Spring 2022

# Characterizing Prospective Memory Errors and their Neuropsychological Correlations in Persons with MS

Caitlyn Nguyen
caitlyn.nguyen@trincoll.edu

TRINITY COLLEGE

# CHARACTERIZING PROSPECTIVE MEMORY ERRORS AND THEIR NEUROPSYCHOLOGICAL CORRELATIONS IN PERSONS WITH MS

By

Caitlyn Nguyen

A THESIS SUBMITTED TO THE FACULTY OF THE NEUROSCIENCE PROGRAM IN THE CADIDACY FOR THE BACCALAUREATE DEGREE WITH HONORS IN NEUROSCIENCE

Characterizing Prospective Memory Errors and their Neuropsychological Correlations in Persons with MS

By

Caitlyn Nguyen

Honors Thesis Committee

Approved:

_____
Sarah Raskin, PhD., Thesis Advisor

_____
Michael Puljung, PhD., Thesis Committee

_____
Sarah Raskin, PhD., Director, Neuroscience Program

Date: _____

## Table of Contents

Characterizing Prospective Memory Errors and their Neuropsychological Correlations in Persons with MS


## Abstract

**Background**: Prospective memory (PM) or "remembering to remember" is an important cognitive domain for everyday tasks. PM errors (e.g., loss of content, task substitution, or loss of time) have been noted in certain neurological disorders, with detrimental effects on a person's quality of life and independent functioning. While PM deficits have been documented in multiple sclerosis (MS), little is known about the specific errors made.

**Objectives**: 1) To characterize types and frequencies of PM errors and 2) investigate whether other cognitive processes (i.e., processing speed and verbal learning) or personality traits (i.e., Five Factor Model of Personality) are associated with PM errors in persons with MS (PwMS).

**Methods:** Participants (n = 111) were PwMS who completed the Memory for Intentions Test (MIST) as part of a cross-sectional study. As part of the assessment battery, participants also completed the Symbol Digits Modalities Test (SDMT), Rey Auditory Verbal Learning Test (RAVLT), and NEO Five Factor Inventory-3 (NEO FFI-3). Descriptive statistics were used to characterize PM errors, with chi-squares used to examine frequency differences in the types of errors. Spearman's correlations were run between the number of PM errors and the cognitive processes and personality traits. Variables with a p-value of <.1 were entered into a linear regression with PM errors as the outcome and age, gender, and education as covariates, with non-significant factors manually removed.

**Results:** About 92% of participants made at least one PM error. There was an overall difference in the type of PM error ($\chi^2(3) = 98.71$, $p < .001$), with loss of content errors (45%) being the most common. PwMS were also more likely to make errors on time-based tasks ($\chi^2(1) = 43.35$, $p < .001$). RAVLT total learning ($b = -0.58$, $p < .001$) and SDMT ($b = -0.42$, $p = .003$) were both significantly associated with PM errors. There were no significant relationships between PM errors and personality traits ($ps \geq .116$).

**Conclusion**: PM errors are common in PwMS, particularly loss of content errors and errors on time-based tasks. Verbal learning and processing speed are also negatively associated with the number of PM errors, suggesting that deficits in these cognitive domains likely contribute to PM difficulties.

## Introduction

### *Background on Multiple Sclerosis*

Multiple sclerosis (MS) is a debilitating neurological disease that is caused by immune-mediated demyelination of the myelin sheath in the central nervous system (CNS) (Ercolini & Miller, 2006). The autoimmune response results in inflammatory attacks on the myelin sheaths of the CNS neurons, damaging the brain, spinal cord, and optic nerve, resulting in "scarring" and lesions (plaques) (National Multiple Sclerosis Society, n.d.). Depending on where the lesions are, patients can exhibit cognitive, behavioral, and physical deficits that impact their daily living and quality of life. It is estimated that nearly one million people in the United States are living with MS, with the average age of diagnosis being in the early to mid-30s (The Multiple Sclerosis International Federation, 2020). It universally affects women more frequently than men (Harbo, et al., 2013). Furthermore, there are currently no cures or ways to prevent the disease from developing.

MS can present as three different subtypes: relapse remitting MS (RRMS), secondary-progressive MS (SPMS), and primary progressive MS (PPMS). RRMS is the most common type of multiple sclerosis. It is estimated that 85% of MS patients are first diagnosed with RRMS when clinically examined for MS (National Multiple Sclerosis Society, n.d.). RRMS is characterized as periods of attack (i.e., relapse), which are followed by sessions of recovery (i.e., remission) (Dobson & Giovannoni, 2018). During the period of relapse, neurological symptoms persist until the recovery period where symptoms may disappear or partially remain (National Multiple Sclerosis Society, n.d.). Over time, persons with RRMS may go onto develop SPMS, in which they gradually suffer nerve damage or loss instead of lesions due to inflammatory attacks (National Multiple Sclerosis Society, n.d.). Depending on the individual, those with SPMS may

or may not continue to experience inflammatory attacks on myelin on the neuronal axons (relapses) (National Multiple Sclerosis Society, n.d.). Individuals with an initial progressive form of MS without distinct periods of relapses and remissions are diagnosed with PPMS. PPMS involves less inflammation resulting in fewer lesions in comparison to those with relapsing MS (National Multiple Sclerosis Society, n.d.). However, PPMS patients tend to have more lesions in their spinal cords than the brain making it harder to diagnose in comparison to relapsing MS patients (National Multiple Sclerosis Society, n.d.).

