COGNITIVE DEFICITS IN MENTAL ROTATION IN PARKINSON’S DISEASE

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COGNITIVE DEFICITS IN MENTAL ROTATION IN PARKINSON’S DISEASE

By

Debra L. Nyman

THESIS

Submitted to

Northern Michigan University
In partial fulfillment of the requirements
For the degree of

MASTER’S IN EXPERIMENTAL PSYCHOLOGY

Graduate Studies Office

2011
This thesis by Debra Nyman is recommended for approval by the student's Thesis Committee and Department Head in the Department of Psychology and by the Dean of Graduate Studies.

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**NAME:**

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July 02 1956
The purpose of this study was to explore the possibility that a simple computerized mental rotation task (MRT) might help to detect early cognitive deficits in Parkinson’s disease (PD) patients and lead to earlier diagnoses. The 51 participants in this study consisted of three groups: participants with PD (n=9), an age-matched control group (n=20), and college students (n=22). Participants were assessed for the presence of dementia and memory function using the Mini Mental Status Exam (MMSE). No participants were recruited if they showed signs of more than the presence of mild dementia. The Stroop Color Test (SCT) was administered to assess attention and executive control. Lastly, the MRT was given to test reaction time and mental imagery manipulation. Results showed that the MRT was not a good indicator of early cognitive deficits in this group of PD participants. The MMSE was not only an easier test to administer, but appeared to be a better indicator of cognitive impairment. Independent of the MRT and the MMSE, the SCT showed attention deficits which were only correlated with age in this sample.
Dedication

To my sister Sandy, my inspiration and life-line, who taught me the value of an education.
Acknowledgement

A special thanks must be extended to the PD Support Group of Escanaba, MI. Without their participation this study would not have been possible.
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ABBREVIATIONS

AD: Alzheimer’s Disease; BA: Brodmann Area; DLPFC: DA: Dopamine; Dorsolateral Prefrontal Cortex; fMRI: functional magnetic resonance imaging; GPi: Globus Palidus Internal Part; HD: Huntington’s Disease; IQ: Intelligence Quota; MGH: Marquette General Hospital; MR: Mental Rotation; MRT: Mental Rotation Task; MD: Muscular Dystrophy; MMSE: Mini Mental Status Exam; MS: Multiple Sclerosis; NMU: Northern Michigan University; PD: Parkinson’s Disease; PS: Picture Sequencing; : SCT: Stroop Color Test; VTA: Ventral Tegmental Area; W: Wisconsin Card Sorting Task.
INTRODUCTION

This thesis follows the format prescribed by the APA Style Manual and the Department of Psychology.

The purpose of this exploratory study is to assess the ability of a simple Mental Rotation Task (MRT) to detect visual-spatial deficits in people with Parkinson’s Disease (PD). It is based on the knowledge that PD is associated with cognitive deficits as well as motor impairments (Banich, 2004) and the similarity of the neural pathways involved in PD and those apparently involved in a MRT (Crucian, et al., 2003).

General Characteristics of PD and Psychomotor Impairments Exhibited

PD is known for its physical symptoms of resting tremor, muscle rigidity, imbalance, and slowness of movement (Tinaz, Schendan, & Stern, 2006). PD is a neurodegenerative disorder characterized by dopamine depletion in the substantia nigra and affects the frontal lobe area and stimulation of the primary motor cortex (Banich, 2004) leading to motor disturbances and non-motor symptoms such as sleep disorders, a reduced sense of smell, depression, and dementia (Neese, 2010; Tinaz, et al., 2006).

PD affects one and a half million Americans, more than Multiple Sclerosis (MS) and Muscular Dystrophy (MD) combined (Stern, n.d.). As a neurodegenerative disease, PD is diagnosed second only to Alzheimer’s disease (AD) (Lang, 2005). PD typically progresses slowly; one out of every 100 people over the age of 60 will be diagnosed
with PD, but many times not until the appearance of clear and distinctive physical symptoms (Stern, n.d.).

**PD and Cognitive Functioning and Impairment**

Over fifty percent of people with PD exhibit some form of cognitive impairment, especially when performing tasks requiring working memory (Moberg, n.d.). Cognitive processes including attention, mental processing speed, problem solving or executive function, memory, language, and visual-spatial perceptions are regularly disturbed in PD and tend to be worse for patients displaying symptoms of bradykinesia (slowness of movement) and rigidity (Moberg, n.d.).

The major cause of memory and thought deficits in PD is believed to be due to changes in brain structure and chemistry. The death of neurons in the substantia nigra seems to be tied to damage to the basal ganglia and the resultant decrease in the neurotransmitter dopamine not only produces the motor symptoms typically associated with PD, but is also related to cognitive changes. The nerve pathways between the frontal lobes and the basal ganglia are also affected and may add to difficulties with problem solving, initiation of behavior, and impulsivity (Banich, 2004). Furthermore, fatigue and sleep disturbances as well as depression and anxiety are co-existing conditions that affect thinking and memory (Boeve & Silber, n.d.).

Studies of PD suggest that cognitive deficits resulting from damaged frontal-basal ganglia circuits coincide with motor symptoms and difficulty with sequencing meaningful events (Stamenovic, Djuric, Jolic, Zivadinovic, & Djuric, 2004; Tinaz et al., 2006). Cognitive problems may affect spatial, memory, and executive functions in all
stages of the disease. Although most research studies have concentrated on motor symptoms (e.g., Fillpovic, Rothwell, & Bhatia, 2010; Sabate, Llanos, & Rodriguez, 2008; Amanzio, Monteverdi, Giordano, Soliveri, Filippi, & Gemini, 2009) other areas of PD research have documented deficits in attention shifting, planning, working memory, strategic control, and perceptuomotor (temporal) sequencing (Tinaz et al., 2006; Amick, Grace, & Ott, 2007). Still, there is much to learn about higher level cognitive function in PD (Tinaz et al., 2006), see Figure 1. Neural circuits believed to be involved in PD and those common to PD and mental rotation.

