University of Nevada, Reno

Working Memory in Those with a History of Concussion

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Psychology

By

Jorja Shires

Dr. Marian E. Berryhill – Dissertation Advisor

May, 2024

THE GRADUATE SCHOOL

We recommend that the dissertation
prepared under our supervision by

Jorja Shires

entitled

Abstract and Concrete Stimuli are Maintained Separately in Working Memory; mTBI status and HD-tDCS do not alter Performance

be accepted in partial fulfillment of the
requirements for the degree of

Doctor of Philosophy

Marian E. Berryhill, Ph.D.
Advisor

Edward F. Ester, Ph.D.
Committee Member

Sarah M. Haigh, Ph.D.
Committee Member

Theresa M. Desrochers, Ph.D.
Committee Member

Nicholas G. Murray, Ph.D., M.A.
Graduate School Representative

Markus Kemmelmeier, Ph.D., Dean
Graduate School

May, 2024

Abstract

Mild traumatic brain injury (mTBI), a common head injury, is expected to heal within weeks. However, deficits in visual working memory (WM) persist in undergraduates who report a history of mTBI (hmTBI). This pattern is observed years after injury. MTBI is a heterogenous group in several areas including etiology, treatment, age at injury, sex, and even WM performance. In other words, not all people with hmTBI are impaired in VWM, but a subset are. We proposed several related research questions: 1) are persistent WM deficits attributable to distributions of frontal lobe function, 2) is there a *common* neural signature associated with VWM impairment in hmTBI, and 3) can neuromodulation improve WM function in hmTBI? This dissertation addresses each of these related questions. Aim 1 extended our previous WM findings using a new task relying heavily on frontal lobe regions. We predicted greater deficits on this task compared to our previous WM tasks. Aim 2 investigated whether the subgroup showing WM deficits share an underlying neural signature. Electroencephalogram (EEG) data was used to train a classifier to determine whether a neural signature accurately predicts group membership (control, hmTBI low WM, hmTBI high WM). In Aim 3, we applied transcranial direct current stimulation (tDCS) with the goal of improving WM. The overall goal was to identify *who* has lasting traces of hmTBI, *why* they persist, and *how* to remediate VWM in those with residual deficits.

Our results found no behavioral or neuronal difference between mTBI and controls. There was no group effect regardless of neuromodulation, task demands, or cognitive load. EEG

data was unable to discriminate between hmTBI and controls. However, we did find a significant difference in VWM performance between the dataset collected for this dissertation and a dataset collected pre-COVID. The hmTBI population present at the University of Nevada, Reno may have changed after the pandemic.

Our other major finding was in Aim 1. Performance was significantly higher on ACTS-WM than ACTS despite the increase cognitive load. This finding suggests abstract concepts, such as instructions, and concrete stimuli may be held in WM in separate stores. While our findings were mostly unexpected, they have interesting implications for WM theory and research in special populations.

To my grandparents, who passed on a sense of curiosity and love for science and helped me achieve all of my dreams.

Acknowledgements

I would like to express gratitude to my advisor, Dr. Marian Berryhill, for her endless patience and wisdom. I aspire to love my work as she does. I would like to thank my committee for their comments and suggestions for this dissertation. My committee not only helped shape this dissertation, but their work inspired it. I would like to express gratitude to the members of the Memory and Brain Lab, both current and previous, for their help in data collection, data analysis, coding, and support. I would like to express special thanks to my friend and peer, Jenna N. Pablo, for her unwavering support and assistance in all my scientific endeavors.

Table of Contents

List of Tables

List of Figures

Introduction

Let me begin by orienting the reader to the structure of the following document. In the first few pages of this dissertation, I will present a general content-related background section. For each of the three Aims, there is a corresponding background that is more specialized and specific. At the end of each Aim chapter there will be a discussion of the results. At the end of the dissertation, there will be a general discussion summarizing the predictions and findings. Lastly, there will be a section going over any limitations, theoretical implications, and future directions.

Working Memory

Working memory (WM) is a vital cognitive function that allows us to maintain and manipulate a small amount of information over a brief period of time to accomplish immediate goals. We use WM throughout our days to perform most tasks, for example planning, organizing, and calculating. WM remains incompletely understood, both in terms of behavior and neural mechanism. Our ability to manipulate information in WM can directly affect our ability to live independently as we age, and to achieve academic success in our youth. Below, I will discuss a broad overview of background information characterizing some of the known neural correlates of WM and common WM deficits before expanding into the three specific aims of this dissertation. Importantly, because WM capacity is limited, any change to WM capacity can have a major impact - from academic performance to job ability. One population on campus in whom WM capacity may be affected are those students with a history of mild traumatic brain injury (mTBI). One

overall goal of this dissertation is to understand the breadth of WM deficits in participants with a history of mTBI (hmTBI), commonly referred to as ‘concussion’. [Removed Sentence Here, Disagreed with overall statements about hmTBI]

There is an enormous literature devoted to WM, in particular to determine what is maintained in WM. For this work, the most important empirical approaches include invasive and non-invasive electrophysiology and functional magnetic resonance imaging (fMRI). Seminal research showed WM depended on sustained single-unit activity in monkey prefrontal (Funahashi et al., 1989; Goldman-Rakic, 1995; Miller et al., 1996) and parietal (Constantinidis & Steinmetz, 1996; Owen et al., 2005) cortices. Subsequent neuropsychological studies (Katsuki & Constantinidis, 2013; Ramirez-Cardenas & Nieder, 2019) and non-invasive neuroimaging in humans supported the large role of prefrontal and parietal regions in WM (Cohen et al., 1997; Curtis & D’Esposito, 2003). These approaches reveal consistent activity in anterior-posterior networks including frontal and parietal regions that show sustained activity during WM maintenance (Curtis & Sprague, 2021; Sreenivasan et al., 2014). Coordinated neural activity across frontal and parietal populations form the anterior-posterior neural networks required for WM, such as the Central Executive Network (Daigle et al., 2022; Menon, 2011; Serino et al., 2006; Yu et al., 2023).

Yet, the story is complicated by new data. In particular, the nature of what these fronto-parietal networks reflect is up for renewed debate. One possibility is that information is

maintained for WM within sensory regions (Curtis & Sprague, 2021; Kamitani & Tong, 2005), because multivariate decoding approaches can classify visual items actively held in WM from activity in the visual cortex (Che et al., 2022; Czoschke et al., 2021; Erhart et al., 2021). Other perspectives suggest that silent connections, believed to be altered synaptic weights, retain WM representations without the metabolic cost of action potentials (Muhle-Karbe et al., 2021; Rose et al., 2016). A merging perspective suggests that fronto-parietal activity reflects 'pointers' to reactivate sensory activity (Thyer et al., 2022). In short, there is an on-going debate regarding how, what, and where items are maintained within WM.

