The Relationship Between Information Processing and Functional Performance in Multiple Sclerosis

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Most tasks that have been developed to assess functional performance in Multiple Sclerosis (MS) have limited sensitivity across the spectrum of disease severity. Given that difficulties with information processing are frequently reported early in the disease course, existing functional tools may not accurately detect subtle everyday impairment in early MS when initial cognitive problems emerge. This study examined the relationship between information processing, functional performance, and disease severity (as measured by the Multiple Sclerosis Functional Composite; MSFC) in MS by comparing participants’ performance on functional tasks with increasing cognitive demands.

A total of 23 participants with MS (mean Ambulation Index of 1.7) completed a battery of tests targeting information processing and functional performance which included subtests from the Direct Assessment of Functional Status (DAFS), the Executive Function Performance Test (EFPT), and a virtual reality driving simulator (VRDS).

Information processing measures were related to the cognitive component of the MSFC. There were no significant relationships between disease severity and the primary functional measures; however, a relationship between disease severity (upper extremity function) and response time on the EFPT was found. Although the primary functional measures were not significantly related to information processing performance, response time on the EFPT modestly correlated with processing speed. Taken together, these findings suggest that the DAFS was the least appropriate functional tool to use in a high...
functioning MS sample. Although the EFPT showed more promise, time to completion may be a more sensitive measure in a high functioning sample. Gross measures of driving may not be the best way to capture difficulties in mildly impaired individuals; however, there was more variability in the challenging portion of the drive. Despite the low power and restricted variability, this study adds to the literature concerning the relationship between functional performance and the MSFC. Furthermore, this is one of the few studies of functional performance in MS that includes driving simulation. This study can help inform future research as to which functional measures may be sensitive for capturing impairment in MS.
CHAPTER 1: INTRODUCTION

1.1 Overview

Multiple sclerosis (MS) is a neurological disease primarily caused by the demyelination of axons in the central nervous system (CNS). This demyelination process forms lesions throughout the brain and spinal cord which results in patterns of neurological deficits. On average, the initial clinical presentation of symptoms occurs in the mid-20s, and women are twice as likely to be diagnosed with MS as men (Calabresi, 2004). Although the range of disability is variable, the physical, cognitive, and psychological effects of MS can have a profound impact on several aspects of patients’ lives including employment (Hakim et al., 2000), social functioning (Rao, Leo, & Ellington, 1991) and driving (Schultheis, Garay, & DeLuca, 2001; Schultheis, Garay, Millis, & DeLuca, 2002; Schultheis, Weisser, Manning, Blasco, & Ang, 2008).

MS is characterized by physical and cognitive impairments. In MS, the damage that occurs in the CNS is diffuse and highly variable; however, there are clusters of symptoms that are typically manifested in this population. Somatosensory, motor, and visual disturbances are often the first symptoms reported by the patient (Herndon, 2000; Joy & Johnston, 2001; Sheremata, Honig, & Bowen, 1999). Cognitive difficulties, particularly in the domain of information processing, can emerge early during the disease course, although these impairments may not be assessed until the disease has progressed (Schulz, Kopp, Kunkel, & Faiss, 2006). Individuals with MS are classified into one of four subtypes based on the time course, progression, and objective experience of their symptoms (Blumenthal, 2006). Individuals diagnosed with the relapsing-remitting (RR) subtype experience sudden attacks followed by periods of remission. A diagnosis of
primary progressive (PP) is characterized by an increase in symptoms and gradual neurological decline from the initial diagnosis (Blumenthal, 2006; Joy & Johnston, 2001; Sheremata et al., 1999). The predominant progressive subtype is that of secondary progressive (SP), and many individuals originally diagnosed with RR are later classified as SP after their relapses are relatively more infrequent or absent (Blumenthal, 2006; Joy & Johnston, 2001). As with PP, there is gradual neurological decline. Progressive relapsing (PR) is the third and most rare variant of the progressive subtypes, and includes graded neurological decline with intermittent relapses throughout the course of the disorder (Sheremata et al., 1999).

Across all the subtypes of MS, the most widely used scale for determining the severity of neurological impairment in both clinical care and research is the Expanded Disability Status Scale (EDSS; Kurtze, 1983). Total EDSS scores range from 0.0 (normal neurological exam) to 10.0 (death due to MS). Patients scoring in the range from 1.0 to 4.5 are considered to be ambulatory, whereas individuals in the 5.0 to 9.5 range manifest difficulties with ambulation in addition to impairments in other functional systems. One drawback of the EDSS is that it is more significantly dependent on the presence of physical rather than cognitive symptoms (Coulthard-Morris, 2000). Other limitations of the EDSS are that it is an ordinal (i.e., non linear) scale, can only be administered by physicians, has poor reliability at the lower end of the scale, is less responsive to changes in severely ill patients, and there is subjectivity in determining the rating (Fischer, Rudick, Cutter, & Reingold, 1999). Despite these limitations, the EDSS is often used as a predictor of physical, cognitive, and functional performance in individuals with MS. Another measure of neurologic disability that is often used is the
ambulation index (AI). It is a neurologic rating scale developed by Hauser et al. (1983) that assesses mobility by measuring the time and evaluating the degree of assistance required to walk 25 feet. The AI has demonstrated strong correlations with the EDSS (Deluca, Chelune, Tulsky, Legenfelder, & Chiaravalloti, 2004; Voelbel, Goverover, Gaudino, Moore, Chiaravalloti, & DeLuca, 2011). A more recently developed measure to assess neurological disability and disease progression in MS is the multiple sclerosis functional composite (MSFC). The MSFC was developed in response to the recommendations of a task force for a new outcome measure for use in MS clinical trials. It was developed to address limitations in the existing measures, specifically the EDSS. The task force sought to create a multidimensional measure that reflected the varied clinical symptoms of MS across patients and over time. Other goals of the task force were to develop a composite measure with components that change relatively independently over time, and that also included an assessment of cognitive function. Based on a meta-analysis of primary and secondary outcome assessments in existing clinical trials, the task force chose three tests to fulfill their criteria that measure upper extremity functioning, lower extremity functioning, and cognitive functioning (Fischer et al., 1999).

1.2 Cognitive Impairment in MS

Although physical impairments are considered the hallmark of MS, recent research has demonstrated the existence of cognitive changes in this population as well, with approximately 40-65% of MS patients experiencing cognitive impairments (Sheremata et al., 1999; Rao et al., 1991). Compared to healthy individuals, there is a high degree of variability in cognitive performance in patients with MS (Joy & Johnston,
2001). Early research examining cognitive dysfunction in MS noted the presence of global, rather than specific, cognitive dysfunction in this population. Much of the early research used the EDSS, which entails a brief cognitive exam that focused on gross cognitive impairment only evident at the most advanced stages of the disease process. As such, much research has demonstrated a weak relationship between EDSS score and cognitive function in MS (e.g., Cohen, Kessler, & Fisher, 1993; Rao, Leo, Bernardin, & Unverzagt, 1991). Global assessments of cognitive function were also conducted using the Mini Mental State Exam (MMSE; Beatty & Goodkin, 1990; Rao et al., 1991) and self-reported quality of life measures that entailed questions pertaining to cognitive dysfunction in daily life (Vickrey, Hays, Harooni, Myers, & Ellison, 1995). Similar to findings with the EDSS, research has shown that the MMSE’s sensitivity for the detection of cognitive impairment relative to a comprehensive neuropsychological battery was only 23% (Rao et al., 1991).

More recently, specific aspects of cognitive impairment have been evaluated in MS (e.g., Bobholz & Rao, 2003; Hoffman, Tittgemeyer, & Yves Von Cramon, 2007; Rao et al., 1991). Despite the inter-individual variability of cognitive impairment in MS, one of the most consistent findings using objective neuropsychological tests is reduced information processing, resulting in slower processing speed and impaired working memory (Demaree, DeLuca, Gaudino, & Diamond, 1999; Hoffman et al., 2007; Huijbregts et al., 2004; Schulz, Kopp, Kunkel, & Faiss, 2006). In addition, memory recall is often impaired; however, recognition and implicit memory processes remain relatively unaffected. Individuals with MS have also demonstrated deficits in verbal fluency whereas verbal comprehension remains intact (Henry & Beatty, 2006). Several
aspects of executive functioning such as problem solving and planning can also be compromised. Finally, visuo-spatial and attentional deficits have also been reported (Joy & Johnston, 2001; McCarthy, Beaumont, Thompson, & Peacock, 2005). Converging evidence for specific aspects of cognitive dysfunction in MS has also been found using self-report questionnaires (Lovera et al., 2006; Shevil & Finlayson, 2006; Sullivan, Edgley, & Dehoux, 1990). Using the Perceived Deficits Questionnaire (PDQ), a large community dwelling sample of individuals with MS reported difficulties in the domains of retrospective memory (38%), attention and concentration (22%), prospective memory (17%), and planning/organization (17%) (Sullivan et al., 1990).

1.2.1 Information Processing Impairments in MS

As mentioned, reduced information processing is one of the most common specific neuropsychological impairments found in individuals with MS, and often emerges early after the onset of the disease. Information processing, as defined here, includes both processing speed and working memory. The mechanisms underlying each component of information processing and the assessment tools used to detect impairments are briefly reviewed below.

1.2.1.1 Processing speed. Slowed information processing speed is an early and sensitive marker of cognitive impairment in MS, and has been shown to be related to disease course, employment (Schulz et al., 2006) and quality of life (Barker-Collo, 2006), above and beyond slowed processing due to sensory and motor processes (Demaree et al., 1999; Parmenter, Shucard, & Shucard, 2007). In addition, processing speed has been shown to account for a portion of the variance in other aspects of cognitive impairment (Denny, Lynch, Parmenter, & Horne, 2004). Specifically, impaired processing speed in
MS has been shown to underlie deficits in working memory (Demaree et al., 1999), verbal fluency (Matotek, Saling, Gates, & Sedal, 2001), planning (Denney et al., 2004), story recall (Arnett, 2004), and tasks requiring controlled attention (De Sonneville et al., 2002). Furthermore, it has been repeatedly demonstrated that, if given enough time, persons with MS are able to achieve the same level of accuracy as healthy individuals, providing further support for the existence of reduced processing speed in this population (Arnett, 2004; DeLuca, Chelune, Tulsky, Legenfelder, & Chiaravalloti, 2004; Demaree et al., 1999).

The most common neuropsychological tests used to assess processing speed in this population include the Symbol Digit Modality Test (SDMT), which has been shown to be a sensitive and specific cognitive screening tool (Parmenter, Weinstock-Guttman, Garg, Munschauer, & Benedict, 2007), and the Paced Auditory Serial Addition Test (PASAT; Fischer et al., 1999; Gronwall, 1977). The PASAT has also been modified in both visual and auditory forms (Demaree et al., 1999; Legenfelder, Chiaravalloti, Ricker, & DeLuca, 2003) and for use in neuroimaging studies (Au Doung et al., 2005; Chiaravalloti et al., 2005; Forn et al., 2006; Ranjeva et al., 2006).

1.2.1.2. Working memory. As mentioned, an efficient working memory network is thought to rely, at least in part, on cognitive processing speed (Lengenfelder et al., 2003). This higher-level component of information processing is also impaired in many individuals with MS (DeLuca et al., 2004). Deluca et al. (2004) have extensively studied the interaction between processing speed, working memory, and new learning. They have postulated that in individuals with MS, slowed processing decreases working memory capacity, therefore leading to a reduction in acquired information. This
breakdown in the acquisition of new information is thought to underlie many of the
cognitive problems shown in this population. It has also been shown that although many
individuals with MS manifest slowed processing speed, as task complexity increases,
working memory difficulties become differentially more pronounced in relation to
healthy controls, especially in individuals suffering from the progressive subtypes of the
disease (Parmenter, Shucard, & Shucard, 2007). Therefore, it is presumed that some
individuals with MS have working memory difficulties that cannot be completely
accounted for by processing speed impairments (Parmenter et al., 2007), and other
studies have reported that both of these impairments can occur early in the disorder
(Parmenter, Shucard, Benedict, & Shucard, 2006; Parmenter et al., 2007). The most
common neuropsychological tests used to measure working memory include Digits
Backward and Letter Number Sequencing from the WAIS-III (Wechsler, 1997) and the
PASAT (Gronwall, 1977). In addition, the n-back task has been used to investigate the
neural correlates of the working memory system in MS (Forn et al., 2007; Sweet, Rao,
Primeau, Durgerian, & Cohen, 2006; Wishart et al., 2004).

1.2.2 Information Processing and Cognitive Theory

It has been postulated that the integrity of the information processing network is
fundamental to the efficient operation of higher order cognitive functions such as new
learning in MS (e.g., DeLuca et al., 2004). A model demonstrating the importance of
processing speed to the execution of fluid cognitive functions was developed in the
context of age-related differences in cognition. Across a series of studies, Salthouse
(1991) found that performance on tests of information processing accounted for a
substantial proportion of variance in the performance of fluid cognitive tasks in older
adults. Within this information processing network, perceptual processing speed has also been shown to account for much of the variance in working memory performance of older adults (Salthouse, 1991). Based on these findings, Salthouse (1996) hypothesized a processing speed theory of cognitive aging that attributes the breakdown in cognitive performance between younger and older adults to a decrease in the rate at which cognitive processes can be executed, as well as a reduction in the number of operations that can be conducted simultaneously. Although this theory has been used to explain age-related effects in cognitive performance, it can serve as a useful model to demonstrate the significant role that deficits in information processing, and processing speed in particular, can have for more complex domains of cognition. As noted, information processing has been shown to be an early marker of cognitive dysfunction in MS, therefore, if applied, this model could suggest that individuals with MS who manifest difficulties with information processing may also experience problems in other domains of cognition that rely on these processes to operate efficiently.

1.3 Current State of Cognition in MS

Initial evidence about cognitive impairment in MS focused on global dysfunction assessed by neurological ratings, clinician interviews, and subjective questionnaires. Although these early observations underscored the importance of examining cognitive function in this population, MS is a progressive disorder, and as such, global assessments are not able to differentiate subtle changes in cognition as people move across the spectrum of disease severity. It can be argued that an evaluation of global cognitive dysfunction is needed only in the most advanced cases of MS.
Further research has shown that specific information processing deficits emerge early in the disease course. Objective and subjective tools developed to assess specific aspects of cognitive impairment have led to the identification of subtle changes across the course of the disorder. Further research pertaining to these incremental changes in cognitive function can inform the development of focused treatments prior to the onset of global cognitive impairment, when problems may be less susceptible to remediation efforts.

1.4 Functional Impairment in MS

Across many neurological populations, examination of activities of daily living (ADL) is used to assess the functional performance or disruption of everyday activities that occurs as a result of disease or injury. This reduction in function can negatively impact independence in areas such as employment (Hakim et al., 2000; LaRocca, Kalb, Scheinberg, & Kendall, 1985; Rao et al., 1991), social roles (Hakim et al, 2000), and quality of life (Hakim et al., 2000) in MS. Community surveys have shown that following MS diagnosis, approximately 50 to 75% of individuals were no longer employed (Hakim et al., 2000; LaRocca et al., 1985; Rao et al., 1991), and the standards of living of 37% of individuals declined (Hakim et al., 2000). ADLS are usually divided into two groups based on the type of activity involved. Personal ADLS (P-ADL) involve basic functional tasks such as grooming, toileting, eating, and ambulation; whereas instrumental ADLS (I-ADL) are more complex and require the operation of higher-order cognitively demanding activities such as shopping, cooking, and driving. Given that MS is a progressive disorder, P-ADLS can remain relatively intact at the onset of the disease, but are likely to be reduced as the disease progresses. In contrast, I-ADLS
are likely to be affected earlier in the disease course, which underscores the importance of developing and validating assessment tools that are sensitive to the disruption of I-ADLS across the spectrum of disease severity (Goverover et al., 2005; Shevil & Finlayson, 2006). This information is imperative to the development of rehabilitation and retraining programs aimed at improving day-to-day functioning, independence, and quality of life.

On average, as MS progresses, physical disabilities typically become more severe, but the pattern for cognitive deficits is less clear. Therefore, although physical disabilities may have a great impact on both P-ADL and I-ADLs, declining cognitive status will also play a role, especially at earlier stages of the disorder when physical limitations are not as pronounced (LaRocca et al., 1985). Although most individuals with MS will experience a restriction in functional performance due to physical consequences of the disease, the subset that also suffer from cognitive impairment are likely to be disproportionately more affected in their daily functioning. It has been shown that individuals who were able to maintain employment and reported less barriers to social activity were less likely to be cognitively impaired (Hakim et al., 2000; Rao et al., 1991, Ryan et al., 2009).

