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Research Report

The dissociation of temporal processing behavior in concussion patients: Stable motor and dynamic perceptual timing

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ABSTRACT

Temporal processing is an integral aspect of human cognition and perception. Recent studies have suggested that patients suffering from concussion exhibit a deficit in temporal processing, characterized by poor performance on a variety of timing tasks. However, the majority of studies focusing on temporal processing deficits in concussion have focused on visual timing mechanisms. As temporal processing may be dominant for auditory-based processing, and so less susceptible to noise, we investigated patients with TBI and compared them to normal healthy controls on a battery of temporal processing tasks, including paced finger tapping and temporal bisection with sub-second intervals. The results of our investigation found that traumatic brain patients were unimpaired on the paced finger tapping task, suggesting that temporal processing deficits do not extend into motor timing and rhythmicity domain. In the temporal bisection task, TBI patients maintained precision but had a significantly higher bisection point, characterized by a greater propensity to judge stimuli as "short" and were significantly slower than controls. Analysis with a drift-diffusion model of perceptual decision-making revealed that TBI patients were specifically impaired in evidence accumulation, suggesting a smaller signal to noise ratio. Specifically, it demonstrated that patients had higher decision threshold and slower drift rates for accumulating evidence in order to arrive at a decision. Patients had to surmount higher evidence thresholds to reach a decision and were slower than controls in their rate of evidence accumulation. These results suggest specific deficits in temporal perceptual decision-making may predict the neural temporal pathways that may be compromised or unaffected, paving the way for designing targeted therapies to address these impairments.

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1. Introduction

Time perception and temporal processing represent fundamental aspects of consciousness and cognition. In order to properly attend, react and predict events occurring in the environment, accurate timing is essential. Indeed, organisms are able to regulate their behavior over a wide variety of timescales, from days to milliseconds (Buhusi & Meck, 2005). The shorter timescale, from tens of milliseconds to seconds, may be particularly important, as this temporal domain covers essential motor, language and perceptual skills such as walking, talking and observing stimuli. Temporal processing relies heavily on perception; stimuli with greater salience stand out and are more likely to be processed more efficiently and expeditiously, facilitating easier decision-making about the stimulus and the manifestation of longer subjective time durations (Matthews & Meck, 2016). The stimulus content, complexity, and the speed of the change in perceptual content also impact temporal processing (Roseboom, Fountas, Nikiforou, Bhowmik, Shanahan, & Seth, 2019). The importance of stimulus features has been exemplified in the recent design of an artificial neural system mirroring the human visual system for image classification. The model design has succeeded in activating hierarchical perceptual networks involved in estimating time durations and matching in-person human reports of content gleaned from videos of natural scene processing (Roseboom et al., 2019).

The brain's capacity to process and measure time is compromised following a traumatic brain injury. Traumatic brain injury (TBI) is defined by the American College of Rehabilitative Medicine (ACRM) as an alteration in brain function, or other evidence of brain pathology, caused by an external force (Menon, Schwab, Wright, & Maas, 2010). It is well accepted as a significant public health problem, with an incidence of at least 1.7 million every year. About 75% of TBIs that occur each year are classified as mild TBI (Faul 2010). Mild TBI is commonly referred to as a concussion and the terms are used interchangeably in the scientific literature. The patients in our study all experienced mild TBI and will be referred to as concussion patients, which is aligned with the current terminology.

Post-concussive symptoms can include impaired function in the areas of cognition, mood and behavior, as well as headaches, and vestibular and oculomotor disorders (Kraus, Little, Wojtowicz, & Sweeney, 2010; Kraus, Little, Donnell, Reilly, Simonian, & Sweeney, 2007), all of which can be part of a post-concussion syndrome (Alexander, 1995; Leddy, Sandhu, Sodhi, Baker, & Willer, 2012). More specifically, TBI patients report a number of persistent symptoms affecting language abilities and reaction time, leading to holistic deficits in the processing of environmental stimuli (Mathias & Wheaton, 2007).

TBI patients have also demonstrated deficits in predictive abilities, such as in visual tracking tasks and predictive saccades (Diwakar, 2015; Caeyenberghs et al., 2010; Heitger et al., 2009; Suh, Basu, Kolster, Sarkar, McCandliss, & Ghajar, 2006, Suh, Kolster, Sarkar, McCandliss, & Ghajar, 2006); Kraus et al., 2010, Kraus, Susmaras, Caughlin, Walker, Sweeney, & Little et al., 2007; Kraus, Little et al., 2007. Specifically, researchers have observed deficits in eye tracking, an implicit temporal processing task (Ghajar & Ivry, 2008). TBI victims had reduced target prediction, increased eye position error, and variability in eye position (Suh, Kolster et al., 2006). Eye position and target prediction errors both had a correlation to the modules related to attention and executive functioning on the California Verbal Learning Test (CVLT), thus strengthening the argument that dysregulation in elapsed time perception is associated with cognitive dysfunction (Suh, Kolster et al., 2006). In other studies, patients with mild or moderate/severe TBI were tested on a predictive saccade test to assess procedural learning. The associated deficits were closely connected to injury severity and produced a reduction in the proportion of anticipatory saccades, indicative of lowered learning (Kraus, Little et al., 2007; Kraus, Susmaras et al., 2007). Decrements in oculomotor performance also signaled a deficit in fronto-striatal functionality and gauged neurophysiologic function (Kraus, Little et al., 2007; Kraus, Susmaras et al., 2007).

A crucial overlap among the deficits associated with TBI is the reliance on the shorter timescale domain. Indeed, the deficits apparent in the post-concussive syndrome of TBI patients may be intrinsically related to a deficit in temporal processing, as many of the abilities disrupted rely on an accurate perception of time (Ghajar & Ivry, 2008). Timing deficits have been investigated previously in TBI (reviewed by Mioni, Grondin, & Stablum, 2014); across a variety of studies, TBI patients have been tested on a number of different timing tasks, at several duration ranges. The temporal tasks employed across these studies typically include production, estimation, reproduction and discrimination paradigms, wherein subjects are either required to provide motor or verbal estimates of duration, or to determine the difference in duration between two stimuli. The general finding across these studies is that patients with TBI are more variable than controls, but not necessarily less accurate. This variability may result from an inability to maintain a consistent representation of a time interval (Mioni, Stablum, & Cantagallo, 2013; Mioni et al., 2014; Piras et al., 2014).

There has been debate about whether impairments in temporal processing in TBI patients are due to a primary impairment or a secondary deficit that results from other impaired cognitive functions, such as attention and working memory. For example, the increases in variability on timing tasks, while indicative of impairment, also present a challenge, as these increases may result from the disruption of a number of distinct cognitive operations, such as memory or decision processes (Gibbon, Church, & Meck, 1984).

In this regard, Mioni, Mattalia, and Stablum (2013) demonstrated the difficulty in disentangling time perception from other cognitive operations by administering neuropsychological tests to TBI patients. These authors found that performance on the timing tasks was significantly correlated to performance on attention, working memory, and executive function indices (Mioni, Mattalia et al., 2013). Performance on the Wisconsin Card Sorting Task (WCST), the digit span backward, and divided attention tasks correlated with the results of the timing reproduction task (Mioni, Mattalia et al., 2013). Significant associations in timing performance on the temporal discrimination task were also observed with performance on the divided attention, No-Go tasks, the N-digit

and digit backward tests, the verbal fluency, and WCST. Holistically, this set of studies revealed that memory, attention, and various executive functions are crucial in sub-second duration time perception (Mioni, Mattalia et al., 2013). Essentially, Mioni and colleagues have demonstrated that temporal processing is frequently a secondary deficit in TBI thereby countering studies that describe temporal acuity related to the speed of information processing as a distinct predictor of psychometric intelligence (Helmbold, Troche, & Rammsayer, 2007). In particular, our study is based on the concept that changes in time perceptions between controls and concussion patients are intertwined with other cognitive operations.