However, a consistent WM finding is the engagement of neural populations coordinating to enable behavior. Neural oscillations arise through the rhythmic increase and decrease of neuronal activity of millions of neurons. These oscillations can be classified into five frequency bands: delta (0-4 Hz), theta (4-8 Hz), alpha (8 - 14 Hz), beta (15 - 30 Hz) and gamma (> 30 Hz). For the past few decades, evidence supported the theory that the neural mechanism of WM requires theta and gamma interaction (Lisman & Idiart, 1995; Vosskuhl et al., 2015). Gamma oscillations are nested within slower theta oscillations, a phenomenon known as *phase-amplitude coupling* (PAC). At the peak of a theta oscillation, a gamma burst reinstates the WM representations. Thus, theoretically, if the theta oscillations were slowed, there would be an increase in the temporal duration of its peak, and WM capacity would increase. This possibility was supported by several human neurostimulation studies (Bender et al., 2019; Vosskuhl et al., 2015; Wolinski et al., 2018). Besides frequency, the

phase between theta and gamma must align for successful WM maintenance and retrieval, a measure termed *phase-locking*. As expected, neuronal activity shows phase-locking between theta and gamma oscillations (Canolty et al., 2006; Polanía et al., 2012; Tseng et al., 2018). Altering the phase of either frequency can improve or impair WM performance, depending on the stimulation parameters. For example, an *anti-phase* transcranial alternating current stimulation (tACS) pulse can impair WM performance (Tseng et al., 2018). In our lab, a study pairing tDCS with a WM task performance showed that gains were driven by superior theta-gamma PAC between frontal and parietal regions (Jones et al., 2017, 2020). The changes in PAC were correlated with the WM benefits from tDCS. Furthermore, the strength and timing of the PAC predicted WM performance. Stimulation studies show the successful manipulation of the theta-gamma interaction alters WM capacity and performance. To summarize, a key neural mechanism underlying WM is the connectivity between the frontal and parietal regions in the theta and gamma frequency bands.

WM is a complex cognitive function vital to our everyday lives. It requires the neural coordination of multiple neural populations in multiple frequency bands. In particular, the connection between the theta and gamma within the frontoparietal network has been linked to WM function and capacity. This line of research has been proven useful not only for a basic understanding of neural mechanisms, but also the limitations and changes in WM function. We would expand on this by focusing on those with a deficit in WM. Patients with diverse pathologies present with WM deficits, including various dementias (Foxe et

al., 2020; Zokaei & Husain, 2019), severe mental illness such as schizophrenia (Braun et al., 2021; Yang et al., 2020), mild traumatic brain injury (Arciniega et al., 2019, 2021; Chung et al., 2019; Green et al., 2018; Lawton & Huang, 2019; Quinn De Launay et al., 2021). The aim of this dissertation is to provide insight into the mechanistic failure in a WM deficit to help design and implement recovery strategies.

Mild Traumatic Brain Injury (mTBI)

Mild traumatic brain injury is an injury caused by the brain moving and impacting the skull. MTBI is the most common head injury with ~2.5 million yearly visits to the emergency room in the United States alone (Silverberg et al., 2019). Perhaps surprisingly, the definition and classification of an mTBI, or *concussion* in layman's terms, is an area of debate. The Centers for Disease Control and Prevention (CDC) details 19 guidelines for diagnosis and treatment of an mTBI (Lumba-Brown et al., 2018). Factors such as the mechanism of injury, age, headache severity, vomiting, and Glasgow Coma Scale Score are considered when assessing the severity of the injury (Lumba-Brown et al., 2018). The World Health Organization (WHO) defines an mTBI based on a series of symptoms such as a loss of consciousness (LOC) for <30 minutes. However, the WHO does not clarify a minimum LOC requirement leading to a wide variety of injuries to be classified as mTBI (Lefevre-Dognin et al., 2021). The difference of a moderate and mild TBI has been ill-defined and is an on-going subject of debate (Lefevre-Dognin et al., 2021; Levin & Diaz-Arrastia, 2015). Across all diagnostic criteria, mTBI is a checklist diagnosis that includes a range of symptoms. Unsurprisingly, within the first 48 hours after an mTBI, most

cognitive functions are impaired, and being ‘dazed’ or ‘punch-drunk’ is a classic symptom of mTBI. Other impaired functions include balance, eye-movement, and smooth eye-pursuit (Hossain et al., 2022; Murray et al., 2014, 2019, 2020). While most people recover in a few weeks from an mTBI, ~29% percent develop persistent post-concussion symptoms such as dizziness, headaches, fatigue, problems with memory, etc. (Sterr et al., 2006). Around 50% of those with a previous mTBI show signs of cognitive impairments at 12 months post-injury (Chen et al., 2022). It is clear that for a portion of the mTBI population, the effects of the injury are long-lasting. The overarching goal of this dissertation is further understanding about the long-term outcomes associated with an mTBI and potential nuances of these outcomes.

History of mTBI and mTBI

While this dissertation discusses mTBI, there is an important distinction between the typically studied mTBI population and the population of mTBI in throughout these aims. First, mTBI are usually acute. It is common for testing to occur within days, weeks, or a few months since the injury. The population within this dissertation which we will refer to as those with a *history* of mTBI (hmTBI) are usually years after injury. Second, mTBI are sampled from individuals seeking impact testing or medical attention. Ergo, this population is medically diagnosed while our population is a self-reported without any medical diagnosis. For this dissertation, hmTBI and mTBI will be used when appropriate to indicate when findings were based on a self-reported sample and a medically diagnosed sample.

Working Memory and mTBI

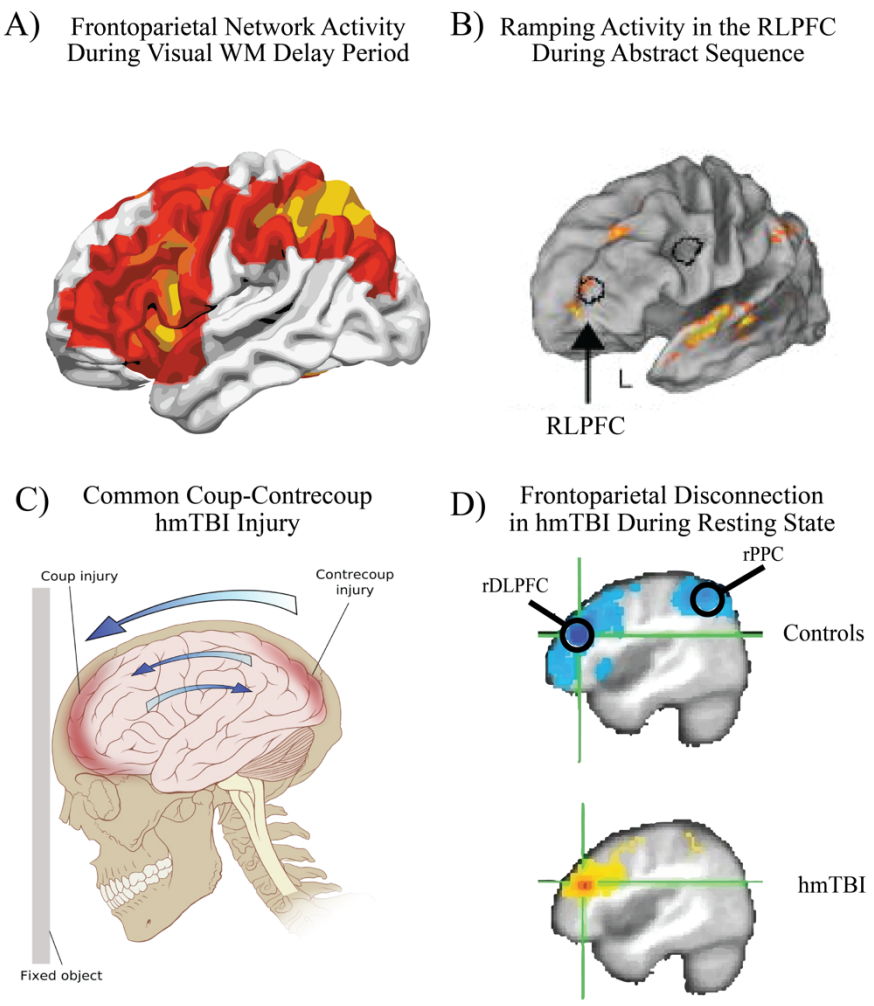

Figure 1. The neural underpinnings of the dissertation: the network activity during a visual WM task (A), the ramping activity during an abstract sequence during an abstract WM task (B), the impact the brain receives during a concussion (C), and the frontoparietal disconnection in chronic mTBI (D). In Aim 1, we test if the mTBI frontoparietal disconnection (D) is focal to the frontal region or both frontal and parietal regions by increasing cognitive demands across the WM network (A) and the RLPFC region with an abstract sequence (B). In Aim 2, we test if the disconnection between the frontal and parietal regions (D) can objectively classify between controls and mTBI. Lastly, in Aim 3, we test if stimulating the parietal region recovers the disconnection (D) by using HD-tDCS during a WM task to stimulate the parietal region. The fMRI data were modified from published papers - A (Li et al., 2022); B (Desrochers et al., 2015); D (Arciniega et al., 2021).