1.4.1 Assessment of Function in MS

Initial research on functional competence in MS tended to focus on P-ADLS, which were typically manifested at later stages of the disorder. However, more recent research has focused on the development of assessment tools designed to evaluate more cognitively based I-ADLS that are more applicable across the spectrum of disease severity. These can be grouped into four main categories of assessment of functional performance: clinician-rated, performance-based: general, self-report, and performance-
based: complex (i.e., driving). Although each of these assessment types has contributed valuable information about the difficulties faced by individuals with MS, there are inherent weaknesses to consider in each category. As a result, assessment of functional performance across the spectrum of MS remains limited.

1.4.1.1 Clinician–rated. Two of the most common clinician-rated tools to assess both P-ADLS and I-ADLS are the Functional Independence Measure (FIM) and the Environmental Status Scale (ESS). In the FIM, the level of disability across a range of physical and cognitive function is determined by the amount of assistance required for completion of a particular activity, and is most often used to assess P-ADLS. The FIM is purported to assess both motor and cognitive difficulties, but recent studies in individuals with MS have shown that it is mostly sensitive to physical disability (e.g., ambulation) (Granger, Cotter, Hamilton, Fiedler, & Hens, 1990) and global cognitive dysfunction (Mansson & Lexell, 2004) and may not capture all of the information processing difficulties reported by individuals in the early stages of MS. Therefore, the FIM may not be sensitive enough to assess functional performance in early MS prior to the onset of physical impairment when P-ADLS are more intact (Mansson & Lexell, 2004).

The ESS is a clinical interview that is conducted with the patient, and if feasible, a significant other (Higginson, Arnett, & Voss, 2000; Rao et al., 1991). Ratings are made using a Likert scale to assess the patient’s difficulty with performing everyday tasks across seven domains: employment status, financial/economic status, modifications to residence, personal assistance, ability to use transportation, community assistance, and social activity. Studies using the ESS have revealed that individuals with MS who are also cognitively impaired were less likely to be working and required greater personal
assistance compared to a cognitively intact group (Rao et al., 1991). In addition, the EDSS has been shown to be a strong predictor of the ESS, suggesting that the ESS may be more sensitive at detecting functional impairments that are a result of physical rather than cognitive difficulties (Higginson et al., 2000). In short, although both the FIM and ESS are easy to administer, the evaluations are not standardized, and appear to be more sensitive at detecting functional problems that focus on more physically loaded functional impairment.

1.4.1.2 Performance-based: General. Another category of functional assessment includes performance-based measures. These tasks were developed to standardize the evaluation of functional performance to ameliorate the subjectivity that may weaken the validity of the results produced by clinician-rated assessments. One of the earliest standardized observation-based measures used in individuals with MS entailed the use of an occupational therapy evaluation conducted in the participant’s home environment (Rao et al., 1991). Therapists rated a participant’s level of dependence across six areas of daily living: dressing, elimination, mobility, bathing/hygiene, eating, and communication. In addition, a homemaking evaluation was included to address higher-level I-ADLs which entailed cooking a simple dessert, operating household appliances, and making a bed. Rao et al. (1991) reported that the MS group with cognitive impairment tended to have more problems with P-ADLS in the areas of bathing, personal hygiene, and utensil usage. For I-ADLS, MS participants with cognitive impairment demonstrated less independence when following a recipe. However, after accounting for upper extremity motor demands, the only significant difference that remained between participants with and without cognitive impairment was assistance needed during the
recipe following task. These results supported the development and use of assessments that examine I-ADL performance independent of motor difficulties. However, shortcomings of this assessment are that it is not feasible to conduct in a restricted setting and entails a complex administration that may limit reliability and repeatability across the disease course.

Another performance-based assessment, the AMPS, was used to evaluate functional impairments in individuals with MS and sought to dissociate the relative impact of motor and cognitive difficulties required for successful ADL completion. The AMPS is individually tailored to the unique functional problems reported by the individual (Doble, Fisk, Fisher, Ritvo, & Murray, 1994). Originally, the AMPS was developed to assess the motor and “process” demands required for performing both P-ADLs and I-ADLs. For example, when asked to complete an ironing task, picking up the iron represented a motor challenge, whereas decision making and organizing the steps to iron a shirt was indicative of a process component. However, for this particular study, Doble et al. (1994) focused on the performance of I-ADLS. Participants were interviewed prior to the evaluation to determine the I-ADLs that were most problematic. Compared to a healthy control group, individuals with MS had AMPS scores that reflected more dependence in completing I-ADLs for both the motor and process abilities. Although both the motor and process scales positively correlated with disease severity as measured by the EDSS, the motor ability scale was more strongly correlated with EDSS score, implying that the process elements of task performance tapped more cognitive, compared to physical, domains of functional performance.
Furthermore, a subsequent study using the AMPS recruited participants with MS in advanced stages of disability (EDSS ranged from 6.0 – 8.5). Unlike the Doble et al. (1994) study, Mannson and Lexell’s (2004) evaluation contained both P-ADL and I-ADL tasks. Problems in P-ADLs were reported in the areas of self-care, transfer, and locomotion, whereas difficulties with the execution of I-ADLs included meal preparation, laundry, and house cleaning (Mannson & Lexell, 2004).

Although the AMPS appeared to be useful for individuals across the spectrum of disease severity, there are several problems that render this assessment as impractical for routine clinical use. First, the AMPS requires a complex administration that is not practical for restricted settings. Furthermore, the AMPS is individually-tailored which makes it highly dependent on the participants’ subjective selection of tasks. This procedure raises questions about the psychometric properties of the assessment.

Another performance-based task was designed to examine the performance of everyday activities that are predominantly instrumental and rely on executive functions. The Executive Function Performance Test (EFPT) is standardized, and scoring is based on the amount and type of cueing required to help the participant complete a series of seven ADLs: hand washing, cooking oatmeal, telephone use, medication management, bill payment, and cooking a casserole (Kalmar, Gaudino, Moore, Halper, & DeLuca, 2008). The cognitively impaired MS group required more cueing overall compared to the healthy control group but not the cognitively intact MS group. More specifically, the cognitively impaired group required more cueing on the bill paying and medication management tasks compared to both the cognitively intact MS and healthy control groups.
Furthermore, in this sample, it was found that performance on the EFPT correlated with performance on neuropsychological tests assessing processing speed, executive function, and new learning but not working memory (Kalmar et al., 2008). Disease severity, as measured by the ambulation index, did not reveal significant differences between the cognitively intact and cognitively impaired MS groups, and reflected a relatively low level of physical assistance for the entire MS group. Although components of this assessment may be applicable across the spectrum of disease severity, the entire assessment entails a complex administration that is not feasible in restricted settings, and may not be practical for repeated assessments that are necessary due to the progressive nature of MS.

Another study examined a performance-based measure of I-ADL in MS that was developed to detect deficits in processing speed which may disrupt functions in everyday life (Goverover, Genova, Hillary, & DeLuca, 2007). This assessment consists of five tasks sampling common I-ADLS: communication (finding a phone number in a phone book), finance (counting change), nutrition (locating and reading ingredients from a can of food), shopping (locating items on a shelf filled with food items), and medicine (locating and reading directions from a medicine bottle). Participants with MS were significantly slower, but just as accurate, on only the nutrition and medication tasks compared to the healthy control group. It was postulated that these tasks were more sensitive at detecting functional impairments in this population because they were more cognitively demanding compared to the communication, finance, and shopping subtests. It should be noted that the disease severity of this group was unknown, so it is difficult to determine at what stage in the disease process these subtests were most sensitive.
Although this assessment seems appropriate for restricted settings and does not require a complex administration, further research is needed to establish the validity of the assessment to functional problems faced by MS individuals on a daily basis. The T-iADL is also highly focused on information processing speed, which does not take into account the influence of other cognitive domains, such as working memory, that have been shown to influence functional performance.

1.4.1.3 Self-report. Another category of functional performance assessments for individuals with MS is self-report inventories. Self-report scales are often given to the patient and a proxy. Specialized questionnaires have been designed to target specific P-ADL or I-ADL problems and others have been developed specifically based on the unique problems faced by the MS population. One questionnaire that was developed to examine functional disability for the performance of ADLs in MS is the Activities of Daily Living Scale (ADL-S; Staples & Lincoln, 1979) covering the following domains: Mobility, Communication, Personal Care, Domestic Activity, Education, Employment, and Social Activity. The ADL-S was positively correlated with EDSS scores, whereby greater functional difficulties were related to more severe neurological impairment. However, physical mobility fully accounted for the relationship, suggesting that the ADL-S was more sensitive as a measure of physical rather than cognitive difficulties in MS (Cohen, Kessler, & Fisher, 1993).

A more current self-reported survey to assess functional impairment specific to the MS population is the Functional Assessment of Multiple Sclerosis (FAMS; Cella et al., 1996). The FAMS scale consists of items divided into six subscales: mobility, symptoms, emotional well-being, general contentment, thinking/fatigue, and
family/social well-being. Although participants with MS reported more problems than matched healthy controls across all six subscales (Goverover et al., 2005), only the mobility subscale was predictive of EDSS score (Cella et al., 1996). In addition, the FAMS did not correlate with the performance-based EFPT, suggesting that it was capturing a different construct of everyday functioning. This lack of a relationship implied that both subjective and objective assessments of everyday functioning should be used in an evaluation to ensure a more comprehensive picture of the functional difficulties experienced by an individual with MS (Goverover et al., 2005).

Another survey used to measure functional performance is the Functional Behavior Profile (FBP) originally developed to assess functional capacity in dementia (Baum, Edwards, & Morrow-Howell, 1993). The FBP is comprised of items that assess the overall capacity of the person to engage in tasks (e.g., takes responsibility), interact socially (e.g., participates in activities), and to problem solve (e.g., problem solves without assistance) in his or her daily activities over the past week. Compared to healthy controls, scores on the FBP for the MS group reflected more difficulties with functional activities across all three facets and the scale significantly contributed to variance in the EFPT after accounting for depression (Goverover et al., 2005).

Self-report inventories are a common mode of assessment for functional performance because they are accessible in restricted settings, standardized, and reliable. However, problems using self-report inventories to evaluate everyday functioning include subjectivity which can be affected by factors such as awareness and depression (Goverover et al., 2005), and validity due to the low concordance between objective and subjective measures of functional performance (Goverover et al., 2005).
1.4.1.4 Performance-based: Complex. One complex behavior that is essential to independence is the ability to drive a motor vehicle. Early work examining driving ability among individuals with MS provided evidence of the existence of difficulties. For example, Knecht et al. (1977) reported that compared to a healthy control group, individuals with MS had a higher frequency of involvement in motor vehicle crashes. Research has also shown that global cognitive impairment negatively affected driving status (Schanke, Grimso, & Sundet, 1995; Ryan et al., 2009), performance on computerized driving tests (Schultheis et al., 2001), accident frequency according to Department of Motor Vehicle (DMV) records (Schultheis et al., 2002), and was a predictor of variability in lane position in a driving simulator (Marcotte, Rosenthal, Roberts, & Lampinen, 2007). Specific aspects of cognition have also been related to driving performance in MS. Reduced information processing abilities have been shown to be related to decreased performance on computerized tests (Sharawyn et al., 2002), increased errors in a driving simulator (Kotterba, Orth, Eren, Fangerau, & Sindern, 2003), and reduced performance on behind-the-wheel road tests (Lincoln & Radford, 2008; Schultheis et al., 2010). In addition, decreased executive function and visuospatial processing have been related to diminished performance in on-the-road evaluations in MS (Lincoln & Radford, 2008).

Although research has demonstrated the importance of examining driving in this population, there are several weaknesses limit the sensitivity of these assessments. The predominant real-world measure of driving performance, DMV records, are biased and underestimate the frequency of traffic violations and crashes, even in healthy populations (Williams, 2003). Computerized measures of driving performance lack validity because
they do not adequately simulate the types of driving environments and hazards encountered in real life (Schultheis et al., 2001). Two studies have employed the use of a driving simulator in individuals with MS; however, these are limited by small sample size and only examined gross measures of driving simulation performance (e.g., crash involvement; lane departure). Finally, behind-the-wheel evaluations are most sensitive for identifying driving difficulties for individuals in the advanced stages of disease severity although cognitive problems can be manifested early on (Lincoln & Radford, 2008; Schultheis et al., 2010).

1.4.1.5 Cognitive Models of Driving Behavior. Recent research has begun to conceptualize driving behavior as a combination of automatic and controlled cognitive processes. Based on the original cognitive theories of Shriffin and Schneider (1977), automatic cognitive processing is fast and effortless, which develops following consistent practice of a certain activity. In contrast, controlled processing is slow and effortful. Much of driving behavior is overlearned and automatic, especially as individuals gain years in driving experience across a variety of driving situations. However, when a novel or unfamiliar driving situation occurs, such as a child chasing a ball into the street, driving becomes more cognitively complex, as the individual is challenged to quickly react to an unanticipated situation. This type of novel situation often entails fast decision making, whereby there is an active consideration of alternative modes of behavior. In challenging or unexpected situations, in a case like the example cited above, if an individual is not able to problem-solve or process information quickly, negative consequences could result (Ranney, 1994).
Although this model can be used to examine the cognitive demands during driving, the efficient shifting between automatic and controlled levels of processing becomes especially salient when examining driving behavior in populations with compromised cognitive capabilities. This process is likely to be disrupted in these populations, whereby unexpected situations that require a shift to controlled processing to quickly find a solution and react to a novel situation may be slowed, or may fail to react at all if the override process does not engage controlled processing (Wickens, Toplak, & Wiesenthal, 2008). Research has shown that these types of cognitive failures are related to aspects of attention (Wickens et al., 2008). As mentioned, information processing deficits can emerge early in MS, so it is worthwhile to examine the potential consequences of these deficits for performance of a functional task like driving that requires both automatic and controlled cognitive processes. Although automatic processes may not be disrupted early on, it is likely that more cognitively demanding, controlled aspects of driving will be influenced by reductions in information processing.

1.5 Current State of Function in MS

Clinician-rated, performance-based: general, self-report, and performance-based: complex tools have been used to examine functional performance in individuals with MS. Although there has been a shift from the assessment of more global, diffuse problems in everyday functioning to the examination of more cognitively-based I-ADL performance, weaknesses of the current assessment tools may limit their feasibility and sensitivity across the spectrum of the disorder. Specifically, the clinician-rated inventories tend to focus on the physical rather than cognitive impairments of the disorder, and may not be sensitive enough to assess functional performance in early MS when information
processing deficits first emerge. Although performance-based ratings offer a more standardized and objective measure of functional performance, they often require a complex administration and may not be feasible in a restricted setting with limited resources which may limit the reliability and repeatability of the assessments over the course of the disorder. Furthermore, although some components of the performance-based assessments were able to discriminate between MS with and without cognitive impairment and healthy controls, the majority of the tasks included in the evaluations only targeted individuals in the most severe range of cognitive impairment. Self-report inventories are typically standardized and reliable, but their validity is in question as the nature of the tools often results in underestimation of the frequency of functional impairment and the demonstrated low concordance between performance-based and subjective reports (Goverover et al., 2005). In addition, self-report surveys can be biased by factors such as insight and depression (Goverover et al., 2005). Lastly, assessments of driving capacity in MS have revealed the existence of driving difficulties in individuals with global cognitive impairment, and has been linked to specific aspects of cognition. However, existing driving tools have limited validity and sensitivity across the spectrum of MS disease severity.

1.6 Next Step

A comprehensive evaluation of functional performance across the spectrum of disease severity in MS will require an assessment tool that addresses the weaknesses found in the current measures. To overcome these shortcomings, the comprehensive evaluation should include the following characteristics: target cognitively (rather than physically) based functional difficulties, be easy to administer, and be replicable over the
course of the disorder. Given these parameters, one approach to developing a systematic assessment of functional performance in MS could include adopting a subset of functional tasks that fulfill these requirements from tools that have already been shown to discriminate between individuals with MS with and without cognitive impairment. The bill-paying and taking medication subtests of the EFPT appear to fit many of these criteria. The entire EFPT is very complex and requires an occupational therapy suite, which makes it impractical for use for repeated and quick assessments over the course of a disorder. However, adopting subtests of the EFPT that can be conducted in a restricted environment is a way to capitalize on the strengths of this assessment, and may be sensitive for individuals in the early to moderate ranges of disability, rather than only those at the most advanced stages of the disease.

