AGE, GENDER, GENERAL INTELLIGENCE AND EDUCATIONAL LEVEL INFLUENCES ON WORKING MEMORY

by

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Abstract

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Working memory plays an important role in normal functioning, and its deficits are central to a number of psychiatric and neurological conditions. Working memory functioning appears to be influenced by a number of demographic factors, including age, gender, as well as educational level and general intelligence. The current study examined the effects of age on working memory changes in younger adults, and investigated relative contributions of gender, education and general intelligence on working memory ability. The current study also addressed the ambiguity in the definition of working memory function by employing a multimeasure battery of tasks, assessing several components of working memory both across the verbal and visual-spatial domains. Data were collected from normal adults (N=403) age 18 to 55 who were tested at the Biopsychiatry department of New York State Psychiatric Institute. Working memory measures included a test of visual spatial maintenance (Spatial Delayed Response task), a test of continuous updating (N-Back test), a test of memory for temporal order (Word Serial Position Test) and a test of mental manipulations within working memory (Letter-Number Sequencing). General intelligence was estimated using the Vocabulary subtest of WAIS-III. The results indicate that working memory declines linearly with age in normal adults between ages 18 and 55. Higher levels of estimated intelligence were predictive of better working memory performance and were also found to be a mediating factor for the

effects of age on the performance of the measure of continuous updating (N-Back task), such that the age associated decrements were more pronounced in those with lower estimated level of intelligence. In individuals with high estimated intelligence, age was found not to be a significant predictor of performance. After controlling for age, gender and general intelligence, education was a significant predictor of working memory performance on selected measures, including the verbal continuous updating task; however, education did not present as a mediating factor for the effects of age. Gender was found to be a significant predictor only on a test of visual spatial working memory, with males performing better than females.

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Introduction

Working memory plays an important role in normal functioning, and its deficits are central to a number of psychiatric and neurological conditions. Working memory functioning appears to be influenced by various demographic factors including age, gender, educational levels and general intelligence. Performance on working memory tests tends to increase through adolescence (Vuontela et al., 2003) and suffers a decline with advanced age (Waters & Caplan, 2005). While few studies have investigated gender effects on working memory, existing research on gender-associated cognitive differences suggests that females tend to perform better on tasks involving verbal material (Maitland et al., 2004; Speck et al., 2000,), while males do better on tasks involving spatial manipulations (Epting & Overman, 1998; Schweinsburg, Nagel & Tapert, 2005). Studies investigating effects of both age and gender on working memory tend to concentrate on peri-puberty (Vuontela et al., 2003) and peri- and postmenopausal stages (Maitland et al., 2004), around the time of the vast endocrine changes that could dramatically impact possible gender differences. No study to date has attempted systematic investigation of age and gender effects on working memory functioning during the normal adult life span, the time which follows adolescence and precedes the onset of changes associated with advanced aging.

Literature on age-related neuroanatomical changes suggests that several brain regions associated with working memory function undergo continuing changes through the adult lifespan (Adler et al 2001; Brickman et al 2006), suggesting the possibility of corresponding changes in working memory ability. In the current study, working memory data collected from a large sample of normal adults, aged 18-55, systematically assessed

on comprehensive battery of working memory tests was examined to evaluate the effects of age and gender on test performance. The use of several working memory measures, tapping various components of this complex function, such as maintenance, continuous updating, memory for temporal order, and mental manipulation, allowed examination of relative changes in each component of working memory, as well as working memory performance as a whole. Finally, the contribution of additional relevant demographic variables, such as education level and an estimate of general intelligence were examined.

Background

Models of Working Memory

Working memory is a limited capacity human memory system that is capable of maintaining and manipulating information (Baddeley, 1996). A wide range of models conceptualizing working memory exists, reflecting certain ambiguity within both cognitive and physiological findings in the area.

Baddeley and Hitch (1974) introduced the most comprehensive model of working memory. According to Baddeley (1996), the concept of working memory stems from an earlier concept of short-term memory as proposed by Atkinson and Shiffrin (1968). Working memory differs from short-term memory in that it is assumed to involve a number of systems, and that it in turn plays a role in other cognitive tasks, such as learning and reasoning. Based on the neuropsychological and experimental evidence, Baddeley and Hitch proposed a tripartite system of working memory, consisting of the central executive, attentional controller, aided by two subsidiary systems—the visuospatial sketchpad that holds and manipulates visual information and the phonological loop that holds and manipulates verbal information (Baddeley 1996).

Maintenance of information in the phonological loop is presumed to take place via subvocal rehearsal, without which the information would fade within 2 to 3 seconds. Baddely placed the phonological store within the left perisylvian region and the rehearsal system within Broca's area. Within the visuospatial sketchpad a distinction is made between visual and spatial types of information. Baddeley points out that there is significantly less known about how information is rehearsed for maintenance within the sketchpad. Within this model, the capacity of the phonological loop and visuospatial sketchpad determines one's memory span.

The attentional controller, an executive mechanism, is very vaguely defined, and may in fact be a series of parallel processes, not a single process. According to Baddeley (1996), the attentional controller is involved in coordinating the activities of the two subordinate systems, a notion that has received some support from dual-task studies that examine the integration of information across visual and verbal modalities (Baddeley, 1996). More recently, a fourth subsystem, the episodic buffer, has been proposed (Baddeley, 2003). The episodic buffer is described as a system that relies heavily on executive processing but still differs from the central executive by its emphasis on storage, rather than attentional control. The episodic buffer is presumed to be responsible for grouping of relevant information, thus allowing for larger capacity of information storage and recall. Like the central executive, the episodic buffer is multimodal in its functioning (Baddeley, 2003).

Goldman-Rakic (1996), pointing to the lack of consistent neurophysiological or neuroanatomical evidence for an attentional controller or a central executive component, suggested instead that parallel processing might better explain integration within working

memory. There is, however, neurophysiological evidence pointing to the working memory neuronal specialization within prefrontal cortex for spatial, visual, and semantic information, offering support for Baddeley's model (Goldman-Rakic, 1996).

Additional attempts at conceptualizing working memory functioning include task-driven separation of associated processes into selective attention to features of a stimulus to be stored in working memory, continuing updating, memory for temporal order, and manipulation of information in working memory (Wager & Smith, 2003). This notion received some support from a number of neuroimaging studies, pointing to differences in brain activation patterns in response to tasks tapping into various components of working memory.

Tasks Used to Measure Working Memory

The variability in definitions of working memory, ranging from simple maintenance of information in a subsection of short-term memory store, to mental manipulation of various complexity of the maintained information, leads to utilization of a large array of diverse tasks to measure this construct. Simple maintenance in working memory is commonly measured using a variation of the Sternberg task (Sternberg, 1966). This task utilizes a delayed match-to-sample paradigm, in which participants are briefly shown a set of stimuli, which then disappears, and is followed by a single (or several) stimuli; the participants are asked to decide whether the single stimulus was a part of a previously presented set (Belger et al., 1998; Finke, Bublak & Zihl, 2006; Glahn et al., 2002; Ranganath, DeGutis & D'Esposito, 2004; Veltman, Rombouts & Dolan, 2003). This task can be performed with or without a distracter task. A commonly used test of spatial working memory, Spatial Delayed Response Test, utilizes this paradigm. In this

task, a participant is asked to remember the spatial position of the stimulus on the screen while performing a continuous-performance type distracter task, which consists of responding every time one sees a target shape, presented intermittently with two nontarget shapes (Bruder et al., 2005; Glahn et al., 2002; Park & Holtzman, 1992). A more complex variation on this task, a Word Serial Position Test, allows examination of memory for temporal order. For this task, participants are presented with a sequence of several words; after a delay, one of the initially presented words is repeated, and participants are asked to indicate the serial position of the target word within the previously presented sequence (Wexler et al., 1998).

N-Back task, in addition to simple maintenance, also tests continuous updating and order memory. Participants are presented with a continuous series of individual stimuli and are asked to respond when the presented stimulus is identical to the one presented *n* positions before. This task is also widely utilized in working memory studies, and several common types of stimuli used for this test include letters or numbers (Bruder et al., 2005; Derrfuss, Brass, & von Cramon, 2004; Owen et al., 2005; Veltman et al., 2003).

Another commonly used measure of working memory is the dual task paradigm (Adcock et al., 2000; Derrfuss et al., 2004; Grabner et al., 2004; Osaka et al., 2003), which requires participants to split attention between two simple tasks, such as count the number of words in a sentence and decide whether it makes sense. Any number of variations on this task exist in the literature, some integrating information from multiple modalities (i.e., visual and verbal), which arguably allows assessment of the central executive component (Adcock et al., 2000). This paradigm may be described as a way of

testing manipulation in working memory, since one may be required to make one or several higher-level decisions about the stimuli, while holding them in memory.

Less often used in research measures of manipulation in working memory are the Digit Span Backward (Sun et al., 2005; Wechsler, 1997), and Letter-Number Sequencing (Bruder, 2005; Tulsky, Zhu & Ledbetter, 1997; Wechsler, 1997) subtests of the WAIS-III. These subtests contribute to the Working Memory Index within the WAIS-III scoring system. Finally, such tasks as Wisconsin Card Sorting Test (WCST; Hartman et al., 2003; Huizinga, Dolan & van der Molen, 2006; McGurk et al., 2004) and Paced Auditory Serial Addition Test (PASAT; Huijbregts et al., 2006; Legenfelder et al., 2006; Ranjeva et al., 2006) are also sometimes referred to in the literature as working memory tests. In the WCST, participants are essentially asked to figure out a rule for matching stimulus cards to one of the four cue cards, using only simple verbal feedback (correct/incorrect) from the examiner. The rule changes once the participant has completed the requisite number of correct trials in a row. In the PASAT, participants are asked to add together single digit numbers presented as an ongoing list, remembering to add each next number to the one presented immediately before it on the list. While both tasks undoubtedly utilize several components of working memory, including maintenance, continuous updating, and cognitive manipulation, it is also clear that a lot more than working memory is involved in completing each task. Some additional executive functions involved in these tasks include problem solving and feedback utilization in the case of WCST, and arithmetic skills and speeded processing in the case of PASAT. Differences in functions that these diverse tasks assess are important considerations in understanding the literature pertaining to working memory.

Certain ambiguity in the definition of working memory, which leads to the development of widely differing means of measuring this construct, also necessitates a more comprehensive means of assessment. It can be argued that no one task adequately measures working memory, and that a valid assessment of this function requires a battery of several measures, taping into several relevant components of working memory, such as maintenance, continuous updating, and mental manipulation.

Neuroanatomy and Neurophysiology of Working Memory

Role of Prefrontal Cortex in Working Memory

Goldman-Rakic (1996) presented neurophysiological evidence of "working memory neurons" within the prefrontal cortex. Evidence from a series of studies in primates using a delayed match to sample paradigm suggests that some neurons within the prefrontal cortex remain active through the delay period of the task. The activation period is relatively short, under 20 seconds, suggesting that the observed activation is not related to long-term memory, and in fact represents the holding space for the information (Goldman-Rakic, 1996). This argues for the primary importance of this brain region in working memory functioning.

Activation within the prefrontal cortex has been widely observed across various working memory tasks using functional imaging (Habeck et al., 2005; Manoach et al., 2003; Passingham & Sakai, 2004; Osaka et al., 2003; Owen et al., 2005; Ranganath, DeGutis & D'Esposito, 2004; Sun et al., 2005; Veltman et al., 2003). However, there is evidence that working memory functioning is associated with a wide range of brain areas spanning frontal, temporal and parietal lobes. Actual areas and patterns of activation seem to depend both on the type of stimulus used (i.e., verbal, visual, or spatial) and on

the type of demand placed on working memory (i.e., simple maintenance, continuous updating, or direct manipulation) (Wager & Smith, 2003).

Neuroanatomy of Verbal Working Memory

Consistent with Baddeley's suggestion of rehearsal within a phonological loop, verbal working memory tasks activate frontal and temporal language areas (Wager & Smith, 2003), and a substantial proportion of studies report increased activation within the left side of the cortex versus right or bilateral activation (Derrfuss et al., 2004; Habeck et al., 2005; Manoach et al., 2003; Owen et al., 2005; Veltman et al., 2003; Wagner & Smith, 2003). In addition, activation of nonlanguage related sites in response to verbal stimuli within the frontal (Habeck et al.; Owen et al.; Passingham & Sakai, 2004 et al; Veltman et al.) and parietal lobes (Habeck et al.; Owen et al.; Veltman et al.), including anterior cingulate cortex (Osaka et al., 2003; Owen et al.), anterior insula (Derrfuss et al.), and cerebellum (Desmond, Chen, & Shieh, 2005) has been reported in the literature.

Neuroanatomy of Visual and Spatial Working Memory

Activation patterns for spatial and visual information tend to be organized along the dorsal/ventral pathways, respectively (Finke, Bublak & Zihl, 2006; Owen, 2004; Wagner & Smith, 2003). Visual working memory, defined as memory for nonspatial visual information, appears to be further subdivided into subtypes of visual information. Thus, a section of fusiform gyrus is implicated in the storage and recognition of facial features (Gazzaley, Rissman & D'Esposito, 2004; Ranganath, DeGutis, & D'Esposito, 2004), while a parahippocampal subregion is implicated in memory for scenery (Ranganath,DeGutis, & D'Esposito, 2004). In the frontal region, visual working memory

appears to activate bilateral middle and left inferior frontal gyri (Belger et al., 1998; Wager & Smith, 2003)

Spatial working memory tasks have shown activation along the dorsal processing and memory stream of intraparietal sulcus and inferior parietal lobule (Belger et al., 1998; Wager & Smith 2003). The right hemisphere, in general, appears to be more involved in processing of spatial information (Adcock et al., 2000; Belger et al.; Finke, Bublak & Zihl, 2006, Wager & Smith 2003). Right dorsolateral frontal cortex appears to play a role in spatial working memory involving maintenance of information (Belger et al.) and damage to the right, but not left, parietal cortex has been associated with a spatial working memory deficit (Finke, Bublak & Zihl, 2006).

Neuroanatomy of Working Memory by Process Type

When examined by the process type, activation patterns change depending on task demands. Simple maintenance, as measured by tasks employing a delayed match-to-sample paradigm, appears to involve the prefrontal cortex (Belger et al., 1998; Glahn et al., 2002; Habeck et al., 2005; Manoach et al., 2003; Passingham & Sakai, 2004; Ranganath, DeGutis, & D'Esposito, 2004; Sun et al., 2005), as well as sensory areas directly implicated in the processing of the task-appropriate sensory input (Belger et al., 1998; Gazzaley, Rissman, & D'Esposito, 2004; Ranganath, DeGutis, & D'Esposito, 2004). Parietal cortex activation also is often cited (Adcock et al., 2000; Belger et al., 1998; Finke, Bublak & Zihl, 2006; Glahn et al., 2002; Habeck et al., 2005; Owen, 2004; Owen et al., 2005). Passingham and Sakai (2004), however, demonstrated that while prefrontal inactivation interferes with sustained memory tasks, parietal inactivation does not have such effect. The cerebellum also may play a role in the encoding and

maintenance of verbal information. A study by Desmond, Chen and Shieh (2005) demonstrated that transcranial magnetic stimulation (TMS) to the right superior cerebellum immediately following the presentation of stimuli interfered with maintenance within the phonological loop, resulting in slower reaction times during recall, which were not related to the motor effects.

Tasks involving continuous updating, such as the N-Back, seem to involve premotor cortex and supplementary motor areas (Derrfuss et al., 2004; Owen et al., 2005; Veltman et al., 2003), in addition to the brain regions involved in simple maintenance. There is also evidence of increased activation of the anterior cingulate gyrus with increase in effort, complexity, and attentional demands, and this region may play a role in error detection and response correction (Owen et al., 2005).

Tasks involving the direct manipulation of information in working memory, such as mental rotation, showed activation within right ventral and anterior prefrontal cortex (Glahn et al., 2002; Wager & Smith, 2003). However, for verbal information, Sun et al (2005) reported instead a selective activation of left prefrontal cortex on a digit span backwards task, suggesting that separate mechanisms may exist for the executive components of verbal and visual spatial working memory. Performance on tasks employing a dual task paradigm showed an increase in activation of areas involved in performance of the individual tasks involved (Adcock et al., 2000; Derrfuss et al., 2004; Glahn et al., 2002; Osaka et al., 2003). No additional regions were activated by the dual task that were not activated by performance of the individual tasks, which can be interpreted as evidence of parallel processing involvement in working memory

functioning, in contradiction to the existence of a central executive, or attentional controller (Adcock et al., 2000).

Differentiation by process type is further supported by findings from a genetic study of working memory (Bruder et al., 2005). The results of this study demonstrated that tasks involving direct manipulation in working memory engage different processes from those involving continuous updating or simple maintenance alone. Only performance on the Wisconsin Card Sorting Test and Letter-Number subtest of the WAIS were related with the COMT genotype, and not the N-Back, or other continuous updating or maintenance tasks.

Converging evidence from neuroimaging and genetic studies for different mechanisms underlying various components of working memory also suggests a need for a comprehensive means of assessment of this construct. While numerous studies of working memory use only one or two measures, it is important to assess a complete range of functions associated with working memory in order to be able to draw legitimate conclusions in this area.

Effects of Age on Working Memory

Overview

Working memory functioning undergoes a number of changes over the course of the lifespan. Through childhood and into adolescence it shows progressive improvement, suggesting functional maturation with age (Vuontela et al., 2003). This most likely reflects myelination of the frontal areas, because the actual areas activated by working memory tasks are the same in children as in adults (Tsujimoto et al., 2004). While both visual and auditory working memory improves with age, visual working memory appears

to develop faster than auditory working memory (Vuontela et al., 2003). Working memory deficits are commonly observed in a number of developmental disorders, such as autism (Williams et al 2005) and attention deficit disorder (Willcut et al., 2005), which can also be viewed as evidence in support of the importance of developmental factors in the physiology of working memory.

