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Abstract

Introduction: Prospective memory (PM) deficits have been documented in multiple sclerosis (MS). This study aimed to explore the specific types of errors made by persons with MS (PwMS), including differences between PwMS and healthy controls (HC) and PwMS who do and do not have impairments in processing speed and/or verbal learning and memory.

Method: PwMS (n = 111) and HC (n = 75) completed the Memory for Intentions Test (MIST), an objective measure of PM that has five types of errors that can be coded (PM failure, task substitution, loss of content, loss of time, and random errors). The number and types of PM errors were calculated for the overall MIST and six subscales, which break down performance by types of delay (2-Minute and 15-Minute), cue (Time and Event), and response (Verbal and Action). Impairment was defined as performing <1.5 SD on either the Symbol Digit Modalities Test (SDMT) or Rey Auditory Verbal Learning Test (RAVLT). Bivariate analyses were used to examine group differences, with post-hoc pairwise comparisons with Bonferroni corrections.

Results: Nearly 93% of PwMS made at least one PM error, compared to 76% of HC (V = .24, p = .001). The most commonly made PM error by PwMS was loss of content errors (45.0%). PwMS made significantly more task substitution errors (26.4% vs. 7.6%, p <.001) and fewer loss of time errors (9.5% vs. 21.2%, p <.001) than HC. Impaired PwMS made more errors than non-impaired PwMS, specifically PM failures on time-based tasks.

Conclusions: PM errors are common in PwMS, particularly when there are longer delays and time-based cues. Not only do PwMS make more errors than demographically similar HC, but they exhibit different cognitive process failures.

Keywords: multiple sclerosis, prospective memory, error analysis, cognitive functioning

Introduction

Multiple sclerosis (MS) is a debilitating neurological disease that affects nearly one million people in the United States (Wallin et al., 2019). A common symptom of MS is cognitive impairment, which affects up to 70% of people with MS (PwMS) (Chiaravalloti & DeLuca, 2008). Many PwMS experience issues with memory, which is thought to be due to impairments in their initial learning (Chiaravalloti & DeLuca, 2008). Reductions in new learning, along with slower processing speed and executive dysfunction, have been connected to difficulties completing functional activities (Kalmar et al., 2008). Furthermore, memory impairments have been associated with unemployment in PwMS (Clemens & Langdon, 2018).

One understudied aspect of memory in MS is prospective memory (PM) or “remembering to remember” (Cohen & Hicks, 2017). PM involves forming new memories and an intention for future action, temporarily storing them, and then retrieving them at a future time (Crystal & Wilson, 2015). As such, individuals need to recall both the content (retrospective component) and the future intention (prospective component) to successfully complete the task. In the four-stage conceptual model of PM (Carey et al., 2006; Raskin et al., 2010), the individual first forms the intention, then must retain that intention while carrying out other tasks, followed by recognition of the cue and correct pairing with the intention, and then finally execution of the intention. The cues to carry out the intention can be time-based, such as a specific time or general deadline (Oates & Peynircioglu, 2014), or event-based, such as a specific event or when a particular action is presented (Strickland et al., 2021). For example, remembering to take a medication at noon is a time-based PM task, while remembering to charge a phone when the low battery alert goes off is an event-based PM task.

Compared to healthy controls, PwMS have greater difficulties with PM (Dagenais et al., 2016; Kardiasmenos et al., 2008; Miller et al., 2014; Raimo et al., 2019; Rendell et al., 2012; Rendell et al., 2007; Weber et al., 2019), particularly on time-based PM (Miller et al., 2014; Raimo et al., 2019; Weber et al., 2019). Several functional issues have been associated with PM deficits in PwMS. For instance, unemployment has been associated with lower PM performance among PwMS, with deficits being a small, yet significant, contributor to reduced work hours, independent of other cognitive difficulties

(Honan et al., 2015). In addition, worse PM has also been associated with poorer medication adherence (Bruce et al., 2010), appointment non-attendance (Gromisch, Raskin, et al., 2023; Gromisch, Turner, et al., 2023), and greater difficulty completing everyday activities (Weber et al., 2019).

While the research in MS has primarily focused on overall PM impairment (Rouleau et al., 2018), the examination of different types of PM errors through error analysis can provide insight into where in the cognitive process the breakdown is occurring. Five types of PM errors have been identified (**Table 1**): PM failure, task substitution, loss of content, loss of time, and random errors (Raskin et al., 2010). Different process failures are thought to result in these different errors. While issues with time monitoring are associated with loss of time errors, prefrontal executive control and retrospective memory failures have been related to task substitution and loss of content errors, respectively (Raskin et al., 2010). In addition, multiple errors can occur during one task. For instance, an individual may have an electric bill due on the 15th but forget the day it is due and which utility to pay. In these situations, there are several cognitive process failures that are contributing to the PM error.

PM errors have been noted to occur in healthy adults with no history of neurological disorder. In the standardization sample for the Memory for Intentions Test (MIST), which included 736 individuals between the ages of 18 and 94, there was a mean error rate of 2.55 (SD = 1.89), with no errors occurring in only 14.5% of the sample (Raskin et al., 2010). PM failure errors were common on Trial 4 (34.8%) and Trial 8 (29.8%), which were both time-based tasks with 15-minute delays (Raskin et al., 2010). Random errors were very uncommon, only occurring in 0.3% of the sample on Trial 4 and 0% on all other tasks (Raskin et al., 2010). More errors were noted in older adults, with the highest rate among individuals 80 years or older (Raskin et al., 2010). It should be noted that an individual could make one or two PM errors on the eight-task MIST and still be classified as “unimpaired.” For example, if a 50-year-old with a college degree made two PM failures on two time-based tasks, the overall performance would be in the 34th percentile, which is considered “average” (Raskin et al., 2010).

Given the dearth of information in this area, this study aimed to explore the types of PM errors made by PwMS. In addition to characterizing the frequency of errors made under different constraints (i.e., different time delays, cue types, and response types), comparisons were made between 1) PwMS and healthy controls (HC) and 2) PwMS with and without impairments in processing speed and/or verbal learning and memory to examine differences in cognitive process failures. It was hypothesized that PwMS would exhibit a greater number of PM errors than HC, given the prevalence of cognitive difficulties in MS (Chiaravalloti & DeLuca, 2008). In addition, it was theorized that non-impaired PwMS would make errors that allowed for partial retrieval (e.g., recalling the correct time but not the correct content) while impaired PwMS would have more complete PM failures.

