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New Insights in Implicit Sequence Learning of Adults With Traumatic Brain Injury: As Measured by an Ocular Serial Reaction Time (O-SRT) Task

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Objective: We investigated the effect of traumatic brain injury (TBI) on implicit sequence learning (ISL) and its relation with demographic, clinical, and working memory (WM) capacity using an eye-tracked variant of the standard serial reaction time (RT; SRT) task. Besides RT, this ocular SRT (O-SRT) task enables generation of correct anticipations (CA) and stucks, reflecting other critical aspects of ISL. ***Method:*** ISL was tested in 26 individuals with TBI and 28 healthy controls using the O-SRT task. Mixed analyses of variance were conducted to analyze RT and CA in three phases: learning, interference, and recovery from interference. The average number of stucks was compared with an independent-samples *t* test. Finally, Pearson correlation analyses of ISL with demographic, clinical, and WM capacity measures were performed. ***Results:*** Based on RT, ISL was impaired in the TBI group. However, CA demonstrated improved learning, but with deficits in the interference and recovery from interference phases. Stucks were more frequent in the TBI group, which affected RT and CA measures. Neither demographic nor clinical factors were associated with ISL. Verbal, but not spatial, WM capacity was impaired in the TBI group, and spatial WM capacity positively correlated with ISL in controls only. ***Conclusion:*** We suggest that the high TBI group stuck rate can be attributed to lack of initiative and/or conservative response bias associated with TBI, and view it as a main cause leading to deficits in ISL. Unlike controls, the TBI group could not muster their relatively preserved spatial WM capacity to support their ISL performance.

Key Points
Question: What is the question this paper addresses? Shedding light on inconsistent findings of implicit sequence learning abilities in individuals with traumatic brain injury (TBI) using an eye tracked version of the serial RT (SRT) task, which besides RT, provides two additional measures: correct anticipations (CA) and stucks. ***Findings:*** What are the primary findings? Analyses of RT and CA revealed impaired implicit sequence learning in TBI which was linked to a higher stuck rate and associated with a lack of initiative and/or conservative response bias in TBI. ***Importance:*** What are the key scientific and practice implications of the findings? Eye movement measures significantly contribute to understanding implicit sequence learning abilities in TBI, as assessed with the SRT task. ***Next Steps:*** What directions should be explored in future research? Evaluating the influence of other factors on ISL in TBI, such as length of learning course as well as gender and long-term TBI effects.

Keywords: implicit sequence learning, procedural learning, eye tracking, SRT, TBI

Traumatic brain injury (TBI) is a health problem with growing incidence worldwide (Dewan et al., 2018), caused by impact to head or body that results in neuropathological damage. The frontal and temporal lobes are particularly susceptible to injury because of their location in the anterior and cranial fossa of the skull (Bigler, 2007), and predominantly impaired in TBI regardless of underlying pathophysiology (Stuss, 2011). Furthermore, occipital regions are also frequently affected along with subcortical regions, including the hippocampus and basal ganglia (Bendlin et al., 2008; Bigler & Maxwell, 2011). Besides damage to neuronal cells and other neuropathology, TBI leads to axonal damage that impairs the interconnection of different sections of the brain (Bigler & Maxwell, 2011; Mckee & Daneshvar, 2015).

TBI leads to serious consequences in cognitive, emotional, and behavioral functioning (Azouvi et al., 2017; Mateer & Sira, 2007; Mckee & Daneshvar, 2015). Frontal lobe injuries in TBI have been

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associated with lack of initiative, impaired organization and planning ability, impulsivity, disinhibition, lack of empathy, and more (Stuss, 2011). Explicit memory impairment is among the most prominent disturbances that occur following TBI (Vakil, 2005), and has been studied extensively. In contrast, only a few studies have been conducted to evaluate aspects of implicit memory such as procedural or skill learning in individuals with TBI. Procedural or skill learning is defined as learning which results following repeated practice. It encompasses the learning of motor, cognitive, and perceptually based procedures, including navigation, sequences, rules, categories, and probabilities. Procedures can be acquired partly through explicit awareness, though primarily they are considered to be learned implicitly, without conscious retrieval of information regarding the procedure (Clegg et al., 1998; Reber, 1993). Different types of tasks have been developed that evaluate various aspects of procedural learning. For an overview of the most prevalently used tasks, see Gofer-Levi et al. (2014). In brief, these assessment tools can be categorized according to their cognitive and attentional demands (e.g., motor, cognitive, conceptual, or perceptual; Vakil & Hoffman, 2004), and type of procedure (e.g., rules, optimal sequence, probabilistic repetition of relations, deterministic repetition of a given sequence).

To date, findings regarding procedural learning in TBI are inconsistent. Due to the low number of studies conducted and the different types of tasks used, as well as the wide range of time after injury onset, it is challenging to draw clear conclusions. Most studies that examined cognitive or conceptual procedural learning assessed with the mental rotation task or tower of Hanoi puzzle did not observe any remarkable deficits in TBI (Ewert et al., 1989; Timmerman & Brouwer, 1999; Vakil & Lev-Ran Galon, 2014), with the exception of Vakil et al. (2001). Similarly, the assessment of perceptual procedural learning with an implicit matrix task or the mirror reading task (Ewert et al., 1989; Nissley & Schmitter-Edgecombe, 2002; Vakil & Lev-Ran Galon, 2014), as well as the testing of manual motor procedural learning with the pursuit rotor task (Ewert et al., 1989; Rigon et al., 2019) revealed no impairments. However, in an oculomotor procedural learning task, deficits were observed in individuals with TBI (Kraus et al., 2010). In this task, participants fixated on a center point, at each side of which a target appeared in the same location in an even rhythm. Participants with TBI anticipated those two targets significantly less often prior to their appearance at their fixed location. Studies that investigated implicit sequence learning (ISL), an essential process underlying procedural learning, provided a mixed picture of either preserved or impaired ISL in TBI (McDowall & Martin, 1996; Mutter et al., 1994; Vakil et al., 2002). ISL is commonly assessed with the serial reaction time (SRT) task (Nissen & Bullemer, 1987), which has become the hallmark task throughout research literature. Unbeknown to participants, in this task they are presented with four squares on the screen appearing in a repeated spatial sequence. Participants are asked to respond as fast as possible by pressing a key whose location corresponds to its position in the appearance of the square. Following several learning blocks (usually 6), a block with a new sequence is presented. ISL is generally expressed in two measures: the first is the decrease in RT during the learning blocks, which has been interpreted to reflect increased correct anticipation of the subsequent spatial locations, and the second is increased RT when the new sequence is introduced. The latter is considered to be a purer measure of ISL, because the former, in addition to ISL, also reflects general learning of the spatial location mapping of the stimuli on the screen and its corresponding key press, which is viewed as stimulus-response (S-R) mapping.

Despite wide use of the SRT task throughout research literature assessing ISL in healthy and clinical populations, studies using this task in TBI samples are sparse. Mutter et al. (1994) tested 12 controls and 23 individuals with TBI that were divided into a mild ($n = 11$) and a moderate-to-severe TBI ($n = 12$) subgroup. Whereas the mild group did not differ from controls, the moderate-to-severe TBI group demonstrated impairments in sequence acquisition. However, this group did not differ from controls when asked explicitly to generate the learned sequence. In contrast, McDowall and Martin (1996) tested individuals with severe TBI ($n = 20$), and although the TBI group was generally slower, no impairment was observed in the acquisition rate of the sequence, compared to controls ($n = 20$). Deficits in both acquisition and generation of the sequence were detected in the severe TBI group ($n = 20$) studied by Vakil et al. (2002). In a follow-up analysis, the authors observed an interference effect (i.e., increased RT when a new sequence is presented) in all controls ($n = 20$), while only about half of the TBI group showed this effect. Subsequently, the TBI group was split into two subgroups according to whether they did or did not show an interference effect. The TBI subgroups did not differ in age, education or severity of injury, nor did any of these measures correlate with the interference score. These results imply that neither demographic nor clinical factors played a significant role in ISL.

One aspect that may have contributed to the different outcome of ISL in TBI is the rather wide range of time after onset. In the study by Mutter et al. (1994) this variable ranged from 112–1,049 days, in the study by Vakil et al. (2002) from 150 to 1,410 days, and in the study by McDowall et al. (1996) participants were at least 180 days postinjury (the maximal time after onset was not mentioned).

Another factor possibly related to ISL may be working memory (WM). Deficits in verbal as well as spatial WM are common in individuals with TBI (Dunning et al., 2016; McAllister et al., 2006), and abnormal frontal brain activation during a WM task has been reported (Kasahara et al., 2011). WM has been associated primarily with the dorsolateral prefrontal cortex (DLPFC). The facts that in healthy participants, noninvasive brain stimulation of the DLPFC increases WM performance, as revealed in the meta-analyses of Brunoni and Vanderhasselt (2014), and that the same region was reported to be activated during the assessment of ISL by the SRT (Willingham et al., 2002), points to a link between WM and ISL. Nevertheless, this relationship is debatable (Janacsek & Nemeth, 2013). For example, Bo et al. (2011) found that better ISL was related to higher verbal and visuospatial WM in young adults, and in older adults only to verbal WM. On the contrary, the study by Virag et al. (2015) detected a negative correlation between verbal WM measures and ISL: namely, the lower the verbal WM, the better the ISL. To the best of our knowledge, the effect of WM on ISL has not yet been investigated with individuals who have sustained TBI.