Although the majority of symptoms of an mTBI abate within the first few weeks, some are left with persistent, long-term effects (Dailey et al., 2018; Keatley et al., 2023; Mollica et al., 2022; Skjeldal et al., 2022; Sterr et al., 2006). In our lab, we found undergraduate

college students with chronic (injury >6 months old) perform worse on a range of WM tasks compared to their neurotypical peers (Arciniega et al., 2019, 2021; Chung et al., 2019; Green et al., 2018; Kumar et al., 2013; Quinn De Launay et al., 2021). Undergraduates with a previous hmTBI show WM impairment compared to controls when maintaining 3 items. We further tested if their impairment was affected by WM maintenance duration, performance feedback, and retrieval demands, and found consistent deficits that could not be clearly linked to any stage of WM (Arciniega et al., 2019). We replicated this visual WM impairment across multiple studies in >150 hmTBI participants (Arciniega et al., 2019, 2020, 2021).

The aim of the current dissertation is to explore the intersection of hmTBI and WM further to explore the long-term impact of a hmTBI on WM. The results of these three aims will contribute to our understanding of the behavioral and neural basis of hmTBI deficits (Fig. 1). The long-term goal of this line of research is to design evidence-based protocols for detection and risk assessment of an hmTBI, and then to develop interventions to remediate identified deficits.

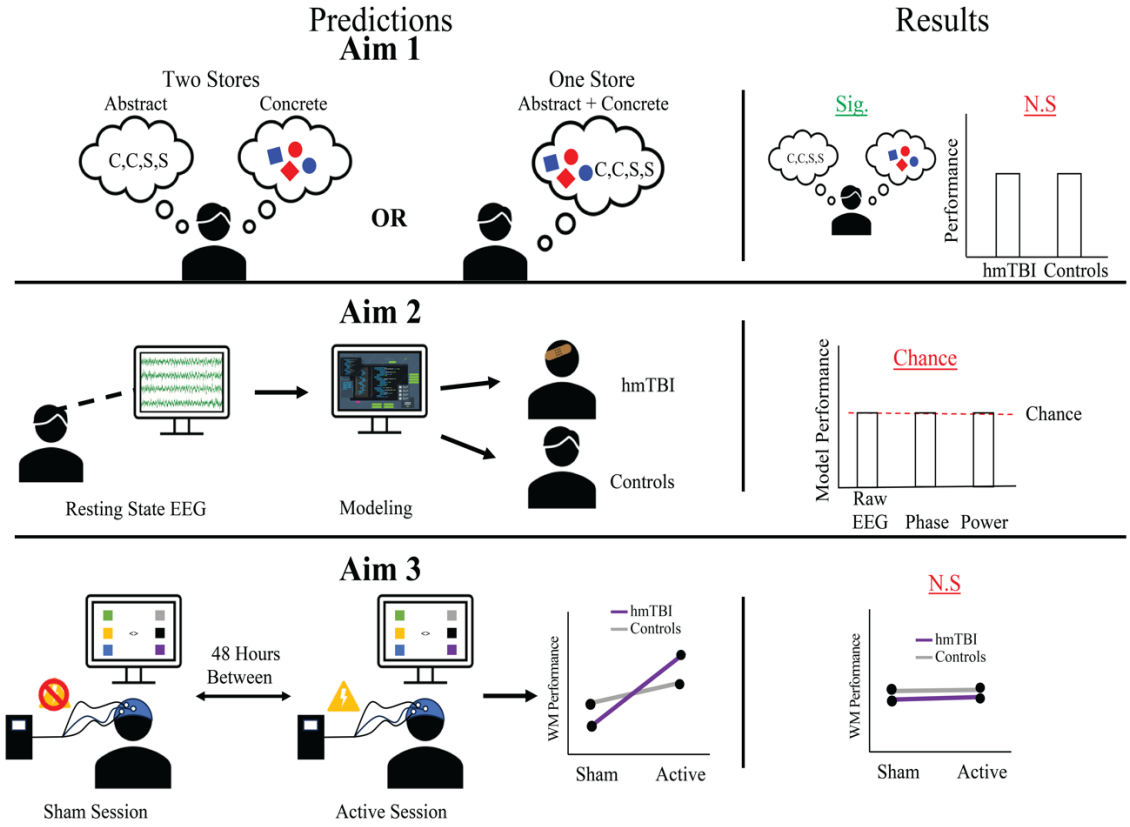

Figure 2. A visual summary of the dissertation aims predictions and results.
Top: **Aim 1** tests if abstract and concrete items are held in different WM stores. We predicted a single WM store with performance impaired when the task required holding both the visual item (e.g., shape) and an abstract sequence (e.g., a set of instructions). Additionally, we predicted that the hmTBI would show impairment at the tasks with an increased impairment as the WM load increased. Our results did not show a difference between hmTBI and controls. Surprisingly, participants were better when holding both abstract and concrete items.
Middle: **Aim 2** tests if resting state EEG can classify hmTBI and controls. We predicted it would be able to with certain metrics (i.e., raw EEG signal, power, phase) being better for classification. All models performed at chance. Bottom: **Aim 3** tested if non-invasive neurostimulation could improve WM performance in the hmTBI population. We found no behavioral benefit of stimulation or difference between hmTBI and controls. Note: © Stan Tiberiu / Adobe Stock; © mix3r / Adobe Stock

In this dissertation, we proposed three aims to investigate WM capacity and how it changes after a head injury (Fig. 2). In Aim 1, a new paradigm using abstract sequences tested if abstract instructions and concrete stimulus items are held in separate WM stores. Aims 2 and 3 tested whether neural mechanisms differ in hmTBI to controls. In Aim 2, we used a data-driven approach to isolate neural correlates of concussions during resting state EEG. In Aim 3, we used high density transcranial direct current stimulation (HD-tDCS) to test

whether it can improve WM performance in those with low WM capacities, especially those with a history of concussions. In summary, the aims of this dissertation are to isolate neural mechanisms of WM and to improve WM performance through techniques such as stimulation.

Aim 1. Are Abstract and Concrete Stimuli Held in Separate Stores?

Abstract Cognitive Task Sequences

Daily tasks often involve an overarching set of abstract goals. For example, an abstract goal (e.g., *have a productive day*) includes a host of secondary tasks (e.g., *work out, complete jobs, finish tasks*). This kind of hierarchical complexity is rarely captured by typical working memory (WM) paradigms used in research studies. A newly designed paradigm, termed Abstract Cognitive Task Sequences (ACTS), addresses this gap (Desrochers et al., 2015). ACTS captures the abstract and the concrete demands of executive function by requiring participants to remember a sequence of *instructions*; (Fig. 3). The instructions are held in WM and the participant must apply the appropriate instruction to whatever input stimuli follow. Each input stimulus is subjected to an instructed operation based on its position within a sequence. For example, participants might be asked to report stimulus features of an item. The instruction sequence may require reports of either color or shape in alternating fashion, e.g., 'Color, Shape, Color, Shape...'. To perform well, participants must keep track of the appropriate *instruction* for each trial while retaining the stimuli themselves. This is distinct from the specifics of the required motor responses, and separable from a priori verbal strategies because the WM stimuli are

unknown when the sequence of instructions are provided. ACTS creates a unique neural signature of ramping activity in the rostrolateral prefrontal cortex (RLPFC) associated with reducing error throughout the sequence. In summary, ACTS requires WM maintenance of unique abstract sequences and engages an error-monitoring circuit within the RLPFC. The following section will go over typical behavioral and neuronal findings during an ACTS task.

