HHS Public Access

Author manuscript

J Clin Exp Neuropsychol. Author manuscript; available in PMC 2023 July 25.

Published in final edited form as:

J Clin Exp Neuropsychol. 2022 April ; 44(3): 210–225. doi:10.1080/13803395.2022.2101620.

Temporal Order Memory Impairments in Individuals with Moderate-Severe Traumatic Brain Injury

Michael R. Dulas[1,2], **Emily L. Morrow**[3], **Hillary Schwarb**[1,4], **Neal J. Cohen**[2,4], **Melissa C. Duff**[3]

[1]Beckman Institute, University of Illinois at Urbana-Champaign, Urbana (IL)

[2]Department of Psychology, University of Illinois at Urbana-Champaign, Urbana (IL)

[3]Department of Hearing and Speech Sciences, Vanderbilt University Medical Center, Nashville (TN)

[4]Interdisciplinary Health Sciences Institutes, University of Illinois at Urbana-Champaign, Urbana (IL)

Abstract

Introduction: Temporal order memory is a core cognitive function that underlies much of our behaviour. The ability to bind together information within and across events, and to reconstruct that sequence of information, critically relies upon the hippocampal relational memory system. Recent work has suggested traumatic brain injury (TBI) may particularly impact hippocampally-mediated relational memory. However, it is currently unclear whether such deficits extend to temporal order memory, and whether deficits only arise at large memory loads. The present study assessed temporal order memory in individuals with chronic, moderate-severe TBI across multiple set sizes.

Method: Individuals with TBI and Neurotypical Comparison participants studied sequences of three to nine objects, one a time. At test, all items were re-presented in pseudorandom order, and participants indicated the temporal position (i.e., first, second, etc.) in which each object had appeared. Critically, we assessed both the frequency and the magnitude of errors (i.e., how far from its studied position was an item remembered).

Results: Individuals with TBI were not impaired for the smallest set size, but showed significant impairments at 5+ items. Group differences in the frequency of errors did not increase further with larger set sizes, but group differences in the magnitude of these errors did increase with larger memory loads. Individuals with TBI showed spared performance for the first object of each list (primacy) but were impaired on the last object (recency), though error frequency was better for last compared to middle items.

Conclusions: Our findings demonstrate that TBI results in impaired temporal order memory for lists as small as five items, and that impairments are exacerbated with increasing memory loads.

Correspondence: Michael R. Dulas, Ph.D., Beckman Institute, 405 N Mathews Ave, Urbana, IL 61801, mrdulas@illinois.edu, +1-585-732-0276.

Disclosure statement

No potential conflicts of interest were reported by the authors.

Assessments that test only small set sizes may be insufficient to detect these deficits. Further, these data highlight the importance of additional, sensitive measures in the assessment of cognitive impairments in TBI.

Keywords

traumatic brain injury; relational memory; hippocampus; temporal memory; assessment

INTRODUCTION

Temporal order memory is a critical cognitive operation that underlies many everyday tasks, from scheduling and attending appointments, to effectively retracing one's steps to find a misplaced item (Beaver & Schmitter-Edgecombe, 2017; Cohen, 2015; van der Meer, Beyer, Heinze, & Badel, 2002). Indeed, when we recall the events of our daily lives, we remember not only what events happened but also when, and in what order, they happened (St Jacques, Rubin, LaBar, & Cabeza, 2008). Temporal order memory places high demands on relational memory/processing, as it requires the *binding* of arbitrary relations between the elements of experience (temporal and spatial) into durable representations and the *flexible* expression of these representations in novel settings, i.e., in different contexts from encoding (Eichenbaum & Cohen, 2001; Rigon, Schwarb, Klooster, Cohen, & Duff, 2020; Rubin, Schwarb, Lucas, Dulas, & Cohen, 2017). In this way, relational memory supports a range of temporal goals, such as using representations of temporal relations from past experiences to recall the sequence of events to tell a story or the order and timing of steps to prepare a meal.

The hippocampus plays a critical role in relational memory processing (Cohen et al., 1999; Eichenbaum & Cohen, 2014). Data from patients with focal, bilateral hippocampal lesions have demonstrated that damage to the hippocampus impacts relational memory across domains, types of stimuli, and time scales (Konkel, Warren, Duff, Tranel, & Cohen, 2008; Monti et al., 2014). For example, previous research has shown that individuals with bilateral hippocampal damage demonstrate impairments in memory for binding items to contexts (Hannula, Ryan, Tranel, & Cohen, 2007; Hannula, Tranel, & Cohen, 2006), for the locations of objects in space (Horecka et al., 2018; Lucas, Duff, & Cohen, 2019; Watson, Voss, Warren, Tranel, & Cohen, 2013), and for the order in which objects were presented (Konkel et al., 2008). Thus, deficits in relational memory are linked to hippocampal damage, and such deficits are likely to be present across conditions where hippocampal damage and dysfunction are prevalent, including traumatic brain injury (TBI).

Indeed, in TBI, memory deficits are among the most commonly reported and treated consequences of injury (Cicerone et al., 2011; Murray, Ramage, & Hopper, 2001; Vakil, 2005; Wilson, 1998). Critically, the structure and function of the hippocampus and medial temporal lobe regions are highly vulnerable to injury, including the pathophysiological consequences of TBI, such as from hypoxia and seizure. Such hippocampal damage likely underlies the memory deficits (e.g., episodic memory impairments) that are so common in TBI (Atkins, 2011; Irimia & Van Horn, 2015; Palacios et al., 2013; Tate & Bigler, 2000; Vespa et al., 2010). More recent studies, however, have characterised the impact of TBI across a range of relational memory domains beyond episodic or autobiographical memory.

One study to assess relational memory deficits in individuals with TBI asked participants to learn and remember item-context pairings (Monti et al., 2013). Participants studied faces paired with unique scenes, and later were tested on their memory for those pairings. Specifically, they were asked whether they could identify whether each scene was paired with the same face as before (intact), or whether the face belonged with a different scene (re-pair). This same paradigm has been used with individuals with focal hippocampal damage, who showed significant deficits in face-scene relational memory compared to matched control participants (Hannula et al., 2007). Middle-aged adults with a mild TBI in the remote past were impaired on this relational memory task compared to participants with no history of TBI. Further, neuroimaging revealed that individuals with a history of mild TBI, showed a decrease in the size of the hippocampi and reductions in hippocampal activity during relational memory retrieval. More recently, we employed a continuous version of this face-scene task in individuals with chronic, moderate-severe TBI (Morrow, Dulas, Cohen, & Duff, 2020). In this variant, instead of separate study and test phases, the task was continuous in nature, with test trials appearing at various intervals throughout the ongoing task. Critically, the study was designed so that participants were tested on their memory for a face-scene pairing after a moderate delay or immediately after studying that face-scene pairing. This task had been previously used to demonstrate that hippocampal damage results in relational memory deficits even at short time scales (Hannula et al., 2006). Results showed that individuals with moderate-severe TBI were impaired on relational memory for face-scene pairings, not just after a long delay, but even when tested immediately after studying the face-scene pairing. These results demonstrate that relational memory deficits in TBI are not confined to traditional concepts of “long-term” memory, but impact the use of relational information even in the moment.

Relational memory deficits in individuals with TBI also extend to spatial memory. In a recent study using a spatial reconstruction task, participants studied an array of five objects, and then, after a short delay, were asked to reconstruct that array (Rigon et al., 2020). This task has previously demonstrated that hippocampal damage is tied to specific deficits in spatial reconstruction performance (Horecka et al., 2018). That is, while the ability to reconstruct the overall shape of an array is relatively spared, individuals with hippocampal lesions show deficits in placing objects in their exact locations (identity-location binding) and show larger errors in the distance between the studied location of an object and their reconstructed location of that object (misplacement). Using this same task with individuals with chronic, moderate-severe TBI (Rigon et al., 2020), the results mirrored the findings from individuals with focal hippocampal lesions: Individuals with TBI showed deficits in the same two aspects of spatial reconstruction performance relative to non-injured participants, again with a spared ability to reconstruct the general shape of the array. Thus, even in a condition that causes diffuse neurological damage, the similarity in the presence, and patterns, of relational memory deficits between individuals with moderate-severe TBI and individuals with focal hippocampal lesions is striking.

The focus of the current study is to extend the examination of relational memory in individuals with TBI to temporal order memory. We should note that disruptions in temporal processing in individuals with TBI are well documented (e.g., Mioni, Grondin, & Stablum, 2014; Mioni, Mattalia, & Stablum, 2013; Mioni, Stablum, & Cantagallo, 2013),

particularly in time discrimination, perception, and estimation. However, less is known about temporal order memory, and existing results are equivocal. In one study of temporal order memory, individuals with TBI completed eight cognitive tasks during the acute phase of their recovery and were tested immediately and approximately one year later (Schmitter-Edgecombe & Seelye, 2012). At both time points, participants were asked to recall the eight tasks, as well as to reproduce the temporal order in which the tasks were completed. Relative to neurotypical comparison participants, individuals with moderate-severe TBI were impaired in free recall and temporal order memory of the tasks at both time points, although temporal order memory improved across time for the participants with TBI. This finding was in contrast to a similar study where the authors found no group differences between individuals with and without TBI on temporal order memory for completing the eight tasks at a single time point (Schmitter-Edgecombe & Wright, 2003). Previous work has also used temporal order tasks to test the benefits of verbal encoding conditions (e.g., incidental vs intentional; automatic vs. effortful) on memory performance with variable outcomes, assessing whether temporal order memory in TBI can look better or worse based on training condition (Cooke & Kausler, 1995; Vakil, Blachstein, & Hoofien, 1991; Vakil, Sherf, Hoffman, & Stern, 1998; Vakil & Tweedy, 1994; Wright et al., 2014). These previous studies of temporal order memory in TBI differed in their goals (e.g., to study recovery of temporal order memory; to assess if different training conditions improve performance), but a common factor is that they have used a fixed stimuli set size across groups ranging from approximately 8 to 24 items or activities. Yet, it is unknown if temporal order memory is impaired in TBI across all set sizes, or if the presence or magnitude of a temporal order memory deficit might expand as set size and memory load increase. Moreover, these various tasks have differences in the environmental support afforded to the participant. As mentioned, some tasks employed various training conditions (Cooke & Kausler, 1995; Vakil et al., 1991; Vakil et al., 1998; Vakil & Tweedy, 1994; Wright et al., 2014), assessed memory for sequences of performed tasks (Schmitter-Edgecombe & Wright, 2003), and some even incorporated cumulative timelines of events during study (Heaton et al., 2014). While these methods may be more naturalistic in some cases, such environmental support may mask underlying core temporal memory deficits.

Furthermore, there is interest in the extent to which temporal order memory may be associated with performance on standardised neuropsychological tests. For example, Schmitter-Edgecombe and Seeley (2012) found that in individuals with TBI, temporal order memory performance was correlated with their two neuropsychological measures of medial temporal lobe ability (Rey Auditory Verbal Learning Test trials 1-5 and long delay) at the immediate time point, but not at the one-year time point. Temporal order memory performance was not correlated with any of the five measures of frontal lobe ability (e.g., Trails Making Test, Controlled Oral Word Association Test) at the immediate time point, although there was a correlation with performance at the one-year time point on one measure of frontal lobe ability (Letter-Number Sequencing). We have also been interested in these associations in our own work on relational memory in TBI. In both of our recent studies with individuals with moderate-severe TBI (Morrow et al., 2020; Rigon et al., 2020), some participants with TBI showed spared performance on standardised neuropsychological assessments of episodic memory while performing at least 1.5 standard deviations below the

average of the neurotypical participants on the experimental tasks. We speculate that some standardised neuropsychological tests may not sufficiently tap into the relational memory processes impacted by TBI, or may lack the sensitivity to detect such relational memory deficits, including deficits in temporal order memory.