In the present study ISL was tested in individuals following TBI, using the oculomotor activated version of the ocular SRT (O-SRT). The O-SRT is an eye tracked variant of the SRT task, developed by Vakil et al. (2017). The advantage of using eye

tracking is that it enables generation of a new measure called correct anticipation (CA), in addition to RT, which is typically generated from this task. Eye tracking enables measurement of the number of CAs by recording whether the eyes move toward the next correct position during the 500-ms interval between targets (Vakil et al., 2017). This measure reflects CA of the subsequent spatial location directly, whereas the RT measure is an indirect measure of CAs. Presumably, CA of the spatial location of the next stimulus yields a faster RT. In addition to the CA measure, this paradigm enables us to generate a "stucks" measure, namely, the number of times the participant remains fixated on the previous location and then moves to the next location only when the new stimulus appears, rather than during the 500-ms delay between stimuli.

The O-SRT test also allows measurement of RT in two ways: first, the standard RT by key press as assessed in the manually activated (MA) version. Second, RT based on eye movements when using the oculomotor activated (OA) version. In the OA version, an eye fixation on target for 100 ms replaces key pressing. Results of the OA version and of the standard MA version yielded similar sequence learning rates (although the OA RT was faster overall than the MA RT; Vakil et al., 2017). Consistent with previous findings in the literature (Ferraro et al., 1993; Vakil et al., 2002), when the new sequence was introduced, RT in the MA version did not revert to baseline level because of the general skill (S-R) learned, and was carried over to the new sequence. However, in the OA version RT returned to baseline level because it does not involve the general skill of associating spatial location with the corresponding key. The researchers interpreted this finding as an indication that the OA version of the O-SRT task generates purer sequence learning measures.

The goal of the present study was to elucidate the underlying cognitive processes of ISL following TBI, by analyzing and integrating the three oculomotor measures: RT, CA and stucks. Furthermore, we were interested in investigating ISL at a relatively early post TBI phase, and therefore limited our sample to a maximum of one year post injury. We also aimed to minimize the range of time after onset in order to have a more homogenous sample, in comparison to previous SRT studies (Mutter et al., 1994; Vakil et al., 2002) that used a longer range of time after onset. In addition, evaluation of the impact of demographic and clinical factors, as well as the role of WM capacity in acquisition of ISL, will provide further information contributing to the complex picture of ISL in TBI.

Method

Participants

Two groups participated in the present study: a group following TBI and a control group (without brain injury). A total of 28 individuals with TBI participated in the study. Two participants had to be excluded due to technical registration problems (connection loss) of the eye tracker device, resulting in a sample of three females and 23 males, with ages ranging from 19 to 53 years (M = 31.7, SD = 11.9). Individuals with TBI were recruited from a population of patients admitted to the Loewenstein Rehabilitation Center (Israel), for rehabilitation following TBI. The diagnosis of TBI was made by a physician, based on anamnestic, clinical, and computed tomography (CT) data. Participants included were individuals with complicated mild, moderate, or severe TBI with maximum time after onset of 1 year, in stable medical condition, and at least 2 weeks beyond post traumatic amnesia. Exclusion criteria included sustained penetrating TBI, prior sustained TBI, eye movement disorder, visual field impairment to an extent that would not permit task performance, history of alcohol or drug abuse, and premorbid psychiatric or neurological diagnoses. All individuals with TBI had normal or corrected vision and all were hospitalized at the time of assessment and exposed to the same rehabilitation setting. Most participants (n = 19) of the TBI group received medical treatment such as analgesics (n = 9), antidepressants (n = 5), antiepileptics (n = 8), anxiolytics (n = 1), dopaminergic anamnestic medication (n = 3), neuroleptics (n = 6), and stimulants (n = 1). The group consisted of individuals with complicated mild (n = 3), moderate (n = 4), and severe TBI (n = 19), estimated according to the Glasgow Coma Scale (GCS), ranging from 3 to 15 (M = 6.7). The individuals included with complicated mild TBI were classified as complicated mild TBI since all had prominent brain injury as evaluated with CT (Table 1) and clinically apparent symptoms. The time after onset of all TBI group participants ranged from 14 to 309 days (M = 97.8 days). Causes that led to TBI included motor vehicle accidents (n = 20) and falls from height (n = 6). Several of the participants sustained orthopedic injuries such as amputation of the digits (n = 1), fractures of the femur (n = 3), ilium (n = 1), limbs (n = 3), knee (n = 1), pelvis (n = 8), radius (n = 1), tibia (n = 3) and vertebrae (n = 2). According to CT data, most individuals sustained a focal injury in the frontotemporal lobes (see Table 1 for detailed information). Due to the local clinical conventions that defined CT as the default imaging assessment, no neuroimaging data (e.g., structural MRI, diffusion tensor imaging [DTI], etc.) suitable to evaluate white matter damage was available. However, according to neuropathology studies evaluating affected brain regions in TBI, we can assume that frontotemporal damage as well as diffuse axonal injury and other neuropathology in other brain regions is likely to be the case in our sample (Bigler, 2007; Mckee & Daneshvar, 2015; Stuss, 2011). Detailed demographic, clinical, and imaging (i.e., CT) information per participant of the TBI group is presented in Table 1. The control group consisted of 28 individuals (3 females and 25 males), with normal or corrected vision. Two individuals participated voluntarily, 10 participated in return for a payment of 40 NIS (~10 USD), and 16 were undergraduate students at Bar-Ilan University who took part in the experiment to fulfill academic requirements. Their ages ranged from 18 to 55 years (M = 31.2, SD = 10.7). The group's ages, $t(52) = 0.15$, $p = .88$, as well as their educational level, $t(52) = -1.62$, $p = .11$, did not differ significantly. Written informed consent was obtained from all participants. The study was approved as required by the Helsinki Committee at the Loewenstein Rehabilitation Center.

Procedure

Participants completed the study procedures in a single testing session lasting approximately 50 min. First, participants signed the informed consent form and completed a short demographic ques-

Table 1
Traumatic Brain Injury Group: Demographic, Clinical, and Imaging Data

P	Sex	Age	Edu	GCS	TAO	Location and pathology of brain injury (CT)	Orthopedic injuries	Medication	Cause
1	M	53	13	3	156	Lt temporal epidural hematoma, Bi frontal and Lt temporal contusions, SAH		AD	mv
2	M	51	12	3	189	Rt fronto-parietal contusion	amputation of Rt digits	AD, AE, St	mv
3	M	43	14	14	91	Rt frontal contusion, Lt SAH, small SDH	multiple fractures of Rt upper limp and ilium	NOAn	fall
4	F	46	13	3	81	Bi frontal, Lt temporal contusion			mv
5	M	48	15	7	20	Lt frontal and temporal contusions			fall
6	M	29	15	8	41	DAI (Rt frontal, Lt parietal)	Rt knee injury		mv
7	M	19	12	3	66	Lt occipital infarction		AD, OAn	mv
8	F	38	17	6	97	Lt cerebellar and Lt occipital infarction			mv
9	M	21	12	6	78	no pathology on early CT	fractures; pelvis, femur, lumbar vertebrae	AE, N, AX, OAn	mv
10	M	22	10	6	309	Bi frontal contusions, Lt thalamic hemorrhage	fracture left radius	D	mv
11	M	21	12	8	109	no pathology on late CT	fracture pelvis	NOAn	fall
12	M	28	12	3	108	DAI (Grade III—hemispheres, focal lesions in corpus callosum, midbrain)	fracture knee	AD, N	mv
13	M	46	10	14	29	Bi prefrontal and Lt temporal contusions, SAH		AE, N, NOAn	fall
14	M	27	14	10	216	DAI	fracture pelvis	AE, NOAn	mv
15	M	47	12	10	112	Rt frontal SAH, Bi SDH	fractures; pelvis, vertebrae	AD	mv
16	M	20	10	4	51	DAI	fracture Rt femur	AE, N	mv
17	M	19	12	3	33	fracture of parietal bone, small tentorial SDH, no pathology on late CT			mv
18	F	23	12	6	235	Lt temporal contusion, Lt craniectomy	fracture Lt tibia	AE	mv
19	M	21	12	15	14	Lt frontal contusion, SAH	fracture Rt tibia	AE, OAn	mv
20	M	30	15	8	69	Bi frontal contusions, Bi SDH on early CT, large Lt frontal injury on late CT.		N	mv
21	M	22	10	3	129	Lt temporal hypodense area, Lt basal ganglia lacunar lesion	fractures; pelvis, limbs	NOAn	mv
22	M	20	12	10	52	Rt parietal hypodense area		N, D	mv
23	M	47	13	5	49	Bi small frontal and Lt parietal contusions	fractures; pelvis, limbs	OAn	fall
24	M	25	12	3	50	Bi frontal contusions, SAH			fall
25	M	35	17	9	26	Bi prefrontal contusions, suspected temporal poles involvement			mv
26	M	23	12	3	135	Bi frontal contusions, SAH, Lt SDH on early CT, enlargement of Rt lateral ventricle on late CT	fractures; pelvis, Rt tibia, femur	D	mv