Performance on most visual, spatial, and verbal (Waters & Caplan, 2005), although not emotional (Mikels et al., 2005), working memory tasks tends to decline with age. Wecker et al. (2005), in a study using a test of executive functioning with a working memory component (Trails B), found a steady decline in performance with age through the adult life span, with accelerated decline past the age of 50. Similarly, in a series of experiments, Foos (1989) found reduced working memory storage among older participants (aged 60-79), as compared to the younger participants. Mattay et al. (2006) reported similar performance in older and younger participants on a 1-Back version of N-back task, but comparatively reduced performance on 2- and 3-back versions in older participants, suggesting an increase in deficit with an increase in demand.

Effects of Age on Specific Components of Working Memory

Investigation of the age-related reduction in specific components of working memory may help in understanding the effects of age on this function and clarify the uneven findings in the area. Several authors have reported a decline in the executive component of working memory, suggesting reduction in attentional capacity, including increased distractibility and poor monitoring as it relates to working memory. De Fockert (2005) reported specific age-related reduction in the ability to disassociate information to be stored from that to be ignored, which accounts for some of the reduction in working

memory performance. Reduction in monitoring abilities in performance on working memory tasks was also reported by Chavtor and Schmitter-Edgecombe (2004). Holtzer, Stern, and Rakitin (2004) observed disproportionate interference with encoding during a dual-task type test in older participants, while Hancock, Lesch, and Simmons (2003), in an ecological study of driving while talking on a phone, observed strong age effects in reaction times to a light change while listening to the phone.

There is some evidence in support of the notion that increased cognitive load has a more taxing effect in older individuals than in younger ones. Bopp and Verhaeghen (2005) concluded from a meta-analysis of the verbal-span tasks that age effect increased from simple memory span to digit backward span to still more complex working memory tasks. However, the findings of increased age related effects in working memory tasks as compared to the simple storage have been inconsistent, and Wilde, Strauss and Tulsky (2004), as well as Hester, Kinsella and Ong (2004), failed to find age-related performance decrements when comparing forward and backward span tasks. This can be interpreted as either indicating general decline in memory span, but a not specific decline in the executive component of working memory, or greater importance of executive control in forward span than has been previously suggested.

Related functions, such as ability to switch between tasks (Reimer & Maylor, 2005; Wecker, 2005) also tend to change through the lifespan, and Reimer and Maylor demonstrated that switch costs on performance declined in children up until age 18, and increased linearly from then on. Finally, an increase in reaction times with age, which could have an impact on task performance, also have been reported consistently (Chavtor & Schmitter-Edgecombe, 2004; Mattay et al., 2006; Waters & Caplan, 2005).

Observed changes in individual components of working memory, versus a general decline, suggest a differential rate and magnitude of functional changes with age. A comprehensive assessment of age-associated changes in working memory would benefit from a systematic study of relevant functions, utilizing several measures instead of a single task.

Age-Associated Neuroanatomical and Neurophysiological Changes

A number of neuroimaging studies have investigated the effects of aging on relevant brain structures. Brickman et all (2006) in an MRI study of age-related changes in regional white matter demonstrated that frontal and temporal white matter volumes were particularly sensitive to age, and the changes were seen across the lifespan and not limited to older adults. Cabeza et al. (2004) in an fMRI study of activation patterns during performance of working memory tasks in older versus younger adults found reduction in hemispheric asymmetry and in activation of sensory areas. Simultaneous increase in activation of prefrontal and parietal areas also was observed, reflecting possible compensatory mechanisms (Cabeza et al., 2004). A blood-oxygen-level-dependent fMRI study by Mattay et al. (2006), demonstrated that when performing within capacity, defined as the same level of task performance in younger and older participants, older participants showed increased activation within frontal areas. On more demanding tasks, when older participants performed below younger ones, the frontal activation in older participants also was reduced as compared to activation in younger participants. This activation pattern suggests compensatory mechanism at work for within-capacity tasks, allowing maintenance of performance level, which breaks down with an increase in demand. A meta-analysis of fMRI and PET studies of working

memory (Rajah & D'Esposito, 2005) suggests that age related changes within prefrontal cortex are not homogeneous, with different change patterns seen in different regions. The authors hypothesized that observed deficits in function in the right dorsal and anterior prefrontal cortex might be compensated by left dorsal and anterior prefrontal cortical regions (Rajah & D'Esposito, 2005).

Temporal lobe gray matter appears to gradualy decline in volume with age (Sullivan et al., 1995). In particular, hippocampal activation patterns appeared to change through the lifespan, starting with younger adults (Adler et al., 2001), with weaker activation observed in older individuals (Adler et al., 2001; Cabeza et al., 2004). Neuroanatomical changes within these regions have been shown to correlate to changes in the corresponding cognitive functions (Lazeron, et al., 2005).

Working memory functioning also closely relates to the dopaminergic activity (Lewis & Miall, 2006) and dopamine receptor agonists have been shown to enhance cognitive performance, including on working memory tasks (Mehta & Reidel, 2006). Chen et al. (2005), in a study utilizing single photon emission computed tomography, demonstrated that performance on working memory measures accounted for the most variance in striatal dopaminergic (D2/D3) receptor density. Both striatal (Chen et al., 2005) and extrastriatal (Inoue et al., 2001; Ota et al., 2006) dopaminergic receptor binding shows gradual decline with age, with most rapid rate of decline (13.8% per decade) observed within the frontal lobes (Inoue et al., 2001).

Findings of continuing anatomic and neurophysiological changes in brain structures involved in working memory function through the lifespan argue against the

stepwise decline in cognitive functioning, suggested by studies comparing groups of young and old individuals, and instead imply a much more gradual process.

Gender Effects in Working Memory

Neuroanatomy of Gender Differences in Working Memory

Gender differences in brain structure are widely documented. Men tend to have larger brain volumes, while the gray-to-white ratio tends to be greater in females (Allen et al., 2003; Gur et al., 1999). Additional differences are observed in activation patterns in response to various tasks, suggesting complex effects of gender on neural structure and function (Bell et al., 2006; Speck et al., 2000).

Gender effects in working memory are not well researched; however, the existent studies support presence of the sexual dimorphism in brain activation patterns within the structures underlying working memory functioning (Bell et al., 2006; Goldstein et al., 2005; Speck et al., 2000). Functional neuroimaging studies examining gender differences in verbal working memory found differences in activation patterns, with women exhibiting greater changes in signal intensity in the middle, inferior, and orbital prefrontal cortices than men (Goldstein et al., 2005). In addition, in an fMRI study of several verbal working memory tests, Speck et al. (2000) found greater activation in the left hemisphere in females, while males showed either bilateral activation or right-sided dominance for prefrontal cortex, parietal cortex and caudate (Speck et al., 2000). Bell et al. (2006) measured blood-oxygen-level-dependent magnitude during the performance of a working memory task with five-digit numbers, utilizing a delayed recall paradigm with a distracter task. The results showed greater mean activation in males than in females, especially in

the right superior parietal gyrus, right inferior occipital gyrus, and left inferior parietal lobe (Bell et al., 2005).

Differences in brain activation are also commonly observed in response to visual spatial tasks. Gur et al. (2000) noted gender differences in brain activation patterns in response to a judgment of line orientation task, with males showing right-lateralized increase in activation compared to females. On a spatial working memory task, males demonstrated increased anterior cingulate activation and greater response in frontopolar cortex than females (Schweinsburg, Nagel, & Tapert, 2005).

Gender Effects in Cognitive Performance on Working Memory Test

Behavioral studies suggest that there is some female advantage in performance on verbal working memory tests (Speck et al., 2000) and on verbal tests with working memory components, such as complex verbal fluency tasks (Maitland et al., 2004). Male advantage has been observed on tests with visual spatial demands (Epting & Overman, 1998), including spatial working memory tests (Schweinsburg, Nagel, & Tapert, 2005). Such selective gender differences in cognitive performance have been observed both in humans (Epting & Overman, 1998; Maitland et al., 2004; Speck et al., 2000) and in primates (Lacreuse et al., 1999), suggesting biological, rather than social bases of this phenomenon. Some evidence of endocrine involvement on cognitive performance, which may be responsible for some of the observed gender differences, was seen in performance of women through the menstrual cycle on spatial tasks (mental rotation), with higher testosterone levels associated with enhanced performance, and higher estradiol levels associated with decreased performance (Hausmann et al., 2000).

The above reviewed evidence suggests a complex relationship between working memory performance and gender differences and appears to suggest strong mediation by the type of stimuli (i.e., verbal versus visual spatial). This would suggest that within the Baddeley model, the gender effects manifest at the level of the visual spatial sketchpad and phonological loop. Possible gender differences at the level of the central executive are not currently addressed in the literature.

A direct and comprehensive investigation of gender effects on both verbal and visual spatial working memory tasks would elucidate the relationship between gender and working memory function beyond the well-documented gender differences on verbal and visual spatial tasks.

Interaction Between Age and Gender in Cognitive Functioning

A comprehensive study of gender effects across the adult life span in working memory functioning has not been undertaken; however, a developmental study with children between ages 6 and 13 years showed significant age or gender interaction effect for accuracy rates on the N-Back task, with the initial girls' advantage on the task diminishing with age (Vuontela et al., 2003). This suggests that working memory functioning changes differently in males and females for at least a part of a lifespan.

Neuroanatomical and Neurophysiological Evidence of Gender Dimorphism in Age Effects

Neuroimaging studies provide some evidence of an interaction between gender and age effects on brain volumes through the life span, from childhood through the advanced stages of aging. Primary volumetric differences between genders are in overall brain volumes, with male brains appearing to be larger than female brains (Gur, 1991;

Larkin, 1998; Murphy et al., 1996), even in young children aged 4-18 (Giedd et al., 1997). According to some studies, this effect is primarily due to differences in white-matter volumes (Passe et al., 1997), although this is not a consistent finding (Nopolous et al., 2000). Age effects in older adults are associated with reduction in gray matter (Passe et al., 1997), and there is some interaction between age and gender in that domain. In children ages 6-17, males show greater gray matter decrease and white matter increase with age than females (De Bellis et al., 2001). In adults, male brains show a steeper regression in volume with age (Gur, 1991; Larkin, 1998; Murphy et al., 1996), and a greater increase in CSF volumes, primarily in the sulcal, not ventricular regions (Gur et al., 1991), possibly reflecting white matter loss. The rate of age-associated decrease appears to increase significantly in older adults, with the changes becoming more prominent in males over the age of 60, and females over the age of 50 (Hatazawa et al., 1982).

Various brain regions appear to change at different rates in men and women, with males showing greater decrease in volume for the left hemisphere, while in women the changes in hemispherical volumes appear to be more symmetrical (Gur et al., 1991). Frontal regions in general show greater volume decline with age than other brain regions (Cowell et al., 1994; Murphy et al., 1996), and the prefrontal cortex, which is involved in working memory functioning, seems to be particularly sensitive to age-associated changes (Raz et al., 2004; Tisserand & Jolles, 2003; Tisserand et al., 2002). Age-related changes within the frontal (Cowell et al., 1994) and prefrontal cortex appear to be gender-dimorphic. Gur et al., (2002) in an MRI study of young adults (18-49 years old) found that with age, men experienced a greater decrease in dorsolateral prefrontal cortex

volume than women. The gender effects in the age-associated changes appear to level off with age, and in older adults (over 70), frontal brain volumes appear to change at an equal rate in both men and women (Coffey et al., 1998; Lemaitre et al., 2005).

Nonfrontal brain regions also show considerable gender dimorphism through the life span, with Murphy et al. (1996), Cowell et al. (1994), and Xu et al. (2000) demonstrating that in addition to frontal lobes, temporal lobe volume appeared to decline more in men than in women. The findings for the hippocampal and parietal regions were inconsistent, with Murphy et al. (1996) reporting greater volume loss in women than in men, while Xu et al. (2000) reported no significant gender differences in the rate of decline for these regions. Coffey et al. (1998) also demonstrated that unlike in the frontal regions, in other brain regions, including parieto-occipital region, strong age-gender interactions, in the direction of greater decline in males than in females, were observed even among the older adults (over 70). Not all brain structures showed age or gender differences, with cerebellar volumes showing neither (Luft et al., 1997). The volumetric changes in the brain were observed not only in the cross-sectional studies, but also in a longitudinal study involving adults aged 59-84, further confirming the validity of such findings (Rettmann et al., 2005).

Brain chemistry, especially within the frontal lobes, also appears to change with age, and vary by gender. Grachev and Apkarian (2000) measured concentrations of N-acetyl aspartate, choline, glutamate, glutamine, GABA, inositol, glucose, and lactate relative to creatine within six distinct brain regions, noting that total concentration of the metabolites was highest within the prefrontal regions, and it appeared to increase with age. Women also demonstrated higher metabolite concentrations than men (Grachev &

Apkarian, 2000). Glucose metabolism in the brain shows both age and gender effects. Age effects manifested in decreases of global and widespread cortical and anterior paralimbic glucose metabolism, and metabolical increases were observed within the cerebellum, thalamus, and occipital areas (Willis et al., 2002). Men had lower global as well as regional cortical and subcortical metabolism than women, but there appeared to be no significant interaction between age and gender (Willis et al., 2002).

Relationship Between Neuroanatomical and Cognitive Findings

Volumetrical changes in the brain anatomy can have an effect on corresponding cognitive functions. White matter volumes in multiple sclerosis patients (Sanfilipo et al., 2006), and in normal controls (Brickman et al., 2006) were associated with mental processing speed and working memory, while gray matter volumes were predictive of verbal memory. Medial temporal lobe atrophy in nondemented stroke patients was associated with deficits in learning, story recall, visual reproduction, constructional abilities, and mental speed (Jokinen et al., 2004). Executive functions, including verbal fluency, complex attention, and working memory, were associated with lower volumes within frontal, temporal, and parietal lobes in patients with multiple sclerosis (Lazeron, et al., 2005). Decline in prefrontal cortex volumes were associated with increase in perseverative errors on WCST (Guning-Dixon & Raz, 2003). In patients with schizophrenia, reduction in dorsolateral prefrontal cortex was associated with poorer performance on tests of attention, reasoning, and executive functions (Seidman et al., 1994; Gur et al., 2000). Immediate memory was also affected by the decrease in prefrontal gray matter volumes in patients with schizophrenia (Baare et al., 1999). Volume of supplementary motor cortex correlates with variability in time estimation in

older adults (Gunstad et al., 2006). Age-related decreases in thalamic volumes were associated with decreased performance on tests of cognitive speed (Van Der Werf et al., 2001). Allen et al. (2006) found that anoxic patients with severe amnesia had a 36% reduction in their hippocampal volumes compared to normal controls, while patients with mild or no amnesia had normal hippocampal volumes. A similar correlation between hippocampal volumes and performance on memory scales was observed by Wang, Liu, and Lin (2006) in patients with mild cognitive impairment. Changes in hippocampal volume associated with normal aging also were correlated with performance on memory tests (Persson et al., 2006; Petersen et al., 2000).

Working memory, as measured with a variant of a dual task paradigm, was significantly correlated with the prefrontal cortex volumes in older adults (50-80 years old); however, this relationship did not hold when corrected for age (Gunning-Dixon & Raz, 2003; Raz et al., 1998). While prefrontal cortex volume failed to predict performance on a working memory test beyond the effects of age on performance, it nevertheless can be argued that the age effects observed in performance on working memory are mediated via age related decreases in the prefrontal cortex volume.

Volumetric changes in brain structures have been shown to have an effect on corresponding cognitive functions in both patient populations and in normal aging. While no studies to date have demonstrated gender dimorphism in age-associated decline in working memory performance, evidence from the neuroanatomical studies involving relevant brain regions (Cowell et al., 1994; Gur et al., 2002; Murphy et al., 1996) lends support to such notion.

Contribution of the Education Level and Overall Intelligence to Working Memory

Additional demographic factors that can influence performance on working memory tasks include level of education and overall intellectual capacity (sometimes referred to as "g"). In a recent meta-analysis of 86 studies relating working memory to the overall intellectual capacity, Ackerman et al. (2005) concluded that the average correlation between working memory factor and g is approximately 0.48. Such a high correlation may indicate either an important role played by working memory in general intellectual functioning, or an interrelation of the two constructs.

Premorbid levels of intelligence have been shown to relate to better survival in Alzheimer disease (Pavlik et al., 2006). Age-related cognitive decline in normal adults has also been shown to be mediated by intelligence, such that individuals with lower premorbid intelligence appeared to decline more than those with high premorbid intelligence (Corral et al., 2006). This effect is consistent with a notion of cognitive reserve (Stern, 2002), which suggests that a higher level of premorbid cognitive functioning may serve as a protective agent, resulting in better prognosis and recovery in conditions such as stroke (Nichols-Larsen et al., 2005) and degenerative disorders (Sanches, Rodriguez & Carro, 2002).

Educational level has been shown to relate to performance on tasks of attention and executive functioning, including working memory (Gomez-Perez & Ostosky-Solis, 2006). In addition, education has been shown to have a "protective" or "buffering" effect on age-associated decline in cognitive performance in general, such that individuals with higher levels of education appear to decline less with age (Meguro et al., 2001; Staff et

al., 2004). Possible mediating effects of education on age-associated changes within working memory have not so far been undertaken.