Material and Methods

Participants and Procedures

PwMS Group: This study was a secondary analysis of a cross-sectional study conducted at two community-based MS centers (Gromisch et al., 2021). The study procedures were approved by the Trinity Health Of New England Institutional Review Board (IRB), with the one-time data collection completed between June 2019 and September 2020. To qualify for the parent study, individuals needed to have a definite diagnosis of MS made by a center neurologist using on the McDonald criteria (Thompson et al., 2018), be between the ages of 18 and 89 (actual age range was between 21 and 74), be able to read and write in English, and have not experienced a relapse within the past two months. For the current analyses, participants needed to complete the entire MIST to ensure the PM error data were available for all eight trials. One participant was excluded due to not fulfilling the criteria, resulting in 111 PwMS being included in the analyses. Demographics are reported in **Table 2**.

HC Group: HC data were extracted from two previous studies (Raskin et al., 2010; Raskin et al., 2011), which were approved by the Trinity College IRB. These individuals had no histories of neurological, psychiatric, cardiovascular, or substance use disorders, or visual impairments that would interfere with testing. The HC did not complete any other tests besides the MIST. Selected HC (n = 75) were between the ages of 21 and 73 to match the ages of the PwMS group. They did not differ from the PwMS group in terms of age, education, or race, although there was a higher percentage of men (**Table**

2).

Measures

All demographics were self-reported, with MS-related disability measured using the Patient Determined Disease Steps (PDDS) (Hohol et al., 1995, 1999; Learmonth et al., 2013; Marrie & Goldman, 2007). The primary outcome was the MIST, an objective measure of PM with eight trials (four time-based and four event-based) (Raskin et al., 2010). The MIST has strong internal consistency and interrater reliability, and it has been validated in PwMS (Raskin et al., 2010). In addition to a total score for overall PM performance, six subscales can be calculated, which further break down PM performance by time delay (2-Minute Time Delay and 15-Minute Time Delay), cue type (Time Cue and Event Cue), and response type (Verbal Response or Action Response). Four trials were included in each subscale. For example, Trial 4 was included in the 15-Minute Time Delay, Time Cue, and Verbal Response subscales, as the task involved the examinee saying a specific statement 15 minutes after it was given.

Errors were recorded if the examinee performed the trial incorrectly, which could be a PM failure, task substitution, loss of content, loss of time, or random error. Descriptions of each error type are provided in **Table 1**. For event-based trials, a loss of time error could be coded if the examinee did not provide a response within one minute of the cue being provided. Only two random errors were noted in the HC group, which were both associated with Trial 4, as were the random errors in the MIST standardization sample (Raskin et al., 2010). These random errors were associated with Trial 4 (15-minute delay, time cued trial task with a verbal response) as they occurred around the time frame of that task but not within the possible time for a different task. In addition, the random errors were verbal responses and thus were not related to the adjacent action trials. For both HC, the adjacent trials were answered correctly and would not have an error coded. It was possible for two errors to occur within one trial (e.g., the examinee forgot the content of the trial (loss of content error) and responded at the incorrect time (loss of time error)). The total number of errors made on the MIST were calculated, along with the percentage of each type of error made. This process was repeated for the six subscales of the MIST as well to examine the conditions under which the different errors occur.

Two measures were used to classify PwMS as cognitively impaired/non-impaired: the oral version of Symbol Digit Modalities Test (SDMT), a brief measure in which examinees match the number to a simple geometric design (Smith, 1982), and the Rey Auditory Verbal Learning Test (RAVLT), a 15-item list learning test with five learning trials and immediate and delayed recalls (Schmidt, 1996). The SDMT was selected as it is a sensitive, though not specific, measure of cognitive functioning in MS that is related to deep grey matter structures, whole brain volume, and total white matter volume (Benedict et al., 2017; Pitteri et al., 2021; Sandry et al., 2021; Spain et al., 2023). The RAVLT was selected as impaired new learning is associated with PM difficulties (Chiaravalloti & DeLuca, 2008), and retrospective memory is a component of the PM model (Carey et al., 2006; Raskin et al., 2010). The selection of these two measures was confirmed by the significant, positive associations between the total MIST score and the SDMT (ρ = .50, p < .001) and RAVLT total (ρ = .44, p <.001), immediate (ρ = .37, p < .001), and delayed (ρ = .44, p <.001) recalls. MS regression-based norms were used to calculate the SDMT z-scores (Parmenter et al., 2010), while age-based metanorms were used to calculate z-scores for the RAVLT total, immediate, and delayed recalls (Strauss et al., 2006). Impairment was defined as performing <-1.5 standard deviations (SD) on at least one of these measures. A total of 57 PwMS (51.4%) were classified as impaired based on this criterion, with 47.4% impaired only on the SDMT, 29.8% on both measures, and 22.8% only on the RAVLT.

Statistical Analysis

SPSS v26 was used to analyze the data. Differences in demographics between the PwMS and HC groups were examined using t-tests (age and education), chi-square (gender), and Fisher's exact test (race). Descriptive statistics were used to characterize the frequency of errors made on the overall MIST and each subscale by PwMS. For each type of constraint (i.e., time delays, cue type, and response type), Wilcoxon signed-rank test (effect size reported as *r*) and McNemar's test were run to explore whether there were differences in the number of errors made and percentage of PwMS who did not make any errors, respectively.

Mann-Whitney U tests (effect size reported as *r*) were used to compare the number of errors made by PwMS and HC on the overall MIST and each subscale, while chi-squares (effect size reported as Cramer's *V*) were used to evaluate the percentage who did not make any errors and differences in the types of errors made by these two groups. If there was a significant overall difference, post-hoc pairwise comparisons were conducted with Bonferroni corrections ($p < .006$ for four error types and $p < .005$ for five error types). Similar analyses were used to compare the number of errors and error types between impaired and non-impaired PwMS, with Fisher's exact test used when there were frequencies below five. The analyses were repeated to only include persons with relapsing remitting MS (RRMS) to explore whether the observed differences changed when individuals with progressive forms of MS were excluded.

Results

Errors on the Overall MIST

PwMS made a median of three errors, with 24.0% making no errors on the MIST. The most common error type was loss of content (45.0%), followed by task substitutions (26.4%). Compared to HC (**Table 3**), PwMS made more errors on the MIST, with the number of individuals making no errors being significantly lower. There was a significant difference in the types of errors made (**Figure 1**), with PwMS making made more task substitution errors and fewer loss of time errors. The observed differences in the frequency (**Supplementary Table 1**) and types of errors made (**Supplementary Table 2**) between HC and PwMS did not change when only persons with RRMS were examined. Impaired PwMS made more overall errors than non-impaired PwMS (**Table 3**), as well as more PM failure errors (**Figure 1**). These results did not change when only persons with RRMS were included in the analyses (**Supplementary Tables 1 & 2**).