An important distinction in this regard is that all of the studies surveyed by Mioni and colleagues tested subjects on tasks with visual stimuli. There is substantial evidence that the visual modality is less precise for temporal processing than the auditory modality (Wiener, Thompson, & Coslett, 2014; Cicchini, Arrighi, Cecchetti, Giusti, & Burr, 2012; Grondin, 2010; Penney, Gibbon, & Meck, 2000), suggesting that the auditory modality, with greater temporal resolution (Kanabus, Szelag, Rojek, & Poppel, 2002), is dominant for time perception (Kanai, Lloyd, Bueti, & Walsh, 2011; Burr, Banks, & Morrone, 2009; Guttman, Gilroy, & Blake, 2005). Indeed, auditory deficits have been demonstrated as a persistent problem for mild patients (Mayer et al., 2009; Arciniegas, Topkoff, & Silver, 2000). It is possible, then, that the timing impairments observed for TBI patients in these studies may have been exacerbated or masked by the use of visual stimuli.

Neuronal deficits resulting from TBI also present a vexing problem in clinical research. The damage resulting from a concussion typically does not result in a discrete lesion on clinical imaging, but rather what is referred to as diffuse or traumatic axonal injury to white matter tracts between regions, that can be difficult to detect (Shenton et al., 2012). The cognitive deficits in TBI are thought to result from dysfunction of the white matter tracts due to the primary mechanical trauma, as well as secondary mechanisms, impacting critical connections between the prefrontal cortex, a vital region for higher cognitive functions, and other areas that are crucially involved in perception and planning (Kraus, Little et al., 2007; Kraus, Susmaras et al., 2007). Indeed, deficits in timing and predictive functions have been suggested to result from disconnections between coordinated areas responsible for forming expectations (Ghajar & Ivry, 2008). Timing tasks, in this regard, may be particularly useful. Cognitive studies of time perception have traditionally been interpreted within the framework of a unified timing system or centralized "clock" that tracks elapsed time by summating pulses from a pulse-generating pacemaker (Gibbon et al., 1984) in order to perceive intervals (Allman & Meck, 2012). At a certain switch point, the accumulator records the pulses, stores it into working memory, and transfers the trace into reference memory, which is then compared to the current clock value in the comparator module (Gibbon et al., 1984). At this time, the brain makes a decision and a response occurs (Gibbon et al., 1984).

Neuroscience studies from the past fifteen years have now demonstrated a fractionation of timing systems within the brain, depending on a variety of experimental factors, such as the range of intervals tested (above or below one second) or the means by which those intervals are demarcated (motor or perceptual) (Merchant, Harrington, & Meck, 2013; Wiener, Turkeltaub, & Coslett, 2010). Whether the timing task involves an explicit or implicit measurement of time (collision judgments, temporal cuing) also impacts what neural regions are activated (Coull & Nobre, 2008). Additional differences have been suggested between the rhythmic or discrete presentation of durations (Teki, Grube, Kumar, & Griffiths, 2011), or the modality of presentation (Bueti, 2011). Thus, a growing debate in studies of temporal processing is whether there is a single, amodal timing mechanism in the brain, disparate, yet coordinated modality-specific timing mechanisms (Ivry & Schlerf, 2008) or a state-dependent network of sub-second timing derived from intrinsic local neuronal dynamics and time-dependent activity patterns which fluctuate with time (Goel & Buonomano, 2014). It has been further suggested that these separate timing networks may be flexibly invoked when the appropriate task context occurs and that there are gradients and varying activation patterns even within one neural location (Wiener, Matell, & Coslett, 2011). Recent progress has also been made in mapping these distinct yet overlapping neural networks and the tasks they are utilized for (Wiener et al., 2010). The potential implication of this fractionation for studies of TBI is that, if separate timing tasks are used, each potentially invoking a separate timing network depending upon the experimental characteristics, and a timing-specific deficit is found, then one may infer that a particular network has been disrupted. The present study sought to take advantage of the distinct timing systems within the brain by testing TBI patients on two well-established timing tasks that each may invoke separate timing networks and draw attention to specific timing deficits.

Potentially related to the disruption of white matter, evidence has suggested that TBI patients exhibit a specific impairment in thalamic and basal ganglia circuitry and have damage in cortical-subcortical pathways (Fridman, Beattie, Broft, Laureys, & Schiff, 2014; Little et al., 2010). Diffusion tensor imaging and fractional anisotropy of the thalamus of mild and moderate/severe TBI patients showed damage to the thalamic projection fibers and were correlated with deficits in executive function, attention, and memory (Little et al., 2010). This has raised the intriguing possibility that diffuse axonal injury, although widespread and heterogeneous across participants, leads to a common deficit in projections to the basal ganglia-thalamic circuitry. The plausibility of this theory is driven by the wealth of projections from disparate cortical modules to the basal ganglia, such as to striatal spiny neurons, which may integrate anywhere from 10,000 to 30,000 inputs (Dube, Smith, & Bolam, 1988). With respect to time perception, this also presents an interesting connection; currently, one of the dominant neural theories of time perception is Striatal Beat Frequency (SBF; Matell & Meck, 2004), which posits that dopaminergic projections to the basal ganglia act as a coincidence detection mechanism for oscillatory input from widespread cortical neurons. The basal ganglia may also represent a special node in studies of time perception, as distinct sub-regions are activated across the entire corpus of

timing task contexts studied previously. Indeed, the basal ganglia could thus operate as a key integrator for different timing modules (Merchant et al., 2013).

With respect to the increased variability observed in timing tasks for TBI patients, one way in which these findings could be further disentangled is by the application of cognitive models. Well-validated cognitive models offer the opportunity to decompose the variability observed in a number of distinct components, depending on the exact pattern of behavior that is observed (Wiecki, Poland, & Frank, 2015). For example, the Wing-Kristofferson model (Wing & Kristofferson, 1973) of paced finger tapping offers a means for disentangling motor and central aspects of rhythmic tapping performance, by which one can assess whether observed deficits are the result of a cognitive impairment, or simply due to a motor slowing aspect (Ivry & Keele, 1989). Similarly, the drift-diffusion model of Ratcliff (1978) offers a parsimonious way of decomposing responses on a two-alternative forced choice task (2AFC) in which a subject selects one stimulus following the presentation of the target and an alternative option. Responses on the 2AFC are parsed into different components related to perceptual decision-making using the drift-diffusion model. This model was recently adapted to explain time perception processes (Simen et al., 2009; 2011), and has been further expanded to cover temporal decision-making (Balci & Simen, 2014).

Under this framework, the Time-adaptive opponent Poisson Drift Diffusion Model (ToP-DDM) of temporal decision making consists of a two-stage process (Balci & Simen, 2014). In the first stage, a drift-rate process is initiated at the onset of a to-be-timed signal that accumulates at a given rate until the stimulus duration has elapsed. At this point, a second-stage drift diffusion process is initiated, in which evidence accumulates to one of two boundaries, such as whether the perceived signal was “long” or “short”, relative to a reference. Changes in the pattern of responses may thus be ascribed to the threshold bounds for reaching a particular decision, the rate at which information is accumulated to either of the boundaries, or the residual motor speed for producing the response, termed the non-decision time. Crucially, the accumulated output of the first-stage drift process determines the starting point, direction, and strength of the second-stage drift, with longer durations leading to faster drifts to the “long” duration boundary (Balci & Simen, 2014).

The present study was therefore designed to ascertain impairments in distinct timing mechanisms in TBI patients compared to healthy controls by using two auditory timing tasks, one which is mainly motor oriented and involves rhythmic tapping activity while the other task is perceptual in nature and focuses on assessing sound durations. Based on previous studies of temporal perception and the wide variety of timing systems in the brain, we hypothesize that performance with regards to accuracy will remain the same between TBI patients and controls. However, we conjecture that there will be greater variability or less precision in maintaining a specific time interval or consistently identifying a temporal window of time. Furthermore, by using cognitive models, such as Ratcliff's drift-diffusion model, we will discern specific decrements related to perceptual temporal decision-making.