Note. In this table age was rounded off to full year of age; in analyses the exact age was used (decimal). P = participant; Edu = years of education; CT = computed tomography; GCS = Glasgow Coma Scale; TAO = time after onset in days; Bi = bilateral; DAI = diffuse axonal injury; Lt = left; Rt = right; SAH = subarachnoid hemorrhage; SDH = subdural hemorrhage. Medication categories: AD = antidepressant; AE = antiepileptics; Ax = anxiolytics; D = dopaminergic; NOAn = nonopioid analgesics; N = neuroleptics; OAn = opioid analgesics; St = stimulants. Cause: mv = motor-vehicle accident; fall = fall from height.

tionnaire. They were then tested with the OA version of the O-SRT task, lasting approximately 20 min. Subsequently, the Digit Span and Spatial Span subtests of the Wechsler Memory Scale (WMS-III; Wechsler, 1997) were administered. Three participants of the TBI and one of the control group did not take part in the Digit Span and Spatial Span assessment.

Test Material

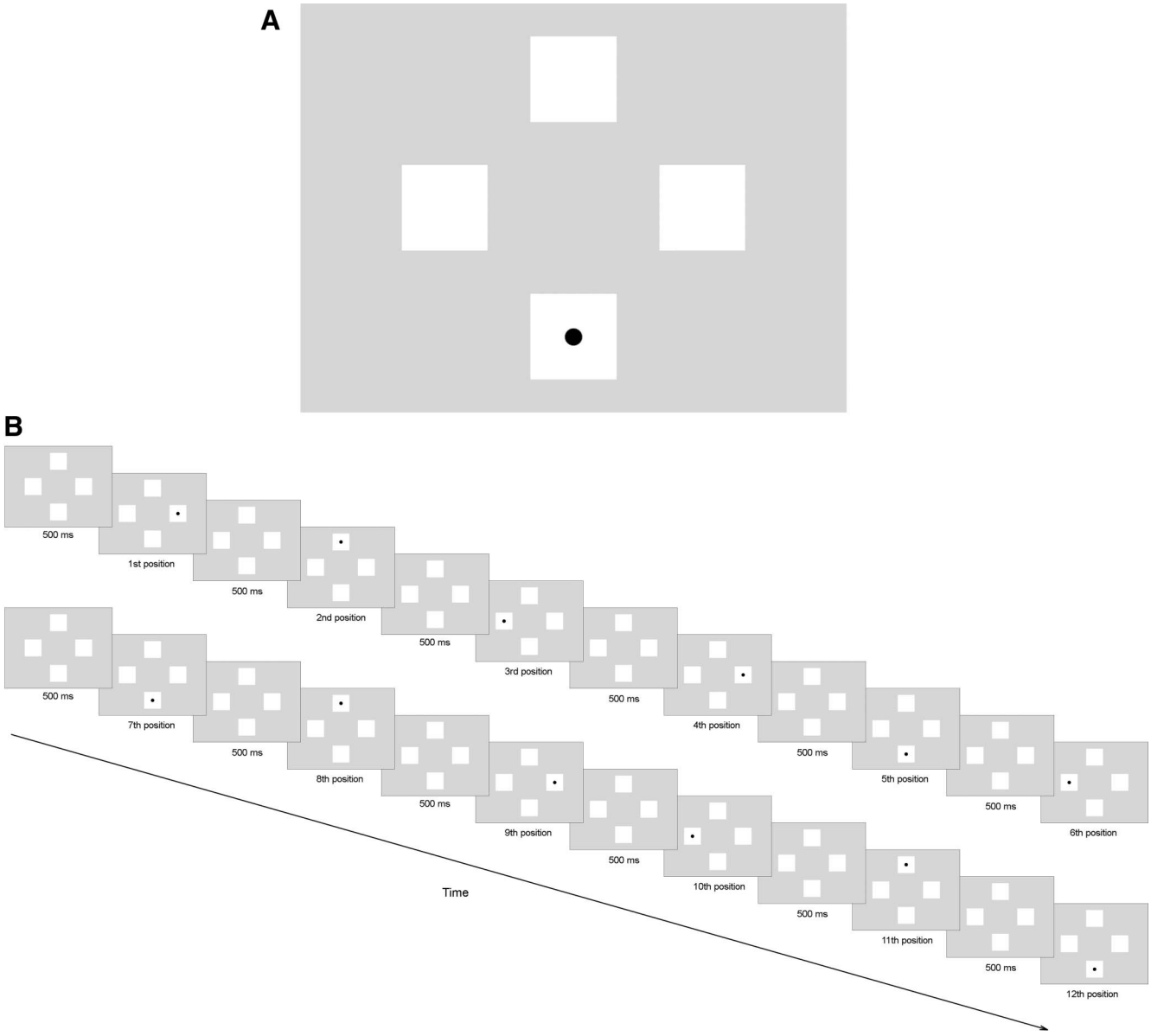
O-SRT

The SRT design used for this experiment was a replication of the OA version of the O-SRT task in the study by Vakil et al. (2017). The task was programmed in E-Prime 2.0. Eye movements were recorded by the SMI iView 120 REDm Eye Tracker (SensoMotoric Instruments, Teltow, Germany), at a sample rate of 120 Hz. Stimuli were presented on an LCD computer screen (size 42 × 24 cm; resolution 1,600 × 900 pixels). The recording device was installed beneath the screen. Participants were seated in front of the screen, approximately 60 cm away from it. Calibration was performed once at the beginning of every task session, using a standard 5-point grid for both eyes.

Stimuli

Stimuli consisted of five slides (Figure 1A), each with a resolution of 1,400 × 900 pixels. Each stimulus included four white squares arranged in a diamond shape on a gray background. Four slides contained a black dot (indicating the target) in one of the four white squares. One slide, which was used to measure antici-

Figure 1
Illustration of the Ocular Serial Reaction Time (O-SRT) Task



Note. (A) An example of a target slide. This slide was activated by 100 ms of fixation on the white square, or at the latest after 1,000 ms if no fixation had occurred. (B) Illustration of one of the sequences used in the experiment design of the O-SRT. A sequence consisting of 12 elements (= positions) was repeated nine times per Block. At the start and in between the target slides, an empty slide containing only the squares was presented for 500 ms in order to measure correct anticipations (CA) and stucks. The same sequence (A) had been displayed in Blocks 1–6, followed by an interference block 7 carrying a different sequence (B) and terminated by the recovery block 8 with the original sequence (A).

pation, contained only the four white squares, without a black dot in any of the squares. The size of each square was 6 × 6 cm and the diameter of the dot was 1.5 × 1.5 cm.

O-SRT Procedure

Computerized target slides were presented with a black dot (the target stimulus) that appeared in one of four white squares arranged in a diamond shape (see Figure 1A). Before each target slide, a blank slide with four empty squares was shown for 500 ms (i.e., the anticipation slide). Each block consisted of a 12-element sequence repeated nine times (see Figure 1B), which resulted in 108 anticipation and 108 target slides. The sequence in each block began from a different element of the sequence, that is, a different starting point. No first-order predictive information was provided in the sequence (i.e., each location was preceded by the same location only once). Each element in the sequence was matched

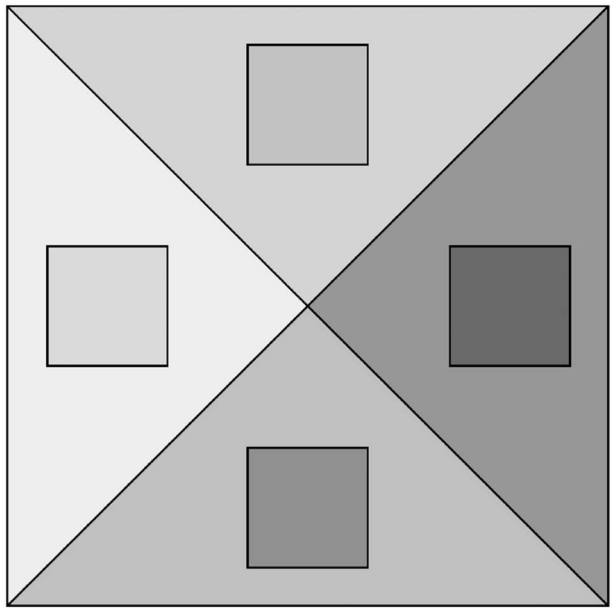
with one of the four squares: 1, 2, 3, and 4 to correspond with down, left, right, and up, respectively. Two sequences were used in the O-SRT which were adopted from Gabriel et al. (2013): Sequence A (3–4–2–3–1–2–1–4–3–2–4–1; the original sequence) and Sequence B (3–4–1–2–4–3–1–4–2–1–3–2; the interference sequence). Figure 1B presents an illustration of Sequence A.

