996).

Hypotheses

The purpose of this study is to investigate the applicability of the prefrontal cortex theory to cognitive aging in a sample of healthy, older adults. The main premise of this study is that the prefrontal cortex is critically important for the integration, formation, and execution of complex, novel behavioral structures and temporal gestalts, which supports the direction of behavior in an orderly, purposeful manner. This integrative function is subserved by four secondary processes, identified by West (1996): provisional/retrospective memory, prospective memory, interference control, and inhibition of prepotent responses. Table 1 provides a summarized description of these processes. For the purpose of this investigation, the concepts of provisional memory and prospective memory will be considered together as the concept of "working memory". The following hypotheses will be tested:

1) The three-factor model of prefrontal cortex function (working memory, interference control, and inhibition of prepotent responses) will be analyzed using confirmatory factor analytic techniques (see Figure 1). The three-factor measurement model of prefrontal cortex function will fit better than a one- or two- factor model (see Figure 2). In the case of a poor fit, an exploratory factor analytic representation of prefrontal cortex function variables will be generated and used for subsequent analyses.

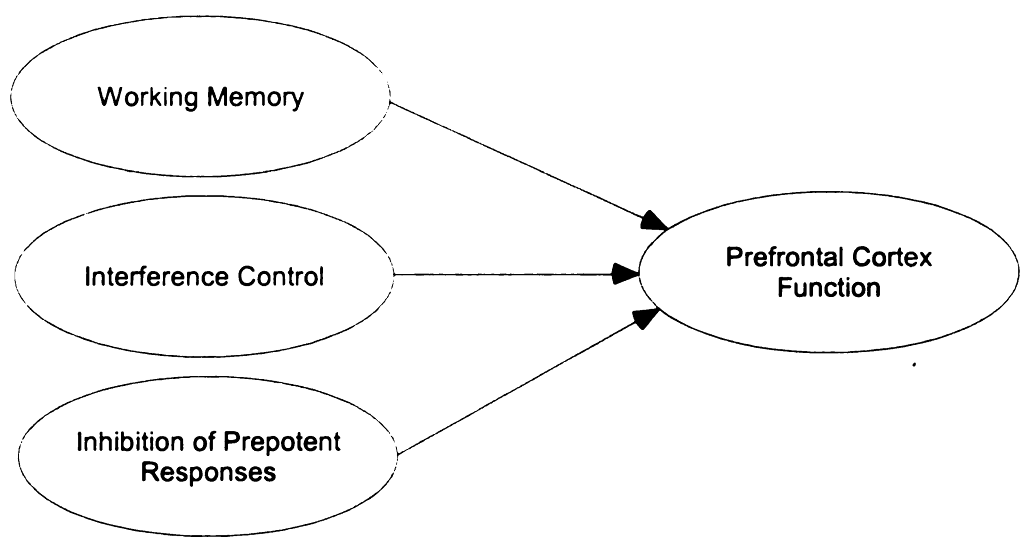

Figure 1. Three – Factor Model of Prefrontal Cortex Function

The factor representing the ability to inhibit prepotent responses is hypothesized to be comprised of the Stroop color-word naming trial score, and perseverative errors scores from the WCST, Ruff Figural Fluency Test, and California Verbal Learning Test (CVLT). The factor representing working memory is hypothesized to be comprised of total scores from the Digit Span (DSp) and Visual Memory Span (VMSp) subtests from the Wechsler Memory Scale-Revised (WMS-R; Wechsler, 1987) and the WCST total categories achieved score. The final factor representing interference control is hypothesized to be comprised of scores from the Trailmaking Test Parts A and B, the total score from the Symbol Digit Modalities Test , and the CVLT proactive interference score.

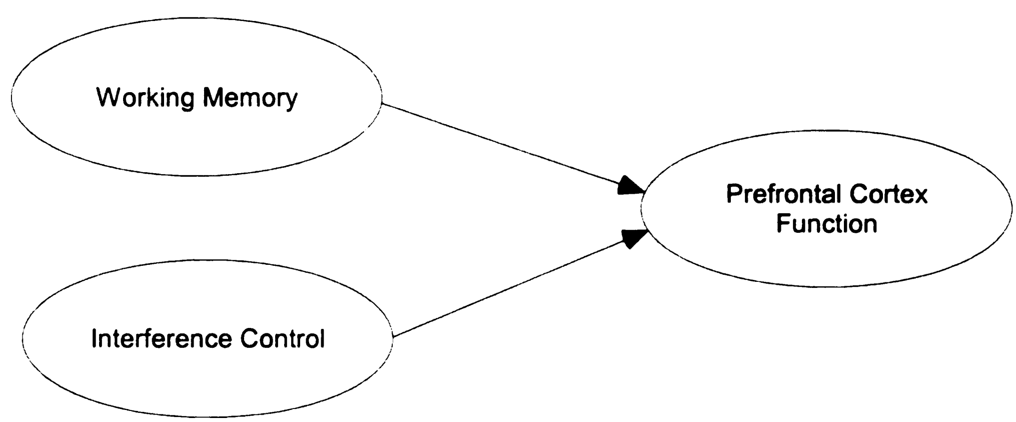

Figure 2. Two – Factor Model of Prefrontal Cortex Function

2) Causal models will be tested in which prefrontal cortex function will mediate the association between age and verbal memory measures (see Figure 3), with decline in prefrontal cortex functioning mediating the decline in verbal memory performance with advancing age. Because verbal memory performance is often chosen as a key measure in

evaluating changes with advancing age because of its direct, pragmatic application to daily functioning, it was utilized in this study to investigate the hypothesized mediating role of prefrontal cortex function on cognitive aging.

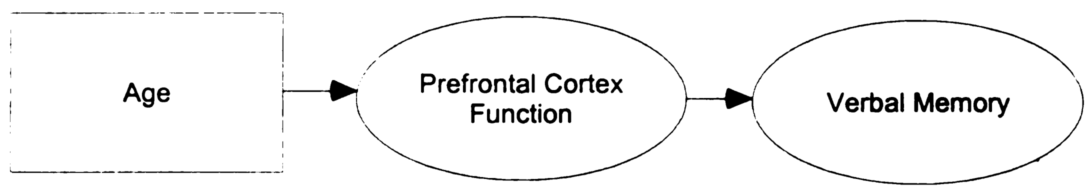

Figure 3. Causal Model of Prefrontal Cortex Function as a Mediator

METHOD

Participants

One hundred nine community dwelling, independently-living older adults were drawn from a larger intervention study that recruited participants from the greater Lansing, Michigan area through newspaper advertisements. Those who scored at 24 or better on the Mini Mental Status Examination and reported no significant history of severe neurological or medical problems likely to adversely affect their cognitive abilities (e.g., stroke, major ischemia, terminal illness, significant traumatic brain injury) on a self-report medical history questionnaire were included. The 60 women and 49 men ranged in age from 55 to 88 years old (M = 70.2; SD = 6.9) and had a mean education of 16.4 years (SD = 2.9).

Procedure

Participants were assessed at MSU's Psychological Clinic. The entire assessment for each participant, including measures unrelated to this study, required from two to two-and-one-half hours. Participants were unaware of the hypotheses of this study when they participated in the assessment. Assessments were conducted and scored by the author and graduate level students enrolled in MSU's Clinical Psychology program who have experience in administering and scoring these tests. The author and two other graduate students specializing in neuropsychology re-checked the scoring on all tests. Upon completing the assessment, participants were enrolled in a bi-weekly support group that focused on instruction in mnemonic memory training strategies and either attention retraining or relaxation techniques. Groups lasted four weeks, after which time participants were re-administered the assessment battery and then received feedback about their performance as compared to others their age. One test that required correct color vision (Stroop Color Word Test) could not be completed by four male participants who were determined to be color vision-deficient.

Measures

Measures of Prefrontal Cortex Functioning

Wisconsin Card Sorting Task (WCST)

The WCST assesses the ability to generate and test hypotheses and to shift and maintain cognitive sets. Described by many as a measure of working memory, it contains 128 cards which the participant attempts to discover three different rules/categories for sorting multidimensional stimuli by matching each card to one of four key cards. Feedback is provided when cards are matched correctly or incorrectly. After the participant matches 10 cards of a given category, the examiner changes the matching category, without indicating this to the participant. Each category has to be discovered twice. This test yields four measures: total categories achieved (WCSTcat); perseverative errors involving continuation of sorting based on an immediately preceding rule (WCSTpe); and nonperseverative errors (WCSTnp).

The WCST is widely used in clinical settings to detect cognitive impairments associated with frontal lesions (Stuss & Benson, 1986). Spreen and Strauss (1991) critiqued the WCST, reporting that studies have generally confirmed that this test is sensitive to frontal functioning, although some have reported more perseveration in patients with right as compared to left prefrontal damage. Drewe's (1974) investigation of patient's with schizophrenia who had undergone frontal leucotomy demonstrated significant difficulties with perseveration on the WCST. Milner (1963) found that patients with dorsolateral frontal excisions demonstrated significantly poorer performance on this task when compared to those with orbitomedial and posterior lesions. Specifically, those with dorsolateral lesions showed an inability to shift from one sorting principal to another. The work of both Taylor (1979) and Hermann et al. (1988) supported these findings and suggested that the WCST is sensitive to function in dorsolateral areas of both frontal lobes, but more to the left than to the right. Most recently, Ragland et al. (1997) found that WCST performance was associated with increased PET rCBF activity in the dorsolateral prefrontal cortex. Notably, participants with the highest WCST scores activated dorsolateral prefrontal and inferior frontal regions, exclusively.

Stroop Color and Word Test (Stroop)

The Stroop measures the ease with which a person can shift perceptual set to conform to changing demands and suppress a habitual or prepotent response in favor of an unusual one. This test yields three basic scores: word naming (Stroopw) determined by the number of words (red, green, or blue) read correctly in 45 seconds; color naming (Stroopc) determined by the number of colors (red, green, or blue) named correctly in 45 seconds; color-word naming (Stroopcw) determined by the number of correct responses in 45 seconds. The Stroop-cw trial consists of color words printed in incongruous colored ink (e.g., the word "blue" printed in red ink). The participant is asked to name the color of ink in which the word is printed, requiring them to suppress a highly prepotent response (reading the word). The extent to which the tendency to read the word intrudes upon the color naming assignment, referred to as the interference effect, is calculated from the three basic scores.

Regard (1981) reported that patients with frontal lobe damage performed significantly worse on the Stroop-cw when compared to patients with lesions in other areas of the cortex. Uchiyama et al. (1994) found Stroop-c and Stroop-cw score to be two of the most sensitive measures for predicting frontal lobe functioning in both geriatric and non-geriatric samples. Vendrell et al. (1995) demonstrated that the brain region most related to errors on the Stroop-cw was the right prefrontal lateral cortex utilizing magnetic resonance imaging (MRI). In their review of PET studies, Cabeza and Nyberg (1997) found that the ability to select between competing processing alternatives on the basis of some pre-existing internal, conscious plan, as evidence by Stroop performance, was consistently related to increased activity in the anterior cingulate. Spreen and Strauss (1991) reported a one month test-retest reliability for each page of the Stroop to be .90, .83, and .91, respectively.

Paced Auditory Serial Addition Test (PASAT)

The PASAT (Brittain, LaMarche, Reeder, Roth, & Boll) is designed to measure sustained attention and information processing abilities. A pre-recorded tape delivers a random series of 61 numbers from 1 through 9. The respondent is instructed to add pairs of numbers such that each number is added to the one immediately preceding it: the second number is added to the first, the third to the second, the fourth to the third, and so on. The same 60 numbers are given in four different trials at differing presentation rates (2.4, 2.0, 1.6, and 1.2 seconds). This test requires an individual to comprehend the auditory input, respond verbally, inhibit encoding of one's own response while attending to the next stimulus in a series, and perform at an externally determined pace (Spreen & Strauss, 1991).

The PASAT has good internal consistency, with a split-half reliability of .96 (Egan, 1988). O'Donnell, et al.'s (1994) factor analytic study of a numerous neuropsychological tests demonstrated that the PASAT was one of the measures that defined an attentional factor. Brittain et al. (1991) examined the effect of age, gender, race, IQ, and education on PASAT performance in healthy adults aged 17-88. Age and IQ were found to significantly affect PASAT results. A mildly significant effect was observed for gender as well, with males performing slightly better than females. Schmidt, Trueblood, Merwin, and Durham's (1994) factor analytic study of attention tests included the PASAT as one of the measures of a global construct of attention.

Ruff Figural Fluency Test (RUFF)

A measure of design fluency, the RUFF (Ruff, Allen, Farrow, Niemann, & Wylie, 1994) assesses spontaneous flexibility, the ready flow of ideas or answers in a response to a single questions. Requiring divergent thought and production, successful performance on the RUFF also relies on self-monitoring, remembering, and creative imagination. Participants are required to generate as many different designs as they can by connecting dots in a specific configuration within a one minute time limit. Five trials, each with a different dot configuration pattern or different background on which the dots are to be connected, are given. Performances are scored for number of unique patterns (productivity - RUFFdes) and for number of repetitions of patterns (perseverations - RUFFper).

Age and education have been shown to affect RUFF productivity scores in normative studies (Ruff et al., 1994). Productivity scores have also been shown to discriminate mild from severe head trauma patients and both groups from normal control participants (Lezak, 1995). Furthermore, perseverative responses increased from control (5.8) to mildly injured (8.8) to severely injured (10.1).

Trailmaking Test A & B (TMT)

TMT (Reitan & Wolfson, 1985) assesses speed of information processing, attention, mental flexibility, and visuomotor tracking. It requires participants to join randomly located numbers in numerical sequence (TMTa) and in alternate numerical-alphabetical sequence (TMTb) as quickly as possible. Resulting scores are based on time taken to successfully complete each task.

Normative studies have shown that performance times increase significantly in each succeeding decade (Stuss, Stethem, & Poirier, 1987). Drebing et al. (1994) found the TMT to be one of the most sensitive and specific neuropsychological tests to detect early cognitive decline in higher cognitively functioning older adults. Factor analytic studies have demonstrated that TMT performance consistently loads on a factor generally described as "attention" (O'Donnell et al., 1994; Schmidt et al., 1994; Uchiyama et al., 1994). Scores are strongly influenced by level of education (Spreen & Strauss, 1991). Retest reliability over a six month interval was reported as .98 for TMTa and .67 for TMTb (Lezak, 1995).

Symbol-Digit Modalities Test (SDMT)

SDMT (Smith, 1973) is a measure of processing speed, sustained attention, and visual-motor scanning. It requires the matching of numbers to symbols within a 90 second time constraint. The score is based on the number of successfully matched symbol-number pairs. This test is similar to the Wechsler Digit Symbol subtest except the matching is inverse.

Smith (1973) found the SDMT to possess good predictive validity in dissociating normal adults from those with brain-damage. A number of factor analytic studies have included the SDMT in factors described as information processing and visuo-motor scanning (Schmidt et al., 1994).

Controlled Oral Word Association Test (COWAT)

A measure of verbal fluency, the COWAT (Benton & Hamsher, 1983) also assesses spontaneous flexibility. Participants are asked to produce as many words as possible that begin with a designated letter of the alphabet. Three trials are conducted using the letters "C", "F", and "L", with a one-minute time limit imposed for each trial. The score is the sum of all admissible words for the three letters.

Frontal lesions, regardless of side, tend to depress fluency scores, with left frontal lesions resulting in lower word production than right frontal ones (Miceli et al., 1981, Benton, 1968). Eslinger and Grattan (1993) demonstrated that COWAT performance, as well as performance on other measures of spontaneous flexibility, was markedly decreased in persons with frontal lobe lesions. Martin, Wiggs, LaLonde, and Mack (1994) demonstrated that verbal fluency places greater demands on frontal lobe mediated strategic search processes than on temporal lobe mediated semantic knowledge. A PET-scan study (Parks et al., 1988) with normal volunteers indicated that verbal fluency activated frontal and bilateral temporal lobes. A rCBF study (Gourovitch et al., 2000) with normal volunteers found that during a verbal fluency task, the anterior cingulate, left prefrontal regions, thalamus, and cerebellum were activated. Education and age have been shown to influence COWAT performance. Retest reliability with adults after 19-24 days was reported as .88. (Spreen & Strauss, 1991).

Wechsler Memory Scale-Revised Digit Span (DSp)

DSp (Wechsler, 1987) assesses verbal/auditory attention, short-term memory, and/or working memory. Aural presentation of digits made to participants must be repeated back to the examiner in either a forward or backward sequence. DSp performance has been shown to decrease with age and in some studies has been positively associated with higher levels of education (Lezak, 1995; Ryan, Lopez, & Paolo, 1996). Shimamura, Janowsky, and Squire (1991) found that patients with frontal lobe lesions exhibited significant impairment on the DSp when compared to controls.

Wechsler Memory Scale-Revised Visual Memory Span (VMSp)

VMSp (Wechsler, 1987) is the visual-spatial analog to DSp. It assesses visual attention, short-term memory, and/or working memory. Participants are required tap a sequence of colored blocks in either the same forward or backward order as the examiner has tapped. VMSp performance has demonstrated the same relationship to age and education at DSp (Lezak, 1995).