Figure 1. Neural pathways involved in Parkinson’s Disease and visual-spatial processing necessary for the mental rotation task. Pathways are based on those shown in or discussed by Tinaz, et al., 2008; Yoshzaki, et al., 2007; Tinaz, et al., 2006; Banich, 2004; Crucian, et al., 2003; Barone, 2001.
In addition to the main symptoms of rigidity, gait disorders, bradykinesia, and tremor, cognitive impairments often follow and are frequently a forerunner of dementia. Cognitive impairments in patients diagnosed with PD are often found in the early stages of the disease with the help of neuropsychological tests (Banich, 2004). The purpose of this paper is to examine whether mental rotation (MR) can be used to detect early cognitive deficits in patients with PD.

**Visual-Spatial Changes and the MRT**

PD has been associated with deficits in visual-spatial and mental object rotation ability for decades (Crucian, et al., 2003). One idea is that frontal-striatal and frontal-parietal dysfunction in PD is caused by dopamine depletion and, hence, disrupts working memory (Crucian et al., 2003). A study conducted by Tinaz and colleagues (2006) to examine the functional integrity of the frontal-basal ganglia circuits in PD patients found that semantic event sequencing incorporated crucial brain components including the dorsolateral prefrontal cortex (DLPFC) and the globus palidus internal part (GPi), especially in the left hemisphere. They found PD patients to show hypoactivation in the premotor/inferior frontal areas, the right dorsolateral prefrontal cortex, the left caudate and orbitofrontal regions, and the bilateral sensorimotor cortices. In addition, abnormal resting brain activity was found (Tinaz, et al., 2006).

Hypoactivation of the DLPFC part of the circuit (right BA [brain area] 9) (Sternberg, 2006) may impair patients suffering from PD in picture sequencing (PS) tasks. Hypoactivation was also observed outside the DLPFC circuit in the precentral/inferior frontal gyri. In addition, hyperactivation was found in the left middle
frontal gyrus (BA 8) which is involved in maintaining visual-spatial information in working memory. Thus, compensatory activity may be required for PD patients to achieve levels of normal working memory and executive function (Tinaz, et al., 2006).

Moreover, the inactivation of default areas implicated when the brain is in a state of rest may be linked to the inability to shift attentional resources from internally driven, self-referential processing to task processing which relies on external cues (Tinaz, et al., 2006). PD sufferers have a more difficult time planning and initiating strategies and, if no external cue is available as a guide for an event sequencing task, cognitive deficiencies cause internally driven cues to make demands on additional cortical regions. Left caudate hyperactivation may reflect compensatory brain activity linked to working memory demands and right hemisphere recruitment shows a pattern of heightened activity in general for patients with PD (Tinaz, et al., 2006). Other neuropsychological studies have found cognitive deficits in medicated PD patients even though dopaminergic medication has normalizing effects on motor performance and brain activation patterns (Davidsdottir, Wagenaar, Young, & Cronin-Colomb, 2008; Boeve & Silber, n.d.).

Deficits related to executive brain functions and the frontal lobes include attention, concentration, sequencing, and set-shifting. Visual-spatial abilities involve several cognitive processes and mental rotation (MR) relies on visual-spatial skills (Crucian, et al., 2003). Controversies arise as to whether deficits are specific to visual-spatial abilities or due to general slowing in psychomotor and mental processing speed generally associated with PD (Cronin-Golomb & Braun, 1997).
Neuropsychological Tests and Treatment

Neuropsychological tests are of great value in identifying the early cognitive disturbances connected to PD. MR is dependent on multifaceted cognitive functions which are in turn dependent on basal ganglia connections to the frontal lobe and parietal brain regions and PD is largely a disorder of the basal ganglia (Crucian et al., 2003). The primary pathology of PD involves the loss of dopaminergic cells in the substantia nigra and the ventral tegmental area and these two subcortical sites project into brain systems important for normal motor, cognitive, and affective functioning. See Figure 1. There appears to be an impaired awareness (anosognosia) in PD sufferers when it comes to their own movement disorders including dyskinesias, hypokinesias, and motor fluctuations. The degeneration of dopaminergic neurons in the substantia nigra leads to dopaminergic denervation of the striatum. Over time other dopaminergic systems deteriorate, such as the mesocorticolimbic system and the ventral striatum, leading to executive function deficits which elicit behavioral changes (Amanzio, Monteverdi, Giordan, Soliveri, Filippi, & Geminiani, 2009).

Current treatments, in particular the treatment of PD with levodopa, create additional complications due to motor fluctuations caused by on-off states. An “on” state is a time of relief from PD symptoms due to medication and an “off” episode is the time when PD symptoms reappear even though the patient continues to be medicated (Amanzio, et al., 2009). Amanzio and colleagues (2009) conducted one of the first studies to analyze motor deficit awareness in PD patients in the on-off states in order to assess cognitive and behavioral functioning. Their data showed that PD patients were
more aware of their motor deficits and, hence suffered greater psychological distress, in the off state. They were more troubled by their motor disabilities which resulted in additional mood disorders. While patients were in the on state, however, they showed a selective reduction of awareness of their movement disorders. These findings suggest that dopaminergic overstimulation of mesocorticolimbic pathways may mask awareness in executive function (Amanzio, et al., 2009).

