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Abstract

Prospective memory deficits are common after brain injury and can create impediments to independent living. Most approaches to management of prospective memory deficits are compensatory, such as the use of notebooks or electronic devices. While these can be effective, a restorative approach, in theory, could lead to greater generalization of treatment. In the current study a metacognitive technique, using visual imagery, was employed. This was employed under conditions of rote repetition and spaced retrieval. Treatment was provided in an AB-BA crossover design with A as the active treatment and B as a no-treatment attention control to twenty individuals with brain injury. A group of 20 healthy participants served to control for effects of re-testing. Individuals with brain injury demonstrated improvement on the main outcome measure of prospective memory, the Memory for Intentions Screening Test, only after the active treatment condition. In addition, some generalization of treatment was measured in daily life. Moreover, treatment gains were maintained for one year after treatment was completed.

Keywords: Traumatic brain injury, cognitive rehabilitation, prospective memory

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Introduction

The ability to complete intended actions, prospective memory, is critical for independent functioning. Successful performance is essential for managing in vocational, home and community settings. Many activities of daily living (e.g., taking medications, attending appointments, purchasing food) depend upon intact prospective memory. Survivors of brain injury (BI) report failures relating to prospective memory (PM) (e.g., I forget to take my medicine) as their most frequent memory problem (Kliegel, Jager, Altgassen, & Shum, 2008; Mateer, Sohlberg, & Crinean, 1987). In fact, they perceive prospective memory deficits as more important to their daily lives than their significant others do (Huang, Fleming, Pomery, Chan, & Shum, 2014). However, in spite of the importance of PM in everyday functioning and findings of deficits after brain injury or illness, there have been relatively few studies investigating the treatment of prospective memory deficits (e.g., Knight, Harnett, & Titov, 2005; Raskin & Sohlberg, 2009).

In everyday life, successful PM performance depends on many factors, including the ability to pay attention, to maintain the intention in working memory, to call the intention to mind at the appropriate time and to recall the content of the intention (Groot, Wilson, Evans, & Watson, 2002). In addition, metacognitive abilities such as monitoring ongoing performance, evaluation of outcome, and awareness of PM limitations are required (Guynn, 2003). In any one individual, more than one of these underlying abilities may be affected. Thus, rehabilitation efforts may need to be multifaceted, taking into account the different underlying reasons for failure at PM tasks in each individual in what has been referred to as precision medicine.

Cognitive rehabilitation approaches traditionally group cognitive rehabilitation therapy (CRT) into interventions that are considered compensatory and those that are considered restorative approaches (Sohlberg, 2006). It could be argued that metacognition or self-regulation interventions constitute a third category (Kennedy et al., 2007). An example of a metacognitive approach would be training people in the use of strategies or systems that facilitate self-monitoring during PM task completion (Levine et al., 1998). All three of these rehabilitation approaches have been evaluated for their potential to address deficits in PM functioning.

Compensatory Approaches

The most commonly used compensatory technique for PM deficits is the use of diaries or notebooks (Sohlberg, 2005). For comprehensive discussions of the use of memory notebooks and the importance of training individuals to use them effectively, see Sohlberg and Mateer (2001) as well as McKerracher, Powell, and Oyebode (2005). There are several difficulties with the use of notebooks. These include the need for extensive training in their use, the need to have a system to keep them from becoming misplaced, and the need to have a PM span of at least five minutes to use them effectively (Raskin & Sohlberg, 2009). In a randomized controlled trial, a number of compensatory aids were used for veterans with mild brain injury in a treatment referred to as Cognitive Symptom Management and Rehabilitation Therapy (CogSMART). Cognitive rehabilitation therapy targeted not just PM but also attention and vigilance; learning and memory; and executive functioning. After 12 weeks PM was the only function that showed significant improvement (Twamley, Jak, Delis, Bondi & Lohr, 2014) and this improvement in PM functioning was maintained after one year (Twamley et al.,2015).

A number of electronic aids have also been evaluated to assist with PM deficits. The strongest evidence supporting the use of PM task prompting comes from a randomized, controlled trial evaluating the use of alphanumeric pagers to prompt certain simple routing behaviors (Wilson et al., 2001). When prompted with these pagers, individuals increased completion of daily tasks from approximately 47% to 75% follow through (Emslie, Wilson, Quirk, Evans, & Watson, 2007; Wilson, Emslie, Quirk & Evans, 2001; Wilson, Emslie, Quirk, Evans & Watson, 2001; Wilson, Scott, Evans, Emslie, 2003). Moreover, some patients were able to remember daily activities even after the pager was removed, suggesting an internalization of the external prompt.