Measures of Verbal Learning and Memory

California Verbal Learning Test (CVLT)

The California Verbal Learning Test (CVLT; Delis, Kramer, Kaplan, & Ober, 1984) involves learning lists of words presented in successive trials in the same sequence. Its scoring system provides information on the quantity of material learned, as well as for: rate of learning over several trials, the encoding strategy employed (semantic versus serial clustering), the types of recall errors made, vulnerability of memory to time and interference conditions, and the degree to which memory performance improves with assisted recall cues.

Rosenbaum's (1984) reported that the CVLT is an extremely sensitive instrument for detecting subtle memory deficits; however, this high sensitivity comes at the expense of more false-positive errors. Over a one-year interval, CVLT test-retest reliability coefficients ranged from .26 (percent middle recall) to .79 (long-delay cued recall). Total immediate recall of List A across the five trials correlated .66 with the WMS-R General Memory Index and in the .60s with several other WMS-R variables (Delis, Kramer, Kaplan, & Ober, 1987). These authors also factor analyzed all CVLT intercorrelations and found that its multiple indices identified theoretically meaningful factors consonant with the constructs they were designed to measure. An additional factor analytic study demonstrated that verbal memory, as measured by the CVLT, consisted of a number of theoretically meaningful component factors reflecting learning strategy, acquisition rate, serial position effect, discriminability, and learning interference (Delis, Freelan, Kramer, & Kaplan, 1988). Multiple CVLT studies of selected neurological groups (chronic alcoholics, Parkinson's, Huntington's, and Alzheimer's disease) have yielded results commensurate with each group's previously determined memory problems. Four measures from the CVLT were used in analyses as verbal memory variables: CVLTtot – free recall total from trials 1 through 5; CVLTsf – short-delay free recall; CVLTlf – long-delay free recall; CVLTrec – recognition hits. Total perseverative errors (CVLTper) and the proactive interference score (CVLTpi) were used as measures of prefrontal cortex functioning.

Logical Memory (LM)

Immediate recall total of stories A and B from the Wechsler Memory Scale-Revised (WMS-R; Wechsler, 1987) represents the recall of two verbal passages immediately after each is presented. Total recall scores for LM can range from 0 to 46, with higher scores reflecting more information units recalled. It has an average test-retest stability of .79 over 4-6 weeks (Bowden & Bell, 1992) and has consistently shown to load on the verbal memory factor in numerous factor analyses (Prigatano, 1978). It is strongly correlated with both CVLTtot (.79) and CVLTlf (.93; Spreen & Strauss, 1998). Clinical investigations using LM found it sensitive to memory disturbances in patient groups including older adults with age-associated memory impairment, dementia, multiple sclerosis, neurotoxin exposure, and depression (Spreen & Strauss, 1998).

Measure of Mental Status

The Mini-Mental Status Exam (MMSE) is a 30-item test created to briefly screen for level of cognitive functioning. It assess orientation, immediate recall, attention, calculation, language abilities, and constructional dyspraxia. Scores can range from 0, indicating severe impairment to 30, indicating unimpaired mental status. It was standardized on a sample of healthy older controls (M = 74 years) whose scores ranges from 24.6 to 27.6 (Folstein, Folstein, & McHugh, 1975). Demented persons scored between 9.6 to 12.2, with no overlap between these two groups. A cut-off score of 24 is often used to identify scores more suggestive of impairment (Lezak, 1995).

Measure of Depression

The 30 yes-no Geriatric Depression Scale (GDS) items assesses mood and psychological symptoms of depression. Respondents answer each question according to how they feel at the time of administration. GDS scores range from 0, indicating no depressive statements were endorsed, to 30, indicating severe depression. The item-total correlations ranged from .32 to .83 ($M = .56$), while internal consistency and split-half reliability were both .94. The test-retest reliability over one month was .85 (Koenig, Meador, Cohen, & Blazer, 1988).

Factor analysis of the GDS identified a major factor of general depression and minor factors of worry/obsessive thoughts, and apathy/withdrawal (Parmalee et al., 1989). Criterion validity with the Research Diagnostic Criteria was found to be .82. Concurrent validity with the Hamilton and Zung Depression Scales appear good (.83 and .86, respectively; Yesavage et al., 1986). Stebbins and Hopp (1990) reported that the GDS successfully discriminated between mildly demented depressed, and non-depressed individuals.

RESULTS

Missing Data

Precautionary steps during data collection were taken to ensure a complete data set. This included making alternative arrangements and multiple attempts to finish data collection if a participant indicated they wished to discontinue with the testing. Following data collection, if data were found missing, information was obtained from the clinician who conducted the testing to determine the reason(s) for the missing data. Data from seven participants were eliminated from analyses. These included three participants who discontinued testing before the delayed recall trials could be administered on both verbal memory measures and four male participants who were color vision-deficient and unable to complete the Stroop. Thus, the total number of participants used for all analyses was 102. No data were missing for any of these 102 participants.

Preliminary Data Examination

In order to examine the relationship between variables, Pearson product-moment coefficients were calculated for all measures used in the study. In examining the relationship between prefrontal cortex function measures, age, and education (see Appendix A), the correlations between age and prefrontal cortex function variables were significant, consistent with West's theory, and demonstrated declining performance with advancing age, with a few exceptions. The magnitude of the significant correlations between prefrontal cortex functioning measures and age ranged from .24 to .53. Perseverative errors on the RFFT and the CVLT, performance on the Stroop word-naming trial, Digit Span total score, the proactive interference score from the CVLT, and verbal fluency were not significantly related to age. Regarding the relationship between education and performance on prefrontal cortex function measures, only Digit Span total score, perseverative errors on the CVLT, and RUFF total designs were significantly related to education. The magnitude of these significant relationships ranged from .20 to .27. The remaining relationships between education and prefrontal cortex function variables were not significant.

Analysis of variance (ANOVA) was used to examine the relationship between gender and performance on prefrontal cortex function measures. Only four prefrontal cortex function variables were significantly related to gender (see Appendix B). Males performed significantly better on the PASAT, completed more designs on the RUFF, made fewer perseverative errors on the CVLT, but made more non-perseverative errors on the WCST than females.

Depression was significantly negatively related to seven prefrontal cortex function measures (see Appendix C). Performance on Trailmaking Test Parts A and B, Visual Memory Span total, the color-word naming trial of the Stroop, PASAT total score, and RUFF total designs all were lower with higher levels of depressive symptomatology, whereas the number of perseverative errors on the WCST was higher with higher levels of depressive symptomatology. The magnitude of significant correlations ranged from .20 to .33. Notably, the average GDS score for this sample was well below the accepted cut-off score of 10 ($\underline{M}$ = 6.77, $\underline{SD}$ = 6.66), indicating a very low frequency of reported depressive symptomatology in this sample.

Appendix D illustrates the relationship between measures of prefrontal cortex function. The majority of prefrontal cortex function variables were significantly related to each other, with a few exceptions. The magnitude of significant correlations ranged from .21 to .76. Total score on the SDMT was the only measure that was significantly related to all other prefrontal cortex function variables. Perseverative errors on the RUFF was not significantly related to any other prefrontal cortex function variable. The proactive interference score on the CVLT was significantly related only to the verbal fluency score, with higher proactive interference scores being associated with poorer verbal fluency scores. Perseverative errors on the CVLT was significantly related only to total categories achieved on the WCST and to WCST non-perseverative errors, with greater perseverative CVLT errors associated with fewer categories achieved on the WCST and greater WCST non-perseverative errors.

The relationship between prefrontal cortex function and verbal memory measures is illustrated in Appendix E. Only two prefrontal cortex function measures were significantly related to all verbal memory measures: fewer non-perseverative errors on the WCST and stronger performance on the color-word naming trial of the Stroop were associated with stronger performance on all verbal memory measures. The total immediate recall score from trials 1-5 on the CVLT was significantly related, in the expected direction (i.e., stronger performance on the prefrontal cortex function measure was associated with stronger verbal memory performance), to the majority of prefrontal cortex function variables. The magnitude of significant relationships between verbal memory and prefrontal cortex function measures ranged from .21 to .45. In contrast, total recognition hits on the CVLT was significantly related to only two prefrontal cortex function measures: stronger performance on the color-word naming trial of the Stroop and fewer non-perseverative errors on the WCST were associated with greater recognition hits.

Hypothesis 1: Examination of the 3-factor Model of Prefrontal Cortex Function

The three-factor model of prefrontal cortex function (working memory, interference control, and inhibition of prepotent responses) was analyzed using the following steps:

1. Correlations of manifest variables (specific test scores) for each corresponding latent variable (each proposed factor) were examined.
2. Principal components analysis (PCA), constraining the data to three factors, was employed to determine the fit of the three-factor model.

As proposed, if the three-factor model of prefrontal cortex function was determined to not offer the best fit to the data, then a new measurement model would be determined through exploratory factor analysis.

Correlations of manifest variables to their corresponding latent variable

The relationship between specific test scores hypothesized to comprise each of the three factors representing prefrontal cortex function was examined using Pearson product moment correlations. Specific test scores/measures or manifest variables proposed to comprise each latent variable were chosen on the basis of previous studies that had indicated that these variables were related and theorized to be measuring the same or similar cognitive processes. Table 2 presents the Pearson product moment correlations between manifest variables comprising each latent variable. Only two of the measures hypothesized to comprise the factor representing ability to inhibit prepotent responses (Stroopcw and WCSTper) were significantly related. Similarly, only two of the three measures (Dsptot and VMSptot) hypothesized to comprise the working memory factor were significantly related. The final measure, WCSTcat, was unrelated to either measure. In contrast, all measures hypothesized to comprise the interference control factor were significantly related.

In conclusion, two of the three factors proposed to represent prefrontal cortex function were comprised of measures that were not highly homogeneous. While Cattell (1982) has demonstrated that the best validity of a factor may be reached with a certain moderate calculable homogeneity versus the highest homogeneity that can be achieved, the low level of homogenity between some of the above measures strongly suggested that another possible combination might provide a better representation of the three factors proposed to comprise prefrontal cortex function.

Table 2

Correlations of Manifest Variables for Each Latent Variable

Ability to Inhibit Prepotent Responses

	Stroopcw	WCSTper	RFFTper	CVLTper
Stroopcw	1.0	-.44**	.01	-.03
WCSTper		1.0	-.08	-.11
RFFTper			1.0	-.04

Working Memory

	Dsptot	WCSTcat	VMSptot
Dsptot	1.0	.07	.38**
WCSTcat		1.0	.02

Interference Control

	PASAT	TMTa	TMTb	SDMT
PASAT	1.0	-.41**	-.41**	.58**
TMTa		1.0	.53**	-.60**
TMTb			1.0	-.56**
CVLTpi	-.02	.03	-.17	.08

Note: * $p \leq .05$; ** $p \leq .01$. PASAT = Paced Auditory Serial Addition Test; STROOPcw = Stroop Color-Word Test – color-word naming trial; TMTa = Trailmaking Test Part A; TMTb = Trailmaking Test Part B; Dsptot = Digit Span total score; VMSptot = Visual Memory Span total score; WCSTcat = Wisconsin Card Sorting Test total categories achieved; WCSTper = Wisconsin Card Sorting Test perseverative errors; RFFTper = Ruff Figural Fluency Test total perseverative errors; CVLTper = California Verbal Learning Test total perseverative errors; CVLTpi = California Verbal Learning Test proactive interference score; SDMT = Symbol Digit Modalities Test.

Principal components analysis (PCA) of three-factor model of prefrontal cortex function

A PCA was conducted on the 12 prefrontal cortex function measures. The purpose of PCA is to reduce large data items into a few meaningful components based on the intercorrlations among the items. Because PCA explains the variation that is unique to an item and its error variance, as well (Pedhazur & Schmelkin, 1991), it was chosen as the best data reduction method. The rule of eigenvalues greater than one (Johnson & Wichern, 1992) was utilized to determine which components to retain. The Varimax rotation method using generalized least squares was used to determine the best factor solution. It was chosen in order to maximize the variances of the factors without changing the mathematical properties of the solution (Tabachnick & Fidell, 1996).

Sample size restricted the number of measures that could be subjected to the PCA. Using the rule of a minimum of 10 participants for each measure subjected to the components analysis (Bryant & Yarnold, 1995), the current data set allowed for only 10 measures to be used in the PCA. Measures to be eliminated from the PCA were determined by examining loading coeffecient scores prior to and after rotation. As seen in Table 3, three measures had coeffecient loading scores below 0.2 (RFFTper, CVLTper, and CVLTpi). Comrey and Lee (1992) suggest that loadings below .32 (10% overlapping variance) are "poor" measures of a component/factor. These three measures were eliminated and the remaining 9 measures were subjected to PCA.

Table 3

Communalities of 12 Original Prefrontal Cortex Function Variables

Variable	Shrunken r^2	Final
PASAT	.472	.583
STROOPcw	.518	.601
TMTa	.457	.850
TMTb	.504	.613
Dsptot	.319	.457
VMSptot	.349	.427
WCSTcat	.573	.893
WCSTper	.583	.669
SDMT	.595	.683
RFFTper	.007	.116
CVLTper	.131	.216
CVLTpi	.119	.217

Note: Extraction Method: Generalized Least Squares; PASAT = Paced Auditory Serial Addition Test; STROOPcw = Stroop Color-Word Test – color-word naming trial; TMTa = Trailmaking Test Part A; TMTb = Trailmaking Test Part B; Dsptot = Digit Span total score; VMSptot = Visual Memory Span total score; WCSTcat = Wisconsin Card Sorting Test total categories achieved; WCSTper = Wisconsin Card Sorting Test perseverative errors; SDMT = Symbol Digit Modalities Test; RFFTper = Ruff Figural Fluency Test total perseverations; CVLTper = California Verbal Learning Test total perseverative errors; CVLTpi = California Verbal Learning Test proactive interference score.

The resulting three-factor structure is shown in Table 4. Eigenvalues for the three-factor solution were between 1.1 to 2.6 and accounted for 60.4% of the variance. All items loaded on at least one of the three factors with loading coefficients ranging from .42 to .81. However, measures comprising the three factors did not fit the model of prefrontal cortex functioning that was originally proposed. The first factor, accounting for 29.1% of the variance, was comprised of PASAT, Stroopcw, TMTa, TMTb, VMSptot, and SDMT. The measures comprising this factor appear to represent a combination of attention, concentration, set-shifting, and interference control. The second factor was comprised of both WCST measures and accounted for 18.7% of the variance. This factor is consistent

Table 4

Varimax 3-Factor Structure (Factor-Variable Correlations) of Retained Original Variables

Variable	Factor 1	Factor 2	Factor 3	Communalities Shrunken r^2	Final
PASAT	**.61**	.13	.34	.46	.53
Stroopcw	**.60**	.38	.24	.51	.57
TMTa	**-.69**	-.13	.03	.40	.52
TMTb	**-.63**	-.20	-.27	.46	.54
Dsptot	.23	.04	**.87**	.31	.81
VMSptot	**.54**	-.09	.33	.36	.42
WCSTcat	-.20	**.85**	-.01	.54	.73
WCSTper	-.20	**-.83**	-.06	.57	.74
SDMT	**.79**	.21	.17	.57	.70
% Variance	29.1	18.7	12.6		

Note: Extraction Method – Generalized Least Squares; Rotation Method – Varimax with Kaiser Normalization; PASAT = Paced Auditory Serial Addition Test; STROOPcw = Stroop Color-Word Test – color-word naming trial; TMTa = Trailmaking Test Part A; TMTb = Trailmaking Test Part B; Dsptot = Digit Span total score; VMSptot = Visual Memory Span total score; WCSTcat = Wisconsin Card Sorting Test total categories achieved; WCSTper = Wisconsin Card Sorting Test perseverative errors; SDMT = Symbol Digit Modalities Test.

with one of the three originally proposed factors, working memory. The final factor was comprised of one measure, DSptot, and accounted for 12.6% of the variance. In conclusion, the nine originally proposed variables, when constrained to three factors, did not adequately capture or represent the three identified constructs of prefrontal cortex functioning.

<u>Identification of a new measurement model of prefrontal cortex functioning</u>

Since results of the PCA when the data was constrained to three factors demonstrated that the proposed measurement model was not the best representation of the factors underlying prefrontal cortex function, as proposed by West (1996), a series of steps was undertaken to determine a new, more robust representative measurement model based upon the data. These steps were as follows:

1. Five additional measures of prefrontal cortex function that have been previously identified by numerous other studies as measures of prefrontal cortex function were added for subsequent analysis to determine potential contribution to the measurement model: Wisconsin Card Sorting Test, non-perseverative errors (WCSTnp), Stroop word naming trial score (Stroopw), Stroop color naming trial score (Stroopc), Ruff Figural Fluency Test total designs (RFFTdes), and the total score from the Controlled Oral Word Association Test (Vfluency).
2. A series of exploratory factor analyses were used to determine two- and three-factor models of prefrontal cortex function.
3. Chi-square test was used to evaluate the goodness-of-fit of the two- and three-factor models in order to determine which factor model best fit the data to be used as the final measurement model testing the last hypothesis investigating the mediating role of prefrontal cortex function between age and verbal memory performance.