Purpose of the Current Study

In this study, we undertook comprehensive assessment of age and gender effects on working memory functioning through the adult lifespan. In addition, mediating effects of general intelligence and education on age-associated changes in working memory were examined. The working memory construct was examined as a whole, and separate analyses were conducted to investigate relevant age and gender effects in verbal and spatial working memory, as well as across working memory domains, including simple maintenance, continuous updating, temporal order, and direct mental manipulations.

Significance

Working memory plays an important role in normal functioning. Deficits in working memory are observed across a wide range of psychiatric and neurological disorders, highlighting the importance of this ability for normal functioning. Most notably, working memory impairments are associated with schizophrenia (Barch, 2005; Honey & Fletcher, 2005; Smith, Park, & Cornblatt, 2005), bipolar disorder (Doyle et al., 2005), and major depression (Rose & Ebmeier, 2005). Working memory impairments are also seen in early stages of Alzheimer disease (Germano & Kinsela, 2005) and multiple sclerosis (Morgen et al., 2005), as well as in developmental disorders such as autism (Williams et al., 2005), attention deficit/hyperactivity disorder (Willcut et al., 2005), and learning disabilities (Gathercole et al., 2005). For all its importance in normal day-to-day functioning, relatively little is known about the gender differences in working memory, or how working memory ability changes across the adult life span following adolescence

and preceding the onset of advanced age. Our findings may clarify both the course of normal age-associated working memory changes in younger adults, and identify possible gender-related differences in such course. This study will also comprehensively assess the construct of working memory function by employing a multimeasure battery of tasks, assessing several components of working memory both across the verbal and visual-spatial domains, instead of relying on any single task to measure the construct. Finally, by examining the contribution of general intelligence and levels of education to the course of changes within working memory, we will inspect possible mediating factors affecting functioning in this area.

Hypotheses

This study tests the following hypotheses:

Hypothesis 1. Working memory function will show linear decline across the normal adult life span.

We expect to find a decline in performance on working memory tests with age, based on previous findings of the decline in performance in this area in older adults compared to the younger adults. Based on the previous findings of gradual lifelong changes in the neuroanatomy of relevant brain regions (Adler et al., 2001; Brickman et al., 2006), we expect the performance on the working memory tests to decline linearly and gradually through the adult life span in individuals ages 18 to 55.

Hypothesis 2. Working memory function will differ between genders, with females showing selective advantage on tasks of verbal working memory and males having advantage on tasks of visual-spatial working memory.

Previous research suggests a female advantage on verbal tasks and a male advantage on visual-spatial tasks, and this is expected in the current study. Additional gender differences may be expected in the rates of age-associated changes in working memory performance. Based on evidence from the literature, we hypothesize that there will be a decrease in gender differences with an increase in age.

Hypothesis 3. Estimated level of intelligence will be predictive of higher performance on working memory tasks, and will moderate the effects of age on performance.

Higher levels of intelligence have been shown to be associated with better performance on working memory tasks. We expect to find a strong correlation between estimated level of verbal intelligence and performance on all working memory tests. In addition, higher level of intelligence is expected to serve as a cognitive buffer, reducing the rate of age-associated decline on working memory performance.

Hypothesis 4. Levels of education will be predictive of higher performance on working memory tasks beyond the effect of intelligence level, and will mediate the effects of age on performance.

Education level has been shown to be associated with enhanced performance across several cognitive domains, including working memory, and we expect to find a positive correlation between educational attainment and performance on all working memory measures. Higher educational levels are also expected to serve as a cognitive buffer, reducing the rate of age-associated decline on working memory performance. The effects of education on performance are expected to extend beyond those accounted for by verbal intelligence.

Methods

Participants

Participants were recruited from Internet-based advertisements and from postings at the Columbia Presbyterian medical center and local colleges. Exclusion criteria included unfamiliarity with English language (nonfluent comprehension, reading, and speaking skills), self-reported past or current neurological and psychiatric disorders, and substance abuse. An inclusion criterion was age between 18 and 55 years old. A total of 403 healthy adults have been recruited as part of a larger study of genetics of working memory (Bruder et al, 2005).

Study Group Demographics

The average age of the participants was 30.04 (*SD* = 8.805) years old, with the range between 18 and 55 years old. The average number of years of education was 15.68 (*SD* = 2.191), with a range between 9 and 24 years of education. Of the 403 participants, 174 were male, and 229 were female. Fifty-four percent of the sample (219 participants) was composed of Non-Hispanic Caucasians; 10% (42 participants) were Hispanic; 20% were African American (78 participants); 10% (40 participants) were Asian, and 6% (25 persons) were mixed or other. Demographics of this study group (age, education, sex, and race/ethnicity) are presented in Table 1.

Procedure

Prior to enrolment in the study, all potential participants were screened over the phone for the past or current neurological or psychiatric disorders and substance abuse. All participants gave written informed consent at the time of study enrolment.

Participants were interviewed to obtain demographic information, and participants completed several self-rating scales for assessing psychopathology. Participants were tested with a comprehensive battery of working memory tests and an estimate of general intellectual ability was obtained. Participants received monetary compensation ($40) upon completion of testing for their participation in this study.

Data Collection

Demographic and Clinical Information

Demographic information, including age, gender, and years of education, was obtained by interview with the prospective participant at the time of recruitment. The participants also completed self-rating scales for assessing psychopathology, including the Beck Depression Inventory (BDI-II; Beck et al., 1961) and the Hopkins Symptom Checklist (SCL-90; Derogatis et al., 1974) at the time of the assessment, prior to the administration of the neuropsychological tests.

Neuropsychological Assessment Procedures

A 2-hour battery of neuropsychological measures comprised of four tests of working memory and a measure of vocabulary for estimation of general intelligence were administered to each participant in this study. Testing was performed by trained psychometricians.

The vocabulary subtest is a good correlate of overall IQ on the WAIS-III and was administered to obtain an estimate of general level of intellectual ability (Tulsky, Zhu & Ledbetter, 1997; Wechsler 1997). The working memory tests were chosen to assess the major components of working memory as outlined in Wager and Smith (2003). These

included maintenance of information in memory, continuous updating of information, memory for temporal order, and direct manipulation of information in memory. Measures of both verbal and visual working memory were used. The tests chosen for this study are widely utilized in research on working memory and have been previously discussed in relevant literature.

Tests of Working Memory

The following tests of working memory were administered to all participants:

Spatial Delayed Response (SDR) Test

A computerized version of this test (Lyons-Warren et al., 2004) was used to provide a measure of simple retention of visuospatial information over brief time delays (Park & Holzman, 1992). While the participant fixates on a central cross on a monitor screen, a dot appears for 150 msec in one of 32 possible locations at a 4.5 inch radius from the central cross. During a delay period of 2, 5, 15, or 30 sec, a series of geometric shapes appears in place of the fixation cross, and the participant presses a space bar whenever a diamond shape appears. After the delay, the fixation cross returns and the participant's task is to point to the location on the computer screen where he or she remember seeing the dot. There were eight trials at each delay. The mean error in millimeters (distance between the recalled position and the actual target) was calculated for each delay and averaged across delays. The log of the mean error in millimeters was used as the dependent variable because there were outliers with large errors. This transformation normalized the distribution of scores and reduced outlier influence on statistical analyses.

Word Serial Position Test (WSPT)

A six-word version of the auditory WSPT (Wexler et al., 1998) provided a measure of verbal working memory in a delayed-response paradigm requiring the retention of both item content and serial order. Each trial begins with six nouns spoken with 1 second intervals between words. After a delay of 9 seconds, one of these words is repeated. The participant is instructed to remember the six words in the order presented and to indicate the serial position of the repeated word by pressing one of six keys (labeled 1 to 6) on the computer keyboard. After practice, each participant is tested in 36 trials with a random order of the six serial positions. The outcome measures are the percent correct responses for all serial positions and for each position separately.

N-Back Task

This N-back is a continuous working memory task (adapted from Cohen et al., 1997) that requires participants to monitor a series of letters presented sequentially on a computer screen and to respond when a letter is identical to the one that immediately preceded it (1-back condition), one presented two letters back (2-back), or three letters back (3-back). As each new letter is presented, the participant is required to update his or her temporary storage of previous letters (the number depending on the condition). Sixty letters were presented in each block of items, the 2- and 3-back conditions were each presented twice (1-back performance is generally at or near ceiling levels in non-patient samples; repeating it provides little additional variability in scores). Stimuli were presented for 500 msec, with 2500-msec interstimulus intervals. A total of 12, 20 and 20 targets were presented for the 1-, 2-, and 3-back conditions, respectively. An overall measure of sensitivity (d') for detecting targets and avoiding non-target responses (which

controls for differences in response bias) was computed for all conditions and for 2- and 3- back conditions separately.

Letter-Number Sequencing

The Letter-Number Sequencing subtest from the WAIS-III (Tulsky, Zhu & Ledbetter, 1997; Wechsler, 1997) is an auditory task that requires participants to store and reorder (recite in numerical and alphabetical order) strings of intermingled letters and numbers. The dependent measure is the total number of correct strings. The subtest loads on the working memory factor extracted from among WAIS-III subtests (Tulsky, Zhu & Ledbetter, 1997).

Statistical Analyses

Data Normalization and Construction of a Working Memory Factor.

A log transformation was applied to the raw scores on the SDR test to correct for skewed distribution. Scores on the N-Back, Letter-Number Sequencing and WSPT tests were not normally distributed, reflecting uneven demographical distribution of the sample. Because normality of the original score distribution is not an assumption for the regression analysis, these distributions were left un-corrected for ease of the interpretation. Distributions of the residuals were normally distributed; however, given the large sample size, even non-normally distributed residuals were not expected to present problems with the interpretation of either significance tests or confidence intervals (Cohen, Cohen, West & Aiken, 2003).

Following this normalization procedure, we computed standardized scores (*z* scores). To develop standardized scores, means and *SD*s for the sample were calculated for each measure. The sample mean was subtracted from the raw test scores and then

divided by the sample standard deviation. This procedure was adopted because there is no published normative data for several tests, while the normative data available for the WAIS-III subtests corrects for the effects of age, which is one of the variables of interest. Finally, normative groups are demographically dissimilar with respect to the current study population.

A principle component analysis (PCA) was performed on the correlation matrix of overall accuracy scores for the four working memory tests to determine whether performance across these tests could be characterized in terms of a single or multiple working memory factors.

Data Analysis

Hierarchical multiple regression analyses were used to determine the magnitude of the gender, age, intelligence level and education effects, as well as selective interactions on each of the tests and extracted factors. Multiple regression analysis was chosen because a combination of categorical and continuous variables were used in this study, and multiple regression analysis has been shown to be both better suited and more sensitive for this type of analysis (Cohen et al., 2003). To determine whether the linear model was the best fit, a curve estimation analysis was performed. Linear representation was the best fit for all tests, with significance levels exceeding $p < 0.01$ (See Table 2). The order in which variables were entered into the hierarchical regression was guided by the primary goals of this study, with considerations for control of the relevant covariates.

Hypotheses 1 and 2: Effects of Age and Gender on Working Memory.

We hypothesized that working memory functioning will decline linearly between the ages of 18 and 55. To test this hypothesis, we used multiple linear regressions to

examine the main effect of age on performance on each of the working memory measures, as well as on the working memory factor score. The age variable was centered (converted to deviation scores so that each variable has a mean of zero) to avoid problems with multicollinearity (Cohen et al., 2003).

To test the hypothesis that there are selective gender advantages on performance of verbal and visual-spatial tests, a main effect of gender on performance on each task was examined. For this analysis, the gender variable was numerically coded, with 1 signifying male gender and 0 signifying a female gender. A separate analysis was conducted for each test.

We also hypothesized that gender-related differences in performance would diminish with age. This hypothesis implies an interaction between age and gender effects. An interaction term was made available for the analysis by creating a new independent variable that is a cross-product of two original independent variables (age and gender), and including it with the originals in the analysis. A significant interaction would be interpreted to signify that the relationship between gender and performance on working memory measures varies as a function of age. We expected to find smaller gender advantage in older individuals than in younger ones.

Hypotheses 3 and 4: Effects of General Intelligence and Education on Working Memory:

To test our hypothesis that general level of intelligence will be predictive of a higher level of performance on working memory tests, we examined the main effect of Vocabulary test scores on performance on each of the tests and on the working memory factor. The raw scores on this test were converted to *z* scores, and these were used in the analysis. We did not use the scaled scores for the Vocabulary subtest because they correct

for several relevant demographic variables and do not provide an accurate representation of our sample. The vocabulary scores were entered into the regression after the age, gender and age-gender interaction, thus producing a demographically-corrected measure of the effects of general intelligence on working memory performance.

We examined our hypothesis that a higher level of intelligence would serve as a buffer against effects of age on working memory performance by analyzing the interaction effects between age and Vocabulary scores for each test and for the working memory factor as a whole.

Post-hoc procedures were conducted to follow-up significant interactions in order to compare the difference in relationship between age and working memory performance as a function of intelligence. The procedure for post hoc tests is outlined in Aiken and West (1991). This procedure involves the computation of two conditional group variables for intelligence level, one in which the low intelligence group is defined as those with Vocabulary *z* scores lower than 1 *SD* below the mean and one in which the high intelligence group is defined as those with Vocabulary z scores above 1 *SD* from the mean. One regression generated the slope for the lower intelligence group and a second regression generated a slope for the higher intelligence group. These slopes were then used to plot regression lines on the basis of two equations, substituting high (1 *SD* above the mean) and low (1 *SD* below the mean) values for Vocabulary *z* scores in each equation.

To test our hypothesis that a higher level of education will correspond to better performance on working memory tests, we examined the main effect of education on working memory performance. In order to assess the effects of education beyond those

accounted for by general intelligence, we entered the education variable after the Vocabulary variable into the stepwise regression, thus accounting for the possible variance attributable to the general intelligence before examining the education effects. The education variable was centered (converted to deviation scores so that each variable has a mean of zero) to avoid problems with multicollinearity (Cohen et al., 2003).

We examined possible buffering effects of educational level on age-related decline in working memory performance by exploring the interaction between education and age variables. The interaction effects were examined separately for each of the tests and for the working memory factor as a whole.

Results

Generalizability of Results

Study group demographic characteristics are represented in Table 1. Overall, the sample was positively skewed with regard to the age variable, with more of younger persons taking part in the study (mean age of participants was 30 years old). The study group was also negatively skewed with regard to the education and estimated intelligence measures. Average level of education was college (16 years), and average vocabulary score, used as index of intelligence, was one standard deviation above the published norms (13).

Of the working memory measures used in this study, only the Letter-Number Sequencing subtest of WAIS-III has been previously normed. This study group performed on average one standard deviation higher than the published average score. This performance is consistent with the negative skew seen on other cognitive performance indicators in this study—the educational levels and estimated IQ.

Demographic characteristics split by gender are represented in Table 1. The two groups did not differ significantly in age ($t = 1.753$, $p = 0.08$, $df = 401$) or amount of education ($t = -1.18$, $p = 2.38$, $df = 401$). The two groups were also compared on their performance on the Vocabulary subtest of WAIS-III, which was used as an estimate of intelligence level. The mean Vocabulary scaled score was 12.80 (SD 3.18) for the males, and 13.36 (SD 3.22) for the females. The two means were not significantly different ($t = -1.733$, $p = 0.084$, $df = 402$). Males and females were demographically similar enough to allow valid comparisons between their respective performances on working memory tasks.

Data Reduction.

Raw Data

Means and standard deviations for participants' scores on the four working memory tests are represented in Table 3. When compared to the maximal test score values, it can be seen that a ceiling effect was not operative.

As shown in Table 4, we examined the normality of the test scores' distribution using Kolmogorov-Smirnov tests. All raw test scores were significantly abnormal in distribution: test scores were negatively skewed and some displayed leptokurtis and platykurtis. In order to normalize the distributions, a logarithmic correction was applied to the SDR distribution. N-Back, Letter-Number Sequencing and WSPT scores were not correctable by traditional transformations, and these test scores were used with no additional transformation in the regression analyses in order to preserve the original scale and ease interpretation.

Working Memory Factor

Principle component analysis was performed on the correlation matrix of the raw accuracy scores on the four working memory tests to determine whether performance across these tests could be categorized in terms of a single or multiple working memory factors. Only one factor was sufficiently common across tests to yield an eigenvalue greater than 1 (i.e., 2.214, 55.4% variance accounted for). All tests were weighted approximately equally (loading for SDR = 0.62; WSPT = 0.79; N-Back = 0.78; Letter Number Sequencing = 0.77), lending support to a notion of a single factor underlying working memory test performance.

Working memory factor values were converted to *z*-scores by calculating a mean and standard deviations of the factor distribution, subtracting the mean value from each score, and dividing the result by the standard deviation. The assumption of a normal distribution of the working memory factor was examined using the Kolmogorov-Smirnov test. The distribution was not significantly different from the normal distribution ($p = 0.106$).

Inter-correlations of test scores among each other and with the working memory factor are presented in the Table 5. While correlation coefficients of individual scores with the working memory factor score ranged from 0.59 to 0.79, inter-correlations between the individual tests were lower, but still significant, ranging from 0.30 to 0.50, accounting for a relatively smaller proportion of variance, and suggesting that the tests measured somewhat distinct aspects of working memory.

Demographic Influences on Working Memory Performance: Multivariate Model

The impact of demographic variables on performance on working memory tests was assessed using separate hierarchical linear regression analyses for each test, and for the working memory factor. The test and factor scores were entered into the analysis as dependent variables. Demographic variables were entered as independent variables. The assumption of normality of the distribution of residuals for each test and for the Working Memory Factor was examined using Kolmogorov-Smirnov test. The results are presented in Table 6. The distributions were not significantly different from the normal distribution, thus satisfying the assumption of normality of the residuals; however, for large sample sizes, such as the one presented here, even non-normally distributed

residuals would not have had a significant effect on the significance tests or confidence intervals (Cohen et al., 2003).