According to research conducted by Vitale and colleagues, other studies have shown frontotemporal cortical dysfunction in AD patients, but lack of awareness in PD patients appears to be associated with both cortical and subcortical brain regions more similar to those suffering from Huntington’s disease (HD). The unawareness level of PD patients was inversely related to dyskinesia severity while in HD it was related directly to disease duration (Vitale, et al., 2001). Another study conducted in 2001 compared AD and PD patients and supported findings that PD is more strongly related to poor overall cognitive function, especially when assessing memory, although PD patients with intact cognitive functioning displayed a preserved awareness of their motor deficits (Seltzer, Vasterling, Mathias, & Brennan, 2001). However, a later study conducted in 2004 of non-demented PD patients did show discrepancies between patient and caregiver reports. In this study, patients who described themselves as less impaired exhibited more left side motor symptoms, hence more extensive right basal ganglia dysfunction, which may alter the patient’s insight. Thus, the frontal lobe-basal ganglia connection may help to explain the unawareness of deficits in ostensibly cognitively intact PD patients (Amanzio et al., 2009).
In the on state, PD patients showed better motor and overall cognitive performance. In the off state, patients showed higher levels of anxiety, depression, and apathy. Although no subjects were clinically depressed, apathetic behavior could have been related to physical discomfort, but dopaminergic treatment appears to affect apathetic symptoms associated with PD (Czernecki et al., 2002). Alternatively, levodopa treatment may also produce detrimental effects on the functioning of the orbitofrontal and cingulated frontal-subcortical loops critical in awareness (Leritz et al., 2004; Seltzer et al., 2001). Low awareness of dyskinesias in the on state was found to be related to poorer performances on the WCST (Wisconsin Card Sorting Task) and memory tasks. PD patients exhibited a reduction in functioning of the anterior cingulated cortex and striatum (ventrolateral and posterior prefrontal cortex), which play essential roles in awareness phenomena, Lumme, Aalto, Ilonen, Nagren, & Hietala, 2007; Monchi, Petride, Petre, Worsley, & Dagher, 2001) and they were less able to inhibit errors and self-correct during cognitive tasks. These awareness based cognitive functions, inhibition and self-correction, should also become apparent when attention or awareness tests such as the SCT is administered. The apparent importance of judgment and metacognitive competencies in daily self-assessment during routine activity while not affecting a global cognitive awareness consciousness is supported by these results (Amanzio, 2009). While levodopa treatments help with PD motor symptoms, the treatments may also lower cognitive awareness. On the other hand, if the side effects can be tolerated by patients suffering from PD, the benefits of this treatment for motor
symptoms might outweigh what may be lost cognitively until better drug treatment is available (Amanzio, et al., 2009).

**PD and Executive Function**

Executive function is the ability to self direct information flow and is tied to working memory (Pashler, 1998). PD impairments in cognition which accompany motor symptoms are greatest in executive control (Park & Schwarz, 2000). Research indicates that increased intellectual effort worsens motor disorders and affirms the importance of the role of the basal ganglia (Banich, 2004). In addition, deficits in procedural learning have been documented albeit task dependent. Cognitive deficits are common in PD and include deficits in attention, concentration, memory, visual observation, visuospatial orientation, visuomotor abilities, conceptual thinking, visuoperceptive analysis (Stamenovic et al., 2004), and internally controlled task set shifting (Cools, Barker, Sahakian, & Robbins, 2001). Anxiety and depression are often commonplace in patients with PD in addition to fewer novelty seeking behaviors which may lead to social avoidance (Stamenovic et al., 2004). Working memory is universally impaired and cognitive and memory deficits consistently emerge. The basal ganglia play a critical role in the selection and inhibition of opposing motor and cognitive agendas. Patients with PD may have problems with internal strategies, organization, and long term memory retrieval. The latter may indicate the importance of working memory to memory recall. Since the basal ganglia have numerous connections with the prefrontal and limbic cortical areas in addition to the motor cortex, dopaminergic reduction also leads to deficits in several kinds of processing (Stamenovic et al., 2004).
Research using high functioning PD patients conducted by Mohr and colleagues appears to show some selective deficits in the areas of cognition and memory. Although verbal skills and higher executive functions remained relatively intact, their research showed some reduction in episodic memory and visuospatial performance. Additionally, overall intelligence quota (IQ) scores were shown to deteriorate even though verbal aptitude remained at a superior level and executive functioning appearing to be uncompromised for the most part. However, tests on memory conversely demonstrated a substantial decline as scores on the Wechsler Memory Scale were significantly reduced. High functioning PD patients retained premorbid verbal abilities and preserved executive function with compromised visual-spatial function. Episodic memory and attention was influenced by apparent functional and effortful compromises and, overall, research studies have shown that complex tasks showed some impairment while simpler tasks did not (Mohr, 1990). It appears that deficits in executive control in the majority of cognitive areas appear in the later stages of PD. Could cognitive tests, such as the SCT or MR which rely on executive functions, detect compromised cognition earlier and lead to earlier diagnosis of PD?