Participants were instructed to look as quickly as possible at the target dot when it appeared in one of the four squares arranged in a diamond shape. For the purpose of measuring anticipation of the subsequent target location, a blank slide (i.e., the anticipation slide) was presented for 500 ms in between the target slides. Importantly, participants were not aware that a blank slide appeared, since it is perceived as a continuous flow from one to the next target slide. The target slides were oculomotor activated, meaning that when the square with the target was fixated for a minimum of 100 ms, the blank slide was displayed, followed by the next target slide.

The O-SRT task was constructed out of a total of eight blocks, divided into three phases. First, the learning phase—the presentation of six Blocks (1–6) containing the original Sequence A. Second, the interference phase—the presentation of one block with the interference Sequence B (Block 7). Third, the recovery from interference phase—the presentation of one block with the original Sequence A (Block 8). After each block, a 1-min break was given before starting the next block. Participants received no prior information about the nature of the task (i.e., that the dots appear in a sequential order) nor the number of blocks.

Figure 2

Areas of Interest (AOIs) Used for Calculating Correct Anticipations



Note. Each triangle was considered the AOI for the square that was positioned inside of it.

Data Analysis

Eye movement data was registered using iView (SensoMotoric Instruments, Teltow, Germany), and BeGaze (SensoMotoric Instruments, Teltow, Germany), was used to generate eye-tracking parameters. Three dependent measures were used: speed (RT to target), number of CAs and number of stucks.

Reaction Time (RT)

Median RT was calculated for each 12-item sequence (i.e., the median of the 12 trials that constituted 1 repetition of a sequence). Then, the mean of medians of RT per block (i.e., 9 sequences of 12 items each; 108 trials) was analyzed.

Number of CAs

Number of CAs was evaluated by tracking the transition of the participant's gaze to the correct subsequent position during the blank slide between target slides presentation. We used the function area of interest (AOI) in the BeGaze program and enlarged the squares into triangles, so that four triangles covered the four squares and the center point of the screen Figure 2. All trials in which participants fixated at least once on the AOI of the correct subsequent sequence location (where the next target was going to appear) were classified as CAs. The number of CAs per block was summarized (i.e., the maximum possible number per Block is 108). This established the CA score for each block for all participants.

Analysis of ISL

Performance of ISL using the RT and CA measures was analyzed in the following three phases:

Learning. A mixed-design analysis of variance (ANOVA; 2 × 6) was used to analyze the effects of the between-subjects condition factor of Group (TBI and controls) and the within-subjects factor of Learning (Blocks 1–6).

Interference. A mixed-design ANOVA (2 × 2) was used to explore the effect of the between-subjects condition factor of Group (TBI and controls) and the within-subjects factor of Interference (Block 6 vs. Block 7).

Recovery From Interference. A mixed-design ANOVA (2 × 2) was used to explore the effect of the between-subjects condition factor of Group (TBI and controls) and the within-subjects factor of Recovery from Interference (Block 7 vs. Block 8).

ISL Scores

For each participant, scores describing the extent of ISL, for the learning as well as the interference phases, for both the RT and CA measures, were computed as follows:

1. **ISL Learning score:** Block 6 was subtracted from Block 1 for the RT measures and vice versa, Block 1 was subtracted from Block 6 for the CA measures, thereby resulting in RT and CA learning scores.

2. **ISL Interference score:** Block 7 was subtracted from Block 6 for the RT measures and vice versa, Block 7 was subtracted from Block 6 for the CA measures, which resulted in RT interference and CA interference scores.

For all computed score accounts, the higher the score the stronger the learning or interference effect. The ISL scores were viewed

as indicators of how well the sequence was learned. In order to evaluate possible influences of clinical, demographic and WM measures on ISL, these ISL scores were used to perform bivariate Pearson correlation analyses.

Number of Stucks

Stucks were evaluated by tracking the participant's gaze which remained at the previously presented target position during the blank slide between target slides presentation. The procedure for computing stucks was similar to that of CAs. The same AOIs (i.e., four triangles covering the four squares as illustrated in Figure 2) were used in order to identify the trials where participants were stuck. Then, the sum of stucks was calculated for each block separately. We were primarily interested in the number of stucks during the learning phase, and therefore computed the average stucks of Blocks 1–6. We compared this measure between the groups by conducting an independent-samples *t* test.

Digit and Spatial Span

We assessed verbal and spatial WM capacity by applying the Forward and Backward Digit and Spatial Span subtests of the WMS-III (Wechsler, 1997). The total score (sum of Forward and Backward Span) was used in both tasks to perform independent-samples *t* tests to compare the groups, as well as to perform bivariate Pearson correlation analyses with the RT and CA ISL scores.

Results

Reaction Time

The mean of the medians of RT as a function of Blocks 1 to 8 of the O-SRT for both groups is presented in Figure 3.

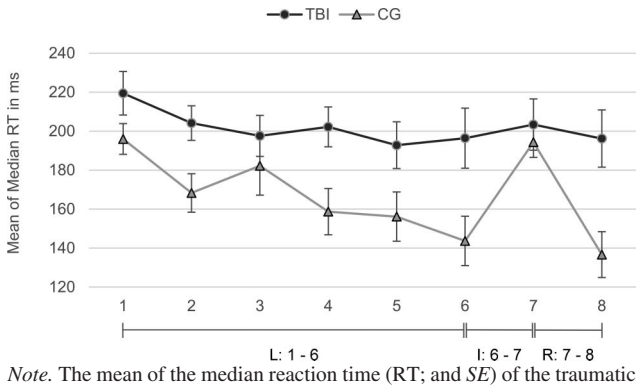
Learning

A mixed ANOVA with a Greenhouse-Geisser correction revealed that there was a significant reduction in RT over Blocks 1–6, $F(3.96, 206.07) = 8.37$, $p < .001$, $\eta_p^2 = .14$. The main effect of Group, $F(1, 52) = 8.04$, $p < .01$, $\eta_p^2 = .13$, as well as the Group × Learning interaction, $F(3.96, 206.07) = 2.42$, $p < .05$, $\eta_p^2 = .05$, reached significance as well. To understand the source of the interaction, we performed follow up analyses (i.e., separate repeated measures ANOVA with a Greenhouse-Geisser correction for each group), which demonstrated that the Learning effect was significant only in the control $F(3.57, 96.27) = 9.4$, $p < .001$, $\eta_p^2 = .26$, but not in the TBI group $F(2.82, 70.73) = 1.9$, $p = .14$, $\eta_p^2 = .07$). These results indicate that only the control group significantly reduced RTs during the learning phase. Additionally, the TBI group performed generally slower than the control group (see Figure 3).

Interference

Interference main effect, $F(1, 52) = 15.24$, $p < .001$, $\eta_p^2 = .23$, interaction of Group and Interference, $F(1, 52) = 9.06$, $p < .01$, $\eta_p^2 = .15$, and Group effect, $F(1, 52) = 5.78$, $p < .05$, $\eta_p^2 = .10$ were all significant. Follow-up analyses revealed that only the control group showed a significant Interference effect (TBI: $F(1, 25) = 0.38$, $p = .54$, $\eta_p^2 = .02$, controls: $F(1, 27) = 25.17$, $p < .001$, $\eta_p^2 = .48$). These results indicate that interference only affected the control group, which demonstrated higher RTs when a different sequence was presented (see Figure 3).

Figure 3
Reaction Time



Note. The mean of the median reaction time (RT; and *SE*) of the traumatic brain injury (TBI) and control group is displayed from Blocks 1–8. In the learning phase (L) Sequence A was presented from Block 1–Block 6. The seventh Block contained the different Sequence B (I = interference phase) and finally in Block 8 the original Sequence A was presented again (R = recovery from interference phase). RT was measured as the time starting from the onset of the target slide until the first fixation on the square containing the dot on the target slide.

Recovery From Interference

All three effects reached significance: Recovery from Interference main effect, $F(1, 52) = 17.31$, $p < .001$, $\eta_p^2 = .25$, Group × Recovery From Interference interaction, $F(1, 52) = 10.39$, $p < .01$, $\eta_p^2 = .17$ and Group main effect, $F(1, 52) = 6.80$, $p < .05$, $\eta_p^2 = .12$. The follow- up analyses revealed that the main effect for Recovery from Interference stemmed only from the control group ($F(1, 27) = 24.27$, $p < .001$, $\eta_p^2 = .48$). The TBI group did not show a significant Recovery from Interference effect, $F(1, 25) = 0.50$, $p = .49$, $\eta_p^2 = .02$. As can be seen in Figure 3, in contrast to the TBI group, RTs of the control group were remarkably reduced when the original sequence had been reintroduced.