*Cognitive Deficits in Multiple Sclerosis*

A common symptom of MS is cognitive impairment, which affects up to 70% of persons with MS (Chiaravalloti & DeLuca, 2008). These cognitive deficits manifest as problems with attention, information processing speed, episodic memory, executive functions, visuospatial perception, and prospective memory (Jongen, et a., 2012). Furthermore, MS research has determined that the most common cognitive impairments patients suffer from are episodic memory and processing speed deficits (Sumowski et al., 2018). Approximately 28% to 52% of persons with MS are impaired on processing speed tests such as the Paced Auditory Serial Addition Test and the Symbol Digit Modalities Test (SDMT) and about 30% to 55% on memory tests such as the California Verbal Learning Test second edition (CVLT-II) and the Brief Visuospatial Memory Test-Revised (BVMT-R) (Sumowski et al., 2018). Despite these new findings, MS research in cognitive improvement and treatment is still lacking.

*Cognition, Prospective Memory & Cue Types in Multiple Sclerosis*

Prospective memory (PM) is the process of "remembering to remember." (Cohen & Hicks, 2017). It is the action of forming new memories for future action, temporarily storing them, and then being able to retrieve them at a future time (Crystal et al., 2015). The two main categories for prospective memory are those that rely on time-based cues and those that rely on event-based cues. These cues help trigger the retrieval of memories and initiate prospective memory. Time-based cues in PM are considered the "to-be-completed" tasks at a specific time or general deadline (Oates & Peynircioglu, 2014). For example, remembering to pick up your sibling from school at 2 pm, or calling your parents at noon are considered time-based cues. On the other hand, event-based cues are the to-be-completed tasks when a particular action is presented or when participants encounter a specific event (Strickland et al., 2021). For example, when someone opens your bedroom door, you remember to close it afterwards, or when the bell rings, you remember to leave the classroom. Usually when these PM tasks are given, there is also an ongoing task as well. When these cues are properly completed, PM can be considered intact and working well in a person. However, problems arise when these cue types are not followed, typically indicating a memory problem. It recent studies, it was discovered that individuals with MS had impaired time-based PM compared to healthy individuals (Raimo et al., 2019).

There are also objective and subjective methods to assess a person with MS's cognitive abilities. Objective measures include the Brief Repeated Batter of Neuropsychological Tests (BRB-N) that consist of the selective reminding, 10/36 spatial recall, symbols digit modalities, paced auditory serial addition (PASAT), and word list generation tests (Bever Jr et al., 1995). The subjective measure to determine a persons' cognitive abilities are the Self-Reported

Perceived Deficits Questionnaire – Prospective Memory (PDQ-PM) (Visser & Hiele, 2014). In persons with MS, it was discovered that objective measures accurately depicted patient's cognitive abilities (Bever Jr et al., 1995). However, in subjective measures, researchers discovered that 15% overestimated their executive performance and demonstrated executive dysfunction on testing ((Visser & Hiele, 2014). Furthermore, approximately, 15% underestimated their executive performance and self-reported executive function disturbances, but showed normal executive performance (Visser & Hiele, 2014). Overall, it seems that objective measures for determining PM in persons with PM are more reliable than self-reporting measures.

In persons with MS, it was discovered that PM is negatively impacted by MS. Previous research has indicated that persons with MS have a diminished PM compared to control groups in the Memory for Intentions Screening Test (MIST) results (Miller et al., 2014). Additional research has supported this conclusion by stating that persons with MS have a significantly impaired PM performance and this was discovered when they were undergoing PM tasks (Rendell et al., 2014). Therefore, this PM impairment and cognitive deficit easily transfers to difficulties in performance on cognitive tasks, which impact their quality of life (Honan et al., 2015). Additionally, PM deficits in persons with MS can also be seen in early stages of the disease (Rouleau et al., 2017). Fortunately, studies have concluded that implementation interventions can help improve PM tasks in patients with MS (Kardiasmenos et al., 2008).

*Prospective Error Types in Multiple Sclerosis*

Prospective memory errors in MS can be used to understand deficits in a person's cognitive ability and provide insight into how these deficits impact their quality to life.

According to the MIST, there are five types of PM errors: no response errors (prospective memory failures errors), task substitution errors, loss of content errors, loss of time errors, and random errors (Raskin, 2004). No response errors are scored if the examinee does not provide a response at the specified time or event (Raskin, 2004). Task substitution errors are when the participant provides an inappropriate response to a cue, such as performing an action for a verbal item or giving a verbal response for an action item (Raskin, 2004). Loss of context errors are if the participant recalls that a task needs to be completed at the correct time but cannot remember the content of the task (Raskin, 2004). Loss of time errors are when the participant recalls the content of a task correctly, but at the wrong time (Raskin, 2004). Finally, random errors are when the participant's error does not fit into any category already stated (Raskin, 2004). Overall, these five types of PM errors can be used to categorize deficits in PM in persons with MS.