Similar electronic systems have been employed to call individuals' mobile phones, such as Postie (Kirsch, et al., 2004) the Yahoo-Calendar System (O'Connell, Mateer, & Kerns, 2003) and Mobile Extensible Memory and Orientation System (MEMOS; Thone-Otto & Walther, 2003) and this prompting technology has shown its utility in improving PM functioning (Van den Broek, Downes, Johnson, Dayus, & Hilton, 2000; Wade & Troy, 2001; Yasuda, Misu, Beckman, Watanabe, Ozawa, & Nakamura, 2002). However, these studies have been single case studies with no experimental control, so it is difficult to generalize from the results.

Current research demonstrates the promise of assistive technologies to help people with PM impairments (Gillette & DePompei, 2008; Kirsch et al., 2004; Wong, Sinclair, Seabrook, McKay & Ponsford, 2016). However, high tech devices are still not widely used by many people with brain injuries who demonstrate deficits in PM (Evald, 2015;Evans, Wilson, Needham, & Brentnall, 2003). Identified barriers for long term use include problems with a range of device characteristics, such as being overly complex or having inaccessible interfaces (LoPresti, Mihailidis, & Kirsch, 2004; Stock, Davies & Gillespie, 2013), lack of training in their use (Wong, Sinclair, Seabrook, McKay & Ponsford, 2016) and especially cost, and fears of losing the device (Evald, 2015). This digital divide between those with access to mobile devices and those without (Gonzales, 2016) is seen in the brain injury community (e.g., Bryan, Carey, & Friedman, 2007; Newman, Browne-Yung, Raghavendra, Wood, & Grace, 2016). For a discussion of why technologies are used or not used see Scherer and Federici (2015). Thus, non technological approaches are still needed.

Restorative Approaches

A restorative approach has the potential of improving functions in all aspects of a person's life, not just those directly trained. The theoretical basis of restorative approaches derives from studies of repetitive activity, which appear to facilitate neuroplasticity. That is, repeated use of a particular cognitive process should strengthen connections in the underlying neural circuitry and lead to an increase in the ability to perform that task (Kolb, Cioe, & Williams, 2011).

Sohlberg, White, Evans, & Mateer (1992) reported on a case study of PM restoration with a person with BI. Using a within-participant repeated measures design they implemented repetitive practice, carrying out target tasks at increasingly longer time intervals. Measurement using probes to evaluate generalization revealed a steady increase in the person's PM span. However, the training and generalization data were somewhat ambiguous, as improvement occurred in both the experimental and control conditions. In a study by Raskin and Sohlberg (1996), participants with traumatic BI were required to execute actions at future designated times. As participants became more proficient, the length of time between task assignment and task execution was systematically increased (similar to spaced retrieval approaches). Results supported the ability to increase participants' PM span. Participants improved on both naturalistic probes (e.g. laboratory tasks that simulated real-world tasks, such as "When this session is over, please remind me to call your physician") and performance in daily life

A similar spaced-retrieval approach was used in a study of individuals with cognitive impairments secondary to schizophrenia (Kurtz, Moberg, Mozley, Swanson, Gur, & Gur, 2001). These data are somewhat difficult to interpret as all participants received both attention training and PM training, so the individual effects of each type of training could not be determined. Additionally, in a study of individuals with Parkinson's disease, training in set-shifting, another metacognitive approach, resulted in improved PM performance such that the group that underwent the experimental treatment improved significantly from pre-treatment to post-treatment; however, this was not true for the placebo group (Costa, Carlesima, & Caltagirone, 2012).

Metacognitive Approaches

In a comprehensive review of the literature on executive function treatment, Kennedy et al. (2007) found substantial evidence from 11 intervention studies that training individuals with BI to use metacognitive regulation strategies improved problem solving, planning, and organization necessary for carrying out goal directed activity. An example of a metacognitive intervention pertinent to managing PM impairment is to provide individuals with reminders to self -regulate that can later be faded. Manly et al. (2001) presented participants with BI audible tones to cue them *to do the next task* in a series of 6 “hotel” tasks that were multifaceted and complex. Fish et al. (2007) also performed a study evaluating an alerting strategy. Individuals with BI were sent a text message of “stop” at varying points during the day. The message carried no content information and was not sent at the time that the activity (calling a voicemail service) needed to be performed. Nevertheless, the authors reported improvement in PM performance on the days that the message was sent, with a medium to large effect size. This suggests that nonspecific cuing can lead to enhanced goal monitoring in these individuals.