PD produces an impairment of visual-spatial perception which includes difficulty in the evaluation of the position of objects in space, integrating those objects into a coherent spatial framework, and performing mental operations which involve spatial concepts (Crucian, 2003). Thus, MR experiments may have diagnostic value in cognitive dysfunction detection.
PD and the MRT

A MRT consists of objects or letters which are either the same image rotated by degrees (0-180 degrees) or a mirror image of the object or letter. The experimental subjects are rated on accuracy and response time as they differentiate between the images (Forster, Gebhardt, Lindlar, Siemann, & Delius, 1996). MR tests may be conducted with the use of computers or as simple paper and pencil test for identifying shape as a function of the difference in the orientations. While paper and pencil tests of MR (e.g., Vandenberg & Kuse, 1978) are convenient, they do not allow the detailed analysis of a computerized MRT. The computerized MRT, unlike the paper and pencil task, allows one to separate reaction time speeds from the actual MR time. In addition, when repeated training occurs one can easily look at learning in both simple rotation time and the rotation activity may be measured.

Roger Shepard and Jacqueline Metzler (1971) found that reaction time in the MR task increases linearly with the image’s angle of rotation. Shepard and Cooper (1982) found that response time depended largely on the degree the object was rotated, opposed to the axis on which the object was rotated from picture plane or depth. Additionally, R. J. Sternberg (2006) found a decrease in MR response time with practice suggesting a reduction in the time needed to mentally rotate a given image. MR has been used for decades to evaluate visual-spatial ability and to study cognitive performance (Riecansky & Fedor, 2008). Recent technological advances, such as magnetic resonance imaging (MRI), have supported early theories regarding MR by
confirming brain area activation in areas used in the MRT that are similar to those affected by PD (Yoshizaki, Banich, & Weissman, 2007). See figure 1.

MR is a complex task which increases in difficulty with the degree of image rotation (Shepard & Metzler, 1971). MR requires higher executive brain function ability in the frontal-striatal and/or frontal-parietal systems, as well as, cognitive processes such as working memory and visual-spatial calculations. These higher cognitive processes are compromised with dopamine depletion in the frontal-basal ganglia neural circuitry which is critical to many operations including attention, concentration, sequencing, set shifting (Crucian, et al., 2003), and problem solving (Cronin-Golomb & Braun. 1997).

Similar deficits are found with those suffering from basal ganglia dysfunction and studies of PD suggest that cognitive deficits may be a product of damage to frontal-basal ganglia circuits (Banich, 2004; Lang, 2005; Tinaz, 2008; Moberg, n.d.). In addition, cognitive deficits in concentration and the learning of new manual skills are found in PD patients before mental deterioration is obviously apparent (Stamenovic, et al., 2004) which suggests that learning in MR might be used to obtain data on cerebral dysfunction.

It was suggested in a pilot study (Pascoe, et al., 2003) conducted on a small sample of PD patients in an assisted living facility that the ability of PD patients to perform a computerized MRT might be compromised. The results suggested that reaction time (speed) improved with practice while the MR rate (spin) did not show learning. The researchers attributed this pattern of performance to PD and
recommended that future research could use the apparent difference between speed (simple reaction time) and spin (rate of rotation or time added when object is shown in a different orientation) to explore the role of the basal ganglia in cognitive performance (Pascoe, et al., 2003).

Consequently, this study’s primary concern is to explore the possibility that learning in a simple repeated MRT might help assess early cognitive dysfunction in PD patients and might become an additional tool in screening for cognitive loss. The MRT data derived from a suspected PD sufferer may be compared to the data derived from the Mini Mental Status Exam (MMSE) and a Stroop task and benefit medical professionals by allowing for earlier and more accurate diagnoses.

The MMSE offers a fast and easy way to quantify cognitive function in the areas of orientation, attention, calculation, recall, language and motor skills. The Stroop task tests attention deficits and an individual’s ability to inhibit errors and self correct responses. The addition of a computerized MRT may give medical and research professionals additional information and more accurate information and data with which to work. Therefore, MR might become a valuable tool for early diagnostic purposes in PD and PD rehabilitation, in addition to, future research in other areas of disease.

Because PD has been associated with visual-spatial impairment and because of the outcome of the Pascoe (2003) pilot study, I hypothesized that both the reaction time (speed) and the rotation rate (spin) would differ significantly between the PD group and the student control group. I also hypothesized that both speed and spin would not differ
significantly between the PD group and the age match control group. Furthermore, I hypothesized that speed and spin would differ significantly between the two control groups.
METHODS

Research Participants and Demographic Data

This study was approved by the NMU Institutional Review Board (approval letter attached).

The participants in this study consisted of three groups: a group of nine male participants diagnosed with idiopathic PD (mean age=76.1); a student group consisting of 13 females and 9 males, (mean ages=22.3, 24.1, total M=23); and a non-PD age match group consisting of 14 females and 6 males, (mean ages=82.6, 71.2, total M=79.2).

Because of equipment failure, fatigue, and failure to follow instructions, the number of subjects on each cognition task varied. Table 1 shows the total number and the number of females and males who provided data for each task. The low number of student MRT data resulted from a glitch in the MRT which was not immediately recognized. In all groups the majority of participants had at least some college education; only two participants did not have a high school diploma or better. Student subjects were recruited from the NMU campus. PD and age match control participants were recruited from Mill Creek Assisted Living Facility, D.J. Jacobetti Home for Veterans, the PD Support Group of Escanaba, MI and other varying off campus sources such as caregivers and family members (N=51). All participants were able to give their own consent. As it happened, all but one of the PD participants was living independently, while 75% of the age match group was in an assisted living facility. Thus, inadvertently the PD diagnosis and assisted living status were largely unconfounded in this experiment compared to
the pilot study. Among the PD patients, Parkinsonian symptom onset was documented at the mean age of 71.1 with PD subjects being diagnosed between the years 2002 to 2008. The student control subjects recruited from Northern Michigan University (NMU) received course credit for their participation. The age match control group volunteers from Jacobetti Home for Veterans and Mill Creek Assisted Living benefited only from the extra attention and time spent with the researcher which they appeared to enjoy. There was no benefit to the PD support group with the exception of satisfying the desire to possibly help PD patients in the future. All subjects consented to participate in this study after full disclosure of potential risks and benefits.