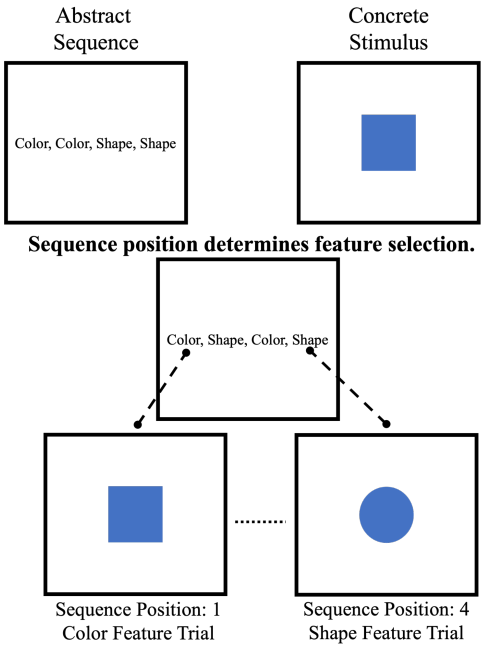

Figure 3. Examples of an abstract sequence and a concrete stimulus with a diagram to show how the two interact on a given trial. The abstract sequence is a series of instructions. In this case, features to report about a concrete stimulus (e.g., a blue square). The position within the sequence determines what feature must be reported about the concrete stimulus.

ACTS: Behavioral and Neuronal Findings

A series of research studies from the Desrochers' lab using the ACTS paradigm provides key findings linking structure and function. Across several studies, they report a behavioral switch cost in response time when changing from one instruction to another within a sequence (Desrochers et al., 2015). Their finding is consistent with previous research

reporting reliable switch costs even after extensive training in a motor response task requiring alternating between two distinct visual-motor response mappings (Berryhill & Hughes, 2009; Koch et al., 2018). The Desrochers' lab also found that the first item in any sequence is processed less efficiently, an effect they term the *initiation cost* (Desrochers et al., 2015). Importantly, this is not limited to the first trial after learning a sequence but continues for each sequence initiation within a sequence block. Activity in the rostrolateral prefrontal cortex (RLPFC) increases as the sequence progresses (Desrochers et al., 2015, 2019). The increase in RLPFC activity remained unchanged even in the absence of memory cues (Desrochers et al., 2019). Further, task performance was disrupted when TMS was applied to the RLPFC, but not to other frontal areas (Desrochers et al., 2019). In summary, RLPFC plays an important role in ACTS by marking the position in the sequence correctly while integrating other important task information.

ACTS and Working Memory

ACTS experiments required maintenance of *only* the abstract sequence in WM but not the stimuli themselves. This raises a theoretical question: is this *abstract* information maintained in the same WM store as the stimuli, or separately? Many tasks in our daily lives require holding both an abstract sequence and stimuli such as cooking, chores, etc. Our understanding of the interaction between the abstract and concrete stimuli may help understand its limits and why the function may be impaired in special populations.

To test this question, we made several modifications of the ACTS paradigm. By increasing the WM task demands we can try to push the interaction between ACTS and WM may reveal insight into how WM representations are maintained. Most visual WM paradigms require maintaining visual stimuli. On the other hand, ACTS requires the maintenance of *instructions*. The representation for these two types of information may differ. For example, if the representations are hierarchical, you would expect a decrease in performance for the representation lower in the hierarchy. Performing ACTS engages the prefrontal cortex differential than a non-sequential WM task, in particular the RLPFC. The ramping activity in the anterior prefrontal cortex may indicate the abstract component requires additional WM resources. Alternatively, the abstract sequences of instructions may be maintained separately and not affected by the maintenance of the relevant concrete visual stimuli (Fig. 4). Here, we bridge this gap by testing the capacity of ACTS with items in WM.

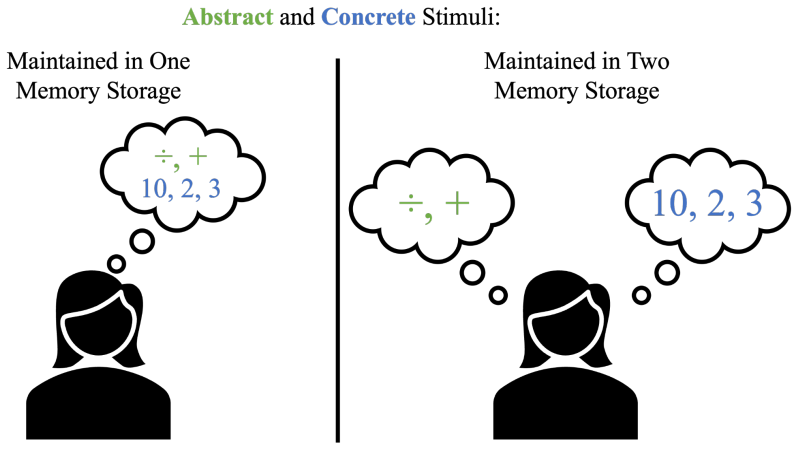

Figure 4. Two competing ideas for how WM maintains abstract (e.g., instructions; green) and concrete (e.g., visual stimuli; blue) items. On the left, the information is maintained in one memory storage. On the right, the two memory storages for each stimuli type. There are two major implications from these ideas. First, if the one-store model is true, WM capacity will be quickly reached with simple math operations. Conversely, under the two-store model, each storage may have a capacity. The second implication of these hypotheses is the existence or non-existent double dissociation between abstract and concrete WM items.

ACTS, WM, and hmTBI

Research in the mTBI population has suggested visual WM deficits in several studies (Arciniega et al., 2019, 2021; Chung et al., 2019; Green et al., 2018; Kumar et al., 2013; Quinn De Launay et al., 2021). However, the exact cause of these WM deficits are unknown. Most of the long-term cognitive effects of hmTBI are an open research question. The hmTBI is a highly heterogeneous group making finding underlying neural mechanisms difficult. In this study, we investigated if WM deficits in hmTBI were more localized to the frontal lobe than the general WM network or the parietal lobe. The ACTS and ACTS-WM tasks can neatly address this gap of knowledge by adding cognitive load to the frontal lobe while engaging the rest of the WM network simultaneously. If WM deficits post-hmTBI are more localized frontally, then we would predict worse performance on the ACTS-WM task than the ACTS or WM task. Alternatively, if it were not localized to the frontal lobe, we would predict around equal performance on all three tasks in the hmTBI.