Visual imagery is another self-regulation strategy that has been evaluated for its potential to improve PM deficits. While creating an image is not, in and of itself, a metacognitive regulation strategy, we would argue that using the creation of an image to increase awareness of the intention to be performed and the planning of when to respond is one. It has been demonstrated that individuals have good metacognitive awareness of their own mental images and that this can affect performance (Pearson, Rademaker, & Tong, 2011). Studies using visual imagery to improve prospective memory have been designed not to learn to create images, per se, but to use image generation to increase awareness of when a cue arrives and a response is required. Kaschel et al. (2002) trained nine patients to use visual imagery to imagine themselves fulfilling the PM task at the correct time or to the correct cue. Individuals who received 20 sessions of the imagery training showed higher rates of keeping appointments than the control group of memory impaired patients who received standard memory rehabilitation strategies. Similarly, Potvin et al. (2011) used a five-stage training program to train individuals with BI to visualize cues in a PM task. They also reported that individuals with BI demonstrated improvements in PM in daily life. On a self-report measure of PM failures, a significant reduction in failures was reported following three months for the treatment group but not for the control group. Grilli and McFarland (2011) used a technique previously found to be effective in retrospective episodic memory recall to train individuals with neurological impairment in visual imagery techniques. They reported that self-imaging resulted in better PM performance and postulated that this is due to a superiority based on mnemonic mechanisms specifically related to the self. These studies show that visual imagery has excellent promise. However, the studies have been short-lived, despite evidence from cortical plasticity that repetition over time is necessary for successful long-term change in brain organization and have not measured generalization to daily life.

Combination approaches. Clinically, practitioners often combine the use of external compensatory aids and metacognitive strategies to address PM deficits in patients. Fleming, Shum, Strong, and Lightbody (2005) evaluated a multi-component intervention in three individuals with BI. These interventions included self-awareness training, teaching organizational strategies, and selection of a compensatory device (e.g., notebook, electronic diary). The authors reported an improvement in PM performance based on objective memory assessments. In a follow up randomized controlled trial, with four groups of participants, the groups with compensatory prospective memory training demonstrataed greater improvement than those given self-awareness training alone (Shum, Fleming, Gill, Gullio, & Strong, 2011). In a study that combined spaced-retrieval with elaborated encoding, Kinsella, Ong, Storey, Wallace, and Hester (2007) reported that individuals with early Alzheimer's disease were able to increase prospective remembering with the combination of these two approaches but not with spaced-retrieval alone.

The current study used a combination approach with the two most promising techniques. Individuals with BI were trained in visual imagery techniques, but under conditions of rote repetition, thereby taking advantage of both the effect of self-reference and the effect of repetition. Treatment was provided on an individualized basis.

It was hypothesized (hypothesis one) that the magnitude of change for the outcome measures (MIST, neuropsychological tests, generalization measures) would be significantly greater following the active treatment (A condition) than following the active control (B condition). It was also hypothesized (hypothesis two) that the individuals with BI would perform significantly more poorly on the MIST at baseline than the healthy participants overall and would exhibit significantly more prospective memory (no response) errors. Finally, it was hypothesized (hypothesis three) that treatment gains would be maintained for one year after treatment, such that there would be no significant difference between scores immediate post-treatment and those at one year follow-up for any of the outcome measures.

Research Design and Method

Methods

<u>Participants.</u> There were 20 adult individuals with BI (12 male, 8 female) and 20 healthy adults (10 male, 10 female) in the study. Participants with BI were recruited through the Brain Injury Alliance of Connecticut website, the Hartford Healthcare Head Injury Clinic and local support groups. The healthy participants were relatives or companions of those with BI or were employees of Trinity College. In the BI group, all individuals were at least one-year post injury but not more than five years, had obtainable medical records that included brain imaging, and all had a baseline PM performance of less than 10 minutes. Glasgow Coma Scale score (Teasdale & Jennett, 1974) from the scene of the accident or the emergency room was used to identify severity of injury. Only those with moderate to severe brain injury (GCS 12 or less) were included. All received traumatic brain injuries (12 motor vehicle accidents, 5 falls, 3 struck by object).