*Prospective Memory & Personality*

Personality traits have been analyzed in the context of several neurological diseases and have been found to impact factors such as cognition and behavioral patterns. Personality can be categorized using the Neuroticism-Extraversion-Openness Five-Factor Inventory (NEO-FFI-3). The NEO-FFI-3 is used assess personality traits and categorize patients into five factor domains, neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness (Costa et al., 1989). Neuroticism personality trait is the disposition to experience negative effects such as anger, anxiety, self-consciousness, irritability, emotional instability, and depression (Widiger & Oltmanns, 2017). Persons with neuroticism tend to respond poorly to environmental stress and interpret normal situations at threatening (Widiger & Oltmanns, 2017). Extroversion personality trait is the disposition to be more sociable and assertive (Thomas, 2021). Those with openness

tend to have a disposition for intellectual curiosity and creative imagination (Thomas, 2021). A person with agreeableness has a disposition for compassion and respectfulness (Thomas, 2021). Finally, a person with conscientiousness has a disposition that includes high levels of thoughtfulness, impulse control, and goal-directed behaviors (Thomas, 2021). Overall, these personality traits indicate that those with certain personality traits are more likely to act, behave, and react to certain situations differently.

In relation to MS, studies have indicated that personality traits might be correlated to PM errors. It was determined that individuals with a higher conscientiousness had higher estimated PM compared to individuals lower on the conscientiousness dimension (Smith et al., 2011). Therefore, further investigation into personality traits and its correlations to PM errors can give insight into MS and its effect on cognition.

By correlating personality traits to PM errors in persons with MS, psychologists can help determine whether persons with certain traits are at higher risk for developing certain PM errors and so that psychologists can determine the best treatment plan for patients.

*Neuropsychological Examinations*

Neuropsychological examinations are used to assess prospective memory errors and their neuropsychological correlates in persons with MS. These examinations are the Memory for Intentions Test (MIST), which evaluates PM through comparing event-based and time-based cues in clinical populations (Raskin, 2009); the Symbol Digit Modalities Test (SDMT), to examine cognitive processing speed (Benedict et al., 2017); Rey Auditory Verbal Learning Test (RAVLT) Trial 1, Total Learning, and Trial B to assess attention, memory, and learning ability through an auditory-verbal exam (Correia & Osorio, 2013); Neuroticism-Extraversion-Openness

Five-Factor Inventory (NEO-FFI-3) to determine personality types (McCrae et al., 1991); and the Self-reported Perceived Deficits Questionnaire – Prospective Memory (PDQ-PM) to assess patients' and significant others' perceptions of cognitive abilities and concerns (Strober et al., 2016). The MIST consists of 8 times-delayed PM tasks that provides a comprehensive measure of many aspects of PM functioning (Raskin, 2009). It is commonly used in brain trauma research to assess patient prospective memory capabilities (Hicks et al., 2021); however, new MS research is attempting to apply its methodology to better understand prospective memory in patients with MS. In MS, the MIST is used to characterize types and frequencies of PM errors. The SDMT is used to detect cognitive impairment by testing information processing speed, visual scanning, and motor ability (Benedict et al., 2017). The RAVLT is used to evaluate verbal memory in patients and to monitor changes in memory function over time. Specifically, it is used to measure a person's ability to encode, combine, store, and recover verbal information at different stages of immediate memory (Neurol, 2016). Moreover, a cognitive distractor (Trial B) is included to further assess prospective memory in patients. The NEO-FFI-3 is used assess personality traits and categorize patients into five factor domains, neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness (Costa et al., 1989). The PDQ is used as a method of patient self-reporting to monitor cognitive dysfunction such as attention, retrospective memory, prospective memory, and planning and organization (National Multiple Sclerosis Society). Specifically, the PDQ-PM monitors the prospective memory of cognitive dysfunction in patients with MS.

*This Study*

In this study, PM error types and frequencies, in persons with MS, were characterized and analysis into whether they differ by cue types will also be conducted. A separate investigation into whether other cognitive processes and personality types contribute to prospective memory will also be explored. Preexisting data (2019-2021) from Dr. Gromisch's Lab at the Mandell Center for Multiple Sclerosis in Hartford, CT will be used in this study. Data were extracted from the MIST, SDMT, RAVLT Trial 1, Total Learning, and Trial B, NEO-FFI-3, and the PDQ-PM and it will be used to determine PM errors and their neuropsychological correlations to persons in MS. By characterizing prospective memory errors and their neuropsychological correlations in patients with multiple sclerosis, this study hopes to inform rehabilitation and treatment approaches to improve quality of life in persons with multiple sclerosis.