Errors by Time Delay

PwMS made more errors when there was a 15-minute delay compared to a 2-minute delay ($r = .73$, *p*

< .001; **Table 3**). In addition, fewer PwMS made no errors when there was a 15-minute delay (8.1% vs 45.0%, $p < .001$). The most common error type at both time delays was loss of content (46.9% for 2-minutes and 44.3% for 15-minutes).

Compared to HC (**Table 3**), PwMS made more errors and were less likely to make no errors at both time delays, which was also observed when only persons with RRMS were examined (**Supplementary Table 1**). While there was an overall difference on the types of errors made with the 2-minute delay (**Figure 2**), none of the pairwise comparisons were significant after the Bonferroni corrections. This overall difference became shy of significance when only persons with RRMS were in the sample (**Supplementary Table 2**). However, there was a significant difference with the 15-minute delay (**Figure 2**), with PwMS making more task substitution errors and fewer loss of time errors. In the RRMS only sub-analysis, the loss of time errors difference was no longer significant (**Supplementary Table 2)**.

Impaired PwMS significantly differed from non-impaired PwMS in terms of the number (**Table 3**) and types of errors (**Figure 2**) made with the 2-minute delay, although none of the pairwise comparisons were significant following the Bonferroni correction. While impaired PwMS made a greater number of errors when there was a 15-minute delay (**Table 3**), there was no difference in the types of errors (**Figure 2**). These observed differences were maintained when only persons with RRMS were analyzed, except for the types of errors made with the 2-minute delay which became shy of significance (**Supplementary Tables 1 & 2**).

Errors by Cue Type

PwMS had a greater number of errors on time-based tasks compared to event-based tasks ($r = .69$, $p < .001$; **Table 3**). Fewer PwMS also made no errors when there were time cues (8.1% vs 40.5%, $p <.001$). Loss of content errors were the most common for both cue types (45.8% for time and 4.4% for event), although task substitutions were frequent for event cues (42.5%).

Compared to HC (**Table 3**), PwMS had a higher number of both time-based and event-based errors. In addition, there were significantly fewer PwMS who made no errors in either cue type. Although there was an overall difference on the types of errors made when there was a time cue (**Figure 3**), none of the post-hoc comparisons were significant after correction. Errors made on event-based tasks, however, did differ significantly, with PwMS making more task substitution errors and fewer loss of time errors (**Figure 3**). None of these results changed when only persons with RRMS were examined (**Supplementary Tables 1 & 2**).

Impaired PwMS made more errors than non-impaired PwMS on both time- and event-based tasks (**Table 3**). There was a significant difference on the types of errors made on time-based tasks, with impaired PwMS making more PM failures, but not on the types of errors made on event-based tasks (**Figure 3**). These observed differences remained the same when only persons with RRMS were included in the sample (**Supplementary Tables 1 & 2**).

Errors by Response Type

The number of errors made by PwMS did not significantly differ by response type (r = .14, p = .145; **Table 3**), nor was there a difference in the percentage who did not make any errors on verbal versus action responses (18.9% vs 15.3%, p = .119). PwMS primarily made loss of content errors on both verbal (51.8%) and action (38.9%) tasks, although task substitutions were also frequent for the latter (31.9%).

Compared to HC (**Table 3**), PwMS made more errors under both response conditions and there was a significantly lower percentage of PwMS who had no errors for either one. While there was an overall difference in the types of errors for verbal responses **(Figure 4**), the post-hoc comparisons were non-significant after correction. There was a significant difference in error type for action responses (**Figure 4**), with PwMS making more task substitution errors. These results did not change in the RRMS only sub-analyses (**Supplementary Tables 1 & 2**).

Impaired PwMS had a greater number of errors on both verbal and action tasks compared to non-impaired PwMS (**Table 3**), but there were no differences in the types of errors made in either condition (**Figure 4**). None of these results changed when only persons with RRMS were examined (**Supplementary Tables 1 & 2**).

Discussion

This is the first study to not only explore the type of PM errors made by PwMS, but also examine whether there are cognitive process failure differences between 1) PwMS and HC and 2) PwMS with and without impairments in processing speed and/or verbal learning and memory. Overall, PM errors were common among PwMS, with 92.7% making at least one error; the average number of errors was three. PwMS tended to make more errors when there was a 15-minute delay or time-based cue, two conditions that have higher cognitive demands (Matos et al., 2020). Loss of content errors were the most frequently made error, which was noted across all conditions. No random errors were made by PwMS, with loss of time errors occurring less than 10% of the time.

As hypothesized, PwMS made more PM errors than HC. In addition, there was a significantly lower percentage of PwMS who made no errors compared to HC across all time delays, cue type, and response type. These findings suggest that PwMS experience a higher rate of cognitive process failures, regardless of the condition in which the PM task is presented. One explanation may be differences in semantic networks between HC and PwMS. It has been proposed that these networks are altered in PwMS, affecting activation of semantic associations when recalling information (Pitteri et al., 2020). Furthermore, PwMS can be more susceptible to both proactive and retroactive semantic interference (Matias-Guiu et al., 2020). These issues may culminate in errors through different stages in the PM model. If there are alterations in the semantic network connectivity affecting how much information is stored (Pitteri et al., 2020), this may affect encoding of how the task will be carried out (first stage) (Carey et al., 2006; Raskin et al., 2010). Reductions in connections affecting retrieval (Pitteri et al., 2020) or interference from competing tasks may cause disruptions in the third stage, where the individual must recognize the cue and correctly pair it with the intention (Carey et al., 2006; Raskin et al., 2010). Slightly less than half of the sample did not have impairments in processing speed and/or verbal learning and memory. It should be noted that issues with PM errors (possibly indicative of semantic network alterations) were noted in PwMS without verbal memory impairments, suggesting that this process may be more subtle than what is measured on traditional neuropsychological assessments (Pitteri et al., 2020). Clinically, this may translate to PwMS reporting problems with everyday tasks but not exhibiting significant impairment on standardized testing. Rather, they may be experiencing a subclinical level of cognitive impairment, evidenced by an elevated number of PM errors in relation to HC.