2. Methods

2.1. Subjects and study design

Twenty-one normal, healthy right-handed controls ages 20–59 (mean = 30.7 ± 10.09) with twelve females and nine males were recruited using flyers around the GMU campus. We encountered data transfer issues with one control female participant resulting in incomplete temporal bisection data. Additionally, two male participants had values that were ±3 standard deviations from the mean. Of the two participants, one male subject had low carryover and another presented with high clock/motor variances so these participants were removed from the final data analysis. The final data analysis was performed on eighteen normal, healthy right-handed control subjects ages 20–59 (mean = 30.3 ± 10.45, 7 males, 11 females). Researchers gave each subject a questionnaire to determine eligibility. Participants with any neurological and psychological disorders, hospitalization for a psychological disorder, or diagnosis or treatment for substance abuse were excluded.

Twenty-three traumatic brain-injury victims ages 21–62 (mean = 37.43 ± 12.1), including seven males and 16 females were evaluated and diagnosed by a physician (author M.K.) at the Traumatic Brain Injury and Concussion Clinic at George Washington University Medical Center. Patients were asked if they desired to participate in the research study. If permission was granted, they were enrolled in the study. Excluding the gender and name, the researchers administering both timing tasks were blind to all patient characteristics and medical history, including the severity of the injury and location. All participants gave their written consent to perform the study and were approved by the Institutional Review Boards at GMU and GWU. All patients were at minimum two months post-injury. Note that two male patients were removed due to severe TBI and tumor resection, respectively. Another male participant was excluded because his data exceeded 3 SD from the mean for the total and clock variances. The final data analysis was performed on twenty patients ages 21–62 (mean 35.9 ± 11, 4 males, 16 females).

2.2. Control and patient characteristics

Twenty patients ranging in age from 21 to 62 years of age (mean = 35.9 ± 11.0, 4 males) participated in the study. Eighteen controls ranging in age from 20 to 59 years of age (mean = 30.3 ± 10.45, 7 males) were also enrolled. According to Fisher's test, gender was not significantly different for either groups ($p = .288$, odds ratio = .393). The difference in ages between the groups was also not significant $t\ (36) = -1.579$, $p = .123$ (d = .509).

All of the patients tested had a concussion (mild TBI). The mechanisms of injury were motor-vehicle accidents (35%), falls (25%), assaults (15%), and accidents (25%). Of the 17 patients that had imaging results (MRI or CT scans), 59% had normal CT or MRI scans (negative findings), 18% had incidental findings of cavernoma (2 patients) and meningioma (1 patient), and the rest (23%) had positive findings on their MRI or CT. Positive findings ranged from one subdural hematoma,

one temporal/occipital bone fracture, one spinal cord injury of C3–C5, and one hemorrhage of the left parietal cortex (see Table 1).

Post-injury times ranged from 2.3 to 69.6 months with a mean of 18.6 ± 19.1 months. Of the 12 patients with available loss-of-consciousness (LOC) data, only two had suffered from LOC. Post-traumatic amnesia was reported in six of the sixteen patients with those data. While all patients were currently diagnosed with concussions, we also examined previous concussion history. Data was only available for previous concussions in 18 patients. Of those, nine patients had never had a concussion, six patients were either diagnosed or possibly had one concussion, and three patients had suffered three to ten concussions.

2.3. Tasks

All tasks were administered on a laptop computer. Participants sat at a comfortable distance from the computer and performed the Paced Finger Tapping first and Temporal Bisection second. Auditory stimuli were delivered from the laptop's internal speakers, with the volume individually adjusted by the subject beforehand so that it was at a comfortable level and did not induce headaches or discomfort. Experimental tasks were presented using PsychoPy (Peirce, 2007). To enable proper timing of auditory stimuli, we utilized the 'pyo' sound library within Python, which consistently shows accurate timing (see https://www.psychopy.org/api/sound.html).

2.3.1. Paced finger-tapping

The first task to be administered is the paced finger tapping task, which measures the examinee's propensity for tapping in sync with an externally produced beat. This task has a synchronization and a continuation phase. Isochronous tones (50-msec duration, 400-msec inter-stimulus interval) are played by the computer's audio and the participant is asked to listen for the first few tones and then requested to begin to tap in sync with the beat using the spacebar key once they are comfortable with the rhythm. Participants can listen for as short or as long of a time as they need in order to master the beat before they commence tapping with the tones. Starting with the first keypress, participants tapped in time with the rhythm for 14 consecutive taps. After the 14th tap, the synchronization phase ended and the continuation phase began which encompassed 31 taps. Participants were directed to keep tapping in sync until 31 total taps were collected and a message on the computer indicated they cease tapping. Feedback in the form of a ratio of an intertap interval (ITI) divided by the interbeat interval (IBI) was presented at the end of each trial. The interbeat interval remained constant at 400 msec while the intertap interval varied since it was the rate at which the participant is tapping. A score of one was deemed as perfect performance and participants were encouraged to aim for a ratio that was close to one as possible. Ratios greater than one were deemed too slow and ratios less than one were deemed to be too fast. Each participant underwent 24 trials with 12 trials using the left hand and 12 trials with the right hand. The hand for tapping was chosen randomly by the program at the beginning of the trial.

For data analysis, the inter-tap-intervals were partitioned using the Wing-Kristofferson model of paced finger tapping. Only data from the continuation phase were analyzed. The first tap in each sequence was removed from the analysis. The remaining 30 taps were fit on each trial with a linear regression; the residuals from each regression line were then used to calculate the lag 1 autocovariance, so as to further calculate motor and central (clock) variance scores (Vorberg & Wing, 1996, pp. 181–262). The Wing-Kristofferson model presumes that inter-tap-intervals will negatively covary with one another as the subjects attempt to maintain the standard inter-tone-interval from the synchronization phase. However, when this prediction does not hold and taps positively covary, the model is violated. A variety of means for correcting for these violations has been suggested, each with negligible differences on the overall results (O'Boyle et al., 1996). In this instance, we dealt with violations using the method of Ivry and Keele (1989), where the motor variance was set to zero, and the central (clock) variance was set to equal the total variance of that trial. The average proportion of violations for both the control and the TBI patient groups were 10%. TBI patients had an average of 2.4 ± 2.4 violations whereas patients had an average of 2.6 ± 1.98 violations. According to the Mann Whitney *U* test, the difference in the number of violations between the patients and the controls was not significant ($U = 166.500$, $z = -.400$, $p = .689$).

In the tapping task, three dependent measures were extracted and calculated from the inter-tap interval: motor variance (MV), clock variance (CV), and total variance (TV). The motor and clock variances were the temporal characteristics of the self-paced phase of the tapping with the "clock" entrained to the metronomic beat and the "motor" variance related to the delay in the activation of the motor system in initiating the pressing of the response key (O'Boyle, Freeman, & Cody, 1996). The total variance was the sum of the clock and the motor variance.

2.3.2. Temporal bisection task

Next, the subjects participated in a speeded temporal bisection task with auditory stimuli (Wiener, Coslett & Thompson, 2014). In this task, subjects were presented with a white noise burst on each trial that persisted for one of seven possible, log-spaced durations between 300 and 900 msec. On each trial, subjects were required to judge whether the stimulus presented was "long" or "short", based on their own subjective feeling, and press one of two response keys for each choice. Subjects were additionally instructed to make each response as quickly, yet as accurately as possible, and not to over-think their responses. At the beginning of the experiment, subjects were presented with three stimuli at the geometric mean of the stimulus set (520 msec) as an example of the average stimulus duration and for comparison purposes for the first few trials. Each trial consisted of the presentation of a centrally presented fixation point for 500 msec, followed by the presentation of the stimulus for a variable duration (without the fixation point), followed by a blank screen that was terminated by a choice response. Subjects experienced 64 trials at each duration, for a total of 448 trials, presented in a first-order counterbalanced order, such that every interval in the stimulus set proceeded every interval an equal number of times (see Fig. 1).