Exclusion criteria for all participants included the following: under 19 years of age, previous neurological or psychiatric illness, diagnosis of a learning disability, non-English speaking, severe depression or anxiety (measured with the Beck Depression Inventory and the

Beck Anxiety Inventory), significant visual or hearing deficit, seizure in prior six months, dementia (measured with the Dementia Rating Scale), and illiteracy. All participants received the National Adult Reading Test as an estimate of premorbid intelligence. Demographic information on all participants and injury information for those with BI are provided in Table 1. This study was approved by the Trinity College Institutional Review Board.

Materials. Several assessments were used to measure change as a result of treatment. All assessment materials were chosen because they had alternative forms and in all cases alternative forms were used for pre-testing versus post-testing. It should be noted that the MIST has four alternate forms so no form was repeated in any condition for any one participant.

Prospective Memory Assessment. The primary outcome measure was the Memory for Intentions Test (MIST; Raskin, 2004), which is a 30-min, 8-trial test during which participants engage in a word search puzzle as the ongoing task. A complete description of the MIST administration and scoring procedures can be found in Raskin (2009) and Woods et al. (2008). The following primary MIST variables were examined: 1) summary score; 2) time-based scale; and 3) event-based scale. The MIST is comprised of four trials with event-based cues (e.g., "When I hand you a postcard, self-address it.") and four trials with time-based cues (e.g., "In 15 minutes, tell me it is time to take a break."), with each item scored from 0-2 points; thus, the separate event-based and time-based scales have scores ranging from 0 to 8. The time- and event-based trials are balanced for delay interval (i.e., 2- and 15-min delay periods) and response modality (i.e., verbal and action responses). The MIST allows for separate scoring of time-based trials (8 points possible), event-based trials (8 points possible), 2-minute delay periods (8 points possible), 15-minute delay periods (8 points possible), verbal response trials (8 points possible) and action response trials (8 points possible), which are summed for a total of 48 possible points. However, this involves inclusion of the score of each trial three times in the total score (e.g., Trial 1 is a 2-minute delay trial, time-based cue, and verbal response, thus contributing to the 2-minute delay, time-based cue, and verbal response scores). A large digital clock is in full view of the participant at all times. For the event-based trials, the cues are considered to be ecologically relevant, meaning they are related to the response required and could naturally elicit that required response (e.g., When I hand you a request for records form, please write your doctors' names on it). The ongoing task is non-focal as the word search is not related to the prospective memory items. Prior studies support the reliability (Raskin, 2009; Woods et al., 2008) and construct validity (e.g., Raskin & Buckheit, 2001; Woods et al., 2008) of the MIST.

At the completion of the eight MIST trials, participants were given eight multiple choice recognition items (e.g., "At any time during this test, were you supposed to: 1) tell me to make an appointment; 2) tell me when I can call you tomorrow; 3) tell me to call for a prescription."). The recognition scale was included as a way to determine whether PM failures were due to encoding versus retrieval failures. Impairment on recognition items is likely to reflect deficits in retrospective rather than prospective memory functions. Furthermore, a 24-hr delay trial was administered for which examinees were instructed to leave a voicemail message for the examiner the day after the exam indicating the number of hours the participant slept the night after the evaluation. In addition, the following error types were coded: 1) no response (i.e., response omission errors); 2) task substitutions (e.g., replacement of a verbal response with an action or vice-versa); 3) loss of content (e.g., acknowledgment that a response was required for a cue, but failure to recall the content); and (4) loss of time (i.e., performance of an intention greater than ± 15% before or after the target cue). No response errors were presumed to be directly due to failure of PM (i.e., cue detection). Task substitution errors (e.g., intrusions and perseverations) were likely multi-determined, but presumed to be due to executive control deficits (e.g., Carey et al., 2004). Loss of content errors most likely reflected retrospective memory failures and loss of time errors seemed to be due to difficulty with strategic monitoring or timing.

Neuropsychological Assessment. All participants were given a battery of neuropsychological measures to assess attention, retrospective memory, and executive functioning. These measures were the Trail Making Test, the Brief Test of Attention, and the Hopkins Verbal Learning Test.