While both PwMS and HC made loss of content errors the most frequently, differences emerged in the number of task substitution and loss of time errors they made. PwMS made more task substitution errors, specifically when there were 15-minute delays, event cues, and verbal responses. HC, on the other hand, made more loss of time errors, particularly when there were 15-minute delays and event cues. These findings suggest that PwMS and HC have different cognitive process failures during the third stage of PM (Carey et al., 2006; Raskin et al., 2010). PwMS experience more difficulty pairing the correct cue and intention but have fewer issues than HC with recognizing that it is time to respond to the cue. As noted above, alterations in PwMS' semantic networks (Pitteri et al., 2020) and susceptibility to intrusions (Matias-Guiu et al., 2020) could explain why PwMS demonstrated a higher rate of task substitution errors compared to HC. In addition, as new learning can be impaired in PwMS (Chiaravalloti & DeLuca, 2008), PwMS may have greater difficulty processing and properly assigning the correct retrospective component (content) with the prospective component (intention), resulting in the substitution. Furthermore, if their attentional focus is on the time that they need to complete the task, it may have affected their efficiency of encoding the retrospective component information.

While it has been suggested that time-based PM issues in PwMS were due to issues with time monitoring (Raimo et al., 2019), the current results showed that PwMS made *fewer* loss of time errors than HC. In addition, loss of time errors were the least commonly made PM error by PwMS (9.5%), suggesting that time monitoring is not necessarily their primary issue. PwMS still exhibit more problems with time-based PM than HC, with loss of content (45.8%), PM failures (22.5%), and task substitution errors (18.6%) being more common than loss of time errors (13.1%) on these tasks. As to why PwMS made fewer loss of time errors than HC, there are some potential explanations. It is possible that PwMS were paying more attention to the clock, knowing that they would have to provide a response at a certain time even if they could not recall its content. Self-awareness of executive dysfunction has been associated with cognitive abilities in PwMS (Goverover et al., 2005). Theoretically, if a PwMS was aware that they would struggle recalling both the time and intention, they may have focused their efforts on just remembering the time when they needed to respond. However, a stark contrast was noted on event-based tasks (1.8% versus 20.0%), in which a loss of time error was given if a response was not provided within one minute of the cue. While the examinee still needs to keep track of the time in relation to discontinuing the distractor task and engaging in the intended task, loss of time errors on event-based tasks may be less suggestive of a time monitoring issue and more so a delayed recall response. When taking a closer look at the specific event-based tasks where HC made errors, 71.4% of them were made on Trials 5 and 6, which both had a 15-minute delay and examinees had been given instructions for seven out of the eight tasks. This may suggest that these HC needed additional time to correctly connect the intention with the cue when there was a longer delay and larger cognitive load. Similar to other 15-minute delay tasks, PwMS had a higher number of task substitution errors compared to HC (40.0% versus 5.9%) on these two trials, suggesting that they quickly respond, knowing they have been cued for a task, but they could not correctly connect the intention with that cue.

Across all conditions, PwMS with impaired processing speed and/or verbal learning and memory made more PM errors than PwMS without those cognitive deficits. They exhibited more prospective memory failures (i.e., no response), particularly on tasks where there was a time-based cue. This suggests that when PwMS have slowed processing speed and/or difficulty encoding new information, they experience a breakdown during the initial formation of the intention (first stage) (Raskin et al., 2010). This issue becomes more evident when there is not an external cue, like an event, and the individual must track both the time and content of the task, thus increasing the cognitive demands. Notably, both groups had similar amounts of task substitution errors across all conditions, suggesting that deficits in processing speed, learning, and memory alone do not account for these types of errors. Task substitutions have been attributed to issues with prefrontal executive control (Raskin et al., 2010), and executive dysfunction was not measured as part of this study. As such, further examination of PM errors with a larger neuropsychological assessment battery is needed to fully understand the underlying cognitive processes contributing to these errors, as well as identify PwMS with cognitive impairments not captured by the two measures used, which can then be used to inform interventional approaches for addressing PM issues in PwMS.

Given its functional implications for PwMS (Bruce et al., 2010; Gromisch, Raskin, et al., 2023; Gromisch, Turner, et al., 2023; Honan et al., 2015; Weber et al., 2019), there is a need to recognize and address PM in clinical practice. Even when an individual does not reach the threshold for cognitive impairment, they still may be making occasional PM errors that may manifest as forgetting to take one's medication or mail a bill one time or two times, which can be distressing. As such, if a PwMS endorses cognitive-related functional issues but their performance does not reach the level of clinical impairment, clinicians may explore the types of errors they are making, which can help inform compensatory strategy recommendations. Given that recalling the correct content is an underlying issue for PwMS who do and do not reach that threshold, strategies that assist with retrospective recall may be considered, such as diaries and planners. While there is limited information on interventional approaches for PwMS (Rouleau et al., 2018), there is emerging evidence supporting the implementation of intentions technique in PwMS (Kardiasmenos et al., 2008), which involves establishing cues for the task using 'if' 'then' statements along with visualization. This strategy has been beneficial for improving PM in other populations, such as traumatic brain injury, mild Alzheimer's disease, and HIV (Pennar et al., 2018; Raskin et al., 2019; Shelton et al., 2016).

When interpreting the findings of this study, a number of limitations need to be considered. In addition to the lack of executive functioning measures in the battery used to classify PwMS as impaired/non-impaired, the low number of errors in certain conditions may have affected detection of certain differences. For example, although more than 24% of impaired PwMS made PM failures on the 2-minute delay tasks compared to 8.8% of non-impaired PwMS, this difference was non-significant. For the MIST subscales, there are only four tasks, resulting in a limited number of errors that can be made and thus examined. It should also be noted that because of the low number of potential errors, small differences may result in a significant skew and the results may not be generalizable to the larger population. This may be addressed in future studies with the inclusion of additional PM tasks, which would not only provide more confidence that differences in error frequencies occur between PwMS and HC but could allow for an examination of whether there is a threshold of PM errors made and evidence of real-world functional difficulties. A larger, more diverse sample size is also needed to better understand how PM errors differ by MS subtype. Although most results did not change when only persons with RRMS were examined, the number of persons with progressive forms of the disease was not large enough to compare the different subgroups. Cognitive impairment is frequently seen in progressive MS (Wachowius et al., 2005), underscoring the need to examine PM in these disease types.