Table 1: Number of Participants (Female, Male, and Total) on Each Task

<table>
<thead>
<tr>
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<th>Stroop</th>
<th>MR</th>
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</tr>
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</table>
Apparatuses and Instruments

Examples of all tasks can be found in Appendix 2.

**MMSE.** The presence of dementia was assessed with the commonly used MMSE (Folstein, Folstein, & McHugh, 1975) by testing short-term memory and assessing basic situational awareness with a cut-off criterion of 20/30. An MMSE score of 25 or above indicates that cognitive function is intact, 21-24 indicates mild dementia, 10-20 moderate, and a score of 9 or less is used to determine severe cognitive impairment (Crum, Anthony, Bassett, & Folstein, 1993) although motor or physical symptoms may affect scoring and should be noted (Mungas, 1991). No participants exhibited physical symptoms or motor deficits that would affect their MMSE score and the mean of each group was above 25. This task took less than 10 minutes.

**SCT.** The Stroop Color Test (SCT) was administered in a counterbalanced design with the MMSE to access the subject’s attention ability under conditions of interference or conflict (Stroop, 1935). According to the 3rd edition of Neuropsychological Assessment, the Stroop task has been used to measure response conflict and inhibition and the failure of selective attention. More commonly today the task is considered a good measure for difficulties in concentration (Lezak, M., 1990). There is no brief, standardized SCT and so a short two-card version was used (Mitrushina, M., Boone, K., & D’Elia, L., 1999). Two timed variations of the task were given to each subject: participants were first asked to name the color of each of 25 colored blocks printed on a single page and second they were asked to once again name the block color while ignoring a color-word written within the block which was the name of a different color.
(a red block would have the word green written in it, for example). Each task was timed with a stopwatch and the number of mistakes made was recorded. Appendix 3 has a copy of each SCT sheet used. The SCT took less than five minutes and participants were allowed restart if they became distracted or did not understand the instructions.

**MRT.** Participants were informed that the Mental Rotation Task (MRT) was concerned with the basic principles of cognition and mental imagery and assesses nonverbal memory function. The PD and age-match subjects were tested individually on a Toshiba personal laptop computer. The students were tested on a desk-top windows-based computer. Subjects were first warmed up and trained on large “yes” (green button, letter is facing in the correct direction) and “no” (red button, letter is a mirror image) buttons, developed for testing MR in the NMU psychology department, by going through two sets of ten trials on which they only had to indicate whether the word yes or no was on the screen. This first trial set was called button training and enabled the subject to get comfortable in position and with the equipment. The participant would simply press the green button if the word “yes” appeared on the screen and the red button if the word “no” was shown. After button training, the actual mental rotation test began. Subjects were given three blocks of 56 mental rotation trials. Each block included eight warm up presentations of the letter \( \mathbf{F} \). \( \mathbf{F} \) was presented at four angles (0, 45, 90, and 135 degrees of relative rotation) in the proper orientation (yes) trials and at four mirror image presentations (no) trials. The subject was asked to press the green button if the letter was facing the correct way and the no button if the letter was a mirror image. After the presentations of the \( \mathbf{F} \)-stimuli, another 48 trials were
presented. These 48 presentations include three passes on the letters R and G in either correct or mirror-image presentations at each of the four angles (0, 45, 90, 135-degrees of rotation). On each trial a single letter was presented. Table 2 shows three examples of the presentation trial.

Table 2: Examples of Mental Rotation Trials

<table>
<thead>
<tr>
<th>“Yes with no rotation”</th>
<th>“Yes with 45-degree Rotation”</th>
<th>“No with 90-degree Rotation”</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>R</td>
<td>B</td>
</tr>
</tbody>
</table>

Each participant was instructed to work as quickly as possible without sacrificing accuracy. The computer program automatically recorded, in milliseconds, the time to respond once the stimulus was shown on the screen. The data analyzed consisted of the correct “yes” responses. This is consistent with the procedures of Shepard and Metzler (1971). Participants were given the opportunity to rest between MRT blocks. Few took the time. The MRT took about 10 minutes.

PD participants were screened for depression as part of the participant information questionnaire form. The majority stated they did feel some depression and/or anxiety because of their disease. Additionally, an equal number of PD participants said they felt they had either none or some cognitive impairment (on a 1-3 point scale with none being the lowest and some being the highest) with one participant stating he felt that he had very little. The PD participants also rated their motor
symptoms and most rated the severity of their motor symptoms as moderate (1-3 point scale: minimal, moderate, and severe) with the remaining rating symptoms as minimal. None felt their motor symptoms were severe.

**Procedure**

Each participant was run individually, at his/her place of residence for the older adults and in a standard research room at NMU for the students. The entire experiment took less than an hour, usually about 30 minutes. Participants were allowed to rest between tasks. Each participant was given a debriefing sheet at the end of the experiment and was asked if he/she had any final questions or comments about the study and were thanked for participating. Additional follow up thank you notes were mailed after completion at each off-campus facility.
RESULTS

All data were analyzed using Micro-Soft Excel and IBM PASW (SPSS, version 18).