Table 1 – Traumatic brain injury patient characteristics.

Patients	Gender	Age	Months Post- Injury	Cause of Injury	Imaging Findings	Handedness	Loss of Consciousness	Past History of Concussions	Post-Traumatic Amnesia
l	F	34	7.5	Fall	Negative	R	n/a	0	n/a
2	F	40	3.0	Accident	Negative	R	n/a	0	N
3	F	33	2.3	Car	n/a	n/a	N	1 (possible)	Y brief possibly
4	F	27	18.4	Fall	n/a	R	N	0	N
5	F	34	17.3	Assault	Negative	R	N	Not formally diagnosed but possible	N
6	F	21	32.1	Car	Negative	R	N	3	N
7	F	62	65.2	Accident	Incidental meningioma	R	Y	1 (as a child)	Y
8	F	47	6.5	Car	Patient has C5–C7 spinal injury	n/a	n/a	0	Y
9	F	42	36.4	Car	Negative	n/a	Y	0	N
10	F	35	12.5	Accident	n/a	R	N	0	N
11	F	55	7.7	Assault	Minimal punctuate densities and hemorrhage to the left parietal cortex	R	N	3	N
12	F	24	28.0	Accident	Incidental cavernoma	R	N	Sub-concussive due to sports but no diagnosis (possible)	Y
13	M	33	2.7	Car	Negative	R	n/a	0	N
14	F	36	10.7	Car	Negative	R	N	0	Y
15	F	40	7.7	Car	Incidental cavernoma	R	N	1	N
16	F	28	69.6	Accident	Negative	R	n/a	~10 sports related	N
17	M	25	10.0	Assault	Negative	R	N	1	n/a
18	M	49	14.7	Fall	Subdural hematoma	R	n/a	0	Y
19	M	31	5.4	Fall	Temporal or occipital bone fracture	n/a	n/a	n/a	n/a
20	F	21	15.4	Fall	Negative	L	n/a	n/a	n/a
	Mean	35.9	18.6	Car	Negative (normal)	R	Y	Y	Y
	(SD)	(11.0)	(19.1)	35%	59%	93.8%	16.7%	50%	37.5%

Patient Demographics and Injury Characteristics of the TBI Concussion Patients (n = 20). The table provides information on the cause of injury, post-injury months, the imaging findings, handedness, and past and present history of loss of consciousness, previous concussion history, and post-traumatic amnesia. The average number of previous loss-of-consciousness episodes includes all patients with any number of possible or diagnosed LOC events.

The data were analyzed similarly to our previous investigations (Wiener et al., 2014). All trials were filtered by a 1000 msec reaction time (RT) cutoff, such that trials for which the RT exceeded 1000 msec were discarded. Trials which were less than 200 msec RT were also filtered and discarded. Psychometric curves were generated by plotting the proportion of "long" response choices for each of the seven tested durations; these points were then fit by a sigmoidal, logistic curve using the *psignifit* version 2.5.6 software package for Matlab (see http://bootstrap-software.org/psignifit). We used the Maximum Likelihood method outlined by Wichmann and Hill (2001), and implemented it using the *BootstrapInference* function for Psignifit 3.0 The results of this analysis yielded the bisection point (BP; the time value at which subjects were equally likely to judge the stimulus as long or short), the difference limen [DL; the difference between the upper (75%) and lower (25%) threshold values divided in half], and the coefficient of variation (CV; DL/BP). The BP thus reflects the subjective midpoint of the range of tested durations, while the CV reflects the normalized variability of measurements. Chronometric curves were constructed by plotting the RT for each of the seven possible durations.

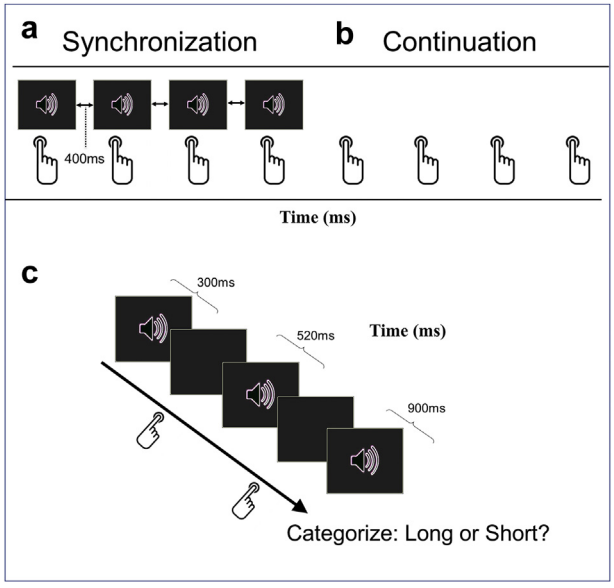

Fig. 1 – a.) Task Schematic for the Synchronization phase of the Paced Finger Tapping Task. The task starts with an auditory metronome that is played at 400 msec intervals. Participants are instructed to listen and to start tapping in sync with the rhythm at any point during the loop for the first 14 taps. b.) Task Schematic for the Continuation phase of the Paced Finger Tapping Task. After the 14 taps, the auditory metronome ended, but the participant was instructed to continue tapping in the absence of the rhythm until the instructions indicated that tapping should cease. There are a total of 31 taps in the continuation phase. Feedback was provided for all trials and the tapping is alternated between the right and left hands for each trial. c.) Task Schematic for the Temporal Bisection Task. Participants listened to seven logarithmically spaced durations auditory stimuli presented one at a time. The auditory stimuli comprised of Gaussian white noise bursts played from the computer speakers. Participants were instructed to categorize each sound as short or long based on their subjective experience with previously experienced auditory stimuli durations.

Variables relating the bias in the previous trial to the current trial were also extracted. For example, the prior decision bias estimate was calculated by examining the signed difference between the bisection points for each prior condition [(prior rLong)-(prior rShort)], with rLong being the bisection point for trials on which the previous trial's response was "long", and rShort being when the previous trial's response was "short". Carryover is another variable that incorporates the previous trial response; in this case, seven psychometric curves are constructed for trials on which each of the seven intervals in the stimulus set was presented on the previous trial. The bisection points (BP) are fitted with a simple linear regression [$BP = m(\text{time}) + b$] and the slope (m) determines the degree and direction of the carryover effect of prior trial duration. Positive slopes show a negative impact of prior trial duration; longer prior trial durations are associated with judging the present trial duration as short. Negative slopes show a positive influence of the previous trial; longer prior trial durations are associated with judging the present trial duration as long (Wiener et al., 2014; Wiener & Thompson, 2015; Wiener, Parikh, Krakow, & Coslett, 2018).

Individual subject trial choice and RT data were additionally decomposed using Ratcliff (1978) drift-diffusion model. We applied non-hierarchical estimation for the drift-diffusion model by using routines provided by the HDDM toolbox for Python (Wiecki, Sofer, & Frank, 2013). To construct the model, we used the HDDM StimCoding() class, which formulates a model of choice and reaction time with duration as a within-subject feature. We decomposed choice and reaction time data to obtain four measures: threshold (a), drift-rate (v), bias (z), and non-decision-time (t); each parameter varied by the tested duration (Wiener et al., 2018; Tipples, 2018). Model fitting was applied to each subject independently and fits for the parameter values were minimized using the HDDM.Optimize() for quantile optimization function, which applies Maximum Likelihood estimation to the cumulative distribution of reaction times (Ratcliff & Tuerlinckx, 2002).