Greater diversity should be considered as the homogeneity of the sample precluded examination of cultural differences that may have influenced performance and need to be considered by clinicians when addressing PM issues. Although HC did not differ from PwMS in terms of age and education, there was a discrepancy in terms of gender. While the MS sample's gender distribution is congruent with the larger MS population (The Multiple Sclerosis International Federation (MSIF), 2020), men with MS can present with more cognitive impairment than women (Benedict & Zivadinov, 2011). Besides matching on gender, future analyses may stratify PwMS and HC by age group to examine whether PM error patterns differ in younger versus older adults, and if factors like disease duration contribute to the number of errors being made. Finally, the MIST in the PwMS and HC groups were administered by different examiners, so there is the possibility of disagreements in the error code assignment. That said, the MIST has good inter-rater reliability for error coding, with the intraclass correlations ranging from 0.81 to 0.96, with 100% agreement on Trial 7 (Raskin et al., 2010).

Overall, PM errors are common among PwMS, even in the absence of processing speed and/or verbal learning and memory deficits. PwMS tend to make more errors when there are longer delays and time-based cues, with loss of content errors being the most frequently made error. PwMS have a higher rate of PM errors than HC, with PwMS making more task substitution errors and fewer loss of time errors. Impaired PwMS made more errors than non-impaired PwMS, exhibiting more prospective memory failures during time-based tasks. These findings highlight the different cognitive process failures that result in PM issues among PwMS and HC.

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The views and opinions expressed in this article reflect those of the authors and do not necessarily reflect those of the United States Department of Veterans Affairs.

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Declaration of Interest

Dr. Sarah Raskin is the developer of the MIST. The authors have no other competing interests to declare.

References

Benedict, R. H., DeLuca, J., Phillips, G., LaRocca, N., Hudson, L. D., Rudick, R., & Consortium, M. S. O. A. (2017). Validity of the Symbol Digit Modalities Test as a cognition performance outcome measure for multiple sclerosis. *Mult Scler*, *23*(5), 721-733.

Benedict, R. H., & Zivadinov, R. (2011). Risk factors for and management of cognitive dysfunction in multiple sclerosis. *Nature Reviews Neurology*, *7*(6), 332-342.

Bruce, J. M., Hancock, L. M., Arnett, P., & Lynch, S. (2010). Treatment adherence in multiple sclerosis: association with emotional status, personality, and cognition. *Journal of behavioral medicine*, *33*(3), 219-227.

Carey, C. L., Paul Woods, S., Rippeth, J. D., Heaton, R. K., Grant, I., & Group, H. N. R. C. (2006). Prospective memory in HIV-1 infection. *Journal of clinical and experimental neuropsychology, 28*(4), 536-548.

Chiaravalloti, N. D., & DeLuca, J. (2008). Cognitive impairment in multiple sclerosis. *The Lancet Neurology, 7*(12), 1139-1151.

Clemens, L., & Langdon, D. (2018). How does cognition relate to employment in multiple sclerosis? A systematic review. *Multiple sclerosis and related disorders, 26*, 183-191.

Cohen, A.-L., & Hicks, J. L. (2017). *Prospective memory: Remembering to remember, remembering to forget*. Springer.

Crystal, J. D., & Wilson, A. G. (2015). Prospective memory: a comparative perspective. *Behavioural processes, 112*, 88-99.

Dagenais, E., Rouleau, I., Tremblay, A., Demers, M., Roger, É., Jobin, C., & Duquette, P. (2016). Role of executive functions in prospective memory in multiple sclerosis: Impact of the strength of cue–action association. *Journal of clinical and experimental neuropsychology, 38*(1), 127-140.

Goverover, Y., Chiaravalloti, N., & DeLuca, J. (2005). The relationship between self-awareness of neurobehavioral symptoms, cognitive functioning, and emotional symptoms in multiple sclerosis. *Multiple Sclerosis Journal, 11*(2), 203-212.

Gromisch, E. S., Raskin, S. A., Neto, L. O., Haselkorn, J. K., & Turner, A. P. (2023). Appointment attendance behaviors in multiple sclerosis: Understanding the factors that differ between no shows, short notice cancellations, and attended appointments. *Multiple sclerosis and related disorders, 70*, 104509.

Gromisch, E. S., Turner, A. P., Neto, L. O., Haselkorn, J. K., & Raskin, S. A. (2023). Identifying prospective memory deficits in multiple sclerosis: Preliminary evaluation of the criterion and ecological validity of a single item version of the memory for intentions test (MIST). *The Clinical Neuropsychologist, 37*(2), 371-386.

Hohol, M., Orav, E., & Weiner, H. (1995). Disease Steps in multiple sclerosis A simple approach to evaluate disease progression. *Neurology, 45*(2), 251-255.

Hohol, M., Orav, E., & Weiner, H. (1999). Disease steps in multiple sclerosis: a longitudinal study comparing disease steps and EDSS to evaluate disease progression. *Mult Scler, 5*(5), 349-354.

Honan, C. A., Brown, R. F., & Batchelor, J. (2015). Perceived cognitive difficulties and cognitive test performance as predictors of employment outcomes in people with multiple sclerosis. *Journal of the International Neuropsychological Society: JINS, 21*(2), 156.

Kalmar, J. H., Gaudino, E. A., Moore, N. B., Halper, J., & DeLuca, J. (2008). The relationship between cognitive deficits and everyday functional activities in multiple sclerosis. *Neuropsychology, 22*(4), 442.

Kardiasmenos, K. S., Clawson, D. M., Wilken, J. A., & Wallin, M. T. (2008). Prospective memory and the efficacy of a memory strategy in multiple sclerosis. *Neuropsychology, 22*(6), 746.

Learmonth, Y. C., Motl, R. W., Sandroff, B. M., Pula, J. H., & Cadavid, D. (2013). Validation of patient determined disease steps (PDDS) scale scores in persons with multiple sclerosis. *BMC Neurol, 13*(1), 37.

Marrie, R. A., & Goldman, M. (2007). Validity of performance scales for disability assessment in multiple sclerosis. *Mult Scler, 13*(9), 1176-1182.

Matias-Guiu, J. A., Cortés-Martínez, A., Curiel, R. E., Delgado-Álvarez, A., Fernández-Oliveira, A., Pytel, V., Montero, P., Moreno-Ramos, T., Loewenstein, D. A., & Matías-Guiu, J. (2020). Memory impairment in relapsing-remitting multiple sclerosis using a challenging semantic interference task. *Frontiers in neurology, 11*, 309.

Matos, P., Pereira, D. R., Albuquerque, P. B., & Santos, F. H. (2020). How does performing demanding activities influence prospective memory? A systematic review. *Advances in Cognitive Psychology, 16*(3), 268.

Miller, A. K., Basso, M. R., Candilis, P. J., Combs, D. R., & Woods, S. P. (2014). Pain is associated with prospective memory dysfunction in multiple sclerosis. *Journal of clinical and experimental neuropsychology, 36*(8), 887-896.