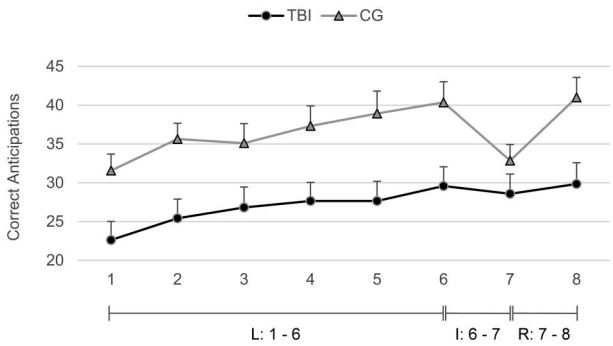
Number of CAs

The average CA as a function of blocks 1 to 8 of the O-SRT for both groups is presented in Figure 4.

Learning

The Learning main effect of a mixed ANOVA with a Greenhouse-Geisser correction, $F(3.81, 198.12) = 9.73$, $p < .001$, $\eta_p^2 = .16$, and effect for Group, $F(1, 52) = 9.87$, $p < .01$, $\eta_p^2 = .16$ were significant. The Group × Learning interaction did not reach significance, $F(3.81, 198.12) = .41$, $p = .79$, $\eta_p^2 = .01$. Overall, these results (see Figure 4) indicate that as the session progressed, both groups showed a similar increase in the number of CAs, whereas the overall number of CAs was significantly lower in the TBI group.

Figure 4
Correct Anticipations



Note. The average number (and *SE*) of correct anticipations (CA) of the ocular serial reaction time (O-SRT) task for the TBI and the control group is displayed from Blocks 1–8. In the learning phase (L) Sequence A was presented from Block 1–Block 6. The seventh Block contained the different Sequence B (I = interference phase), and finally in Block 8 the original Sequence A was presented again (R = recovery from interference phase).

Interference

All three effects were significant: the Interference main effect, $F(1, 52) = 8.92$, $p < .01$, $\eta_p^2 = .15$, Group × Interference interaction $F(1, 52) = 5.21$, $p < .05$, $\eta_p^2 = .10$, and Group main effect $F(1, 52) = 5.69$, $p < .05$, $\eta_p^2 = .10$. Follow-up analyses (i.e., separate repeated measures ANOVA for each group) revealed that the Interference effect was driven by the performance of the control group, ($F(1, 27) = 11.74$, $p < .01$, $\eta_p^2 = .30$). The Interference effect of the TBI group was not significant, $F(1, 25) = .32$, $p = .58$, $\eta_p^2 = .01$. This outcome implies that only the control group was disturbed significantly by the different sequence that led to the reduced number of CAs (see Figure 4).

Recovery From Interference

All three effects were significant: the Recovery from Interference main effect, $F(1, 52) = 11.09$, $p < .01$, $\eta_p^2 = .18$, Group × Recovery from Interference interaction, $F(1, 52) = 5.91$, $p < .05$, $\eta_p^2 = .10$, and Group main effect, $F(1, 52) = 5.74$, $p < .05$, $\eta_p^2 = .10$. Follow-up analyses (i.e., separate repeated measures ANOVA for each group) revealed that the Recovery from Interference effect was only significant in the control group, $F(1, 27) = 12.91$, $p < .01$, $\eta_p^2 = .32$. The TBI group did not reach a significant effect, $F(1, 25) = .61$, $p = .44$, $\eta_p^2 = .02$. Thus, as illustrated in Figure 4, when presenting the original sequence again, only controls demonstrated a significant increase in CAs.

Number of Stucks

The average number of stucks from Block 1–Block 6 differed significantly between the groups, $t(52) = 3.284$, $p < .01$. The TBI group was stuck more often at the same location ($M = 46.63$, $SD = 19.63$), compared to the controls ($M = 29.49$, $SD = 18.72$).

Percentage of CAs

The higher numbers of stucks found in the TBI group has an implication for the CA measure. That is because a higher number of stucks results in a lower number of available trials in which participants could make correct or incorrect anticipations. We were therefore interested in evaluating performance of CAs in proportion to incorrect anticipations (i.e., eye fixation on a triangle other than the preceding or subsequent target), regardless of the number of stucks. Thus, we calculated the percentage of CAs out of the total number of correct and incorrect anticipated trials. This established the percentage of CAs score (Percentage CA) for each block for all participants. In order to compare the groups, we computed the average of the percentage CA in the learning phase and conducted an independent-samples t test. This analysis revealed that groups had a similar average percentage CA (TBI: $M = 46.04$, $SD = 5.88$, control group: $M = 48.40$, $SD = 5.86$) and did not differ significantly, $t(52) = -1.473$, $p = .15$.

Digit and Spatial Span

Digit Span differed significantly between groups, $t(48) = -6.02$, $p < .001$. The control group reached a higher total Digit Span score ($M = 18.07$, $SD = 3.75$) than the group with TBI ($M = 12.18$, $SD = 2.92$). Although the control group achieved higher results in the total Spatial Span ($M = 16.44$, $SD = 2.85$) than the group with TBI ($M = 14.70$, $SD = 3.20$), this difference did not reach significance on the Bonferroni corrected significance level ($p < .025$), $t(48) = -2.05$, $p = .046$.

Correlation Analyses

Bivariate Pearson correlation analyses revealed no significant ($p < .05$) correlations between demographic (i.e., age, education) and ISL scores of RT and CA in both groups. Furthermore, these measures also did not correlate with the clinical factors (i.e., GCS, time after onset) in the TBI group. However, and only in the control group, we found a significant correlation between the Spatial Span and the ISL scores of CA and RT. There were no significant correlations between Digit Span and the ISL scores. The Pearson product–moment correlation coefficients of these analyses for both groups are presented in Table 2. Since literature is inconsistent regarding the contribution of WM to ISL, and to the best of our knowledge, the present study is the first to test this relation in individuals following TBI, we followed an exploratory approach. Therefore, we corrected for multiple comparisons of the number of correlation analyses conducted per study group that resulted in a Bonferroni corrected threshold level of $p < .006$. Only the correlation between CA Learning score and Spatial Span ($r(27) = .589$, $p < .001$) of the control group reached this level of significance.

Discussion

The present study investigated ISL in individuals that had sustained TBI at a maximum of 1 year postinjury, using the OA version of the O-SRT task. Compared to the original MA version of the SRT that measures primarily manual RT, aside from OA RT, the O-SRT provides additional measures such as number of CAs and number of stucks. Whereas RT is considered to be an indirect measure of ISL, the CA measure allows direct assessment of whether a sequence has been learned or not, and to what extent. Furthermore, the OA measure of RT is itself a purer measure than

Table 2
Pearson Correlation Matrix of Working Memory Capacity and Implicit Sequence Learning Scores

	ISL scores			
	Learning		Interference	
Group subtests	RT	CA	RT	CA
TBI				
Digit Span	−.073	.094	.089	.062
Spatial Span	−.115	−.014	−.134	.017
Controls				
Digit Span	−.033	−.060	.107	.296
Spatial Span	.472*	.589**†	.456*	.412*

Note. TBI = traumatic brain injury; RT = reaction time; CA = number of correct anticipations; RT Learning = RT Block 1 minus Block 6; RT Interference = RT Block 7 minus Block 6; CA Learning = CA Block 6 minus Block 1; CA Interference = CA Block 6 minus Block 7.
† Reaching Bonferroni corrected threshold level of $p < .006$. * $p < .05$. ** $p < .01$, two-tailed.

the MA measure of RT, because it does not involve the general skill learning of mapping the spatial location of the screen stimulus to the corresponding key (S-R). All three measures such as OA RT, CA, and stucks provide important information allowing characterization of different ISL aspects.

Generally, the TBI group performed slower than controls as expressed by the group main effect of the RT measures, which is consistent with a slower processing speed typically associated with TBI (e.g., Johansson et al., 2009). The aim of the present study was to investigate the learning characteristics of ISL in individuals with TBI. Therefore, our focus is on the learning rate measures which are independent of the speed of processing. The comparison between the multiple measures generated by the O-SRT task provided us with some insights into the underlying cognitive processes involved in the acquisition phase of ISL in individuals with TBI versus controls. Consistent with previous findings (Vakil et al., 2017), ISL in controls was expressed in RT and CA measures. In contrast, the TBI group showed impaired ISL in all three phases (i.e., learning, interference and recovery from interference) compared to controls using the RT measure. The performance according to the CA measure revealed a slightly different picture. Although the TBI group reached a significantly lower number of CAs in the learning phase, the increase in CA was significant in both groups. However, the introduction of the interference sequence had no significant impact on the TBI group (indicating impaired ISL), as compared to the controls who were significantly disturbed by it. Similarly, in the recovering from interference phase, only the control group recovered significantly and was able to increase the CAs. Thus, the CA analyses revealed that the TBI group showed impairment, expressed primarily by the absent Interference effect upon presentation of a different sequence. Yet, at the same time it indicates that their learning rate was similar to that of controls.