Measures of Generalization. Several questionnaires were used to evaluate everyday PM functioning including: The Prospective Memory Questionnaire (PMQ; Hannon et al.1995), The Everyday Memory Questionnaire (EMQ; Mateer, Sohlberg, & Crinean, 1987), and the WHO-QoL-BREF (Skevington, Lofty, O'Connell, & WHOQOL Group, 2004). A pre- post-test diary study was used to measure performance on PM tasks in daily life (Raskin & Sohlberg, 1996). The diary study involved keeping data for one week on ten PM tasks that are part of the participants' regular daily routine. Ten items are identified by the participant and examiner that must be completed in the following week. A significant other is then shown how to keep track of the participant's performance during the week. Scoring was based on a 2-point scale with 1 point=correct time or task and 2=correct time and task.

Procedure

All participants were administered the MIST, the neuropsychological tests, and the generalization measures at the beginning of the study. Treatment was provided in an AB-BA within-subjects crossover design. The BI participants received the MIST in between the two conditions of training. Once training was completed, all participants again received all tests and again one year after completion of training. For a schematic of the study procedures see Table 2. Testing performed before and after training and at one-year follow-up was performed by an experimenter with no knowledge of the treatment condition of the participants.

Training Procedures. Only the BI group participated in the training. All participants received training in one-hour sessions, one or two times per week, for a total of six months.

This was judged to be adequate time to allow for any changes that might be due to cortical reorganization and is modeled after studies of motor and sensory plasticity (e.g., Morris, Crago, DeLuca, Pidikiti, & Taub, 1997). Participants began with the PM training at one minute beyond their baseline ability. They were given an ongoing task to perform in that period of time, such as computer games or paper and pencil puzzles. Training of visual imagery followed that of Potvin, et al.(2012) and Grilli and McFarland, (2011. Participants were given events as cues. They were asked to imagine as much about the cue as possible from their own personal perspective and to describe in as much detail as possible. In particular they were asked to answer the following questions: 1) What will you see when the event occurs? 2) If it is a visual cue, what color will it be? 4) What size will the event be? 3) What will you hear when the event occurs? 4) How will you feel when the event occurs? 5) Do you have any specific thoughts about the event? 6) Please imagine yourself performing the task. Due to findings of improved performance under errorless conditions (Fish et al., 2015), training began well within the range of a participant's successful perofmrance. As the participant became proficient at a time span (defined as five consecutive trials of getting both the time and task correct), the delay time was increased by one minute and participants were instructed not to guess but only to answer if they were sure they were correct. The method described above, using visual imagery, was the A condition. For half the participants, this was followed by the B condition or active control condition. The B condition consisted of the same number and frequency of sessions. Rather than receiving imagery training, participants performed a task analogous to PM training, but which has been demonstrated not to improve performance (Raskin & Sohlberg, 1996). This required participants to perform a task identical to that used in the PM training (e.g., sign your name), then after a specific period of time, the examiner asked the participant to recall the task performed (e.g., "Can you recall what I asked you to do exactly 2 minutes ago?"). The other half of the BI participants received the B condition first and then the A condition. Training conditions were given in blocks. All cues were EB.

In order to offset the difficulties of having the participants participate in a control condition, the final 15 minutes of each session in both conditions was a program of education about brain injury. Thus, these individuals were not asked to make special trips for sessions that were known to be of no value to them.

Results

Performance on training tasks. McNemar's Test for Change indicated that all participants showed an increase in the time they were able to recall the PM tasks (mean increase 2.51 minutes, standard deviation 1.85; *d'*=1.36).

Performance on the measure of PM. Following from Hypothesis One, anaylsis of variance (ANOVA) was performed on the MIST scores in each condition. Differences between treatment conditions were evaluated using linear mixed models. Total MIST scores represented the dependent variable, while treatment (A vs. B) and time (pre- vs. post-treatment) were included as within-subjects explanatory variables. All multi-way interactions were considered and the correlation between repeated measures on an individual was modeled using random effects and/or structured variance-covariance matrices. There was a significant interaction ($p<.001$) explained by pre-post difference for treatment A, but not B. See Figure 1 for the BI data.