Oates, J. M., & Peynircioglu, 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.

Parmenter, B. A., Testa, S. M., Schretlen, D. J., Weinstock-Guttman, B., & Benedict, R. H. (2010). The utility of regression-based norms in interpreting the minimal assessment of cognitive function in multiple sclerosis (MACFIMS). *Journal of the International Neuropsychological Society, 16*(1), 6-16.

Pennar, A., Naar, S., Woods, S., Nichols, S., Outlaw, A., & Ellis, D. (2018). Promoting resilience through neurocognitive functioning in youth living with HIV. *AIDS care*, *30*(sup4), 59-64.

Pitteri, M., Galazzo, I. B., Brusini, L., Cruciani, F., Dapor, C., Marastoni, D., Menegaz, G., & Calabrese, M. (2021). Microstructural MRI correlates of cognitive impairment in multiple sclerosis: The role of deep gray matter. *Diagnostics*, *11*(6), 1103.

Pitteri, M., Vannucci, M., Ziccardi, S., Beccherle, M., Semenza, C., & Calabrese, M. (2020). False memories in relapsing remitting multiple sclerosis patients: A preliminary investigation with the DRM paradigm. *Multiple sclerosis and related disorders, 37*, 101418.

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.

Raskin, S. A., Buckheit, C., & Sherrod, C. (2010). Memory for intentions screening test: Manual. *Psychological Assessment Resources, Inc., Lutz, FL*.

Raskin, S. A., Smith, M. P., Mills, G., Pedro, C., & Zamroziewicz, M. (2019). Prospective memory intervention using visual imagery in individuals with brain injury. *Neuropsychological rehabilitation, 29*(2), 289-304.

Raskin, S. A., Woods, S. P., Poquette, A. J., McTaggart, A. B., Sethna, J., Williams, R. C., & Tröster, A. I. (2011). A differential deficit in time-versus event-based prospective memory in Parkinson's disease. *Neuropsychology, 25*(2), 201.

Rendell, P. G., Henry, J. D., Phillips, L. H., De la Piedad Garcia, X., Booth, P., Phillips, P., & Kliegel, M. (2012). Prospective memory, emotional valence, and multiple sclerosis. *Journal of clinical and experimental neuropsychology, 34*(7), 738-749.

Rendell, P. G., Jensen, F., & Henry, J. D. (2007). Prospective memory in multiple sclerosis. *Journal of the International Neuropsychological Society: JINS, 13*(3), 410.

Rouleau, I., Dagenais, E., Tremblay, A., Demers, M., Roger, É., Jobin, C., & Duquette, P. (2018). Prospective memory impairment in multiple sclerosis: a review. *The Clinical Neuropsychologist, 32*(5), 922-936.

Sandry, J., Simonet, D. V., Brandstadter, R., Krieger, S., Sand, I. K., Graney, R. A., Buchanan, A. V., Lall, S., & Sumowski, J. F. (2021). The Symbol Digit Modalities Test (SDMT) is sensitive but non-specific in MS: Lexical access speed, memory, and information processing speed independently contribute to SDMT performance. *Multiple sclerosis and related disorders, 51*, 102950.

Schmidt, M. (1996). *Rey auditory verbal learning test: A handbook*. Western Psychological Services Los Angeles, CA.

Shelton, J. T., Lee, J. H., Scullin, M. K., Rose, N. S., Rendell, P. G., & McDaniel, M. A. (2016). Improving prospective memory in healthy older adults and individuals with very mild Alzheimer's disease. *Journal of the American Geriatrics Society, 64*(6), 1307-1312.

Smith, A. (1982). *Symbol digit modalities test: Manual*. Western Psychological Services.

Spain, R. I., Hildebrand, A., Waslo, C. S., Rooney, W. D., Schwartz, D. L., Paz Soldan, M. M., Gross, R. H., & Turner, A. P. (2023). Processing speed and memory test performance are associated with different brain region volumes in Veterans and others with progressive multiple sclerosis. *Frontiers in neurology, 14*, 1188124.

Strauss, E., Sherman, E. M. S., & Spreen, O. (2006). *Compendium of neuropsychological tests: Administration, norms, and commentary*. Oxford University Press.

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*.

The Multiple Sclerosis International Federation (MSIF). (2020). *Part 1: Mapping multiple sclerosis around the world, key epidemiology findings* (Atlas of MS, Issue. https://www.msif.org/wp-content/uploads/2020/09/Atlas-Epidemiology-report-Sept-2020-Final-EN.pdf

Thompson, A. J., Banwell, B. L., Barkhof, F., Carroll, W. M., Coetzee, T., Comi, G., Correale, J., Fazekas, F., Filippi, M., & Freedman, M. S. (2018). Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *The Lancet Neurology, 17*(2), 162-173.

Wachowius, U., Talley, M., Silver, N., Heinze, H.-J., & Sailer, M. (2005). Cognitive impairment in primary and secondary progressive multiple sclerosis. *Journal of clinical and experimental neuropsychology*, *27*(1), 65-77.

Wallin, M. T., Culpepper, W. J., Campbell, J. D., Nelson, L. M., Langer-Gould, A., Marrie, R. A., Cutter, G. R., Kaye, W. E., Wagner, L., & Tremlett, H. (2019). The prevalence of MS in the United States: A population-based estimate using health claims data. *Neurology*, 10.1212/WNL. 0000000000007035.

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: JINS*, *25*(10), 1035-1043.

Tables

Table 1

Different Types of Prospective Memory Errors, Their Corresponding Process Failure, and Real-World Examples

Error Type	Description	Process Failure[1]	Time-Based Example	Event-Based Example
Prospective memory failure	The individual has had a complete failure, in which no response or recognition of the need for a response is given.	Prospective memory	*Task*: “Take your medication at 2 pm.” *Response*: None	*Task:* “Take your medication when lunch is served.” *Response:* None
Task substitution	While the individual responds at the correct time, the content of the task has been switched with another one.	Prefrontal executive control	*Task:* “Take your medication at 2 pm.” *Response:* Pays phone bill at 2 pm.	*Task:* “Take your medication when lunch is served.” *Response:* Checks voicemail when lunch is served.
Loss of content	The individual recognizes that they had a task to complete but cannot remember what they were supposed to do.	Retrospective memory	*Task:* “Take your medication at 2 pm” *Response:* “I know I’m supposed to be doing something at 2 pm, but I can’t remember what.”	*Task:* “Take your medication when lunch is served.” *Response:* “I know I’m supposed to be doing something when lunch is served, but I can’t remember what.”
Loss of time	The individual recalls the correct content of the task but performs it at the incorrect time (± 1 minute window for both time- and event-based tasks).	Time monitoring	*Task:* “Take your medication at 2 pm.” *Response:* Takes medication at 10 am.	*Task:* “Take your medication when lunch is served.” *Response:* Takes medication when dinner is served.
Random error	The individual provides a random response at a random time.	Unclear	*Task:* “Take your medication at 2 pm.” *Response:* Calls doctor at 11 am.	*Task:* “Take your medication when lunch is served.” *Response:* Pays phone bill at 10 am.