The current study tested temporal order memory in individuals with chronic, moderate-severe TBI across various set sizes to determine whether temporal order memory deficits exist for short lists but are, in turn, exacerbated by longer lists. As we are interested in whether there is a core deficit in temporal order memory, we have minimised any environmental support, which, while perhaps less naturalistic, could mask underlying temporal memory deficits. Further, we capitalise on the sensitive measures we have already developed in our previous studies of spatial relational memory (Horecka et al., 2018) to assess not only the frequency of errors, but also their magnitude. We predict the following:

1. Individuals with moderate-severe TBI will show a higher frequency of errors at all set sizes, and their errors will be greater in magnitude than neurotypical participants.
2. These group differences in both metrics will become more pronounced as the number of items to-be-remembered (set size) increases.

Critically, such a temporal order task allows us to assess additional facets of memory that do not exist in spatial memory, namely primacy and recency effects (Murdock Jr, 1962; Neath, 1993). In free recall tasks, these effects reflect superior performance for the first (primacy) and last (recency) items on a list, often with a U-shaped function of performance across serial position. Similar results have been demonstrated in temporal order tasks, where the position of the first and last items of lists are best remembered, suggesting that the start and end of lists serve to anchor relative temporal order information (Henson, 1998, 1999). Thus, as an exploratory analysis, we assess whether individuals with TBI may show spared memory for the first and last items of our lists, even in the face of overall deficits in temporal order memory. Further, given our assertion that standardised neuropsychological assessments may be less sensitive to relational memory deficits (Morrow et al., 2020; Rigon et al., 2020), we include a second exploratory analysis, in which we relate performance on our experimental measure of temporal order memory with the NIH Toolbox's Episodic Memory subtest (Heaton et al., 2014), which assesses memory for the temporal order of a series of images.

METHOD

Participants

Participants were 40 individuals with moderate-severe TBI (22 female, 18 male) and 40 neurotypical comparison participants (29 female, 11 male). Six participants with TBI and one comparison participant were left-handed. All participants were between the ages of 18 and 55. Neurotypical comparison (NC) participants were recruited from Nashville and the surrounding areas and had no history of neurological or cognitive disability. The mean age for the participants with TBI and the healthy comparison participants were 35.9 (SD = 9.1) and 33.5 (SD = 9.9) years, respectively, and did not differ statistically ($t(78) = 1.12$,

$p = 0.27$). The mean level of education in years for the participants with TBI and the NC participants were 15.0 (SD = 2.2) and 15.6 (SD = 1.9), respectively, and also did not differ statistically ($t(78) = 1.21$, $p = 0.23$).

Participants with TBI were recruited through the Vanderbilt Brain Injury Patient Registry. All participants with TBI were in the chronic phase of injury (>6 months post-injury), sustained a single instance of TBI, and sustained their injuries in adulthood (i.e., after age 18). Thus, participants' neuropsychological profiles were in the chronic and stable phase (Salmond, Menon, Chatfield, Pickard, & Sahakian, 2006). Average time since injury was 68.6 months (SD = 87.3). Participants with TBI did not have a history of neurological or cognitive disability prior to the qualifying brain injury. TBI severity was determined using the Mayo Classification System (Malec et al., 2007). Participants were classified as having sustained a moderate-severe TBI if at least one of the following criteria was met: (1) Glasgow Coma Scale (GCS) <13 within 24 hours of acute care admission (i.e., moderate or severe injury according to the GCS), (2) positive neuroimaging findings (acute CT findings or lesions visible on a chronic MRI), (3) loss of consciousness (LOC) >30 minutes, or (4) post-traumatic amnesia (PTA) >24 hours. Injury-related information was collected from available medical records and a semi-structured interview with participants.

GCS was available for 33 participants (Median = 10, ranging from 3 to 15); loss of consciousness (LOC) information was available for 35 participants; post-traumatic amnesia (PTA) information was available for 39 participants; acute imaging information was available for 38 participants (36 with positive findings). Causes of injury were motor vehicle accidents (18), falls (6), motorcycle or snowmobile accidents (4), being hit by a car as a pedestrian (5), non-motorised vehicle accidents (5), assault (1), or being hit by a moving object (1). See Table 1 for demographic and injury information for participants with TBI.

Temporal Order Task

Stimuli and Design—The Temporal Order Task stimuli included 300 × 300 pixel, colourised line drawings of 120 common, uniquely nameable objects (Snodgrass & Vanderwart, 1980). An additional 11 objects were used for instructions and practice. The 120 test objects were divided into 20 sets of items, with each set consisting of 3, 5, 7, or 9 items. Then, these sets were divided into five blocks, each containing one of each set size. Each block, therefore, consisted of four runs, one of each set size, which included a study phase and a test phase. During the study phase of each run, participants were first alerted to what set size they would be studying. Then objects appeared, one at a time, in the centre of the screen for 1000 ms, with a 500 ms fixation cross between items. After all the items had been presented, participants were alerted that they would now be tested on their memory for the temporal position of each item. During each trial of the test phase, participants were again shown each item, one at a time, in the centre of the screen. The order of the items was pseudorandomised so that there was no correlation between study position and test position across runs. Below the item, the possible ordinal positions from the list were present (e.g., 1, 2, and 3 for a 3 item set; 1, 2, 3, 4, and 5 for a 5 item set, etc.). Participants were tasked with selecting which number corresponded to each item's place in the temporal order by pressing the corresponding key on the keyboard. Participants were

given unlimited time to respond. All position options were available even if the participant had previously selected that number for a prior object. Thus, participants needed to recall the temporal position of each individual item while it appeared alone, so that performance was neither supported nor constrained by previous responses. For both phases, objects were presented electronically using the E-Prime 3.0 software (E-Prime 3.0 software (Psychology Software Tools, Pittsburgh, PA) on a 1280×1024 pixel display. Examples of the study phase and test phase for a Set Size 3 list are shown in Figure 1A and 1B, respectively.

Procedure—Data collection for the Temporal Order Task was conducted as part of an initial visit for the Vanderbilt Brain Injury Patient Registry, during which participants complete consent forms and an intake interview. After obtaining informed consent and completing the intake interview, the experimenter explained the task via both on screen and verbal instructions, as well as by walking each participant through an example of a Set Size 3 item set. Participants then completed practice trials for a set of 3 and then a set of 5 items. Participants were allowed to practice as many times as needed to feel comfortable with the task. After completing practice, participants started the first block of the experiment. Within each block, the order of set sizes was pseudorandomised, but every participant completed the blocks in the same order. Each participant was then tested individually, with a short (few minutes) break between blocks if needed. In total, the entire task (including training and all five experimental blocks) took approximately 15 minutes to administer, with blocks lasting 2-3 minutes each.

Neuropsychological Testing—For the majority of participants, we were also able to administer the Episodic Memory subtest from the Cognition Battery of the NIH Toolbox as a standardised neuropsychological assessment of memory (Heaton et al., 2014). We have previously used the NIH Toolbox as a comparison point (Morrow et al., 2020; Rigon et al., 2020), as it is widely used and recommended for use in TBI research (e.g., NIH Common Data Elements). Participants completed the Cognition Battery on an iPad during a separate session from the temporal order task; average time between the two sessions was 3.7 weeks. The NIH Toolbox was either administered as the only neuropsychological measure during a given session, or as the first measure if other neuropsychological assessments were administered. For the present study, the Episodic Memory (Picture Sequence Memory) subtest was specifically selected due to its nature of being a temporal order memory task. The subtest involves recalling series of illustrated activities, which increase in length as the subtest continues. Participants must recall the sequence of activities over two learning trials. Sequences vary in length from 6-18 pictures, depending on the participant's age, and participants receive credit for each adjacent pair of pictures they place correctly. The subtest took approximately 10-15 minutes to administer, and we used both raw and age-corrected standard scores as outcome measures. The number of correct adjacent pairs is converted to a theta score, then a nationally normed standard score based on the participant's age (National Institutes of Health, 2016). Critically, while this test does have increasing set sizes, this factor is used to adjust for age/education differences, and is not a variable assessed itself in the calculation of raw scores.

Statistical Analysis—There were two dependent variables of interest for the Temporal Order Task, each measured separately for the four set sizes. The first variable of interest was the number of Exact Hits, i.e., on how many trials did a participant assign the correct ordinal position to an item at test. This is akin to the identity-location binding metric we have previously used in our spatial reconstruction tasks (Cannavale et al., 2019; Horecka et al., 2018; Rigon et al., 2020). The proportion of Exact Hits for each participant reflects the **frequency** of errors. The second variable of interest was Misplacement, i.e., how many positions off from the correct placement was each item. For example, pressing "2" for the second item in a list (an Exact Hit) would be a Misplacement of 0, but pressing "1" for the third item in the list would be a misplacement of 2. This measure is akin to the Misplacement metric we have used in our spatial reconstruction tasks, with ordinal position distance filling in for spatial distance. The Misplacement for each participant reflects the **magnitude** of errors. To account for differences across Set Sizes in the opportunities for errors, we calculated Misplacement as the average magnitude of error at the level of a single item, so that the total number of errors did not impact the calculation of their magnitude. Example responses and their corresponding misplacement scores are shown in Figure 1B. Repeated-measures analyses of variance (ANOVAs) were used to assess Group and Set Size effects and interactions for each of these variables, with planned subsidiary t-tests included to determine the source of effects where necessary. In instances where sphericity was violated, reported statistics were corrected using Huynh-Feldt corrections. Further, in instances where ceiling level effects suggested non-normal distributions, we also conducted Mann-Whitney U (or Wilcoxon rank sum) tests to confirm significant differences. However, in all cases, analyses using t-tests and Mann-Whitney U tests revealed complementary results. Thus, for simplicity, we only report the t-tests.

Further, we conducted exploratory analyses of Primacy and Recency effects. Performance scores for the first studied item (Primacy) and last studied item (Recency) of each set were combined across all blocks and Set Sizes to assess whether performance was preserved for the first and last item of each list, in line with previous studies suggesting the beginning and end of lists have improved memory relative to the middle (Henson, 1998, 1999). Group differences on these metrics were assessed using the same ANOVA, t-test, and Mann-Whitney U test parameters as the main analyses. Again, as these the t-tests and U-tests showed complementary results, for simplicity, we only report the t-tests.

All statistical tests were conducted in jamovi version 1.2 (The jamovi project, 2020, retrieved from https://www.jamovi.org), with an alpha of 0.05.

RESULTS

Temporal Order Task

Exact Hits—The percentage of Exact Hits for each group across set sizes are shown in Figure 2. An ANOVA, with factors of Set Size (3, 5, 7, 9) and Group (NC, TBI) showed main effects of Set Size [$F(3,234) = 217.09$, $p < 0.001$, $\eta^2p = 0.74$] and Group [$F(1,78) = 9.67$, $p = 0.003$, $\eta^2p = 0.11$], but a non-significant interaction [$F(3,234) = 2.54$, $p = 0.06$, $\eta^2p = 0.03$]. Given that the interaction approached significance, and visual inspection of the data suggested that the effect of Group was likely non-significant at Set Size 3, we conducted

follow-up t-tests between groups at each Set Size. Results revealed no significant group difference at Set Size 3 [$t(78) = 1.08$, $p = 0.29$, Cohen's d = 0.24], but significant differences at all other Set Sizes [$t(78)$'s > 2.61, p's < 0.01, Cohen's d's > 0.58]. Further, the magnitude of the group differences did not increase with Set Size after Set Size 3, with differences being 0.096, 0.102, and 0.087 for Set Sizes 5, 7, and 9, respectively. Thus, while both Groups had a similar percentage of Exact Hits for Set Size 3, individuals with TBI showed impairments, relative to the NC group, for sets of 5 or more, though these impairments did not increase with Set Size.