We chose this model because it conforms to previous work done on drift-diffusion modeling application to temporal bisection data (see Tipples, 2018 and Wiener et al., 2018 for further discussion). Briefly, the Time-Adaptive Opponent Processes Drift Diffusion Model (TopDDM) model, as discussed above, postulates a two-stage process in the case of temporal bisection; a first-stage which acts as a "timer" and a second-stage which acts as a "decider" and typically begins at the stimulus offset. Notably, in their original formulation of the model, Balci and Simen (2014) determined that modeling the second-stage alone was sufficient to capture the necessary pattern of responses; this finding was confirmed by further reports finding that modeling the second stage, which conforms to a standard DDM, replicated findings of the full, two-stage model (Wiener et al., 2018; Tipples, 2018). These include 1) an increased second-stage drift rate from the short to long duration boundary with increasing duration, 2) a u-shaped

pattern in the threshold boundary with increasing duration and 3) a linear increase in the starting point with increasing duration. For these reasons, along with our earlier work (Wiener et al., 2018), we modeled the second-stage process alone.

2.4. Statistical analysis

The behavioral data analyses were carried out using SPSS 19.0 (IBM, SPSS) with alpha set to .05 (two-tailed). The paced tapping study data were not normally distributed according to the Shapiro Wilks and visual inspection of the Q–Q plots confirmed this finding; therefore, the assumptions for the Bartlett test were violated. Therefore, we performed the non-parametric Mann–Whitney *U* test to compare data on the motor, central, and total variances between the TBI and healthy control groups.

For the temporal bisection data, the coefficient of variation, the variable related to the prior decision for responding short or long, and the perceptual carryover were normally distributed and the assumptions of the Bartlett test were not violated so we performed independent t-tests. In contrast, the bisection point data was not normally distributed; therefore we conducted the Mann–Whitney *U* test. We also performed a Repeated Measures Analysis of Variance for the two groups (healthy controls and TBI patients) for reaction times, with duration as a within-subject factor.

Eta squared values were calculated for the motor, clock, and total variances in the healthy controls and TBI patients in the tapping study and the bisection point in the temporal bisection task using the effect size calculator for non-parametric tests and the equation ($U^2/\sqrt{(n)}$) (Lenhard & Lenhard, 2016). Cohen's d was calculated for the coefficient of variation, carryover, and prior decision in the temporal bisection task using the same effect size calculator.

3. Results

3.1. Paced finger-tapping study data

Both TBI patients and controls performed the task appropriately. Using the Wing-Kristofferson model to separate the different motor and clock components and the Mann–Whitney U to detect differences, we found no significant difference in total variances ($U = 165$, $z = -.439$, $p = .661$, $\eta^2 = .005$), clock variances ($U = 170$, $z = -.292$, $p = .770$, $\eta^2 = .0023$) or motor variances ($z = -.672$, $U = 157$, $p = .501$, $\eta^2 = .0122$). All participants made less than 30% violations (see Fig. 2).

3.2. Temporal bisection data

Both patients and controls performed this task appropriately. Bisection is the time in seconds at which a participant has an equal probability of responding to a given duration with short or long. According to the Mann–Whitney *U* test, TBI patients (mean = .542 ± .057 SD) bisected at a significantly higher point than healthy normal controls (mean = .505 ± .054 SD) ($U = 109$, $z = -2.076$, $p = .038$, $\eta^2 = .1164$), indicating a greater propensity to judge stimuli as "short."[1] Variability was assessed by the coefficient of variation and healthy controls (mean = .123 ± .036 SD) and patients (.112 ± .037 SD) were not significantly different $t(36) = .994$, $p = .351$ ($d = .307$) (see Fig. 3). Examination of the carryover variable, which evaluates the influence of the previous trial duration on the current trial also exhibited no significant differences $t(36) = 1.925$, $p = .062$ ($d = .625$). Calculations of prior decisions were also not significantly different $t(36) = -1.284$, $p = .207$ ($d = .417$).

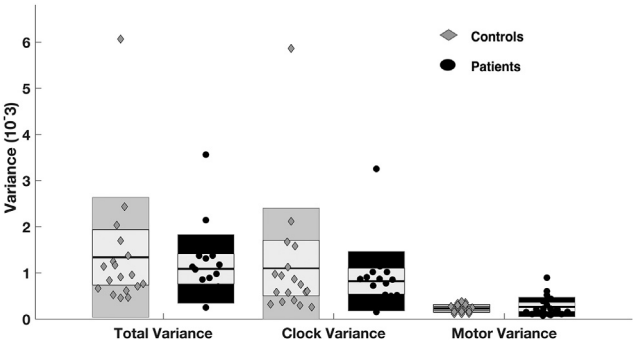

Fig. 2 – Paced Finger Tapping Task Performance. Total variance (TV), clock variance (CV) and motor variance (MV) are all plotted in one graph and were not significantly different between patients and controls. The diamonds represent individual healthy control TV, CV, and MVs whereas the dots represent the patients. The solid black horizontal lines represent the averages, 95% confidence intervals are represented by the outer boxes, and ± one standard deviation are represented by the inner boxes.

Analysis of the chronometric functions for responding showed that the reaction times for controls were faster than for patients [$F(1,36) = 7.387$, $p = .010$, $\eta^2 = .17$]. Within-subjects there was a significant main effect of duration [$F(2.174, 78.259) = 73.968$, $p < .001$, $\eta^2 = .673$], but no interaction between duration and group [$F(2.174, 78.259) = 2.484$, $p = .085$].

We used non-hierarchical drift-diffusion models to further evaluate the temporal decision-making and perceptual abilities and report all significant within and between subject results, including interactions. The threshold shifted quadratically in a U-shaped curve with duration length values, in a manner where the lowest thresholds were observed for mid-range durations, with higher thresholds for more extreme durations, consistent with previous investigations (Balci & Simen, 2014; Wiener et al., 2018). Thresholds were higher in the patients compared to the normal healthy controls [$F(1,36) = 10.238$, $p = .003$, $\eta = .221$] and exhibited a significant main effect of duration within subjects [$F(3.248,116.938) = 11.457$, $p < .001$, $\eta = .241$]. Drift rates also displayed a significant main effect of duration within subjects [$F(1.872, 67.397) = 193.217$, $p < .001$, $\eta = .843$] and had a linear shaped curve. Between subjects, the control drift rates were

[1] A version of the dataset with the excluded participants was re-analyzed using non-parametric tests and compared to dataset without outliers. Values for the majority of the temporal bisection measures were identical; however, for the bisection point measure, when we included the outliers, it led to different results and no statistical significance between the groups.