MMSE

No participants were recruited for this study if they showed signs of more than the presence of mild dementia and no participants tested scored less than 23/30 on the MMSE. The mean score of the non-demented PD group measured 27.67, the age match non-PD group measured 27.75, and the student group measured 29.24. One student was eliminated due to incomplete data (N=50). A one-way ANOVA showed a significant difference between the three groups $F(2,47) = 5.233$, $p = .009$. A post-hoc Tukey Test showed that the students had higher MMSE scores than the two older adult groups, $p < .05$, $StDev_{pooled} = .67$, $g = .84$. The minimum score for the PD group was 26, maximum 30; the same as the student group. The minimum score for the age match group was 23, maximum 30. However, when taken as a whole, the mean score for the PD group (27.67) was closer to the age match group (27.75) than it was to the student group (29.34). A copy of the MMSE form used can be found in Appendix 2. These scores are shown in Figure 2.

SCT

The SCT (N=51) was administered in two separate sections by first using color blocks only and then color blocks plus words and appeared to be the best indicator of cognitive impairment in the PD group. Figure 3 shows the mean color only and color with words times for each group.
A three by two (group by trial) mixed-model ANOVA, with repeated measures on trial, showed a significant effect of Trial, $F(1,48)=54.93, p=.001$, Group, $F(1,48)=54.93, p=.001$; and an interaction of Trial and Group, $F(2,48)=5.88, p=.005$. All groups showed the Stroop interference effect, longer times, on the second trial (color with color word
superimposed); the students were faster and showed less interference than the older adults. The difference in times were 30.33 seconds (SD=15.66) for the PD participants, 25.05 (SD=27.23) for the age-match participants, and 8.63 (SD=7.83) for the students.

If the differences in time scores are converted to the percentage of increase from the color only trial the increases are 121% for the PD participants, 106% for the age-match, and 68% for the students. These differences were not significantly different, but the power of the test was low (power = .46) suggesting that the sample sizes were not large enough to detect a difference. The estimated size of effect, $g=.55$) of the older adults compared to the students is worth noting, see Figure 4.

![Figure 4. Mean percent increase on Stroop trial with words.](image)

A correlation between age and Stroop percent change was run for all subjects. The correlation with age was significant, $r(49) = .30$, $p = .01$, two-tailed.

**MRT**

Because the first block of mental rotation trials shows a good deal of variability and many errors, the MRT analysis will proceed in two parts. First the three blocks of rails will be analyzed for basic learning effects, then a separate analysis of speed and
spin in blocks two and three will be completed. The three blocks of trials were analyzed in a group (3) by blocks (3) by angles (4) mixed model ANOVA with blocks and angles as repeated measures on the original raw data. Because there was lack of sphericity on the repeated measures variables, the df and probability values presented reflect the Greenhouse-Geisser correction. The data for this analysis are shown in Figure 5.

![Figure 5](image)

Figure 5. Performance at each angle in each block of training trials for three groups of participants.

There was a significant between groups effect of participant group, $F(2,34) = 8.91, p = .001$. The students responded faster than either of the older groups. There was also a significant effect of blocks, $F(1.86,68) = 7.51, p = .002$; Responding, in general became faster over blocks. The blocks effect is an indication of learning. There was also a main effect of angles, $F(1.76, 102) = 26.61, p < .000$; responding was faster to smaller angles of rotation. This is the mental rotation effect, response times increase as the degrees of rotation increase. There was also an angle by group effect, $F(3.52, 102) = 5.55, p = .001$, indicating the angles effect was not the same for each group. Viewing Figure 5, one can see that the angle effect was smaller for the PD and student groups.
than for the age-control group. A trend analysis of the blocks and angles effect showed
the primary component and only significant component to be linear, $F(1,34) = 12.95$, $p = .001$ for blocks and $F(1, 34) = 38.01$, $p < .001$, for angles.

In summary, the overall analysis of the mental rotation data shows that learning
did occur, primarily between blocks 1 and 2 and that the rotation rates (angles by group)
were different for different groups of participants.

**MR Speed.** Figure 6 shows the mean reaction time at no/zero rotation. A three
(group) by two (block) mixed model ANOVA showed a significant effect of group, $F(2,35)$
$= 8.286$, $p = .001$, and a significant interaction between block and group, $F(2,35) = 3.29$, $p = .049$.

![Figure 6](image_url)

Figure 6. Speed, mean reaction time with no rotation, for three groups of participants over two training blocks.

The students performed better than either older adults in absolute reaction time
with no rotation and the PD and student participants showed improvement between
blocks 2 and 3, while the age control slowed down, if anything. Clearly the PD
participants showed the largest improvement between the two blocks.
**MR Spin.** Spin is the rotation rate or msec per degree added as the letter is rotated out of the upright (zero rotation) position. It is also the average slope of the line through the angles of rotation. An average rotation was calculated for each subject separately and then analyzed again in a three (groups) by two (blocks) mixed model ANOVA. These data are presented in Figure 7.

![Figure 7](image)

Figure 7. Spin, mean rotation rate, msec per degree, over two blocks for three participant groups.

There was only a significant effect of group in this analysis, $F(2,35) = 5.79$, $p = .007$. Clearly, the PD and student participants were rotating at the same rate and the age control was considerably slower. The mean over the two blocks for the PD participants was 1.47 msec per degree and for the students was 1.60 msec per degree. The rotation rate for the age control over the two blocks was 8.18 msec per degree.

**Correlations Between Measures**

Finally, correlations were run between measures on the three tests and group, age, and education. This was essentially a division between demographic and performance measures. Note that in this table, group is a nominal variable (PD=1, Age
control=2, and Student=3) so you would not expect linear relationships between other variables and this grouping variable. Table 3 shows these correlations and the significant correlations are indicated by shading. For the MRT data, performance on blocks 2 and 3 are averaged. The significant correlations are highlighted.