Misplacement—The average Misplacement for a single item (including Exact Hits as 0 Misplacements) is shown in Figure 3, divided by Group and Set Size. An ANOVA, with factors of Set Size (3, 5, 7, 9) and Group (NC, TBI) showed main effects of Set Size [$F(2.17,169.00) = 215.16$, $p < 0.001$, $\eta^2p = 0.73$] and Group [$F(1,78) = 9.41$, $p = 0.003$, $\eta^2p = 0.11$], as well as a significant interaction [$F(2.17,169.00) = 4.47$, $p = 0.01$, $\eta^2p = 0.05$]. Follow-up t-tests again revealed no significant Group difference at Set Size 3 [$t(78) = 1.18$, $p = 0.24$, Cohen's d = 0.26], but significant differences at all other Set Sizes [$t(78)$'s > 2.30, p's < 0.024, Cohen's d's > 0.51]. Moreover, the magnitude of the group differences increased with increasing Set Size even beyond Set Size 3, with group differences being 0.024, 0.130, 0.213, and 0.266 for Set Sizes 3, 5, 7, and 9 respectively. Thus, while groups showed similar performance at Set Size 3 for Misplacement, individuals with TBI showed increased impairments in Misplacement with increasing Set Size. Given that these Group differences increased for Misplacement, but not for Exact Hits, this suggests that while the frequency with which individuals with TBI were incorrect (Hits) did not increase with increasing Set Size, the magnitude of their errors (Misplacement) did. While not an initial variable of interest, we note that, despite group differences in Exact Hits and Misplacement across Set Sizes 5, 7, and 9, there were no significant differences in group variances (as assessed by Levene's test; p's > 0.21).

Exploratory Analyses of Primacy and Recency—Given that many memory studies show better memory for the first (Primacy) and last (Recency) items on a to-be-remembered list (Dewar, Brown, & Della Sala, 2011; Henson, 1998; van Asselen, Van der Lubbe, & Postma, 2006), we sought to assess whether, despite overall group differences, individuals with TBI demonstrated similar benefits in memory for first and last items. Namely, we wanted to assess whether performance was spared in individuals with TBI for first and/or last items despite overall temporal order memory impairments. Primacy and Recency scores for Exact Hits were created by calculating the percentage of correct responses on the first and last items, respectively, collapsed across Set Sizes 5, 7, and 9[1]. Set Size 3 was excluded as there were no group differences for Set Size 3 overall, and both groups were at/near ceiling for all ordinal positions for Set Size 3 (i.e. accuracy was >94% and misplacement was under 0.1 for both groups). Further, for comparison, we also extracted the middle item of each Set, so as to have a middle comparison to infer whether Primacy and Recency performance were indeed superior to the middle of the list. These values are shown in

[1]These values were collapsed as there were not enough trials to have sufficient power to assess each value. However, it should be noted that the ANOVAs for Primacy and Recency with factors of Set Size and Group showed no significant Set Size by Group interactions [F's < 1.80, p's > 0.17], suggesting collapsing in this way did not mask group differences across Set Sizes.

Figure 4. An ANOVA of Type (First, Middle, Last) and Group showed main effects of Type [$F(2,158) = 130.44$, $p < 0.001$, $\eta^2p = 0.63$] and Group [$F(1,78) = 11.20$, $p = 0.001$, $\eta^2p = 0.13$], modified by a Type x Group interaction [$F(2,158) = 5.63$, $p = 0.004$, $\eta^2p = 0.07$]. Follow-up independent samples t-tests showed that there were no significant group differences for the Primacy effects [$t(78) = 0.77$, $p = 0.44$, Cohen's d = 0.17], but that individuals with TBI showed reduced performance for Middle and Last items compared to NC's [$t(78)$'s > 2.89, p's < 0.01, Cohen's d's > 0.63]. Further, as can be seen in Figure 4, for both groups, first items were remembered the best, followed by last items, with middle items being the worst [$t(39)$'s > 3.33, p's < 0.011, Cohen's d's > 0.53]. These data suggest that while individuals with TBI show more frequent errors generally, they are spared for the first item of each list, and also show a somewhat spared Recency effect relative to middle items.

This analysis was then repeated for Misplacement for the first and last items of each list for Set Sizes 5-9. These values are shown in Figure 5. The ANOVA of Type (First, Middle, Last) and Group showed main effects of Type [$F(1.72,134.20) = 62.60$, $p < 0.001$, $\eta^2p = 0.45$] and Group [$F(1,78) = 9.36$, $p = 0.003$, $\eta^2p = 0.11$], modified by a Type x Group interaction [$F(1.72,134.20) = 6.24$, $p = 0.004$, $\eta^2p = 0.07$]. Follow-up independent samples t-tests again showed that there were no significant group differences for the Primacy effects [$t(78) = 0.85$, $p = 0.39$, Cohen's d = 0.19], but that individuals with TBI showed reduced performance for middle and last items compared to NC's [$t(78)$'s > 3.01, p's < 0.01, Cohen's d's > 0.67]. Interestingly, the paired samples t-tests showed a different pattern for Misplacement than for Exact Hits. In NC's, First items showed a lower magnitude of error than middle or last items [$t(39)$'s > 5.39, p's < 0.001, Cohen's d's > 0.85] but no difference in error magnitude between middle and last items [t(39) = 0.62, $p = 0.54$, Cohen's d = 0.10]. However, in individuals with TBI, while again first items showed the lowest error magnitude [$t(39)$'s > 7.30, p's < 0.001, Cohen's d's > 1.16], middle items showed a lower error magnitude than last items [$t(39) = 2.53$, $p = 0.02$, Cohen's d = 0.40], despite middle items having a higher frequency of errors.

Exploratory Analysis NIH Toolbox Episodic Memory Task—36 participants with TBI and 33 comparison participants completed neuropsychological testing via the NIH Toolbox[2]. Participants who did not complete the NIH Toolbox were unable to return to the lab to complete the assessment or had moved away. These results are shown in Table 2. We sought to assess whether our Temporal Order Task was more sensitive to memory deficits than the NIH Toolbox's Episodic Memory Subtest, itself a test of temporal order memory. First, group differences were assessed with an independent t-test on the raw adjacency scores. This t-test showed no group difference [$t(67) = 1.84$, $p = 0.07$, Cohen's d = 0.44]. The same t-test run on the fully-corrected (for age and education) T-scores did show a significant group difference [$t(67) = 2.09$, $p = 0.04$, Cohen's d = 0.50]. We also assessed how many participants scored 1.5 standard deviations below the neurotypical participants' average, a common cut-off used in standardised assessments and one we have used previously (Morrow et al., 2020; Rigon et al., 2020). Only four of the 36 participants

[2]This subset of participants still had no significant group differences in age, education, or sex [p's > 0.28]. The previous analyses of the Temporal Order Task were conducted again with only this subset of participants; all statistical results were the same with regards to significance, confirming that this subset of participants performed in line with reported results.

with TBI scored more than 1.5 standard deviations below the neurotypical participants' average. Meanwhile, nine of the 36 participants were 1.5 standard deviations below the neurotypical participant's average performance on Misplacement in the Temporal Order Task at even Set Size 5. It should be noted that fully corrected T-scores significantly correlated with performance on the Temporal Order Task for Set Sizes 5-9 in both groups [r's > −0.41, p's < 0.015]. Thus, while both tasks assess temporal order memory, a great deal of variance in performance may be attributed to the environmental support provided by the NIH Toolbox's task, including the timeline during, semantic framing, and non-random testing.

Ad-Hoc Correlations with Injury Severity and Time Since Injury—Per reviewer request, we also assessed whether initial injury severity, as measured by the Glasgow Coma Scale (GCS), or time since injury (TSI) were correlated with our main outcome measures of error Frequency and Magnitude. Note, age was significantly correlated with performance across both groups for Set Sizes 5-9, wherein older individuals committed more frequent errors [r's > 0.31, p's < 0.006], and older individuals made larger errors [r's > 0.37, p's < 0.001], fitting with evidence that age negatively impacts relational memory performance. Education was not significantly correlated with performance at any Set Size [r's < 0.13, p's > 0.26]. Thus, we conducted partial Correlations, controlling for age. Only 33 of the 40 individuals with TBI had GCS scores. All correlations of these measures with TSI at all set sizes and with GCS for Set Sizes 5-9 showed non-significant correlations [r's < 0.23, p's > 0.22]. There were significant correlations between error frequency and magnitude with GCS for Set Size 3 when uncorrected, [Frequency: $r = 0.42$, $p = 0.02$, Magnitude: $r = 0.38$, $p = 0.04$]; however these correlations were non-significant when correcting for multiple comparisons (Bonferroni p-value = 0.013, when correcting for even just four comparisons within measure). Thus, the present data suggest that temporal order memory impairments observed in moderate-severe TBI are not predicted by injury severity or time since injury.

DISCUSSION

We sought to determine whether relational memory deficits in individuals with moderate-severe TBI extended to temporal order memory, and, if so, whether these deficits were exacerbated by increased set size/memory load. As predicted, relative to neurotypical comparison participants, individuals with chronic, moderate-severe TBI showed deficits in how frequently they remembered the correct ordinal position of objects (Exact Hits), as well as the magnitude of their errors when they misplaced an object in order (Misplacement). However, performance was spared on both metrics at the smallest set size, three objects, with both groups performing at/near ceiling. Further, group differences increased with increasing set sizes for the magnitude of errors, but not the frequency of errors. Interestingly, regardless of set size, individuals with moderate-severe TBI showed no deficits in the frequency of errors for the first item in each list (primacy) but did show deficits in the magnitude of such errors. The frequency and magnitude of errors were both significantly greater in individuals with TBI for the last item of each list (recency). We discuss these findings in more detail below.

Individuals with TBI showed spared performance at Set Size 3, with both groups showing at/near ceiling performance for both Hits and Misplacement. Based on our previous finding in the face-scene task (Morrow et al., 2020), which showed that even with an immediate test, individuals with TBI showed relational memory deficts, we expected to see similar deficits at our smallest set size. However, the face-scene task involved an ongoing task wherein the appearance of test trials were unpredictable to the participant. In the present task, participants knew how many objects they would be shown, and had alerts between study and test to prepare them for each phase. With only three items, it is possible that short term memory may have been sufficient to support performance (Cowan, 2001). For example, given that the stimuli in the present study were unique, nameable objects, participants may have been able to utilise a rehearsal strategy (e.g., Dewar et al., 2011) that was effective for three items, but not more. That said, other studies should assess memory deficits in other domains using multiple set sizes or cognitive loads to confirm whether similar patterns exist across domains. Regardless, even a modest increase in set size, to five, resulted in significant performance deficits in the TBI group. Critically, some frequently used formal (e.g., Mini-Mental State Exam) and informal (ad-hoc, idiosyncratic, or in-house assessment batteries) cognitive evaluations and screening tools include simple memory tasks that only require the individual to remember three items, sometimes without needing to remember them in order. While further work is needed to assess whether memory for three items is spared in TBI even in a delayed test, our results suggest that tests of only a few items may be insensitive to the relational memory deficits observed in TBI, and further point to the need for more sensitive measures to capture relational memory deficits. Assessments that tap into relational processing and use measures with increased sensitity would not only assist in documenting relational memory deficits, but also in tracking and monitoring change or recovery across time.