Gender, a categorical variable, recoded with 1 representing males, and 0 representing females, was entered into the analysis first. Because the males and females in the study did not differ significantly with respect to the demographics, there was no need to control for such variables as age, education and estimated intelligence in examining group differences. Age was entered as a continuous variable after the gender, controlling for possible sex differences in calculating the age-related changes in performance. In order to test our hypothesis that age effects will differ between the genders, an interaction term was added next. The interaction was made available for the analysis by creating a new independent variable that is a cross-product of two original independent variables (age and gender).

The general level of intelligence, estimated by the scores on the Vocabulary subtest was entered into the regression after age and gender. Level of education was entered after the Vocabulary scores. This order of variables allowed us to control for the effects of demographic variables of age and gender on working memory performance prior to considering the effects of general intelligence and education. Given the negatively skewed age distribution, this may be of particular importance. Level of education was entered into the equation after the Vocabulary scores to allow for examination of the effects of education beyond natural ability. To test our hypotheses that levels of intelligence and education can have buffering effects on the age-related decline in working memory, two interaction variables consisting of the cross-products of age, with vocabulary and education, respectively, were then entered into the regression.

Two three-way interactions of age, gender and vocabulary and age, gender and education were entered as a final step, to determine if any buffering effects of general intelligence and education on age-related changes in functioning may be gender specific.

For all analyses, vocabulary scores, education, and age variables were centered (converted to deviation scores so that each variable has a mean of zero) to avoid problems with multicollinearity (Aiken & West, 1991). Results of the final regression model for each test and for the working memory factor are presented in Table 7. Significance was judged at a value of $p < 0.05$ for all analyses. The significant findings are summarized in Table 8.

Age and Gender Influences on Working Memory

We hypothesized that performance on all working memory tests and on the working memory factor would decline linearly with age. The gender effects were expected to be in the direction of a female advantage on measures of verbal working memory and male advantage on a test of spatial working memory. The interaction between age and gender was expected to be in the direction of declining gender-related differences with increased age.

The main effect of age was statistically significant for all tests and for the working memory as a whole, consistent with our hypothesis of gradual decline in working memory performance with age. The regression lines representing age-associated changes for all tests and for the working memory factor are presented in Figure 1. The corresponding scatterplots of the *z*-scores for each test and working memory factor scores are represented in Figures 1a through 1e. The summaries of the raw scores for all tests and for the working memory factor across different age groups are presented in Table 10.

The regression slopes for each of the tests were compared to that of the working memory factor in order to assess whether age had a significantly greater effect on participants' performance on any of the individual tasks when compared to the overall working memory factor. This was accomplished by examining the interaction effect of the type of the test as compared to the working memory factor and age. Four new variables, one for each task, signifying the interaction terms between variable type and age, with the working memory factor serving as a comparison variable, have been entered into the regression analysis, following the procedure described in Cohen et al. (2003). The results of this analysis indicate that performance on the Letter-Number Sequencing task was significantly less affected by age-associated changes than the working memory factor (ß = 0.062, $p = 0.031$).

The main effect of gender was significant only for the Spatial Delay Recall task (ß = 0.103, $p = 0.04$); (Model $R^2 = .120$), with males performing better than females. Further probing, consisting of calculating separate regression equations for each difficulty level of the test (2-second, 5-second, 15-second and 30-second delays), revealed that gender was a significant predictor of performance only for the 5-second and 15-second conditions, and not for the 2-second or 30-second conditions (see Table 10 for a summary of the gender effects across different levels of SDR). This finding is independent of the floor or ceiling effects, which were not contributory, and suggests that the observed gender advantage is most relevant on tasks that depend more heavily on visual spatial working memory (5-second and 15-second delay tasks), than on pure visual-spatial skills (2-second delay condition) or on longer retention intervals (30-second delay condition). Main effect of gender was not significant for the verbal working memory tasks, or for the

working memory factor as a whole. The age-gender interaction was not significant on any task or for the working memory factor.

General Intelligence and Education Influences on Working Memory

We hypothesized that performance on all working memory tasks and on the working memory factor would correlate positively with particpants' level of education and with estimated general intelligence. These effects would be significant after accounting for the effects of age on performance, and the influence of education on working memory performance was assessed after correcting for the general level of intelligence. The interaction between general intelligence and age effects and between education and age effects was expected in the direction of buffering of expected age-associated decline.

The main effect of generalized intelligence was significant across all tests and for the working memory factor. As expected, greater levels of estimated intelligence were associated with better performance on all working memory measures. The summary of the raw scores for all tests and for the working memory factor across different levels of estimated general intelligence are presented in Table 11. Analysis of the inter-correlations between the scaled scores on the vocabulary subtest, representing estimated intelligence, and performance on the working memory tests and factor scores are presented in Table 12. Correlation coefficients for the estimated intelligence and working memory measures ranged from 0.222 for the scores on the SDR to 0.505 for the working memory factor. These values are similar to those reported in the literature for the correlations between working memory and general intelligence (Ackerman, Beier & Boyle, 2005).

The regression slopes for each of the tests were compared to that of the working memory factor in order to assess whether intelligence is a significantly greater predictor of performance on any of the individual tasks than for the overall working memory factor. This was accomplished by examining interaction effects for type of the test, as compared to the working memory factor and vocabulary *z*-scores. Four new variables, one for each task (signifying the interaction terms between variable type and general intelligence, with the working memory factor serving as a comparison), were entered into the regression analysis following the procedure described in Cohen et al. (2003). The results of this analysis indicated that the effects of general intelligence on performance on the SDR were significantly lower than on the working memory factor as a whole (ß = -0.111, $p < 0.001$). All other tests were not significantly different from the working memory factor with regard to the influence of estimated general intelligence on test performance.

The interaction between age and general intelligence was significant for the N-Back task (ß = 0.138, $p = 0.045$) but not for any other tests or for the working memory factor. The presence of the significant interaction informed us that the relationship between the predictor (Age) and the outcome (N-Back score) differed depending on the level of the moderator (general intelligence). It was then necessary to follow-up this interaction with post-hoc procedures in order to test our hypothesis that higher intelligence would minimize the age-associated decline seen in performance on the N-Back task.

Post-hoc probing of the significant moderator effect was conducted as outlined in Aiken and West (1991). This procedure allows one to generate two simple slopes, one

slope depicting the relationship between the predictor (i.e., age) and the outcome (i.e., N-Back score) at a low level of the moderator (i.e., intelligence), and the other slope depicting this relationship at a high level of the moderator. This approach also permits one to test whether either of the simple slopes is significantly different from zero. To accomplish this, two new conditional group variables for performance on the Vocabulary test were computed, one in which the low general intelligence group was defined as performance of 1SD below the mean Vocabulary score and one in which the high general intelligence group was defined as performance of 1SD above the mean Vocabulary score. We then ran two regression analyses incorporating each of these new variables. One regression analysis generated the slope for the lower estimated intelligence group (1 SD below the mean; Vocabulary SS score equivalent = 10), and a second regression generated a slope for the higher estimated intelligence group (1 SD above the mean; Vocabulary SS score equivalent = 16). Post-hoc regression analyses revealed that for participants with lower estimated intelligence (i.e., Vocabulary Z Score < -1.00), more advanced age was significantly associated with lower scores on N-Back test (ß = -0.496, $p < 0.001$). However, for participants with higher estimated intelligence (i.e., Vocabulary *z* Score >1), the association between age and N-Back score was not significant (ß = -0.247, $p = 0.083$). The general level of intelligence moderated the relationship between scores on N-Back and age, such that at lower levels of general intelligence, participants showed greater decline in performance on N-Back test with age than did participants with higher level of intelligence. The observed difference in the rate of age-associated decline is statistically significant, as is evident from the significance of the age-general intelligence interaction effect. Figure 2 shows the slopes of the regression lines for high

and low estimated levels of intelligence, 1SD above and below the mean, respectively, and reflects the relationship described above.

Because our sample was negatively skewed with respect to general intelligence and because the average Scaled Score for the Vocabulary subtest in this sample was 13, we re-calculated selected regression equations to estimate the relationship between N-Back scores and age for those participants of average intelligence (SS = 10), and for participants who fell one *SD* above and below this mean (*SS* = 7 and *SS* = 13 respectively). The resulting regression lines are represented in Figure 3. The relationship remains as mentioned above.

The main effect of education was computed after accounting for the effects of general intelligence. Significant results were observed for the working memory factor as a whole (ß = 0.109, $p = 0.015$) and for N-Back task (ß = 0.099, $p = 0.038$), but not for other tests. There was no significant interaction between education and age, counter to our predictions. The summary of the raw scores for all tests and for the working memory factor across different levels of education is presented in Table 13.

Discussion

Summary of Regression Findings

The current study examined the relative contributions of age, gender, general level of intelligence and educational attainment on working memory functioning in normal adults. A comprehensive battery of four verbal and visual spatial working memory tests was utilized for this study, and a common working memory factor was derived from the obtained scores. Age emerged as a significant predictor of working memory functioning on all individual measures and for the working memory factor. Working memory showed a linear decline with age in normal adults. General intelligence was also found to be a significant predictor of performance across all working memory measures, and for the working memory factor, and higher levels of estimated intelligence were associated with better performance on working memory. Gender was found to be a significant predictor only on a test of visual spatial working memory, with males performing better than females. Education was a significant predictor of performance on the working memory factor as a whole, and on a verbal continuous updating task, after controlling for age, gender and general intelligence. Higher levels of education corresponded to enhanced performance on these measures of working memory.

General intelligence was also found to be a mediating factor for the effects of age on the performance of the N-Back task, a test of continuous updating, such that the age associated decrements were more pronounced in those with lower estimated levels of intelligence. In individuals with high estimated intelligence, age was found not to be a significant predictor of performance.

Age Effects on Working Memory

As expected, age was found to be a significant predictor of performance on working memory tasks. Performance on all measures showed gradual and linear decline with age. Working memory functioning declined at a rate of one quarter to one third of a standard deviation every decade, dependent on the measure. Performance on the Letter-Number Sequencing test, which examines direct manipulation within working memory, declined significantly less with age than overall working memory factor, highlighting the variations in functions assessed by different tasks.

Gender Influences on Working Memory

As was hypothesized, gender was a significant predictor of working memory performance on the test of visual-spatial working memory, Spatial Delayed Recall test. As expected, males performed better than females on this task. However, contrary to our predictions, gender was not a significant predictor of the performance on any of the verbal working memory tests. Based on the previous findings in the literature of a female advantage on verbally mediated cognitive tasks, including tests of verbal working memory (Speck et al 2000), we expected to find a female advantage on performance of the WSPT, N-Back, and Letter-Number Sequencing tests. The tests used by Speck et al. (2000) were different from those used in this study (four tasks adapted from California Computerized Assessment Package, including single letter versions of 1- and 2- Back task and sequential single digit number (1- and 2-increment) tasks), which may help explain this discrepancy in findings. The tests utilized by Speck were continuous updating tasks, with the most challenging condition being 2-back, which relied more heavily on the attentional component of the test. In our battery, the continuous updating

task consisted of the combined performance on 1-, 2-, and 3-Back number tasks, and was more complex and presumably more taxing on working memory than the 1-, and 2-back tasks used by Speck. In addition, our battery included verbal working memory tests assessing memory for temporal order (WSPT) and mental manipulation within working memory (Letter-Number Sequencing). No other study investigating gender differences has used a set of tests similar to ours, but it is possible that the female advantage in verbal performance is more relevant on tasks that rely more on attention and general verbal abilities rather than actual verbal working memory.

The working memory factor as a whole was not influenced by gender. This suggests that overall working memory functioning is similar in males and females. This finding could also have been influenced by a relatively larger loading of the verbally mediated tasks, which, in contrast to the visual-spatial task, do not appear to be gender sensitive.

We hypothesized that gender effects would diminish with age. On the task of visual-spatial working memory, the age-gender interaction was not found to be significant; however, the findings were in the predicted direction. Since no gender differences were found for the remainder of the working memory tasks, this hypothesis has not been confirmed for verbal working memory. Overall, there were no gender differences in the rate of age-associated changes. Because there is some evidence for endocrine mediation of cognitive functioning in both animal (Sutcliffe, Marshall & Neill, 2007) and human (Hausmann et al., 2000) studies demonstrating fluctuation in cognitive performance as a function of hormonal levels, the lack of findings of the gender-mediated

differences in the age-associated changes might reflect the relatively similar endocrine effects in males and females during this period in life.

The Influences of General Intelligence on Working Memory Performance.

As expected, levels of estimated intelligence showed a strong positive relationship with performance on working memory as a whole, as well as on all measures administered in this study. Intelligence was the strongest predictor of the working memory factor scores and of the performance on the Letter-Number Sequencing and Word Serial Position tests. Off all tests, intelligence was least associated with the performance on the Spatial Delayed Recall. This may reflect the fact that we used a verbal measure (Vocabulary subtest of the WAIS-III) to estimate intelligence; however, this association was still statistically significant.

While there is a strong observed relationship between working memory performance and our estimates of general intelligence, the two constructs do not appear to be one and the same. Analysis of intercorrelations between scores on the working memory tests and performance on the Vocabulary subtest revealed correlation coefficients ranging from 0.222 for Spatial Delayed Response test to 0.436 for Letter-Number Sequencing, while the working memory factor correlated with the Vocabulary scores at 0.505. This suggests that there is a large proportion of variance that the two measures do not share. In a meta-analysis of studies that relate working memory to intelligence, Ackerman, Beier and Boyle (2005) observed similar correlations. The authors concluded, after examining a large number of relevant variables, that this relationship does not constitute unity of two paradigms, because the two constructs only share approximately 25% of variance. Criticisms of Ackerman et al. by Kane, Hambrick

and Conway (2005) and Oberauer et al (2005) suggest that their analysis underestimates the true relationship between general intelligence and working memory, and that working memory may explain up to 50% of the variance in general intelligence scores (Kane, Hambrick & Conway, 2005; Oberauer et al., 2005). However, such criticism does not imply that working memory and intelligence are isomorphic, instead proposing that working memory may be an explanatory construct for intelligence (Oberauer et al., 2005).

Intelligence levels also moderated the effects of age on performance of the N-Back task, with lower levels of intelligence associated with a steeper rate of age-associated decline. At one standard deviation above the mean in the current sample (corresponding to two standard deviations above the mean in the WAIS-III normative sample), the age–associated decline in performance on the N-Back was not statistically significant. This implies that in persons with very high levels of intelligence, age associated changes in continuous updating are negligible within the time frame between ages of 18 and 55. Intelligence level did not appear to moderate age-associated changes on any other measure, or on the working memory factor as a whole, suggesting a complex relationship between various components of working memory, age and intellectual capacity.

Education and Working Memory Functioning.

Education emerged as a significant predictor for scores on the working memory factor and for performance on the N-Back test of continuous updating. Higher levels of education were associated with better performance on the N-Back task and with higher scores on the working memory factor, even after correction for general intelligence. This

is consistent with our predictions, and further confirms the importance of education in cognitive functioning (Gomez-Perez & Ostosky-Solis, 2006; Meguro et al., 2001; Staff et al., 2004), above and beyond the effects of general intelligence.

Contrary to our expectation, education was not a significant predictor for the performance on WSPT, Letter-Number Sequencing test, or Spatial Delayed Response test. We also failed to find an interaction between level of education and age effects, suggesting that in our sample education did not serve as a protective factor for age-associated changes in working memory function. It is possible that our use of Vocabulary scores to estimate intelligence has diminished the observed values for the effects of education, since vocabulary is highly sensitive to educational level, and the main and interaction effects of education were calculated after correcting for general intelligence. In addition, past research suggests that there might be ceiling effects to the protective properties of education for cognitive functioning. In a longitudinal study of normal adults, educational levels below 8th grade were associated with higher cognitive decline with age; however, educational levels beyond 9th grade were not associated with additional reduction in the rate of decline (Lyketsos, Chen & Anthony, 1999). Because our sample largely consisted of persons with higher than a high school level of education, our failure to observe the buffering effects of education on age-associated changes in working memory performance may be due to the low threshold for benefit of education.

Assessment of Working Memory Function –Differences Between Various Aspects of Working Memory.

The results of the principle component analysis demonstrated the existence of a single factor underlying all four working memory tests, lending support to the notion of

working memory as a cohesive cognitive function. The working memory factor appeared to be susceptible to the effects of age and also was influenced, in a similar fashion, by level of general intelligence. Educational level appeared to have a positive effect on working memory but gender differences were not found to be significant in this sample. While positively correlated with the working memory scores, neither education nor vocabulary appeared to have a buffering effect for age-associated changes, as is evident from the lack of significant age or education and age or intelligence interactions. However, the exact degree to which various demographic variables contributed to the performance on individual measures varied between tests, suggesting variations in mechanisms underlying the performance on different working memory tests.

Verbal Versus Visual-Spatial Working Memory

While age and general intelligence appeared to affect performance on verbal and visual-spatial working memory in similar ways, only visual-spatial working memory, and not verbal working memory, showed a gender effect. Visual-spatial working memory, assessed by the Spatial Delayed Response Task, appeared to be better in males than in females. This effect appears to be independent of the well-documented male visual-spatial advantage (Epting & Overman, 1998; Gur et al., 2000; Lacreuse et al., 1999). No significant gender differences were observed on the 2-second delay condition, which relies heavily on attention (ability to attend to the presented stimulus) and general visual-spatial skills (ability to point on the screen to the location of the stimulus), but not on actual working memory (ability to hold the information within active memory store for a short period of time). Similarly, no gender differences were observed on the 30-second delay condition, which taxes more of one's actual memory capacity than working

memory per se. Significant gender effects were obtained only for the 5-second and 15-second delay conditions, which rely primarily on actual working memory by requiring the participant to hold the information "online" for a brief period of time.