## Methods

### *Note on Previously Collected Data*

The data used in this study were previously collected at two community-based MS centers in Hartford, CT that shared the same health care system. It was previously collected for a study investigating the biopsychosocial correlates of overall and individual self-management, while incorporating demographics of co-occurring medical diagnoses, cognition, personality traits, and psychosocial and physical functioning as variables (Gromisch et al., 2021). The data were conducted between June 2019 and September 2020, and this study was approved by the Trinity Health of New England Institutional Review Board (Gromisch et al., 2021). For the purpose of the current study the MIST, SDMT, RAVLT, and NEO-FFI-3 measures were used.

### *Participants*

Participants (n=111) had a definite diagnosis of MS and were between the ages of 18 and 89. The sample size was comprised of females (n=82) and males (n=29) whose average age of education was 15.23 years. Furthermore 90 participants had relapse remitting MS (RRMS), 12 participants had secondary progressive MS (SPMS), and 9 participants had primary progressive MS (PPMS). The average MS duration from diagnosis was $14.40 \pm 9.31$ years with a range from 0 to 45 years. Additionally, 75 participants were undergoing infusion disease modifying treatment (DMT), 14 were taking oral DMT, 9 were undergoing injectable DMT, and 14 were not undergoing any DMTs. All participants spoke English and had not experienced a relapse within the past 2 months before the study evaluations were conducted. Participants who previously indicated that they were interested in participating in research studies were contacted through emails, phone calls, and mail. Additionally, paper flyers were placed in waiting rooms in

the community-based MS centers and community rooms. This study originally had 112 participants; however, 1 participant was excluded due to incomplete neuropsychology assessments. Demographic and clinical information was collected (Table 1). (Gromisch et al., 2021).

**Table 1**: Participant demographic and clinical information

**Participant Demographic & Clinical Information**

| | N (%) | Mean (SD) | Median (Range) |
|---|---|---|---|
| Age | | 51.03±12.23 | 52.50 (21-74) |
| Years of Education | | 15.21±2.29 | 15.50 (10-25) |
| Employment Status | | | |
| No | | 65 (58.0%) | |
| Yes, Part Time | | 16 (14.3%) | |
| Yes, Full Time | | 31 (27.7%) | |
| MS Duration | | 14.40±9.31 | 12.00 (0-45) |
| Type of MS | | | |
| Relapsing Remitting | 90 (80.4%) | | |
| Secondary Progressive | 12 (10.7%) | | |
| Primary Progressive | 9 (8.0%) | | |
| Not Sure | 1 (0.9%) | | |
| Gender | | | |
| Female | 83 (74.1%) | | |

| | | | |
|---|---|---|---|
| Male | 29 (25.9%) | | |
| Race | | | |
| White | 96 (85.7%) | | |
| African American | 10 (8.9%) | | |
| Other | 4 (3.6%) | | |
| Multiple | 2 (1.8%) | | |
| History of Depression | 48 (42.9%) | | |
| History of Anxiety | 35 (31.3%) | | |
| PDQ | | | |
| Attention | | 10.73±3.99 | 11.00 (2-20) |
| Retrospective Memory | | 9.56±4.03 | 9.50 (0-18) |
| Prospective Memory | | 7.84±3.43 | 7.00 (1-19) |
| Planning and Organization | | 9.48±3.95 | 9.00 (1-19) |

(Gromisch et al., 2021)

*Clinical Materials*

The primary outcome was the 24-item MS Self-management Scale-Revised (MSSM-R). The scale analyzed the person's ability to take care of their own condition by measuring their collaboration with providers and their coping and health behaviors. After collecting total score data, 5 subscales were also kept into account: Health-care Provider Relationship/Communication, Treatment Adherence/Barriers, Social/Family Support, MS knowledge and information, and Health Maintenance Behaviors. The higher the score was, the better the self-management. The participants' processing speed and working memory were also evaluated using the oral SDMT. Retrospective verbal learning and memory were assessed using

the RAVLT, and the MIST was used to measure prospective memory. Additionally, personality traits were determined using the NEO-FFI-3. Finally, participants self-reported cognitive, psychosocial, and physical functioning using the Illness Intrusiveness Ratings Scale, Hospital Anxiety and Depression Scale, Modified Fatigue Impact Scale-5, Pain Effects Scale, Perceived Deficits Questionnaire, Multiple Sclerosis Quality of Life-29, Multiple Sclerosis Resiliency Scale, and University of Washington Self-efficacy Scale. (Gromisch et al., 2021).

*Procedure*

In-person testing was conducted by a neuropsychologist from June 2019 to September 2020. Participants were required to fill out an informed consent form and then asked to complete an eligibility screening. They then underwent a one-time assessment that contained MS-validated measures and participants received a $40 financial compensation for their participation in this study (Gromisch et al., 2021).

*The Current Study*

In the current study, we analyzed previously collected data to characterize types and frequencies of PM errors and to determine if other cognitive processes or personality traits are associated with PM errors in persons with MS. First it was determined how many errors were made in total, how many of each type, and how many errors were time-based, or event-based. Then for each participant, the same categorization was applied. Afterwards, the data were compared to see if there was a difference through a 2x1 contingency table. Next, investigation into the relationship between PM errors, personality traits, and other cognitive processes such as

processing speed, total learning, initial learning, proactive interference, and distractor encoding was conducted.