In addition, virtual reality technology can be used to target specific aspects of functional performance. A driving simulator is a tool that can be used as a quick assessment of functional performance, is standardized, requires minimal administration, and can be easily administered over multiple sessions. Furthermore, a driving simulator can include established gross measures of driving performance (e.g., speed deviation, lane management), as well as specific measures in baseline driving (e.g., straight road, curves) and challenging driving scenarios (e.g., pedestrian running into the street, car running red light) to provide a more real-world assessment of driving and functional performance in a manner not clinically available.

1.7 Current Study

There has been much research documenting the existence of cognitive impairments in individuals with MS; however, less attention has been paid to how these
cognitive problems affect performance in everyday life. Research with cognitive function in MS has shifted from a global approach, which tended to only capture cognitive problems at the most advanced stages of disease severity, to the examination of more specific aspects of cognition that are disrupted throughout the course of the disease. In contrast, most tasks that have been developed to assess functional performance have limited sensitivity across the spectrum of disease severity, and only capture global functional impairment evident in the more advanced stages of the disease. Given that difficulties with information processing are frequently reported early in the disease course, existing functional tools may not accurately detect subtle everyday impairment in early MS when initial cognitive problems emerge. The gap that exists between the assessment of cognitive and functional performance in early MS can be addressed by adopting a systematic approach to functional assessment across the course of disease severity. Understanding the impact of cognitive impairment on functional performance across the spectrum of disease severity can help clinicians identify at which point cognition impacts a person with MS and how this disruption affects the performance of everyday activities.

The overarching objective of this study is to examine the relationship between a specific domain of cognition, information processing abilities, and functional performance across the spectrum of disease severity in MS. The domain of information processing was chosen as the focus of this study because it has been shown to emerge early in the disease course in MS (Hoffman et al., 2007; Schultz et al., 2006), and it underlies performance in higher order cognitive functions (DeLuca et al., 1994; Salthouse, 1991, 1996). This relationship will be evaluated by comparing participants’
performance on functional tasks that range from simple to complex according to the
cognitive demands required for successful performance.

The original aims were as follows:

**Aim 1. To examine the relationship between information processing capacity and
disease severity in MS.**

As noted, information processing is related to the integrity of more complex
cognitive functions. Although research has identified that information processing is an
early and sensitive marker of cognitive dysfunction in MS, less is known about how
information processing changes as a function of disease severity. Knowledge about how
this domain changes over the disease course could provide insight into the subtle
cognitive changes that occur in order to better inform clinical treatment.

**Aim 2. To examine the sensitivity of functional performance tests that range from
simple to complex according to the cognitive demands required for successful
performance across the spectrum of disease severity in MS.**

Although functional performance has been investigated in MS, weaknesses in the
assessments may restrict the usability of these tools. Therefore, this study is interested in
developing better functional tools that address the limitations of the current approaches.
This includes selecting a functional assessment that targets higher-order cognitive
domains, is easy to administer, and is replicable over the course of the disorder. As such,
subtests of the DAFS will be included because they are similar to functional tasks that are
used in a variety of ADL assessments. In addition, subtests of the EFPT which have been
shown to be sensitive in MS will be included in the assessment. Also, a driving simulator
will be used because it provides more specific and objective measurements of driving
performance that are not available with many of the driving tools commonly used with this population.

**Aim 3. To examine the relationship between information processing abilities and functional performance across the spectrum of disease severity in MS.**

Although it is known that both information processing and functional performance are disrupted in MS, less is known about the specific ways in which information processing affects functional performance. It is worthwhile to examine how information processing capabilities and functional performance interact at different points in the disease course. Understanding the impact of information processing difficulties on functional performance may help clinicians identify at which point deficits in information processing affect a person with MS, and the consequences these impairments may have for functional performance.

**CHAPTER 2: METHODS**

2.1 Participant Recruitment

A total of 23 participants were recruited through the use of flyers and advertisements distributed throughout local chapters of the National Multiple Sclerosis Society (NMSS) and through the MS clinic at Thomas Jefferson University in Philadelphia, Pennsylvania. Participants were screened over the telephone and those who met the eligibility requirements were invited to participate. To be included in the study, participants had to be diagnosed with MS according to the revised McDonald criteria (2001). Participants with all four subtypes (RR, PP, SP, and PR) were included. To be eligible for inclusion, participants with MS must have had been diagnosed for at least one year prior to enrollment in the study. Participants had to be between the ages of 21 and
60, because of the rarity of individuals under 21 in MS and to reduce the potential effects of aging on cognitive performance. Potential participants were included in the study if they did not have a history of head injury, stroke, seizures, or any other significant neurological history other than MS. Participants could not have been diagnosed with a significant psychiatric illness (e.g., medical history of psychosis, schizophrenia) or have a documented substance abuse history. Participants were excluded if they experienced an exacerbation of symptoms within 30 days prior to testing. They were also required to be on a stable regimen of medications for 30 days, and could not be on corticosteroid therapy. Since virtual reality driving was a component of the study, participants included in the study had to have at least one year of driving experience, be continuously licensed for the past five years, were “active” drivers at the time of study participation, and could not use adaptive driving equipment (e.g., hand controls, steering wheel turn knob, adaptive mirrors) due to constraints imposed by the simulator. Further, individuals with a history of known motion sickness were excluded from the study due to the risk of simulator sickness during the driving simulation.

A total of 81 individuals expressed interest in the study. Thirty of the screened individuals did not meet inclusion criteria or declined to participate. The 23 individuals who were ineligible were excluded for the following reasons: 6 (26.09%) had a diagnosis of vertigo or extreme motion sickness, 4 (17.39%) for driving reasons (e.g., adaptive controls, no license), 3 (13.04%) had a neurological illness other than MS, 3 (13.04%) exceeded age criteria, 2 (8.7%) had not been diagnosed at least one year, 2 (8.7%) had substantial visual impairment, 2 (8.7%) were currently pregnant, and 1 (4.35%) was not a native English speaker. Twenty-two of the individuals were repeatedly contacted without
success and were consequently not screened for participation, and four persons were in the process of being scheduled. A total of 25 individuals were scheduled, but two canceled due to unexpected personal circumstances. All sessions were conducted in the Applied Neurotechnologies Laboratory at Drexel University in Philadelphia, Pennsylvania. At the beginning of the session participants were required to undergo IRB-approved written informed consent including HIPPA. As part of the informed consent, they were asked to complete a questionnaire that assessed their understanding of the study as well as its risks and benefits. Participants were also required to sign a release of information waiver that allowed us to obtain information from their treating neurologist to verify a clinically definite diagnosis of MS including years since onset, subtype, and severity of disease progression according to the EDSS.

2.2 Measures

All study participants were administered a battery of tests and questionnaires to examine aspects of 1) cognition, 2) functional performance, 3) motor function, 4) visual function, and 5) self-reported functioning across several domains. Cognitive domains were examined using standardized and research-based measures that are commonly used in individuals with MS to assess general intellectual function, learning and memory, verbal fluency, and information processing. Functional performance was assessed using subtests from the Direct Assessment of Functional Status (DAFS), the Executive Function Performance Test (EFPT), and a Virtual Reality Driving Simulator (VRDS). Given that many of the functional tasks included in the study required physical movements, upper and lower extremity motor function was assessed to account for potential motor impairments that could affect functional performance independent of
information processing abilities. Also, because visual difficulties are commonly seen among patients with MS and can impact functional performance (Jacobs & Galetta, 2004; Mowry, Balcer, & Galetta, 2007), a brief visual examination was conducted. Finally, because cognition and functional performance can be adversely affected by emotionality (Arnett et al., 1999; Goverover et al., 2005) and fatigue (Joy & Johnston, 2001; Strober & Arnett, 2005), several questionnaires quantifying the levels of these factors were administered.

2.3 Cognitive Measures

2.3.1 Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999). The two-subtest form (Vocabulary and Matrix Reasoning) was used as a basic screening of cognitive performance by providing a Full Scale IQ score based on age corrected norms. This test was used to rule out pre-morbid deficits of general intelligence (i.e., IQ score of 69 or below).

2.3.1.1 Vocabulary (VOCAB). The vocabulary subtest of the WASI assesses semantic word knowledge and is considered an estimate of pre-morbid verbal ability that is relatively robust to changes in neurological compromise. For this subtest, the raw score was converted to an age-corrected T-score (VOCAB-T).

2.3.1.2 Matrix Reasoning (MR). The MR subtest of the WASI assesses untimed visuo-perceptual reasoning and pattern analysis. For this subtest, the raw score was converted to an age-corrected T-score (MR-T).

2.3.2 Brief Repeatable Battery of Neuropsychological Tests (BRB-N; Rao et al., 1990). This battery was designed as a brief (i.e., 20 to 30 minute) screen to assess
impairment in patients with MS in domains that have been found to be compromised in this population. It has 15 forms which are purported to be psychometrically similar.

2.3.2.1 Selective Reminding Test (SRT; Rao et al., 1990). The SRT is included as part of the BRB-N to assess verbal learning and memory. The SRT consists of 12 words that are to be remembered across six list-learning trials. Only words that are not recalled are presented in a subsequent trial. After a 10-minute delay, long term retention of the words was assessed. The dependent variables were the number of total words included in long term storage (i.e., any word that is spontaneously recalled, without reminding, and is identified by two consecutive recalls of the word) converted to an age matched T-score (SRT-Total-T) and the total number of words recalled following the delay period (SRT-Delay).

2.3.2.2 10/36 Spatial Recall Test (SPART; Rao et al., 1990). The SPART is included as part of the BRB-N to assess visual learning and memory. For this task, the participant was presented with a 6x6 board with 10 dots placed in random locations. The board was presented for 10 seconds, removed, and the participant was required to recall the location of the dots using checkers. This process was repeated two additional times and they were asked to recall the design following a 10-minute delay. The dependent variables were the total number correct across the three trials (SPART-Total) and the total number correct following the delay period (SPART-Delay).

2.3.2.3 Word List Generation (WLG; Rao et al., 1990). The WLG is included as part of the BRB-N to assess phonemic verbal fluency. The participant was given one minute to name as many words as possible that begin with a given letter.
process was repeated for three letters. The dependent variable was the total number of correct words generated (WLG-Total).

2.3.2.4 Paced Auditory Serial Addition Test (PASAT; Gronwell, 1977). Complex information processing including processing speed, working memory, and sustained attention was assessed by means of the MSFC modified version of the PASAT (Fischer et al., 1999). The PASAT has been shown to be predictive of an individuals’ return to work after head injury (Gronwall, 1977), and has been adapted as the cognitive component of the MSFC due to its sensitivity in the MS population (Fischer et al., 1999). This task required the participant to add 61 aurally presented single digits so that each digit was added to the one immediately preceding it. Participants were given detailed instructions and a practice trial prior to starting the task. Participants completed an initial trial with an inter-stimulus interval of 3.0 seconds. Following a short break, the participant completed a practice trial and a test trial with a 2.0 second inter-stimulus interval. The dependent variables were the total number correct on each trial corrected for education and converted to a T-score (Rao et al., 1990; PASAT-2-T and PASAT-3-T).

2.3.2.5 Symbol Digit Modalities Test (SDMT; Smith, 1982). Cognitive processing speed will be assessed using the oral SDMT given the presence of motor disturbances in MS. This measure has demonstrated sensitivity and specificity for information processing difficulties in early MS, and has also been suggested as a screening tool for individuals with early MS (Parmenter et al., 2007). The oral version of the SDMT has been normed according to age and education level, and has been shown to have good psychometric properties across many samples of participants (Smith, 1982). For this task, participants were given a sheet of paper with a set of nine geometric
symbols paired with numbers from one to nine. Participants were required to say out loud the number that corresponds to the geometric symbol. There are a total of 90 symbols to be matched as quickly as possible. The dependent variable was the number of correctly matched items in 90 seconds converted to an age and education matched T-score (SDMT-T).

2.3.3 Digit Span (DS; Wechsler, 1997). The Digit Span task, a subtest of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III), is a standardized working memory and sustained attention task. Stimuli in this task consist of number series beginning with a two-number sequence. In the Digits Forward task, participants verbally repeated the number series verbatim and were given increasingly longer digit series upon meeting the performance criterion. Two trials were presented for each digit series length, and the task was discontinued following a failure on both trials. The second portion of the test, Digits Backward, follows the same procedure except the participant must recite the numbers in reverse order. The dependent variable was the total number of correct trials across Digits Forward and Digits Backward converted to an age corrected T-score (DS-T).

2.3.4 Letter Number Sequencing (LNS; Weschler, 1997). The LNS task, a subtest of the WAIS-III, is a standardized working memory task. Stimuli in this task are comprised of alternating letter and number series beginning with a two-letter sequence. Participants verbally repeated the letter-number series verbatim and were given increasingly longer letter-number series upon meeting the performance criterion. Three trials were presented for each digit series length, and the task was discontinued following
a failure on all trials. The dependent variable was the total number of correct trials converted to an age corrected T-score (LNS-T).

2.3.5 Verbal N-Back. The n-back task has been used to measure both processing speed and working memory in individuals with MS, and may be a more sensitive measure of working memory impairment compared to traditional neuropsychological measures (Parmenter et al., 2006). This sensitivity can be accomplished by modifying the traditional n-back task to tease apart the components of information processing by including a baseline condition whereby processing speed can be dissociated from working memory demands (Parmenter et al., 2006; 2007). This reduces the problem of inter-task variability in administration, novelty, and demands, and can be used to subtract the effects of simple motor and sensory processing speed (Parmenter et al., 2006; 2007).

The n-back task adopted in this study was similar to that used with MS patients by Parmenter et al. (2007), and was developed and presented using E-prime software (E-prime v. 2.0, Psychology Software Tools). Stimuli included upper and lower case letters presented at fixation. Individual letters were displayed for 400 milliseconds (ms), with a 2000 ms inter-stimulus interval. The n-back task had four conditions: 0-back, 1-back, 2-back, and 3-back. For 0-back, which is the baseline condition, the participant was instructed to respond each time the letter X was presented. For the 1-back, 2-back, and 3-back conditions, participants were instructed to attend to each letter, and to respond with the “same” key if the current letter was the same as the one presented “n” letters back, and the “different” key if the current letter was different from the letter presented “n” letters back. Prior to each condition (0, 1, 2, and 3), participants were given detailed instructions and several examples followed by a practice session.
Given that research has demonstrated that the two-back condition discriminates between individuals with MS and healthy controls (Parmenter et al., 2007), data collected from this condition was used to assess working memory demands. One of the dependent variables was the total number correct (2-back-ACC) which was measured by calculating the number of correctly identified targets. A second dependent variable was the mean reaction time collected during correct responses for the two-back condition, adjusted to reflect “complex processing speed” by subtracting basic processing speed demonstrated in the zero-back condition (2-back-RT).

2.4 Functional Performance Measures

2.4.1 Direct Assessment of Functional Status (DAFS; Loewenstein et al., 1989). The DAFS is a standardized, performance-based measure of ADL that has shown high inter-rater and test-retest reliability, convergent, and discriminant validity in a sample of individuals with Alzheimer’s disease and other related memory disorders (Loewenstein et al., 1989). The DAFS has also been validated in individuals with mild dementia (Razani, Casas, Wong, Alessi, & Josephson, 2007) and in older individuals with schizophrenia (Klapow et al., 2007). Seven functional abilities are assessed including: time orientation (assesses the person’s orientation to person, place, and time), communication skills (ability to dial a telephone, mail a letter, and write a check), transportation (patient’s knowledge of road signs and driving rules), financial (ability to perform tasks such as balancing a checkbook or counting correct change), shopping (ability to “shop” from a mock grocery store by recalling shopping items they are to memorize and to provide a written shopping list), grooming (ability to perform certain basic skills, including the
ability to comb hair or use a toothbrush), and eating (ability to perform tasks such as using utensils).

For the purposes of this study, only two subtests from the DAFS will be included to assess functional activities presumed to require simple cognitive demands. These tasks will be included to target individuals in the severe range of impairment, and are similar to functional tasks that are used in a variety of ADL assessments across many neurological populations. The tasks that were selected for inclusion are subcomponents of the financial (Counting Change) and communication (Using a Telephone) categories.

2.4.1.1 Counting Change. Administration and scoring criteria for each subtest will be adapted from Lowenstein et al. (1989). For the counting change subtest, the participant was presented with the following quantities and types of currency: 1-$10 dollar bill, 1-$5 dollar bill, 3-1$ bills, 3 quarters, 2 dimes, 1 nickel, and 3 pennies. The participant was asked to count the correct amount of change for the following amounts in this order: 6 cents, 102 cents (in change), $6.73, and $12.17. Participants were assigned one point for the correct completion of each operation. Scores can range from 0 to 4, with higher scores indicating better functional performance.