<u>Selection of additional variables</u>

While difficulties with the measurement of functions associated with the prefrontal cortex have been previously addressed, significant evidence exists to suggest that there are a number of neuropsychological tests that appear to consistently relate to functions subserved by the prefrontal cortex. Ideally, those measures that have consistently demonstrated, through neuroimaging studies, to be associated with prefrontal activation would have been utilized to represent one of the three underlying factors comprising prefrontal cortex function. These would have included: 1) a version of the n-back test during which participants observe or listen for sequences of letters presented one at a time and respond to an identified letter only when it follows another identified letter (Smith et al., 1998; Barch et al., 1997; Braver et al., 1997; & Jonides et al., 1993); 2) an additional measure of sustained attention, such as the Conners' Continuous Performance Test or the Attention Capacity Test (Chao & Knight, 1997; Parasuraman & Giambra, 1991; Wilkings, Shallice, & McCarthy, 1987); 3) a prospective memory measure (Einstein et al., 1992; McDaniel & Einstein, 1992; and West, 1988); and 4) a measure of source memory (Spencer & Raz, 1994; Schacter et al., 1994; Schacter et al., 1991; and Craik et al., 1990).

Studies demonstrating the reliability and validity of the five additional measures of prefrontal cortex function selected have been previously reviewed. An additional score from the WCST was chosen because it was strongly correlated with the two other scores from the WCST, as well as with other measures of prefrontal cortex function. It was added to provide another potential measure of working memory, since the current working memory factor was comprised of only two variables. The word- and color-naming trials from the Stroop were added because both were strongly correlated with a number of other prefrontal cortex function measures related to attention, concentration, and interference control, as well as to the color-word naming trial score from the Stroop and because they provide additional measures of processing speed. Total scores from both the Ruff Figural Fluency Test and the Controlled Oral Word Association Test were added because of their strong correlational relationship to numerous other prefrontal cortex function measures and because numerous neuroimaging studies have consistently identified both as measures of spontaneous flexibility that are associated with areas within the prefrontal cortex (Gourovitch et al., 2000; Parks et al., 1988; Jason, 1985).

Results of exploratory factor analyses

An EFA was conducted with the nine retained original prefrontal cortex function measures and the five added prefrontal cortex function measures. Again, because of restrictions due to sample size, measures were eliminated from the EFA based upon factor loading coefficient scores prior to rotation. The five variables with the smallest factor loading coefficients were eliminated prior to constraining the data to three factors. As seen in Table 5, five measures had coefficient loading scores below 0.5 (TMTa, DSptot, VMSptot, Vfluency, and RFFTdes) and were eliminated from subsequent analyses. EFA was conducted with the final, nine retained prefrontal cortex function measures, constraining the data into both two- and three-factor solutions.

Table 5

Communalities of Retained Original Prefrontal Cortex Function Variables and Added Relevant Variables

Variable	Shrunken r^2	Final
PASAT	.498	.588
STROOPw	.516	.666
STROOPc	.626	.794
STROOPcw	.667	.757
TMTa	.443	.577
TMTb	.504	.682
Dsptot	.342	.474
VMSptot	.407	.566
WCSTcat	.667	.769
WCSTper	.626	.710
WCSTnp	.712	.871
SDMT	.628	.702
Vfluency	.322	.473
RFFTdes	.398	.420

Note: Extraction Method: Generalized Least Squares; PASAT = Paced Auditory Serial Addition Test; STROOPw = Stroop Color-Word Test – word naming trial; STROOPc = Stroop Color-Word Test – color naming trial; STROOPcw = Stroop Color-Word Test – color-word naming trial; TMTa = Trailmaking Test Part A; TMTb = Trailmaking Test Part B; Dsptot = Digit Span total score; VMSptot = Visual Memory Span total score; WCSTcat = Wisconsin Card Sorting Test total categories achieved; WCSTper = Wisconsin Card Sorting Test perseverative errors; WCSTnp = Wisconsin Card Sorting Test non-perseverative errors; SDMT = Symbol Digit Modalities Test; Vfluency = Verbal Fluency; RFFTdes = Ruff Figural Fluency Test total designs.

The resulting three-factor structure is shown in Table 6. Eigenvalues for the three-factor solution ranged from 1.6 to 2.4 and accounted for 66.4% of the variance. All items loaded on at least one of the three factors with loading coefficients ranging from .53 to .87. The first factor, which accounted for 26.2% of the variance, was comprised of the three WCST measures and is consistent with the originally proposed working memory factor. The second factor, accounting for 22.5 % of the variance, was comprised of the three Stroop measures. This factor appears to represent a combination of processing speed and inhibitory control. The final factor was comprised of PASAT, TMTb, and SDMT, accounted for 17.5% of the variance. This factor is comprised of variables measuring sustained attention, mental flexibility, and interference control.

Table 6

Varimax 3-Factor Structure (Factor-Variable Correlations) of Final Variables

				Communalities	
Variable	Factor 1	Factor 2	Factor 3	Shrunken r^2	Final
PASAT	-.15	.40	**.53**	.43	.53
TMTb	.13	-.18	**-.75**	.41	.63
SDMT	-.20	.50	**.60**	.57	.67
WCSTcat	**-.84**	.07	.09	.66	.76
WCSTper	**.77**	.10	-.26	.61	.68
WCSTnp	**.91**	-.14	-.08	.70	.87
Stroopw	.07	**.67**	.25	.46	.57
Stroopc	-.18	**.87**	.18	.59	.82
Stroopcw	-.36	**.60**	.44	.63	.69
% Variance	26.2	22.5	17.5		

Note: Extraction Method – Generalized Least Squares; Rotation Method – Varimax with Kaiser Normalization; PASAT = Paced Auditory Serial Addition Test; STROOPcw = Stroop Color-Word Test – color-word naming trial; TMTb = Trailmaking Test Part B; Dsptot = Digit Span total score; VMSptot = Visual Memory Span total score; WCSTcat = Wisconsin Card Sorting Test total categories achieved; WCSTper = Wisconsin Card Sorting Test perseverative errors; SDMT = Symbol Digit Modalities Test.

The results of the two-factor structure are shown in Table 7. Eigenvalues for the two-factor solution were 3.0 and 2.4 and accounted for 60.5% of the variance. Loading coefficients ranged from .52 to .87. The first factor was comprised of PASAT, TMTb, SDMT, and all three Stroop measures and accounted for 33.6% of the variance. It is comprised of variables measuring sustained attention, interference control, processing speed, and inhibitory control. While this factor is not a pure measure of interference control, it was named "interference control" for subsequent analyses because interference control is one of the major constructs that underlies performance on all of the tests comprising this measure and to remain consistent with the language of the proposed theory of prefrontal cortex functioning. The final factor was comprised of the three WCST measures and accounted for 26.9% of the variance. This factor was named "working memory" for subsequent analyses.

The goodness-of-fit test was used to determine the best measurement model to use for subsequent analyses. The 3-factor model yielded a chi-square value of 16.1 (df = 12) and was significant (p = .03). In contrast, the goodness-of-fit test for the 2-factor model was not significant (p = .19) and yielded a chi-square value of 32.6 (df = 19). Thus, the two-factor model of prefrontal cortex functioning, comprised of the interference control and working memory factors, was used as the measurement model in subsequent analyses.

Table 7

Varimax 2-Factor Structure (Factor-Variable Correlations) of Final Variables

Variable	Factor 1	Factor 2	Communalities Shrunken r^2	Final
PASAT	**.64**	-.17	.43	.52
TMTb	**-.56**	.17	.41	.53
SDMT	**.76**	-.22	.57	.67
WCSTcat	.12	**-.85**	.66	.77
WCSTper	-.23	**.78**	.61	.68
WCSTnp	-.15	**.91**	.70	.87
Stroopw	**.69**	.07	.46	.59
Stroopc	**.79**	-.18	.59	.73
Stroopcw	**.75**	-.34	.63	.71
% Variance	33.6	26.9		

Note: Extraction Method – Generalized Least Squares; Rotation Method – Varimax with Kaiser Normalization; PASAT = Paced Auditory Serial Addition Test; STROOPcw = Stroop Color-Word Test – color-word naming trial; TMTb = Trailmaking Test Part B; Dsptot = Digit Span total score; VMSptot = Visual Memory Span total score; WCSTcat = Wisconsin Card Sorting Test total categories achieved; WCSTper = Wisconsin Card Sorting Test perseverative errors; SDMT = Symbol Digit Modalities Test.

Structural Equation Modeling

Hypothesis 2 that the relationship between age and verbal memory performance is mediated by prefrontal cortex function was tested by comparing three structural equation models. Model 1 tested the hypothesized direct effect of age on verbal memory performance without taking prefrontal cortex function (as represented by interference control and working memory) into consideration. Model 2 tested the hypothesized indirect effects of age on verbal memory performance taking prefrontal cortex function into consideration. Model 3 tested the hypothesized direct and indirect effects of age on verbal memory performance taking prefrontal cortex function into consideration. AMOS

4 (Arbuckle & Wothe, 1999) was used to obtain generalized least squares estimates of the model coefficients.

Model 1

The purpose of model 1 was to evaluate the significant direct effect of age on verbal memory. The Chi-Square [χ^2 (df = 62, N = 102) = 80.95, $p > .05$] was not significant for model 1, but the RMSEA (.06) was large, and the GFI (.88) and the CFI (.80) were small. However, the data fit the rule of thumb that an acceptable fit exists if two times the degrees of freedom exceeds the χ^2 [df = 62 x 2 = 124; 124 > 80.95]. Taken together, the fit indices provide evidence for an adequate fit between the model and the data.

The standardized path coefficients for model 1 are presented in Figure 4. Relationships in the model are all in the expected direction and all are significant, with one exception. Age directly affected verbal memory performance, with advancing age resulting in poorer verbal memory performance (standardized coefficient = -.30). Age directly affected interference control and indirectly affected working memory performance. Advancing age predicted poorer performance on interference control measures (standardized coefficient = -.70). In turn, poorer performance on interference control measures predicted poorer performance on working memory measures (standardized coefficient = .29). However, advancing age did not significantly, directly predict poorer performance on working memory measures. This model, with the uni-directional arrow from interference control and working memory, was chosen because it offered the best fit to the data, when compared to all other models evaluated.

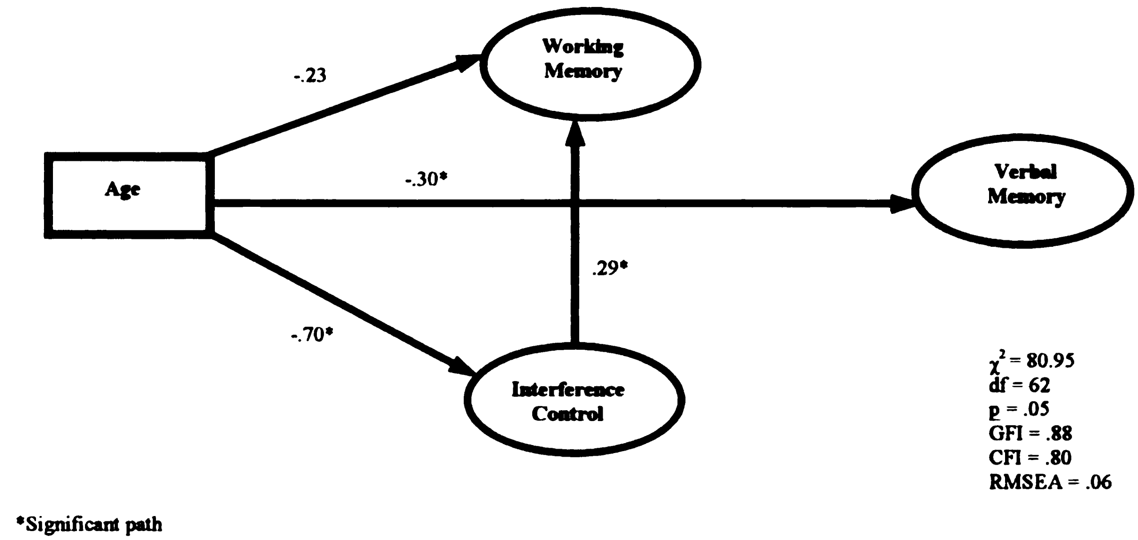

Figure 4. Standardized Path Coefficients of Model 1 – Direct Effects Model

Model 2

The purpose of model 2 was to evaluate the significant, indirect effect of age on verbal memory performance when prefrontal cortex function was taken into account. Model 2 resulted in a strong fit between the data and the model. Not only was the Chi-Square non-significant [χ^2 (df = 60, N = 102) = 68.27, p = .22], the GFI (.90) and the CFI (.91) were large and the RMSEA (.04) was small.

The standardized path coefficients for model 2 are presented in Figure 5. All relationships in the model are significant and in the hypothesized direction with the same exception as demonstrated in model 1. Two of the same paths, as found significant in model 1, were found significant in model 2. Additionally, the direct paths from working memory and interference control to verbal memory were significant. Age indirectly affected verbal memory performance. Advancing age resulted in poorer performance on interference control measures (standardized coefficient = -.58). Poorer performance on interference control measures predicted poorer performance on verbal memory measures

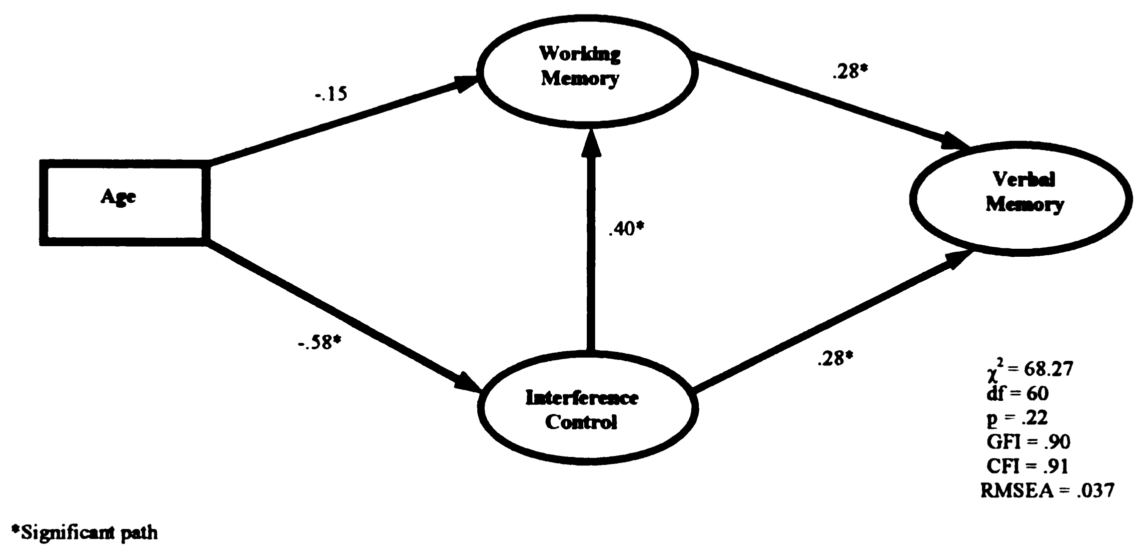

Figure 5. Standardized Path Coefficients of Model 2 – Indirect Effects Model

(standardized coefficient = .28). Poorer performance on interference control measures also predicted poorer performance on working memory measures (standardized coefficient = .40). In turn, poorer performance on working memory measures resulted in poorer performance on verbal memory measures (standardized coefficient = .28). The results indicate that performance on measures of interference control and working memory significantly influence the relationship between advancing age and declining verbal memory performance.

Model 3

The purpose of model 3 was to demonstrate that the direct effect between age and verbal memory became insignificant when it was considered in conjunction with the indirect effect between these two constructs, taking prefrontal cortex function into consideration. This would confirm that prefrontal cortex function was mediating the relationship between age and verbal memory. The results of model 3 were nearly identical to those of model 2 and demonstrated a strong fit between the data and the model. The Chi-Square [χ^2 (df = 59, N = 102) = 68.00, p = .20] was non-significant, the GFI (.90) and the CFI (.91) were large, and the RMSEA (.04) was small.

The standardized path coefficients for model 3 are presented in Figure 6. The same four paths, as found significant in model 2, were found significant in model 3. However, the direct effect of age on verbal memory was insignificant. Age indirectly affected verbal memory performance. Advancing age resulted in poorer performance on interference control measures (standardized coefficient = -.58). Poorer performance on interference control measures predicted poorer verbal memory performance (standardized coefficient = .32). Poorer performance on interference control measures also predicted poorer performance on working memory measures (standardized coefficient = .40). In turn, poorer performance on working memory measures predicted poorer verbal memory performance (standardized coefficient

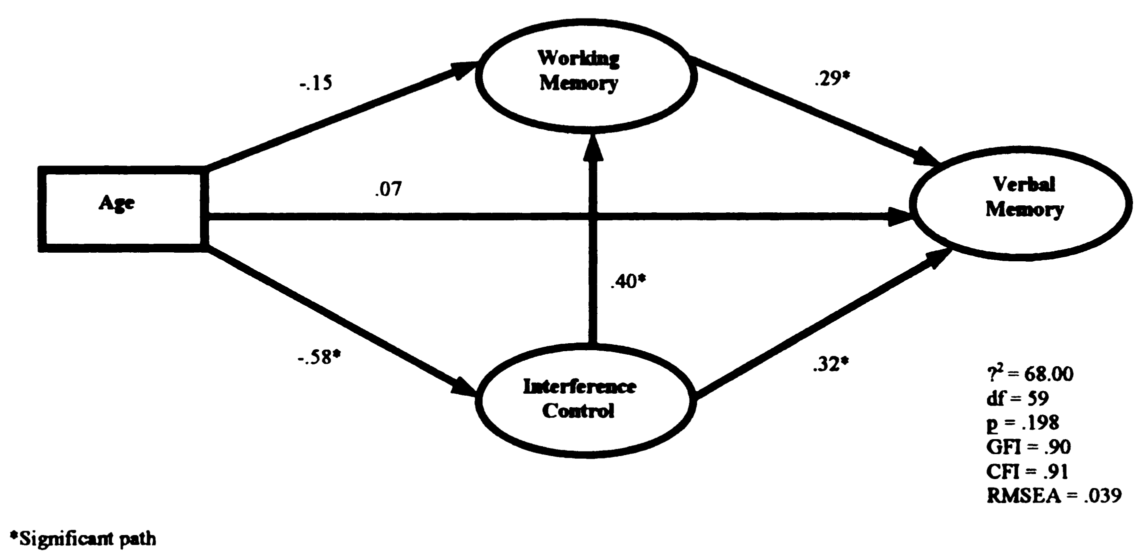

Figure 6. Standardized Path Coefficients of Model 3 – Mediation Model

= .29). The direct effect of advancing age on verbal memory performance became non-significant when considered along with the significant effect that age had on performance on prefrontal cortex function measures, which in turn significantly negatively impacted verbal memory performance. The results indicate that performance on measures of interference control and working memory mediate the effects of advancing age on declining verbal memory performance, supporting hypothesis 2.