Education was not correlated with any performance measure. Group was correlated, but probably represents the correlation with age, which is moderate to somewhat strong across the performance measures. Mental rotation performance (spin) was only related to age and the speed component to the MRT. The Stroop performance is related only to age itself. That is, it appears to be independent of the other measures of cognitive ability.

Table 3: Correlations Between Demographic and Performance Measures

<table>
<thead>
<tr>
<th>Demographic Measures</th>
<th>Performance Measures</th>
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<tbody>
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<td></td>
<td>Group</td>
</tr>
<tr>
<td>----------------------</td>
<td>-------</td>
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<td>Group</td>
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<tr>
<td></td>
<td></td>
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<tr>
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<td>Pearson r</td>
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<td></td>
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Table 3: Correlations Between Demographic and Performance Measures

<table>
<thead>
<tr>
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<th>Stroop Difference</th>
<th>Stroop Difference PCT</th>
<th>Speed zero23</th>
<th>Spin slope 23</th>
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Discussion

This study was undertaken to explore the possibility of using a simple computerized MRT for early detection of cognitive deficits in potential PD patients and to check the results from a 2003 pilot study of MR and learning in PD. MR is frequently administered as a paper and pencil task. The 2003 pilot study was administered by computer and the data indicated that the PD patients were able to improve their response time, but unable to improve MR time with practice because there is overlap in the brain areas that affect PD and which are used by MR. Both PD and MR use brain pathways from the substantia nigra leading into the primary motor cortex and from the ventral tegmental area to the ventral striatum and preceding to the frontal lobe (“PD: Hope Through Research”, 2010) it seemed reasonable that MR performance might be affected by PD.

I hypothesized that both the reaction time (speed) and the rotation rate (spin) would differ significantly between the PD group and the student group. This hypothesis was shown to be false. Although the PD group was more like the age match control group in the area of speed they showed similar results in the area of spin to the students which did not support the 2003 finding. The PD participants in this study, however, were not recruited from a nursing home or assisted living facility as they were in the pilot study. Instead, a second age match control group was recruited for data comparison. Performance of this assisted living group did match the pilot study pattern and this result suggests that the pilot study outcome was caused by whatever
cognitive/performance issues that led to assisted living arrangements. The PD sample size was smaller than what would be considered optimal due to the rural area in which the data were collected, but larger than the PD sample used in the pilot study. I also hypothesized that both speed and spin would not differ significantly between the PD group and the age match control group. This hypothesis was also shown to be false for the reason that the age matched control did not show improvement in the rotation component of the task. Furthermore, I hypothesized that speed and spin would differ significantly between the two control groups. The data showed this hypothesis to be true as the age match group was slower than the students in both reaction time and rotation time.

The MRT used here may not be a good diagnostic tool to use when testing the aged because the measure of interest (speed and spin) are derived from reaction times, which grow slower and more inconsistent with age. The MMSE is easier to administer than a computerized MRT and appears to be a more useful indicator of cognitive ability than MR. The SCT appears independent of both MR and the MMSE and according to the data collected in this study is a better diagnostic test to administer to PD sufferers to test for cognitive impairment. The SCT is also a quick and easy task to run. Although the present MRT may be a poor diagnostic tool the results from this study indicate that MR continues to be a potential research tool. In particular it should be noted that the PD participants showed relatively poor performance on the SCT, but retained a quite good performance on the learned spin measure. If this pattern is unique to PD patients it may become a useful marker for early cognitive decline in PD.
Education level appeared to have no relationship to scores in any of the tests conducted. Eighty-eight percent of the PD participants had at least some college education, as did fifty-five percent of the Age Match Controls, and one hundred percent of the student group.

Age was related to all performance measures. The MMSE was correlated \(-.597\) to the speed aspect of the MRT \((p=.000)\), but not to the SCT \((r=.106, p=.465)\). Absolute SCT difference was related to age \((r=.467, p=.001)\), but not to MRT performance measures, but was related to group \((r=-.425, p=.002)\) and to age \((r=.467, p=.001)\).

According to the data collected in this study, there appears to have been a confound unaccounted for in the 2003 pilot data. The pilot study recruited PD participants from an assisted living facility while the majority of the PD participants in this study were living at home. Future research might want to explore the reasons a PD sufferer becomes a resident at such a facility, other than the fact that they have become more than mildly cognitively impaired, to eliminate additional confounds. Future research is also needed in the area of the effect of medications used in the treatment of Parkinson’s on cognitive performance. This study was limited as the PD participant medical records were not requested. Because age was the best indicator of impairment in all tasks, it would be interesting to compare PD participants across age groups with repeated MRTs over a longer period of time. These conclusions are also limited by the specific sample of the study and the small sample size.
**Conclusion**

Advancement in the understanding and treatment of PD has developed substantially in recent years. Research being done today in the area of PD considers stopping the progression of PD, restoration of lost functioning, and preventing PD entirely to be realistic goals in the years to come (NINDS, 2010). While PD patients normally show the preservation of higher executive function and verbal skills, they typically exhibit significantly reduced visual-spatial function along with the typically seen motor impairments that are the usual focus of treatments. Subtle cognitive and memory deficits are also known to be consistent features of PD (Mohr, 1990) and may contribute to the co-morbid symptoms of anxiety and depression. It is of utmost importance that accurate and easy to administer tests are available to spot cognitive deficits quickly in order to help PD patients get on an appropriate and effective treatment plan as soon as possible.
References


APPENDICES

1. IRB Approval

2. Task Examples

   Mini-Mental Status Exam -- MMSE

   Stroop Color Test -- SCT

   Example Mental Rotation Items
Appendix 1.