2.4.1.2 Using the Telephone. For the Using the Telephone task, the participant was presented with a standard handheld telephone and a local white pages phone book. The participant was asked to perform the following series of steps: dial the operator, dial a pre-determined number from the phone book, and dial a number presented orally by the evaluator. Participants were also evaluated on whether they were able to pick up the receiver, dial the numbers, and hang up the phone, as well as whether they completed the last three steps in the appropriate order. One point was assigned for
the correct completion of each operation. Scores can range from 0 to 8, with higher scores indicating better functional performance.

2.4.1.3 Composite. A composite DAFS (DAFS-Total) score will be used as the dependent measure for this task, and will be calculated by summing the scores for the Counting Change and Using the Telephone tasks. Scores for the DAFS-Total can range from 0 to 12 points, with higher scores indicating better functioning. The scoring criteria for each task are located in Appendix B.

2.4.2 Executive Function Performance Test (EFPT; Baum, Morrison, Hahn, & Edwards, 2007). The EFPT was developed by occupational therapists as a standardized functional assessment tool to examine cognitive functioning in an ecologically valid context (Baum & Edwards, 1993). Rather than focus on what individuals cannot do, the EFPT employs a cueing and scoring system that characterizes what functions a person can still do within four domains: simple cooking, telephone use, medication management, and bill payment. The EFPT has been validated in geriatric populations (Baum & Edwards, 1993), individuals with cerebrovascular accidents (Baum et al., 2008), schizophrenia (Katz, Tadmor, Felzen, & Harman-Macir, 2007), and MS (Goverover et al., 2005). The EFPT was administered according to the test protocol written by Baum et al. (2007). These tasks are presumed to reflect moderate cognitive demands, and will be included to target individuals in the moderate range of impairment. Within these four domains, the EFPT evaluates a person’s ability in the following categories: initiation, execution (specifically organization, sequencing, judgment and safety), and completion.
Initiation is the motor action in which the participant engages at the beginning of a task, such as walking toward a table where task materials are located and gathering items needed to accomplish the specific test. The execution component entails the correct completion of each step of the specific task and encompasses three individual requirements: organization, sequencing, and judgment. Organization includes the physical arrangement and utilization of the space and materials to allow for appropriate performance of the various steps involved in the task. Sequencing involves the correct ordering of the steps involved in the task. This component includes devoting an appropriate amount of attention to each step, and being able to efficiently switch to the next step without perseveration. The next component, judgment and safety, allows reasoning on the part of the participant to avoid physically, emotionally, or financially dangerous situations. This component can entail both avoidance and prevention behaviors depending on the particular step or task. Completion is the final component of the model. This component involves inhibition, rather than initiation, of the motor behaviors needed to indicate that the participant is finished with the task. This step typically involves the person stepping away from the materials and communicating to the experimenter that the task has been completed.

For each of the five components outlined above, there are strict guidelines for how and what type of cueing to administer. The cueing ranges from no cues (0 points), then progresses in the following order: indirect verbal guidance (1 point), gestural guidance (2 points), direct verbal assistance (3 points), physical assistance (4 points), and unable to complete without assistance (5 points). The type and level of cueing required by the participant will reflect their level of functional performance, with higher scores
indicating poorer performance. For each task, the score can range from 0 to 25 across the five components listed above.

For each of these components and subcomponents, specific cueing guidelines are followed by the evaluator to obtain an overall subtest score. In general, the experimenter will not interfere with the completion of the task unless the participant is obviously struggling with the next step in the sequence. Before providing any cues, the experimenter will wait for 10 seconds to observe the participant’s behavior. If a cue is provided, the experimenter must give two cues of the same level before moving on to the next cueing level, and must provide the cues according to the hierarchy outlined above. Each of these cueing guidelines is relevant for each step within a subtest. If a participant requires more than one level of cueing during a task, his or her score should reflect the highest level of cueing used during the entire task assessment. For this study, only the two subtests that discriminated between individuals with and without cognitive impairment in MS and between MS and healthy controls will be adopted (Goverover et al, 2005; Kalmar et al., 2008). These tasks include the Taking Medication and Bill Paying tasks. Examples of cueing for the subtests included in this study will be provided below.

2.4.2.1 Taking Medication. For the Taking Medication task, the required items included a medicine bottle with the person’s name on it filled with sugar-free candy, a medicine bottle with a different person’s name on it filled with sugar-free candy, a vitamin bottle filled with sugar-free candy, a drinking cup, and a magnifying glass. The instructions to the participant were “I need you to pretend you have a prescription in the box. Find your prescription and do what the instructions tell you to do. The pills in the
bottle are safe—they are sugar free candy.” Following the instructions, the participant was not given any further instructions unless cueing was required according to the guidelines outlined above. Indirect verbal assistance is the first level of cueing, and is delivered in the form of general questions to help the participant such as “What is the next step? or “What else do you need?”. Gestural guidance is the next level and would involve the experimenter mimicking an action that is required for that step of the task such as pointing to a specific item, or mimicking the motions necessary to open the pill bottle or use the drinking cup. Direct verbal assistance is the next level of cueing and required the experimenter to give specific cues about a step involved in the task such as “take the bottle out of the box” or “swallow the pills”. Physical assistance is the next cueing level and involved physically manipulating items necessary to aid the participant in completing the next step of the task such as loosening the cap on the medicine container. The last level of cueing, and the one requiring the most dependence, is completing the task for the participant.

2.4.2.2 Bill Paying. For the Bill Paying task, the required items included two bills (one cable and one phone) mixed with five other pieces of mail in a Ziploc bag, blank checks, a balance sheet (account register) with a balance $5.00 less than the bills total, pen, stamps, and a calculator. The instructions to the participant were “I need you to take what you need to pay the bills out of the bag, find the bills, pay them, and balance the account. These are fake bills and this is not your account but I need you to pretend that these are your bills and your account as this is part of the assessment.” Following the instructions, the participant was not given any further instructions unless cueing was required according to the guidelines outlined above. Indirect verbal assistance would be
the same as the Taking Medication task, and would entail general questions such as “What is the next step? or “What else do you need?”. An example of gestural guidance would be mimicking the motions necessary to place the stamp in the correct location on the envelope. Direct verbal assistance would be comprised of questions from the evaluator such as “pick up the pen” or “put the check in the envelope”. An example of physical assistance would include holding the checkbook while the participant writes. Finally, as with Taking Medication, the last level would require completing the task for the participant.

2.4.2.3 Composite. A composite EFPT (EFPT-Total) score was used as the dependent measure for this task, and was calculated by summing the scores for the Taking Medication and Bill Paying tasks. Scores for the EFPT-Total can range from 0 to 50 points, with higher scores indicating poorer functioning. Although accuracy was the primary dependent variable, to assess potential effects of cognitive reserve, the amount of time taken to complete each subtest was recorded and combined (EFPT-RT). The item requirement, administration instructions, tasks steps, and scoring criteria are located in Appendix C. Given the nature of the cueing and scoring system for the EFPT, research assistants were trained using a manual that clearly outlines the steps necessary for completion of the task as well as appropriate times to cue the participant. Research assistants were trained using live “mock” participants to learn the appropriate times to cue and the detailed scoring criteria, and were observed testing real participants. An effort was made to videotape the EFPT to increase the reliability of scoring. However, technical difficulties resulted in only seven participants being videotaped while completing the EFPT. Therefore, inter-rater reliability could not be calculated.
2.4.3 Virtual Reality Driving Simulator (VRDS). Driving simulation has been used in several other studies with various clinical populations (Lengenfelder, Schultheis, Ali-Shihabi, DeLuca, & Mourant, 2002; Schultheis et al., 2004; Schultheis et al., 2006). The current study used a Virtual Reality Driving Simulator (release 1.2) developed by Digital Media Works Inc. in collaboration with Maria Schultheis, Ph.D. The VRDS was designed to be a clinically accessible simulator, relies on commercially available hardware and software, and does not require specialized training and/or large space. Previous studies have found that VRDS measures performance of cognitive domains known to be relevant to driving performance (Schultheis et al., 2004), and that VRDS measures can differentiate performance between clinical populations and healthy controls (Schultheis et al., 2004). Moreover, the VRDS has been shown to generate more specific driving measures than traditional clinical driving tests (Schultheis, Rebimbas, Mourant & Millis, 2007).

The simulator allows for a large variety of vehicle types using real-world dynamics to be utilized in a variety of pre-programmed driving scenarios. Driver input is provided via a commercially available steering column and foot pedals. This study incorporated three 21-inch flat-screen monitor displays to provide an adequate sense of immersion and believability to the driver.

Administration of the VRDS takes approximately 30 minutes and included two virtual drives. The first drive was a standardized training session that allowed the participant to become familiar with the driving simulator on both a highway and residential section. For the second drive the participant drove through the VRDS route and was presented with specific driving challenges. The participant navigated the route
based on verbal instructions delivered by the examiner. Each participant completed the same route. The driving system included five types of driving zones: rural, highway, residential, school, and commercial. These zones were specifically selected from clinical driving specialists to capture real life driving situations. This study required every participant to drive though each zone once, as instructed by the examiner. Information was generated by the computer and sampled every 200 milliseconds during driving. The simulator is able to sample driving parameters including speed (mph), lane deviation (in inches), acceleration and deceleration rates (mph), and stopping behavior.

For the current study, two components of driving were assessed: Basic Driving and Challenges. Based on the model of driving theory outlined above, the challenge portion of the task was proposed to be more sensitive than basic driving across the spectrum of disease severity (Ranney, 1994).

2.4.3.1 Basic Driving. Basic driving was assessed by examining performance when driving on straight roads and curved roads. The components that were examined included two straight sections of road (both a rural highway and a regular highway). From these sections, the following measures were collected: maximum speed (mph), average speed (mph), standard deviation of speed (mph), standard deviation of deviation from the center of the line (inches), as well as the number of times the participant crossed over the lane (lane bust). The estimates of standard deviation were included to assess speed and lane management across the sections. For these sections, some aspects of performance were compared to a normative sample of age, education, and gender matched individuals (n = 13) from another study. The specific variables and
scoring system are detailed in Appendix D. The total score that can be earned from Basic Driving (BASIC) was 22 points, with higher scores reflecting better driving performance.

2.4.3.2 Challenges. The challenges component examined more cognitively complex behaviors including stopping and navigating an intersection in both a residential and rural setting. Behaviors that were sampled included whether the participant came to a complete stop and the amount of time they waited before accelerating compared to the normative group. A second challenge was how the participant responded in a construction zone. This challenge required a reduction in speed (from 55 to 30 mph), as well as navigating around construction barriers. A third challenge was when the participant encounters a child chasing a ball into the street in the residential area. Here, points were assigned according to whether the participant came to a complete stop. The last challenge variable included an assessment of whether the participant had an accident with people, objects, or other vehicles throughout the entire virtual environment. The total score that can be earned from the Challenges drive (CHALLENGE) was eight points, with higher scores reflecting better driving performance. Detailed scoring criteria are presented in Appendix E.

2.5 Motor Measures

This study relied on prior MS research and employed the physical components of the NMSS recommended measure, the MSFC (Fischer et al., 1999). Specifically, the MFSC measures leg function/ambulation (Timed Walk Task) and arm/hand function (Nine Hole Peg).

2.5.1 Timed Walk Test (TWT; Fischer et al, 1999). The TWT was used to examine lower extremity functioning, and is the time it took a participant to walk 25 feet
with usual aids. Two trials were performed and an average time was calculated for each participant. Mean performance time served as the dependent measure of lower extremity functioning (TWT).

2.5.2 Nine Hole Peg (9HPT; Fischer et al., 1999). The 9HPT was used to examine upper extremity functioning. Specifically, the 9HPT is a timed task that required the person to put nine pegs into a pegboard in any order and to subsequently remove them as quickly as possible. Two trials were conducted for both the dominant and non-dominant hands, and the average of the four total trials was used as the score. Mean performance time served as the dependent measure of upper extremity functioning (9HPT).

2.6 Visual Measures

2.6.1 Visual Acuity. Due to documented visual problems in MS (Jacobs & Galetta, 2004; Mowry et al., 2007) a standard Snellen vision test was used to determine visual acuity. The Snellen chart consists of eleven lines of block letters that decrease in size from top to bottom. A visual acuity score was computed for the right eye, left eye, and binocular vision.

2.6.2 Contrast Sensitivity (Dougherty, Flom, & Bullimore, 2005) Contrast sensitivity is another aspect of vision that can be disrupted in MS. Contrast sensitivity was tested using the Mars Letter Contrast Sensitivity Test.

2.6.3 Color Perception (Ishihara, S., 1917). Color perception can also be affected in MS and was assessed using the standard Ishihara Test.

2.7 Clinical Measures

2.7.1 Ambulation Index (AI; Hauser, 1983). The AI for each participant was estimated using information from the TWT, and the type of assistance (e.g., cane) used
during the walk. Estimates of gait difficulties and fatigue were derived from self reports of the participants. Scores range from 0 (asymptomatic and fully active) to 9 (restricted to wheelchair; unable to ambulate independently). This score is determined by having the individual walk a marked 25-foot course as quickly and safely as possible. The time it takes the person to walk the course and the type of assistance (e.g., cane, walker, crutches) required were used to determine the rating. The AI has demonstrated good test-retest, inter-rater, and convergent validity.

2.7.2 Multiple Sclerosis Functional Composite (MSFC, Fischer et al., 1999). The MSFC is a composite score that takes into account three aspects of functioning: lower extremity (TWT), upper extremity (9HPT), and cognition (PASAT-3). Each participant’s raw scores are converted to a z-score based on means and standard deviations derived from the Task Force Dataset that includes a broad spectrum of MS patients (Cutter et al., 1999). The computed z-scores are then averaged to create an overall MSFC score. Across many studies, the MSFC has demonstrated strong psychometric properties including inter-rater reliability, construct validity, and concurrent validity and is strongly correlated with the EDSS (Cutter et al., 1999; Fischer et al., 1999; Polman & Rudick, 2010). The advantages of the MSFC compared to the EDSS are that it is cost effective, practical, and does not require a physician for administration. In addition, given that the individual and composite scores are standardized, it overcomes the non-linearity problem inherent in the EDSS. One drawback of the MSFC is that the resultant z-scores can change depending on the reference population (or baseline performance) chosen, making it difficult to determine cut-off scores or to compare samples across studies. Studies have shown that the MSFC has predicted MRI status (Rudick et al., 2001), employment status
(Honarmand, Akbar, Kou, & Feinstein, 2011), and is related to quality of life (Miller, Rudick, Cutter, Baier, & Fischer, 2000) and driving skills on computerized measures (Shawaryn, Schultheis, Garay, & DeLuca, 2002).

2.8 Self-report Questionnaires

2.8.1 Fatigue Severity Scale (FSS; Krupp, LaRocca, Muir-Nash, & Steinberg, 1989). The FSS is a 9-item self-report inventory commonly used in individuals with MS to evaluate their subjective level of fatigue over the past week using a 7-point Likert scale. It was developed to differentiate fatigue from clinical depression as they share several common clinical features and can lead to misdiagnosis in neurological populations (Strober & Arnett, 2005).

2.8.2 Visual Analog Scale of Fatigue (VAS; Kos, Nagels, D’Hooghe, Duportail, & Kerckhofs, 2006). The VAS is a visual analogue scale used to assess levels of state fatigue. Participants marked their current level of fatigue on a line 10 centimeters long. It was administered five times throughout the testing day to monitor the effects of fatigue.

2.8.3 Chicago Multi-Scale Depression Inventory (CMDI; Nyenhuis et al., 1995; 1998). The CMDI was developed to assess depression in medical patients and the mood subscale has been validated for use in MS. The mood subscale contains items that measure depression without taking into account neurovegetative effects that are often present in persons with MS. Participants were asked to rate the extent to which each item described the way they have been feeling over the past week, including today, with “1” indicating that the item does not apply to them, and with “5” indicating that the item extremely applies to them. Scores for each of the scales (mood, evaluative, and vegetative) were converted into T-scores compared to a healthy control group (Nyenhuis et al., 1995).
2.8.4 Simulation Sickness Questionnaire (SSQ; Kennedy, Lane, Berbaum, & Lilienthal, 1993). Some drivers are at risk for "simulator sickness". The current protocol has several modifications to minimize this risk. Although potential participants will be screened for susceptibility to motion sickness prior to enrollment, immediately prior to the first VR drive, participants will again be asked to complete a modified version of the Pre-Exposure Symptom Checklist to assess potential risk for simulator sickness at the time of testing. Participants identified at high risk for simulator sickness will be excluded from the VRDS component of the study.