We predicted that group differences in both the frequency and magnitude of errors would increase with increasing set size. However, group differences in Exact Hits (frequency) plateaued after set size 5. We previously used a similar measure in our assessements of spatial relational memory in focal hippocampal lesion patients (Horecka et al., 2018) and individuals with TBI (Rigon et al., 2020). The hippocampal lesion study also included an analysis of multiple set sizes (2, 3, 4, and 5). Similar to the current error frequency results, group differences between hippocampal lesion patients and comparison participants increased from 3 to 4 items per spatial set, but plateaued between 4 and 5 item sets. While additional, larger set sizes were not assessed, these data do suggest a similar pattern of findings between the hippocampal lesion patients and the individuals with TBI, lending further credence to the suggestion that hippocampal dysfunction underlies relational memory deficits in individuals with TBI. It should be noted that perhaps if memory were taxed even further, with larger lists than 9 items, group differences may begin to increase as well for error frequency. However, in contrast, despite group differences in the frequency of errors plateauing between five and nine items, the magnitude of these errors (i.e., Misplacement) continued to increase with increasing set size. We previously assessed group differences between hippocampal lesion patients and comparison participants in misplacement across set sizes (again 2, 3, 4, and 5 items per set) in spatial relational memory (Watson et al., 2013). Results showed a visual (though not statistically significant)

trend of increasing group differences in magnitude of errors with nameable objects. Given that the set sizes in the present study spanned a larger range, these data seem in line with the present findings that magnitude of errors increase with increasing set size. Taken together, these data suggest that looking at hit rate, or error rate, is not sufficient to capture performance deficits in relational memory; the magnitude of such errors should be assessed as well when possible. This magnitude effect may result in larger mistakes in real-world circumstances when individuals with TBI need to juggle more information.

We also conducted an exploratory analysis of group differences in primacy and recency effects. Previous work with temporal order memory has suggested that temporal order is mostly relative, rather than absolute, but that the first and last items serve as anchors for those relative positions, as compared to items appearing in the middle of a list (Henson, 1998, 1999). There were no group differences in error frequency or magnitude for the first item on each list, regardless of set size, suggesting relatively preserved memory for these items in individuals with TBI. However, group differences were present for both the frequency and magnitude of errors for the middle and final item of each list. With regards to error frequency, both groups showed the standard skewed U-shaped function (Henson, 1998), with performance for the earliest items being the best, but performance for the last items being superior to those in the middle of the list. Thus, when only considering the frequency data, our results would demonstrate that while individuals with TBI have overall relational memory deficits, they still show intact primacy and recency effects, at least relative to their performance on the middle items of lists. Interestingly however, while the size of group differences were equal for middle vs. last items when comparing error frequency, last items showed larger group differences than middle items when comparing error magnitude. That is, despite both groups making fewer errors for last compared to middle items, when individuals with TBI did make an error on a final item, it was on average a larger error compared to middle items. While there is technically more “room for error” for final items (i.e., a middle item can only be half the list off, while the final item can be off by the whole length of the list), this is true for both groups. Thus, our results suggest that, while individuals with TBI may be less likely to forget the final item of the list or series of events, when that item or event is forgotten, little information for its position will be maintained. These results are in line with work that suggests that even individuals with medial temporal lobe lesions can show intact primacy effects when using a cumulative rehearsal strategy (Dewar et al., 2011). Moreover, these results diverge from evidence that individuals with frontal lobe lesions show both impaired primacy and recency effects (Capitani, Della Sala, Logie, & Spinnler, 1992; Eslinger & Grattan, 1994), suggesting frontal dysfunction may not be the primary underlying cause of the present memory deficits. Further, these data again echo the assertion that assessments of error magnitude may be sensitive to memory deficits not detected by error frequency.

The importance of the increased sensitivity to memory deficits using misplacement is further magnified when compared to our standard neuropsychological assessment (NIH Toolbox’s Episodic Memory subtest), which identified fewer participants with temporal memory deficits than our temporal order task. This finding of decreased sensitivity from standard neuropsychological memory assessments echoes results found in our previous relational memory studies with individuals with TBI (Morrow et al., 2020; Rigon et al.,

2020), as well as the suggestion of others that additional temporal order measures be added to standardised assessments (see Vakil, 2006 for further discussion). Together, these results demonstrate that widely used neuropsychological tests may be insufficiently sensitive to underlying memory deficits across all patients and further echo calls for the field to combine the advances of cognitive neuroscience with the standardised testing of neuropsychology (McAndrews, Cohn, & Gold, 2020). As noted, many neuropsychological measures (such as initial screening tests) include too small of a set size to detect memory deficits in individuals with TBI. Further, other standardised tests employ measures of memory that are may not be sufficiently sensitive to such relational deficits. Our results have direct clinical relevance, suggesting future clinical assessments should employ more sophisticated methods for assessing memory deficits in patients. As demonstrated here, these assessments need not be long, as even short, five item temporal order tests show significant deficits in individuals with traumatic brain injury that are present, on average, years after their injury. Furthermore, educational attainment can buffer deficits observed in neurological populations on standardised tests. However, the present results showed no correlation with education. Further, even in our present sample, whose average educational attainment was above the average range for individuals who sustain a TBI (Gauthier et al., 2018), we still observe striking deficits in temporal order memory performance.

It is also important to note that temporal order memory performance in TBI varies depending on the structure of the task. The present task employed an intentional learning paradigm (i.e., participants were told that their memory for item order would be tested) and showed a deficit in participants with TBI in temporal order memory for objects at a set size of five and larger. However, previous work (Vakil et al., 1991) demonstrated that individuals with TBI and non-injured comparison participants show similar verbal temporal order memory abilities under incidental learning conditions (i.e., when participants are not told that their memory for item order will be tested), even when participants with TBI showed deficits under intentional learning instructions. Furthermore, in the NIH Toolbox subtest, the scenes share a theme, they are presented along with a timeline that has additional time to be studied, and participants get to visually reconstruct that timeline. It has been previously suggested that such environmental support may improve memory performance (Dulas & Duarte, 2013, 2014; Luo & Craik, 2008) and act to “scaffold” cognition (Park & Reuter-Lorenz, 2009; Reuter-Lorenz & Park, 2014), overcoming underlying deficits. Such scaffolding may underlie our finding that many participants showing impairments on our task were within the normal range for the NIH Toolbox assessment. It should be noted that the present design may be less naturalistic than previous experiments, such as those wherein participants are asked to remember a sequence of tasks they performed (Schmitter-Edgecombe & Seelye, 2012; Schmitter-Edgecombe & Wright, 2003). However, these more naturalistic tasks showed conflicting results, with one showing evidence of a temporal order memory deficits in TBI (Schmitter-Edgecombe & Seelye, 2012), while the other did not (Schmitter-Edgecombe & Wright, 2003). Therefore, it is important that future work attempts to identify contexts in which temporal order memory deficits may be minimised or even eliminated. Naturalistic settings may serve to support temporal order memory for some types of information, but everyday situations where someone needs to remember the order in which things happened, other forms of environmental support is rarely present, and

assessments that offer such support may be masking underlying deficits, which in turn may result in under-identification, and treatment, of such deficits.

Our finding of temporal order memory impairments in individuals with chronic, moderate-severe TBI, at set sizes as small as 5, adds to a growing body of evidence of relational memory deficits in TBI (Monti et al., 2013; Morrow et al., 2020; Rigon et al., 2020). Previous work has demonstrated that the hippocampus is critical for all forms of relational memory (Eichenbaum & Cohen, 2014; Konkel et al., 2008; Monti et al., 2014), and that damage to this region and its connections results in impaired relational binding and use of relational memory representations, including temporal order memory (Konkel et al., 2008). The prefrontal cortex has also been shown to contribute to temporal order memory (Duarte, Henson, Knight, Emery, & Graham, 2009; Rajah, Ames, & D'Esposito, 2008), and frontal lobe damage can impair temporal order memory performance (e.g., Shimamura, Janowsky, & Squire, 1990). That temporal order memory would be impaired in TBI makes sense given the vulnerabiltiy of both the medial temporal lobes and frontal lobes to TBI mechanisms (e.g., Adams et al., 1985; Atkins, 2011; Irimia & Van Horn, 2015; Palacios et al., 2013; Tate & Bigler, 2000; Vespa et al., 2010). Interestingly, in the TBI literature, temporal order memory (often referred to as context memory) is linked (sometimes exclusively) with frontal lobe function, while item memory (often referred to as content memory) is linked with medial temporal lobe function (Schmitter-Edgecombe & Seelye, 2012; Vakil et al., 1998; Wright et al., 2014). Yet, in at least one study, individuals with focal medial temporal lobe damage were similarly impaired on a temporal order task compared to those with focal frontal lobe lesions, while individuals with damage to both regions showed even larger temporal order memory deficits (Shimamura et al., 1990). In another study, temporal order memory performance correlated more often with measures of medial temporal lobe function than with measures of frontal lobe function in TBI (Schmitter-Edgecombe & Seelye, 2012). Thus, while damage to either the medial temporal lobes or the frontal lobes appears to place an indivdual at risk for deficits in temporal order memory, increased consideration of the role of the hippocampus and medial temporal lobes in temporal order memory in individuals with TBI is warranted. Indeed, in our own work on relational memory impairments in TBI, we have been struck by the success of tasks developed to recruit and measure the functions of the hippocampus in capturing relational memory deficits in TBI, and by the similiarity in deficit patterns between individuls with TBI and individuals with focal bilateral hippocampal damage, including in temporal order memory. That said, further clinical and imaging work is necessary to truly assess whether dysfunction in the hippocampus, prefrontal cortex, or in their interactions, underlies relational memory deficits in individuals with TBI. Indeed, there will likely be individual differences in the nature of dysfunction underlying such relational memory deficits.

Consideration of the role of relational memory (dys)function in individuals with TBI may be beneficial more broadly and may advance our understanding and remediation of a range of cognitive abilities that support behavioural performance and success in everyday settings. For example, hippocampal and medial temporal lobe function, and likewise dysfunction, have been linked to a myriad of seemingly disparate cognitive abilities, including those not typically considered to be within the confines of memory. These include communication and language (Duff & Brown-Schmidt, 2012), social cognition (Beadle, Tranel, Cohen, & Duff,

2013; Davidson, Drouin, Kwan, Moscovitch, & Rosenbaum, 2012; Spreng, 2013), decision-making (Gupta et al., 2009; Schlichting & Preston, 2017), perception (Aly, Ranganath, & Yonelinas, 2013; Aly & Turke-Brown, 2017; Barense, Gaffan, & Graham, 2007; Lee, Yeung, & Barense, 2012), and spatial navigation and environmental exploration (Maguire, Nannery, & Spiers, 2006; Voss, Gonsalves, Federmeier, Tranel, & Cohen, 2011; Voss, Warren, et al., 2011; Yee et al., 2014). Characterization of deficit profiles and treatment outcomes have long been hampered by issues of heterogeneity among individuals with TBI (Covington & Duff, 2021). However, we suggest that the presence and severity of relational memory impairments may provide a unifying account of these seemingly disparate behavioural deficits across cognitive domains, providing a new direction in TBI research worth further study.