DISCUSSION

In the past decade, there has been considerable effort to attempt to identify the mechanism(s) by which cognitive aging occurs. Because of the expanding body of evidence suggesting a selective, age-related decline in performance on neuropsychological measures identified as sensitive to frontal lobe dysfunction, a growing number of researchers, clinicians, and theorists have suggested that the cognitive processes supported by the frontal lobes, and more specifically the prefrontal cortex, are among the first to decline with advancing age. West (1996) proposed a prefrontal cortex function theory of cognitive aging which predicted that functions largely dependent on frontal regions are selectively negatively impacted by aging. Specifically, age-related declines in cognitive processes supported by the prefrontal cortex should emerge at an earlier age and should be of greater magnitude than age-related declines observed in cognitive processes supported by nonfrontal regions. West identified four specific processes underlying prefrontal cortex function (prospective memory, retrospective memory, interference control, and inhibition of prepotent responses) that demonstrated strong ability to account for age-related declines in a number of cognitive functions including verbal memory.

The purpose of this study was to evaluate the applicability of West's prefrontal cortex function theory of cognitive aging to a sample of healthy, independently living older adults. The first step involved examining to what extent the four specific processes (of which the first two were combined in this study and labeled as "working memory") underlying prefrontal cortex function, as identified by West, were discernable with multiple neuropsychological measures that have been consistently identified as measuring prefrontal cortex or executive function. It was hypothesized that the data would fit a three-factor model of prefrontal cortex functioning, with factors representing interference control, inhibition of prepotent responses, and working memory. Secondly, the mediating strength of the identified underlying prefrontal cortex processes was examined in the relationship between age and verbal memory performance. Verbal memory performance was chosen to investigate the hypothesized mediating role of prefrontal cortex function because of its wide use in investigations of cognitive aging and because of its direct, pragmatic application to daily functioning. It was hypothesized that the three-factor measurement model of prefrontal cortex functioning would mediate the relationship between advancing age and declining performance on verbal memory measures.

The Model of Prefrontal Cortex Function

Neither correlational analyses nor initial principatl components analysis (PCA) supported the proposed 3-factor model of prefrontal cortex function. Tests proposed to measure interference control, the ability to "clear out" action-irrelevant information from working memory, were all significantly related. In contrast, only two of the three tests proposed to measure working memory, the ability to maintain relevant task information "on-line" while performing mental operations, were significantly related. Only two of the four tests proposed to measure the ability to inhibit prepotent responses, preventing an action sequence from being "captured" by a dominant internal response pattern or highly salient environmental stimuli, were significantly related.

The originally proposed measures of interference control were tests that required sustained attention, concentration, processing speed, and the ability to quickly shift conceptual sets. Thus, none directly measured what West (1996) described as interference control; however, stronger performances on all of these tests undoubtedly related to how effectively a person could keep task-irrelevant information from interfering with subsequent efforts to attend, processes information quickly, and set shift. Numerous studies have shown that older adults demonstrate greater buildup of interference over trials, as evidenced by measures such as proactive interference, and declining ability to sustain attention, both of which can be attributable to a decreased ability to clear task-irrelevant information from working memory (Nyberg et al., 1997; O'Donnell et al., 1994; Shimamura & Jurica, 1994; Parasuraman & Giambra, 1991; and Dobbs et al., 1989). It was based on this rationale and research that that aforementioned tests were selected. However, a more effective, efficient way to have measured interference control would have been to utilize a version of the Brown-Peterson Consonant Trigram Test or other tasks on which strong performance depends upon release from proactive interference. Consistent declines with advancing age on the Brown-Peterson task have been demonstrated, regardless of the length of the retention interval (West, 1996). In this study, a measure of proactive interference from the CVLT was included as part of the subsequent EFA's to determine a prefrontal cortex measurement model. However, this measure, CVLTpi, was found to be significantly related to only one other measure of prefrontal cortex function (Vfluency) and had one of these lowest factor loading scores of all of the prefrontal cortex function measures. This suggests that it was either a poor measure of proactive interference for this sample (due to lack of specificity and/or sensitivity) or that the originally proposed measures of interference control represented constructs that were not sensitive or specific enough measures of interference control.

Of the three originally proposed measures of working memory, only two were significantly related (DSp and VMSp). Correlations between these measures and the final working memory measure, WCSTcat, were extremely low ($\leq .1$). While scores on the WCST have been consistently described as measures of working memory (Robbins et al., 1998; Cabeza & Nyberg, 1997; Ragland et al., 1997; Libon et al., 1994; Parkin & Walter, 1991; Spreen & Strauss, 1991), data on performance on both Digit and Visual Memory

Span tests is less consistent (Reynolds, 1997; Ryan, Lopez, & Paolo, 1996; and Lezak, 1995). Both Digit and Visual Memory Span have been purported to measure auditory/visual attention, short-term memory, and working memory. Backward memory span, in particular, requires not only sustained attention, but the ability to hold information "on-line" while actively reversing the sequence of digits presented. Thus, backward memory span performance relies more on working memory ability. Reynolds (1997) reviewed previous studies and conducted factor analyses including forward and backward span recall, concluding that these scores should not be combined for clinical analysis because the cognitive skills required for both are distinct. Thus, using only digit and visual memory span backwards scores in this study may have provided a more specific and sensitive measure of working memory. Combining both forward and backward performances may have resulted in a measure that represented both more passive attention or short-term memory skills with more active attentional and working memory ability. This may have made it a less specific measure of working memory (yet still a potentially good measure of general prefrontal cortex function), making it insignificantly related to WCST performance.

None of the four originally proposed measures of the ability to inhibit prepotent responses were significantly related. Furthermore perseverative errors on the RUFF was not significantly related to any other prefrontal cortex function measure and perseverative errors on the CVLT was related to only two other prefrontal cortex function measures (WCSTcat and WCSTnp). Perseverative errors represent an inability to prevent an action sequence from being captured by a dominant internal response pattern that may have been previously rewarded. Thus, measures of perseverative errors provide a method of analyzing the ability to suppress a prepotent response. Numerous studies have demonstrated a relationship between perseverative errors and prefrontal cortex function (Raz et al., 1998; Burgess and Shallice, 1996; Stuss et al., 1994). It is therefore puzzling that none of the perseverative error scores were significantly related to one another in this study. While each measure of perseverative errors was generated from tests that each required somewhat different cognitive skills (i.e., the WCST is a working memory test; the CVLT is a verbal memory test; the RUFF is a test of figural fluency), the reason for making perseverative errors on each of these tests is theorized to be the same mechanism. Processing speed may have played a role in the lack of a relationship between RUFFper and other measures. Specifically, this was the only perseverative error measure that was generated under a time constraint.

The remaining measure of the ability to inhibit prepotent responses, the color-word naming trial of the Stroop, has been one of the most widely documented and accepted measures of this construct (Spieler, Balota, & Faust, 1996; West, 1996; Vendrell et al., 1995; Uchiyama et al., 1994; and Houx et al., 1993). Strong performance on the Stroopcw requires inhibitory control, as well as the ability to process information quickly. While it was insignificantly related to the perseverative measures previously discussed, Stroopcw was strongly, significantly related to all other measures of prefrontal cortex function.

Results of the EFA that confined the data to three factors indicated that the proposed three-factor model of prefrontal cortex function did not fit the current data set. This may have been attributable to a number of issues, including: 1) a more appropriate underlying factor structure of prefrontal cortex function existed; 2) tests were misidentified as to the functions measured; 3) tests were unable to specifically discern underlying functions comprising prefrontal cortex function; 4) selection of measures was not well suited to evaluation of West's model; and 5) sample characteristics (such as level of education) significantly influenced the measurement and identification of the underlying factor structure of prefrontal cortex function.

Alternative Models of Factors Comprising Prefrontal Cortex Function

A series of exploratory factor analyses (EFA) conducted suggested alternative two- and three-factor prefrontal cortex function solutions. Notably, some of the originally identified measures of prefrontal cortex function demonstrated weak factor loadings during the series of EFA's and were subsequently dropped from analyses. These included: perseveration error scores on the CVLT and RUFF, the CVLT proactive interference score, Trail Making Test A, and total scores on Digit Span and Visual Memory Span. Furthermore, some tests not originally proposed as measures of one of the underlying constructs of prefrontal cortex function were found to significantly contribute to the measurement model of prefrontal cortex function in this study. These included: non-perseverative errors on the WCST and scores from the Stroop word- and color-naming trials.

Factor loading scores for CVLTper, RUFFper, and CVLTpi were extremely low ($\leq .13$), suggesting that these scores represent functions essentially different from the remaining prefrontal cortex function measures. Likewise, factor loadings for DSp and VMSp were also low ($\leq .35$). As previously discussed, both of these scores may represent a combination of passive and active attentional abilities, short-term memory, and working memory. Although both were significantly correlated with a number of prefrontal cortex function measures, sensitivity and specificity of these measures may be less than that of other prefrontal cortex function measures, resulting in them being related to, yet not strongly representative of, the specific constructs underlying prefrontal cortex function. The lower factor loading score of TMTa may be a function of its validity as a measure of prefrontal cortex function. Specifically, it may predominantly represent processing speed and visuomotor tracking, versus performance on TMTb, which requires both of these skills, in addition to mental flexibility and cognitive set-shifting skill. Processing speed measures have been shown to be significantly negatively affected by advancing age (Fristoe, Salthouse, & Woodard, 1997; Fisk & Warr, 1996; Salthouse, Fristoe, & Rhee, 1996; Salthouse, 1994; and Tun et al., 1992) and may be reliant, in part, on the integrity of prefrontal cortex function. The extent to which performance on TMTa is related to processing speed may make it essentially different from functions measured by the remaining prefrontal cortex function tasks in this sample. In conclusion, measures eliminated through EFA appear to be a combination of test scores that are less sensitive and specific than other measures of prefrontal cortex function.

Rationale for including the five additional measures of prefrontal cortex function, as previously addressed, was based predominantly on: previous research that had demonstrated consistent relationships between selected measures and activation of areas of the prefrontal cortex in neuroimaging studies; other research demonstrating relationships between selected measures and other tests purported to measure prefrontal cortex function; and the strong correlational relationships between selected measures and other prefrontal cortex function measures in this study. WCSTnp was added because it was strongly correlated with the two other scores from the WCST, as well as with other measures of prefrontal cortex function. It was added with the assumption that it would provide another potential measure of working memory. This assumption was supported, as all WCST scores consistently loaded independently of other prefrontal cortex measures during EFA's. Numerous recent factor analytic studies examining the WCST and other neuropsychological measures have demonstrated that subtest scores on the WCST typically load independently of other neuropsychological measures or with other tests designed to be administered, scored, and interpreted in the same manner (such as the Booklet Category Test – Reitan & Wolfson, 1985) (Boone et al., 1998; Greve, Ingram, & Bianchini, 1998; and O'Donnell et al., 1994). This is consistent with current EFA results that demonstrated that the three selected measures of the WCST loaded together and contributed uniquely as a construct of prefrontal cortex function. Notably, other studies examining the factor structure and construct validity of the WCST have demonstrated both two- and three-factor solutions (Greve, Bianchini, Hartley, & Adams, 1999; Greve Ingram, & Bianchini, 1998; Greve et al., 1997; and Goldman et al., 1996). However, the sample in each of these studies was significantly different (i.e., healthy, middle-aged adults, persons who have had strokes) from the current study. No WCST factor analytic studies with a sample of healthy older adults could be located through extensive literature reviews. It is possible that the WCST could be measuring slightly different constructs depending upon the sample of participants used, or that the WCST is more or less sensitive to the construct(s) measured, depending upon the sample. This is supported by Burgess et al.'s (1998) study of the ecological validity of tests of executive functioning that included the WCST. Study findings indicated that while the WCST was found to be one of the most highly sensitive measures of overall neuropsychological dysfunction, it was strongly related to behavioral characteristics defined as reflecting inhibition (response suppression problems, impulsivity, disinhibition) and executive memory (confabulation, temporal sequencing problems, perseveration).

While the word- and color-naming trials from the Stroop have been predominantly identified as measures of processing speed, because both were significantly related to the majority of prefrontal cortex measures and because they also require sustained attention ability, they were added to subsequent EFA's. During all subsequent EFA's, the added Stroop scores demonstrated strong factor loadings ($\geq .52$). When prefrontal cortex function variables were constrained to three factors, all three scores from the Stroop loaded together on a factor, independent of all other prefrontal cortex function variables. This factor was interpreted to represent a combination of processing speed and inhibitory control. When prefrontal cortex function variables were constrained to two factors, the WCST scores loaded independently on one factor and all three Stroop scores loaded with the remaining prefrontal cortex function variables (PASAT, TMTb, and SDMT). This latter factor was interpreted to represent a construct comprised of interference control, sustained attention, processing speed, inhibitory control, and mental flexibility.

Notably, although both the RUFF and Vfluency have been associated with prefrontal cortex function (Gourovitch et al., 2000; Parks et al., 1988; Jason, 1985) and were related to the majority of prefrontal cortex function measures in this study, they demonstrated weak factor loadings during EFA's. Thus, both were eliminated from further EFA's. Burgess et al. (1998) found that verbal fluency was highly insensitive to general neurological pathology and executive functioning in sample of both mixed etiology neurological patients and normal, age-matched controls. It is possible that either RUFF and Vfluency were not sensitive enough measures of the constructs identified in this study or that each measured a separate but related prefrontal cortex function construct from the remaining tests in this study.

The final two- and three-factor models of prefrontal cortex function generated both included a factor comprised of all three WCST measures that was labeled working memory. This is consistent with West's (1996) theory, as well as with previously cited factor analytic studies of prefrontal cortex function measures. However, the remaining factors generated in both the two- and three-factor models did not directly fit the remaining secondary processes of prefrontal cortex function, as proposed by West. In the three-factor model, the factor comprised of all three Stroop scores appears to represent a combined measure of processing speed and inhibitory control. The remaining factor is comprised of measures of sustained attention, interference control, processing speed, and mental flexibility. In the two-factor solution, the final factor is a combination of measures of sustained attention, processing speed, inhibitory and interference control, and mental flexibility. These results are generally consistent with other factor analytic studies of tests identified as prefrontal cortex function measures. Boone et al. (1998) conducted a factor analytic study including WCST, Vfluency, Stroop, DSp, a sustained attention test similar to the PASAT, and a test nearly identical to SDMT on data collected from a sample consisting of patients referred for neuropsychological testing and healthy volunteers (mean age = 56.0; mean education = 14.0 years). Results yielded a three-factor solution. One factor contained all WCST scores, the second was comprised of Vfluency, all Stroop scores, and SDMT, and the final factor contained DSp, the sustained attention test, IQ, and memory retention scores. A factor analytic study of the PASAT, WCST, TMTb, a visual attention test, and a test similar to the WCST conducted on a sample of persons referred for rehabilitation services at a state agency (mean age = 30.2; mean education = 12.4) yielded two factors (O'Donnell et al., 1994). The first factor included PASAT, TMTb, and the visual attention test and the second factor was comprised of WCST and the test similar to the WCST. A factor analytic study of numerous attention tests conducted on a sample of outpatients referred for neuropsychological evaluation (mean age = 34.9; mean education = 12.9) that included PASAT, TMT, DSp, VMSp, and Stroop found that all of these tests loaded on the same factor (Schmidt et al., 1994). Notably, in all of these studies, participants were significantly younger and less educated than persons in this study. Additionally, most participants in these studies were referred for neuropsychological testing because of some identified neurologic problem. Nonetheless, results from these studies are similar to current study findings. This suggests that regardless of the age, level of education, and type of impairment a person may have, the tests of prefrontal cortex function utilized in this study appear to be related in a manner reflecting a working memory factor and an attentional/processing speed factor. This is consistent with the two-factor model of prefrontal cortex functioning being a better fit for this data set (as well as possibly other data sets). It is possible that the attention/processing speed factor may be a general measure of a person's inhibitory and interference control and that current prefrontal cortex function measures are not sensitive enough to discern these underlying constructs.