In order to investigate Hypothesis Two, prior to training, both groups were compared on the variables from the Memory for Intentions Screening Test (MIST) (Raskin, Buckheit, & Sherrod, 2010). A repeated measures analyses of variance (ANOVA) for time delay (2 minute, 15 minute) x group (HA, BI) revealed a significant main effect for time delay ($F(1,18)=72.71$, $p<.001$), such that performance was superior at 2 minute delays compared to 15 minute delays; the main effect for group was also significant ($F(1, 18)=32.78$, $p<.001$), such that healthy adults showed superior performance to those with brain injury; but the interaction was not significant.

For type of cue (event, time) x group (HA, BI), the main effect for type of cue was also significant $F(1,18)=32.29$, $p<.001$, such that performance for event-based cues was superior to performance for time-based cues overall. The main effect for group was significant (F (1, 18)=39.44, p<.001). The interaction was not significant.

For type of response (action, verbal) x group (HA, BI), the main effect of type of response was significant (F(1, 18)=15.67, p<.001), such that performance on verbal response tasks was superior to that of action response tasks. The main effect of group was significant with the HA group performance superior to the BI group (F(1,18)=23.23, p<.001. The interaction was significant (F (1, 18)=17.82, p<.01) such the group with BI was significantly worse than the HA group for action responses but that there were no differences between the groups for verbal responses.

A series of Student's t – tests was used to compare the two groups on each type of error on the MIST. Individuals with BI had significantly more PM (no response) errors, indicating no recall of the need to perform an intention (t (19)=8.67, p<.01). They also performed significantly more poorly on the recognition items, indicating that RM is also impaired (t (19) =9.33, p<.01). On the more naturalistic 24-hour recall task, there was no difference between the groups. See Tables 3 and 4 for the performance of the two groups on the MIST. There were no significant differences between the immediate post-testing and one-year follow up on the MIST.

<u>Performance on neuropsychological measures.</u> As a further test of Hypothesis Two, comparisons were made between groups on the neuropsychological measures. At pre-treatment BI participants performed poorly on tests of complex attention, executive functioning and retrospective memory. In order to investigate the effect of treatment on the neuropsychological measures, scores were compared pre-treatment and post-treatment. Post-treatment performance indicated change only on measures of complex attention and executive functioning for both groups. These data are presented in Table 6. Correlational analyses were used to compare the MIST total score with each neuropsychological measure. MIST summary score was significantly related to measures of executive functioning (Trail Making Test Part B)

(r=.71; p<.001) but not the other measures. At one year there were no significant differences as compared to the immediate post-testing on any of the measures.

Performance on generalization measures. Finally, comparisons were made between the groups on the measures of generalization. Using McNemar's test for change, there were no significant differences found for the WHO-QoL-BREF, or the Prospective Memory Questionnaire before or after treatment. However, there were significant improvements measured using McNemar's test for change on the Everyday Memory Questionnaire (*p=.022)* and the performance on the Diary Measure (*p=.003)*. At one year scores on the measures of generalization were not significantly different than those at the immediate post-testing. See Table 4.

Correlations between the MIST scores and the generalization measures

Correlational analyses revealed that MIST Total (r=.74; p<.001), MIST EB (r=.70; p<.01) and PM errors (r=.73;p<.001) but not MIST TB were significantly related to the Diary Measure.

Discussion

This study has a small number of participants, but given the within-participants design, these data provide another increment of evidence that PM may be one area of cognitive functioning that is amenable to this kind of restorative approach. Perhaps because of the nature of the underlying cognitive systems, these processes may be more adaptable than other memory regions. It is of note that the participants in this study improved on the task given in session but that they also improved on unrelated neuropsychological tasks and generalization measures of PM performance in daily life. Further, they continued to maintain the gains at one year after treatment was concluded.

In terms of PM performance in this population, the date from the MIST add to the growing literature reporting deficits in this area of cognitive functioning. In terms of time delay, individuals with BI were impaired compared to healthy participants on both the short and the long delay, but were not differentially impaired by the long delay. This suggests that any PM impairments are already measureable at two minutes. It might be interesting to investigate whether shorter time delays would still yield deficits. For type of cue, both groups showed significantly reduced performance on time-based cues as compared to event-based cues. This has been demonstrated in both BI and healthy populations previously, and is presumed to be due to the greater cognitive control required for time-based cues (Raskin, Buckheit & Waxman, 2011; Shum, Valentine, Cutmore, 1999). Again, it is of note that the difference between these types of cues was not greater in the BI group. Finally, in terms of type of response, it is of note that the group with BI actually demonstrated reduced performance on action responses relative to verbal responses. Thus, it is possible that they are not able to take advantage of the action superiority effect (Pereira, Ellis & Freeman, 2012).