2.8.5 Quality of Life in Multiple Sclerosis (MSQOL-54; Vickrey et al., 1995). Quality of life will be examined using the MSQOL–54 instrument which has been shown to have good reliability (internal consistency, .75 to .96; test-retest, .66 to 96) and construct validity (Vickrey et al., 1995). This is a 54-item measure that assesses overall quality of life, and contains subscales that represent the following domains: physical function, role limitations (physical and emotional), pain, emotional well-being, energy, health perceptions, social and cognitive function, and health distress. From these domains, two composite scores (physical and mental) were calculated. Each composite score can range from 0 to 100, with 100 reflecting a higher quality of life.

2.9 Procedure

All of the participants recruited through the NMSS or by word of mouth (n = 20) participated in one four to five hour session completed at Drexel University. The session was broken up by a lunch break in the middle of the day. Taking this break into account, the testing sessions were split into two parts (I and II) which were counterbalanced to eliminate order and fatigue effects. However, certain measures were always administered at
the beginning and end of the testing day. Details regarding administration are outlined below. The participants that were recruited through Thomas Jefferson University (n = 3) completed only a subset of the tasks at Drexel University.

Following informed consent, all participants were asked to provide a brief medical and psychosocial history. Participants were then administered the CMDI, FSS, and initial VAS scale to obtain a pre-testing rating of fatigue.

Participants were randomly assigned to complete either session I or session II prior to a lunch break, and then completed the remaining session following the break. Part I was comprised of the measures described above in the following order: TWT, 9HPT, WASI (VOCAB, MR), RAO BRB-N (SRT-IMMEDIATE, SPART-IMMEDIATE, SDMT, PASAT, SRT-DELAY, SPART – DELAY, WLG), DS, and LNS. After these tasks were completed the participant was given a VAS to assess fatigue prior to the break.

Part II was comprised of measures described above in the following order: VAS, Visual Acuity, Contrast Sensitivity, Color Blindness, DAFS, EFPT, VRDS Training, and VRDS Challenge Drive. Prior to and following the VRDS component, participants completed the SSQ Symptom checklist to assess symptoms of simulator sickness at the time of testing. Participants were again given the VAS.

The last measure to be administered at the end of the entire session was the N-back task, followed by the final VAS.

Participants were given the MS-QOL-54 self-report questionnaire to complete during the break or when there was downtime in between tasks. At the end of the study participants were debriefed, provided with a resource packet, and compensated $50 for their time.
2.10 Summary of Modifications

Although the original overarching objective of the study was to examine the relationship between information processing and functional performance across the spectrum of disease severity, the original aims, hypotheses, and statistical analyses had to be slightly modified due to several unanticipated factors. One challenge was difficulty obtaining an EDSS score (the proposed measure of disease severity) for the majority of the participants in the study. When requesting data from treating neurologists it was discovered that many of the local physicians do not routinely employ this measure. This is in contrast to the fact that it is often used to measure severity and progression in clinical trials and research studies. Although we were unable to obtain EDSS scores for this sample, a proxy measure of disease severity was established using an estimated AI described earlier. Although not as comprehensive as the EDSS as it relies solely on ambulation and type of assistance to derive the score, it does provide some information as to the level of disease severity in this sample, and it has been shown to correlate with the EDSS. Although the AI will be used to describe the characteristics of the sample, it will not be used in the analyses as the primary indicator of disease severity or disease progression. Rather, the MSFC was chosen as the measure to replace the EDSS due to its advantages that were detailed earlier. As described, it has also been shown to correlate with the EDSS. In addition to measuring the overall influence of disease severity using the composite score, each of the three components can also be compared to cognitive and functional performance.

Another difficulty this study encountered that affected the original aims and hypotheses is the small sample size. Difficulty with recruitment resulted in a small
number of participants. As such, the current sample reflects a restricted range of disease severity and variability. A comparison between individuals in the mild, moderate, and severe stages of disease severity was initially proposed. Based on data available from the AI and MSFC, as well as the small sample size, it does not appear that this particular sample spans the spectrum of disease severity. Thus, this sample likely reflects the lower end of disease severity and progression, and is relatively high functioning, thereby presenting a restricted range (limited variability) in some of the primary variables of interest. Although it was anticipated that it would be difficult to recruit individuals in the severe range, there was also likely a self-selection bias. The original aims and hypotheses were outlined above. The following changes were made to the aims, hypotheses, and data analysis plan based on the modifications thus described. Specifically, Aim 1 and Hypothesis 1 essentially remained the same except the hypothesis was reworded to reflect the distribution of the MSFC. Aim 2 was reframed to examine the sensitivity of the functional tests within this particular sample instead of across the spectrum of disease severity. Hypotheses 2a, 2b, and 2c were also changed to reflect the examination of the relationship between the MSFC and the functional tasks. Aim 3 was initially proposed to examine whether disease severity or information processing was more predictive of functional performance. This aim was changed to examine the relationship between information processing measures and the functional performance tests. Lastly, Aim 4 is new and was added to assess the relationship between the functional tasks and other domains of cognition that are relevant in MS.
2.11 Statistical Analyses

IBM SPSS Statistics Version 19.0.0 was used to conduct all analyses. Preliminary analyses were conducted to determine whether age or education had an influence on the primary clinical, cognitive, and functional measures. If so, these were used as covariates to control for the effects of these variables. The data was checked to ensure that the assumptions for each test were not violated. If assumptions were not met, data transformations, other remedial procedures, or the use of non-parametric tests were undertaken to account for the violations.

**Aim 1. To examine information processing across the spectrum of disease severity in MS.** This aim was still examined but the MSFC was used in place of the EDSS. As described, although we are not capturing the entire spectrum of disease severity, there is still some variability in functioning within the sample. Subsequently, the following changes were made to the hypothesis:

**Hypothesis 1.** Information processing capacity will be significantly positively related to disease severity.

One-tailed Pearson correlations were performed to assess the relationship between the MSFC and information processing abilities. Five correlations were conducted to evaluate the relationship between MSFC and 1) DS-T, 2) LNS-T, 3) SDMT-T, 4) 2-Back-ACC, and 5) 2-Back-RT. The use of the PASAT was originally proposed but will no longer be used because the MSFC contains data from the PASAT-3.

A bivariate regression was conducted to examine whether information processing is predictive of disease status as measured by the MSFC. Due to concerns with low statistical power, an information processing composite score (IPS) was calculated for
each participant by averaging the T-scores from the DS-T, LNS-T, and the SDMT-T. To examine this relationship, a bivariate regression was conducted with IPS as the predictor variable and the MSFC as the outcome variable.

**Aim 2. To examine the sensitivity of functional performance tests that range from simple to complex according to the cognitive demands required for successful performance across the spectrum of disease severity in MS.** Given the modifications discussed above, this aim was able to be partially examined. It was originally hypothesized that as the cognitive demands of a functional task increase, the task would be more sensitive at detecting impairments across a wider range of disease severity. Since the range of disease severity in the current sample is limited and likely within the mild range, this aim was reframed to examine the sensitivity of these functional tests within this particular sample. This also has an effect on the proposed hypotheses and related statistical analysis.

**Overall Hypothesis.** There will be a stronger relationship between the MSFC and a functional task as the cognitive demands of a functional task increase.

**Hypothesis 2a.** There will not be a significant relationship between disease severity (MSFC) and performance on the DAFS which reflects easy cognitive demands.

Given that traditional hypothesis testing is less risk-averse to Type II error, special caution was taken when testing a proposed null finding and evaluating the results. To conclude a null finding, the critical significance level ($p$) must have exceeded .10, and the obtained effect size ($r^2$) must have been less than .09, which represents a small effect size (Cohen, 1988). Given the limited variability in performance on the DAFS, a logistic
regression was conducted with MSFC as the predictor variable and DAFS-Total as the outcome variable.

**Hypothesis 2b.** There will be a significant relationship between disease severity and performance on the EFPT, which reflects moderate cognitive demands.

Due to the violation of assumptions in the EFPT-Total, rather than the proposed regression analysis, a Kendall’s Tau b correlation was conducted between the MSFC and the EFPT-Total. To examine the effects of cognitive reserve, a bivariate regression was conducted with the MSFC as the predictor and EFPT-RT as the outcome variable.

**Hypothesis 2ci.** There will not be a significant relationship between disease severity and performance on the VRDS BASIC drive.

Again, to conclude a null finding, the critical significance level ($p$) must have exceeded .10, and the obtained effect size ($r^2$) must have been less than .09, which represents a small effect size (Cohen, 1988). Due to non normality and a restricted range in the VRDS BASIC, a two-tailed Kendall’s Tau b correlation was conducted to examine the relationship between basic driving and disease severity.

**Hypothesis 2cii.** There will be a significant relationship between disease severity and performance on the VRDS CHALLENGE drive.

A bivariate regression was conducted with the MSFC as the predictor variable and the VRDS CHALLENGE as the outcome variable.

**Aim 3. To examine the relationship between information processing abilities and functional performance.**

The original intent of this aim was exploratory and sought to examine whether information processing or disease severity played more of a role as the cognitive
demands of a functional task increase. This aim was reframed to focus on the relationship between the information processing variables and functional performance. It is expected that as the cognitive demands of a functional task increase, information processing measures will correlate more strongly to functional performance.

To examine this relationship, two-tailed correlations were performed between the three functional tests and the following information processing variables: 1) DS-T, 2) LNS-T, 3) SDMT-T, 4) PASAT-3-T, 5) 2-Back-ACC, and 6) 2-Back-RT. Correlational analyses between the information processing variables and the DAFS-Total were conducted using a point-biserial correlation. Analyses between the information processing variables and the EFPT-Total were conducted using a Kendall’s Tau b correlation due to the violation of assumptions. Pearson correlations were conducted to determine the relationship between the information processing variables and the EFPT-RT. Correlational analyses between the information processing variables and the VRDS BASIC were conducted using Kendall’s Tau b. Pearson correlations were conducted between the information processing variables and the VRDS CHALLENGE.

**Aim 4. To examine the relationship between functional performance and the cognitive domains of verbal ability, visuoperceptual reasoning, and verbal and visual learning and memory.**

Although not part of the original aims and hypotheses, the relationship between the functional tasks and additional cognitive domains (other than information processing measures) including measures of verbal ability (WLG), visuoperceptual reasoning (MR-T), and learning and memory (SRT-IMM-T, SRT-Delay, SPART-IMM, SPART-Delay) were examined as these are areas of cognitive functioning that are often reduced in
individuals with MS, or have been shown to be previously related to functional abilities. All correlations were two-tailed.

Correlational analyses between the cognitive variables and the DAFS-Total were conducted using a point-biserial correlation. Analyses between the cognitive variables and the EFPT-Total were conducted using a Kendalls Tau b correlation due to assumption violations. Pearson correlations between the cognitive variables and the EFPT-RT were also conducted. Correlational analyses between the cognitive variables and the VRDS BASIC were conducted using Kendall’s Tau b. Pearson correlations were conducted between the cognitive variables and the VRDS CHALLENGE.

CHAPTER 3: RESULTS

3.1 Characteristics of the Sample

The sample consisted of 23 participants with a diagnosis of MS. Two of the participants were male (8.7%) and 21 (91.3%) were female. Participants had a mean age of 46.22 ($SD = 8.95$) years. The mean education for the sample was 14.87 years ($SD = 1.96$). The mean IQ for the participants was 108.95 ($SD = 12.45$), which is within the average range. Regarding disease characteristics, 19 (82.6%) participants were diagnosed with the relapsing-remitting subtype, two (8.7%) with the secondary progressive subtype, one (4.3%) with the primary progressive subtype, and one (4.3%) with the progressive-relapsing subtype. On average, participants had been diagnosed with MS for 8.78 years ($SD = 6.75$), and reported an average of 11.5 years ($SD = 7.5$) since the onset of their symptoms. The mean AI for this sample was 1.70 ($SD = 1.60$; Median = 1.00; range from 0 to 6). The mean MSFC composite z-score was .12 ($SD = .56$; range from -.83 to .95). The mean z-score for the upper extremity (9HPT) was -.04 ($SD = .94$; range from -1.38 to
2.15), the mean $z$-score for the lower extremity component (TWT) was .20 ($SD = .34$; range from -1.17 to .52), and the mean $z$-score for the cognitive component (PASAT 3) was .26 ($SD = .88$; range from -1.41 to 1.16). Additional characteristics of the sample are detailed in Table 1. Correlations between the clinical outcome measures can be found in Table 2. Although the range in the sample is limited, it is comparable to a previous study from our laboratory that examined driving in MS. That study contained 66 participants with a mean age of 43.24 ($SD = 8.07$) years, mean education of 15.29 ($SD = 2.07$) years, an AI of 1.83 ($SD = 1.61$) and a mean EDSS of 3.41 ($SD = 1.76$). Other studies have also demonstrated comparable, relatively high functioning samples (Kalmer et al., 2008; Parmenter et al., 2007; Schultheis et al., 2008).

3.1.1 Emotional

Data on depression from the CMDI was available for 21 of the participants. Compared to a healthy control group including 87 control participants (mean age 49.6; $SD = 11.6$; Nyenhuis et al., 1995); the current MS sample had a mean mood $T$-score of 52.25 ($SD = 12.59$), a mean evaluative $T$-score of 50.78 ($SD = 11.97$), and a mean vegetative $T$-score of 69.26 ($SD = 17.40$). These results suggest that compared to healthy individuals, this sample of MS participants had a current level of depressive mood and evaluative symptoms within the average range; however, their increased number of vegetative symptoms is not surprising given the high frequency of these symptoms in individuals with MS.

The mean level of general fatigue in the sample was 4.41 ($SD = 1.72$), suggesting a moderate amount of fatigue. Regarding quality of life, their average self report of mental health was 71.59 ($SD = 19.15$) out of a possible 100 points, whereas their average report
of physical health was 58.90 (SD = 19.35). There was a significant difference between the mental and physical quality of life (F(1,22) = 14.91, p = .001), with individuals reporting higher mental health despite the relatively low level of physical impairment in this sample. Correlational analyses between the emotional factors are displayed in Table 3.

3.1.2 Visual

All participants had binocular acuity of at least 20/40 which is in accordance with the Department of Transportation for New Jersey and Pennsylvania. No participants were deemed to be color blind.

3.1.3 Functional

Although this study did not contain a stand-alone self-report questionnaire of cognitive or everyday functioning, general questions were asked regarding whether individuals perceived themselves as experiencing cognitive or functional difficulties. Across the sample, 18 (78.3%) participants reported physical difficulties. Seventeen participants (73.9%) reported cognitive difficulties and six (26.1%) individuals reported difficulties in activities of daily living. More specifically relating to the I-ADLs, only two (8.7%) participants indicated that they may need verbal assistance during the medication-taking test, whereas only one participant (4.3%) reported that they may need verbal assistance during the bill-paying test.

Regarding driving, the MS participants had an average of 28.76 (SD = 10.1) years of driving experience. They drove a mean of 5.48 days per week (SD = 1.83). Six (26.1%) of the participants reported a change in driving since their diagnosis. However, eight (34.8%) individuals reported that they had changed their driving behavior as a result
of their MS. Furthermore, 15 (65.2%) participants reported that their employment status changed since being diagnosed with MS.

Taken together, although the current sample may be restricted in terms of disease severity, based on self report they are still experiencing some reductions in quality of life, cognitive and physical difficulties, and changes in functional performance, in particular in the areas of driving and occupational status.

3.2 Primary Analyses

To address the aims, correlational and regression analyses will be used. When appropriate, $r^2$ will be used as a measure of effect size. The following guidelines were used to determine the magnitude of the effect based on Cohen (1988): small: $0.01 < 0.09$; medium: $0.09 \leq t < 0.25$; large: $t \geq 0.25$. When Kendall’s Tau non-parametric correlational analyses were used, effect sizes were typically not calculated as there is suggestion that they underestimate the amount of shared variance between the variables compared to parametric correlations or alternative non-parametric correlations (e.g., Spearman’s rho) (Strahan, 1982). Given the exploratory nature of this study, correction for multiple comparisons (e.g., bonferroni correction) was not used and alpha was set at .05.