Measurement of Prefrontal Cortex Function with Neuropsychological Tests

The neuropsychological tests used in this study to measure prefrontal cortex functioning are some of the most popular and widely researched and used instruments to assess frontal or executive functioning. These tests are proposed to be selectively sensitive to frontal lobe dysfunction. However, there are problems with both the sensitivity and specificity of these tests as indicators of prefrontal cortex dysfunction (Phillips & Della Sala, 1999; Phillips, 1997; Reitan & Wolfson, 1994). In addition to measuring prefrontal cortex function, performance on these tests may also be affected by lesions/impairment elsewhere in the brain, in part, because of the extensive connections between the frontal lobes and other cortical and subcortical areas. Some studies have demonstrated that persons with frontal lobe lesions and persons with extensive frontal lobe damage who have demonstrated problems in managing their daily lives perform well on numerous tests of frontal functioning (Anderson et al., 1991; Shallice and Burgess, 1991). Furthermore, some studies have demonstrated insignificant correlations between tests of frontal functioning and behavioral problems commonly presented by persons with frontal lobe lesions (Burgess et al., 1998; Baddeley et al., 1997; Alderman, 1996). However, all of these studies demonstrating weak or a lack of a significant relationship between frontal lobe lesions/damage, behavior, and performance deficits on tests purported to measure frontal functioning were conducted on persons with identified, significant frontal cortex damage through neuroimaging studies. Even though numerous neuroimaging studies of older adults have demonstrated neurological changes in the prefrontal cortex, these changes are usually described as being less severe than the acquired brain lesions/damage that result from cerebral vascular disease or other head trauama. Presumably, the effects of age-associated prefrontal cortex neurological changes would be less than those evidenced by more severely neurologically impaired persons. This suggests that the specific measurement of prefrontal cortex dysfunction in older adults by identified tests of frontal lobe functioning is an even more difficult endeavor.

Additionally, as was the case in this study, age differentially relates to and effects performance on various measures of frontal lobe functioning (Phillips & Della Sala, 1999; Moscovitch & Winocur, 1995; Shimamura, 1994). While some prefrontal cortex function measures in this study were not significantly related to age (Vfluency, DSp, perseverative errors on CVLT and RUFF, Stroop word naming trial, CVLT proactive interference score) others were very strongly related ($p \geq .40$; TMTa, SDMT, Stroop color- and color-word naming trials, and WCSTnp).

Furthermore, numerous studies have demonstrated that there is a significant amount of shared variance between tests of prefrontal cortex function (Robbins et al., 1998; Fisk & Warr, 1996; Salthouse et al., 1996; Salthouse 1992). The majority of these studies have shown that controlling for the effects of processing speed eliminates a significant proportion of the age effects on performance on tests of prefrontal cortex or executive functioning. This may be an explanation for the EFA results in this study. Specifically, the final two-factor solution of prefrontal cortex function in this study contains one factor comprised of WCST scores that do not involve a time constraint and thus are most likely not related to processing speed. The remaining factor is comprised of numerous tests that are all dependent, to some degree, on processing speed. Thus, it provides a measure of how quickly a person can process information while sustaining their attention, shifting mental sets, and inhibiting prepotent responses.

Relationship Between Measured Cognitive Functions and Neuroanatomical Substrates

The aging brain loses weight, volume, and neurons and experiences an increased number of pathological structures and changes in neurochemistry. These changes have been demonstrated to be disproportionally greater in the prefrontal cortex when compared to other areas of the brain in post-mortum and neuroimaging studies (Fabiani, Friedman, & Cheng, 1998; Raglund et al., 1997; Haug & Eggers, 1991; Gur et al., 1987; Squire, 1987; Gerard & Weisberg, 1986; Strubel et al., 1985; Shaw et al., 1984; Scheibel et al., 1975). However, some findings have been less conclusive and have indicated that other brain regions demonstrate similar or even greater deterioration that the prefrontal cortex (Coffey et al., 1992; Giaquinto, 1988; de Leon et al., 1984). In her critical review of the frontal aging hypothesis, Greenwood (2000) concluded that while there were clear effects of aging on brain structure and physiology which may underlie the altered patterns seen in blood flow and metabolism during task performance, the evidence that prefrontal areas are more vulnerable than other brain regions to these aging effects is weak.

Others have emphasized that the changes in cognition with advancing age that have been largely attributed to a decline in frontal lobe function cannot exclude the role that the frontal-striatal and frontal-temporal-parietal circuits play in promoting cognitive function. For example, Rubin (1999) demonstrated, through a neuroimaging study, that the decrease in the size of the caudate is proportional to that of the prefrontal cortex and that this volume change is accompanied by declines in inhibitory processes, executive control, and cognitive speed similar to that demonstrated in normal aging. Schumacher et al.'s (1996) PET study investigating performance on a verbal working memory task consistently demonstrated overlapping activation of the dorsolateral prefrontal cortex, Broca's area, bilateral superior and posterior parietal cortices, anterior cingulate, and right cerebellum. Thus, in addition to measuring prefrontal cortex function, performance on tests purported to measure prefrontal cortex function such as those used in this study are most likely also affected by lesions/impairment elsewhere in the brain, in part, because of the extensive connections between the frontal lobes and other cortical and subcortical areas.

The frontal lobes have been described as an executive for the rest of the brain and have thus been referred to by many as the central executive. Parkin (1998) has argued that the central executive does not exist. Specifically, he has stated that there is no localization evidence, based on his review of neuroradiological and neuropsychological studies, for a central executive and that tests identified as measuring executive function should do so in a "qualitative way" rather than assuming that a range of specific tests represent a unitary construct. Greenwood's (2000) conclusion is similar in her critical review of West's (1996) prefrontal cortex theory of cognitive aging. She stated that while the frontal lobes are subject to age-related changes reflected in both behavior and pathology, evidence for a prefrontal cortex function theory of cognitive aging is both weak and conflicting. She argues that a network-based theory of cognitive aging spanning more that one area of the brain is more appropriate. This is consistent with one of Salthouse et al.'s (1996) conclusions that the source of the shared variance in different cognitive measures purported to measure frontal functioning is not discrete and localized, but instead corresponds to anatomical and/or physiological characteristics distributed across many regions of the brain.

However, both West (2000) and Baddeley (1998) have argued in response to both Parkin and Greenwood that significant and sufficient evidence exists to demonstrate that the prefrontal cortex/central executive plays a substantial role in cognitive aging. Both acknowledge that the prefrontal cortex/central executive does not exclusively and unitarily control the aging process or the effects of cognitive aging as demonstrated by current neuropsychological measures. Baddeley (1998) argues that the central executive exists as a "concept" that provides a useful basis for studying the complexities of executive control and identifying subprocesses that may then be mapped on to their anatomical substrate(s).

The theoretical debate about the accuracy and applicability of the prefrontal cortex function theory to cognitive aging contributes to increased difficulties in validity of measurement of prefrontal cortex functions. While some neuropsychological tests such as those employed in this study may not be able to be definitively identified as measures of specific prefrontal cortex functions because of the aforementioned issues, a review of more recent neuroimaging studies with many of the measures in this study demonstrates a significant, strong trend towards prefrontal cortex involvement. Additionally, one of the ways to interpret the large amount of shared variance between tests purported to measure frontal functioning is that all of these measures may be dependent upon the integrity of a single neuroanatomical structure or system. The prefrontal cortex circuits (i.e., prefrontal-striatal and prefrontal-parietal circuits) may be the best candidate currently for this single structure or system.

In conclusion, the neuropsychological tests used in this study to measure prefrontal cortex function most likely do not reflect functioning in discrete and independent structures, nor are the age-related effects on them exclusively determined by distinct and unique sets of influences. However, this does not necessarily mean that some level of specificity and localization could not exist. Many of the prefrontal cortex meausures in this study that have been shown, through functional MRI studies, to be related to specific, increased activity in the prefrontal cortex were found to be strongly related. Furthermore, when combined with study findings demonstrating that prefrontal cortex function strongly mediated the relationship between aging and poorer verbal memory performance, results from this study are believed to support West's and Baddeley's belief that the prefrontal cortex/central executive plays a substantial role in cognitive aging. Functional MRI studies with healthy older adults that allow for the elimination of the contributions of other areas of the brain to performance on the prefrontal cortex function tests used in this study would provide further insight as to the localizability of such measures.

Sample Characteristics

The older adults in this study comprised a unique sample of highly educated, non-depressed, independently living individuals. Education has been proposed to provide protection against both normal and pathological aging processes (Stern et al., 1994; Katzman, 1993; Mortiner, 1988). Capitani, Barbarotto, and Laicana (1996) proposed that three different patterns of association could be expected between age-related decline and education: 1) parallelism: age-related decline runs the same course in different educational groups, so that no interaction is observed; 2) protection: age-related decline is attenuated in well-educated participants; and 3) confluence: the initial advantage of well-educated participants in middle age is reduced in later life. Several studies have demonstrated a strong association between educational level and performance on various neuropsychological tests (Ardila, Ostrosky-Solis, Rosselli, and Gomez, 2000; Ardila, Rosselli, & Ostrosky, 1992; and Heaton, Grant, & Mathews, 1986). Given these findings, it could be assumed that the high level of education in the current sample, coupled with the fact that many of the participants were retired university faculty and thus were more familiar (and perhaps comfortable) with the use of testing/evaluations, would have significantly attenuated findings. Interestingly, the data do not appear to directly support this assumption. Only three measures of prefrontal cortex function were significantly positively associated with education and none of these measures were included in the final measurement model of prefrontal cortex function. One of these measures, Digit Span total score, had been previously shown to be associated with education (Ryan, Lopez, & Paolo, 1996 and Powell &Whitla, 1994). However, a number of studies support current findings that performance on measures of prefrontal cortex function may be minimally affected by level of education in studies with older adults. In particular, Lowe and Reynolds (1999) found that education was significantly negatively related only to the number of random responses made on a test of verbal set-shifting and rule-induction similar to the WCST. Christensen, Korten, Jorm, and Henderson (1997) found that education has also been shown to be unrelated to processing speed, verbal memory, and reaction time in older adults. In contrast, Ardilla et al. (2000) found that while education had a protective influence on a test measuring phonemic fluency, it had a confluent influence Digit Span-backwards scores. However, in this study, the mean level of education for the most highly educated group of adults ages 66 to 85 was 13.5 years, substantially lower than that of the current sample. However, in a sample of older adults with a minimum of 16 years of education, Powell and Whitla (1994) found that education was significantly positively related to performance on tests of auditory attention and verbal and non-verbal reasoning.

Notably in the Powell and Whitla (1994) study, the cognitive benefit of education was strongest for women, especially on tests of reasoning. Since it was highly unusual for women to attain advanced degrees in the 1940's , it is likely that highly educated women, like those in this study, may have been brighter, more highly motivated, and/or came from homes that strongly valued intellectual activities. However, very few significant differences were found between the performance of men and women on tests of prefrontal cortex function in this study. Despite the fact that the level of education was not significantly different for men and women in this study, males performed significantly better on the PASAT, completed more designs on the RUFF, and made fewer perseverative errors on the CVLT. However, males made more non-perseverative errors on the WCST. Overall, gender and level of education appeared to have had a minimal impact on the final results of this study.

Depression has been demonstrated to have a negative effect on memory skills, attention, verbal fluency, processing speed, and performance on tasks similar to the WCST (King, Cox, Lyness, & Caine, 1995; LaRue, 1992; Rubin et al., 1991; and Emery & Breslau, 1989). However, other studies have failed to replicate these findings (Boone et al., 1995 and Abas et al., 1990). Although the mean score on the depression measure (GDS) for this sample was well below the cut-off suggestive of significant depressive symptomatology, scores on the GDS were significantly negatively related to a number of measures of prefrontal cortex functioning, including four measures used in the final measurement model (PASAT, TMTb, WCST perseverative errors, and the Stroop color-word naming trial). This finding has significant treatment and research implications. First, it suggests that participants in this study, who were highly educated and functioned independently, may be more sensitive to and thus more affected by even minimal levels of depressive symptomatology. Professionals working with these individuals would therefore need to be more alert to even subtle observed or reported changes in mood, as this could have a significant, negative effect on cognitive functioning. Second, it suggests that research investigating the effects of level of depression on cognitive functioning in older adults that classifies participants as "depressed" or "non-depressed" may be overlooking subtle but significant differences within classified groups that could have a major impact upon cognitive and psychosocial functioning.

The Mediating Role of Prefrontal Cortex Function

The second hypothesis, that prefrontal cortex function mediates the relationship between age and verbal memory performance, was strongly supported. The direct effect of age on verbal memory performance became insignificant when the indirect effect of prefrontal cortex function, as represented by working memory and interference control, was considered. In fact, the direct effect of age on verbal memory performance became almost negligible (standardardized coefficient = .07), indicating that prefrontal cortex function accounted for nearly all of the decline in verbal memory performance with advancing age in this sample of healthy, independently living older adults. While the direct effects model evaluating the relationship between age and verbal memory performance was the weakest of the three models evaluated, the direct, significant relationship between increasing age and poorer verbal memory performance had already been previously demonstrated through correlational analyses.

These results are consistent with both neuroimaging and neuropsychological studies demonstrating relationships between age, prefrontal cortex functioning, and verbal memory. Shallice et al. (1994) demonstrated that verbal episodic memory involves a network of specific prefrontal and posterior structures in healthy middle-aged adults. Petrides, Alivisatos, and Evans' (1995) functional MRI study of healthy young adults found that the mid-ventrolateral frontal cortex was directly involved in active retrieval mechanisms during a verbal memory task and the mid-dorsolateral frontal region participated in free recall, which they concluded was a result of working memory requirements during the verbal memory task. In Stuss et al.'s (1994) study examining organizational strategies of patients with unilateral or bilateral frontal lobe injuries on a word list learning task, all patients with frontal lesions demonstrated impaired verbal recall due to poor higher order organization of learning. In particular, those patients with right frontal lesions demonstrated excess intralist repetitions/perseverations. Parkin and Walter (1991) examined the relationship between age, short-term memory, and frontal dysfunction and found that age-related differences on a verbal memory task reflected a deficit in initial acquisition and a retrieval deficit stemming from the frontal atrophy known to be associated with normal aging. In a conditional associative learning (CAL) study that compared the performances of patients with frontal lobe lesions to healthy older adults, both groups demonstrated impaired CAL performance, but the deficit was greater in the former group where it was specific to patients with dorsolateral prefrontal cortex lesions (Levine, Stuss, & Milberg, 1997). The authors concluded that the congruence between older adults and frontal lobe patients suggested that age-related decline in inhibitory processes is due to dorsolateral prefrontal cortex dysfunction. Current study results support this conclusion. Reuter-Lorenz (2000) studied PET activation patterns of younger and older adults during both letter identity and spatial location memory tasks. Younger adults showed left-sided frontal activation for the letter identity task and right-sided frontal activation for the spatial location task, whereas older adults showed bilateral frontal activation for both tasks. These results were interpreted to suggest that the greater demands on storage and maintenance in older adults or an increased need to elaborate stimulus representations that have been less well-encoded lead to bilateral frontal activation. Another possibility is that prefrontal/executive processes are selectively impaired in older adults and that the effort to recruit all available prefrontal cortical resources results in increased activation of prefrontal areas in older but not younger adults.

The current mediating model of prefrontal cortex function indicates a strong, direct relationship between age and interference control, which then indirectly, significantly affects verbal memory performance. Thus, decline in verbal memory performance is a result of declining sustained attention, processing speed, interference and inhibitory control skills, which are negatively influenced by advancing age. This same indirect relationship was not demonstrated with working memory. While working memory had a significant, indirect effect on verbal memory performance, its role as a mediator between age and verbal memory performance was significantly influenced by interference control. This indicates that for the older adults in this study, the negative effect of advancing age did not have a significant direct effect on working memory skills. Rather, advancing age significantly negatively influenced interference control skills that then significantly affected working memory performance, leading to a decline in verbal recall. Theoretically, this is consistent with West's (1996) theory. Task irrelevant information needs to be cleared from working memory stores (interference control) and an action sequence must be prevented from becoming influenced by a dominant internal response pattern (inhibition of prepotent responses) in order for working memory skills to be optimized. Interpretation with the current measurement model suggests that attention must be sustained, information must be processed quickly, interfering information must be controlled, and previously rewarded internal response patterns must be inhibited in order to be able optimize working memory ability. Once this occurs, working memory performance then mediates the relationship between age and verbal memory performance.

Consistent with this interpretation of current study findings, Chao and Knight (1997) found that the percentage of perseverative errors and overall performance on the WCST were positively correlated with measures of distractibility and sustained attention during a event-related potential study using an auditory delayed match-to-sample task comparing the performances of younger and older adults. Additional support for the aforementioned interpretation of current study findings is found in the expanding body of research implicating the significant role of processing speed in the relationship between age and performance on neuropsychological measures. Measures of executive functioning were found to be less important in accounting for age differences between younger and older adults on a verbal associative learning task than measures of the learners' perceptual speed (Fisk & Warr, 1998). These same researchers (1996) demonstrated age differences in central executive functioning are primarily attributable to a decline in the rate at which information is activated within the working memory system. In a study examining the effect of fluid intelligence and processing speed on performance of frontal lobe function measures, Parkin and Java (1999) concluded that a large proportion of the age-related variance on measures of frontal lobe function may be attributable to a more general factor characterized jointly by fluid intelligence and processing speed. Salthouse has demonstrated, in a number of studies, that slower processing speed mediates the relationship between age, performance on executive measures, and memory (Fristoe, Salthouse, & Woodard, 1997; Salthouse et al., 1996; Salthouse, 1994).