On neuropsychological measures of attention, memory and executive functioning, the BI group demonstrated significantly lower performance in all domains when compared to the healthy participants. When examining the relationship between the MIST and the neuropsychological measures, the only significant relationship was found between the MIST and the measures of executive functioning. This is consistent with previous studies that have suggested that PM is most closely linked to executive functioning and likely to be mediated by prefrontal structures (e.g., Neulinger, Oram, Tinson, O'Gorman, & Shum, 2016).

Importantly, individuals demonstrated generalization of treatment in daily life as measured by the diary study, confirming previous findings of a relationship with (Raskin & Sohlberg, 2009), but not a relationship with self-report questionnaires (Raskin, Buckheit & Waxman, 2011). It is essential that treatment studies plan for and empirically measure generalization to ensure that treatment effects are valid (Sohlberg & Raskin, 1996). In addition, the MIST total score and EB items were related to this measure of generalization but the TB items were not. This may be because a greater number of the diary measures were EB in nature and those that were TB were of much longer duration than that seen in the MIST, allowing for a greater margin of error. It would be interesting in future studies to carefully control the items on the diary measure to ensure a balance of TB and EB items and to more carefully monitor whether the TB items were completed at the appropriate time.

In addition, all of the items on the MIST have a high cue-intention relationship, that is the intention to be performed follows naturally from the cue (e.g., “When I hand you an envelope, please self-address it”). Thus the cue itself may spontaneously evoke the response. While this was intentionally designed into the MIST, in order to most close resemble real world functioning, it may also play a role in the greater relationship between MIST items and EB items in daily life (Pereria, Ellis, & Freeman, 2012). It would be interesting to look at this variable in future studies of rehabilitation.

Perhaps most importantly, improvements on the main outcome measure and the generalization measure were maintained for one year after the completion of treatment with no further intervention. While there were no significant differences between the post-testing and the one-year follow-up on any measure, in fact, some of the data were in the direction of continued improvement. This suggests the possibility that the changes made as a result of treatment are not only lasting but that they may allow the individual to practice successful performance regularly, thus continuing to strengthen these abilities.

In addition to the small sample size, this study has limitations related to the study design. Research is needed that uses larger randomized controlled designs. While large-scale or multi-site intervention studies may not, in fact, be the goal, given the need for individualized treatment, studies need to use appropriate single-case designs in order to be interpreted as efficacious. Many studies have not measured generalization to daily life and outcome measures may not be clearly defined. Many of these concerns have been summarized in the National Institutes of Health Consensus Development Panel on the Rehabilitation of Persons with Traumatic Brain Injury (1998). In addition, this treatment needs to be compared to other possible treatments to ensure that this particular combination is the most effective.

Research on PM is an area of increasing interest. As researchers in the field gain greater understanding of the mechanisms required for successful PM performance, it will become easier to develop effective rehabilitation strategies. Success to date has been documented with compensatory approaches, meta-cognitive strategies, and restorative approaches.

Metacognitive strategies promise for gains in daily functioning, since a large part of successful PM performance is based on the ability to evaluate one's own performance. And metacognitive strategies may show the greatest generalization as individuals are able to evaluate when PM functioning is required and the best method for successful implementation. Moreover, combination strategies may be the most useful approach and will allow for treatment that meets the individual needs of each person.

PM may be one of the few cognitive rehabilitation domains that respond to restorative approaches. This study lends support to the notion that a restorative approach shows promise for the remediation of PM deficits in individuals with brain injury. In addition, these gains demonstrated generalization to daily life on a measure that is individual and specific to the treatment. As more research on neuroplasticity is applied to brain injury rehabilitation, it should become more clear which approaches to restoration are most beneficial. However, current data suggest that rote repetition, based on the consistent finding that change in the brain requires repetition, seems like a critical approach. Some reasons for the superiority of rote repetition might be that repetition appears key to experience- based cortical plasticity, there are ample opportunities for testing, it is error-free, it provides multiple examples to avoid stimulus-bound learning, it is self-generated, and it may increase automatization. Finally, combination approaches are likely to have the most lasting and profound effects.