Differences by Type of Process

The tests chosen for this study were selected to measure various aspects of working memory, including continuous updating, memory for temporal order, and direct manipulation within working memory. Previous literature reports differences in neurophysiological processing associated with these functions, involving diverse brain structures and patterns of activation in response to tasks measuring different aspects of working memory (Wager & Smith, 2003). Similarly, we found that while age and general intelligence were significantly associated with performance on all tests, the degree to which various tasks were affected by these demographic variables varied from task-to-task. Additional demographic variables, gender and education, had only a selective effect on performance on some and not other working memory tests, further supporting the notion of different mechanisms involved in performance of these tests.

Maintenance of Information in Memory

Maintenance of information in memory was assessed with a visual delayed match-to-sample task, Spatial Delayed Response. This function appears approximately as susceptible to the effects of age as the working memory factor, and tends to decline at an approximate rate of one quarter of standard deviation per decade between the ages of 18 to 55. Performance on the Spatial Delayed Response task was significantly less related to general intelligence than other functions. This may be an artifact of the fact that this test is primarily visual, while the IQ estimate was derived from a verbal measure

(Vocabulary). However, in the literature, short-term memory is also less associated with the intelligence measures than working memory (Ackerman, Beier & Boyle, 2005). This suggests that maintenance aspect of working memory, which may be closer to the construct of short-term memory in that it involves a minimal amount of manipulation within the memory store, may in fact be less influenced by general intelligence than other aspects of working memory.

Continuous Updating

Continuous updating was assessed with the N-Back Task. Performance on this task showed relatively greater age-associated changes than on other tasks. This may relate to the heavy reliance on sustained attention placed by this task. Previous research demonstrates that distractibility is an age-sensitive function, with older individuals demonstrating significantly greater susceptibility to distraction than younger ones (Lustig, Hasheer & Tonev, 2006). It may also be reflection of the speeded nature of this task. Speed of processing also tends to show a significant age-associated decline, affecting a wide range of cognitive domains (Lindenberger, Mayr & Kliegl, 1993).

The effects of age on continuous updating were modulated by intelligence levels, such that in persons with relatively lower levels of estimated intelligence the age-associated changes were statistically significant, while in those with high estimated intelligence the age-associated decline was not significant. In addition, continuous updating was the only aspect of working memory that showed improvement with increased levels of education. These findings could be interpreted as evidence of cognitive reserve mediation in working memory functioning, because increase in cognitive functioning that is reflected in higher educational attainment is associated with

the corresponding increase in performance on the N-Back test. Alternatively, since the causality of this relationship is difficult to establish, this can indicate the importance of continuous updating in intellectual and educational achievement.

Memory for Temporal Order

Memory for temporal order was measured with the Word Serial Position Test. For this measure, of all demographic factors examined, estimated level of intelligence was the strongest predictor of performance. While this may be in part due to the verbal nature of the measure that we used to estimate intelligence (Vocabulary), it is unlikely, because the words used in this test are very common, and are not likely to present a challenge even to the less articulate participants. It is also possible that memory for temporal order is closely related to memory span. Presumably, greater memory span could contribute to a larger fund of knowledge by allowing greater amount of information to be encoded into a long-term memory over time, resulting in an observed correlation with the measures of general knowledge. The relationship between the WSPT scores and those on the Vocabulary test is likely based on common factors contributing to both measures, rather than causative (greater general intelligence-greater working memory).

Accuracy rates examined as function of serial position on WSPT are presented in Table 14. There is an expected position effect, with highest accuracy rates achieved for the words presented in the first and last positions within the sequences. The effect of general intelligence(vocabulary) on WSPT performance tended to be greatest for most difficult serial positions (third and fourth positions) where accuracy was least, although relative differences in slopes were not significant Age effects were significantly stronger for the items presented later in the sequence (particularly in the fourth and fifth positions)

than for those presented earlier in the sequence, suggesting that primacy effect is relatively less susceptible to age associated decrements than recency effect.

Direct Manipulation in Working Memory:

Mental operations within working memory were assessed with the Letter-Number Sequencing test. Performance on this task showed significantly less decline with age than other measures, at just under one fifth of a standard deviation per decade. This function appears to be most closely related to the estimated intelligence in a pattern similar to performance on the WSPT. While both the WSPT and Letter-Number Sequencing assess order memory, Letter-Number Sequencing places greater demands on executive systems, because participants have to remember not only the information provided, but also mentally reorder that information. Relatively lower age-associated changes in performance on this task suggest that the higher level executive functions are relatively more preserved within the adult span. This finding is consistent with that of several previous studies (Hester, Kinsella & Ong, 2004; Wild, Strauss & Tulsky, 2004) that failed to find a significantly greater decrease on tasks of working memory with a strong executive component versus those that rely primarily on maintenance.

Previous findings by Bruder et al. (2005) and Wager and Smith (2003) suggested different genetic and neuroanatomical bases underlying performance on various working memory measures. Current findings provide further support for the notion that a number of different and separate processes comprise the working memory system, as is evident from variances in demographic influences on these processes. Examining working memory functioning by process type offers valuable insights into the mechanisms underlying this cognitive ability. Current findings suggest that observed age-associated

changes in working memory are likely related to decreases in mental storage capacity and processing speed. The actual ability to manipulate information within the memory store remains relatively stable between the ages of 18 and 55.

Generalizability of Results

The participant group was examined with regard to the demographic factors to determine whether study results could be generalized to other populations. Our participants differed from the general population in several relevant aspects. The age distribution of the study cohort was positively skewed, with more younger than older participants taking part in this study. This likely reflects the relatively high number of students enrolled in this study, as testing took place during work hours. In addition, because part of the recruitment was accomplished via the Internet, younger and more computer-savvy participants were likely to respond to the ads. However, given a large sample size and reasonable number of participants in each age group, this skew is not expected to distort the results of the regressions, suggesting valid results.

The racial background of the participants was broken down as follows: 54% Caucasians (219 participants); 10% Hispanic (42 participants); 20% African American (78 participants); 10% Asian (40 participants), and 6% mixed or other (25 persons). This breakdown was similar to that of the residents of this area, with the exception of the Hispanic participants, who were underrepresented in this study. According to the US census, Hispanic participants constitute 27% of people living the NY metropolitan this area, while only 10% of our study group was Hispanic. Only fluent English speakers were recruited into this study, possibly limiting Hispanic participants from enrolling. Given the large size of the study group and its substantial diversity, with all major

ethnicities represented, we believe that the results of this study are valid and can be generalized to the general population of US residents.

All study participants completed at least 9 grades of education, and the majority completed or was enrolled in college. In our sample, 97 % had completed high school, and 65% had completed college. This is significantly higher than the census for New York City, where 86% were high school graduates, and 30% had at least a college education. However, given that there was a significant number of participants without a college education, and some with less than 12 grades of education, we believe that the results of this study can be generalized to at least 86% of the local population (those with at least a high school education). Overall, the results of this study may more validly represent people with at least a high school diploma than those with less than 9 years of education.

Strengths of the Current Study

The current study systematically assessed demographic influences on working memory using several working memory tests, instead of relying on generalizations drawn from a single measure. The relative lack of clarity in the definition of working memory, combined with a wide range of highly diverse tasks claiming to assess it, make the use of a single assessment instrument of limited value in estimating the underlying function. The use of a battery of working memory tasks allowed both a more accurate estimate of working memory functioning as a whole, and permitted examination of the demographic influences on individual functions within the working memory construct.

Our large sample size permitted a valid study of the working memory functioning in the normal adult population. Despite some limitations of our sample, it was quite

heterogeneous, with participants enrolled from a range of racial, ethnic and educational backgrounds; we believe our is a valid representation of the large New York City population.

In terms of statistical methodology, examining the effects of age, general intelligence, and education as continuous predictor variables in the multiple regression analysis is more informative than performing an analysis of variance, since this approach uses all of the information available in the predictor variables to provide direct estimates of the effect sizes and percent of variance accounted for (Aiken & West, 1991). Researchers have frequently utilized median splits or taken upper and lower quartiles for their variables when using analysis of variance. While splitting a continuous variable is common practice in research, this approach results in the loss of information and reduces the power of the statistical test.

Limitations of the Current Study

There were several limitations to this study:

1. Higher than average levels of education and estimated intelligence: Participants in our study had completed at least 9 years of formal education, and the average estimated intelligence was one standard deviation higher than the average adult in the standardization sample. While we were able to detect the effects of intelligence on working memory measures, the effects of education might have been obscured by a constricted range of education in our participants. Ardila et al. (2000) reported that in illiterate participants in Mexico, maximal scores on a number of cognitive domains, including working memory, were observed not in the younger adults, but in the older group. This pattern held for participants with up to 4 grades of education, and was

reversed in more educated participants (Ardila et al.). The rate of age-associated decline is also reported to be different in persons with lower levels of education than in those with higher education (Ardila et al.; Lyketsos et al., 1999); however, education-mediated decrease in cognitive decline was not significant beyond 9 grades of education (Lyketsos et al.). Because our participants had a minimum of 9 grades of education, we did not observe a robust effect of education, although higher educational levels were still associated with stronger performance on some measures.

2. Younger cohort: The age of the participants in this study was kept under 55 in order to examine changes in working memory functioning prior to the onset of changes associated with aging. While this provides an estimate of age-associated changes in working memory functioning within a portion of the life-span, it does not allow for the examination of the changes through the entire life-span. Use of a compatible testing battery to assess working memory functioning both in younger and older adults would make it easier to understand the changes that take place as part of the normal aging process. A comprehensive assessment of changes within the working memory system through the entire life span could be considered a direction for future research.

3. Limitations of the battery: Our working memory test battery was relatively brief, utilizing four measures. The goal was to assess both visual-spatial and verbal working memory, and to evaluate maintenance, continuous updating, memory for temporal order, and direct manipulation in working memory. Therefore, a single test was chosen to assess each of these domains of working memory, with emphasis placed on choosing the measures commonly used in research. One of the measures was visual-spatial, and three were verbal, with numerical, verbal and mixed stimuli. While this

provides a concise measure of all aspects of working memory, it makes some of the contrasts more difficult to make. For example, the Spatial Delayed Recall task is used to assess maintenance within working memory, and at the same time to draw conclusions about visual-spatial working memory functioning as a whole. One of the advantages of using a concise testing battery is that it is less taxing on the participants, and therefore a greater number of individuals could be recruited into the study. Participants who are able to take part in a shorter study are also likely to be more demographically diverse than those who are able to devote a greater part of their day time during a work week. However, in future studies, matching of visual-spatial and verbal tasks for each aspect of working memory, as well as matching for difficulty level, could be considered to provide a more balanced and comprehensive assessment.

General Intelligence Estimate: In this study, general intelligence was estimated using scores from the Vocabulary subtest of the WAIS-III. While this measure shows a close correlation with overall intelligence (Tulsky, Zhu & Ledbetter, 1997; Wechsler 1997), it reflects a general fund of knowledge and is also strongly associated with educational attainment. Education effects on working memory performance were examined after correcting for general intelligence. However, given that our estimate for intelligence was Vocabulary, it is possible that we underestimated the effects of education on working memory. Nevertheless, education was a significant predictor of the performance on working memory as a whole, and on the test of continuous updating (N-Back), suggesting that the effect was preserved at least to some extent.

Intelligence estimate measures based on demographic factors, such as the Barona index (Barona, Reynolds, and Chastain, 1984), which estimates intelligence based on

such variables as age, educational, and occupational attainment, could be utilized; however, given that this study concentrated on demographic variables as predictors of working memory functioning, that type of IQ estimate may not have been appropriate. In addition, demographically-based IQ estimates may be less accurate in younger adults, which have not as yet completed their education or obtained a job. A more desirable alternative for future research is the use of a brief battery assessing more than one aspect of intelligence as a means of providing a more balanced estimate of overall cognitive ability.

4. Recording Years of Education as an Index of Educational Attainment:

In the current study, we used the number of completed years of education as a measure of educational attainment. It can be argued that quantity of education is not equivalent to quality of education, as schools differ dramatically in the type of education they provide to students (Manly et al., 2002). Measures of educational attainment that focus on on qualitative factors, such as literacy levels, may better capture the quality of education than years of education alone (Manly, Touradji, Tang, & Stern, 2003; Stern, 2003). Measures like the National Adult Reading Test (NART) could be considered estimates of the quality of education; however, since we used the WAIS-III Vocabulary subtest as an estimate of intelligence, we could not use a word-reading test as a measure of education, because the two measures would be very closely related. It is recommended that future studies consider using a combination measure of years of education and literacy to assess the quality of education and to diminish possible bias from cultural or economic influences on availability or utilization of formal education.

5. Cross-sectional design: The inherent confound of a cross-sectional design is the cohort effect – that is that the observed differences in performance are produced not only by age, but also by the cohort-relevant experiences, including such variables as differences in quality of education in different decades, or impact of various historical events on development. While a longitudinal design would be able to avoid such confounds, the cross-sectional design enables examining of a much greater age-span, making possible inferences about life-long changes in a given domain. There were also practical (e.g. money, time) constraints that prevented use of a longitudinal design.

Conclusions

This study aimed to clarify the contributions of age, gender, intelligence and education on working memory functioning in normal adults. The majority of studies examining age-associated changes in cognitive functioning, including working memory, have concentrated on the decline associated with more advanced aging (Brickman et al., 2007; Nebes et al., 2006). By concentrating on the normal adult life span, following adolescence and preceding the onset of the changes associated with advanced aging, this study examined normal changes in the relatively less-studied age group. In addition, by examining the age-associated changes on a continuum, as opposed to the more common approach of comparing age groups, such as "younger", "middle" and "older" adults (Brickman et al., 2006), this study allowed us to establish that the age associated changes in this function are linear and to estimate the rate of decline.

This study also addressed the complex relationship between gender and working memory in cognitively normal adults. While gender differences in neuronal activity during performance of working memory tasks have been consistently reported in

literature (Bell et al., 2006, Schweinsburg, Nagel & Tapert, 2005; Speck et al., 2000), the behavioral findings have been more controversial. A male advantage has been documented for the visual spatial tasks (Epting & Overman 1998, Gur et al., 2000), though not specifically for the working memory tasks (Schweinsburg, Nagel, & Tapert, 2005), and a female advantage has been observed on a continuous updating task by Speck et al. (2000). Previous studies investigating gender differences in working memory performance tended to have a relatively small sample size (under 50 participants) and often employed a single measure to assess working memory function. The current study employed a battery of working memory tests and examined performance of a large group of participants (over 400) on each measure, as well as on the extracted working memory cluster, allowing for a more reliable assessment of possible gender differences. Our findings suggest an absence of gender differences in overall working memory, as suggested by the lack of gender effects on the working memory factor score. While previous studies reported a female advantage on verbal tasks and a male advantage on spatial tasks, the current study failed to find a female advantage on verbal working memory tasks, and observed a male advantage on the visual spatial task that seemed independent of the overall visual spatial abilities involved in performance of that test. This also suggests that working memory functioning is different and relatively independent from the linguistic and visual spatial functions that underlie it.

The current study addressed the implications of overall intelligence and educational levels for working memory functioning. Our findings support the previously reported strong positive correlation between working memory and overall intelligence (Ackerman, Beier & Boyle, 2005). In addition, our findings suggest that at least for

selected domains of working memory (i.e., continuous updating), general intelligence may serve as a buffer against the effects of age. Level of education, above and beyond the effects of general intelligence, was found to be a strong predictor of working memory performance as a whole and continuous updating in particular. These findings are consistent with the notion of cognitive reserve (Stern, 2002), but have not been previously studied with regard to normal working memory functioning in younger adults. However, given that only selected aspects of working memory showed the buffering effects of general intelligence, and education has not been shown to have protective properties against the effects of aging as we anticipated, further studies would be necessary to clarify the role of cognitive reserve in age-related changes within the adult life span.

The current study is the only one to date to examine the contribution of demographic factors to various components of working memory. While our findings support the existence of an overall working memory factor, observed differences in the relative influences of various demographic factors on subcomponents of working memory suggests several distinct mechanisms at play.

The current study emphasized the complexity of working memory function by highlighting commonalities and differences in the effects of demographic factors on various components of working memory. Our findings contribute to the body of work suggesting that several diverse processes are grouped together under the general heading of working memory. This has implications for assessment, in that generalizations about working memory functioning in an individual stemming from a single measure may be of limited value due to the variability between the different components of working

memory. The current study suggests that of the four measures that were used in this study, the Spatial Delayed Response test had the lowest loading on the working memory factor, and would be least informative as an estimate of working memory as a whole. All of the verbal tasks used in this study showed approximately the same relationship with the overall factor score, and could be used as reasonable predictors of this function.