*Statistical Analysis*

SPSS v26 was used to analyze the data. Any variables with a low cell count (<5%) were excluded from the analyses. MSSM-R total and subscale cores were nonnormally distributed and ordinal and scale variables were analyzed using nonparametric bivariate analyses and Spearman correlations. Mann Whitney U was used for nominal variables and Kruskal-Wallis tests were used for multicategorical variables. Variables with a P value < 0.1 were analyzed as an ordinary least squares linear regression. Nonsignificant variables were analyzed to find the optimal combination of factors and multicollinearity, homoscedasticity and linearity, independence of errors, and normal distribution of residuals were analyzed through variance inflation factor and tolerance statistics, scatterplots and partial regression plots, Durbin-Watson test, and Kolmogrov-Smirnow test. Since, MSSM-R total score was the primary outcome, the variables that were significant were kept because the purpose was to identify the specific individual variables that independently explained the outcome.

## Results

*Objective 1 Results*

The objective of this experiment was to characterize the types and frequencies of PM errors. For each participant, the total number of PM errors, the number of each type of error, and the number of time-based errors and the number of event-based errors were calculated. Differences between each type of error were analyzed using a 2x1 contingency table and percentages were determined. Descriptive statistics were used to characterize PM errors. It was discovered that 92.87% (n=103) of participants made at least one PM error on the MIST. Among those who made an error, the median number was 3 and the range was from 1 to 8 number of errors. Based on descriptive statistics, loss of content errors (45%) were the most common PM error made by those with PwMS (Table 2). Time-based tasks were also more frequently made in PwMS (67.6%) (Table 3). After descriptive statistics, chi-squares were used to examine frequency differences in the types of errors ($\chi^2(3) = 98.71$ $p < .001$) (Table 2) and time-based and event-based PM errors (Table 3) ($\chi^2(1) = 43.35$, $p < .001$). Chi-square analysis determined that there is a significant difference between the expected and actual data.

**Table 2:** Descriptive data depicting the frequency of the type of PM errors made (n=395).

| | Number of errors (n) | Percentage % |
|---|---|---|
| Loss of Content | 157 | 45 |
| Task Substitution Errors | 96 | 27.2 |
| Prospective Memory Failures | 67 | 19.2 |
| Loss of Time Errors | 30 | 8.6 |

$\chi^2$ (3) = 98.71, p<.001

**Table 3:** Descriptive data depicting the frequency of time-based and event-based PM errors.

| | Number of errors (n) | Percentage % |
|---|---|---|
| Time-based Errors | 236 | 67.6 |
| Event-based Errors | 113 | 32.4 |

$\chi^2$ (1) = 43.35, p<.001

*Objective 2 Results*

The number of PM errors were non-normally distributed resulting in Spearman Correlations data analysis. Spearman's correlations were run between the number of PM errors and the cognitive processes and personality traits. Specifically, correlations between the number of PM errors and SDMT 2-score, RAVLT Trial 1 2-score, RAVLT Trial B 2-score, RAVLT Total Learning 2-score, RAVLT proactive interference ratio, and NEO FFI-3 T-scores were conducted (Table 6).

**Table 4:** Spearman's correlations depicting the relationship between PM errors & cognitive processes.

| | Correlation (rho) | p-value |
|---|---|---|
| SMDT z-score | -.38 | <.001* |
| RAVLT Trial 1 z-score | -34 | <.001* |
| RAVLT Trial B z-score | -.33 | <.001* |
| RAVLT Total Learning z-score | -.41 | <.001* |
| RAVLT Proactive Interference Percentage | -.07 | .462 |

* = significance (p<.001)

**Table 5:** Spearman's correlations depicting the relationship between PM errors and personality traits (NEO-FFI-3).

| | Correlation (rho) | p-value |
|---|---|---|
| Neuroticism | -.01 | .919 |
| Extraversion | .08 | .382 |
| Openness | -.15 | .116 |
| Agreeableness | .02 | .856 |
| Conscientiousness | .01 | .953 |

From the analysis, SDMT 2-score, RAVLT trial 1 z-score, RAVLT trial B z-score, and RAVLT total learning z-score were deemed significant ($p<.001$) (Table 6). There were no significant relationships between PM errors and personality traits. Significant variables were further analyzed as independent variables using a linear regression to determine the most predictive of PM errors out of the variables used. The variables were added from the correlation matrix and compared to the number of PM errors as the outcome. Covariates for this analysis were age, gender, and years of education. Non-significant variables were manually removed one at a time, starting from the highest p-value. The variables that were removed after linear regression analysis were the RAVLT trial 1 z-score ($p=.996$) and the RAVLT trial B z-score ($p=.922$) (Table 6). Remaining variables were the SDMT z-score ($p=.003$) and the RAVLT total learning z-score ($p<.001$) (Table 6). A final model was conducted to determine goodness of fit of the linear regression model ($F(5,105) = 13.16$, $p<.001$). It was determined that there was an overall significance of the variables compared to PM errors in PwMS (Table 5).