Extending ACTS to WM and to the hmTBI population

In Aim 1, we wanted to test two things. First, we wanted to test the hierarchical nature of WM, by examining whether we can maintain: 1) abstract instructions, and 2) concrete items separately or whether they tap a single WM store. A major limitation of WM is the strict capacity limit of ~4+/-1 item (Cowan, 2010; Gilchrist et al., 2008). Decades of neuroimaging (D'Esposito & Postle, 2015) and neuropsychological (Kolb et al., 1983; N. G. Müller & Knight, 2006; Paulraj et al., 2018) research reveal varied WM deficit after fronto-parietal lesions. But ACTS shows a much broader neural basis that includes the RLPFC. A tantalizing question is whether there is a store for abstract WM content, such as

the instructions for upcoming stimuli that have yet to enter WM, separate from concrete WM content. This finding would align with recent research into how WM indexes multiple items in WM (Thyer et al., 2022). This research suggests WM holds 'pointers' which keep track of the number of items in WM but hold no content about the item itself. They may indicate where the stimuli content is stored in other regions, such as sensory regions (Thyer et al., 2022). The instructions may act as a pointer to the visual stimuli. Furthermore, this research provides insight into how WM is used in complex real-life situations and, potentially, a new insight into nuanced WM impairments. To answer this question, we expanded the ACTS paradigm to require additional maintenance of the visual stimulus features.

Second, as noted, a subset of people who experience hmTBI show lasting WM deficits, even years after injury. There is great interest in determining the mechanism of lasting deficits so that we can predict in whom they will emerge. This is particularly challenging because of the heterogeneity surrounding all aspects of hmTBI, including etiology, premorbid cognitive ability, and health status, treatment, etc. Yet, there are certain regularities in brain architecture in hmTBI: frontal and parietal disconnection (Arciniega et al., 2021). These are the key networks associated with executive function tasks: WM, ACTS. Linking task performance with anatomy may be an efficient way to determine who will show lasting deficits post hmTBI.

To address our first question, we compare performance when items in WM are abstract, concrete, or both. If abstract and concrete items are held within the same WM store, we expect the lowest performance when participants had to maintain both types due to limited resources. Alternatively, if the stores are separate, performance would be relatively similar between the three tasks.

If the WM deficit in some hmTBI survivors is disproportionately due to frontal damage, specifically rostrolateral impacts, then we predict an interaction showing increasingly poor performance on the ACTS and ACTS-WM paradigms in the hmTBI participants. This subset of hmTBI should be visually obvious in a graphical distribution of the data which will allow us to decide criteria to determine hmTBI with and without WM deficits. On the other hand, if it is due to a disconnection in the frontal-parietal network, we would predict that the deficit in the hmTBI would be *smallest* in the ACTS task (Fig. 5).

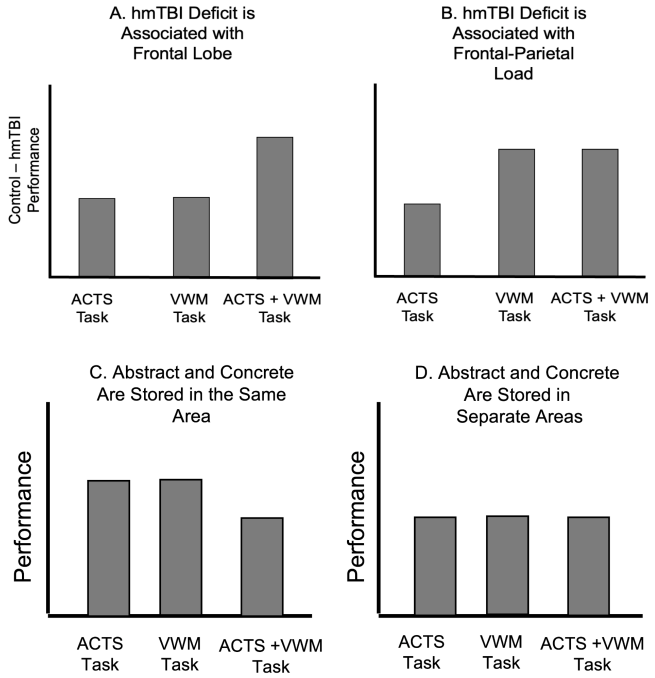

Figure 5. The predictions for Experiment 1; the top row of graphs illustrates the predictions for the hmTBI group; the bottom row shows the prediction for the tasks. **A-B.** The two predictions for the hmTBI group. One (A), that hmTBI injury is located mostly in the prefrontal lobe. Thus, the greater load on the prefrontal lobe will increase the difference between them and controls. Two (B), hmTBI injury is at a network level with a general WM deficit. **C-D.** The two predictions for the maintenance of abstract and concrete items. One (C), the outcomes if abstract and concrete items are maintained in the same WM store. The performance would decrease when having to maintain both types of items. Two (D), the outcomes if the abstract and concrete items were maintained in separate stores. The performance among all the tasks would be around the same, regardless of WM load.

Methods

Participants

All participants read an assent form prior to participation and indicate they read and understood the form. The consent form and all procedures were approved by the University of Nevada Institutional Review Board.

We collected data from 112 SONA participants (Age: M = 19.94, SD = 1.76; Female = 74, Male = 37, Non-Binary = 1). Participants completed 77.69% of the tasks on average. Of these, n= 27 self-reported a history of hmTBI (Mean time since injury = 62.48 months;

5.21 years). We also collected data from Amazon MTurk (Mechanical Turk). We excluded this dataset for reasons detailed below.

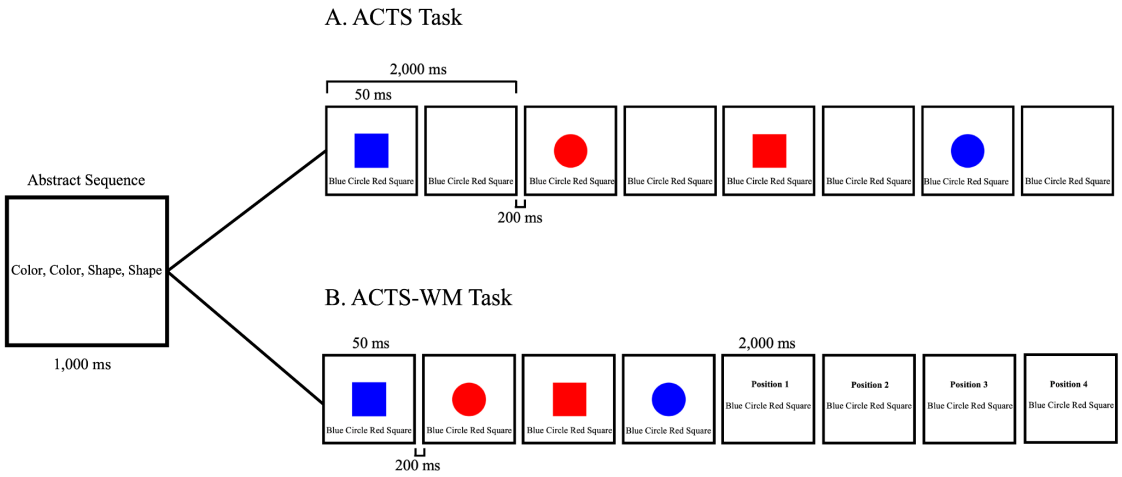

Figure 6. The task paradigms of the two ACTS tasks. **A.** In the ACTS task, participants held onto a sequence of instructions (see 'Abstract Sequence') to make judgements about the following shapes. As stimuli were presented, participants responded with the corresponding feature judgment (e.g., 'blue' for the first answer in Fig.). Participants could respond as stimuli appeared. **B.** In the ACTS-WM task, participants held the sequence and the features in WM. The responses were collected after all stimuli for a sequence were presented.

Exclusion Criteria

The data we collected online required several cleaning procedures to extract any meaningful conclusions we could be confident in. During data processing, single trials were eliminated if they had any of the following:

1) no response recorded;

2) their response time was faster than 200 milliseconds;

3) had a response time longer than 4,000 milliseconds. This criteria was set to 2,000 milliseconds longer than the response time limit, but this accounted for any small lags due to internet or Qualtrics. Accuracy was based on the total number of trials passing the criteria.