Table 1

Demographics of the Study Sample

Race/ethnicity	Gender (*N*)	*M*/*SD* age (range)	*M*/*SD* education (range)	Total *N*
African-American	Male (30)	34.00/8.22 (18-52)	14.70/2.04 (11-18)	78
	Female (48)	33.00/10.69 (19-48)	14.40/2.48 (9-20)	
Asian	Male (15)	25.00/4.78 (19-32)	17.53/3.07 (14-24)	40
	Female (25)	28.00/8.90 (19-54)	16.52/1.98 (13-20)	
Caucasian	Male (97)	30.00/8.65 (18-55)	15.69/1.93 (10-20)	218
	Female (121)	28.13/7.27 (18-51)	16.21/1.85 (11-22)	
Hispanic	Male (25)	33.00/8.58 (18-47)	14.76/1.94 (12-18)	42
	Female (17)	29.06/8.27 (20-50)	14.88/1.76 (12-18)	
Other	Male (7)	32.71/10.44 (22-50)	15.43/3.05 (11-20)	25
	Female (18)	27.00/9.00 (19-54)	16.56/2.1 (13-20)	
Total	Male (174)	31.76/8.76 (18-55)	15.53/2.22 (11-24)	403
	Female (229)	29.92/8.58 (18-54)	15.79/2.16 (9-22)	

Table 2

Coefficient of Linear Fit for Working Memory Tests

Test	F	Significance
SDR (log transformed)	33.41	0.000
WSPT	42.33	0.000
N-Back	66.68	0.000
LN	32.03	0.000

Table 3

Study Group Test Performance Means and SD (Raw Scores) and Maximal Test Performance Values

Test	Mean	SD	Maximal Score
Letter-Number Sequencing	12.819	3.188	21
N-Back test (D' total score)	3.371	0.773	5.10
Spatial delayed response task (total error (in pixels) score)	1031.699	367.068	0.00
Word serial position test (proportion correct score)	0.682	0.169	1.00

Table 4

Results of Kolmogorov-Smirnov Test of Normality of the Distribution

Test	Statistic	Significance
Letter-Number Sequencing	0.098	0.000
N-Back test	0.049	0.026
Spatial delayed response task	0.115	0.000
Word serial position test	0.068	0.000

Table 5

Correlation Coefficients (Sig) of Test Scores and Working Memory Factor Scores

	Word serial position task	N-Back test	Letter-Number Sequencing	Working memory factor
	Word serial Position Task	N-Back Test	Letter-Number Sequencing	Working Memory Factor
Spatial Delayed Response Task	0.312 (p=0.000)	0.303 (p=0.000)	0.300 (p=0.000)	0.590 (p=0.000)
Word Serial Position Test	1.000	0.487 (p=0.000)	0.502 (p=0.000)	0.794 (p=0.000)
N-Back Test	0.487 (p=0.000)	1.000	0.452 (p=0.000)	0.777 (p=0.000)
Letter-Number Sequencing	0.502 (p=0.000)	0.452 (p=0.000)	1.000	0.769 (p=0.000)
Working Memory Factor	0.794 (p=0.000)	0.777 (p=0.000)	0.769 (p=0.000)	1.000

Table 6

Results of Kolmogorov-Smirnov Test of Normality of the Distributions of the Residuals

Test	Statistic	Significance
Letter-Number Sequencing	0.030	0.200
N-Back Test	0.041	0.134
Spatial Delayed Response Task	0.040	0.151
Word Serial Position Test	0.039	0.176
Working Memory Factor	0.029	0.200

Table 7

Summary of the Final Regression Model for Working Memory Factor and All Tests

	Working Memory Factor		Letter-Number Sequencing		N-Back Test		Spatial Delayed Response Task		Word Serial Position Test	
	β	p	β	p	β	p	β	p	β	p
Gender	0.021	0.610	0.024	0.590	-0.063	0.151	0.106	0.027	0.029	0.529
Age	-0.342	0.000	-0.198	0.001	-0.353	0.000	-0.258	0.000	-0.259	0.000
Age x Gender	-0.043	0.450	-0.025	0.678	0.008	0.898	-0.034	-0.515	-0.037	0.555
Vocabulary	0.387	0.000	0.383	0.000	0.278	0.000	0.147	0.005	0.313	0.000
Education	0.109	0.015	0.057	0.238	0.099	0.038	0.074	0.155	0.083	0.092
Age x Vocabulary	0.041	0.536	-0.039	0.577	0.138	0.045	0.061	0.429	-0.050	0.486
Age x Education	-0.078	0.234	-0.007	0.913	-0.121	0.071	-0.036	0.641	-0.078	0.270
Age x Gender x Vocabulary	-0.029	0.647	0.046	0.487	-0.050	0.448	-0.036	0.615	-0.011	0.870
Age x Gender x Education	0.081	0.192	0.085	0.202	0.064	0.315	-0.002	0.979	0.067	0.328

Table 8

Summary of the Significant Findings (Marked with X) for Working Memory Factor and All Tests

	Working memory factor	Letter-Number Sequencing	N-back test	Spatial delayed response task	Word serial position test
Gender				X	
Age	X	X	X	X	X
Age x Gender					
Vocabulary	X	X	X	X	X
Education	X		X		
Age x Vocabulary			X		

Table 9

Effects of Age on Working Memory

Test	Gender	Age (mean [Sd])				
		< 20 yo (n = 36)	20-29 yo (n = 199)	30-39 yo (n = 94)	40-49 yo (n = 59)	> 50 yo (n = 15)
Working Memory Factor (Total Error)	Male	0.761 (0.862)	0.279 (0.957)	-0.267 (1.029)	-0.658 (1.121)	-1.089 (0.738)
	Female	0.455 (0.746)	0.263 (0.856)	-0.160 (0.962)	-0.608 (0.908)	-0.951 (0.438)
Letter-Number Sequencing	Male	15.571 (3.101)	13.281 (3.467)	12.419 (3.141)	11.231 (3.089)	11.000 (2.915)
	Female	13.846 (2.853)	13.289 (3.025)	12.820 (2.833)	11.625 (2.981)	9.667 (1.211)
N-Back test D’	Male	3.628 (0.722)	3.493 (0.722)	3.098 (0.881)	2.908 (0.654)	2.592 (0.751)
	Female	3.642 (0.672)	3.622 (0.670)	3.339 (0.743)	2.897 (0.713)	2.875 (0.447)
Spatial Delay Response Task	Male	795.607 (223.250)	928.526 (276.629)	1081.506 (397.583)	1135.966 (474.956)	1236.136 (233.712)
	Female	911.471 (156.216)	986.533 (300.849)	1134.7158 (526.489)	1199.093 (382.731)	1198.11 (248.941)
Word Serial Position Test	Male	0.739 (0.114)	0.720 (0.161)	0.654 (0.158)	0.587 (0.217)	0.568 (0.148)
	Female	0.749 (0.099)	0.715 (0.158)	0.643 (0.166)	0.617 (0.176)	0.577 (0.117)

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Table 10

Effects of Gender Across Different Levels of Spatial Delayed Recall Task

SDR subtest	Mean (*SD*) error in pixels		Mean (*SD*) Z scores		Gender main effect	
	Males	Females	Males	Females	β	p
2-second delay	818.460 (356.803)	861.972 (342.409)	0.078 (1.018)	-0.047 (0.977)	0.076	0.130
5-second delay	902.213 (418.721)	1003.643 (473.924)	0.131 (0.908)	-0.089 (1.028)	0.125	0.013
15-second delay	1054.982 (488.971)	1122.898 (548.444)	0.088 (0.909)	-0.038 (1.020)	0.101	0.035
30-second delay	1242.463 (613.669)	1210.915 (591.331)	-0.022 (1.018)	0.029 (0.981)	0.003	0.949

Table 11

Effects of General Intelligence on Working Memory

	Estimated level of intelligence (mean [SD])		
	Below average IQ (Voc SS < 7)	Average IQ (Voc SS 7-13)	Above average IQ (Voc SS <13)
Working memory factor	-1.11 (0.884)	-0.365 (0.933)	0.434 (0.870)
Letter-Number Sequencing	8.73 (2.724)	11.904 (2.687)	13.985 (3.204)
N-Back test	2.73 (0.932)	3.144 (0.757)	3.632 (0.670)
Spatial delayed response task	1187.11 (322.662)	1091.193 (421.964)	963.744 (291.658)
Word serial position test	0.56 (0.096)	0.629 (0.169)	0.741 (0.148)

Table 12

Correlation Coefficients (Sig) for the Vocabulary Scaled Scores and z-Scores for the Working Memory Tests and Working Memory Factor

	Vocabulary Scaled Scores
Spatial Delayed Response Task	0.222 (0.000)
Word Serial Position Test	0.415 (0.000)
N-Back test	0.404 (0.000)
Letter-Number Sequencing	0.436 (0.000)
Working Memory Factor	0.505 (0.000)

Table 13

Effects of Education on Working Memory

	Level of Education (mean [SD])		
	Up to College (< 12 years)	College (13-16 years)	Postgraduate (>16 years)
Working memory factor	-0.599 (1.223)	-0.024 (1.040)	0.278 (0.945)
Letter-Number Sequencing	11.189 (3.635)	12.804 (2.983)	13.443 (3.230)
N-Back test	2.917 (0.949)	3.363 (0.723)	3.535 (0.792)
Spatial delayed response task	1213.717 (467.008)	1014.269 (422.036)	1010.352 (317.384)
Word serial position test	0.642 (0.198)	0.670 (0.180)	0.720 (0.142)

Table 14

Accuracy at Each Serial Position on WSPT and Effects of Vocabulary and Age

Serial Position	Accuracy Mean (*SD*)	Vocabulary main effect	Age main effect
WSPT 1	0.78 (0.229)	0.196 (0.00)	-0.132 (0.05)
WSPT 2	0.65 (0.252)	0.197 (0.00)	-0.157 (0.02)
WSPT 3	0.59 (0.282)	0.229 (0.00)	-0.146 (0.03)
WSPT 4	0.54 (0.301)	0.204 (0.00)	-0.238 (0.00)
WSPT 5	0.65 (0.263)	0.189 (0.00)	-0.303 (0.00)
WSPT 6	0.86 (0.213)	0.165 (0.00)	-0.194 (0.00)

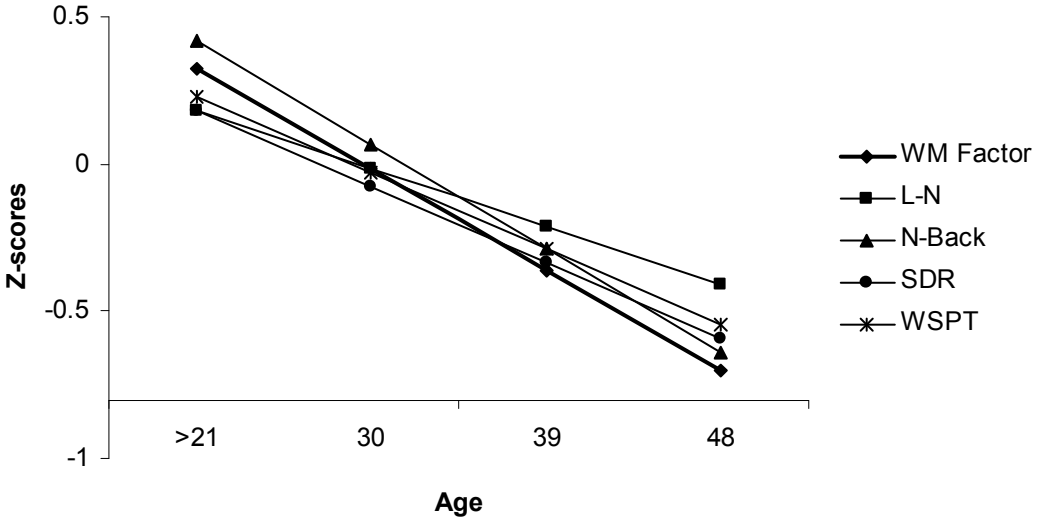

Figure 1. Age associated changes in performance on working memory tests and working memory factor.

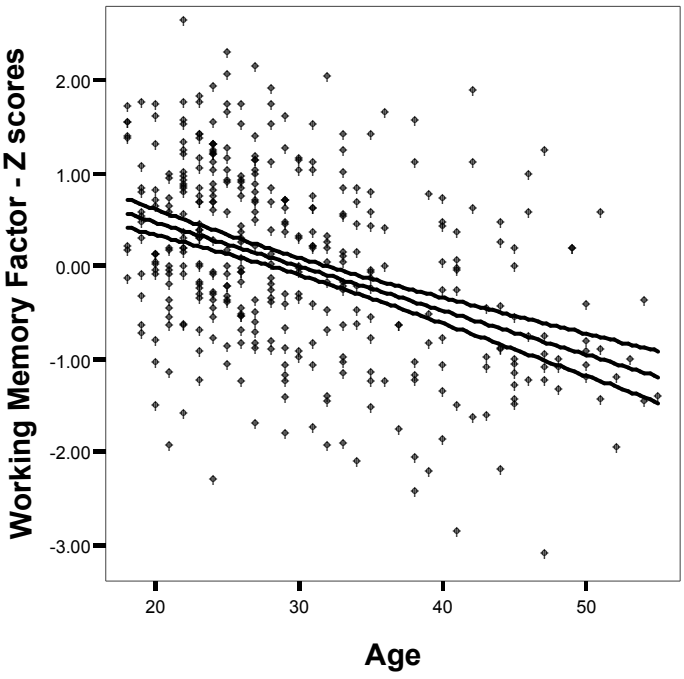

*Figure 1a.*Age associated changes in performance on working memory factor (Regression line is represented with the 95 % confidence interval)

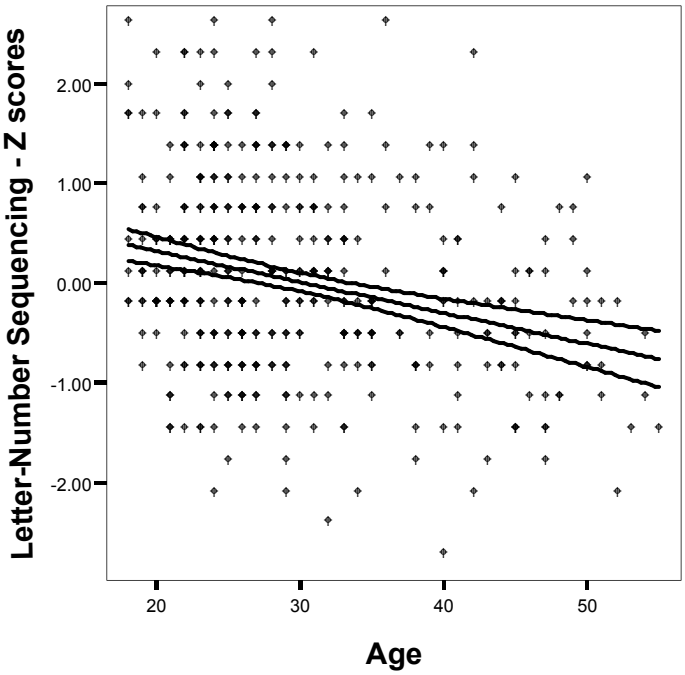

Figure 1b. Age associated changes in performance on Letter-Number Sequencing Test (Regression line is represented with the 95 % confidence interval)

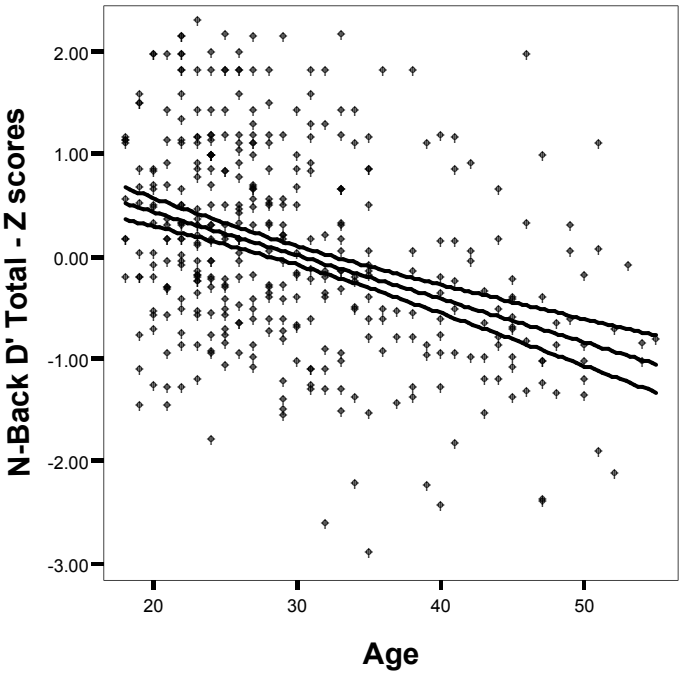

Figure 1c. Age associated changes in performance on N-Back test (Regression line is represented with the 95 % confidence interval)

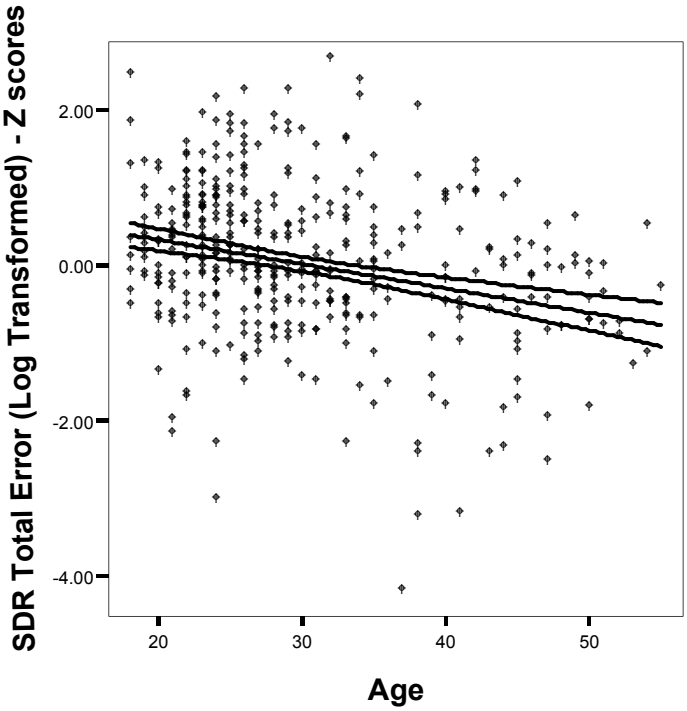

Figure 1d. Age associated changes in performance on Spatial Delayed Response test (Regression line is represented with the 95 % confidence interval)