**Table 5:** Linear regression of significant Spearman's correlation variables with PM errors as the outcome.

| | B(SE) | 95% Confidence Interval (Lower Bound, Upper Bound) | $\beta$ | p-value |
|---|---|---|---|---|
| Age | .06 (.01) | .03, .08 | .36 | <.001* |
| Education | .04 (.07) | -.09, .18 | .05 | .514 |
| Gender | -.01 (.36) | -.73, -.15 | -.00 | .980 |
| SDMT z-score | -.42 (.14) | -.70, -.15 | -.27 | .003* |
| RAVLT Total Learning z-score | -.58 (.14) | -.86, -.31 | -.41 | <.001* |

* = significance (p<.01)

## Discussion

### *Interpretation of Results*

This study aimed to characterize the types and frequencies of PM errors and to investigate whether other cognitive processes (i.e., processing speed and verbal learning) or personality traits (i.e., neuroticism, extraversion, etc.) are associated with PM errors in persons with multiple sclerosis.

For the first objective, it was discovered that PM errors occur frequently in persons with MS as 92.87% (n=103) of participants who came to the clinics for the study made at least one PM error on the MIST. Interestingly, these participants with MS did not complain about PM deficits before coming into the clinic, however, a significant number of participants with MS suffer from PM deficits. In contrast to previous studies, the most common cognitive impairments persons with MS suffered from were episodic memory and processing speed deficits (Sumowski et al., 2018). However, this study differs from prior MS research, and indicates that prospective memory is a frequent cognitive impairment that impacts persons with MS. Additionally, it was revealed that loss of content errors are the most common PM error made since 45% of all errors made on the MIST were loss of content errors (Table 2). This finding is new to MS research and indicates that persons with MS often forget what they need to do at certain times and events, and this may reflect a deficit in the retrospective recall aspect of PM. Errors on time-based tasks were also found to occur more frequently since in persons with MS since 67.6% of all errors made were on items with time-based cues (Table 3). This finding supports previous research that determined persons with MS performed significantly worse on time-based tasks than event-based tasks (Weber et al., 2019). This is likely because time-based tasks require cognitive control and the added need to monitor time passing.

For the second objective, it was discovered the number of PM errors persons with MS make are negatively associated with their performance on tests examining processing speed, initial verbal learning, and overall verbal learning. These findings support prior research that concluded that patients with MS have significantly slower information processing speed (Demaree et al., 1999). Furthermore, research has also indicated that verbal learning and memory deficits are some of the most common in persons with MS (Pitteri et al., 2020). Hence, this may explain the loss of content errors occurring in persons with MS. However, the number of PM errors are not associated with learning interference or personality traits. In the context of proactive learning interference, prior research has determined that proactive interference is unaffected in persons with MS (Griffiths et al., 2005). Therefore, our findings align with previous learning proactive interference conclusions in MS research. On the other hand, prior research has determined that some personality traits negatively affected cognitive domains, mood, and impacted a persons' psychological well-being (Maggio et al., 2020). Hence, our findings contradict prior personality research in persons with MS and how it impacts cognition. After further analysis, it was further determined that age, processing speed and verbal learning are associated with greater number of PM errors made in persons with MS. Overall, PM is a cognitive domain that needs to be further researched in MS since most persons with MS suffer from PM impairments and deficits that affect their daily living and ability to independently function.

*Conclusion*

From the current study, it was determined that PM errors occur frequently in persons with MS. Specifically, we discovered that persons with MS tend to make more errors on time-based

tasks in comparison to event-based tasks. Furthermore, loss of content errors were found to be the most common error made in persons with MS. Additionally, persons with MS have a slower processing speed and reduced verbal learning and this is positively associated with a greater number of PM errors made on neuropsychological assessments. Moreover, it was determined that personality traits do not contribute to the number of PM errors made by persons with MS. Ultimately, persons with MS are detrimentally impacted by the disease as it negatively impacts their PM and results in an increase in PM deficits.

*Limitations*

The most significant limitation from this study is the composition of the sample size. Although the sample size was 111 persons with MS, most of the participants were women (n= 82). Additionally, the majority of participants had relapsing remitting MS (RRMS) (n=90) and were taking infusion disease modifying treatments at the time of evaluation. Due to these variables, the sample size should increase to account for other factors that might be impacting PM error results. Additionally, most of the data were collected from two community-based MS centers in Hartford, CT, limiting the geographical area of where the data were collected from. Due to the limited geographical area, participant PM error data can be skewed due to similar external factors, and it is not representative of the entire population of persons with MS in the United States and internationally.

*Future Studies*

This study is an exploratory retrospective study into PM deficits in persons with MS. Based on prior cognitive domain research in persons with MS, more research into PM needs to

be done as a significant amount of the research is only addressing PM to a certain extent. Furthermore, research into PM errors in persons with MS is also very limited. If more research can fully investigate the impacts of PM deficits on the daily living and functioning of persons with MS, it is possible to improve their lives. Ultimately, by conducting research into intervention studies to prevent the progression of PM deficits in persons with MS, we can help improve their lives.