In order to gain a better understanding of the divergent outcome of the RT and CA analyses, we looked closer at the stucks measure and its relation to the RT and CA measures. We observed the following pattern, which we view as a key finding for understanding the ISL process in individuals with TBI compared to that of controls. The fact that the TBI group had a remarkably higher number of stucks has a direct implication on the total number of their possible CAs. In other words, the higher the stucks rate, the lower the possible number of CAs, because the total number of possible CAs is finite (i.e., a maximal 108 possible CAs per Block). Therefore, we hypothesized that the TBI group would perform proportionally at a CA rate during learning similar to that of controls. Using the percentage measure of CAs (Percentage CA) this analysis confirmed our assumption. Thus, in absolute terms, the TBI group had a significantly lower CA rate, but when correcting for the number of stucks and looking at proportional CA relative to total anticipations (i.e., including correct and incorrect anticipations, but excluding stucks), the difference between the groups disappeared. Consequently, the tendency to remain in the old stuck position drives the difference in CA between the groups.

By integrating all these findings, the picture emerging is that individuals with TBI tend to be reluctant to make an anticipation move toward the next possible location of the subsequent appearing stimulus during the time delay of 500 ms in between the preceding and subsequent appearing stimulus. This behavior is expressed in a higher rate of stucks. This could be due to their lack of initiative associated with TBI (Arnould et al., 2016; Godfrey et al., 2003; Oddy et al., 2008; Prigatano, 1992; Vallat-Azouvi et al., 2018) and frontal lobe injury in TBI (Stuss, 2011; Zappalà et al., 2012), or lack of confidence in knowing the correct location, or both. The tendency to remain stuck more often at the "old" position, together with the lower processing speed as mentioned above, may also explain the higher RT as compared to controls. Unlike controls, participants with TBI performed a move toward the next location that would have shortened their RT less frequently. Instead they waited for the stimulus to appear, and only then moved toward it. The higher stucks rate in the TBI group also had implications for their CA rate, as explained above. Their hesitation expressed in a higher number of stucks suggests that individuals with TBI have a conservative response bias compared to controls. This means that they make an anticipatory move when they feel quite confident about the accuracy of their move. This leads to the finding that they did not differ from controls on the Percentage CA rate. Nevertheless, the fact that they were not significantly disturbed by the interference sequence clearly reflects their impairment in ISL.

In sum, by taking into account all three measures used in the present study, namely RT, CA, and number of stucks, we concluded that the TBI group tested in our study was impaired in ISL, but not to such an extent as the RT analyses alone would imply. We propose that the lack of initiative associated with frontal lobe injuries in TBI (Stuss, 2011; Zappalà et al., 2012) and/or the conservative response prevalent in TBI (Campbell et al., 1990; Paniak et al., 1989; Whyte et al., 1995) resulted in a higher stucks rate, which was the main factor leading to impaired ISL in the TBI group. Nevertheless, we cannot exclude the possibility that affected brain regions other than frontal lobes, such as basal ganglia or fronto-striatal connections, were related to this behavior. These regions are also frequently impaired following TBI (Mckee & Daneshvar, 2015) and were previously linked with lack of initiative (Moretti & Signori, 2016; Palmisano et al., 2020). No imaging data (e.g., MRI, DTI) suitable to test this assumption was available, which together with the fact that our sample was characterized by rather heterogenic brain injuries (i.e., in terms of affected brain re-

gions and brain pathology) limits the results of our study. However, based on the literature (Bigler, 2007; Stuss, 2011) we assume that most participants sustained frontal lobe injuries, which we see as a key impairment in association with lack of initiative and/or conservative response bias, as being responsible for the observed deficits of ISL in TBI.

We were further interested in learning whether clinical (GCS, time after onset) or demographic variables such as age and education have an impact on ISL. Consistent with the results of Vakil et al. (2002), ISL (i.e., ISL scores of RT and CA) was not associated with clinical measures such as GCS or time after onset. Furthermore, a study assessing explicit sequence learning, did not detect any relation between sequence learning and clinical measures (Korman et al., 2018). Education was not related to ISL in either the control or the TBI group, and in contrast to the findings of Lukács & Kemény (2015), we did not observe a correlation between age and ISL scores. In their study, the effect of age on ISL was systematically tested, and the authors reported a peak that occurred between ages 18–35 and then started to decline. We do not exclude the possibility that age affected ISL in our samples, as the group sizes may have been too small to detect it. This, however, was also not the focus of our study. Based on the results of our age-matched samples, we do assume that if age affected ISL, it occurred in both groups in a similar way.

WM is another domain that may influence ISL. Since individuals with TBI have been frequently reported to be impaired in WM (Dunning et al., 2016; McAllister et al., 2006), we assessed the Digit and Spatial Span of the WMS-III (Wechsler, 1997). Our analysis revealed that after correction for multiple comparisons, verbal but not spatial WM capacity was significantly impaired in the TBI group. This pattern has been observed similarly in previous studies (Kraus et al., 2010; Little et al., 2014; Vallat-Azouvi et al., 2009; Vallat-Azouvi et al., 2007). At the same time, we would like to note that by using a larger sample size, we might also have detected a significant difference in spatial WM capacity. However, considering the very low p value of the Digit Span group comparison, we suggest that our tested TBI group was predominantly impaired in verbal rather than spatial WM capacity. Furthermore, we were interested in examining the impact of WM capacity on ISL. We found that Spatial Span, after correcting for multiple comparisons, was positively correlated with the CA Learning score in the control group. This finding may be related to the spatial arrangement of the target dots in our O-SRT version. The study by Robertson et al. (2001) that compared learning on a spatial versus nonspatial cued response sequence task by applying repetitive inhibitory transcranial magnetic stimulation to the DLPFC, does point to this link. Since learning was disrupted only during the spatial cued response task, the authors concluded that previously reported activation of the DLPFC during ISL is specifically related to the processing of spatial cues in WM. Interestingly, although spatial WM performance was not significantly impaired in our TBI group, we did not detect a relation between Spatial Span and the ISL scores. We relate this pattern to the impact of brain damage to frontal structures which results in failure of the "implementation of strategic approach and conceptual elaboration of information" (p. 997) as described by Vakil (2005). In other words, although the TBI group had sufficient spatial WM ability, individuals with TBI were not able to use this ability during performance on the O-SRT.

In previous publications, ISL was found to be affected by medications in a variety of clinical populations, either by an enhanced, decreased, or no effect on ISL. Dopaminergic treatment (i.e., levodopa) rather enhanced ISL (Beigi et al., 2016; Rösser et al., 2008), neuroleptics, depending on the class type led to enhanced or reduced ISL (Kumari et al., 2015) and antidepressants seemed not to affect ISL (Pedersen et al., 2009). Most of the participants in our TBI group received an individually catered medication treatment plan, and therefore the medication profile in our TBI group is rather heterogenic. Thus, given the findings in the literature and considering the heterogeneity of the medication treatment in our TBI sample, we assume that on the group level possible medication effects on ISL were counterbalanced, but we cannot exclude that medications did affect their ISL on an individual level.

In conclusion, our study demonstrates the benefit of using eye tracking in the assessment of ISL, as it can potentially unveil learning strategies and/or cognitive processes which remain hidden when using standard behavioral assessments. Using the O-SRT task enabled the generation of new measures in addition to the RT measure used in the standard SRT task. It is evident from this study that RT provides only a partial picture of the sequence learning process. This could also explain the inconsistent findings in the literature, because it seems that individuals post-TBI are capable of learning to some extent (i.e., as expressed by the significant learning effect of CAs), but this is not necessarily reflected in the RT measure. Thus, our results point to a significant ISL impairment in individuals with TBI, yet more research is needed to understand whether other factors, for example lengthening the learning phase, may lead to better ISL performance. In view of the fact that elements of procedural learning are frequently implemented in physical, behavioral, and cognitive rehabilitation settings, it is highly relevant to study procedural learning abilities in TBI. Rehabilitation settings cater to the learning of new skills in order to cope with TBI-related difficulties during activities of daily living (Skidmore, 2015). Our study provides novel insights into ISL in TBI which may be implemented in rehabilitation. The finding that individuals post TBI were more stuck during learning of a sequential procedure probably because of their lack of initiative or hesitation due to feelings of insecurity, eventually leading to impaired learning, may be a critical point to be addressed in therapeutic settings. In addition, such settings may also consider our finding that despite relatively preserved spatial WM, individuals with TBI may not be able to apply this ability to support their skill learning. Future research is needed to replicate our findings and to better understand the influence of other factors, such as the length of the learning course. Our finding that the TBI group expressed a learning effect of CAs, may also imply that individuals with TBI are slower in acquiring the sequence and do need more repetitions in order to learn. At the same time, exposing individuals with TBI to a longer learning phase may result in fatigue effects (Johansson et al., 2009). Therefore, a possible approach to study the influence of the length of the learning course may be to spread the learning over several sessions. Furthermore, other aspects worth study-

ing are gender effects, recently reported to play a critical role in ISL of male and female veterans who had sustained TBI (Waltzman et al., 2017). Finally, long-term effects of TBI and the influence of targeted interventions on ISL, are additional relevant questions to be investigated, since their outcome may be highly important in terms of being implemented in clinical settings and/or daily routines of individuals post TBI.