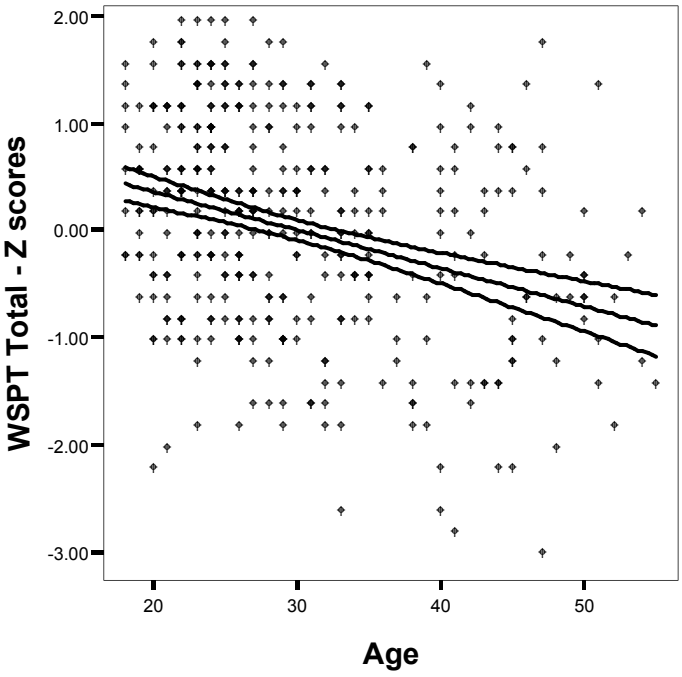

Figure 1e. Age associated changes in performance on Word Serial Position Test (Regression line is represented with the 95 % confidence interval)

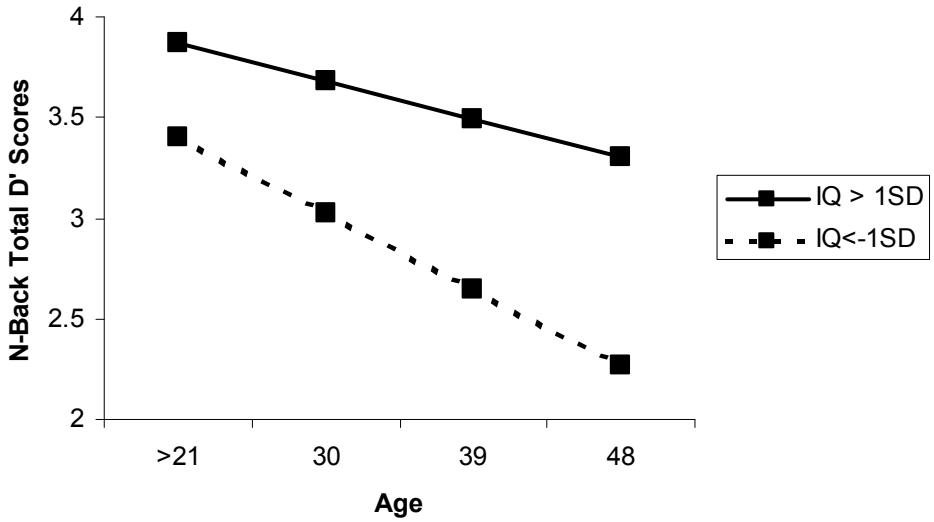

Figure 2. Age-related changes in performance on N-Back task for participants with high (>1SD) versus low (<-1SD) estimated level of intelligence.

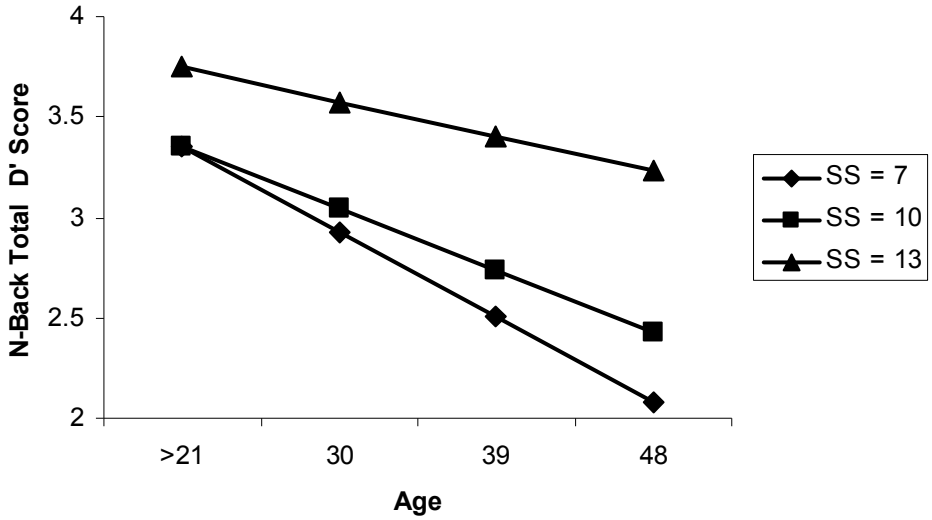

Figure 3: Age-related changes in performance on N-Back task for participants with high average (>1SD; SS = 13), average (SS = 10), and low average (<-1SD; SS=7) scores on Vocabulary test.

REFERENCES

Ackerman, P. L., Beier, M.E., & Boyle, M. O. (2005). Working memory and intelligence: The same or different constructs? *Psychological Bulletin, 131*(1)*,* 30-60

Adcock, R. A., Constable, R. T., Gore, J. C., & Goldman-Rakic, P. S. (2000). Functional neuroanatomy of executive processes involved in dual-task performance. *Proceeds of National Academy of Science, USA, 97,* 3567-3572.

Adler, C. M., Holland, S. K., Enseleit, S., & Strakowski, S. M (2001). Age-related changes in regional activation during working memory in young adults: An fMRI Study. *Synapse, 42,* 252-257.

Aiken, L. & West, S. (1991). *Multiple regression: Testing and interpreting interactions*. Thousand Oaks, CA: Sage.

Allen, J. S., Damasio, H., Grabowski, T. J., Bruss, J., & Zhang, W. (2003). Sexual dimorphism and symmetries in the gray-white composition of the human cerebrum. *Neuroimage, 18,* 880-894.

Allen, J. S., Tranel, D., Bruss, J., & Damasio, H. (2006). Correlation between regional brain volumes and memory performance in anoxia. *Journal of Clinical Experimental Neuropsychology, 28,* 457-476.

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

Atkinson, R. C. & Shiffrin, R. M. (1968). *The psychology of learning and motivation: Advances in research and theory* (Vol. 2, pp. 89-195). New York: Academic.

Baare, W. F., Hulshoff Pol, H. E., Hijman, R., Mali, W. P., Viergever, M. A., & Kahn, R. S. (1999). Volumetric analysis of frontal lobe regions in schizophrenia: relation to cognitive function and symptomatology. *Biological Psychiatry, 45,* 1597-1605.

Baddeley, A. (1996). The fractionation of working memory. *Proceeds of the National Academy of Science, USA, 93,* 13468-13472.

Baddeley, A. (2003). Working memory and language: and overview. *Journal of Communication Disorders, 36,* 189-208.

Baddeley, A. D. & Hitch, G. (1974). *The psychology of learning and motivation* (Vol. 8, pp. 47-89). New York:Academic.

Barona, A., Reynolds, C.R., & Chastain, R. (1984). A demographically based index of premorbid intelligence from the WAIS-R. *Journal of Consulting and Clinical Psychology, 52*, 885-887.

Beck, A. T., Ward, C.H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry, 4,* 561-571

Belger, A., Puce, A., Krystal, J. H., Gore, J. C., Goldman-Rakic, P., & Mc.Carthy, G. (1998). Dissociation of mnemonic and perceptual processes during spatial and nonspatial working memory using fMRI. *Human Brain Mapping, 6*(1)*,* 14-32.

Bell, E. C., Willson, M. C., Wilman, A. H., Dave, S. & Silverstone, P. H. (2006). Males and females differ in brain activation during cognitive tasks. *Neuroimage, 30,* 529-538.

Brickman, A. M., Habeck, C., Zarahn, E., Flynn, J., & Stern, Y. (2007). Structural MRI covariance patterns associated with normal aging and neuropsychological functioning. *Neurobiology of Aging, 28,* 284-295.

Brickman, A. M., Zimmerman, M. E., Paul, R. H., Grieve, S. M., Tate, D. F., Cohen, R. A., Williams, L. M., Clark, C. R. & Gordon, E. (2006). Regional white matter and neuropsychological functioning across the adult lifespan. *Biological Psychiatry, 60,* 444-453.

Bopp, K. L. & Verhaeghen, P. (2005). Aging and verbal memory span: a meta-analysis. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 60,* 223-233.

Bruder, G. E., Keilp, J. G., Xu, H., Shikhman, M., Schori, E., Gorman, J. M., & Gilliam, T.C. (2005) Catechol-O-methyltransferase (COMT) genotypes and working memory:Associations with differing cognitive operations. *Biological Psychiatry, 58,* 901-907.

Cabeza, R., Daselaar, S. M., Dolcos, F., Pricne, S. E., Budde, M., & Nyberg, L. (2004). Task-independent and task-specific age effects on brain activity during working memory, visual attention and episodic retrieval. *Cerebral Cortex, 14,* 364-375.

Chavtor, N. & Schmitter-Edgecombe, M. (2004). Working memory and aging: a cross-sectional and longitudinal analysis using a self-ordered pointing task. *Journal of International Neuropsychological Society, 10,* 489-503.

Chen, P. S., Yang, Y. K., Lee, Y. S., Yeh, T. L., Lee, I. H., Chiu, N. T., & Chu, C. L. (2005). Correlation between different memory systems and striatal dopamine D2/D3 receptor density: a single photon emission computed tomography study. *Psychological Medicine, 35,* 197-204.

Coffey, C. E., Lucke, J. F., Saxton, J. A., Ratcliff, G., Unitas, L. J., Billig, B., & Bryan, R. N. (1998). Sex differences in brain aging: A quantitative magnetic resonance imaging study. *Archives of Neurology, 55,* 169-179.

Cohen, J., Cohen, P., & West, S.G., & Aiken, L.S. (2003). *Applied multiple regression/correlation analysis for the behavioral science–Third edition.* Upper Saddle River, NJ*:* Lawrence Erlbaum.

Cohen, J.D., Perlstein, W.M., Braver, T.S., Nystrom, L.E., Noll, D.C., Jonides, J., & Smith, E.E. (1997). Temporal dynamics of brain activation during a working memory task. *Nature, 386,* 604-608

Corral, M., Rodriguez, M., Amenedo, E., Sanchez, J.L. & Diaz, F. (2006). Cognitive reserve, age, and neuropsychological performance in healthy participants. *Developmental Neuropsychology, 29,* 479-491

Cowell, P. E., Turetsky, B. I., Gur, R. C., Grossman, R. I., Shtasel, D. L., & Gur, R. E. (1994). Sex differences in aging of the human frontal and temporal lobes. *Journal of Neuroscience, 14,* 4748-4755.

De Bellis, M. D., Keshavan, M. S., Beers S. R., Hall, J., Frustaci, K., Masalehdan, A., Noll, J., et al. (2001). Sex differences in brain maturation during childhood and adolescence. *Cerebral Cortex, 11,* 552-557.

De Fockert, J. M. (2005). Keeping priorities: the role of working memory and selective attention in cognitive aging. *Science of Aging Knowledge Environment, 44,* 34-39.

Derogatis, L.R., Lipman, R.S., Rickels, K., Uhlenhuth, E.H., & Covl, L. (1974): The Hopkins symptom checklist (HSCL): A self-report symptom Inventory. *Behavioral Science, 19,* 1-15

Derrfuss, J., Brass, M., & von Cramon, D. Y. (2004). Cognitive control in the posterior frontal cortex: evidence from common activations in task coordination, interference control, and working memory. *Neuroimage, 23,* 604-612.

Desmond, J. E., Chen, S. H. A., & Shieh, P. B. (2005). Cerebellar transcranial magnetic stimulation impairs verbal working memory. *Annals of Neurology, 58,* 553-560.

Epting L. K. & Overman, W. H. (1998). Sex-sensitive tasks in men and women: A search for performance fluctuation across the menstrual cycle. *Behavioral Neuroscience, 112,* 1304-1317.

Finke, K., Bublak, P., & Zihl, J. (2006). Visual spatial and visual pattern working memory: Neuropsychological evidence for a differential role of left and right dorsal visual brain. *Neuropsychologia, 44,* 649-661.

Foos, P. W. (1989). Adult age differences in working memory. *Psychology of Aging, 4,* 269-275.

Giedd, J. N., Castellanos, F. X., Rajapakse, J. C., Vaituzis, A. C., & Rapoport, J. L. (1997). Sexual dimorphism of the developing human brain. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 21,* 1185-1201.

Glahn, D. C., Kim, J., Cohen, M. S., Poutanen, V-P., Therman, S., Bava, S., Van Erp, T. G. M., Manninen, M., et al.. (2002). Maintenance and manipulation in spatial working memory: Dissociation in the prefrontal cortex. *Neuroimage, 17,* 201-213.

Goldman-Rakic, P. S. (1996). Regional and cellular fractionation of working memory. *Proceeds of the National Academy of Science, USA, 93,* 13473-13480.

Goldstein, J. M., Jerram, M., Poldrack, R., Anagnoson, R., Breiter, H. C., Makris, N., Goodman, J. M., Tsuang, M. T., & Seidman, L. J. (2005). Sex differences in

prefrontal cortical brain activity during fMRI of auditory verbal working memory. *Neuropsychology, 19,* 509-519.

Gomez-Perez, E. & Ostosky-Solis, F. (2006). Attention and memory evaluation across the life span: heterogeneous effects of age and education. *Journal of Clinical Experimental Neuropsychology, 28,* 477-494.

Grabner, R. H., Fink, A., Stipacek, C., Neuper, A. C., & Neubauer, A. C. (2004). Intelligence and working memory systems: evidence of neural efficiency in alpha band ERD. *Cognitive Brain Research, 20,* 212-225.

Grachev, I. D. & Apkarian, A. V. (2000). Chemical heterogeneity of the living human brain: a proton MR spectroscopy study on the effects of sex, age, and brain region. *Neuroimage, 11,* 554-563.

Gunning-Dixon, F. M., & Raz, N. (2003). Neuroanatomical correlates of selected executive functions in middle-aged and older adults: a prospective MRI study. *Neuropsychologia, 41,* 1921-1941.

Gunstad, J., Cohen, P. A., Paul, R. H., Luyster, F. S., & Gordon, E. (2006). Age effects in time estimation: relationship to frontal brain morphometry. *Journal of Integrated Neurosciences, 5,* 75-87.

Gur, R. C., Alsop, D., Glahn, D., Petty, R., Swanson, C. L., Maldjian, J. A., Turetsky, B. I., et al. (2000). An fMRI study of sex differences in regional activation to a verbal and a spatial task. *Brain and Language, 74,* 157-170.

Gur, R. E., Cowell, P. E., Latshaw, A., Turetsky, B. I., Grossman, R. I., Arnold, S. E., Bilker, W. B., et al. (2000). Reduced dorsal and orbital prefrontal gray matter volumes in schizophrenia. *Archives of General Psychiatry, 57,* 761-768.

Gur, R. C., Gunning-Dixon, F. M., Turetsky, B. I., Bilker, W. B., & Gur, R. E. (2002). Brain region and sex differences in age association with brain volume: a quantitative MRI study of health young adults. *American Journal of Geriatric Psychiatry, 10,* 72-80.

Gur, R. C., Mozley, P. D., Resnick, S. M., Gottlieb, G. L., Kohn, M., Zimmerman, R., Herman, G., et al. (1991). Gender differences in age effect on brain atrophy measured by magnetic resonance imaging. *Proceeds of the National Academy of Sciences, USA, 88,* 2845-2849.

Gur, R. C., Turetsky, B. I., Matsui, M., Yan, M., Bilker, W., Hughett, P., Gur, R. E. (1999). Sex differences in brain gray and white matter in healthy young adults: correlations with cognitive performance. *Journal of Neuroscience, 19,* 4065-4072.

Guzzaley, A., Rissman, J., & D'Esposito, M. (2004). Functional connectivity during working memory maintenance. *Cognitive, Affective, and Behavioral Neuroscience, 4,* 580-599.

Habeck, C., Rakitin, B. C., Moeller, J., Scarmeas, N., Zarahn, E., Brown, T., & Stern, Y. (2005). An event-related fMRI study of the neural networks underlying the encoding, maintenance, and retrieval phase in a delayed-match-to-sample task. *Cognitive Brain Research, 23,* 207-220.

Hancock, P. A., Lesch, M., & Simmons, L. (2003). The distraction effects of phone use during a crucial driving maneuver. *Accident Analysis & Prevention, 35,* 501-514.

Hartman, M., Steketee, M. C., Silva, S., Lanning, K. & Andersson, C. (2003). Wisconsin Card Sorting Test performance in schizophrenia: The role of working memory. *Schizophrenia Research, 63,* 201-217.

Hatazawa, J., Ito, M., Yamaura, H., & Matsuzawa, T. (1982). Sex difference in brain atrophy during aging: a quantitative study with computed tomography. *Journal of the American Geriatric Society, 30,* 235-239.