**Acknowledgments**

I would like to thank my thesis advisor, Dr. Elizabeth S. Gromisch for her constant support, patience, and encouragement throughout my time at the Mandell MS Center in Hartford, CT. I was able to pursue my interest in multiple sclerosis research because of her and I would not be where I am today without her generosity and guidance. I would also like to thank Lindsay Neto for her constant support and assistance throughout my senior thesis, and Dr. Zaenab Dhari for teaching me how to analyze MRI scans and understand multiple sclerosis from a radiology perspective. Furthermore, I would like to thank my Trinity College thesis advisor, Dr. Sarah Raskin for helping me understand prospective memory and her guidance throughout my time at Trinity College. I would not be where I am today without the help from all my advisors and mentors, and I greatly appreciate their impact on my life. I would also like to thank my senior thesis second reader Dr. Michael Puljung for his edits on my senior thesis. Finally, I would like to thank the Mandell MS Center and Trinity College Neuroscience Program for making this research possible.

The views and opinions expressed in this paper reflect those of the authors and do not necessarily reflect those of the United States Department of Veteran Affairs. Furthermore, this study was funded as a pilot grant from the National MS society (PP-1901-33103).

## References

Benedict, R. H., DeLuca, J., Phillips, G., LaRocca, N., Hudson, L. D., & Rudick, R. (2017). Validity of the Symbol Digit Modalities Test as a cognition performance outcome measure for multiple sclerosis. *Multiple Sclerosis (Houndmills, Basingstoke, England)*, *23*(5), 721–733. https://doi.org /10.1177/1352458517690821

Bever, C. T., Grattan, L., Panitch, H. S., & Johnson, K. P. (1995). The Brief Repeatable Battery of Neuropsychological Tests for Multiple Sclerosis: A preliminary serial study. *Multiple Sclerosis (Houndmills, Basingstoke, England)*, *1*(3), 165–169. https://doi.org/10.1177/135245859500100306

Chiaravalloti, N. D., & DeLuca, J. (2008). Cognitive impairment in multiple sclerosis. *The Lancet. Neurology*, *7*(12), 1139–1151. https://doi.org/10.1016/S1474-4422(08)70259-X

*Cognition in multiple sclerosis | Neurology*. (n.d.). Retrieved November 22, 2021, from https://n.neurology.org/content/90/6/278

Cohen, A.-L., & Hicks, J. (2017). *Prospective Memory: Remembering to Remember, Remembering to Forget*. https://doi.org/10.1007/978-3-319-68990-6

Dobson, R., & Giovannoni, G. (2019). Multiple sclerosis – a review. *European Journal of Neurology*, *26*(1), 27–40. https://doi.org/10.1111/ene.13819

Ercolini, A. M., & Miller, S. D. (2006). Mechanisms of Immunopathology in Murine Models of Central Nervous System Demyelinating Disease. *The Journal of Immunology*, *176*(6), 3293–3298. https://doi.org/10.4049/jimmunol.176.6.3293

Griffiths, S. Y., Yamamoto, A., Boudreau, V. G., Ross, L. K., Kozora, E., & Thornton, A. E. (2005). Memory interference in multiple sclerosis. *Journal of the International Neuropsychological Society: JINS*, *11*(6), 737–746. https://doi.org/10.1017/S135561770505085X

Gromisch, E. S., Neto, L. O., & Turner, A. P. (2021). What Biopsychosocial Factors Explain Self- management Behaviors in Multiple Sclerosis? The Role of Demographics, Cognition, Personality, and Psychosocial and Physical Functioning. *Archives of Physical Medicine and Rehabilitation*, *102*(10), 1982-1988.e4. https://doi.org/10.1016/j.apmr.2021.05.012

Harbo, H. F., Gold, R., & Tintoré, M. (2013). Sex and gender issues in multiple sclerosis. *Therapeutic Advances in Neurological Disorders*, *6*(4), 237–248. https://doi.org/10.1177/1756285613488434

Jongen, P. J., Ter, H. A., & Brands, A. M. (2012). Cognitive impairment in multiple sclerosis. *Minerva Medica*, *103*(2), 73–96.

Jongen, P. J., Ter Horst, A. T., & Brands, A. M. (2012). Cognitive impairment in multiple sclerosis. *Minerva Medica*, *103*(2), 73–96.

KHOSRAVI FARD, E., L. KEELOR, J., Akbarzadeh BAGHEBAN, A., & W. KEITH, R. (2016).

Comparison of the Rey Auditory Verbal Learning Test (RAVLT) and Digit Test among Typically Achieving and Gifted Students. *Iranian Journal of Child Neurology*, *10*(2), 26–37.