In conclusion, the present study demonstrated that individuals with chronic, moderate-severe TBI exhibit relational memory deficits for temporal order information in lists as small as five items. Further, the magnitude of their errors increased with larger set sizes, demonstrating that cognitive load may be an important variable to consider in future studies, and that other assessments of relational memory may benefit from including a similar, highly sensitive measure of magnitude. Further, we note that the present temporal order memory deficits likely reflect a broader swath of deficits in relational memory and flexible cognition, potentially tied to underlying dysfunction in the hippocampus and its interactions with the PFC. Critically, we demonstrated that these relational memory impairments may not be sufficiently detected by commonly-used neuropsychological tests. Future studies may build on the present findings by assessing the relatonship between hippocampal dysfunction in TBI with other cognitive domains, as well as assessing individual differences in performance and underlying dysfunction. As impairments in relational memory underlie deficits in many behaviours needed for successful community reintegration, such work has the long-term possibility of leading to better predictions of functional outcomes and individualised cognitive rehabilitation after TBI.

Acknowledgments

This work was supported by NINDS grant R01 NS110661 to MCD and NJC.

We thank Nirav Patel for his help with data collection and all of the individuals who participated in this study. Portions of this work were previously presented at the International Brain Injury Association's 13th Annual World Congress on Brain Injury in Toronto, ON, Canada in March 2019.

References

Adams JH, Doyle D, Graham DI, Lawrence AE, McLellan DR, Gennarelli TA, … Sakamoto T. (1985). The contusion index: a reappraisal in human and experimental non-missile head injury. Neuropathol Appl Neurobiol, 11(4), 299–308. doi: 10.1111/j.1365-2990.1985.tb00027.x [PubMed: 4058674]

Aly M, Ranganath C, & Yonelinas AP (2013). Detecting Changes in Scenes: The Hippocampus Is Critical for Strength-Based Perception. Neuron, 78, 1127–1137. doi: 10.1016/j.neuron.2013.04.018 [PubMed: 23791201]

Aly M, & Turke-Brown NB (2017). How Hippocampal Memory Shapes, and Is Shaped by, Attention. In Duff MC & Hannula DE (Eds.), The Hippocampus from Cells to Systems (pp. 369–404): Springer.

Atkins CM (2011). Decoding hippocampal signaling deficits after traumatic brain injury. Translational Stroke Research, 2, 546–555. doi: 10.1007/s12975-011-0123-z [PubMed: 23227133]

Barense MD, Gaffan D, & Graham KS (2007). The human medial temporal lobe processes online representations of complex objects. Neuropsychologia, 45, 2963–2974. doi: 10.1016/j.neuropsychologia.2007.05.023 [PubMed: 17658561]

Beadle JN, Tranel D, Cohen NJ, & Duff MC (2013). Empathy in hippocampal amnesia. Front Psychol, 4, 1–12. doi: 10.3389/fpsyg.2013.00069 [PubMed: 23382719]

Beaver J, & Schmitter-Edgecombe M (2017). Multiple Types of Memory and Everyday Functional Assessment in Older Adults. Arch Clin Neuropsychol, 32(4), 413–426. doi: 10.1093/arclin/acx016 [PubMed: 28334170]

Cannavale CN, Hassevoort KM, Edwards CG, Thompson SV, Burd NA, Holscher HD, … Khan NA (2019). Serum Lutein is related to Relational Memory Performance. Nutrients, 11(4). doi: 10.3390/nu11040768

Capitani E, Della Sala S, Logie RH, & Spinnler H (1992). Recency, primacy, and memory: reappraising and standardising the serial position curve. Cortex, 28(3), 315–342. doi: 10.1016/s0010-9452(13)80143-8 [PubMed: 1395637]

Cicerone KD, Langenbahn DM, Braden C, Malec JF, Kalmar K, Fraas M, … Ashman T. (2011). Evidence-based cognitive rehabilitation: Updated review of the literature from 2003 through 2008. Archives of Physical Medicine and Rehabilitation, 92, 519–530. doi: 10.1016/j.apmr.2010.11.015 [PubMed: 21440699]

Cohen NJ (2015). Navigating life. Hippocampus, 25(6), 704–708. doi: 10.1002/hipo.22443 [PubMed: 25787273]

Cohen NJ, Ryan J, Hunt C, Romine L, Wszalek T, & Nash C (1999). Hippocampal system and declarative (relational) memory: summarizing the data from functional neuroimaging studies. Hippocampus, 9(1), 83–98. doi: 10.1002/(SICI)1098-1063(1999)9:1<83::AID-HIPO9>3.0.CO;2-7 [PubMed: 10088903]

Cooke DL, & Kausler DH (1995). Content memory and temporal memory for actions in survivors of traumatic brain injury. J Clin Exp Neuropsychol, 17(1), 90–99. doi: 10.1080/13803399508406585 [PubMed: 7608307]

Covington NV, & Duff MC (2021). Heterogeneity is a hallmark of traumatic brain injury, not a limitation: A new perspective on study design in rehabilitation research. American journal of speech-language pathology, 30(2S), 974–985. [PubMed: 33556261]

Cowan N (2001). The magical number 4 in short-term memory: a reconsideration of mental storage capacity. Behav Brain Sci, 24(1), 87–114; discussion 114–185. doi: 10.1017/s0140525x01003922 [PubMed: 11515286]

Davidson P, Drouin H, Kwan D, Moscovitch M, & Rosenbaum R (2012). Memory as social glue: close interpersonal relationships in amnesic patients. Fronteirs in Psychology, 3, 1–9. doi: 10.3389/fpsyg.2012.00531

Dewar M, Brown GD, & Della Sala S (2011). Restoring primacy in amnesic free recall: evidence for the recency theory of primacy. Cogn Neuropsychol, 28(6), 386–396. doi: 10.1080/02643294.2012.665802 [PubMed: 22360707]

Duarte A, Henson RN, Knight RT, Emery T, & Graham KS (2009). Orbito-frontal cortex is necessary for temporal context memory. J Cogn Neurosci, 22(8), 1819–1831. doi: 10.1162/jocn.2009.21316

Duff MC, & Brown-Schmidt S (2012). The hippocampus and the flexible use and processing of language. Front Hum Neurosci, 6, 1–11. doi: 10.3389/fnhum.2012.00069 [PubMed: 22279433]

Dulas MR, & Duarte A (2013). The influence of directed attention at encoding on source memory retrieval in the young and old: an ERP study. Brain Res.

Dulas MR, & Duarte A (2014). Aging Affects the Interaction between Attentional Control and Source Memory: An fMRI Study. J Cogn Neurosci doi: 10.1162/jocn_a_00663

Eichenbaum H, & Cohen NJ (2001). From Conditioning to Conscious Recollection: Multiple Memory Systems of the Brain.

Eichenbaum H, & Cohen NJ (2014). Can we reconcile the declarative memory and spatial navigation views on hippocampal function? Neuron, 83, 764–770. doi: 10.1016/j.neuron.2014.07.032 [PubMed: 25144874]

Eslinger PJ, & Grattan LM (1994). Altered serial position learning after frontal lobe lesion. Neuropsychologia, 32(6), 729–739. doi: 10.1016/0028-3932(94)90032-9 [PubMed: 8084427]

Gauthier S, LeBlanc J, Seresova A, Laberge-Poirier A, A Correa J, Alturki AY, … de Guise E (2018). Acute prediction of outcome and cognitive-communication impairments following traumatic brain injury: The influence of age, education and site of lesion. Journal of Communication Disorders, 73, 77–90. doi: 10.1016/j.jcomdis.2018.04.003 [PubMed: 29709658]

Gupta R, Duff MC, Denburg NL, Cohen NJ, Bechara A, & Tranel D (2009). Declarative memory is critical for sustained advantageous complex decision-making. Neuropsychologia, 47, 1686–1693. doi: 10.1016/j.neuropsychologia.2009.02.007 [PubMed: 19397863]

Hannula DE, Ryan JD, Tranel D, & Cohen NJ (2007). Rapid onset relational memory effects are evident in eye movement behavior, but not in hippocampal amnesia. J Cogn Neurosci, 19(10), 1690–1705. doi: 10.1162/jocn.2007.19.10.1690 [PubMed: 17854282]

Hannula DE, Tranel D, & Cohen NJ (2006). The long and the short of it: Relational memory impairments in amnesia, even at short lags. Journal of Neuroscience, 26, 8352–8359. doi: 10.1523/JNEUROSCI.5222-05.2006 [PubMed: 16899730]

Health, N. I. o. (2016). NIH Toolbox Scoring and Interpretation Guide for the iPad.

Heaton RK, Akshoomoff N, Tulsky D, Mungas D, Weintraub S, Dikmen S, … Gershon R (2014). Reliability and validity of composite scores from the NIH toolbox cognition battery in adults. Journal of the International Neuropsychological Society, 20, 588–598. doi: 10.1017/S1355617714000241 [PubMed: 24960398]

Henson RN (1998). Short-term memory for serial order: the Start-End Model. Cogn Psychol, 36(2), 73–137. doi: 10.1006/cogp.1998.0685 [PubMed: 9721198]

Henson RN (1999). Positional information in short-term memory: relative or absolute? Mem Cognit, 27(5), 915–927. doi: 10.3758/bf03198544

Horecka KM, Dulas MR, Schwarb H, Lucas HD, Duff M, & Cohen NJ (2018). Reconstructing relational information. Hippocampus, 28, 164–177. doi: 10.1002/hipo.22819 [PubMed: 29232494]

Irimia A, & Van Horn JD (2015). Functional neuroimaging of traumatic brain injury: Advances and clinical utility. Neuropsychiatric Disease and Treatment, 11, 2355–2365. doi: 10.2147/NDT.S79174 [PubMed: 26396520]

Konkel A, Warren DE, Duff MC, Tranel DN, & Cohen NJ (2008). Hippocampal amnesia impairs all manner of relational memory. Front Hum Neurosci, 2, 15. doi: 10.3389/neuro.09.015.2008 [PubMed: 18989388]

Lee ACH, Yeung LK, & Barense MD (2012). The hippocampus and visual perception. Front Hum Neurosci, 6, 1–17. doi: 10.3389/fnhum.2012.00091 [PubMed: 22279433]

Lucas HD, Duff MC, & Cohen NJ (2019). The Hippocampus Promotes Effective Saccadic Information Gathering in Humans. J Cogn Neurosci, 31(2), 186–201. doi: 10.1162/jocn_a_01336 [PubMed: 30188777]

Luo L, & Craik FI (2008). Aging and memory: a cognitive approach. Can J Psychiatry, 53(6), 346–353. [PubMed: 18616854]

Maguire EA, Nannery R, & Spiers HJ (2006). Navigation around London by a taxi driver with bilateral hippocampal lesions. Brain, 129, 2894–2907. doi: 10.1093/brain/awl286 [PubMed: 17071921]

Malec JF, Brown AW, Leibson CL, Flaada JT, Mandrekar JN, Diehl NN, & Perkins PK (2007). The Mayo classification system for traumatic brain injury severity. Journal of Neurotrauma, 24, 1417–1424. doi: 10.1089/neu.2006.0245 [PubMed: 17892404]

McAndrews MP, Cohn M, & Gold DA (2020). Infusing cognitive neuroscience into the clinical neuropsychology of memory. Curr Opin Behav Sci, 32, 94–101. doi: 10.1016/j.cobeha.2020.01.011

Mioni G, Grondin S, & Stablum F (2014). Temporal dysfunction in traumatic brain injury patients: primary or secondary impairment? Front Hum Neurosci, 8, 269. doi: 10.3389/fnhum.2014.00269 [PubMed: 24817847]

Mioni G, Mattalia G, & Stablum F (2013). Time perception in severe traumatic brain injury patients: a study comparing different methodologies. Brain Cogn, 81(3), 305–312. doi: 10.1016/j.bandc.2012.12.005 [PubMed: 23395855]

Mioni G, Stablum F, & Cantagallo A (2013). Time discrimination in traumatic brain injury patients. J Clin Exp Neuropsychol, 35(1), 90–102. doi: 10.1080/13803395.2012.755151 [PubMed: 23259647]

Monti J, Cooke G, Watson P, Voss M, Kramer A, & Cohen N (2014). Relating hippocampus to relational memory processing across domains and delays. Journal of Cognitive Neuroscience, 27, 234–245. doi: 10.1162/jocn

Monti JM, Voss MW, Pence A, McAuley E, Kramer AF, & Cohen NJ (2013). History of mild traumatic brain injury is associated with deficits in relational memory, reduced hippocampal volume, and less neural activity later in life. Front Aging Neurosci, 5, 1–9. doi: 10.3389/fnagi.2013.00041 [PubMed: 23430962]

Morrow EL, Dulas MR, Cohen NJ, & Duff MC (2020). Relational Memory at Short and Long Delays in Individuals With Moderate-Severe Traumatic Brain Injury. Front Hum Neurosci, 14, 112. [PubMed: 32327986]

Murdock BB Jr (1962). The serial position effect of free recall. Journal of Experimental Psychology, 64(5), 482.