**Aim 1: To examine information processing across the spectrum of disease severity in MS.**

Descriptive data for the information processing measures can be found in Table 4. The results of the correlations between disease severity and the independent information processing variables demonstrated that there was a significant positive relationship between disease severity and SDMT-T ($r = .43, p = .02, r^2 = .18$), such that 18 percent of the variance in disease severity could be explained by performance on the
SDMT, which is classified as a medium effect size. There was also a significant positive relationship between disease severity and DS-T ($r = .36, p = .05, r^2 = .13$), whereby 13 percent of the variance in disease severity could be explained by performance on DS, which was again a medium effect. The relationship between disease severity and LNS-T ($r = .19, p = .19, r^2 = .04$), 2-Back-ACC ($r = .27, p = .12, r^2 = .07$), and 2-Back-RT ($r = .09, p = .35, r^2 = .01$) did not reach significance and demonstrated small effect sizes.

To further determine which aspect of the MSFC contributed to the significant relationships, two-tailed Pearson correlations were run between each component of the MSFC (upper, lower, and cognitive), the SDMT-T, and DS-T. Both the SDMT ($r = .62, p = .002, r^2 = .38$) and the DS ($r = .53, p = .009, r^2 = .28$) were significantly positively correlated with the cognitive (but not the upper or lower extremity) components of the MSFC, and both demonstrated large effect sizes. These correlations, measures of effect size, and confidence intervals are displayed in Table 5.

When information processing was regressed on disease severity, there was a trend for the IPS to significantly predict disease severity, $a = -1.03, b = .02, SE_b = .01, p_b = .07, r^2 = .15$. Thus, although the relationship approached significance, 15 percent of the variance was shared between information processing and disease severity, accounting for a medium effect size.

Aim 2. To examine the sensitivity of functional performance tests that range from simple to complex according to the cognitive demands required for successful performance across the spectrum of disease severity in MS.

Descriptive statistics for all of the functional tests are located in Table 6.
**Hypothesis 2a.** Given that 17 (73.9%) participants achieved a perfect (i.e., 12 points) score on the DAFS-Total and the remaining six (26.1%) participants scored 11 points, a logistic regression was conducted. When disease severity was regressed on DAFS performance, $a = 1.02$, $b = 1.58$, $SE_b = .996$, $Exp(b) = 4.84$, $p_b = .11$. The relationship was not significant. As predicted, disease severity was not predictive of performance on the DAFS.

**Hypothesis 2b.** Due to the non-normal, positively skewed distribution of the EFPT-Total, the data was transformed using a logarithmic transformation but still did not achieve normality. As noted, given the non-parametric dependent variable, a Kendall’s Tau b correlation was selected because it is recommended for use with small sample sizes and when ranks are tied. An outlier (above 3 SDs) was also found in the data. Using all participants in the analysis, there was not a significant relationship between disease severity and the EFPT-Total ($r = .01$, $p = .93$). Removing the outlier from the dataset did not affect the outcome ($r = .12$, $p = .46$). Therefore, the hypothesis was not supported.

In contrast, the MSFC was a significant predictor of the EFPT-RT ($a = 518.88$, $b = -118.8$, $SE_b = 49.53$, $p_b = .03$, $r^2 = .22$), such that 22 percent of the variance in the EFPT-RT could be accounted for by the MSFC, which is a medium effect size. Two-tailed Pearson correlations were run to determine which component of the MSFC contributed to this relationship. Only the upper extremity function was significant ($r = -.43$, $p = .04$, $r^2 = .19$). Consequently, a partial correlation was conducted between the MSFC and EFPT-RT while controlling for the effects of upper extremity function, and the relationship was no longer significant ($r = -.19$, $p = n.s.$, $r^2 = .04$).
Hypothesis 2ci. One participant was unable to complete the drive due to the experience of simulation sickness, and another individual was excluded because he or she failed to meet the driving criteria. Due to the non-normal, negatively skewed distribution for the BASIC driving, the data was transformed using a logarithmic transformation but still did not achieve normality. As noted, given the non parametric dependent variable, a Kendall’s Tau b correlation was selected because it is recommended for use with small sample sizes, and when ranks are tied. An outlier (above 3SDs) was found in the data. Removing this outlier from the analysis, there was not a significant relationship between disease severity and the BASIC driving (\( r = -.01, p = .97, r^2 < .001 \)). Keeping the outlier in the dataset did not affect the outcome (\( r = .07, p = .69, r^2 = .005 \)). As such, the hypothesis that disease severity would not be related to BASIC driving skills was supported.

Hypothesis 2cii. Contrary to expectation, when disease severity was regressed on the CHALLENGE driving, \( a = 5.03, b = -.17, SE_b = .58, p_b = .76, r^2 = .005 \), the relationship was not significant and the effect size was small.

Aim 3. To examine the relationship between information processing abilities and functional performance.

There were no significant relationships between any of the information processing measures and the DAFS-Total.

There was a significant negative correlation between the EFPT-Total and the 2-Back-RT (\( r = -.41, p = .03, r^2 = .17 \)). No other correlations between the information processing variables and the EFPT-Total were significant. The positive relationship between the EFPT-RT and the PASAT-3 approached significance (\( r = -.39, p = .07, r^2 = \))
there were no significant correlations between the remaining information processing measures and the EFPT-RT.

For the VRDS, there were no significant correlations between the information processing measures and BASIC or CHALLENGE driving.

The results of the correlational analyses are located in Table 7.

**Aim 4. To examine the relationship between functional performance and the cognitive domains of verbal ability, visuoperceptual reasoning, and verbal and visual learning and memory.**

Descriptive statistics for the cognitive variables can be found in Table 8.

There were no significant relationships between any of the cognitive measures and the DAFS-Total.

There was an inverse relationship between verbal fluency (WLG-Total) and the EFPT-Total ($r = -.36, p = .04, r^2 = .13$). There were no other significant correlations between the cognitive measures and the EFPT-Total. The correlation between the EFPT-RT and verbal memory (SRT-Delay) approached significance ($r = -.43, p = .06, r^2 = .18$); however, there were no other significant correlations between the cognitive measures and EFPT-RT.

For the VRDS, there were no significant correlations between BASIC driving and the cognitive measures. For CHALLENGE driving, the only significant correlation was found for visuoperceptual reasoning (MR-T), $r = .62, p = .004, r^2 = .38$. This constitutes a large effect size, as 38% of the variance in the challenging driving could be accounted for by its relationship with visuoperceptual reasoning.

The results of the correlations between these measures can be found in Table 9.
3.3 Additional Analyses

In this sample, although information processing ability and disease severity generally did not demonstrate a relationship with any of the functional measures, regardless of the level of cognitive demand, a subset of the participants subjectively reported cognitive difficulties, receiving assistance with ADLs, and changes in occupational and driving behavior. Table 10 contains descriptive data comparing the information processing and disease severity of individuals who endorsed changes in their functional status. Given the small and unequal sample sizes, inferential statistics were not performed.

Generally, although a conclusion cannot be ascertained as to whether groups significantly differ, descriptively the data showed that participants who endorsed cognitive difficulties (n = 15) had reduced information processing and higher disease severity compared to those who did not. Regarding the self report of functional difficulties, individuals who generally endorsed these problems (n= 6) were comparable in terms of information processing but had slightly greater disease severity.

Regarding employment, participants who reported a change in their occupational status since their diagnosis of MS (n=15) had lower information processing and higher disease severity than those whose status did not change. Lastly, those who reported a change in their driving status (n = 6) had relatively greater disease severity and reduced scores on information processing measures. Taken together, although it cannot be determined whether these differences are statistically significant or clinically meaningful, much of the descriptive data is in the expected direction, such that individuals who are endorsing cognitive or functional difficulties had relatively reduced information
processing and higher disease severity. The most pronounced differences, at least in terms of mean scores, was between individuals who reported a change in their occupational or driving behavior and those who did not. This discrepancy suggests that individuals who are experiencing reduced cognitive and functional abilities may possess awareness into the potential consequences of these difficulties, and as a result self limit or change their behavior.

CHAPTER 4: DISCUSSION

The current study sought to examine the relationship between information processing and functional performance in individuals with MS. The cognitive domain of information processing was selected because difficulties in this domain typically emerge early in the disease course in MS, and can affect functioning in higher order cognitive domains (DeLuca et al., 1994; Salthouse, 1991). This study was also interested in evaluating the sensitivity of functional performance tests with varying cognitive demands. This aim was of interest due to shortcomings in the functional assessments that have been used and studied in MS. More specifically, many current measures tend to focus on global cognitive decline or personal ADLS and may not be capturing the difficulties individuals with MS are experiencing, especially early in the disease course.

Although this study initially sought to examine information processing and functional performance across the spectrum of disease severity in MS, difficulties with recruitment resulted in a sample with a restricted range of disease severity, within the mild range according to the AI. Even with limited variability in the current sample, it is worthwhile to investigate the functional difficulties of individuals with MS in the mild stages of disease severity given the existence of cognitive problems at that stage.
The initial aim of the study sought to investigate the relationship between information processing and disease severity using the MSFC. Consistent with previous research, there was variability in information processing performance, despite the highly functioning (e.g., high education and mild physical disability) sample. Although the hypothesis was initially supported such that reduced information processing was related to greater disease severity, subsequent analyses determined that the relationship was driven by the cognitive (i.e., PASAT 3) component of the MSFC. This finding reiterates the importance of including a cognitive task sensitive in MS when using a composite measure of disease severity rather than relying solely on measures of physical function.

The second aim examined the sensitivity of the functional measures within this sample and their relationship to disease severity. As expected, there was no relationship between DAFS performance and disease severity. This functional test was initially proposed to only be sensitive to individuals in the severe range of disability given its simple cognitive demands. In this sample there was very limited variability in the data for this measure, with 17 participants achieving a perfect score. In contrast, it was expected that the EFPT would be a sensitive indicator of functional impairment in this sample since it was purportedly tapping moderate cognitive demands. However, this hypothesis was not supported, as the EFPT failed to demonstrate a relationship with disease severity. Although participants’ response time on the EFPT did demonstrate a relationship with disease severity, subsequent analyses revealed that the relationship could be explained by upper extremity functioning. Lastly, although the hypothesis that basic driving would not be related to disease severity was supported, performance on
more cognitively challenging driving scenarios also did not correlate with disease severity and the effect size was small.

At first glance, it was surprising that there was no relationship between the MSFC and the challenging driving scenarios, as previous research has documented that the overall MSFC score and the cognitive component (PASAT 3) were predictive of performance on a selective attention subtest of the Useful Field of Vision (UFOV) and latency measures on the Neurocognitive Driving Test (NDT) (Shawaryn et al., 2002). However, the UFOV and the NDT are comprised of measures that assess visual attention and are sensitive to reaction time. The tests included in the MSFC are also based on speeded processing and motor reaction time. Aspects of driving performance captured in the current paradigm may not be as dependent on visual attention skills and reaction time.

The third aim examined the relationship between the functional tasks and measures of information processing. Although the DAFS did not significantly correlate with any of the measures, the EFPT demonstrated a negative relationship with reaction time on the 2-back test. This was unexpected, as this suggested that quicker reaction times were related to worse performance (i.e., more dependence) on the EFPT. Possibly, this inverse relationship may be a consequence of impulsivity such that participants tended to respond more quickly as the working memory task became more difficult. The lack of a relationship between the EFPT and measures of information processing was surprising given past research that demonstrated correlations between the EFPT and measures of processing speed as measured by the SDMT and PASAT 3 (Kalmar et al., 2008). In previous research, this relationship was found in a sample that also had a mild level of disability (AI = 3.29; SD = 2.18); however, the sample was larger (n = 74) and
the range of disease severity was more variable compared to the participants in the current study (Kalmar et al., 2008). Furthermore, the mean scores on the two subtests of the EFPT from the current sample were comparable to those obtained in the Kalmar et al. (2008) study. However, in the current study the relationship between the PASAT 3 and response time on the EFPT approached significance, indicating that faster processing speed was associated with more rapid completion of the functional measures. This finding is consistent with previous research although past studies have not examined the time taken to complete subtests of the EFPT.

There were no significant correlations between the information processing measures and either driving measure. Based on the theory of automatic versus controlled cognitive processing in driving, it was anticipated that information processing would play more of a role in challenging driving situations (Ranney, 1994; Wickens et al., 2008). As noted, previous research has established a link between driving performance, visual attention, and speeded processing of information (i.e., SDMT, PASAT) using behind-the-wheel, simulated, and computerized measures of driving skills (Kotterba et al., 2003; Lincoln & Radford, 2008; Schultheis et al., 2001; Schultheis et al., 2010). In a study by Schultheis et al. (2010), although processing speed (SDMT) was predictive of whether someone received a “less than perfect” score on a behind-the-wheel assessment, all of the individuals in this category also had an EDSS between 4.5 and 6.5, placing them in the moderate range of disease severity. The milder range of disease severity and limited variability may underlie the weak concordance between processing speed and driving ability in the current sample. Korbetta et al. (2003) conducted a driving simulation study in MS with a sample that was comparable in disease severity (EDSS = 2.8). The findings
from their study demonstrated that poorer performance on the cognitive component of the MSFC was related to a greater number of crashes (quantified as number of accidents that occurred in the environment) throughout a 60 minute virtual drive which spanned several weather (e.g., snow, rain) and daytime conditions. The length of the drive and the increased number of challenging environments compared to the current drive may have made their simulation more sensitive in a higher functioning population, although there remains the question whether this is reflective of a typical driving experience. Lincoln and Radford (2008) reported that tests of concentration and information processing were predictors of driving performance on a behind-the-wheel assessment; however, they included in their analysis individuals who could not drive due to physical limitations (e.g., inadequate eyesight or inadequate power or speed of movement in the limbs).

The fourth aim investigated whether cognitive domains including verbal fluency, visuoperceptual reasoning, and verbal and visual learning and memory were related to the functional measures. These cognitive measures were included because, in addition to information processing, they are common domains of impairment in MS. Consistent with the other findings thus far, none of measures were significantly related to performance on the DAFS. The EFPT did demonstrate a significant relationship with verbal fluency, such that worse performance (i.e. more dependence) on the EFPT was correlated with reduced verbal production. Research has demonstrated that a decline in verbal fluency is related to processing speed, and that verbal fluency can also be affected early in MS (Matotek et al., 2001). This result is consistent with Kalmar et al. (2008) who found that a composite score of executive control measures (i.e., Wisconsin Card Sorting Test (WCST) and Controlled Oral Word Association Test (COWAT)) were negatively related
to performance on the overall EFPT score, bill paying, and medication management subtests. Kalmar et al. (2008) also found a relationship between dependence on the EFPT and new learning and memory which was not replicated in this sample. However, when looking at response time on the EFPT, there was a trend towards a significant relationship with verbal memory.

Although there were no significant correlations between basic driving and the cognitive measures, performance on the challenge drive was positively related to visuoperceptual reasoning, indicating that better driving performance was indicative of stronger spatial reasoning and pattern analysis. Not surprisingly, visuoperceptual skill plays a large role in driving performance, and visuospatial reasoning may contribute to navigating complex driving environments (Lincoln & Radford, 2008).

In bringing these findings together, it is important to consider how this study may help clinicians measure function in MS. Across all of the functional measures, the DAFS was the least appropriate tool to use for functional assessment in this sample given that most individuals performed at ceiling. Although subtests of the DAFS may be useful for individuals with severe global cognitive impairment, it does not appear to be a suitable tool for use in a high functioning sample with MS. The tasks are relatively straightforward and do not rely on processing speed or higher order cognitive abilities. In contrast, the EFPT shows more promise, and the current findings build on prior research which has validated the use of these subtests of the EFPT in persons with MS. However, given the possible range on this test, even individuals with MS (with some cognitive impairment) are able to do relatively well, so it may not be capturing the difficulties they are experiencing in their daily lives. One variation of the EFPT which is not part of the
original administration is the examination of time to complete each subtest. When assessing the time taken to complete the EFPT tasks, there was more variability in the sample and it appears to be more sensitive than a total score that reflects level of dependence. The measurement of response time is particularly important considering the interaction between information processing and cognitive effort, whereby individuals with MS, particularly earlier in the disease course, can perform as accurately as healthy individuals if given unlimited time (Arnett, 2004; DeLuca et al., 2004; Demaree et al., 1999). The research literature reveals that a functional task as multifaceted and complex as driving has been defined and operationalized multiple ways. Based on the current study, which conceptualized two aspects of driving comprised of either basic or challenging tasks, it was found that gross measures such as speed management and lane deviation may not be the best way to capture driving difficulties in this population, especially earlier in the disease course. There was, however, more variability in the challenging portion of the drive, such as when individuals had to navigate an intersection or respond to an unexpected obstacle. It is important to consider which aspects of driving might be compromised in this population and the best way to capture these difficulties. Based on previous studies of cognition and function in this population, the inclusion of more reaction time measures, as well as additional challenging and/or executively demanding scenarios (e.g., navigation, increased decision making), especially under a time demand or increased cognitive load, may be more sensitive at capturing the difficulties these individuals are experiencing in their day-to-day driving. Furthermore, the drive should also be typical of a real driving experience and not merely a series of challenges or unrealistic driving conditions or scenarios (Kotterba et al., 2003).
4.1 Limitations of Current Study

Regarding limitations of the study, due to the small sample size the study suffers from low power and restricted variability, which may have made it difficult to detect effects if they existed. Another limitation concerns the demographic characteristics of the sample in the current study. As noted, although women are twice as likely as men to be diagnosed with MS, the ratio of women to men in the current sample was not reflective of the typical gender distribution which limits the external validity of the results. Furthermore, the rationale for including all subtypes of MS was to increase variability and bolster external validity; however, research has demonstrated that subtypes of the disorder may show different patterns of cognitive impairment (Huijbregts et al., 2006).