There were exclusion criteria for individual participants:

1) Participants were eliminated if they responded to <20% of the trials in any task. This was to ensure each participant's data were based on sufficient trials.

2) Participants were eliminated if their median response time was >2,000 ms. A median response >2,000 ms indicated a majority of trials suffered from lag, suggesting poor internet connection and questionable timing reliability.

3) Outliers (participants performing >2 standard deviations away from the group mean) were removed in the control group. The hmTBI group was excluded from this since we were searching for an impairment and the population is highly heterogeneous in WM performance.

In total, this approach removed **34%** of the Mturk data and 14% of the SONA data. Because a large portion of the Mturk *failed to pass exclusion criteria*, we are not confident in the results drawn from this dataset. Thus, the results and discussion will be based solely on the statistical analysis from the SONA dataset.

Paradigm Materials and Stimuli

All tasks were created using Qualtrics 2023. JavaScript supplemented any features Qualtrics lacked. Data were collected and stored on Qualtrics. Python was used to extract individual trial information and to conduct all numerical analyses.

Stimuli for both ACTS and ACTS-WM consisted of a set of four images: red circle and square (RGB: 234, 51, 38) and blue circle and square (RGB: 0, 0, 245). The stimuli were created in PowerPoint and exported as PNG file images. Image size was set to 300 x 300 pixels through Qualtrics.

Stimuli for the WM task consisted of a set of six color patches: red (RGB: 241, 132, 123), blue (RGB: 102, 102, 249), cyan (RGB: 172, 253, 254), pink (RGB: 241, 132, 250), green (RGB: 172, 252, 147), black (RGB: 102, 102, 102). The mask was a multi-colored circle (yellow: 248, 251, 83; cyan: 110, 237, 248; green: 119, 247, 75; pink: 230, 51, 223). The color patches were created in PowerPoint and exported as PNG file images. Image size was set to 100 x 100 pixels through Qualtrics.

ACTS

There was a total of six blocks, one for each sequence type (sequences: 'CCSS', 'SSCC', 'SCSC', 'CSCS', 'CSSC', 'SCCS'; C = color, S = shape). At the start of each block, participants were shown the sequence for 1 second (Fig. 6). Each sequence showed four judgment instructions (color or shape). Both judgment types were represented equally. Stimuli were presented 50 ms (Fig. 6A). Participants had 2,000 milliseconds to answer with the four possible responses ('Blue', 'Circle', 'Red', 'Square') remaining on screen. They pressed the 'd' key for 'blue', 'f' for square, 'j' for 'circle', and 'k' for 'red'. These keys were chosen so participants could lay their hands naturally on their keyboard. Seven full sets of the sequence were presented and responded. At the end, there was an incomplete

8th sequence to encourage participants to keep track of their position in the sequence. Thus, they ended on either the first, second or third sequence item. After the 8th sequence ended, they were asked to indicate what position they would respond to next. The exact position was counterbalanced between sequence types.

ACTS-WM

The task was the same as the ACTS, except for these changes: four run-throughs of all 6 sequences (16 trials per block, 96 trials all total) - without stopping mid-sequence on the final iteration, a reduction in the total number of trials to hold constant the task duration and, instead of responding while the stimuli were present, participants remembered their answers until after all four stimuli were shown (Fig. 6B). Once the last stimulus had been shown, participants reported the correct feature (color or shape) for each stimulus in order. This task design required participants to keep both the ACTS sequence (e.g., 'CCSS') and a growing item sequence (e.g., 'blue', 'red', 'square', 'circle') in WM. Participants had a limited response window (2,000 ms). For each response, a title at the top of the screen indicated what position the participant was answering. Stimuli were presented for 50 ms. At the start of a block, participants had 1,000 ms to commit the sequence to memory.

Unlike the ACTS task, we did not include a partial sequence.

Change Detection

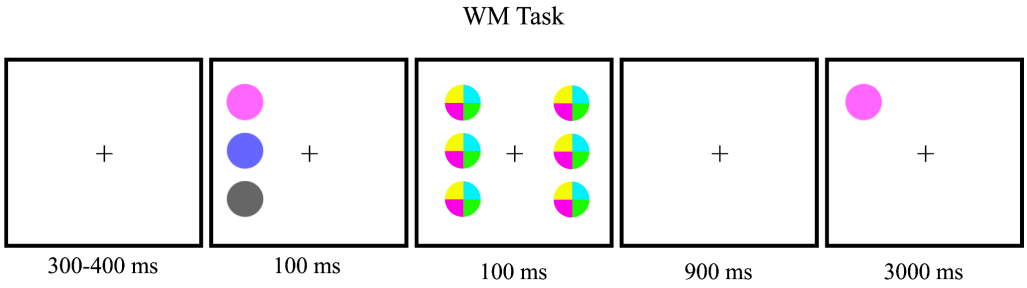

Figure 7. The task diagram of the working memory change detection paradigm. Participants were presented with three stimuli on the left or right of a focus point. The probe was shown on the same side. Participants judged if the probe was among the three presented at the same location. A mask was added after the stimuli to increase difficulty.

The WM change detection task was based on previous change detection tasks used in our lab. Participants were shown three color patches (100 ms), one above the other either to the left or right of a focus point. A brief mask appeared after the stimulus offset because pilot data indicated the task was too easy. The mask was presented for 100 ms. After a delay (900 ms), participants were shown a probe at one of the encoding locations. Participants indicated if the probe was the same stimuli shown at that location. If the probe matched, they pressed 'J'. If it mismatched, they pressed 'F'. Participants had 3,000 ms to respond.

The task began with 10 practice trials, and if >50% correct, there were 40 experimental trials. If practice trial accuracy was <50%, the participant completed a second round of 10 practice trials. If they scored <50% a second time, the participant completed an additional 10 practice trials. After the third set of practice trials, participants completed the task regardless of their practice accuracy.

Results

For all the following statistical analyses, the assumption of normality was violated. However, due to the large sample size and absence of outliers, we used parametric tests. Any condition that did not meet sphericity assumptions was corrected using the Greenhouse-Geisser correction. To address the multiple comparison issues, we used three MANOVAs including accuracy and reaction time. We were unable to conduct one MANOVA due to the metrics (i.e., accuracy) in each analysis being too highly correlated with each other. Because we conducted three separate MANOVAs, we corrected for multiple comparisons using Bonferroni Correction setting the alpha level to 0.02. The post-hoc pairwise comparisons were automatically Bonferroni corrected by SPSS (Version 29) and did not use the same alpha level as the MANOVAs.

Overall Task Performance

The overall accuracy was used to assess performance between the groups (hmTBI, Controls) and between tasks (ACTS, ACTS-WM, WM). We predicted hmTBI would perform worse than controls especially on frontally focused tasks such as ACTS and ACTS-WM. Additionally, we tested if abstract sequences and concrete stimuli were stored in the same store.