Murray BL, Ramage AE, & Hopper T (2001). Memory impairments in adults with neurogenic communication disorders. Seminars in Speech and Language, 22, 127–136. doi: 10.1177/1073858411407206.Epub [PubMed: 11373067]

Neath I (1993). Distinctiveness and serial position effects in recognition. Memory & cognition, 21(5), 689–698. [PubMed: 8412719]

Palacios EM, Sala-Llonch R, Junque C, Fernandez-Espejo D, Roig T, Tormos JM, … Vendrell P (2013). Long-term declarative memory deficits in diffuse TBI: Correlations with cortical thickness, white matter integrity and hippocampal volume. Cortex, 49, 646–657. doi: 10.1016/j.cortex.2012.02.011 [PubMed: 22482692]

Park DC, & Reuter-Lorenz P (2009). The adaptive brain: aging and neurocognitive scaffolding. Annu Rev Psychol, 60, 173–196. doi: 10.1146/annurev.psych.59.103006.093656 [PubMed: 19035823]

Rajah MN, Ames B, & D'Esposito M (2008). Prefrontal contributions to domain-general executive control processes during temporal context retrieval. Neuropsychologia, 46(4), 1088–1103. doi: S0028–3932(07)00370–3 [pii] 10.1016/j.neuropsychologia.2007.10.023 [PubMed: 18155254]

Reuter-Lorenz PA, & Park DC (2014). How does it STAC up? Revisiting the scaffolding theory of aging and cognition. Neuropsychol Rev, 24(3), 355–370. doi: 10.1007/s11065-014-9270-9 [PubMed: 25143069]

Rigon A, Schwarb H, Klooster N, Cohen NJ, & Duff MC (2020). Spatial relational memory in individuals with traumatic brain injury. J Clin Exp Neuropsychol, 42(1), 14–27. doi: 10.1080/13803395.2019.1659755 [PubMed: 31475607]

Rubin RD, Schwarb H, Lucas HD, Dulas MR, & Cohen NJ (2017). Dynamic Hippocampal and Prefrontal Contributions to Memory Processes and Representations Blur the Boundaries of Traditional Cognitive Domains. Brain Sci, 7(7), 1–17. doi: 10.3390/brainsci7070082

Salmond CH, Menon DK, Chatfield DA, Pickard JD, & Sahakian BJ (2006). Changes over time in cognitive and structural profiles of head injury survivors. Neuropsychologia, 44, 1995–1998. doi: 10.1016/j.neuropsychologia.2006.03.013 [PubMed: 16620889]

Schlichting ML, & Preston AR (2017). The Hippocampus and Memory Integration: Building Knowledge to Navigate Future Decisions. In Duff MC & Hannula DE (Eds.), The Hippocampus from Cells to Systems: Structure, Connectivity, and Functional Contributions to Memory and Flexible Cognition (pp. 405–437). New York, NY: Springer.

Schmitter-Edgecombe M, & Seelye AM (2012). Recovery of content and temporal order memory for performed activities following moderate to severe traumatic brain injury. J Clin Exp Neuropsychol, 34(3), 256–268. doi: 10.1080/13803395.2011.633497 [PubMed: 22220505]

Schmitter-Edgecombe M, & Wright MJ (2003). Content memory and temporal order memory for performed activities after severe closed-head injury. J Clin Exp Neuropsychol, 25(7), 933–948. doi: 10.1076/jcen.25.7.933.16493 [PubMed: 13680441]

Shimamura AP, Janowsky JS, & Squire LR (1990). Memory for the temporal order of events in patients with frontal lobe lesions and amnesic patients. Neuropsychologia, 28(8), 803–813. doi: 10.1016/0028-3932(90)90004-8 [PubMed: 2247207]

Snodgrass JG, & Vanderwart M (1980). A standardized set of 260 pictures: norms for name agreement, image agreement, familiarity, and visual complexity. J Exp Psychol Hum Learn, 6(2), 174–215. doi: 10.1037//0278-7393.6.2.174 [PubMed: 7373248]

Spreng NR (2013). Examining the role of memory in social cognition. Front Psychol, 4, 1–2. doi: 10.3389/fpsyg.2013.00437 [PubMed: 23382719]

St Jacques P, Rubin DC, LaBar KS, & Cabeza R (2008). The short and long of it: neural correlates of temporal-order memory for autobiographical events. J Cogn Neurosci, 20(7), 1327–1341. doi: 10.1162/jocn.2008.20091 [PubMed: 18284345]

Tate DF, & Bigler ED (2000). Fornix and hippocampal atrophy in traumatic brain injury. Learning and Memory, 7, 442–446. doi: 10.1101/lm.33000 [PubMed: 11112803]

Vakil E (2005). The effect of moderate to severe traumatic brain injury (TBI) on different aspects of memory: A selective review. J Clin Exp Neuropsychol, 27, 977–1021. doi: 10.1080/13803390490919245 [PubMed: 16207622]

Vakil E (2006). The added value of a temporal order judgment measure to the Rey Auditory Verbal Learning Test (AVLT). In Poreh AM (Ed.), The Quantified Process Approach to Neuropsychological Assessment (pp. 83–92). New York, NY: Taylor & Francis.

Vakil E, Blachstein H, & Hoofien D (1991). Automatic temporal order judgment: the effect of intentionality of retrieval on closed-head-injured patients. J Clin Exp Neuropsychol, 13(2), 291–298. doi: 10.1080/01688639108401044 [PubMed: 1864916]

Vakil E, Sherf R, Hoffman M, & Stern M (1998). Direct and indirect memory measures of temporal order and spatial location: control versus closed-head injury participants. Neuropsychiatry Neuropsychol Behav Neurol, 11(4), 212–217. [PubMed: 9845413]

Vakil E, & Tweedy JR (1994). Memory for Temporal Order and Spatial Position Information: Tests of the Automatic-Effortful Distinction. Cognitive and Behavioral Neurology, 7(4), 281–288.

van Asselen M, Van der Lubbe RH, & Postma A (2006). Are space and time automatically integrated in episodic memory? Memory, 14(2), 232–240. [PubMed: 16484112]

van der Meer E, Beyer R, Heinze B, & Badel I (2002). Temporal order relations in language comprehension. J Exp Psychol Learn Mem Cogn, 28(4), 770–779. doi: 10.1037//0278-7393.28.4.770 [PubMed: 12109767]

Vespa PM, McArthur DL, Xu Y, Eliseo M, Etchepare M, Dinov I, … Hovda D. (2010). Nonconvulsive seizures after traumatic brain injury are associated with hippocampal atrophy. Neurology, 75, 792–798. doi: 10.1212/WNL.0b013e3181f07334 [PubMed: 20805525]

Voss JL, Gonsalves BD, Federmeier KD, Tranel D, & Cohen NJ (2011). Hippocampal brain-network coordination during volitional exploratory behavior enhances learning. Nature neuroscience, 14, 115–122. doi: 10.1038/nn.2693 [PubMed: 21102449]

Voss JL, Warren DE, Gonsalves BD, Federmeier KD, Tranel D, & Cohen NJ (2011). Spontaneous revisitation during visual exploration as a link among strategic behavior, learning, and the hippocampus. Proceedings of the National Academy of Sciences, 108, E402–E409. doi: 10.1073/pnas.1100225108

Watson PD, Voss JL, Warren DE, Tranel D, & Cohen NJ (2013). Spatial reconstruction by patients with hippocampal damage is dominated by relational memory errors. Hippocampus, 23(7), 570–580. doi: 10.1002/hipo.22115 [PubMed: 23418096]

Wilson BA (1998). Recovery of cognitive functions following nonprogressive brain injury. Current Opinion in Neurobiology, 8, 281–287. [PubMed: 9635214]

Wright MJ, Wong AL, Obermeit LC, Woo E, Schmitter-Edgecombe M, & Fuster JM (2014). Memory for performed and observed activities following traumatic brain injury. J Clin Exp Neuropsychol, 36(3), 268–277. doi: 10.1080/13803395.2014.884543 [PubMed: 24524393]

Yee LTS, Warren DE, Voss JL, Duff MC, Tranel D, & Cohen NJ (2014). The hippocampus uses information just encountered to guide efficient ongoing behavior. Hippocampus, 24, 154–164. doi: 10.1002/hipo.22211 [PubMed: 24123615]

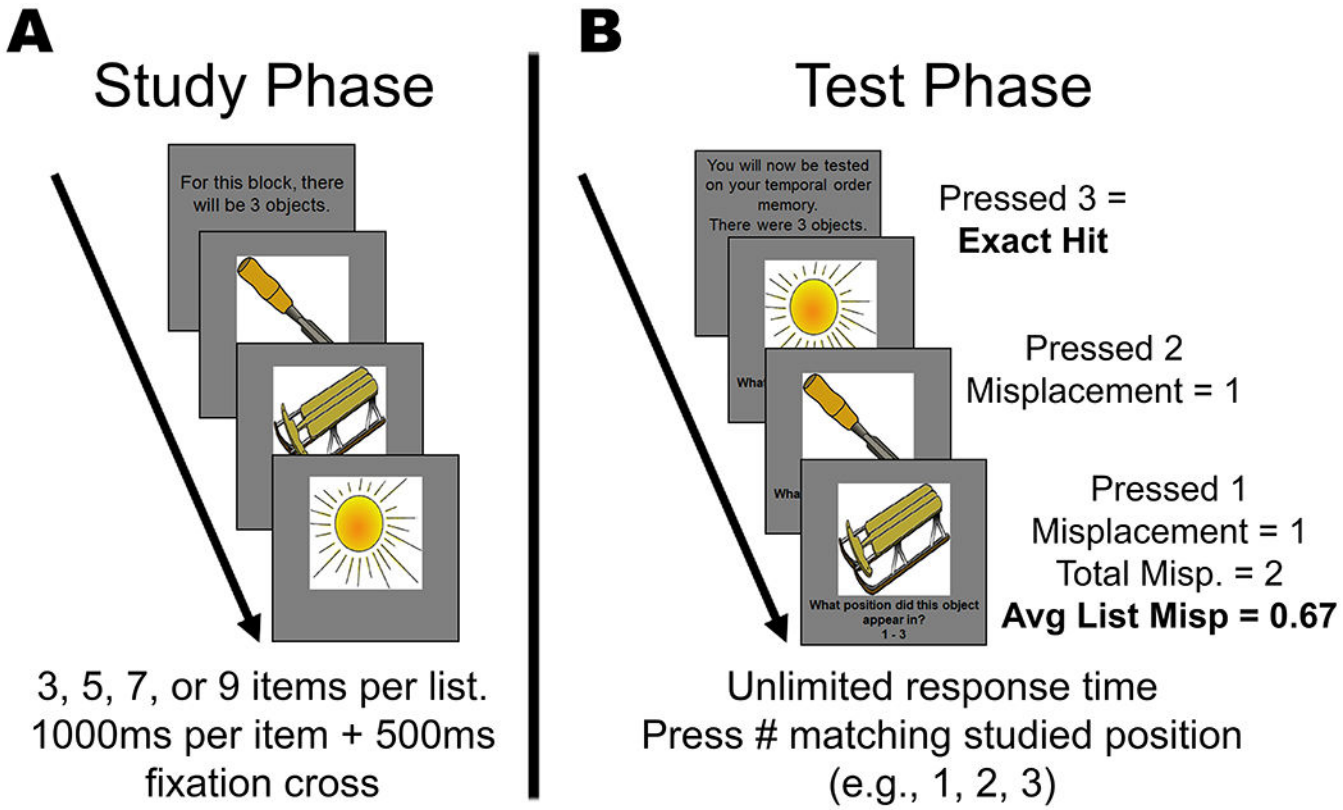

Figure 1. Experimental Paradigm.