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Table 1. Demographic information on both groups and injury information for the BI group

	BI		HA		*t*
	Mean	s.d.	Mean	s.d.	
Age (years)	42.11	13.21	39.15	14.21	1.31
Education (years)	13.64	2.91	14.95	2.78	1.07
Occupation[1]	5.21	2.45	6.13	2.86	1.45
NART-R IQ[2]	106.28	9.78	110.32	9.54	1.79
Time since injury (days)	217.19	198.45	N/A		
Length of PTA[3] (days)	33.67	29.91	N/A		
GCS[4] at admission	7.25	3.89	N/A		

[1]Highest occupation held, using Hollingshead scale (Hollingshead, 1977).
[2]Estimate of IQ from North American Adult Reading Test – Revised (Blair & Spreen, 1989).
[3]Post-traumatic amnesia
[4]Glasgow Coma Scale

Table 2. Format of Study: AB Crossover Design

Pre-Treatment	Between A & B	Post-Treatment	One Year Follow-Up
Neuropsychological		Neuropsychological	Neuropsychological
MIST	MIST	MIST	MIST
Generalization		Generalization	Generalization

Table 3. Performance of the individuals with BI and the healthy adult participants on the first testing with the MIST.

MIST variable	BI (n=20) Mean	s.d.	HA (n=20) Mean	s.d.	p	d'
2 minute delay	4.46	1.42	6.45	1.33	.042	1.45
15 minute delay	2.90	1.76	4.30	1.30	.001	0.90
Event-based cue	3.51	1.62	5.82	1.23	.007	1.61
Time-based cue	2.91	1.38	4.90	1.37	.002	1.45
Action response	3.15	1.01	6.02	1.42	.005	2.33
Verbal response	3.42	1.22	4.55	1.32	.003	0.89
Summary Score	20.78	8.13	32.01	6.55	.003	0.98

Table 4. Performance of the BI participants on the MIST total score, MIST total errors and prospective memory errors at pre-treatment, post-treatment and one year following treatment compared to the first and second testing of the healthy adults (HA)

	BI (n=20) Pre CRT Mean s.d.	BI (n=20) Post CRT Mean s.d.	p	*d'*	BI (n=16) One Year Mean s.d.	HA (n=20) First Test Mean s.d.	HA (n=20) Second Test Mean s.d.
MIST Summary	20.78 8.13	32.01 6.55	.003	0.98	28.86 7.01	32.20 6.10	33.92 6.22
MIST Total Errors	5.23 0.80	2.99 0.77	.002	2.85	1.76 0.07	1.80 0.44	1.89 0.56
PM Errors	5.11 0.54	2.93 0.67	.007	3.60	1.21 0.80	1.08 0.24	1.10 0.13

Table 5. Performance of the individuals with BI on the generalization measures.

	BI (n=20) Pre CRT Mean s.d.	BI (n=20) Post CRT Mean s.d.	p	*d'*	BI (n=16) One Year Mean s.d.
WHO-QoLBREF	26.01 5.23	28.79 3.55	.067	0.63	28.22 5.59
PMQ	12.23 7.47	9.13 3.87	.051	0.55	10.15 5.87
EMQ	19.83 8.22	16.11 4.21	.0004	0.59	16.25 5.89
Diary Study	12.49 4.95	17.22 3.37	.00002	1.14	18.72 5.98

Table 6. Performance of the two groups on the neuropsychological tests

	BI (n=20) Pre CRT Mean s.d.	BI (n=20) Post CRT Mean s.d.	p	*d'*	BI (n=16) One Year Mean s.d.	HA (n=20) First Test Mean s.d.	HA (n=20) Second Test Mean s.d.
Trail Making Part A	55.21 17.73	51.33 9.22	.07	0.27	50.24 9.47	31.04 10.12	27.97 9.23
Brief Test of Attention	10.53 5.40	12.98 5.21	.002	0.46	13.27 4.98	16.52 3.32	17.81 4.22
HVLT Total Recall	20.13 6.98	21.78 7.22	.12	0.23	21.67 7.19	29.21 3.57	28.72 3.21
Trail Making Part B	155.45 21.86	129.71 6.22	.009	0.92	107.42 7.25	83.42 3.50	81.79 3.67

Figure 1. Comparison of Conditions A and B