Another limitation of the study was the lack of a matched control group. The primary aim of the study was to compare information processing and functional performance across the spectrum of disease severity rather than comparing individuals with and without MS. Given that the variability in the MS sample was limited, the inclusion of a demographically matched control group would have allowed for an examination of whether individuals in the mild range of disease severity were experiencing cognitive or functional impairments compared to individuals that were not diagnosed with MS.

Although previous research has demonstrated a low concordance between subjective and objective measures of functional performance (Goverover et al., 2005), the inclusion of a standardized I-ADL measure would have provided a more comprehensive representation of the difficulties these individuals experience on a daily basis. More
Detailed knowledge of the nature and extent of the functional difficulties in persons with MS will increase the ecological validity of functional assessment tools to improve their sensitivity and relevance for this population.

Another limitation of the study was the use of the MSFC as the primary measure of disease severity or progression. Although the EDSS was unavailable for many of the participants, in research studies it remains the gold standard for disease progression and severity despite its disadvantages (e.g., non-linearity, heavily based on ambulation). In particular, clinical trials routinely employ the EDSS to assess the efficacy of drug therapies and intervention tools in MS. For the current study, although the disease severity was estimated using the AI (which correlates highly with the EDSS) it is difficult to directly compare the results from this sample to other research studies that have used the EDSS as their primary measure of disease severity. Although use of the MSFC as an outcome measure of disease progression is gaining popularity due to its advantages over the EDSS (e.g., inclusion of a cognitive component, linearity), there are drawbacks that make it problematic as the sole measure of disease severity. For instance, the MSFC does not include a measure of visual progression, and, unlike the EDSS, cut-off points for determining disease severity (i.e., mild, moderate, severe) have not been established, in particular as the use of different reference populations can influence the resultant z-scores inherent in this measure (Fischer et al., 1999; Polman & Rudick, 2010).

Finally, there were additional limitations due to the methodological and statistical design of the study. Due to the lack of comparison groups, the study design was correlational, which limits the inferences that can be drawn about causality between the variables. As a consequence of low power, some hypotheses were evaluated using a
composite measure of information processing variables. Although cognitive composite scores are often used in research, one drawback is that variables in a composite measure may not be equally weighted, thereby distorting the relationship between the construct and the variable of interest.

4.2 Implications/Future Directions

Thinking about the results of this study in the context of the current sample, one conclusion that may be drawn is that these individuals may not be experiencing functional difficulties, or they may have cognitive impairment but it has not reached a level sufficient enough to interfere with daily functioning. Although a formal, standardized self report of ADLS was not available, based on a brief interview a subset of the individuals reported experiencing cognitive, and to a lesser extent functional, difficulties that were impacting their quality of life and employment status. This suggests that some of these individuals may be experiencing functional impairment that was not being captured in the current assessment. As was reviewed above, perhaps the inclusion of more ecologically valid and cognitively demanding settings or tasks, such as simulation of a work environment, would be a more appropriate assessment for individuals in this range of disease severity. Along those lines, a recent study examined functional performance termed “actual reality” in MS (Goverover, O’Brien, Moore, & DeLuca, 2010). The participants were required to use the internet to purchase airline tickets. Even in a small sample with limited disease severity ($n = 21$; $AI = 2.8$) participants with MS had significantly more difficulty on the task compared to healthy controls, and impaired cognitive functioning was predictive of functional task
performance. Unlike the original EFPT, it also measured time for completion which this study also recommends as an important variable in this population.

Further support for the development of ecologically valid and updated assessment tools is evidenced by the high number of individuals in the current sample that reported using the internet to manage their finances. This is an important consideration as some of the functional tasks that were developed in the past may become obsolete or less relevant as changes in society or technology (e.g., use of internet, cellular communication) influences the way we accomplish everyday tasks. For instance, functional tools such as the DAFS were developed for an elderly dementia cohort in a time when individuals routinely used paper and pencil methods to balance their checkbooks and had limited access to electronic tools to help them manage their finances, operate a telephone, and arrange transportation. The study and development of functional assessment tools will continue to be an evolving area of research as technology changes how we manage and accomplish ADLS. With regards to a neurological disorder like MS, individuals are usually diagnosed in early adulthood when they are typically in the prime of their lives or career. As noted, only three individuals indicated they would need assistance with the medication management and bill paying portions of the EFPT. Although these tests were chosen because previous research has shown that they discriminated between healthy individuals and MS participants with and without cognitive impairment, these aspects of everyday functioning in a high functioning group of individuals may not adequately reflect their difficulties. For instance, a task such as medication management is typically an overlearned, routine task, and individuals are likely more proficient at managing their own medication regimen than those that are artificially simulated in a laboratory.
environment. As such, medication management may not be disrupted until cognitive impairment has progressed. Perhaps the initial breakdown of information processing does not adversely affect a task such medication management, as difficulty in this domain may be more related to compromised executive processing (e.g., source memory) and failures of prospective memory (e.g., remembering when to take medication). It will be important to consider the needs of the MS population with regards to what functional assessments will be most appropriate.

As noted, one unexpected limitation encountered in the current study was the difficulty obtaining current EDSS scores for the research participants. The EDSS is often the primary outcome measure of disease progression in clinical trials and research studies. However, it appeared that few neurologists in the Pennsylvania and New Jersey metropolitan areas were routinely employing this measure. This limitation illustrates the gap that exists between clinical practice and research. Although clinical work should drive and inform research hypotheses, tools that are used in research should also be routinely employed in clinical settings to make the research generalize to clinical work. In the area of functional assessment, much research has focused on using performance-based measures that are typically not employed in outpatient clinical practice. Given the described limitations of self-report measures, increased integration of performance-based tools into clinical practice will be necessary to effectively assess and treat progressive neurological disorders such as MS.

Although the sample in the current study was limited, this research does provide information about the relationship between the MSFC and functional performance. The MSFC has been examined in relation to quality of life (Miller et al., 2000), employment
status (Honarmand et al., 2011), and driving (Shawaryn et al., 2002); however, less is known about its relationship to functional performance in this population. Given that the MSFC is becoming more popular as an outcome measure in research and clinical trials, information about its usefulness with regards for determining functional status is warranted.

Another contribution of the study is that it is one of the few published studies to examine driving in MS using a virtual reality simulator. Information about the usability of this tool in a heterogeneous and progressive disorder such as MS is necessary. Although the sample in the current study was relatively high functioning, a subset of individuals reported a change in driving status or altering their driving behavior, which has also been documented in previous studies (Ryan et al., 2009; Schultheis et al., 2008). Thus, even in the earlier stages of disease severity individuals are noticing difficulties in this domain, so more research is necessary to determine the variables that are relevant in this population (e.g., more novel and challenging driving scenarios, inclusion of reaction time measures).

Defining functional performance is a challenging process, as there are a broad range of activities that fall under the functional domain. Although it is important to examine functioning across the spectrum of disease severity in MS, it is also worthwhile to identify correlates of cognitive and functional impairment earlier in the disease course when individuals will be able to derive the most benefit from rehabilitation techniques or other interventions. More research in this area is necessary to develop functional assessments that are sensitive to the multidimensional and heterogeneous nature of this disorder. Finally, given that MS is a progressive disorder, assessing the repeatability of
functional measures through the use of longitudinal studies will allow for an examination of how cognition and functional performance change over time, and the way they interact to influence daily functioning and quality of life.
List of References


APPENDIX A: Tables

Table 1. Demographic Variables for MS ($n = 23$)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>46.22 (8.95)</td>
</tr>
<tr>
<td>Education (years)</td>
<td>14.87 (1.96)</td>
</tr>
<tr>
<td>Sex % (n)</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>91.3 (21)</td>
</tr>
<tr>
<td>Men</td>
<td>8.7 (2)</td>
</tr>
<tr>
<td>Ethnicity % (n)</td>
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<tr>
<td>Caucasian</td>
<td>91.3 (21)</td>
</tr>
<tr>
<td>African American</td>
<td>8.7 (2)</td>
</tr>
<tr>
<td>Handedness % (n)</td>
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<tr>
<td>Right</td>
<td>95.7 (22)</td>
</tr>
<tr>
<td>Left</td>
<td>4.3 (1)</td>
</tr>
<tr>
<td>Marital Status % (n)</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>39.1 (9)</td>
</tr>
<tr>
<td>Married</td>
<td>60.9 (14)</td>
</tr>
<tr>
<td>Employment % (n)</td>
<td></td>
</tr>
<tr>
<td>Disability</td>
<td>39.1 (9)</td>
</tr>
<tr>
<td>Full Time</td>
<td>30.4 (7)</td>
</tr>
<tr>
<td>Part-Time</td>
<td>13.0 (3)</td>
</tr>
<tr>
<td>Student</td>
<td>4.3 (1)</td>
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<tr>
<td>Other</td>
<td>13.0 (3)</td>
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<tr>
<td>Ambulation Index</td>
<td>1.70 (1.60)</td>
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<tr>
<td>Years since Diagnosis</td>
<td>8.78 (6.75)</td>
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<td>Type of MS % (n)</td>
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<tr>
<td>Relapsing Remitting</td>
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<tr>
<td>Secondary Progressive</td>
<td>8.7 (2)</td>
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<tr>
<td>Primary Progressive</td>
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<tr>
<td>Progressive Relapsing</td>
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NOTE: Data are presented as means and standard deviations (SD) unless otherwise noted.
### Table 2. Correlations between Clinical Outcome Measures

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<tr>
<th></th>
<th>Two tailed</th>
<th>Upper</th>
<th>Lower</th>
<th>Cognitive</th>
<th>AI</th>
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</thead>
<tbody>
<tr>
<td>MSFC (z-score)</td>
<td>0.69**</td>
<td>0.48**</td>
<td>0.49**</td>
<td>-0.41**</td>
<td></td>
</tr>
<tr>
<td>Upper (z)</td>
<td>-</td>
<td>0.52**</td>
<td>0.17</td>
<td>-0.53**</td>
<td></td>
</tr>
<tr>
<td>Lower (z)</td>
<td>-</td>
<td>-</td>
<td>0.16</td>
<td>-0.62**</td>
<td></td>
</tr>
<tr>
<td>Cognitive (z)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-0.04</td>
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</table>

* p < .05  
** p < .01

### Table 3. Correlations between Emotional Measures

<table>
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<th></th>
<th>Two tailed</th>
<th>Physical QOL</th>
<th>CMDI Mood</th>
<th>FSS</th>
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<tbody>
<tr>
<td>Mental QOL</td>
<td>0.67**</td>
<td>-0.79**</td>
<td>-0.49**</td>
<td></td>
</tr>
<tr>
<td>Physical QOL</td>
<td>-</td>
<td>-0.42</td>
<td>-0.71**</td>
<td>0.35</td>
</tr>
<tr>
<td>CMDI Mood</td>
<td>-</td>
<td>-</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* p < .05  
** p < .01

### Table 4. Descriptive Statistics for Information Processing Measures

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDMT Raw</td>
<td>55.91</td>
<td>12.72</td>
<td>57.00</td>
<td>14.00</td>
</tr>
<tr>
<td>SDMT T Score</td>
<td>47.10</td>
<td>13.96</td>
<td>48.22</td>
<td>16.10</td>
</tr>
<tr>
<td>PASAT 3 Raw</td>
<td>48.13</td>
<td>10.57</td>
<td>49.00</td>
<td>15.00</td>
</tr>
<tr>
<td>PASAT 3 T Score</td>
<td>48.87</td>
<td>11.67</td>
<td>48.60</td>
<td>15.46</td>
</tr>
<tr>
<td>PASAT 2 Raw</td>
<td>34.78</td>
<td>11.77</td>
<td>36.00</td>
<td>21.00</td>
</tr>
<tr>
<td>PASAT 2 T Score</td>
<td>46.63</td>
<td>12.28</td>
<td>46.67</td>
<td>19.79</td>
</tr>
<tr>
<td>LNS Raw</td>
<td>10.48</td>
<td>2.31</td>
<td>10.00</td>
<td>3.00</td>
</tr>
<tr>
<td>LNS T Score</td>
<td>51.26</td>
<td>8.52</td>
<td>50.00</td>
<td>14.00</td>
</tr>
<tr>
<td>DS Raw</td>
<td>17.17</td>
<td>4.64</td>
<td>16.00</td>
<td>9.00</td>
</tr>
<tr>
<td>DS T Score</td>
<td>50.87</td>
<td>10.76</td>
<td>47.00</td>
<td>20.00</td>
</tr>
<tr>
<td>2 Back Total (%Acc) (n = 21)</td>
<td>76.35</td>
<td>13.49</td>
<td>79.05</td>
<td>16.22</td>
</tr>
<tr>
<td>2 Back RT (ms) (n = 19)</td>
<td>454.50</td>
<td>218.05</td>
<td>418.07</td>
<td>249.05</td>
</tr>
</tbody>
</table>

Note: SD = standard deviation; IQR = interquartile range
Table 5. Correlations between Information Processing Measures & MSFC

<table>
<thead>
<tr>
<th></th>
<th>One-tailed</th>
<th>MSFC</th>
<th>95% CI</th>
<th>One-tailed</th>
<th>Upper</th>
<th>Lower</th>
<th>Cognitive</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDMT-T</td>
<td>0.43*</td>
<td>0.18</td>
<td>0.02 to .90</td>
<td>SDMT-T</td>
<td>0.18</td>
<td>0.25</td>
<td>0.62**</td>
</tr>
<tr>
<td>DS-T</td>
<td>0.36*</td>
<td>0.13</td>
<td>-.06 to .82</td>
<td>DS-T</td>
<td>0.16</td>
<td>0.22</td>
<td>0.53**</td>
</tr>
<tr>
<td>LNS-T</td>
<td>0.19</td>
<td>0.04</td>
<td>-.25 to .63</td>
<td>LNS-T</td>
<td>0.05</td>
<td>-0.08</td>
<td>0.34</td>
</tr>
<tr>
<td>2-Back-ACC</td>
<td>0.27</td>
<td>0.07</td>
<td>-.16 to .72</td>
<td>2-Back-ACC</td>
<td>-0.06</td>
<td>0.34</td>
<td>0.54*</td>
</tr>
<tr>
<td>2-Back-RT</td>
<td>0.09</td>
<td>0.01</td>
<td>-.35 to .53</td>
<td>2-Back-RT</td>
<td>0.14</td>
<td>-0.20</td>
<td>0.13</td>
</tr>
</tbody>
</table>

*p ≤ .05
**p < .01

Table 6. Descriptive Statistics for Functional Measures

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAFS</td>
<td>11.74</td>
<td>0.45</td>
<td>12.00</td>
<td>1.00</td>
</tr>
<tr>
<td>EFPT-Total (n = 22)</td>
<td>1.91</td>
<td>1.72</td>
<td>1.00</td>
<td>2.25</td>
</tr>
<tr>
<td>EFPT-RT (seconds)</td>
<td>504.68</td>
<td>143.01</td>
<td>470.86</td>
<td>186.00</td>
</tr>
<tr>
<td>Basic Drive (n = 20)</td>
<td>18.45</td>
<td>2.46</td>
<td>19.00</td>
<td>2.00</td>
</tr>
<tr>
<td>Challenge Drive (n = 21)</td>
<td>5.00</td>
<td>1.38</td>
<td>5.00</td>
<td>2.00</td>
</tr>
</tbody>
</table>