IRB Approval Letter
March 10, 2011

TO: Debra Nyman

Psychology

FROM: Terrance Seethoff, Ph.D.
Dean of Graduate Studies & Research

RE: Human Subjects Proposal HS11-398

"Detection of Early Cognitive Deficits in patients with Parkinson Disease"

The Internal Review Board (IRB) has reviewed your proposal and has given it final approval. To maintain permission from the Federal government to use human subjects in research, certain reporting processes are required.

A. You must include the statement "Approved by IRB: Project # (listed above) on all research materials you distribute, as well as on any correspondence concerning this project.

B. If a subject suffers an injury during research, or if there is an incident of non-compliance with IRB policies and procedures, you must take immediate action to assist the subject and notify the IRB chair (dereande@nmu.edu) and NMU's IRB administrator (tseethoff@nmu.edu) within 48 hours. Additionally, you must complete a Unanticipated Problem or Adverse Event Form for Research Involving Human Subjects.

C. If you find that modifications of methods or procedures are necessary, you must submit a Project Modification Form for Research Involving Human Subjects before collecting data.

D. If you complete your project within 12 months from the date of your approval notification, you must submit a Project Completion Form for Research Involving Human Subjects.

E. If you do not complete your project within 12 months from the date of your approval notification, you must submit a Project Renewal Form for Research Involving Human Subjects. You may apply for a one-year project renewal up to four times.

All forms can be found at the NMU Grants and Research website: http://webb.nmu.edu/GrantsAndResearch/SiteSections/Compliance/HumanSubjects.shtml
Appendix 2

Examples of Tasks

Mini-Mental Status Exam
For this study, the attention item was “spell WORLD backwards.”

**The Mini-Mental State Exam**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Examiner</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Maximum</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>( )</td>
</tr>
<tr>
<td>5</td>
<td>( )</td>
</tr>
</tbody>
</table>

**Orientation**

What is the (year) (season) (date) (day) (month)?
Where are we (state) (country) (town) (hospital) (floor)?

**Registration**

3 ( )
Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he/she learns all 3. Count trials and record. Trials ________

**Attention and Calculation**

5 ( )
Serial 7’s. 1 point for each correct answer. Stop after 5 answers. Alternatively spell “world” backward.

**Recall**

3 ( )
Ask for the 3 objects repeated above. Give 1 point for each correct answer.

**Language**

2 ( )
Name a pencil and watch.
1 ( )
Repeat the following “No ifs, ands, or buts”
3 ( )
Follow a 3-stage command:
  “Take a paper in your hand, fold it in half, and put it on the floor.”
1 ( )
Read and obey the following: CLOSE YOUR EYES
1 ( )
Write a sentence.
1 ( )
Copy the design shown.

---

Total Score
ASSESS level of consciousness along a continuum ________
Alert Drowsy Stupor Coma

---

**Stroop Color Test**
Stroop Instructions

Sheet 1: color blocks only

- I want you to name the color in each block as fast as you can.
- I will tell you when to start and keep time with this stop watch.
- I’ll know when you are finished.
- My interest is in how fast you can name the color in each block.
  There are 25 different blocks. The color names are blue, brown, green, purple, and red.
- Do you understand?

Sheet 2: color blocks + words

- Again I want you to name the blocks of color.
  But you must ignore the color name written over the color block. Do not read the word, just name the color block as if the words are not there, just as you did before.

Note: False starts can be restarted. Actual Stroop Sheets are printed to full page size and printed on a glossy photo paper which was inserted into a clear protector envelope.

Color Blocks Only
### Color Blocks with Color Words

<table>
<thead>
<tr>
<th>Blue</th>
<th>brown</th>
<th>purple</th>
<th>green</th>
<th>red</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Green</td>
<td>blue</td>
<td>red</td>
<td>brown</td>
<td>purple</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red</td>
<td>green</td>
<td>blue</td>
<td>brown</td>
<td>purple</td>
</tr>
<tr>
<td></td>
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<tr>
<td>Red</td>
<td>purple</td>
<td>brown</td>
<td>green</td>
<td>blue</td>
</tr>
</tbody>
</table>
Mental Rotation Test

A single letter is shown on screen.

Subject indicates whether each pair is the same or a mirror image, “Different”

Below are two “same” and two “different” examples.

Each block of trials consists of 56 individual trials.

The 8 warm up trials is composed of a single stimulus (F) presented at 4 angles of rotation in both a correct and a mirror image, followed by 48 trials of 2 stimuli (R and G) presented randomly 3 times at each of 4 angles in both a correct and a mirror image.

The computer records the time between the onset of the stimuli and the participant pushing a large “yes” or “no” button.

Participant will be asked to go through the sequence three times with the opportunity to rest as needed.

This task should take less than 10 minutes.
<table>
<thead>
<tr>
<th>Stimulus example</th>
<th>Correct Response</th>
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<tbody>
<tr>
<td>&quot;YES&quot;</td>
<td>Zero (0) Rotation</td>
</tr>
<tr>
<td>G</td>
<td></td>
</tr>
<tr>
<td>&quot;NO” Can not be rotated to original position</td>
<td>Zero (0) Rotation</td>
</tr>
<tr>
<td>D</td>
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<tr>
<td>“YES”</td>
<td>45-Degree Rotation</td>
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<tr>
<td>F</td>
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<td>45-Degree Rotation</td>
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<td></td>
</tr>
</tbody>
</table>