While all of these studies demonstrate that speed of information processing plays a significant role in the relationship between age and performance on both prefrontal cortex function and memory measures, closer examination of the tests used to assess processing speed and prefrontal cortex/executive functioning raises questions as to the definitiveness of some of the conclusions. Many of the measures of processing speed used in the aforementioned studies have been labeled by others (including this author) as tests of prefrontal cortex/executive functioning and nearly all measures require sustained attention ability. For example, the Digit Symbol test from the WAIS-III (Wechsler, 1999), which is nearly identical to the Symbol Digit Modalities Test used in this study, was employed as a measure of processing speed in many of the aforementioned studies (Parkin & Java, 1999; Salthouse, 1994; Fristoe et al, 1997). Performance on this test is not only dependent on processing speed, it also requires sustained attention and working memory skills. In the

Fisk and Warr (1996) study only one measure of working memory span and one measure of executive functioning were used, neither of which were standardized neuropsychological tests. Finally, one of the measures of frontal lobe function, category fluency, that Parkin and Jave (1999) employed has been consistently shown in neuroimaging studies to be weakly or unrelated to prefrontal cortex involvement.

In conclusion, while these measurement issues do not negate the consistent findings that processing speed plays a significant role in the relationship between age, prefrontal cortex function, and memory performance, it is apparent that these studies are also plagued by the issue of difficulty in specifically and selectively identifying and measuring cognitive processes. Salthouse et al. (1996) acknowledge that neuroanatomical and neurophysiological factors responsible for the age-related reduction in processing speed still need to be identified and that speed of information processing plays an important, although not exclusive, role in cognitive aging. Notably, because many of the measures in this study have been found to share a proportion of their age-related variance with other measures, including those related to processing speed, it is likely that the age-related influences on current prefrontal cortex function measures are not independent. However, the use of structural equation modeling to investigate the second hypothesis in this study allowed the investigation of both the common and specific age-related influences that contributed to the relationship between age, performance on prefrontal cortex function measures, and verbal memory. Nonetheless, a consistent theme apparent in current study findings and those summarized above is that processing speed, sustained attention, and the ability to control interfering stimuli play a critical role in verbal memory performance and are negatively influenced by advancing age.

Theoretical Considerations and Future Directions

The results of this study partially supported West's (1996) prefrontal cortex function theory of cognitive aging by demonstrating that prefrontal cortex function strongly mediated the relationship between advancing age and declining verbal memory performance. However, the measurement model of prefrontal cortex function generated from this data set did not support the underlying secondary processes of prefrontal cortex function that West outlined. Instead, it suggested that a factor representing measures of sustained attention, interference control, processing speed, and mental flexibility and a working memory factor provided the best representation of prefrontal cortex or executive function for this sample. While this model still appears consistent with, although less specific than, the model that West (1996) proposed, a brief review of alternative theoretical considerations is warranted.

In Greenwood's (2000) critical evaluation of the prefrontal cortex function theory of cognitive aging, she concludes that there is only "weak and conflicting evidence that frontal regions are selectively and differentially affect by aging" (pp. 705). She suggests that a better approach to conceptualizing the complex effects of aging on cognition is to consider the effects of aging on the integrity of a processing network that involves more than the frontal lobes. Mesulam (1998) has proposed a model of brain organization based on "transmodal areas". These transmodal areas work in combination with primary sensory areas and are divided into five networks, one of which is a "working memory-executive function" network. Greenwood (2000) suggests that Mesulam's theory, in combination with a myelin-based theory of brain aging (which proposes that age-related changes in cognition are the result of deterioration in axonal myelination), could account for much of the evidence on which the frontal aging hypothesis is based. Specifically, processing networks more highly dependent on corticocortical connections, such as the working memory-executive function network, would be increasingly vulnerable to the effects of demyelination with advancing age. Interestingly, this theory does not appear to significantly depart from West's (1996) theory in its emphasis on neurophysiology and prefrontal cortex function. Greenwood's suggested theory emphasized networks as opposed to a specific area/lobe of the brain.

Baddeley (1998) has also suggested this as a more appropriate way to view the role of the prefrontal cortex in cognitive aging. He has proposed that the frontal lobes represent a large and multi-faceted area of the brain which is unlikely to be unitary in function and that is best described as a "central executive" system. Executive processes are likely to involve links between different parts of the brain and hence are unlikely to be exclusively associated with the frontal lobes. Consequently, persons without clear evidence of frontal damage may conceivably have executive deficits, such as those demonstrated with advancing age. Thus, the central executive provides a useful basis for studying the complexities of executive control and identifying subprocesses, which may then be mapped onto their neuroanatomical substrates (Baddeley, 1998).

While current study results strongly supported the mediating role of prefrontal cortex/executive function in the relationship between declining verbal memory performance with advancing age, the underlying processes comprising prefrontal cortex function were somewhat inconsistent with West's (1996) theory. It is possible that with larger sample size, a broader range of education among participants, and additional, more sensitive measures of prefrontal cortex function (such as those previously mentioned), results may have been improved. Furthermore, inclusion of ecologically valid rating scales to be completed by participants and family members (requesting ratings about demonstrated behaviors consistent with prefrontal cortex/executive dysfunction), in combination with the use of functional MRI procedures, would have provided the most comprehensive and accurate way to evaluate the hypotheses in this study.

APPENDIX A

APPENDIX A

Table A-1: Correlations Between Demographic and Prefrontal Cortex Functioning Variables

	Age	Education
PASAT	-.38**	.15
RFFTdes	-.24**	.27**
RFFTper	-.13	.01
STROOPw	-.13	.16
STROOPc	-.45**	-.05
STROOPcw	-.48**	.19
TMTa	.53**	.16
TMTb	.35**	-.09
DSptot	-.17	.20*
VMSptot	-.29**	.08
WCSTcat	-.29**	-.06
WCSTper	.34**	-.02
WCSTnp	.42**	.15
SDMT	-.51**	.07
CVLTpi	-.06	.08
CVLTper	-.08	.25**
Vfluency	-.06	.18

N = 109; * $p < .05$, ** $p < .01$. PASAT = Paced Auditory Serial Addition Test raw score; RFFTdes = Ruff Figural Fluency Test total designs; RFFTper = Ruff Figural Fluency Test total perseverations; STROOPw = Stroop Color-Word Test raw score – word naming trial; STROOPc = Stroop Color-Word Test raw score – color naming trial; STROOPcw = Stroop Color-Word Test raw score – color-word naming trial; TMTa = Trailmaking Test Part A total seconds; TMTb = Trailmaking Test Part B total seconds; Dsptot = Digit Span total score; VMSptot = Visual Memory Span total score; WCSTcat = Wisconsin Card Sorting Test total categories achieved; WCSTper = Wisconsin Card Sorting Test perseverative errors; WCSTnp = Wisconsin Card Sorting Test non-perseverative errors; SDMT = Symbol Digit Modalities Test total score; CVLTpi = California Verbal Learning Test proactive interference score; CVLTper = California Verbal Learning Test total perseverative errors; Vfluency = COWAT total score.

APPENDIX B

APPENDIX B

Table A-2: Relationship Between Gender and Prefrontal Cortex Functioning Variables

	Sum of Squares	F	P
PASAT	11745.88	5.70	.02* (males perform better)
RFFTdes	2085.04	4.60	.03* (males perform better)
RFFTper	286.39	1.62	.21
STROOPw	321.88	1.32	.25
STROOPc	198.41	1.39	.24
STROOPcw	6.86	6.86	.79
TMTa	338.68	2.07	.15
TMTb	1993.78	0.95	.33
Dsptot	31.02	2.36	.13
VMSptot	6.23	0.80	.37
WCSTcat	7.43	2.63	.11
WCSTper	138.54	1.20	.28
WCSTnp	1085.15	11.0	.00** (males make more NPE's)
SDMT	32.29	0.37	.54
CVLTpi	4.09	1.34	.25
CVLTper	89.17	5.45	.02* (males make fewer errors)
Vfluency	15.69	.13	.72

N = 102; df = 100; * $p < .05$, ** $p < .01$. PASAT = Paced Auditory Serial Addition Test raw score; RFFTdes = Ruff Figural Fluency Test total designs; RFFTper = Ruff Figural Fluency Test total perseverations; STROOPw = Stroop Color-Word Test raw score – word naming trial; STROOPc = Stroop Color-Word Test raw score – color naming trial; STROOPcw = Stroop Color-Word Test raw score – color-word naming trial; TMTa = Trailmaking Test Part A total seconds; TMTb = Trailmaking Test Part B total seconds; Dsptot = Digit Span total score; VMSptot = Visual Memory Span total score; WCSTcat = Wisconsin Card Sorting Test total categories achieved; WCSTper = Wisconsin Card Sorting Test perseverative errors; SDMT = Symbol Digit Modalities Test total score; PI = California Verbal Learning Test proactive interference score; CVLTper = California Verbal Learning Test total perseverative errors; Vfluency = COWAT total score.

APPENDIX C

APPENDIX C

Table A-3: Significant Pearson Product-Moment Coefficients for Depression and Prefrontal Cortex Functioning Measures

	PASAT	TMTa	TMTb	VMSp	WCSTper	Stroopcw	RFFTdes
GDS	-.20*	.23*	.32**	-.21*	.23*	-.25*	-.33**

N = 102; * p < .05, ** p < .01. GDS total = Geriatric Depression Scale total score; PASAT = Paced Serial Auditory Addition Test, total score; TMTa = Trailmaking Test Part A; TMTb = Trailmaking Test Part B; VMSp = Visual Memory Span total from the Wecshler Memory Scale-Revised; WCSTper = Wisconsin Card Sorting Test perseverative error score; Stroopcw = Stroop Color-Word Test – color-word naming trial; RFFTdes = Ruff Figural Fluency Test total designs.

APPENDIX D

APPENDIX D

Table A-4: Pearson Product Correlation Coefficients between Prefrontal Cortex Function Measures

	DSp	VMSp	PASAT	Vfluency	SDMT	TMTa	TMTb	CVLTper	CVLTpi
DSp	1.00								.04
VMSp	.38**	1.00							.08
PASAT	.44**	.41**	1.00						-.02
SDMT	.30**	.44**	.58**	.25*	1.00				.08
TMTa	-.13	-.37**	-.41**	-.22*	-.60**	1.00			.03
TMTb	-.38**	-.43**	-.41**	-.23*	-.56**	.53**	1.00		-.17
CVLTper	.03	-.01	.02	.06	.08	-.13	-.09	1.00	-.15
Stroopw	.18	.12	.40**	.40**	.44**	-.26**	-.28**	-.05	-.11
Stroopc	.27**	.26**	.45**	.27**	.60**	- 45**	-.34**	-.01	-.11
Stroopcw	.35**	.37**	.53**	.39**	.60**	-.43**	-.53**	-.03	.05
WCSTcat	.07	.02	.16	.04	.27**	-.24*	-.25*	.22*	.04
WCSTper	-.13	-.05	-.28**	-.21*	-.36**	.25*	.34**	-.11	.04
WCSTnp	-.10	-.04	-.29**	-.05	-.33**	.33**	.21*	-.27**	-.03
RFFTdes	.37**	.32**	.52**	.26**	.51**	-.39**	-.47**	-.02	.01
RFFTper	-.09	.02	.00	.10	.16	-.12	-.14	-.04	.08
Vfluency	.25*	.08	.37**	1.00	.25*	-.22*	-.23*	.06	-.26**
	Stroopw	Stroopc	Stroopcw	WCSTcat	WCSTper	WCSTnp	RFFTdes		
Stroopw	1.00								
Stroopc	.60**	1.00							
Stroopcw	.47**	.66**	1.00						
WCSTcat	.10	.25*	.40**	1.00					
WCSTper	-.14	-.27**	-.44**	-.72**	1.00				
WCSTnp	-.01	-.32**	-.46**	-.76**	.71**	1.00			
RFFTdes	.27**	.36**	.46**	.19	-.25*	-.21*	1.00		
RFFTper	.12	.09	.01	.04	-.08	.01	.00	1.00	

$\underline{N} = 102$; * $\underline{p} < .05$, ** $\underline{p} < .01$. WCSTcat = Wisconsin Card Sorting Test total categories achieved; DSp = Digit Span total from the Wecshler Memory Scale-Revised (WMS-R); VMSp = Visual Memory Span total from the WMS-R; PASAT = Paced Auditory Serial Addition Test total raw score; SDMT = Symbol Digit Modalities Test; TMTa = Trailmaking Test Part A; TMTb = Trailmaking Test Part B; CVLTper = California Verbal Learning Test – total perseverative errors; CVLTpi = California Verbal Learning Test Proactive Interference Score; Stroopw = Stroop Color-Word Test, word naming trial raw score; Stroopc = Stroop Color-Word Test, color naming trial raw score; Stroopcw = Stroop Color-Word Test, color-word trial raw score; WCSTper = Wisconsin Card Sorting Test perseverative error score; WCSTnp = Wisconsin Card Sorting Test non-perseverative error score; RFFTdes = Ruff Figural Fluency Test total designs; RFFTper = Ruff Figural Fluency Test total perseverative errors; Vfluency = Verbal Fluency total score.

APPENDIX E

APPENDIX E

Table A-5: Pearson Product Correlations Between Prefrontal Cortex Function Variables and Verbal Memory Measures

	Lmtot	CVLTtot	CVLTsf	CVLTlf	CVLTrec
PASAT	.33**	.27**	.16	.17	.16
RUFFdes	.18	.21*	.15	.14	.05
RFFTper	.10	.02	.00	.12	-.04
TMTa	-.16	-.25*	-.14	-.17	-.01
TMTb	-.16	-.26**	-.18	-.17	-.06
SDMT	.35**	.32**	.24*	.21*	.02
DSptot	.30**	.20*	.16	.10	.12
VMSptot	.09	.15	.07	-.01	-.11
CVLTper	-.08	.32**	.19	.23*	-.01
CVLTpi	.17	.15	.16	.15	.02
Vfluency	.13	.14	.08	.07	.06
WCSTcat	.25*	.29**	.15	.21*	.15
WCSTper	-.28**	-.28**	-.15	-.19	-.18
WCSTnp	-.36**	-.45**	-.36**	-.41**	-.38**
Stroopw	.16	.12	.02	.06	.04
Stroopc	.18	.31**	.22*	.25*	.12
Stroopcw	.34**	.38**	.25*	.26**	.23*

N = 102, * $p < .05$, ** $p < .01$. LMtot = Logical Memory immediate memory total score; CVLTtot = California Verbal Learning Test total recall trials 1-5; CVLTsf = California Verbal Learning Test short delay free recall total; CVLTlf = California Verbal Learning Test long delay free recall total; CVLTrec = California Verbal Learning Test recognition trial total; PASAT = Paced Auditory Serial Addition Test raw score; RFFTdes = Ruff Figural Fluency Test total designs; RFFTper = Ruff Figural Fluency Test total perseverations; STROOPw = Stroop Color-Word Test raw score – word naming trial; STROOPc = Stroop Color-Word Test raw score – color naming trial; STROOPcw = Stroop Color-Word Test raw score – color-word naming trial; TMTa = Trailmaking Test Part A total seconds; TMTb = Trailmaking Test Part B total seconds; Dsptot = Digit Span total score; VMSptot = Visual Memory Span total score; WCSTcat = Wisconsin Card Sorting Test total categories achieved; WCSTper = Wisconsin Card Sorting Test perseverative errors; Wisconsin Card Sorting Test non-perseverative errors; SDMT = Symbol Digit Modalities Test total score; CVLTpi = California Verbal Learning Test proactive interference score; CVLTper = California Verbal Learning Test total perseverative errors; Vfluency = COWAT total score.

REFERENCES

Abas, M.A., Sahakian, B.J., & Levy, R. (1990). Neuropsychological deficits and CT scan changes in elderly depressives. Psycholgical Medicine, 20, 507-520.

Alderman, N. (1996). Central executive deficit and response to operant conditioning methods. Neuropsychological Rehabilitation, 6, 161-186.

Anderson, S.W., Damasio, A., Jones, R.D., & Tranel, D. (1991). Wisconsin Card Sorting Test performance as a measure of frontal lobe damage. Journal of Clinical and Experiemental Neuropsychology, 13, 909-922.

Arbuckle, J.L. & Wothke, W. (1999). Amos 4.0 user's guide. USA: Small Waters Corporation.

Ardila, A., Ostrosky-Solis, F., Rosselli, M., & Gomez, C. (2000). Age-related cognitive decline during normal aging: The complex effect of education. Archives of Clinical Neuropsychology, 15, 495-513.

Baddeley, A. (1998). The central executive: A concept and some misconceptions. Journal of the International Neuropsychological Society, 4, 523-526.

Baddeley, A., Della Sala, S., Papagno, C., Spinnler, H. (1997). Dual-task performance in dysexecutive and nondysexecutive patients with a frontal lesion. Neuropsychology, 11, 187-194.

Barch, D.M., Braver, T.S., Nystrom, L.E., Forman, S.D., Noll, D.C., & Cohen, J.D. (1997). Dissociating working memory from task difficulty in human prefrontal cortex. Neuropsychologia, 35, 1373-1380.

Benton, A.L. (1968). Differential behavioral effects in frontal lobe disease. Neuropsychologia, 6, 53-60.