An example of a Set Size 3 Study block is shown in A. The corresponding Test Phase is shown in B. Example responses, and the calculations for misplacement (error magnitude) are also shown.

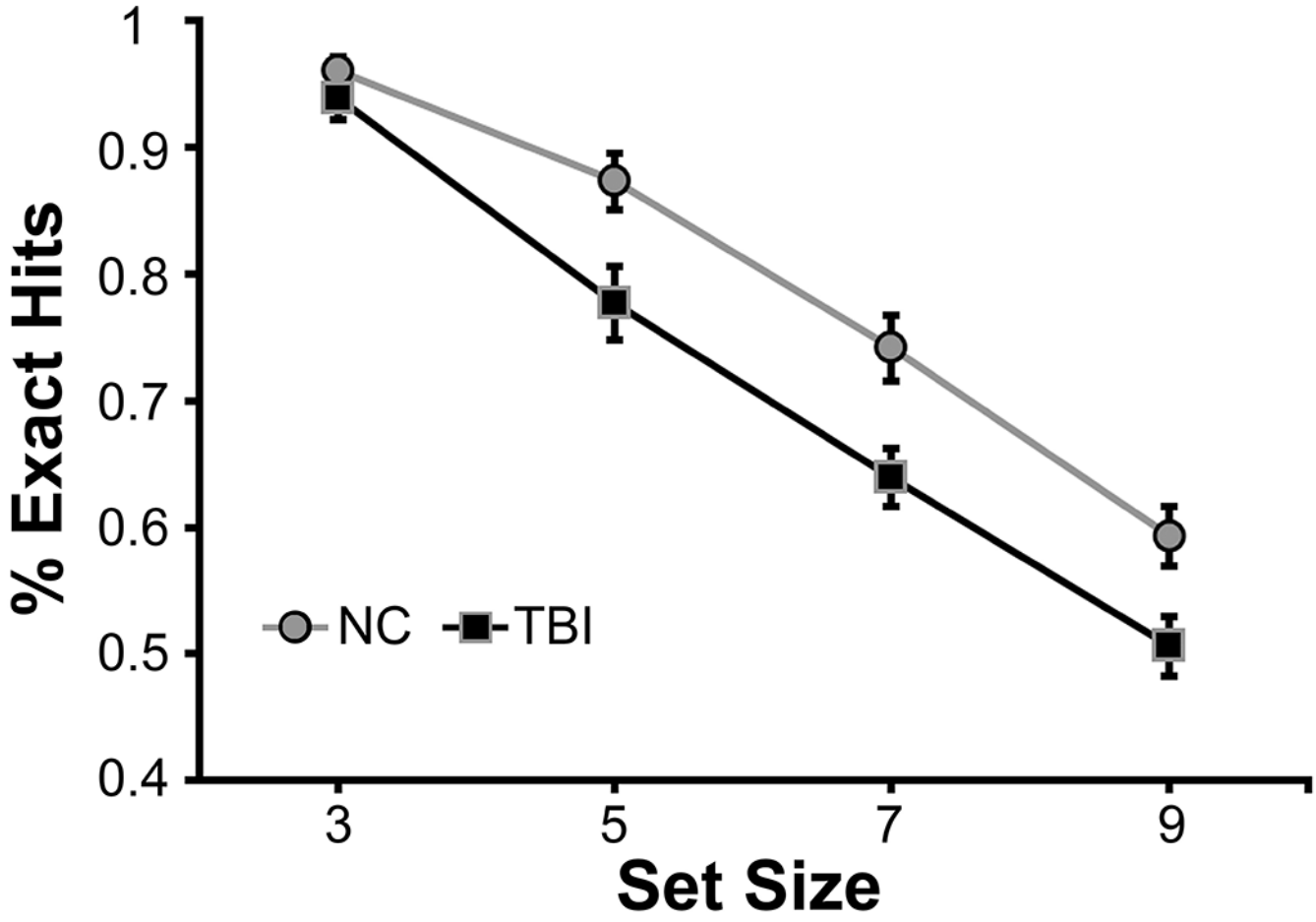

Figure 2. Exact Hits Performance.

Performance is shown as % of Exact Hits (Frequency). NC = Neurotypical Comparison Participants, TBI = Individuals with Traumatic Brain Injury. Error bars represent Standard Error.

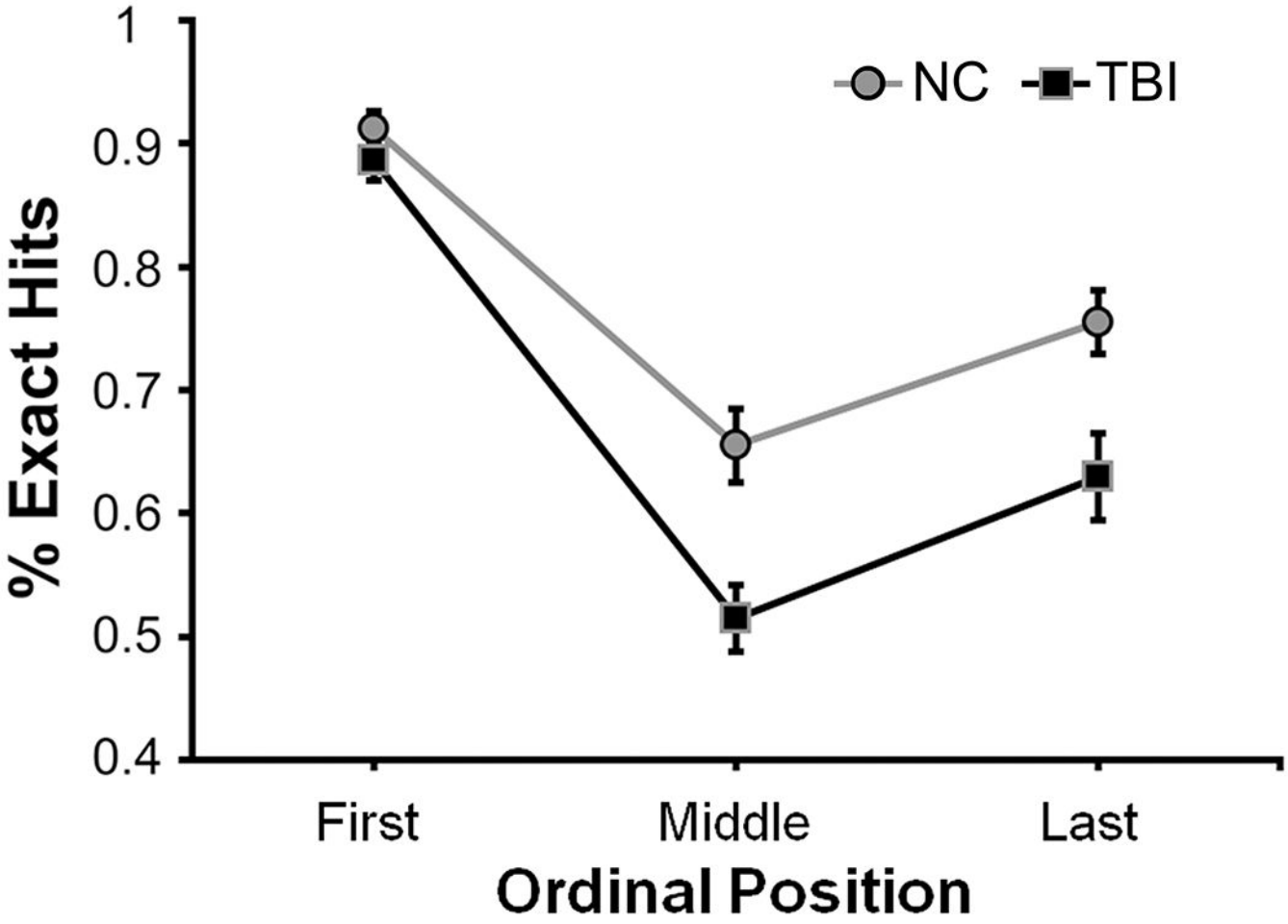

Figure 3. Average Misplacement.

Performance is shown as average absolute misplacement (Magnitude) at the single item level, i.e., how many ordinal positions off were items on average. NC = Neurotypical Comparison Participants, TBI = Individuals with Traumatic Brain Injury. Error bars represent Standard Error.

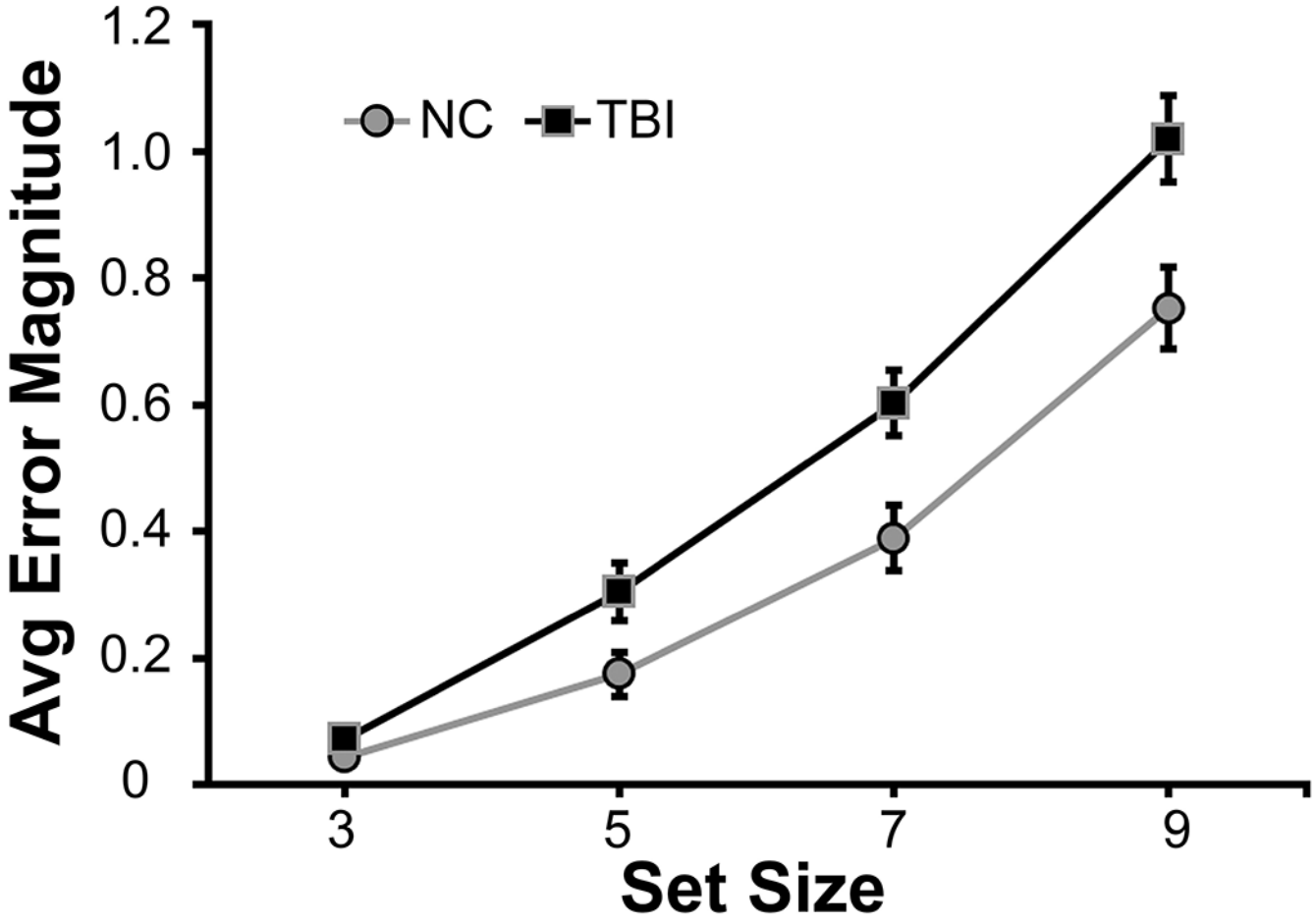

Figure 4. Frequency of Errors for First, Middle, and Last Items.