Hausmann, M., Slabbekoorn, D., Van Goozen, S .H. M., Cohen-Kettenis, P. T., Gunturkun, O. (2000). Sex hormones affect spatial abilities during the menstrual cycle. *Behavioral Neuroscience, 114,* 1245-1250.

Hester, R. L, Kinsella, G. J. & Ong, B. (2004). Effect of age on forward and backward span task. *Journal of International Neuropsychological Society, 10,* 475-481.

Holtzer, R., Stern, Y., & Rakitin, B. C. (2004). Age-related differences in executive control of working memory. *Memory and Cognition, 32,* 1333-1345.

Huijbregts, S. C., Kalker, N. F., de Sonneville, L. M., de Groot, V. & Polman, C. H. (2006). Cognitive impairment and decline in different MS subtypes. *Journal of Neurological Science, 245,* 187-194.

Huizinga, M., Dolan, C. V. & van der Molen, M. W. (2006). Age-related change in executive function: Developmental trends and a latent variable analysis. *Neuropsychologia, 44,* 2017-2036.

Inoue, M., Suhara, T., Sudo, Y., Okubo, Y., Yasuno, F., Kishmoto, T., et al. (2001). Age-related reduction of extrastriatal dopamine D2 receptor measured by PET. *Life Sciences, 69,* 1079-1084

Jokinen, H., Kalska, H., Ylikoski, R., Hietnen, M., Mantyla, R., Pohjasvaara, T., Kaste, M., et al. (2004). Medial temporal lobe atrophy and memory deficits in elderly stroke patients. *European Journal of Neurology, 11,* 825-832.

Kane, M.J., Hambrick, D.Z., & Conway, A.R.A. (2005). Working memory capacity and fluid intelligence are strongly related constructs: Comment on Ackerman, Beier and Boyle. (2005). *Psychological Bulletin, 131*(1)*,* 66-71

Lacreuse, A., Herndon, J. G., Killiany, R. J., Rosene, D. L., & Moss, M. B. (1999). Spatial cognition in rhesus monkeys: Male superiority declines with age. *Hormones and Behavior, 36,* 70-76.

Larkin, M. (1998). Brain shrinkage more rapid in men than in women. *Lancet, 351,* 575-577.

Lazeron, R. H., Boringa, J. B., Schouten, M., Uitdehaag, B. M., Bergers, E., Lindeboom, J., Eikelenboom, M. I., Scheltens, P. H., et al. (2005). Brain atrophy and lesion load as explaining parameters for cognitive impairment in multiple sclerosis. *Multiple Sclerosis, 11,* 524-531.

Lemaitre, H., Crivello, F., Grassiot, B., Alperovitch, A., Tzourio, C., & Mazoyer, B. (2005). Age- and sex-related effects on the neuroanatomy of healthy elderly. *Neuroimage, 26,* 900-911.

Lengenfelder, J., Bryant, D., Diamond, B. J., Kalmar, J. H., Moor, N. B. & DeLuca, J. (2006). Processing speed interacts with working memory efficiency in multiple sclerosis. *Archives of Clinical Neuropsyhology, 21,* 229-238.

Lewis, P.A., & Miall, R.C. (2006). Remembering the time: A continuous clock. *Trends in Cognitive Sciences, 10,* 401-406.

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

Luft, A. R., Skalej, M., Welte, D., Voigt, K., & Klockgether, T. (1997). Age and sex do not affect cerebellar volume in humans. *American Journal of Neuroradiology, 18,* 593-596.

Lustig, C., Hasheer, L., & Tonev, S.T. (2006). Distraction as a determinant of processing speed. *Psychological Bulletin Review, 13,* 619-625

Lyketsos, C.G., Chen, L., & Anthony, J.C. (1999). Cognitive decline in adulthood: An 11.5-year follow-up of the Baltimore epidemiologic catchment area study. *American Journal of Psychiatry, 156*(1)*,* 58-65

Lyons-Warren A., Lillie R., & Hershey, T. (2004). Short- and long-term spatial delayed response performance across the lifespan. *Developmental Neuropsychology, 26,* 661-678

Maitland, S. B., Herlitz, A., Nyberg, L., Backman, L., & Nilsson, L. (2004). Selective sex differences in declarative memory. *Memory and Cognition, 32,* 1160-1169.

Manly, J. J., Jacobs D. M., Touradji, P., & Small, S.A. (2002). Reading level attenuates differences in neuropsychological test performance between African American and White elders. *Journal of the International Neuropsychological Society, 8,* 341-348

Manly, J. J., Touradji, P., Tang, M. X. & Stern, Y. (2003). Literacy and memory decline among ethnically diverse elders. *Journal of Clinical and Experimental Neuropsychology, 25,* 680-690

Manoach, D. S., Greve, N. D., Lindgren, K. A., & Dale, A. M. (2003). Identifying regional activity associated with temporally separated components of working memory using event-related functional MRI. *Neuroimage, 20,* 1670-1684.

Mattay, V. S., Fera, F., Tessitore, A., Hariri, A. R., Berman, K. F., Das, S., Meyer-Lindenberg, A., et al. (2006). Neurophysiological correlates of age-related changes in working memory capacity. *Neuroscience Letters, 392,* 32-37.

McGurk, S. R., Coleman, T., Harvey, P. D., Reichenberg, A., White, L., Friedman, J., Parrella, M. & et al. (2004). Working memory performance in poor outcome schizophrenia: relationship to age and executive functioning. *Journal of Clinical Neuropsychology, 26,* 153-160.

Meguro, K., Shimada, M., Yamaguchi, S., Ishizaki, J., Ishii, H., Shimada, Y., Sato, M., Yamadori, A. & Sekita, Y. (2001). Cognitive function and frontal lobe atrophy in normal elderly adults: Implications for dementia not as aging-related disorders and the reserve hypothesis. *Psychiatry and Clinical Neuroscience, 55,* 565-572.

Mehta, M.A., & Riedel, W.J. (2006). Dopaminergic enhancement of cognitive function. *Current Pharmaceutical Design, 12,* 2487-2500.

Mikels, J. A., Larkin, G. R., Reuter-Lorenz, P. A., & Cartensen, L.L. (2005). Divergent trajectories in the aging mind: changes in working memory for affective versus visual information with age. *Psychology of Aging, 20,* 542-553.

Murphy, D. G., DeCarli, C., McIntosh, A. R., Daly, E., Mentis, M. J., Pietrini, P., Szczepanik, J., et al.. (1996). Sex differences in human brain morphometry and metabolism: and in vivo quantitative magnetic resonance imaging and positron emission tomography study on the effect of aging. *Archives of General Psychiatry, 53,* 585-594.

Nebes, R. D., Meltzer, C. C., Whyte, E. M., Scanlon, J. M., Halligan, E. M., Saxton, J. et al. (2006). The relationship of white matter hyperintensities to cognitive

performance in the normal old: education matters. *Aging, Neuropsychology and Cognition, 13,* 326-340

Nichols-Larsen, D. S., Clark, P. C., Zeringue, A., Greenspan, A. & Blanton, S. (2005). Factors influencing stroke survivors' quality of life during subacute recovery. *Stroke, 36,* 1480-1484.

Nopoulos, P., Flaum, M., O'Leary, D., & Andreasen, N.C. (2000). Sexual dimorphism in the human brain: evaluation of tissue volume, tissue composition and surface anatomy using magnetic resonance imaging. *Psychiatry Research, 98,* 1-13.

Osaka, M., Osaka, N., Kondo, H., Morishita, M., Fukuyama, H., Aso, T., & Shibasaki, H. (2003). The neural basis of individual differences in working memory capacity: an fMRI study. *Neuroimage, 18,* 789-797.

Owen, A. M. (2004). Working memory: Imaging the magic number four. *Current Biology, 14,* 573-574.

Owen, A. M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-Back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. *Human Brain Mapping, 25,* 46-59.

Park, S. & Holtzman, P. S. (1992). Schizophrenics show spatial working memory deficits. *Archives of General Psychiatry, 49,* 975-982.

Passe, T. J., Rajagopalan, P., Tupler, L. A., Byrum, C. E., MacFall, J. R., & Krishnan, K.R. (1997). Age and sex effects on brain morphology. *Progress in Neuro-Psychopharmacology and Biological Psychiatry, 21,* 1231-1237.

Passingham, D., & Sakai, K. (2004). The prefrontal cortex and working memory: physiology and brain imaging. *Current Opinion in Neurobiology, 14,* 163-168.

Pavlik, V.N., Doody, R.S., Massman, P.J., & Chan, W. (2006). Influence of premorbid IQ and education on progression of Alzheimer's disease. *Dementia and Geriatric Cognitive Disorders, 22,* 367-377.

Perlstein, W. M., Carter, C. S., Noll, D. C. & Cohen, J. D. (2001). Relation of prefrontal cortex dysfunction to working memory and symptoms of schizophrenia. *American Journal of Psychiatry, 158,* 1105-1113.

Persson, J., Nyberg, L., Lind, J., Larsson, A., Nilsson, L. G., Ingvar, M., & Buckner, R. L. (2006). Structure-function correlates of cognitive decline in aging. *Cerebral Cortex, 16,* 907-915.

Petersen, R. C., Jack, C. R. Jr., Xu, Y. C., Waring, S. C., O'Brien, P. C., Smith, G. E., Ivnik, R.J., et al., (2000). Memory and MRI-based hippocampal volumes in aging and AD. *Neurology, 54,* 581-587.

Oberauer, K., Schulze, R., Wilhelm, O., & Sub, H.M. (2005). Working memory and intelligence–Their correlation and their relation: Comment on Ackerman, Beier, and Boyle (2005). *Psychological Bulletin, 131*(2),61-65

Ota, M., Yasuno, F., Ito, H., Seki, C., Nozaki, S., Asada, T., & Suhara, T. (2006). Age-related decline of dopamine synthesis in the living human brain measured by positron emission tomography with L-[beta-11C]DOPA. *Life Sciences, 79,* 730-736.

Rajah, M. N. & D'Esposito, M. (2005). Region-specific changes in prefrontal function with age: a review of PET and fMRI studies on working and episodic memory. *Brain, 128,* 1964-1983.

Ranganath, C., DeGutis, J., & D'Esposito, M. (2004). Category-specific modulation of inferior temporal activity during working memory encoding and maintenance. *Cognitive Brain Research, 20,* 37-45.

Ranjeva, J. P., Audoin, B., Au Duong, M. V., Confort-Gouny, S., Malikova, I., Viout, P., Soulier, E., et al. (2006). Structural and functional surrogates of cognitive impairment at the very early stages of multiple sclerosis. *Journal of Neurological Science, 245,* 161-167.

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

Raz, N., Gunning-Dixon, F., Head, D., Rodrigue, K. M., Williamson, A., & Acker, J. D. (2004). Aging, sexual dimorphism, and hemispheric asymmetry of the cerebral cortex: replicability of regional differences in volume. *Neurobiology of Aging, 25,* 377-396.

Reimer, S. & Maylor, E. A. (2005). Task switching across the life span: effects of age on general and specific switch costs. *Developmental Psychology, 41,* 661-671.

Rettmann, M. E., Kraut, M. A., Prince, J. L. & Resnick, S. M. (2006). Cross-sectional and longitudinal analyses of anatomical sulcal changes associated with aging. *Cerebral Cortex, 16,* 1584-1594

Rose, E. J. & Ebmeier, K. P. (2006). Pattern of impaired working memory during major depression. *Journal of Affective Disorders, 90,* 149-161.

Sanches, J. L., Rodriguez, M. & Carro, J. (2002). Influence of cognitive reserve on neuropsychologic functioning in Alzheimer's disease type sporadic in subjects of

Spanish nationality. *Neuropsychiatry, Neuropsychology, and Behavioral Neurology, 15,* 113-122.

Sanfilipo, M. P., Benedict, R. H., Weinstock-Guttman, B., & Bakshi, R. (2006). Gray and white matter brain atrophy and neuropsychological impairment in multiple sclerosis. *Neurology, 66,* 685-692.

Scarmeas, N., Zarahn, E., Anderson, K. E., Honig, L. S., Park, A., Hilton, J., Flynn, J., et al. (2004). Cognitive reserve-mediated modulation of positron emission tomographic activations during memory tasks in Alzheimer disease. *Archives of Neurology, 61,* 73-78.

Schweinsburg, A. D., Nagel, B. J. & Tapert, S. F. (2005). fMRI reveals alteration of spatial working memory network across adolescence. *Journal of International Neuropsychological Society, 11,* 631-644.

Seidman L. J., Yurgelun-Todd, D., Kremen, W. S., Woods, B. T., Goldstein, J. M., Faraone, S.V., & Tsuang, M.T. (1994). Relationship of prefrontal and temporal lobe MRI measures to neuropsychological performance in chronic schizophrenia. *Biological Psychiatry, 35,* 235-246.

Speck, O., Ernst, T., Braun, J., Koch, C., Miller, E., & Chang, L. (2000). Gender differences in the functional organization of the brain for working memory. *NeuroReport, 11,* 2581-2585.

Staff, R. T., Murray, A. D., Deary, I. J. & Whalley, L. J. (2004). What provides cerebral reserve? *Brain, 127,* 1191-1199.

Stern, Y. (2002). What is cognitive reserve? Theory and research application of the reserve concept. *Journal of the International Neuropsychological Society, 8,* 448-460

Stern, Y. (2003). The concept of cognitive reserve: a catalyst for research. *Journal of Clinical and Experimental Neuropsychology, 25,* 589-593

Sutcliffe, J.S., Marshall, K.M., & Neill, J.C. (2007). Influence of gender on working and spatial memory in the novel object recognition task in the rat. *Behavioral Brain Research, 177*(2)*,* 117-125

Sternberg, S. (1966). High-speed scanning in human memory. *Science, 153, 652-654.*

Sullivan, E. V., Marsh, L., Mathalon, D. H., Lim, K. O., & Pfefferbaum, A. (1995). Age-related decline in MRI volumes of temporal lobe gray matter but not hippocampus. *Neurobiology of Aging, 16,* 591-606.

Sun, X., Zhang, X., Chen, X., Zhang, P., Bao, M., Zhang, D., et al. (2005). Age-dependent brain activation during forward and backward digit recall revealed by fMRI. *Neuroimage, 26,* 36-47.

Tisserand, D.J. & Jolles, J. (2003). On the involvement of prefrontal networks in cognitive ageing. *Cortex, 39,* 1107-1128.

Tisserand, D. J., Pruessner, J. C., Sanz Arigita, E. J., van Boxtel, M. P., Evans, A. C., Jolles, J., & Uylings, H.B. (2002). Regional frontal cortical volumes decrease differentially in aging: an MRI study to compare volumetric approaches and voxel-based morphometry. *Neuroimage, 17,* 657-669.

Tsujimoto, S., Yamamoto, T., Kawaguchi, H., Koizumi, H., & Sawaguchi, T. (2004). Prefrontal cortical activation associated with working memory in adults and

preschool children: an event-related optical topography study. *Cerebral Cortex, 14,* 703-712.

Tulsky, D., Zhu, J., & Ledbetter M. F. (1997). *WAIS-III WMS-III technical manual.* San Antonio, TX: Psychological Corporation.

Van Der Werf, Y. D., Tisserand, D. J., Visser, P. J., Hofman, P. A., Vuurman, E., Uyling, H. B., & Jolles, J. (2001). Thalamic volume predicts performance on tests of cognitive speed and decreases in healthy aging. A magnetic resonance imaging-based volumetric analysis. *Cognitive Brain Research, 11,* 377-385.

Veltman, D. J., Rombouts, S. A. R. B., & Dolan, R. J. (2003). Maintenance versus manipulation in verbal working memory revisited: an fMRI study. *Neuroimage, 18,* 247-256.

Vuontela, V., Steenari, M., Carlson, S., Koivisto, J., Fjallberg, M., & Aronen, E. T. (2003). Audiospatial and visuospatial working memory in 6-13 year old school children. *Learning and Memory, 10,* 74-81.

Wager, T. D., & Smith, E. E. (2003). Neuroimaging studies of working memory: A meta-analysis. *Cognitive, Affective, and Behavioral Neuroscience, 3,* 255-274.

Wang, P.N., Liu H.C., & Lin, K.N. (2006). The MCI study in Taiwan. *Acta Neurologica Taiwan, 15,* 66-68.

Waters, G. & Caplan, D. (2005). The relationship between age, processing speed, working memory capacity, and language comprehension. *Memory, 13,* 403-413.

Wechsler, D. (1997). *Wechsler Adult Intelligence Scale-Third Revision (WAIS-III).* San Antonio, TX: Psychological Corporation.

Wexler, B. E., Stevens, A. A., Bowers, A. A., Sernyak, M. J., Goldman-Rakic, P. S. (1998). Word and tone working memory deficits in schizophrenia. *Archives of General Psychiatry, 55,* 1093-1096.

Wecker, N. S., Kramer, J. H, Hallam, B. J., & Delis, D. C. (2005). Mental flexibility: Age effects on switching. *Neuropsychology, 19,* 345-352.

Wilde, N. J., Strauss, E., & Tulsky, D. S. (2004). Memory span on the Wechsler Scales. *Journal of Clinical Experimental Neuropsychology, 26,* 539-546.

Willis, M. W., Ketter, T. A., Kimbrell, T. A., George, M. S., Herscovitch, P., Danielson, A. L., Benson, B.E., et al. (2002). Age, sex, and laterality effects on cerebral glucose metabolism in healthy adults. *Psychiatry Research, 114,* 23-37.

Xu, J., Kobayashi, S., Yamaguchi, S., Iijima, K., Okada, K., & Yamashita, K. (2000). Gender effects on age-related changes in brain structure. *American Journal of Neuroradiology, 21,* 112-118.