Benton, A.L. & Hamsher, K. (1983). Multi-lingual Aphasia Examination. Iowa City: AJA Associates.

Boone, K.B., Lesser, I.M., Miller, B.L., Wohl, M., Berman, N., Lee, A., Palmer, B., and Back, C. (1995). Cognitive functioning in older depressed outpatients: Relationship of presence and severity of depression to neuropsychological test scores. Neuropsychology, 9, 390-398.

Boone, K.B., Ponton, M.O., Gorsuch, R.L., Gonzalez, J.J., & Miller, B.L. (1998). Factor analysis of four measures of prefrontal lobe functioning. Archives of Clinical Neuropsychology, 13, 585-595.

Bowden, S. & Bell, R. (1992). Relative usefulness of the WMS and WMS-R: A comment on D'Elia et al. (1989). Journal of Clinical and Experimental Neuropsychology, 14, 340-346.

Braver, T.S., Cohen, J.D., Nystrom, L.E., Jonides, J., Smith, E.E., Noll, D.C. (1997). A parametric study of prefrontal cortex involvement in human working memory. NeuroImage, 5, 49-62.

Brittain, J., LaMarche, J., Reeder, K., Roth, D., & Boll, T. (1991). Effects of age and IQ on paced Auditory Serial Addition Test (PASAT) performance. The Clinical Neuropsychologist, 5, 163-175.

Burgess, P.W., Alderman, N., Evans, J., Emslie, H., & Wilson, B.A. (1998). The ecological validity of tests of executive function. Journal of the International Neuropsychological Society, 4, 547-558.

Burgess, P.W. & Shallice, T. (1996). Response suppression, initiation and strategy use following frontal lobe lesions. Neuropsychologia, 34, 263-273.

Cabeza, R., Grady, C.L., Nybert, L., McIntosh, A.R., Tulving, E., Kapur, S., Jennings, J.M., Houle, S., & Craik, F.I.M. (1997). Age-related difference in neural activity during memory encoding and retrieval: A positron emission tomography study. Journal of Neuroscience, 17, 391-400.

Cabeza, R. & Nyberg, L. (1997). Imaging cognition: An empirical review of PET studies with normal subjects. Journal of Cognitive Neuroscience, 9, 1-26.

Capitani, E., Barbarotto, R., & Laicana, M. (1996). Does education influence age-related cognitive decline? A further inquiry. Developmental Neuropsychology, 12, 231-240.

Cattell, R.B. (1982). The psychomtry of objective motivation measurement: A response to the critique of Cooper and Kline. British Journal of Educational Psychology, 52, 234-241.

Chao, L.L. & Knight, R.T. (1997). Prefrontal deficits in attention and inhibitory control with aging. Cerebral Cortex, 7, 63-69.

Christensen, H., Korten, A.E., Jorm, A.F., & Henderson, A.S. (1997). Education and decline in cognitive performance: Compensatory but not protective. International Journal of Geriatric Psychiatry, 12, 323-330.

Comrey, A.L. & Lee, H.B. (1992). A first course in factor analysis. (2nd Ed.) Hillsdale, NJ: Erlbaum.

Craik F.I.M., Morris, L.W., Morris, R.G., & Loewen, E.R. (1990). Relations between source amnesia and frontal lobe functioning in older adults. Psychology and Aging, 5, 148-151.

de Leon, M.J., Ferris, S.H., George, A.E., Christman, D.R., Fowler, J.S., Gentes, C., Reisberg, B., Gee, B., Emmerich, M., Yonekura, Y., Brodie, J., Kricheff, I.I., & Wolf, A.P. (1983). Positron emission tomography studies of aging and Alzheimer's disease. American Journal of Neuroradiology, 4, 568-571.

de Leon, M.J., Ferris, S.H., George, A.E., Christman, D.R., Fowler, J.S., Gentes, C., Brodie, J., Reisberg, B., & Wolf, A.P (1984). Positron emission tomography and computed tomography: Assessment of the aging human brain. Journal of Computer Assisted Tomography, 8, 88-94.

Delis, D., Squire, L.R., Bihrle, A., & Massman, P. (1992). Componential analysis of problem-solving ability: Performance of patients with frontal lobe damage and amnesic patients on a new sorting test. Neuropsychologia, 30, 683-697.

Delis, D., Freeland, F., Kramer, J., & Kaplan, E. (1988). Integrating clinical assessment with cognitive neuroscience: Construct validation of the California Verbal Learning Test. Journal of Consulting and Clinical Psychology, 56, 123-130.

Delis, D., Kramer, J., Kaplan, E., & Ober, B. (1984). California Verbal Learning Test Manual. San Antonio: Harcourt Brace Jovanovich.

Denckla, M.B. & Reiss, A.L. (1997). Pre-frontal-subcortical circuits in developmental disorders. In N.A. Krasnegor, G. R. Lyon, & P.S. Goldman-Rakic (Eds.), Development of the Prefrontal Cortex: Evolution, Neurobiology, and Behavior (pp. 283-294). Baltimore: Paul H. Brooks Publishing Company.

Dobbs, A.R., Aubry, J.B., & Rule, B.G. (1989). Age-associated release from proactive interference: A review. Canadian Psychology, 30, 588-595.

Dobbs, A.R. & Rule, B.G. (1989). Adult age difference in working memory. Psychology and Aging, 4, 500-503.

Drebing, C.E., Van Gorp, W.G., Stuck, A.E., Mitrushina, M., & Beck, J. (1994). Early detection of cognitive decline in higher cognitively functioning older adults: Sensitivity and specificity of a neuropsychological screening battery. Neuropsychology, 8, 31-37.

Drewe, E. (1974). The effect of type and are of brain lesion on Wisconsin Card Sorting test performance. Cortex, 10, 159-170.

Dulaney, C.L. & Rogers, W.A. (1994). Mechanisms underlying reduction in Stroop interference with practice for young and old adults. Journal of Experimental Psychology: Learning, Memory, and Cognition, 20, 470-484.

Duncan, J. (1995). Attention, intelligence, and the frontal lobes. In M.S. Gazzaniga (Ed.), The Cognitive Neurosciences. Massachusetts: MIT Press.

Egan, V. (1988). PASAT: Observed correlations with IQ. Personality and Individual Differences, 9, 179-180.

Einstein, G.O., Holland, L.J., McDaniel, M.A., & Guynn, M.J. (1992). Age-related deficits in prospective memory: The influence of task complexity. Psychology and Aging, 7, 471-478.

Emery, O.B. & Breslau, L.D. (1989). Language deficits in depression: Comparisons with SDAT and normal aging. Journal of Gerontology, 44, 85-92.

Eslinger, P.J. & Grattan, L.M. (1993). Frontal lobe and frontal-striatal substrates for different forms of human cognitive flexibility. Neuropsychologia, 31, 17-28.

Fabiani, M., Friedman, D., & Cheng, J.C. (1998). Individual differences in P3 scalp distribution in older adults and their relationship to frontal lobe function. Psychophysiology, 35, 698-708.

Fisk, J.E. & Warr, P. (1996). Age and working memory: The role of perceptual speed, the central executive, and the phonological loop. Psychology and Aging, 11, 316-323.

Folstein, M., Folstein, S., & McHugh, P. (1975). "Mini-Mental State": A practical method for grading the cognitive state of patients for the clinician. Journal of Psychiatric Research, 12, 189-198.

Fristoe, N.M., Salthouse, T.A., & Woodard, J.L. (1997). Examination of age-related deficits on the Wisconsin Card Sorting Test. Neuropsychology, 11, 428-436.

Fuster, J.K. (1980). The Prefrontal Cortex: Anatomy, Physiology, and Neuropsychology of the Frontal Lobes. New York: Raven Press.

Fuster, J.K. (1989). The Prefrontal Cortex. New York: Raven Press.

Gerard G & Weisberg, L. (1986). MRI periventricular lesions in adults. Neurology, 36, 998-1001.

Giaquinto, S. (1988). Aging and the Nervous System. New York: John Wiley & Sons, Ltd.

Gourovitch, M.L.,Kirkby, B.S., Goldberg, T.E., Weinberger, D.R., Gold, J.M., Esposito, G., VanHorn, J., & Berman, K.F. (2000). A comparison of rCBF patterns during letter and semantic fluency. Neuropsychology, 14, 353-360.

Grady, C.L., Maisog, J.M., Horwitz, B., Ungerleider, L.G., Mentis, M.J., Salerno, J.A., Pietrini, P., Wagner, E., & Haxby, J.V. (1994). Age-related changes in cortical blood flow activation during visual processing of faces and location. Journal of Neuroscience, 14, 1450-1462.

Grady, C.L., McIntosh, A.R., Horwitz, B., Maisog, J.M., Ungerleider, L.G., Mentis, M.J., Pietrini, P., Schapiro, M.B., & Haxby, J.V. (1995). Age-related reductions in human recognition memory due to impaired encoding. Science, 269, 218-221.

Greenwood, P.M. (2000). The frontal aging hypothesis is evaluated. Journal of the International Neuropsychological Society, 6, 705-726.

Greve, K.W., Bianchini, K.J., Hartley, S.M., & Adams, D. (1999). The Wisconsin Card Sorting Test in stroke rehabilitation: Factor structure and relationship to outcome. Archives of Clinical Neuropsychology, 14, 497-509.

Greve, K.W., Brooks, J., Crouch, J.A., Williams, M.C., & Rice, W.J. (1997). Factorial structure of the Wisconsin Card Sorting Test. British Journal of Clinical Psychology, 36, 283-285.

Greve, K.W., Ingram, F., & Bianchini, K.J. (1998). Latent structure of the Wisconsin Card Sorting Test in a clinical sample. Archives of Clinical Neuropsychology, 13, 597-609.

Greve, K.W., Williams, M.C., Hassa, W.G., Littell, R.R., & Reinoso, C. (1996). The role of attention in Wisconsin Card Sorting Test performance. Archives of Clinical Neuropsychology, 11, 215-222.

Gronwall, D. & Sampson, H. (1974). The Psychological Effects of Concussion. Auckland: Auckland University Press.

Gronwall, D. & Wrightson, P. (1974). Delayed recovery of intellectual function after minor head injury. Lancet, 2, 605-609.

Goldberg, E. & Bilder, R.M. (1987). The frontal lobes and hierarchical organization of cognitive control. In E. Perecman (Ed.), The Frontal Lobes Revisited (pp. 159-187). New York: The IRBN Press.

Goldman-Rakic (1987). Circuitry of primate prefrontal cortex and regulation of behavior by representational memory. Handbook of Physiology - The Nervous System, 5, 373-417.

Goldman-Rakic, P.S. & Brown, R.M. (1981). Regional changes of monoamines in cerebral cortex and subcortical structures of aging rhesus monkeys. Neuroscience, 6, 177-187.

Gur, R.C., Gur, R.E., Obrist, W.D., Skolnick, B.E., & Reivich, M. (1987). Age and regional cerebral blood flow at rest and during cognitive activity. Archives of General Psychiatry, 44, 617-621.

Guttman, C., Jolesz, F., Kikinis, R., Killiany, R., Moss, M., Sandor, T., & Albert, M. (1998). White matter changes with normal aging. Neurology, 50, 972-978.

Haaland, K.Y., Vranes, L.F., Goodwin, J.S., & Garry, P.J. (1987). Wisconsin Card Sort Test performance in a healthy elderly population. Journal of Gerontology, 42, 345-346.

Hanninen, T., Hallikainen, M.., Koivisto, K., Partanen, K., Laakso, M.P., Riekkinen, P.J., & Soininen, H. (1997). Decline in frontal lobe functions in subjects with age-associated memory impairment. Neurology, 48, 148-153.

Harlow, J.M. (1868). Recovery from the passage of an iron bar through the head. Publications of the Massachusetts Medical Society, 2, 327-346.

Hartley, A.A., Speer, N.K., Jonides, J., Reuter-Lorenz, P.A., & Smith, E.E. (2001). Is the dissociability of working memory systems for name identity, visual-object identity, and spatial location maintained in old age? Neuropsychology, 15, 3-17.

Hasher, L. & Zacks, R. T. (1979). Automatic and effortful processes in memory. Journal of Experimental Psychology: General, 108, 356-388.

Haug, H., Barnwater, U., Eggers, R., Fischer, D., Kuhl, S., & Sass, N.L. (1983). Anatomical changes in aging brain: Morphometric analysis of the human prosencephalon. In J. Cervois-Navarro & H. I. Sarkander (Eds.), Brain Aging: Neuropathology and Neuropharmacology Vol. 21: Aging (pp. 193-225). New York: Raven Press.

Heaton, W.C. (1981). Wisconsin Card Sorting Test. Odessa, TX: Psychological Assessment Resources.

Hecaen, H. & Albert, M. (1978). Human Neuropsychology. New York: Wiley.

Hermann, B., Wyler, A., & Richley, E. (1988). Wisconsin Card Sorting test performance in patients with complex partial seizures of temporal lobe origin. Journal of Clinical and Experimental Psychology, 10, 467-476.

Hultsch, D.F., Hertzog, C., Small, B.J., McDonald-Miszczak, L., & Dixon, R.A. (1992). Short-term longitudinal change in cognitive performance in later life. Psychology and Aging, 7, 571-584.

Haug, H. & Eggers, R. (1991). Morphometry of the human cortex cerebri and corpus striatum during aging. Neurobiology of Aging, 12, 336-338.

Heilbroner, P.L. & Kemper, T. (1990). Cytoarchitectonic distribution of senile plaques in three aged monkeys. Acta Neuropathologica, 81, 60-65.

Houx, P.J., Jolles, J., & Vreeling, F.W. (1993). Stroop interference: Aging effects assessed with the Stroop Color-Word Test. Experimental Aging Research, 19, 209-224.

Janowsky, J.S., Shimamura, A.P., & Squire, L.R. (1989). Source memory impairment in patients with frontal lobe lesions. Neuropsychologia, 27, 1043-1056.

Jason, G.W. (1985). Gesture fluency after focal cortical lesions. Neuropsychologia, 23, 463-481.

Jonides, J., Smith, E.E., Koeppe, R.A., Awh, E., Minoshima, S., & Mintun, M.A. (1993). Spatial working memory in humans as revealed by PET. Nature, 363, 623-625.

Katzman, R. (1991). Education and the prevalence of dementia and Alzheimer's disease. Neurology, 43, 13-20.

Kausler, D.H., Salthouse, T.A., & Saults, J.S. (1987). Frequency of occurrence memory over the adult lifespan. Experimental Aging Research, 13, 159-161.

Kimberg, D.Y. & Farah, M.J. (1993). A unified account of cognitive impairments following frontal lobe damage: The role of working memory in complex, organized behavior. Journal of Experimental Psychology: General, 4, 411-428.

King, D.A., Cox, C., Lyness, J.M., and Caine, E.D. (1995). Neuropsychological effects of depression and age in an elderly sample: A confirmatory study. Neuropsychology, 9, 399-408.

Knight, R.T. & Grabowecky, M. (1995). Escape from linear time: Prefrontal cortex and conscious experience. In N.S. Gazzaniga (Ed.), The Cognitive Neurosciences (pp. 1357-1371). Cambridge, MA: MIT Press.

Koenig, H., Meador, K., Cohen, H., & Blazer, D. (1988). Self-rated depression scales and screening for major depression in the older hospitalized patient with medical illness. Journal of the American Geriatric Society, 36, 699-706.

Koss, E., Ober, B., Delis, D., & Friedland, R. (1984). The Stroop Color and Word Test: Indicator of dementia severity. International Journal of Neuroscience, 24, 53-61.

Kuhl, D.E., Metter, E.J., Riege, W.H., & Hawkins, R.A. (1984). The effect of normal aging on patterns of local cerebral glucose utilization. Annals of Neurology, 15, S133-S137.

LaRue, A. (1992). Cognition in normal aging. In Aging and Neuropsychological Assessment (pp. 47-77). New York: Plenum Press.

Levine, B., Stuss, D.T., & Milberg, W.P. (1997). Effects of aging on conditional associative learning: Process analyses and comparison with focal frontal lesions. Neuropsychology, 11, 367-381.

Lezak, M.D. (1995). Neuropsychological Assessment (3rd ed.). New York: Oxford University Press.

Libon, D.J., Glosser, G., Malamut, B.L., Kaplan, E., Goldberg, E., Swenson, R., & Prouty Sands, L. (1994). Age, executive functions, and visuospatial functioning in healthy older adults. Neuropsychology, 8, 38-43.

Lindenberger, U., Mayr, U., & Kliegl, R. (1993). Speed and intelligence in old age. Psychology and Aging, 8, 207-220.

Lowe, P.A. & Reynolds, C.R. (1999). Age, gender, and education may have little influence on error patterns in the assessment of set-shifting and rule induction among normal elderly. Archives of Clinical Neuropsychology, 14, 303-315.

Luria, A.R. (1973). The Working Brain: An Introduction to Neuropsychology. New York: Basic Books.

Luria, A.R. (1976). The Neuropsychology of Memory. New York: John Wiley.

Luria, A.R. (1980). Higher Cortical Function in Man. New York: Basic Books.

Malloy, P., Bihrle, A., Duffy, J., & Cimino, C. (1993). The orbitomedial frontal system. Archives of Clinical Neuropsychology, 8, 185-201.

Mangles, J.A. (1997). Strategic processing and memory for temporal order in patients with frontal lobe lesions. Neuropsychology, 11, 207-221.