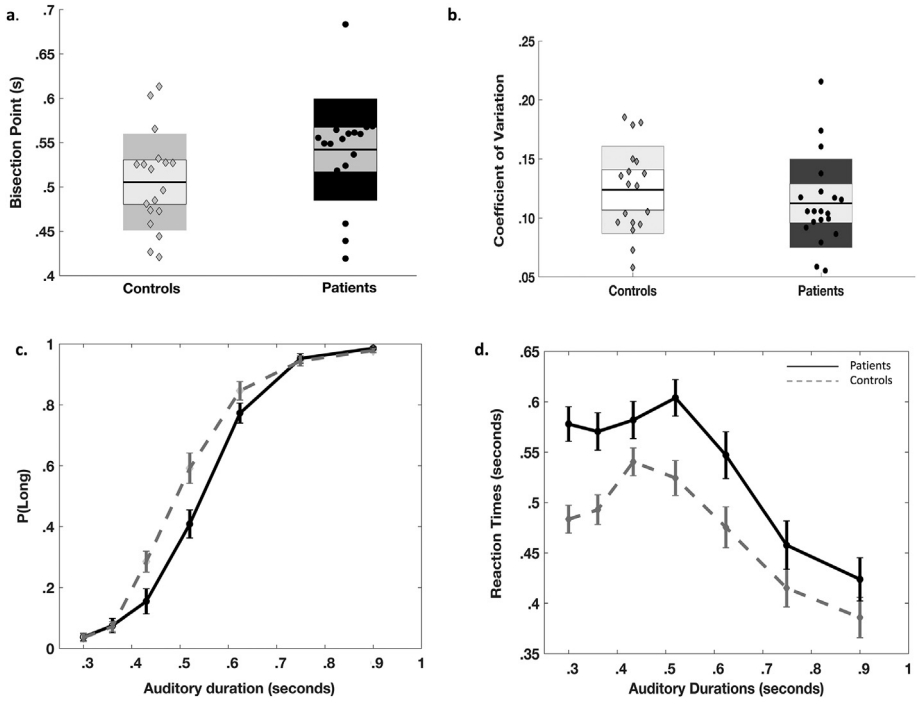

Fig. 3 – a.)Temporal Bisection performance of bisection points in TBI patients and controls. TBI patients bisected at a significantly higher bisection point. Dots represent bisection points for each patient and the diamonds represent each control participant. The solid black horizontal lines represent the averages, 95% confidence intervals are represented by the outer boxes, and ± one standard deviation are represented by the inner boxes. b.) Coefficient of Variation in TBI Patients and Controls. No significant differences in the coefficient of variation were observed between controls and patients. The diamonds represent the individual coefficients of variation for the controls whereas the dots represent the patients. The solid black horizontal lines represent the averages, 95% confidence intervals are represented by the outer boxes, and ± one standard deviation are represented by the inner boxes. c.) Temporal bisection psychometric curve on probability of responding long. Patients were less likely to characterize the auditory stimuli as long but the difference between patients and controls was not significant. The black line represents the patient performance and the dashed line with diamonds represents the control participants. Data expressed in p(Long) ± SEM. d.) Temporal Bisection chronometric curve of stimuli response. Controls had significantly faster reaction times in classifying stimuli. Control participants are denoted by a dashed line with diamonds and the black line represents patient performance. Data are expressed in reaction times ± SEM.

significantly higher than patients [$F(1,36) = 6.293$, $p = .017$, $\eta = .149$] (See Fig. 4). Non-decision response times were similar between the two groups [$F(1,36) = 1.164$, $p = .288$, $\eta = .031$] while within-subjects, there was a significant main effect of duration [$F=(3.844,138.375) = 3.624$, $p = .008$, $\eta = .091$]. Bias for either responding short or long between the two groups was also similar [$F(1,36) = .335$, $p = .565$, $\eta = .009$]. However, within-subjects, bias showed a significant main effect of duration [$F(3.912,140.836) = 30.996$, $p < .001$, $\eta = .463$] and duration by group interaction [$F(3.912,140.836) = 3.012$, $p = .021$, $\eta = .077$], with significance at .36 sec ($t = 2.185$, $p = .036$). Note that Greenhouse-Geisser corrections were applied to all of the data because sphericity was violated (See Fig. 5).

4. Discussion

We performed a study of timing impairments in concussion patients and compared them with normal, healthy controls. Our study accounted for both the motor and perceptual dimensions of temporal processing. We measured the perception of temporal durations with the temporal bisection task and the motor movement involved in synchronizing and continuing with a rhythmic beat using the paced finger tapping task. Both tasks involved cognitive processes such as working memory or attention, suggesting that the measurement of timing is linked to other cognitive operations. Timing impairments in the patient group were related to the perceptual decision-making components. Compared to controls, patients were more likely to have slower reaction times and differences in the perceptual decision-making processes.

No performance differences were detected in the Paced Finger Tapping task when comparing between patients and controls. While this task is a useful measure in approximating disturbances related to motor timing, most of the previous studies on the paced finger tapping task that have demonstrated impairments are related to Parkinson's and Huntington's Disease (O'Boyle et al., 1996; Freeman et al., 1996), Bipolar disorder (Bolbecker et al., 2011), schizophrenia Carroll, O'Donnell, Shekhar, and Hetrick (2009) and cerebellar degeneration (Ivry & Keele, 1989). Decomposition with the Wing-Kristofferson model has been useful for disentangling the

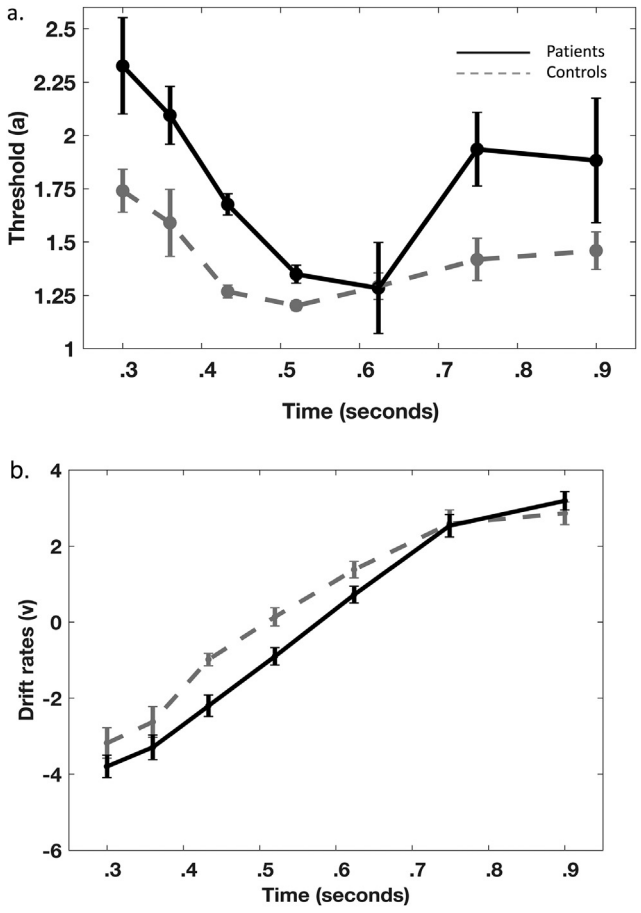

Fig. 4 – a.) Drift Diffusion Performance in TBI patients and control thresholds. Patient thresholds are significantly higher than controls. Data expressed in threshold (a) ± SEM. b.) Drift Diffusion Performance in TBI patients and control drift rates. Generally, controls have significantly faster drift rates than patients. Data expressed in drift rate (v) ± SEM.

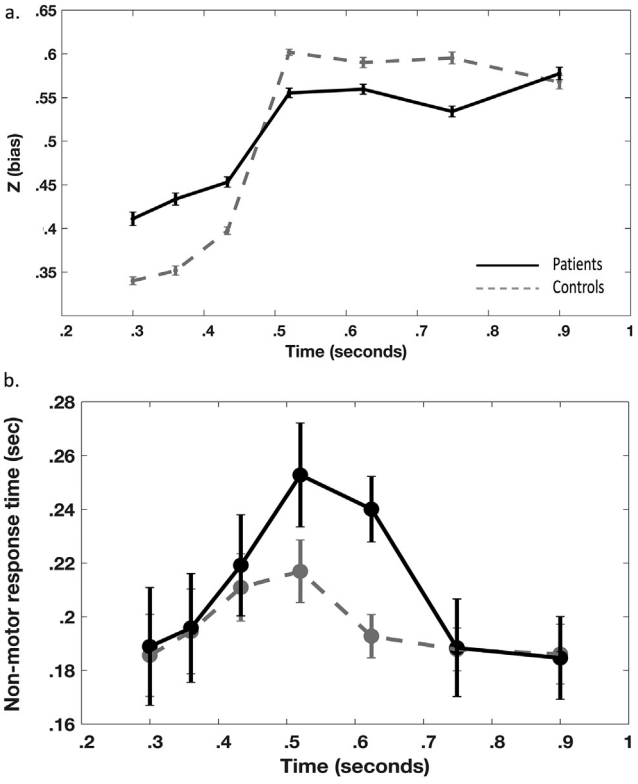

Fig. 5 – a.) Drift Diffusion Performance in TBI patients and control biases. Bias shows a duration by group interaction and a significant difference at .036 sec. Data expressed in bias (z) ± SEM. b.) Drift Diffusion Performance in TBI patients and control non-motor response times. No significant differences are observed between patients and controls. Data expressed in non-motor response times (t) ± SEM.