Performance is shown as % of Exact Hits for the first (primacy), middle, and last (recency) item of each list. NC = Neurotypical Comparison Participants, TBI = Individuals with Traumatic Brain Injury. Error bars represent Standard Error.

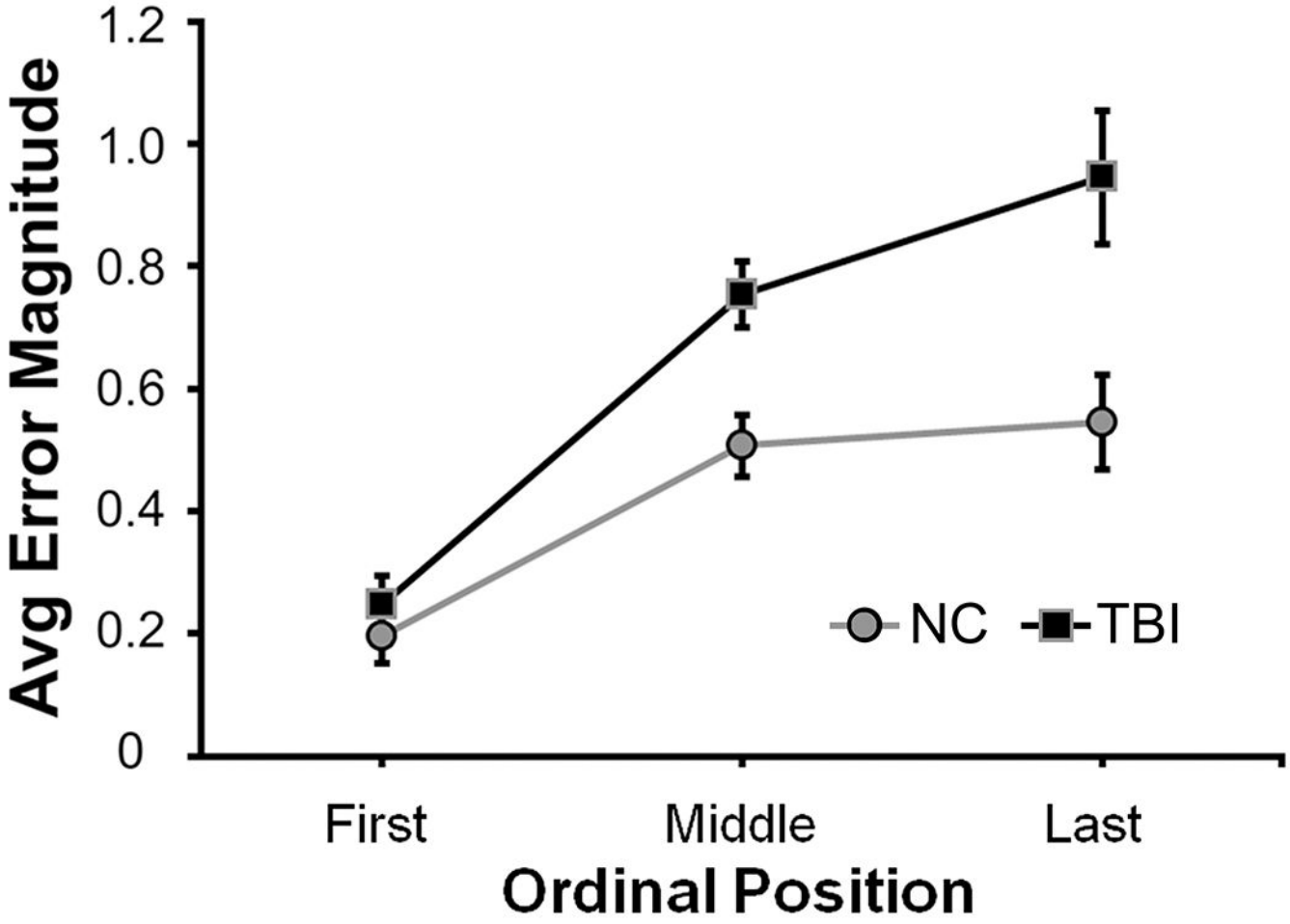

Figure 5. Magnitude of Errors for First, Middle, and Last Items.

Performance is shown as average absolute distance of errors for the first (primacy), middle, and last (recency) item of each list. NC = Neurotypical Comparison Participants, TBI = Individuals with Traumatic Brain Injury. Error bars represent Standard Error.

Table 1.

Demographic & injury information for participants with TBI.

ID	Age	Edu	Etiology	TSO	LOC	Neuroimaging	GCS	PTA
5002	40-45	16	Non-motorised vehicle accident	218	LOC >30 minutes	Intracranial haemorrhage	3	>24 hours
5003	22-27	16	Ped vs. auto	15	N/A	Subdural hematoma	11	>24 hours
5005	29-34	16	MVA	22	LOC >30 minutes	SAH; IVH	14	>24 hours
5006	52-57	12	MCC	406	LOC >30 minutes	Intracranial hematoma	N/A	>24 hours
5010	31-36	16	Ped vs. auto	11	N/A	SAH; intracranial haemorrhage	6	>24 hours
5011	41-46	12	Fall from height	48	N/A	SAH; frontotemporal contusion; epidural hematoma	15	>24 hours
5013	27-32	18	Ped vs. auto	19	No LOC	SAH	15	< 24 hours
5014	48-53	16	MVA	180	LOC >30 minutes	N/A	N/A	>24 hours
5016	18-23	16	MVA	13	LOC >30 minutes	SAH	13	>24 hours
5017	28-33	16	Ped vs. auto	163	LOC >30 minutes	SAH; intraventricular haemorrhage	4	>24 hours
5018	35-40	18	MVA	143	LOC >30 minutes	SAH	3	>24 hours
5019	42-47	16	Ped vs. auto	24	N/A	SAH; SDH	6	>24 hours
5020	46-51	16	MCC	60	LOC >30 minutes	SAH	N/A	>24 hours
5021	38-43	18	MVA	25	LOC >30 minutes	Epidural hematoma; SAH	3	>24 hours
5027	27-32	16	Ground-level fall	10	LOC >30 minutes	SAH	9	>24 hours
5029	30-35	14	Non-motorised vehicle accident	6	LOC < 30 minutes	SDH; intraparenchymal haemorrhage; SAH	14	< 24 hours
5031	51-56	14	Struck by object	7	No LOC	SDH; SAH; IPH	13	N/A
5034	28-33	16	MVA	31	LOC >30 minutes	SAH	3	>24 hours
5036	41-46	16	MVA	6	No LOC	SAH	15	< 24 hours
5037	37-42	12	MVA	37	LOC < 30 minutes	Diffuse intracranial swelling	3	>24 hours
5038	40-45	16	Ground-level fall	18	LOC >30 minutes	SDH; multifocal haemorrhages; post-traumatic haemorrhagic contusions	N/A	>24 hours
5040	37-42	12	MVA	69	LOC >30 minutes	SDH; SAH; uncal herniation	3	>24 hours
5041	30-35	16	MVA	53	No LOC	Negative	10	>24 hours
5042	39-44	16	MVA	20	LOC < 30 minutes	SDH; arachnoid haemorrhage	9	>24 hours
5044	24-29	12	Non-motorised vehicle accident	75	LOC < 30 minutes	SDH; intraparenchymal haemorrhage	15	>24 hours
5046	42-47	18	Non-motorised vehicle accident	46	LOC < 30 minutes	SAH	14	>24 hours
5047	23-28	16	Assault	16	LOC < 30 minutes	SDH	15	< 24 hours
5048	44-49	16	MVA	336	LOC >30 minutes	N/A	N/A	>24 hours
5050	29-34	18	Ground-level fall	16	LOC >30 minutes	SAH; intraparenchymal haemorrhages	15	< 24 hours
5052	44-49	14	MVA	9	LOC <30 minutes	SDH; SAH	9	>24 hours
5054	19-24	12	MVA	33	LOC<30 minutes	SDH	14	>24 hours

ID	Age	Edu	Etiology	TSO	LOC	Neuroimaging	GCS	PTA
5055	27-32	12	MVA	67	N/A	Haemorrhagic shearing; scattered SAH; SDH	4	>24 hours
5056	22-27	12	Non-motorised vehicle accident	30	LOC >30 minutes	Haemorrhagic shear injury	11	>24 hours
5057	21-26	12	MVA	18	No LOC	SDH	N/A	No
5058	29-34	12	MCC	109	LOC < 30 minutes	SAH; SDH; parenchymal haemorrhage	8	>24 hours
5059	27-32	16	MCC	99	Unknown	Extra-axial haemorrhage	14	< 24 hours
5060	36-41	12	MVA	115	LOC >30 minutes	Negative	3	>24 hours
5061	36-41	18	Fall from height	56	LOC < 30 minutes	SDH	N/A	< 24 hours
5062	19-24	12	MVA	81	LOC < 30 minutes	SDH	15	< 24 hours
5068	20-25	16	Fall from height	39	LOC < 30 minutes	Subdural haemorrhage; epidural hematoma	3	>24 hours

ID = participant ID number. Age is presented as a five year range to protect participants' identities. Education (edu) reflects years of highest degree obtained. MVA = motor vehicle accident. MCC includes both motorcycle and snowmobile accidents. Non-motor = non-motorised vehicle accident. Ped vs. auto = participant was hit by car while walking or running. Time since onset (TSO) is presented in months. Loss of consciousness (LOC) is presented in minutes. SDH = subdural haematoma. SAH = subarachnoid haemorrhage. IPH = intraparenchymal haemorrhage. IVH = intraventricular haemorrhage. Glasgow Coma Scale (GCS) is total score at time of first post-injury measurement. PTA = post-traumatic amnesia. Hrs = hours. N/A = information was not available.

Table 2.

NIH Toolbox scores for participants with TBI and comparison participants.

	Raw Adjacency Scores	Fully-corrected T-Scores
TBI	16.80 (SD = 8.65)	52.80 (SD = 11.18)
Comparison	20.50 (SD = 7.73)	58.70 (SD = 12.24)