[1] Adapted from (Raskin et al., 2010)

Table 2
Demographics of PwMS and HC

Variable	PwMS (*n* = 111)	HC (*n* = 75)	p-value
Age (years)	51.12 (12.25)	53.32 (17.65)	.350
Education (years)[a]	15.23 (2.30)	15.09 (2.62)	.721
Gender (% Women)	73.9%	56.0%	.011
Race (% White non-Hispanic)[b]	82.9%	78.7%	.663
MS Type			--
Relapsing Remitting	80.2%	--	
Secondary Progressive	10.8%	--	
Primary Progressive	8.1%	--	
Unsure	0.9%	--	
MS Duration (years)	14.50 (9.30)	--	--
Median PDDS	2 (moderate disability)	--	--

Mean (SD) reported unless otherwise specified
HC: healthy controls; MS: multiple sclerosis; PDDS: Patient Determined Disease Steps; PwMS: persons with MS
[a] *n* = 9 missing in HC group
[b] *n* = 8 missing in HC group

Table 3
Comparison of PM Errors Made on the MIST by PwMS and HC

		PwMS				
Error Data	**HC (*n* = 75)**	**Whole Sample (*n* = 111)**	**Impaired (*n* = 57)**	**Non-Impaired (*n* = 54)**	**All PwMS vs. HC**	**Impaired vs. Non-Impaired PwMS**
Overall MIST						
Number of Errors Made	1 (1)	3 (2)	4 (2)	2 (2.25)	$r = .43$, $p < .001$	$r = .34$, $p < .001$
No Errors Made (%)	24.0%	7.2%			$V = .24$, $p = .001$	
2-Minute Time Delay subscale						
Number of Errors Made	0 (0)	1 (1)	1 (2)	0 (1)	$r = .32$, $p < .001$	$r = .26$, $p = .006$
No Errors Made (%)	78.7%	45.0%			$V = .34$, $p < .001$	
15-Minute Time Delay subscale						
Number of Errors Made	1 (2)	2 (2)	3 (1)	2 (2)	$r = .42$, $p < .001$	$r = .30$, $p = .002$
No Errors Made (%)	26.7%	8.1%			$V = .25$, $p = .001$	
Time Cue subscale						
Number of Errors Made	1 (2)	2 (2)	2 (1)	2 (2)	$r = .41$, $p < .001$	$r = .29$, $p = .003$
No Errors Made (%)	26.7%	8.1%			$V = .25$, $p = .001$	
Event Cue subscale						
Number of Errors Made	0 (0)	1 (2)	1 (2)	0 (1)	$r = .35$, $p < .001$	$r = .31$, $p = .001$
No Errors Made (%)	78.7%	40.5%			$V = .38$, $p < .001$	
Verbal Response subscale						
Number of Errors Made	1 (1)	1 (1)	2 (1)	1 (2)	$r = .33$, $p < .001$	$r = .29$, $p = .002$
No Errors Made (%)	45.3%	18.9%			$V = .28$, $p < .001$	
Action Response subscale						
Number of Errors Made	1 (1)	2 (1)	2 (2)	1 (2)	$r = .40$, $p < .001$	$r = .28$, $p = .004$
No Errors Made (%)	42.7%	15.3%			$V = .31$, $p < .001$	

Median (interquartile range) reported unless otherwise specified
HC: healthy controls; MIST: Memory for Intentions Test; PwMS: persons with multiple sclerosis

Figure Legends

Figure 1

Types of Errors Made on the Overall MIST by PwMS and HC

Note: PwMS vs HC: $V = .26$, $p < .001$; Impaired vs Non-Impaired PwMS: $V = .19$, $p = .006$

$^{*}p < .005$, $^{**}p < .001$

HC; healthy controls; LC: loss of content; LT: loss of time; MIST: Memory for Intentions Test; PMF: prospective memory failure; PwMS: persons with multiple sclerosis; RE: random error; TS: task substitution

Figure 2

Types of Errors Made on Different Time Delays (2-Minute and 15-Minute) on the MIST by PwMS and HC

Note: PwMS vs HC on 2-minute delay: $V = .25$, $p = .032$; Impaired vs Non-Impaired PwMS on 2-minute delay: $V = .28$, $p = .045$; PwMS vs HC on 15-minute delay: $V = .26$, $p < .001$; Impaired vs Non-Impaired PwMS on 15-minute delay: $V = .17$, $p = .061$

$^{*}p < .005$, $^{**}p < .001$

HC; healthy controls; LC: loss of content; LT: loss of time; MIST: Memory for Intentions Test; PMF: prospective memory failure; PwMS: persons with multiple sclerosis; RE: random error; TS: task substitution

Figure 3

Types of Errors Made on Different Cue Types (Time and Event) on the MIST by PwMS and HC

Note: PwMS vs HC on time cue: $V = .20$, $p = .018$; Impaired vs Non-Impaired PwMS on time cue: $V = .21$, $p = .017$; PwMS vs HC on event cue: $V = .44$, $p < .001$; Impaired vs Non-Impaired PwMS on event cue: $V = .17$, $p = .334$

$^{*}p < .005$, $^{**}p < .001$

HC; healthy controls; LC: loss of content; LT: loss of time; MIST: Memory for Intentions Test; PMF: prospective memory failure; PwMS: persons with multiple sclerosis; RE: random error; TS: task substitution

Figure 4

Types of Errors Made on Different Response Types (Verbal and Action) on the MIST by PwMS and HC

Note: PwMS vs HC on verbal response: $V = .24$, $p = .015$; Impaired vs Non-Impaired PwMS on verbal response: $V = .22$, $p = .053$; PwMS vs HC on action response: $V = .30$, $p < .001$; Impaired vs Non-Impaired PwMS on action response: $V = .18$, $p = .111$

**p <.001

HC; healthy controls; LC: loss of content; LT: loss of time; MIST: Memory for Intentions Test; PMF: prospective memory failure; PwMS: persons with multiple sclerosis; RE: random error; TS: task substitution