general level of impairment between motor implementation and central levels. For example, peripheral nerve degeneration has been shown to raise motor, but not central (clock) variance on this task (Ivry & Keele, 1989). The lack of an effect in our group of concussion patients compared to controls suggests that, at least compared to this group, a concussion does not disrupt the ability of a patient to reproduce rhythmic activities, and that this change does not relate to motor timing. TBI patients were able to synchronize their tapping with the external beat and rhythm similarly to controls in paced finger-tapping, demonstrating that this group was still able to capitalize on rhythmic information similarly to healthy participants. Similarly to our work with processing different types of temporal information, a recent study has examined differences in rhythmic-based and aperiodic temporal prediction in two groups of patients, one with cerebellar degeneration and another with Parkinson's Disease. The groups were tested on a visual detection task with stimuli onsets that were rhythmic or single interval (Ivry and Breska, 2018). Expectedly, the Parkinson's Disease patients performed worse on rhythmic-based target detection while cerebellar degeneration patients performed in the opposite pattern (Ivry and Breska, 2018).

In one past study, severely injured TBI patients performed the paced finger tapping task with a slower tempo (1000 msec inter-trial interval) (Perbal, Couillet, Azouvi, & Pouthas, 2003). Results from this study with severe TBI patients were non-significant and consistent with findings from our current experiment. However, there were key differences between our study and this previous experiment; most notably, subjects were simply required to tap at either 1000 msec or a free rate with no external stimulus in either condition. Furthermore, these authors did not parse out the motor, central, and total variances using the Wing-Kristofferson model.

From a neuroanatomical point of view, since the ability to maintain an external beat is associated with a normal functioning basal ganglia and motor cortex, one may conjecture that this part of the basal ganglia circuitry is intact in this set of TBI patients (O'Boyle et al., 1996). Also, due to the sensorimotor coordination involved in producing an action intimately coordinated with a periodic external stimulus, one could conclude that this circuit is also uncompromised in TBI patients (Bavassi, Kamienkowski, Sigman, & Laje, 2017).

Unlike the performance outcomes on the paced finger tapping task, we did observe significant changes in the

temporal bisection task. Patients had a higher bisection point and slower reaction times for responding to the seven durations than controls but no other differences. Typically, humans bisect at the geometric mean (here, 520 msec) in log-spaced intervals while with linear intervals, the bisection is closer to the arithmetic mean (here, 550 msec) (Kopec & Brody, 2010 Dec). The controls in our study bisected at the geometric mean whereas the patients bisected at the arithmetic mean, suggesting that the underlying representation of time between the two groups may differ. Testing at a broader range of durations would provide more evidence for this assertion. Interestingly, compared to past studies, we did not see differences in variability or precision in consistently classifying that set time representation (Mioni, Mattalia et al., 2013). In this regard, the coefficient of variation was not significantly different between groups.

Bisection points are dependent on the ratio of the target intervals, attentional load, inter-trial durations, and the stimuli modality (Levy, Namboodiri, & Shuler, 2015). Since all of these external factors, excluding attentional load, are equivalent in both the patient and control groups, bisection point differences may be attributed to differences in managing attentional load between patients and controls. These factors may also impact memory, which in turn affects the bisection point (Levy et al., 2015). Memory biases may play a role because we used a "no referents" version of the task; therefore, the memory biases remain strong throughout the task. If a fixed referents version of the task (referents provided in each trial) were employed, the memory biases might be reduced. Levy et al. (2015) attempted to address this concern by incorporating an additional temporal production component into the classification component of the temporal bisection task in an attempt to parse out the influence of memory on bisection points. Future studies could modify the task to include a temporal production component.

It is also noteworthy that the two differences (bisection point and reaction time) which were observed in TBI patients in the temporal bisection task were related to independently judging and evaluating temporal durations. Healthy controls and TBI patients had similar results when examining the effect of prior or previous trial temporal judgments on current trial judgments for measures, such as prior decisions and carryovers. These findings signaled that the context-dependent aspects of decision-making of temporal information were uncompromised.

To further understand the reaction time data observed for temporal bisection, we decomposed choice and reaction time data using a DDM model of perceptual decision-making. While researchers have used DDM in a pediatric TBI population to analyze data from a multi-sensory integration and set-shifting paradigm (Königs et al., 2017), our study is the first that we are aware of to apply a DDM to behavioral data from adult TBI patients.

The DDM model was recently adapted to temporal discrimination on a task similar to ours (Balci & Simen, 2014). The general model assumes that timing consists of a two-stage process, wherein subjects first accumulate information during the interval, with the rate of accumulation determining the length of the perceived interval. The second stage initiates when the timed stimulus extinguishes, or when the categorical threshold – in this case, the bisection point – has elapsed. In the second stage, the output of the accumulator sets the starting point for a second drift-diffusion process, by which information accumulates to one of two decision boundaries. The distance between this starting point and the nearest decision boundary determines the drift rate, with faster drift rates for starting points closer to a decision boundary and slower drift rates for starting points closer to the bisection point. The level of noise, in either the first-stage or second-stage process, thus determines the drift rate. Once a decision boundary has been reached, the response is made; any residual time arising from this process is driven by the speed of the motor output, ascribed as non-decision-time. In fitting the DDM to our data, we replicated many of the effects observed previously, with faster drift rates for higher durations and slower drift rates for durations closest to the bisection point and shorter durations. Additionally, we replicate a curious effect where the decision threshold is lowest for intervals near the bisection point and highest for extreme durations. Although the model does not explicitly predict this effect, Balci and Simen (2014) suggest that it may be due to the reward structure of the task, where correct categorization of extreme durations was rewarded; yet, no rewards or feedback were provided in our task. One possibility for decision threshold differences is that these boundaries dynamically change with the amount of evidence accumulation in the second stage. Recent theories of perceptual decision-making suggest that decision boundaries collapse over time, thus triggering decisions with less evidence (Drugowitsch, Moreno-Bote, Churchland, Shadlen, & Pouget, 2012; Bowman, Kording, & Gottfried, 2012). Under particular circumstances (Hawkins, Forstmann, Wagenmakers, Ratcliff, & Brown, 2015), this strategy may afford subjects greater flexibility in their responses. Accordingly, more evidence accumulation is associated with a monotonic collapse in the decision boundary.

When examining the decision-making performance profile of the temporal bisection task between groups, we found that TBI patients differed from controls in the thresholds or the distance between the two boundaries for a response. This boundary separation determines the task strategy most likely to be used and is dependent on the reaction time and accuracy ratios, a reflection of the speed-accuracy trade-off (Wiecki et al., 2013). The larger patient thresholds in our study are indicative of more cautious responding and skewed or slowed response times, a phenomenon that is reflected in other temporal bisection variables (Wiecki et al., 2013). We could infer that patients needed more evidence in order to select a specific response (Wiecki et al., 2013).

Drift rates for patients were also slower than controls, exemplifying slower speeds in accumulating evidence towards the decision to respond either short or long (Wiecki et al., 2013). Drift rates are also linked to the efficiency of information processing and are dependent on signal to noise ratios; subsequently, cleaner signals associated with reduced noise (Wiecki et al., 2013). This is important to note in patients experiencing difficulties with sustained attention (Bonnelle et al., 2011; Cicerone, 1996; Stuss et al., 1989), because longer durations in the stimulus set may have engendered greater noise in the rate of evidence accumulation. Furthermore, since the bisection point was higher in the patient group, the

drift rate was slower due to more evidence needing to be accumulated to reach a decision point.