Maggio, M. G., Cuzzola, M. F., Latella, D., Impellizzeri, F., Todaro, A., Rao, G., Manuli, A., & Calabrò, R. S. (2020). How personality traits affect functional outcomes in patients with multiple sclerosis: A scoping review on a poorly understood topic. *Multiple Sclerosis and Related Disorders*, *46*. https://doi.org/10.1016/j.msard.2020.102560

*Memory for Intentions Test (MIST) | Psychology Resource Centre*. (n.d.). Retrieved November 22, 2021, from https://psycentre.apps01.yorku.ca/wp/memory-for-intentions-test-mist/

Oates, J. M., & Peynircioğlu, Z. F. (2014). The importance of source and cue type in time-based everyday prospective memory. *The American Journal of Psychology*, *127*(3), 343–350.

*Perceived Deficits Questionnaire (PDQ)*. (n.d.). National Multiple Sclerosis Society. Retrieved November 22, 2021, from https://www.nationalmssociety.org/For-Professionals/Researchers/Resources-for-MS-Researchers/Research-Tools/Clinical-Study-Measures/Perceived-Deficits-Questionnaire-(PDQ)

Pitteri, M., Dapor, C., Pisani, A. I., Castellaro, M., DeLuca, J., Chiaravalloti, N., Guandalini, M., Ziccardi, S., & Calabrese, M. (2020). Executive functioning affects verbal learning process in multiple sclerosis patients: Behavioural and imaging results. *Journal of Neuropsychology*, *14*(3), 384–398. https://doi.org/10.1111/jnp.12198

*Primary progressive MS (PPMS)*. (n.d.). National Multiple Sclerosis Society. Retrieved November 21, 2021, from https://www.nationalmssociety.org/What-is-MS/Types-of-MS/Primary-progressive-MS

*Prospective memory and the efficacy of a memory strategy in multiple sclerosis. - PsycNET*. (n.d.). Retrieved November 22, 2021, from https://psycnet.apa.org /doiLanding?doi=10.1037%2Fa0013211

Raimo, S., Trojano, L., Gaita, M., Spitaleri, D., & Santangelo, G. (2019). High openness and high extroversion are linked with better time-based prospective memory in multiple sclerosis. *Journal of Neurology*, *266*(11), 2665–2671. https://doi.org/10.1007/s00415-019-09460-4

Raskin, S. (2009). Memory for Intentions Screening Test: Psychometric Properties and Clinical Evidence. *Brain Impairment - BRAIN IMPAIR*, *10*, 23–33. https://doi.org/10.1375/brim.10.1.23

*Relapsing-remitting MS (RRMS)*. (n.d.). National Multiple Sclerosis Society. Retrieved November 21, 2021, from https://www.nationalmssociety.org/What-is-MS/Types-of-MS/Relapsing-remitting-MS

*Secondary progressive MS (SPMS)*. (n.d.). National Multiple Sclerosis Society. Retrieved November 21, 2021, from https://www.nationalmssociety.org/What-is-MS/Types-of-MS/Secondary- progressive-MS

Smith, R. E., Persyn, D., & Butler, P. (2011). Prospective Memory, Personality, and Working Memory: A Formal Modeling Approach. *Zeitschrift Fur Psychologie*, *219*(2), 108–116. https://doi.org /10.1027/2151-2604/a000055

*Speed of information processing as a key deficit in multiple sclerosis: Implications for rehabilitation | Journal of Neurology, Neurosurgery & Psychiatry*. (n.d.). Retrieved May 9, 2022, from https://jnnp.bmj.com/content/67/5/661

Strickland, L., Heathcote, A., Humphreys, M. S., & Loft, S. (2021). Target learning in event-based prospective memory. *Journal of Experimental Psychology. Learning, Memory, and Cognition*. https://doi.org/10.1037/xlm0000900

Sumowski, J. F., Benedict, R., Enzinger, C., Filippi, M., Geurts, J. J., Hamalainen, P., Hulst, H., Inglese, M., Leavitt, V. M., Rocca, M. A., Rosti-Otajarvi, E. M., & Rao, S. (2018). Cognition in multiple sclerosis: State of the field and priorities for the future. *Neurology*, *90*(6), 278–288. https://doi.org /10.1212/WNL.0000000000004977

Visser, L. H., & van der Hiele, K. (2014). Self-reports of executive functioning in multiple sclerosis: To trust or not to trust. *Neurodegenerative Disease Management*, *4*(2), 109–111. https://doi.org /10.2217/nmt.14.15

Weber, E., Chiaravalloti, N. D., DeLuca, J., & Goverover, Y. (2019). Time-Based Prospective Memory Is Associated with Functional Performance in Persons with MS. *Journal of the International Neuropsychological Society*, *25*(10), 1035–1043. https://doi.org/10.1017/S135561771900095X

*What Are The Big 5 Personality Traits?* (n.d.). Thomas International. Retrieved December 1, 2021, from https://www.thomas.co/resources/type/hr-guides/what-are-big-5-personality-traits

Widiger, T. A., & Oltmanns, J. R. (2017). Neuroticism is a fundamental domain of personality with enormous public health implications. *World Psychiatry*, *16*(2), 144–145. https://doi.org/10.1002 /wps.20411