Supplementary Table 1

Comparison of PM Errors Made on the MIST by PwMS (RRMS Only) and HC

Error Data	HC (n = 75)	PwMS (RRMS Only) Whole Sample (n = 89)	Impaired (n = 46)	Non-Impaired (n = 43)	All PwMS vs. HC	Impaired vs. Non-Impaired PwMS
Overall MIST						
Number of Errors Made	1 (1)	3 (2)	4 (2.25)	2 (2)	$r = .42$, $p < .001$	$r = .40$, $p < .001$
No Errors Made (%)	24.0%	6.7%			$V = .24$, $p = .002$	
2-Minute Time Delay subscale						
Number of Errors Made	0 (0)	1 (2)	1 (2)	0 (1)	$r = .34$, $p < .001$	$r = .28$, $p = .007$
No Errors Made (%)	78.7%	43.8%			$V = .35$, $p < .001$	
15-Minute Time Delay subscale						
Number of Errors Made	1 (2)	2 (2)	3 (1)	2 (1)	$r = .40$, $p < .001$	$r = .36$, $p = .001$
No Errors Made (%)	26.7%	7.9%			$V = .25$, $p = .001$	
Time Cue subscale						
Number of Errors Made	1 (2)	2 (2)	2 (1)	2 (2)	$r = .42$, $p < .001$	$r = .30$, $p = .004$
No Errors Made (%)	26.7%	7.9%			$V = .25$, $p = .001$	
Event Cue subscale						
Number of Errors Made	0 (0)	1 (2)	1 (2)	0 (1)	$r = .33$, $p < .001$	$r = .39$, $p < .001$
No Errors Made (%)	78.7%	43.8%			$V = .35$, $p < .001$	
Verbal Response subscale						
Number of Errors Made	1 (1)	1 (1)	2 (2)	1 (2)	$r = .35$, $p < .001$	$r = .30$, $p = .004$
No Errors Made (%)	45.3%	20.2%			$V = .27$, $p = .001$	
Action Response subscale						
Number of Errors Made	1 (1)	2 (1)	2 (2)	1 (2)	$r = .38$, $p < .001$	$r = .37$, $p < .001$
No Errors Made (%)	42.7%	15.7%			$V = .30$, $p < .001$	

Median (interquartile range) reported unless otherwise specified

HC: healthy controls; MIST: Memory for Intentions Test; PwMS: persons with multiple sclerosis; RRMS: relapsing remitting multiple sclerosis

Supplementary Table 2

Types of PM Errors Made on the MIST by PwMS (RRMS Only) and HC

		PwMS (RRMS Only)		
Error Types	**HC (*n* = 75)**	**Whole Sample (*n* = 89)**	**Impaired (*n* = 46)**	**Non-Impaired (*n* = 43)**
		***Overall MIST*[1]**		
PM Failure	20.3%	20.2%	26.0%*	10.6%
Task Substitution	7.6%	26.7%**	26.6%	26.9%
Loss of Content	49.2%	43.3%	38.2%	51.9%
Loss of Time	21.2%	9.7%*	9.2%	10.6%
Random Error	1.7%	0.0%	0.0%	0.0%
		***2-Minute Time Delay subscale*[2]**		
PM Failure	29.6%	20.7%	25.9%	10.7%
Task Substitution	7.4%	26.8%	31.5%	17.9%
Loss of Content	48.1%	47.6%	37.0%	67.9%
Loss of Time	14.8%	4.9%	5.6%	3.6%
		***15-Minute Time Delay subscale*[3]**		
PM Failure	17.6%	20.0%	26.1%	10.5%
Task Substitution	7.7%	26.7%**	30.3%	24.4%
Loss of Content	49.5%	41.5%	38.7%	46.1%
Loss of Time	23.1%	11.8%	10.9%	13.2%
Random Error	2.2%	0.0%	0.0%	0.0%
		***Time Cue subscale*[4]**		
PM Failure	19.3%	22.3%	30.6%*	11.0%
Task Substitution	9.1%	19.7%	18.0%	22.0%
Loss of Content	47.7%	44.6%	37.8%	53.7%
Loss of Time	21.6%	13.5%	13.5%	13.4%
Random Error	2.3%	0.0%	0.0%	0.0%
		***Event Cue subscale*[5]**		
PM Failure	23.3%	15.5%	17.7%	9.1%
Task Substitution	3.3%	42.9%**	41.9%	45.5%
Loss of Content	53.3%	40.5%	38.7%	45.5%
Loss of Time	20.0%	1.2%**	1.6%	0.0%
		***Verbal Response subscale*[6]**		
PM Failure	20.7%	16.8%	22.6%	7.5%
Task Substitution	10.3%	20.4%	20.2%	20.8%
Loss of Content	43.1%	51.8%	45.2%	62.3%
Loss of Time	22.4%	10.9%	11.9%	9.4%
Random Error	3.4%	0.0%	0.0%	0.0%
		***Action Response subscale*[7]**		
PM Failure	20.0%	23.6%	29.2%	13.7%
Task Substitution	5.0%	32.9%	32.6%	33.3%
Loss of Content	55.0%	35.0%	31.5%	41.2%
Loss of Time	20.0%	8.6%**	6.7%	11.8%

[1] *PwMS vs HC:* $V = .26$, $p < .001$; *Impaired vs Non-Impaired PwMS:* $V = .20$, $p = .014$

[2] *PwMS vs HC:* $V = .25$, $p = .056$; *Impaired vs Non-Impaired PwMS:* $V = .30$, $p = .066$

[3] *PwMS vs HC:* $V = .27$, $p < .001$; *Impaired vs Non-Impaired PwMS:* $V = .19$, $p = .072$

[4] *PwMS vs HC:* $V = .20$, $p = .022$; *Impaired vs Non-Impaired PwMS:* $V = .24$, $p = .011$

[5] *PwMS vs HC:* $V = .47$, $p < .001$; *Impaired vs Non-Impaired PwMS:* $V = .13$, $p = .785$
[6] *PwMS vs HC:* $V = .25$, $p = .021$; *Impaired vs Non-Impaired PwMS:* $V = .22$, $p = .085$
[7] *PwMS vs HC:* $V = .33$, $p < .001$; *Impaired vs Non-Impaired PwMS:* $V = .19$, $p = .162$
* $p < .005$, ** $p < .001$

HC: healthy controls; MIST: Memory for Intentions Test; PM: prospective memory PwMS: persons with multiple sclerosis; RRMS: relapsing remitting multiple sclerosis