Non-decision times were similar between patients and controls. This result indicates that once a decision boundary for short or long had been reached, and the response was made; any residual time arising from this process was driven by the speed of the motor output, ascribed as non-decision-time. The non-decisional time reflects extra-decisional processing, stimulus encoding, and motor preparation along with a response. No detected differences in the non-decision time show that reaction time differences between patients and controls were not due to any extra-decisional processing and conforms with our findings on the paced finger tapping task. Furthermore, the bias for responding short or long was not significantly different between patients and controls and failed to impact the responding time or bisection point.

Our study was able to dissociate specific motor and perceptual temporal processing issues because each task involved a different part of the neural circuitry implicated in timing perception. This elegant parsing of the temporal processing components offered us perspective on the neural region that may have been impacted. The exact location and extent of brain damage may not be clear in a traditional MRI scan without complementary, sophisticated technologies such as diffusion tensor imaging to examine the integrity of the fiber tracts (Kinnunen et al., 2011). This is because TBI frequently involves not only focal damage but also white matter damage or diffuse or traumatic axonal injury which affects connectivity between different neural networks, thereby impacting cognitive and executive functions involved with timing (Kinnunen et al., 2011). Consequently, a major difficulty in the diagnosis and prognosis of TBI patients is discovering which neural regions have been affected by the injury. Although we cannot speak to the precise disconnect pattern affecting timing in the present study as there was no neuroimaging or neurophysiology component to this purely behavioral study, the constellation of deficits allows some speculation. Recent work into time perception has suggested a fractionation of the networks that are invoked for timing across different task contexts (Wiener et al., 2010). As such, the network of regions engaged in sub-second motor timing, as in the case of paced finger tapping, is partially distinct from the network for perceptual timing, as in the case of temporal bisection; this network includes regions of the inferior frontal gyrus, supplementary motor area, basal ganglia, cerebellum and right inferior parietal lobe. In the present study, patients with TBI did not present a gross deficit across all tasks, which suggest that these patients do not suffer from a general impairment that would lead to a global deficit across tasks. Patients did not demonstrate any differences from controls on the paced finger tapping, which indicates that basal ganglia and cerebellar circuitry and their connections with motor cortex are likely intact (Coslett, Wiener, & Chatterjee, 2010; Witt, Laird, & Meyerand, 2008). Instead, differences in the temporal bisection task between patients and controls suggests that these subjects exhibit a specific disconnect between regions of the prefrontal cortex, such as the inferior frontal gyrus and basal ganglia, invoked for similar task contexts (Wiener et al., 2010). Indeed, patients with Parkinson's Disease demonstrate deficits in drift rates during perceptual decision-making that are ameliorated by ablation of the subthalamic nucleus (Obeso et al., 2014). Further, dopaminergic activity in the prefrontal cortex has been linked to the perception of longer intervals (Wiener, Lohoff, & Coslett, 2011), and alterations in dopamine here are suggested to disrupt the signal to noise ratio for temporal integration during working memory (Constantinidis, Williams, & Goldman-Rakic, 2002; Durstewitz, Seamans, & Sejnowski, 2000). Of note, dopaminergic medications have recently been demonstrated to improve symptoms in concussion patients, although the mechanism underlying this improvement is still unknown (Bales, Wagner, Kline, & Dixon, 2009). The findings here would thus suggest that the temporal dysfunction observed in concussion is a result of impaired connectivity between the basal ganglia and prefrontal cortex, mediated by prefrontal dopamine (Winterer & Weinberger, 2004); notably, as paced finger tapping was intact, this suggests that nigrostriatal dopaminergic pathways are unimpaired in these patients (Wiener et al., 2011). If confirmed, this would suggest potential courses of treatment for TBI patients; recent advocates for a network-based approach to concussion suggest that the targeted use of medications or noninvasive brain stimulation may help alleviate cognitive impairments. Of note, TMS of the prefrontal cortex has been demonstrated as an effective tool for inducing dopamine release in the basal ganglia (Strafella, Paus, Barrett, & Dagher, 2001; Pogarell et al., 2007).

Our study had a few limitations which will affect the trajectory of future research. First, it was a small, exploratory study intended to lay the groundwork for a larger more extensive study of motor and perceptual timing differences in the auditory domain between concussion patients and normal, healthy controls. Second, due to the small size, the sample was only matched on age and gender and recruitment was discontinued when it matched on those variables. Future studies should match groups on IQ (Anderson & Schmitter-Edgecombe, 2011), on years of education, and other relevant demographic variables to minimize any other confounds. Thirdly, the testing for the concussion arm of our study was conducted where patients felt most comfortable rather than one central location; therefore, additional studies should occur in one location. Finally, there were more parameters to evaluate in the temporal bisection task as opposed to the paced finger tapping task, increasing the familywise error rate and raising the concern of a greater likelihood of seeing an effect in the perceptual rather than the motor domain. Furthermore, because each task had a different set of requirements and we derived different measurements (bisection point in one case and motor variability in another) for each one, we cannot directly compare differences between the tapping and temporal bisection. Additionally, we administered the paced finger tapping task before the temporal bisection, so any deficits we observe in the sensory task may be due to fatigue arising from not counterbalancing the order in which the tasks were administered. Due to these caveats inherent in a small, exploratory study, our results should be taken with caution and the limitations should be addressed prior to start of a recruitment of a larger study with greater power.

However, our findings still support the suggestion that TBI impacts temporal processing, but provide a more nuanced view on what that impact might be. Specifically, we suggest that TBI impacts connections between the prefrontal cortex and basal ganglia circuitry, supporting the accumulation of temporal information for decision-making. Furthermore, we suggest that TBI leads to changes in perceptual decision-making. The timing tasks used in this study can function as a diagnostic utility for determining the specific timing and rhythm differences in healthy adults and patient populations. In addition to their prognostic value, neurophysiologic assessments that could help assess the course of recovery may also help safely guide TBI management issues such as return to work, school, or athletics. This would be very valuable in reducing subsequent risk of injury, as well as potentially helping guide treatment. Measures of temporal processing show promise in this regard, as their precision could be used for tracking the rate of recovery or indicating the potential risk for re-injury, in addition to designing therapies for treatment. Assessing temporal function can facilitate the development of interventions for concussion patients and can be particularly important in sports-related concussions where timing and rhythm issues impact athletic performance and risk for repeat injury (Harmon et al., 2013). Therefore, there is a high drive within the sports medicine community to further develop the translational potential of assessment tools for the return to play in athletes (Giza, Kutcher, Ashwal, & et al, 2013; Harmon et al., 2013).

Of particular relevance are findings demonstrating that training on a timing task similar to the temporal bisection task in the present study is associated with increases in gray matter and white matter connections in relevant areas (Bueti, Lasaponara, Cercignani, & Macaluso, 2012), which may be useful for improving symptoms in patients with post-concussive syndrome. This training also produced structural changes in the sensory-motor cortices and the cerebellum, highlighting the plasticity of timing-related learning (Bueti et al., 2012). The findings also elaborated on the role of practice in representing and in storing temporal durations (Bueti et al., 2012). One could envision that this type of training paradigm may have implications for clinical populations and possibly traumatic brain injury patients. Therefore, with a better understanding of how timing is encoded in our brain and temporal information is processed in TBI patients, perhaps we can design therapies to address these impairments and enable us to formulate clinical methods to navigate around the temporal dysfunction and perform the acts of daily living.

CRediT authorship contribution statement

Farah Bader: Investigation, Formal analysis, Writing - original draft, Writing - review & editing, Resources, Data curation, Visualization. **William R. Kochen:** Investigation, Resources, Project administration. **Marilyn Kraus:** Resources, Supervision, Project administration. **Martin Wiener:** Conceptualization, Methodology, Writing - review & editing, Software, Data curation, Supervision, Project administration.

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