Note: SD = standard deviation; IQR = interquartile range

Table 7. Correlations between Information Processing and Functional Performance

<table>
<thead>
<tr>
<th></th>
<th>SDMT-T</th>
<th>PASAT-3-T</th>
<th>LNS-T</th>
<th>DS-T</th>
<th>2-B-ACC</th>
<th>2-B-RT</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAFS -Total</td>
<td>0.06</td>
<td>0.08</td>
<td>0.01</td>
<td>-0.12</td>
<td>-0.06</td>
<td>0.16</td>
</tr>
<tr>
<td>EFPT-Total (n = 22)</td>
<td>-0.08</td>
<td>-0.11</td>
<td>-0.13</td>
<td>-0.15</td>
<td>-0.04</td>
<td>-0.41**</td>
</tr>
<tr>
<td>EFPT-RT</td>
<td>-0.10</td>
<td>-0.39*</td>
<td>-0.03</td>
<td>-0.07</td>
<td>-0.12</td>
<td>-0.11</td>
</tr>
<tr>
<td>Basic Drive (n = 20)</td>
<td>-0.05</td>
<td>-0.11</td>
<td>-0.30</td>
<td>-0.18</td>
<td>0.22</td>
<td>0.06</td>
</tr>
<tr>
<td>Challenge Drive (n = 21)</td>
<td>-0.04</td>
<td>0.05</td>
<td>0.12</td>
<td>-0.11</td>
<td>0.01</td>
<td>-0.08</td>
</tr>
</tbody>
</table>

NOTE: B = Back
*p < .07
**p < .05
Table 8. Descriptive Statistics for Cognitive Measures

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>VOCAB Raw</td>
<td>61.22</td>
<td>7.39</td>
<td>61.00</td>
<td>9.00</td>
</tr>
<tr>
<td>VOCAB-T</td>
<td>53.35</td>
<td>7.95</td>
<td>53.00</td>
<td>11.00</td>
</tr>
<tr>
<td>MR RAW ($n = 22$)</td>
<td>25.82</td>
<td>5.02</td>
<td>26.00</td>
<td>7.00</td>
</tr>
<tr>
<td>MR-T</td>
<td>57.00</td>
<td>9.02</td>
<td>58.50</td>
<td>9.00</td>
</tr>
<tr>
<td>WLG-Total ($n = 21$)</td>
<td>32.10</td>
<td>7.44</td>
<td>32.00</td>
<td>10.00</td>
</tr>
<tr>
<td>SPART-Total ($n = 22$)</td>
<td>19.05</td>
<td>6.37</td>
<td>20.00</td>
<td>11.00</td>
</tr>
<tr>
<td>SPART-Delay</td>
<td>6.45</td>
<td>2.65</td>
<td>7.00</td>
<td>5.00</td>
</tr>
<tr>
<td>SRT-Total-T ($n = 20$)</td>
<td>43.58</td>
<td>14.56</td>
<td>44.60</td>
<td>20.74</td>
</tr>
<tr>
<td>SRT-Delay</td>
<td>7.20</td>
<td>3.58</td>
<td>7.00</td>
<td>5.00</td>
</tr>
</tbody>
</table>

Note: SD = standard deviation; IQR = Interquartile Range

Table 9. Correlations between Functional Measures and Cognitive Tasks

<table>
<thead>
<tr>
<th>Measure</th>
<th>WLG</th>
<th>MR-T</th>
<th>SPART Total</th>
<th>SPART Delay</th>
<th>SRT Total-T</th>
<th>SRT Delay</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAFS-Total</td>
<td>-0.22</td>
<td>-0.25</td>
<td>-0.27</td>
<td>-0.11</td>
<td>0.04</td>
<td>-0.09</td>
</tr>
<tr>
<td>EFPT-Total ($n = 22$)</td>
<td>-0.36**</td>
<td>-0.08</td>
<td>0.03</td>
<td>0.06</td>
<td>-0.21</td>
<td>-0.26</td>
</tr>
<tr>
<td>EFPT-RT</td>
<td>-0.29</td>
<td>0.17</td>
<td>0.16</td>
<td>0.14</td>
<td>0.35</td>
<td>-0.43*</td>
</tr>
<tr>
<td>Basic Drive ($n = 20$)</td>
<td>-0.01</td>
<td>0.05</td>
<td>-0.06</td>
<td>0.01</td>
<td>0.07</td>
<td>0.19</td>
</tr>
<tr>
<td>Challenge Drive ($n = 21$)</td>
<td>-0.19</td>
<td>0.61***</td>
<td>0.27</td>
<td>0.11</td>
<td>0.04</td>
<td>-0.10</td>
</tr>
</tbody>
</table>

*p < .06
**p < .05
***p < .01
Table 10. Descriptive Statistics for the Self-Report Functional Variables

<table>
<thead>
<tr>
<th></th>
<th>IPS</th>
<th></th>
<th></th>
<th>MSFC</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Cognitive Difficulty - yes</td>
<td>17</td>
<td>48.51</td>
<td>6.65</td>
<td>0.03</td>
<td>0.55</td>
</tr>
<tr>
<td>Cognitive Difficulty - no</td>
<td>6</td>
<td>52.41</td>
<td>6.65</td>
<td>0.36</td>
<td>0.55</td>
</tr>
<tr>
<td>ADL Difficulty - yes</td>
<td>6</td>
<td>50.66</td>
<td>7.18</td>
<td>-0.10</td>
<td>0.37</td>
</tr>
<tr>
<td>ADL Difficulty - no</td>
<td>17</td>
<td>49.13</td>
<td>9.93</td>
<td>0.20</td>
<td>0.60</td>
</tr>
<tr>
<td>Employment Status - Same</td>
<td>8</td>
<td>54.60</td>
<td>4.44</td>
<td>0.39</td>
<td>0.57</td>
</tr>
<tr>
<td>Employment Status - Different</td>
<td>15</td>
<td>46.82</td>
<td>9.97</td>
<td>-0.03</td>
<td>0.51</td>
</tr>
<tr>
<td>Change in Driving - Yes</td>
<td>6</td>
<td>44.65</td>
<td>9.60</td>
<td>-0.13</td>
<td>0.49</td>
</tr>
<tr>
<td>Change in Driving - No</td>
<td>17</td>
<td>51.25</td>
<td>8.63</td>
<td>0.21</td>
<td>0.57</td>
</tr>
</tbody>
</table>

Note: IPS = Information Processing Composite T-Score (including PASAT-3)  
MSFC = Multiple Sclerosis Functional Composite Z-Score
APPENDIX B: Response Form for the DAFS

**Counting Change**

<table>
<thead>
<tr>
<th>Notes</th>
<th>Correct</th>
<th>Incorrect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 point</td>
<td>0 point</td>
</tr>
</tbody>
</table>

- 6 cents
- 102 cents
- $6.73
- $12.17

Subtotal

**Using the Telephone**

<table>
<thead>
<tr>
<th>Notes</th>
<th>Correct</th>
<th>Incorrect</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 point</td>
<td>0 point</td>
</tr>
</tbody>
</table>

- Dial operator (0)
- Dial number from phone book
- *Mark's Hardwood Floors Co. 215-527-6420*
- Dial number presented orally
- 610-235-9173
- Dial number written down

Hand number to participant.

- Pick up receiver
- Ability to dial
- Hang up phone
- Correct sequence across all previous trials

Subtotal

Total

Notes:
APPENDIX C: Instructions and Response Forms for the EFPT

Medication Taking

Required Items:
- Medicine bottle with instructions on it – with the person’s name on it – filled with sugar-free candy
- Medicine bottle as a distractor (another person’s prescription) – filled with sugar-free candy
- Vitamin bottle (non prescription) as a distractor – filled with sugar free candy
- Water
- Drinking cup
- Magnifying glass

Experimenter Script:
“I need you to pretend you have a prescription in the box. Find your prescription and do what the instructions tell you to do. The pills in the bottle are safe – they are sugar free candy.”

After they take the pills, ask the following questions to rate judgment and safety:
- What times during the day are you supposed to take this medication?
- What are you supposed to take with this medication?
- What do you need to be careful of when you take this medication?

<table>
<thead>
<tr>
<th>Initiation: Upon your request to start, participant moves to table.</th>
<th>Independent</th>
<th>Verbal Guidance</th>
<th>Gestural Guidance</th>
<th>Verbal Direct Instruction</th>
<th>Physical Assistance</th>
<th>Do-For Participant</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Execution: Carrying out the actions without organization, sequencing judgment.</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

Organization: Retrieves needed items
- Sequencing: execution of steps in appropriate order.
- Participant performs steps in appropriate sequence.
- Reads directions on the pill bottle.
- Opens pill bottle.
- Pours pills into hand or on table.
- Chooses correct number of pills according to prescription.
- Puts unused pills back into bottle.
- Puts pills in mouth and swallows.
- Puts cup back on bottle.

Judgment & Safety: avoidance of dangerous situation.
- Participant prevents or avoids danger.
- Takes correct pills.
- Takes correct number of pills.
- Doesn’t put water near edge of table.
- Doesn’t openpill bottle and play with pills.

Completion: Termination of task.
- Participant knows he/she is finished.
- Moves away from the task.
- Doesn’t open pill bottle and play with pills.

Score 0-6
Time to Complete

Total Score
Bill Paying

Required Items:
- Two bills (one cable, one phone) mixed with five other pieces of mail (letter from credit card company, announcement of a sale, etc.) in a Ziploc bag
- Checks
- Balance sheet (account book) with a balance $5.00 less than the bills total
- Pen
- Stamps
- Calculator

Experimenter Script:
“I want you to take what you need to pay the bills out of the bag, find the bills, pay them, and balance the account. These are fake bills and this is not your account but I need you to pretend that these are your bills and your account as this is part of the assessment.”

<table>
<thead>
<tr>
<th>Indication</th>
<th>Independent</th>
<th>Verbal Guidance</th>
<th>Gestural Guidance</th>
<th>Verbal Direct Instruction</th>
<th>Physical Assistance</th>
<th>Do For Participant</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initiation</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Execution</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>5</td>
<td>1</td>
</tr>
</tbody>
</table>

Organization: Retrieves needed items
- Sequencing: execution of steps in appropriate order.
  - Participant performs steps in appropriate sequence.
  - Unlocks the bill.
  - Checks the balance.
  - Writes the check for the correct amount.
  - Puts check in the envelope and address it.
  - Puts stamp on envelope and seals it.
  - Locates second bill, checks balance, etc.

Judgment & Safety: avoidance of dangerous situation.
- Participant prevents or avoids danger.
- Makes check in the correct amount and signs it.
- Verifies correct address.
- Subtracts check amount from the balance.
- Doesn't write second check (not enough money).

Completion: Termination of Task.
- Participant knows he/she is finished.
- Puts down the checkbook.
- Doesn’t continuously write checks or furiously write at the checkbook, etc.
## APPENDIX D: Scoring Form for VRDS-BASIC

<table>
<thead>
<tr>
<th>Topic</th>
<th>Subtopic</th>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Speed</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Highway 1</td>
<td>Max MPH (55 mph; 23-24)</td>
<td>6 to 10 miles over speed limit</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11 to 15 mph over speed limit</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16 to 25 mph over speed limit</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>26 to 30 mph over speed limit</td>
<td>0</td>
</tr>
<tr>
<td>Highway 2</td>
<td>Max MPH (55 mph; 29b-30)</td>
<td>6 to 10 miles over speed limit</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11 to 15 mph over speed limit</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16 to 25 mph over speed limit</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>26 to 30 mph over speed limit</td>
<td>0</td>
</tr>
<tr>
<td>Highway 3</td>
<td>Max MPH (45 mph; 07-09)</td>
<td>6 to 10 miles over speed limit</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11 to 15 mph over speed limit</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>16 to 25 mph over speed limit</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>26 to 30 mph over speed limit</td>
<td>0</td>
</tr>
<tr>
<td>Mean MPH</td>
<td>Highway 1</td>
<td>40.94 to 57.42 -1 SD to 1 SD from normative mean</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; 40.94 or &gt; 57.42 &gt; 1 SD around the normative mean</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Highway 2</td>
<td>32.16 to 51.20 -1 SD to 1 SD from normative mean</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; 32.16 or &gt; 51.20 &gt; 1 SD around the normative mean</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Highway 3</td>
<td>37.09 to 41.92 -1 SD to 1 SD from normative mean</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; 37.09 or &gt; 41.92 &gt; 1 SD around the normative mean</td>
<td>0</td>
</tr>
<tr>
<td>Mean STD MPH</td>
<td>Highway 1</td>
<td>1.28 to 4.38 -1 SD to 1 SD from normative mean</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;1.28 or &gt;4.38 &gt; 1 SD around the normative mean</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Highway 2</td>
<td>2.72 to 7.40 -1 SD to 1 SD from normative mean</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; 2.72 or &gt; 7.40 &gt; 1 SD around the normative mean</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Highway 3</td>
<td>.76 to 3.51 -1 SD to 1 SD from normative mean</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; .76 or &gt; 3.51 &gt; 1 SD around the normative mean</td>
<td>0</td>
</tr>
<tr>
<td><strong>Lane Management</strong></td>
<td>Highway 1</td>
<td>10.35 to 34.99 -1 SD to 1 SD from normative mean</td>
<td>1</td>
</tr>
<tr>
<td>STDoF Lane Deviation</td>
<td></td>
<td>&lt; 10.35 or &gt; 34.99 &gt; 1 SD around the normative mean</td>
<td>0</td>
</tr>
<tr>
<td>Inches</td>
<td>Highway 2</td>
<td>23.63 to 63.65 -1 SD to 1 SD from normative mean</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; 23.63 or &gt; 63.65 &gt; 1 SD around the normative mean</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Highway 3</td>
<td>11.40 to 22.48 -1 SD to 1 SD from normative mean</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; 11.40 or &gt; 22.48 &gt; 1 SD around the normative mean</td>
<td>0</td>
</tr>
<tr>
<td>Lane Busts</td>
<td></td>
<td>&lt;= 2 (Approximate normative mean)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Greater than 2 (Approximate normative mean)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topic</td>
<td>Subtopic</td>
<td>Criteria</td>
<td>Points</td>
</tr>
<tr>
<td>---------------</td>
<td>---------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
<td>--------</td>
</tr>
<tr>
<td><strong>Stopping</strong></td>
<td><strong>Stop Sign 1</strong></td>
<td>Stopped</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>(res1; residential)</td>
<td>Did not Stop</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Waited between 3.35 and 8.75 seconds (1 SD above normative mean)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wait &lt; 3.35 or &gt; 8.75 seconds before driving</td>
<td>0</td>
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<tr>
<td></td>
<td><strong>Stop Sign 2</strong></td>
<td>Stopped</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>(rural 2; rural road)</td>
<td>Did not stop</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Waited between 2.79 and 6.06 seconds (1 SD above normative mean)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wait &lt; 2.79 or &gt; 6.06 seconds</td>
<td>0</td>
</tr>
<tr>
<td><strong>Challenges</strong></td>
<td><strong>Zone 28a-28b</strong></td>
<td>Move to left lane at sign and avoid barriers</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><strong>Construction</strong></td>
<td>Doesn't respond appropriately</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>(30 mph)</td>
<td>25.46 to 36.14</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-1 SD to 1 SD from normative mean</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt; 25.46 to &gt; 36.14</td>
<td>0</td>
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<tr>
<td></td>
<td></td>
<td>&gt; 1 SD around the normative mean</td>
<td></td>
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<tr>
<td><strong>Unexpected Objects</strong></td>
<td><strong>Kid/Ball</strong></td>
<td>Stops when sees ball/kid</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><strong>Zone 06B-08A</strong></td>
<td>Doesn't come to a full stop</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><strong>Throughout</strong></td>
<td>No accident with other vehicles/objects</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><strong>environment</strong></td>
<td>Accident with others</td>
<td>0</td>
</tr>
</tbody>
</table>

Total: 1
VITA

EDUCATION AND TRAINING

2010 - 2011  VA Connecticut Healthcare System, Predoctoral Internship in Clinical Psychology
2006 - 2011  Drexel University, Clinical Psychology Ph.D. (Neuropsychology)
2004 - 2006  Wake Forest University, Master of Arts in Experimental Psychology
1996 - 2000  Emory University, Bachelor of Arts in Psychology

PEER REVIEWED PUBLICATIONS


HONORS AND AWARDS

2009, 2011: Drexel University Office of Graduate Studies, Travel Grant ($500)
2008: Philadelphia Neuropsychological Society, Graduate Student Research Award
2007: Drexel University COAS Research Day, 1st place Graduate Research Poster
2007: Rehabilitation Psychology, Honorable Mention Graduate Student Poster Award
2006: Wake Forest University, Alumni Travel Award ($250)
2005: Wake Forest University, Summer Research Grant ($1000)

TEACHING EXPERIENCE

Instructor: Physiological Psychology, Approaches to Personality
Teaching Assistant: Undergraduate: Introduction to Psychology, Abnormal Psychology
Graduate: Data Analysis I, II, III; Principles of Neuroscience