Marcusson, J., Morgan, D.G., Winblad, B., & Finch, C.E. (1984). Aging and serotonin receptors in the human brain. Clinical Neuropharmacology, 7, 38-39.

Martin, A., Wiggs, C.L., LaLonde, F., & Mack, C. (1994). Word retrieval to letter and semantic cues: A double dissociation in normal subjects using interference tasks. Neuropsychologia, 32, 1487-1494.

McDaniel, M.A. & Einstein, G.O. (1992). Aging and prospective memory: Basic findings and practical implications. Advances in Learning and Behavioral Disabilities, 7, 87-105.

McIntyre, J.S. & Craik, F.I.M. (1987). Age differences in memory for item and source information. Canadian Journal of Psychology, 41, 175-192.

Mesulam, M.M. (1998). From sensation to cognition. Brain, 121, 1013-1052.

Meyer, J.S., Kawamura, J., & Terayama, Y. (1994). Cerebral blood flow and metabolism with normal and abnormal aging. In M.L. Albert & J.E. Knoefel (Eds.), Clinical Neurology of Aging. New York: Oxford University Press.

Miceli, G., Caltagirone, C., Gainotti, G., Masullo, C., & Silveri, M.C. (1981). Neuropsychological correlates of localized cerebral lesions in non-aphasic brain-damaged patients. Journal of Clinical Neuropsychology, 3, 53-63.

Milner, B. (1963). Effects of different brain lesions on card sorting. Archives of Neurology, 9, 90-100.

Mittenberg, W., Seidenberg, M., O'Leary, D.S., & DiGiulio, D.V. (1989). Changes in cerebral functioning associated with normal aging. Journal of Clinical and Experimental Neuropsychology, 11, 918-932.

Mortiner, J.A. & Graves, A.B. (1993). Education and other socioeconomic determinants of dementia and Alzheimer's disease. Neurology, 43, 39-44.

Moscovitch, M. (1994). Cognitive resources and dual-task interference effects at retrieval in normal people: The role of the frontal lobes and medial temporal cortex. Neuropsychology, 8, 524-534.

Moscovitch, M. & Winocur, G. (1995). Frontal lobes, memory, and aging. Annals of the New York Academy of Sciences, 769, 119-150.

Nyberg, L, Winocur, G., & Moscovitch, M. (1997). Correlation between frontal lobe functioning and explicit and implicit stem completion in healthy elderly. Neuropsychology, 11, 70-76.

O'Donnell, J.P., MacGregor, L.A., Dabrowski, J.J., Oestreicher, J.M., & Romero, J.J. (1994). Construct validity of neuropsychological tests of conceptual and attentional abilities. Journal of Clinical Psychology, 50, 596-600.

Panek, P.E., Rush, M.C., & Slade, L.A. 91983). Locus of the age-Stroop interference relationship. Journal of Genetic Psychology, 145, 209-216.

Parasuraman, R. & Giambra, L. (1991). Skill development in vigilance: Effects of event rate and age. Psychology and Aging, 6, 155-169.

Parkin, A.J. (1998). The central executive does not exist. Journal of the International Neuropsychological Society, 4, 518-522.

Parkin, A.J. & Walter, B.M. (1991). Aging, short-term memory, and frontal dysfunction. Psychobiology, 19, 175-179.

Parkin, A.J. & Walter, B.M. (1992). Recollective Experience, Normal Aging, and Frontal Dysfunction. Psychology and Aging, 7, 290-298.

Parkin, A.J., Walter, B.M., & Hunkin, N.M. (1995). Relationships between normal aging, frontal lobe function, and memory for temporal and spatial information. Neuropsychology, 9, 304-312.

Parks, R.W., Loewenstein, D.A., Dodrill, K.L., Barker, W.W., Yoshii, R., Chang, J.Y., Emran, A., Apicella, A., Sheramata, W.A., & Duara, R. (1988). Cerbral metabolic effects of a verbal fluency test: A PET scan study. Journal of Clinical and Experiemental Neuropsychology, 10, 565-575.

Parmalee, P., Katz, I., & Lawton, M. (1989). Depression among institutionalized aged: Assessment and prevalence estimation. Journal of Gerontology, 44, 22-29.

Petrides, M. (1985). Deficits on conditional associative-learning tasks after frontal-and temporal-lobe lesion in man. Neuropsychologia, 23, 601-614.

Petrides, M., Alivisatos, B., & Evans, A.C. (1995). Functional activation of the human ventrolateral frontal cortex during mnemonic retrieval of verbal information. Proceeds from the National Academy of Science, USA, 92, 5803-5807.

Phillips, L.H. (1997). Do 'frontal tests' measure executive function? Issues of assessment and evidence from fluency tests. In P.M.A. Ribbitt (Ed.), Methodology of frontal and executive function (pp. 191-214). Hove: Psychology Press.

Posner, M.I. & Raichle, M.E. (1996). Images of Mind (pp. 153-179). New York: Scientific American Library.

Powell, D.H. & Whitla, D.K. (1994). Profiles in Cognitive Aging (pp. 112-133). Cambridge: Harvard University Press.

Pribram, K.H. (1997). The work in working memory. In N.A. Krasnegor, G. Reid Lyon, & P.S. Goldman-Rakic (Eds.), Development of the Prefrontal Cortex (pp. 359-376). Baltimore: Paul H. Brooks Publishing Company.

Prigatano, G. (1978). Wechsler Memory Scale: A seletive review of the literature. Journal of Clinical Psychology, 34, 816-832.

Raglund, J.D., Glahn, D.C., Gur, R.C., Censits, D.M., Smith, R.J., Mozley, P.D., Alavi, A., & Gur, R.E. (1997). PET regional cerebral blood flow change during working and declarative memory: Relationship with task performance. Neuropsychology, 11, 222-231.

Raykov, T., Tomer, A., & Nesselroade, J.R. (1991). Reporting structural equation modeling results in *Psychology and Aging*: Some Proposed Guildelines. Psychology and Aging, 6, 499-503.

Raz, N., Gunning, F.M., & Acker, J.D. (1998). Neuroanatomical correlates of cognitive aging: Evidence from structural magnetic resonance imaging. Neuropsychology, 12, 95-114.

Raz, N., Gunning, F.M., Head, D., Dupuis, J.H., McQuain, J., Briggs, S.D., Loken, W.J., Thorton, A.E., & Acker, J.D. (1997). Selective aging of the human cerebral cortex observed in vivo: Differential vulnerability of the prefrontal gray matter. Cerebral Cortex, 7, 268-282.

Regard, M. (1981). Cognitive rigidity and flexibility: A neuropsychological study. Unpublished Ph.D. Dissertation, University of Victoria, British Columbia.

Reitan, R.M.& Wolfson, D. (1994). A selective and critical review of neuropsychological deficits and the frontal lobes. Neuropsychology Review, 4, 161-198.

Reuter-Lorenz, P.A., Jonides, J., Smith, E.E., Hartley, A., Miller, A., Marshuetz, C., & Koeppe, R.A. (2000). Age differences in the frontal lateralization of verbal and spatial working memory revealed by PET. Journal of Cognitive Neuroscience, 12, 174-186.

Reynolds, C.R. (1997). Forward and backward memory span should not be combined for clinical analysis. Archives of Clinical Neuropsychology, 12, 29-40.

Robbins, T.W., James, M.,, Owen, A.M., Sahakian, B.J., Lawrence, A.D., Mcinnes, L., & Rabbitt, P. (1998). A study of performance on tests from the CANTAB battery sensitive to frontal lobe dysfunction in a large sample of normal volunteers: Implications for theories of executive functioning and cognitive aging. Journal of the International Neuropsychological Society, 4, 474-490.

Roland, P.E. (1984). Metabolic measurements of the working frontal cortex in man. Trends in Neuroscience, 7, 430-435.

Rubin, D.C. (1999). Frontal-striatal circuits in cognitive aging: Evidence for caudate involvement. Aging, Neuropsychology, and Cognition, 6, 241-259.

Rubin, E.H., Kinscherf, D.A., Grant, E.A., & Storandt, M. (1991). The influence of major depression on clinical and psychometric assessment of SDAT. American Journal of Psychiatry, 148, 1164-1171.

Ruff, R.M., Allen, C.C., Farrow, C.E., Niemann, H., & Wylie, T. (1994). Figural fluency: Differential impairment in patients with left versus right frontal lobe lesions. Archives of Clinical Neuropsychology, 9, 41-55.

Ryan, J.J., Lopez, S.J., & Paolo, A.M. (1996). Digit span performance of persons 75-96 years of age: Base rates and associations with selected demographic variables. Psychological Assessment, 8, 324-327.

Salthouse, T.A. (1985). Speed of behavior and its implications for cognition. In J. Bierren & K. Schaie (Eds.), Handbook of the Psychology of Aging (2nd edition), New York: Van Nostrand Reinhold.

Salthouse, T.A. (1994). The aging of working memory. Neuropsychology, 8, 535-543.

Salthouse, T.A., Fristoe, N., & Rhee, S.H. (1996). How localized are age-related effects on neuropsychological measures? Neuropsychology, 10, 272-285.

Sarno, M.T., Buonaguro, A. & Levita, E. (1985). Gender and recovery from aphasia after stroke. Journal of Nervous and Mental Disease, 173, 605-609.

Schacter, D.L. (1987). Memory, amnesia, and frontal lobe dysfunction. Psychobiology, 15, 21-36.

Schacter, D.L., Kaszniak, A.W., Kihlstrom, J.F., & Valdiserri, M. (1991). The relation between source memory and aging. Psychology and Aging, 6, 559-568.

Schacter, D.L., Osowiecki, D., Kaszniak, A.W., Kihlstrom, J.F., & Valdiserri, M. (1994). Source memory: Extending the boundaries of age-related deficits. Psychology and Aging, 9, 81-89.

Scheibel, M.E., Lindsay, R. D., Tomiyasu, U., & Scheibel, A.B. (1975). Progressive dendritic changes in the aging human cortex. Experimental Neurology, 47, 392-403.

Schmidt, M., Trueblood, W., Merwin, M., & Durham, R.L. (1994). How much do 'attention' test tell us? Archives of Clinical Neuropsychology, 9, 383-394.

Schumacher, E.H., Lauber, E., Awh, E., Jonides, J., & Smith, E.E. (1996). PET evidence for an amodal verbal working memory system. Neuroimage, 3, 79-88.

Seidman, L.J., Oscar-Berman, M., Kalinowski, A.G., Ajilore, O., Kremen, W.S., Faraone, S.V., & Tsuang, M.T. (1995). Experimental and clinical neuropsychological measures of prefrontal dysfunction in schizophrenia. Neuropsychology, 9, 481-490.

Shallice, T. & Burgess, P. (1991). Deficits in stretegy application following frontal lobe damage in man. Brain, 114, 727-741.

Shaw, T.G., Mortel, K.F., Meyer, J.S. Rogers, R.L., Hardenberg, J., & Cutaia, M.M. (1984). Cerebral blood flow changes in benign aging and cerebrovascular disease. Neurology, 34, 855-862.

Shimamura, A.P. (1994). Neuropsychological perspectives on memory and cognitive decline in normal aging. Seminars in the Neurosciences, 6, 387-394.

Shimamura, A.P. (1995). Memory and frontal lobe function. In M.S. Gazzaniga (Ed.), The Cognitive Neurosciences (pp. 803-813). Cambridge, MA: MIT Press.

Shimamura, A.P. & Jurica, P.J. (1994). Memory interference effects and aging: Findings from a test of frontal lobe function. Neuropsychology, 8, 408-412.

Smith, E.E., Jonides, J., Marshuetz, C., & Koeppe, R.A. (1998). Compnents of verbal working memory: Evidence from neuroimaging. Procedes from the National Academy of Sciences, 95, 876-882.

Squire, L.R. (1987). Memory and Brain. New York: Oxford University Press.

Spencer, W.D. & Raz, N. (1994). Memory for facts, source, and context: Can frontal lobe dysfunction explain age-related differences? Psychology and Aging, 9, 149-159.

Spreen, O. & Strauss, E. (1991 & 1998). A Compendium of Neuropsychological Tests. New York: Oxford University Press, Inc.

Spieler, D.H., Balota, D.A., & Faust, M.E. (1996). Stroop performance in healthy younger and older adults and in individuals with dementia of the Alzheimer's type. Journal of Experimental Psychology: Human Perception and Performance, 22, 461-479.

Stern, Y., Gurland, B., Tatemichi, T.K., Tang, M.X., Wilder, D., & Mayeux, R. (1994). Influence of education and occupation on the incidence of Alzheimer's disease. Journal of the American Medical Association, 271, 1004-1010.

Struble, R.G., Price, D.L., Cork., L.A., & Price, D.L. (1985). Senile plaques in the cortex of aged normal monkeys. Brain Research, 361, 267-275.

Stuss, D.T. (1991). Interference effects on memory functions in post-leucotomy patients: An attentional perspective. In H.S. Levin, H.M. Eisenburg, & A.L. Benton (Eds.), Frontal Lobe Function and Dysfunction. New York: IRBN Press.

Stuss, D.T. & Benson, D. F. (1986). The Frontal Lobes. New York: Raven Press.

Stuss, D.T. & Benson, D.F. (1984). Neuropsychological studies of the frontal lobes. Psychological Bulletin, 95, 3-28.

Stuss, D.T., Stethem, L.L., & Poirier, C.A. (1987). Comparison of three tests of attention and rapid information processing across six age groups. The Clinical Neuropsychologist, 1, 139-152.

Suhara, T., Fukuda, H., Inoue, O., Itoh, T., Suzuki, K., Yamasaki, T., & Tateno, Y. (1991). Age-related changes in human D1 dopamine receptors measured by positron emission tomography. Psychopharmacology, 103, 41-45.

Sullivan, E.V., Mathalon, D.H., Zipursky, R.B., Kersteen-Tucker, Z., Knight, R.T., & Pfefferbaum, A. (1993). Factors of the Wisconsin Card Sorting Test as measures of frontal-lobe function in schizophrenia and in chronic alcoholism. Psychiatry Research, 46, 175-199.

Tayor, L. (1979). Psychological assessment of neurological patients. In T. Rasmussen and R. Marino (Eds.), Functional Neurosurgery. New York: Raven Press.

Tulving, E., Kapur, S., Craik, F.I.M., & Moscovitch, M.H.S. (1994). Hemispheric encoding/retrieval asymmetry in episodic memory: Positron emission tomography findings. Proceedings of the National Academy of Sciences, 91, 2016-2020.

Tun, P.A., Wingfield, A., Stine, E.A.L., & Mecsas, C. (1992). Rapid speech processing and divided attention: Processing rate versus processing resources as an explanation of age effects. Psychology and Aging, 7, 546-550.

Uchiyama, C.L., Mitrushina, M.N., D'Elia, L.F., Satz, P., & Mathews, A. (1994). Frontal lobe functioning in geriatric and non-geriatric samples: An argument of multimodal analyses. Archives of Clinical Neuropsychology, 9, 215-227.

Uttl, B. & Graf, P. (1997). Color-word Stroop test performance across the adult life span. Journal of Clinical and Experimental Neuropsychology, 19, 405-420.

Vendrell, P., Junque, C., Pujol, J., Jurado, M.A., Molet, J., & Grafman, J. (1995). The role of prefrontal regions in the Stroop Task. Neuropsychologia, 3, 341-352.

Warren, L.R., Butler, R.W., Katholi, C.R., & Halsey, J.H. (1985). Age differences in cerebral blood flow during rest and during mental activation measurements with and without monetary incentive. Journal of Gerontology, 30, 53-59.

Wechsler, D. (1987). Wechsler Memory Scale-Revised. New York: Psychological Corporation.

Wecker, N.S., Kramer, J.H., Wisniewski, A., Delis, D.C., & Kaplan, E. (2000). Age effects on executive ability. Neuropsychology, 14, 409-414.

West, R. (2000). Reply to Greenwood. Journal of the International Neuropsychological Society, 6, 705-726.

West, R. (1996). An application of prefrontal cortex function theory to cognitive aging. Psychological Bulletin, 120, 272-292.

West, R. & Bell, M.A. (1997). Stroop color-word interference and electroencephalogram activation: Evidence for age-related decline of the anterior attentional system. Neuropsychology, 11, 421-427.

Wiggs, C.L. (1993). Aging and memory for frequency of occurrence of novel, visual stimuli: Direct and indirect measures. Psychology and Aging, 8, 400-410.

Wilkins, A.J., Shallice, T., & McCarthy, R. (1987). Frontal lesions and sustained attention. Neuropsychologia, 25, 359-365.

Winocur, G., Moscovitch, M., & Stuss, D.T. (1996). Explicit and implicit memory in the elderly: Evidence for double dissociation involving medial temporal- and frontal-lobe functions. Neuropsychology, 10, 57-65.

Wong, D.F., Wagner, H.N., Dannals, R.F., Links, J.M., Frost, J.J., Ravert, H.T., Wilson, A.A., Rosenbaum, A.E., Gjedde, A., Douglasse, K.H., Petronis, J.D., & Folstein, M.F. (1984). Effects of age on dopamine and serotonin receptors measured by positron tomography in the living human brain. Science, 226, 1393-1396.

Yesavage, J., Brink, T., Rose, T., Lum, O., Huange, V., Adey, M., & Leirer, V. (1983). Development and validation of a Geriatric Depression Screening Scale: A preliminary report. Journal of Psychiatric Research, 17, 37-49.