References

Arnould, A., Dromer, E., Rochat, L., Van der Linden, M., & Azouvi, P. (2016). Neurobehavioral and self-awareness changes after traumatic brain injury: Towards new multidimensional approaches. *Annals of Physical and Rehabilitation Medicine*, *59*(1), 18–22. https://doi.org/10.1016/j.rehab.2015.09.002

Azouvi, P., Arnould, A., Dromer, E., & Vallat-Azouvi, C. (2017). Neuropsychology of traumatic brain injury: An expert overview. *Revue Neurologique*, *173*(7–8), 461–472. https://doi.org/10.1016/j.neurol.2017.07.006

Beigi, M., Wilkinson, L., Gobet, F., Parton, A., & Jahanshahi, M. (2016). Levodopa medication improves incidental sequence learning in Parkinson's disease. *Neuropsychologia*, *93*, 53–60. https://doi.org/10.1016/j.neuropsychologia.2016.09.019

Bendlin, B. B., Ries, M. L., Lazar, M., Alexander, A. L., Dempsey, R. J., Rowley, H. A., Sherman, H. E., & Johnson, S. C. (2008). Longitudinal changes in patients with traumatic brain injury assessed with diffusion-tensor and volumetric imaging. *NeuroImage*, *42*(2), 503–514. https://doi.org/10.1016/j.neuroimage.2008.04.254

Bigler, E. D. (2007). Anterior and middle cranial fossa in traumatic brain injury: Relevant neuroanatomy and neuropathology in the study of neuropsychological outcome. *Neuropsychology*, *21*(5), 515–531. https://doi.org/10.1037/0894-4105.21.5.515

Bigler, E. D., & Maxwell, W. L. (2011). Neuroimaging and neuropathology of TBI. *NeuroRehabilitation*, *28*(2), 63–74. https://doi.org/10.3233/NRE-2011-0633

Bo, J., Jennett, S., & Seidler, R. D. (2011). Working memory capacity correlates with implicit serial reaction time task performance. *Experimental Brain Research*, *214*(1), 73–81. https://doi.org/10.1007/s00221-011-2807-8

Brunoni, A. R., & Vanderhasselt, M. A. (2014). Working memory improvement with non-invasive brain stimulation of the dorsolateral prefrontal cortex: A systematic review and meta-analysis. *Brain and Cognition*, *86*(1), 1–9. https://doi.org/10.1016/j.bandc.2014.01.008

Campbell, K. B., Suffield, J. B., & Deacon, D. L. (1990). Electrophysiological assessment of cognitive disorder in closed head-injured outpatients. Electroencephalography and clinical neurophysiology. In P. M. Rossini & F. Maugiere (Eds.), *New trends and techniques in clinical neurophysiology*, (pp. 202–215). Elsevier. https://doi.org/10.1016/b978-0-444-81352-7.50025-x

Clegg, B. A., DiGirolamo, G. J., & Keele, S. W. (1998). Sequence learning. *Trends in Cognitive Sciences*, *2*(8), 275–281. https://doi.org/10.1016/S1364-6613(98)01202-9

Dewan, M. C., Rattani, A., Gupta, S., Baticulon, R. E., Hung, Y.-C., Punchak, M., Agrawal, A., Adeleye, A. O., Shrime, M. G., Rubiano, A. M., Rosenfeld, J. V., & Park, K. B. (2018). Estimating the global incidence of traumatic brain injury. *Journal of Neurosurgery*, *130*(4), 1080–1097. https://doi.org/10.3171/2017.10.JNS17352

Dunning, D. L., Westgate, B., & Adlam, A. L. R. (2016). A meta-analysis of working memory impairments in survivors of moderate-to-severe traumatic brain injury. *Neuropsychology*, *30*(7), 811–819. https://doi.org/10.1037/neu0000285

Ewert, J., Levin, H. S., Watson, M. G., & Kalisky, Z. (1989). Procedural memory during posttraumatic amnesia in survivors of severe closed head injury: implications for rehabilitation. *Archives of Neurology*, *46*(8), 911–916. https://doi.org/10.1001/archneur.1989.00520440105027

Ferraro, F. R., Balota, D. A., & Connor, L. T. (1993). Implicit memory and the formation of new associations in nondemented parkinson′s disease individuals and individuals with senile dementia of the alzheimer type: A serial reaction time (SRT) investigation. *Brain and Cognition*, *21*(2), 163–180. https://doi.org/10.1006/brcg.1993.1013

Gabriel, A., Maillart, C., Stefaniak, N., Lejeune, C., Desmottes, L., & Meulemans, T. (2013). Procedural learning in specific language impairment: Effects of sequence complexity. *Journal of the International Neuropsychological Society*, *19*(3), 264–271. https://doi.org/10.1017/S1355617712001270

Godfrey, H. P., Harnett, M. A., Knight, R. G., Marsh, N. V., Kesel, D. A., Partridge, F. M., & Robertson, H. R. (2003). Assessing distress in caregivers of people with a traumatic brain injury (TBI): A psychometric study of the Head Injury Behaviour Scale. *Brain Injury*, *17*(5), 427–435. https://doi.org/10.1080/0269905031000066201

Gofer-Levi, M., Silberg, T., Brezner, A., & Vakil, E. (2014). Cognitive procedural learning among children and adolescents with or without spastic cerebral palsy: The differential effect of age. *Research in Developmental Disabilities*, *35*(9), 1952–1962. https://doi.org/10.1016/j.ridd.2014.04.017

Janacsek, K., & Nemeth, D. (2013). Implicit sequence learning and working memory: Correlated or complicated? *Cortex: A Journal Devoted to the Study of the Nervous System and Behavior*, *49*(8), 2001–2006. https://doi.org/10.1016/j.cortex.2013.02.012

Johansson, B., Berglund, P., & Rönnböck, L. (2009). Mental fatigue and impaired information processing after mild and moderate traumatic brain injury. *Brain Injury*, *23*(13–14), 1027–1040. https://doi.org/10.3109/02699050903421099

Kasahara, M., Menon, D. K., Salmond, C. H., Outtrim, J. G., Tavares, J. V. T., Carpenter, T. A., Pickard, J. D., Sahakian, B. J., & Stamatakis, E. A. (2011). Traumatic brain injury alters the functional brain network mediating working memory. *Brain Injury*, *25*(12), 1170–1187. https://doi.org/10.3109/02699052.2011.608210

Korman, M., Shaklai, S., Cisamariu, K., Gal, C., Maaravi-Hesseg, R., Levy, I., Keren, O., Karni, A., & Sacher, Y. (2018). Atypical within-session motor procedural learning after traumatic brain injury but well-preserved between-session procedural memory consolidation. *Frontiers in Human Neuroscience*, *12*, 10. https://doi.org/10.3389/fnhum.2018.00010

Kraus, M. F., Little, D. M., Wojtowicz, B. S., & Sweeney, J. A. (2010). Procedural learning impairments identified via predictive saccades in chronic traumatic brain injury. *Cognitive and Behavioral Neurology: Official Journal of the Society for Behavioral and Cognitive Neurology*, *23*(4), 210–217. https://doi.org/10.1097/WNN.0b013e3181cefe2e

Kumari, V., Ettinger, U., Lee, S. E., Deuschl, C., Anilkumar, A. P., Schmechtig, A., Corr, P. J., ffytche, D. H., & Williams, S. C. R. (2015). Common and distinct neural effects of risperidone and olanzapine during procedural learning in schizophrenia: A randomised longitudinal fMRI study. *Psychopharmacology*, *232*(17), 3135–3147. https://doi.org/10.1007/s00213-015-3959-1

Little, D. M., Geary, E. K., Moynihan, M., Alexander, A., Pennington, M., Glang, P., Schulze, E. T., Dretsch, M., Pacifico, A., Davis, M. L., Stevens, A. B., & Huang, J. H. (2014). Imaging chronic traumatic brain injury as a risk factor for neurodegeneration. *Alzheimer's & Dementia: The Journal of the Alzheimer's Association*, *10*(35), S188–S195. https://doi.org/10.1016/j.jalz.2014.04.002

Lukács, Á., & Kemény, F. (2015). Development of different forms of skill learning throughout the lifespan. *Cognitive Science*, *39*(2), 383–404. https://doi.org/10.1111/cogs.12143

Mateer, C. A., & Sira, C. S. (2007). Cognitive and emotional consequences of TBI: Intervention strategies for vocational rehabilitation. *NeuroRehabilitation*, *21*(4), 315–326. https://doi.org/10.3233/NRE-2006-21406

McAllister, T. W., Flashman, L. A., McDonald, B. C., & Saykin, A. J. (2006). Mechanisms of working memory dysfunction after mild and moderate TBI: Evidence from functional MRI and neurogenetics. *Journal of Neurotrauma*, *23*(10), 1450–1467. https://doi.org/10.1089/neu.2006.23.1450

McDowall, J., & Martin, S. (1996). Implicit learning in closed head injured subjects: Evidence from an event sequence learning task. *New Zealand Journal of Psychology*, *25*(1), 1–6.