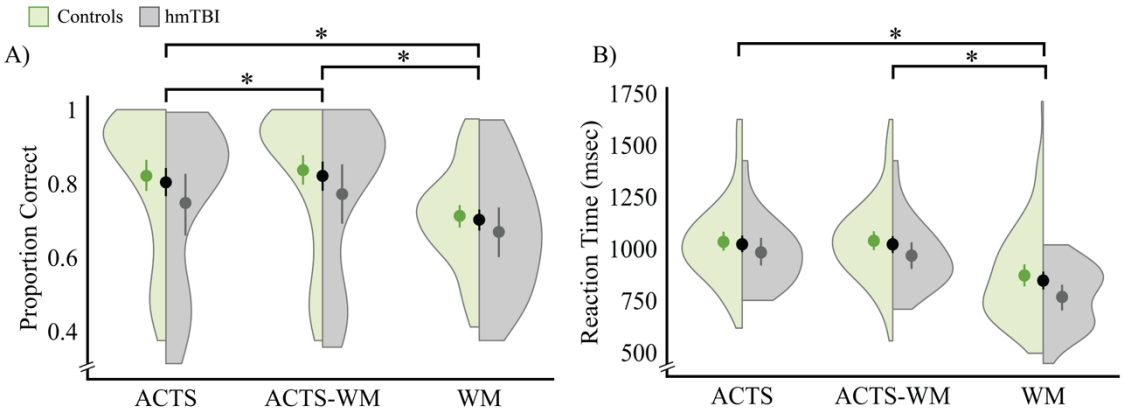

Figure 8. The performance of SONA participants during three online tasks: ACTS, ACTS-WM, and WM**. A**. The accuracy performance across all three tasks. There is a significant main effect of the task with each task being significantly different than each of the others. **B.** This graph shows median correct response times across all three tasks. The violin plots represent the distribution of the data. The dots represent group means. Green represents neurotypical participants. Gray represents participants with a history of hmTBI. The black dots show the group mean collapsed across hmTBI and controls. Error bars on the means are 95% CI. * - p = 0.03; ** - p < 0.001

We conducted a mixed effect MANOVA (*within-factor*: task, *between-factor*: hmTBI group, *measures*: accuracy, reaction time). There was a significant effect of task ($F(4, 440) = 7.9$, $p < 0.001$, $\eta_p^2 = 0.21$) in the multivariate test, but the two-way effect of task and group was not significant ($F(4, 110) = 0.53$, $p = 0.71$, $\eta_p^2 = 0.005$). The univariate tests showed a main effect of task on accuracy ($F(1.06,116.66) = 22.22$, $p < 0.001$, $\eta_p^2 = 0.17$) and reaction time ($F(1.06, 119.92) = 50.44$, $p < 0.001$, $\eta_p^2 = 0.31$). A pairwise comparison revealed that each task was significantly different in accuracy (all ps < 0.001) with the highest accuracy unexpectedly in the ACTS-WM task followed by ACTS task, and then the WM task. The reaction time was only significantly different between the WM and ACTS ($p < 0.001$) tasks, and between the WM and ACTS-WM ($p < 0.001$) tasks. To summarize, we found a significant effect of the task in both accuracy and reaction time. Surprisingly, as we predicted the opposite, the ACTS-WM had the highest accuracy. Response times were faster during the WM task. Furthermore, also contrary to predictions,

there was no evidence of worse performance in any task in the hmTBI group, although there were numeric differences revealing lower accuracy and faster reaction times.

Performance Across Sequence Position

This analysis tested if performance changed across the abstract sequence. We used a mixed effects MANOVA (*within-factor*: task, position; *between-factor*: group, *measures*: accuracy for each position, reaction time for each position). *Note:* The WM task was not considered in this analysis, because it did not have a sequence structure

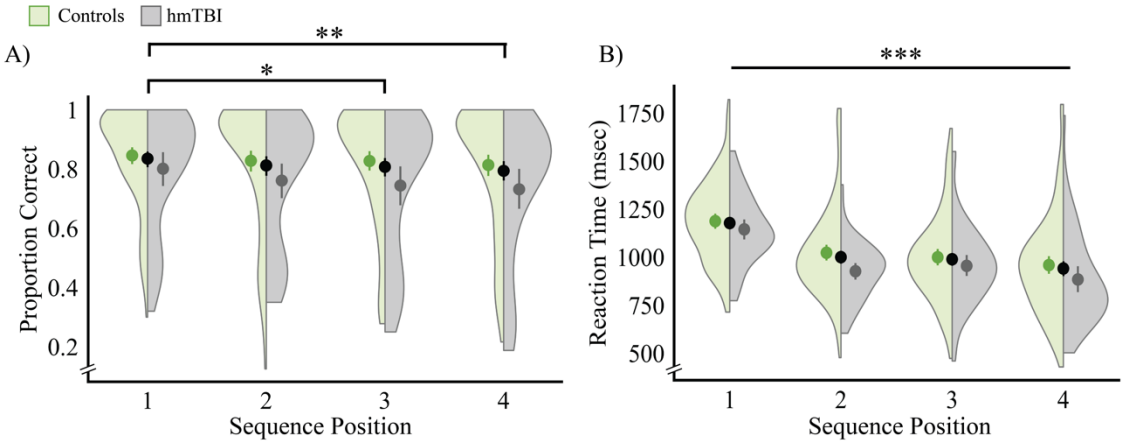

Figure 9. The performance across every position within an abstract sequence, collapsed across tasks. A. This graph shows the accuracy performance with a main effect of position. The first position had a higher accuracy than position three or four. B. This graph shows the response time performance with a main effect of position. Due to the large number of significant pairwise comparisons, they were not illustrated. Position one was slower than all other positions. Positions two and three were slower than position four. For both graphs, there were no significant interactions with group or task. The violin plots show the distribution of data. The dots represent means with 95% CI. Green represents control participants. Gray represents hmTBI participants. The black dots represent collapsed means across group. * - $p = 0.03$; ** - $p = 0.007$; *** - $p < 0.001$

There was a main effect of the task on the multivariate combination of the measures ($F(2, 109) = 9.98$, $p < 0.001$, $\eta_p^2 = 0.16$) and the position ($F(6, 105) = 24.71$, $p < 0.001$, $\eta_p^2 = 0.56$). There was no significant group effect ($F(2,109) = 3.66$, $p = 0.03$, $\eta_p^2 = 0.06$) nor any two-way interactions (Task and Group: $F(2,109) = 1.29$, $p = 0.28$, $\eta_p^2 = 0.98$; Position and Group: $F(6,105) = 0.93$, $p = 0.48$, $\eta_p^2 = 0.05$; Task and Position: $F(6,105) = 0.86$, $p =$

0.52, $\eta_p^2 = 0.05$). The follow-up univariate analysis revealed a significant main effect of task in accuracy ($F(1,110) = 19.78$, $p < 0.001$, $\eta_p^2 = 0.15$), but not reaction time ($F(1, 110) = 0.07$, $p = 0.79$, $\eta_p^2 = 0.001$). Accuracy was higher for the ACTS-WM task than ACTS, as described in the section above. There was a significant univariate main effect of position in both accuracy ($F(2.72, 299.27) = 5.09$, $p = 0.003$, $\eta_p^2 = 0.04$) and reaction time ($F(2.65, 291.41) = 60.74$, $p < 0.001$, $\eta_p^2 = 0.36$). A post-hoc pairwise comparison showed the accuracy on the first sequence item was significantly higher than accuracy for the third ($p = 0.03$) or fourth positions ($p = 0.007$). In reaction time, the responses to the first sequence item were significantly *slower* than to all the other positions (all $ps < 0.001$). This marks the initiation cost. Responses to the fourth position were faster than responses to the second ($p = 0.03$) or third ($p = 0.004$) positions.

To summarize, we found a significant effect of the task, consistent with the previous analysis showing accuracy was higher in ACTS-WM. In this analysis, we tested if the position within a sequence impacts performance. We predicted we would replicate previous findings with the initial position having *worse* performance due to a *sequence initiation cost* (Desrochers et al., 2015, 2019). We observed the initiation cost in slower reaction times, instead of in accuracy. Over the sequence, we observed speedier responses.