Mckee, A. C., & Daneshvar, D. H. (2015). The neuropathology of traumatic brain injury. In J. Grafman & A. M. Salazar (Eds.), *Handbook of Clinical Neurology* (Vol. 127, pp. 45–66). Elsevier. https://doi.org/10.1016/B978-0-444-52892-6.00004-0

Moretti, R., & Signori, R. (2016). Neural correlates for apathy: Frontal-prefrontal and parietal cortical-subcortical circuits. *Frontiers in Aging Neuroscience*, *8*, 289. https://doi.org/10.3389/fnagi.2016.00289

Mutter, S. A., Howard, J. H., Jr., & Howard, D. V. (1994). Serial pattern learning after head injury. *Journal of Clinical and Experimental Neuropsychology*, *16*(2), 271–288. https://doi.org/10.1080/01688639408402638

Nissen, M. J., & Bullemer, P. (1987). Attention requirements of learning evidence from performance measures. *Cognitive Psychology*, *19*(1), 1–32. https://doi.org/10.1016/0010-0285(87)90002-8

Nissley, H. M., & Schmitter-Edgecombe, M. (2002). Perceptually based implicit learning in severe closed-head injury patients. *Neuropsychology*, *16*(1), 111–122. https://doi.org/10.1037/0894-4105.16.1.111

Oddy, M., Cattran, C., & Wood, R. (2008). The development of a measure of motivational changes following acquired brain injury. *Journal of Clinical and Experimental Neuropsychology*, *30*(5), 568–575. https://doi.org/10.1080/13803390701555598

Palmisano, S., Fasotti, L., & Bertens, D. (2020). Neurobehavioral initiation and motivation problems after acquired brain injury. *Frontiers in Neurology*, *11*, 23. https://doi.org/10.3389/fneur.2020.00023

Paniak, C. E., Shore, D. L., & Rourke, B. P. (1989). Recovery of memory after severe closed head injury: Dissociations in recovery of memory parameters and predictors of outcome. *Journal of Clinical and Experimental Neuropsychology*, *11*(5), 631–644. https://doi.org/10.1080/01688638908400921

Pedersen, A., Küppers, K., Behnken, A., Kroker, K., Schöning, S., Baune, B. T., Rist, F., Arolt, V., & Suslow, T. (2009). Implicit and explicit procedural learning in patients recently remitted from severe major depression. *Psychiatry Research*, *169*(1), 1–6. https://doi.org/10.1016/j.psychres.2008.06.001

Prigatano, G. P. (1992). Personality disturbances associated with traumatic brain injury. *Journal of Consulting and Clinical Psychology*, *60*(3), 360–368. https://doi.org/10.1037/0022-006X.60.3.360

Reber, A. S. (1993). *Implicit learning and tacit knowledge: An essay on the cognitive unconscious*. Oxford University Press.

Rigon, A., Klooster, N. B., Crooks, S., & Duff, M. C. (2019). Procedural memory following moderate-severe traumatic brain injury: Group performance and individual differences on the rotary pursuit task. *Frontiers in Human Neuroscience*, *13*, 251. https://doi.org/10.3389/fnhum.2019.00251

Robertson, E. M., Tormos, J. M., Maeda, F., & Pascual-Leone, A. (2001). The role of the dorsolateral prefrontal cortex during sequence learning is specific for spatial information. *Cerebral Cortex*, *11*(7), 628–635. https://doi.org/10.1093/cercor/11.7.628

Rösser, N., Heuschmann, P., Wersching, H., Breitenstein, C., Knecht, S., & Flöel, A. (2008). Levodopa Improves procedural motor learning in chronic stroke patients. *Archives of Physical Medicine and Rehabilitation*, *89*(9), 1633–1641. https://doi.org/10.1016/j.apmr.2008.02.030

Skidmore, E. R. (2015). Training to optimize learning after traumatic brain injury. *Current Physical Medicine and Rehabilitation Reports*, *3*(2), 99–105. https://doi.org/10.1007/s40141-015-0081-6

Stuss, D. (2011). Traumatic brain injury. *Current Opinion in Neurology*, *24*(6), 584–589. https://doi.org/10.1097/WCO.0b013e32834c7eb9

Timmerman, M. E., & Brouwer, W. H. (1999). Slow information processing after very severe closed head injury: Impaired access to declarative knowledge and intact application and acquisition of procedural knowledge. *Neuropsychologia*, *37*(4), 467–478. https://doi.org/10.1016/S0028-3932(98)00085-2

Vakil, E. (2005). The effect of moderate to severe traumatic brain injury (TBI) on different aspects of memory: A selective review. *Journal of Clinical and Experimental Neuropsychology*, *27*(8), 977–1021. https://doi.org/10.1080/13803390490919245

Vakil, E., Bloch, A., & Cohen, H. (2017). Anticipation measures of sequence learning: Manual versus oculomotor versions of the serial reaction time task. *The Quarterly Journal of Experimental Psychology: Human Experimental Psychology*, *70*(3), 579–589. https://doi.org/10.1080/17470218.2016.1172095

Vakil, E., Gordon, Y., Birnstok, S., Aberbuch, S., & Groswasser, Z. (2001). Declarative and nondeclarative sequence learning tasks: Closed-head injured patients versus control participants. *Journal of Clinical and Experimental Neuropsychology*, *23*(2), 207–214. https://doi.org/10.1076/jcen.23.2.207.1209

Vakil, E., & Hoffman, Y. (2004). Dissociation between two types of skill learning tasks: The differential effect of divided attention. *Journal of Clinical and Experimental Neuropsychology*, *26*(5), 653–666. https://doi.org/10.1080/13803390409609789

Vakil, E., Kraus, A., Bor, B., & Groswasser, Z. (2002). Impaired skill learning in patients with severe closed-head injury as demonstrated by the serial reaction time (SRT) task. *Brain and Cognition*, *50*(2), 304–315. https://doi.org/10.1016/S0278-2626(02)00515-8

Vakil, E., & Lev-Ran Galon, C. (2014). Baseline performance and learning rate of conceptual and perceptual skill-learning tasks: The effect of moderate to severe traumatic brain injury. *Journal of Clinical and Experimental Neuropsychology*, *36*(5), 447–454. https://doi.org/10.1080/13803395.2014.901299

Vallat-Azouvi, C., Paillat, C., Bercovici, S., Morin, B., Paquereau, J., Charanton, J., Ghout, I., & Azouvi, P. (2018). Subjective complaints after acquired brain injury: Presentation of the Brain Injury Complaint Questionnaire (BICoQ). *Journal of Neuroscience Research*, *96*(4), 601–611. https://doi.org/10.1002/jnr.24180

Vallat-Azouvi, C., Pradat-Diehl, P., & Azouvi, P. (2009). Rehabilitation of the central executive of working memory after severe traumatic brain injury: Two single-case studies. *Brain Injury*, *23*(6), 585–594. https://doi.org/10.1080/02699050902970711

Vallat-Azouvi, C., Weber, T., Legrand, L., & Azouvi, P. (2007). Working memory after severe traumatic brain injury. *Journal of the International Neuropsychological Society*, *13*(5), 770–780. https://doi.org/10.1017/S1355617707070993

Virag, M., Janacsek, K., Horvath, A., Bujdoso, Z., Fabo, D., & Nemeth, D. (2015). Competition between frontal lobe functions and implicit sequence learning: Evidence from the long-term effects of alcohol. *Experimental Brain Research*, *233*(7), 2081–2089. https://doi.org/10.1007/s00221-015-4279-8

Waltzman, D., Madore, M., McNerney, M. W., Durazzo, T. C., Bhat, J. V., Yesavage, J., Adamson, M. M., & Furst, A. J. (2017). Preliminary investigation of sex differences in procedural skill learning in veterans with co-morbidities. *Journal of Behavioral and Brain Science*, *7*(8), 325–337. https://doi.org/10.4236/jbbs.2017.78024

Wechsler, D. (1997). *Wechsler memory scale (WMS-III; Vol. 14)*. Psychological corporation.

Whyte, J., Polansky, M., Fleming, M., Coslett, H. B., & Cavallucci, C. (1995). Sustained arousal and attention after traumatic brain injury. *Neuropsychologia*, *33*(7), 797–813. https://doi.org/10.1016/0028-3932(95)00029-3

Willingham, D. B., Salidis, J., & Gabrieli, J. D. (2002). Direct comparison of neural systems mediating conscious and unconscious skill learning. *Journal of Neurophysiology*, *88*(3), 1451–1460. https://doi.org/10.1152/jn.2002.88.3.1451

Zappalà, G., de Schotten, T. M., & Eslinger, P. J. (2012). Traumatic brain injury and the frontal lobes: What can we gain with diffusion tensor imaging? *Cortex: A Journal Devoted to the Study of the Nervous System and Behavior*, *48*(2), 156–165. https://doi.org/10.1016/j.cortex.2011.06.020

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