Within-Sequence Feature Switching

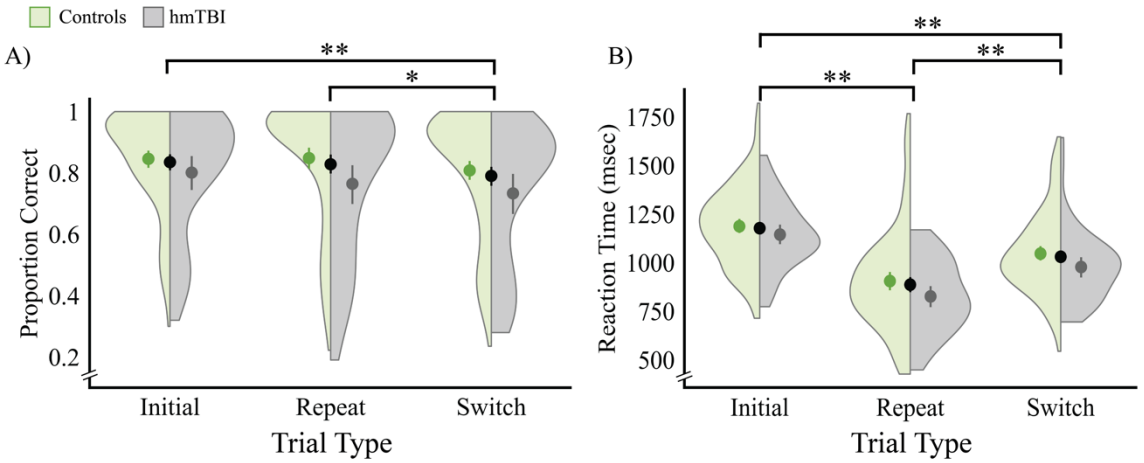

Figure 10. Performance across the different trial types: initial (first trial in a sequence), repeat (current trial instruction matches proceeding), and switch (current trial instruction mismatches proceeding). A. The graph shows the accuracy performance across all three trial types for the two ACTS tasks. Accuracy on switch trials were lower than initial or repeat trials. B. The graph shows the response time across the trial types. Initial trials had the slowest response times. Switch trials were slower than repeat trials. For both graphs, there were no significant interactions with group or tasks. The violin plots show the distribution of data. The dots represent means. Green is control data. Gray is hmTBI data. The black dots represent the mean collapsed across hmTBI and controls. * - $p = 0.02$; ** - $p < 0.02$.

This analysis tested if switching between features within-sequence induced a switch-task cost and if a previous hmTBI further impaired within-sequence feature switching. There are three levels of 'trial type': initial, switch, and repeat. We used a mixed effects MANOVA (*within-factors*: task, trial type; *between-factor*: group, *measures*: accuracy for each trial type, reaction time for each trial type). There was a significant main effect of task ($F(2,109) = 7.89$, $p < 0.001$, $\eta_p^2 = 0.13$) and trial type ($F(4,107) = 49.10$, $p < 0.001$, $\eta_p^2 = 0.65$) on the multivariate combination of accuracy and reaction time. There was no main effect of Group ($F(2,109) = 3.78$, $p = 0.03$, $\eta_p^2 = 0.07$) and no significant two-way interactions (Task and Group: $F(2,109) = 1.45$, $p = 0.24$, $\eta_p^2 = 0.03$; Trial and Group: $F(4,107) = 0.85$, $p = 0.50$, $\eta_p^2 = 0.03$; Task and Trial: $F(4,107) = 0.54$, $p = 0.71$, $\eta_p^2 = 0.02$).

A follow-up univariate showed a significant main effect of task on accuracy ($F(1, 110) = 15.32$, $p < 0.001$, $\eta_p^2 = 0.12$) but were *not* reaction time ($F(1,110) = 1.17$, $p = 0.28$, $\eta_p^2 = 0.01$). The ACTS accuracy was lower than the ACTS-WM across all trial types.

The follow-up univariate test showed the main effect of trial type was present in accuracy ($F(2,220) = 8.10$, $p < 0.001$, $\eta_p^2 = 0.07$) and reaction time ($F(1.64,180.24) = 113.39$, $p < 0.001$, $\eta_p^2 = 0.51$). Accuracy on the switch trials were significantly lower than the initial trials ($p < 0.001$) and repeat trials ($p = 0.02$). In reaction time, each trial type was significantly different from each other with the fastest responses in the repeat trials, then the switch, and the initial trials (all $ps < 0.02$).

To summarize, when we tested if the within-sequence task switch had an effect, we found there was a difference between tasks with *higher* accuracy in ACTS-WM across all sequence positions. This finding agreed with the first MANOVA testing the overall accuracy. Accuracy on switch trials was lower than the initial trial of a sequence or a repeat trial in a sequence. The fastest responses were found in the repeat trials, with some response cost during switch and initial trials.

Performance Across Sequence Position and Type

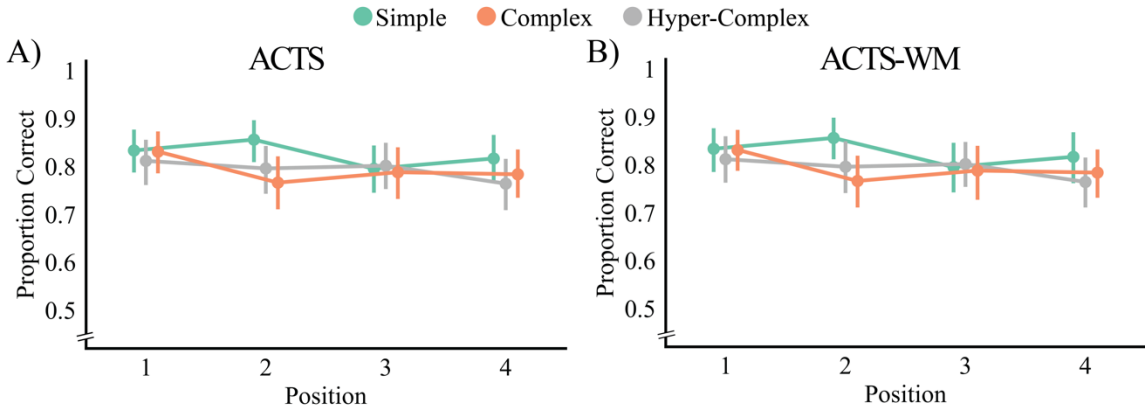

Figure 11. Performance across sequence type and position. Sequences were categorized as simple, complex, or hyper-complex based on the number of feature switching within in each sequence. A. The graph shows the proportion correct across each position and sequence type in the ACTS task. B. The graph shows proportion correct across position and sequence type in the ACTS-WM task. There was no main effect of sequence type or significant interaction.

This analysis tested if accuracy changed across the abstract sequence type and position (Fig. 11). Sequence types were determined by the number of feature switches within the sequence. Simple (AABB) included one switch, Complex (ABBA) included two switches, and Hyper-Complex included three switches (ABAB). We used a mixed effects MANOVA (*within-factor*: task, position, sequence type; *between-factor*: group, *measures*: accuracy for each position). *Note:* One control participant was removed from this analysis because they did not respond for one sequence type at a single position. Additionally, reaction time was not analyzed since multiple participants had 0 correct trials for a given position and sequence. There was no significant main effect of sequence type ($F(2, 218) = 2.34$, $p = 0.09$, $\eta_p^2 = 0.02$) or any two-way interaction with sequence type (Sequence x Group: $F(2, 218) = 3.07$, $p = 0.05$, $\eta_p^2 = 0.03$; Sequence x Position: $F(6,654) = 1.57$, $p = 0.15$, $\eta_p^2 = 0.01$; Sequence x Task: $F(2,218) = 0.66$, $p = 0.52$, $\eta_p^2 = 0.01$).

Subgroups within the Participants

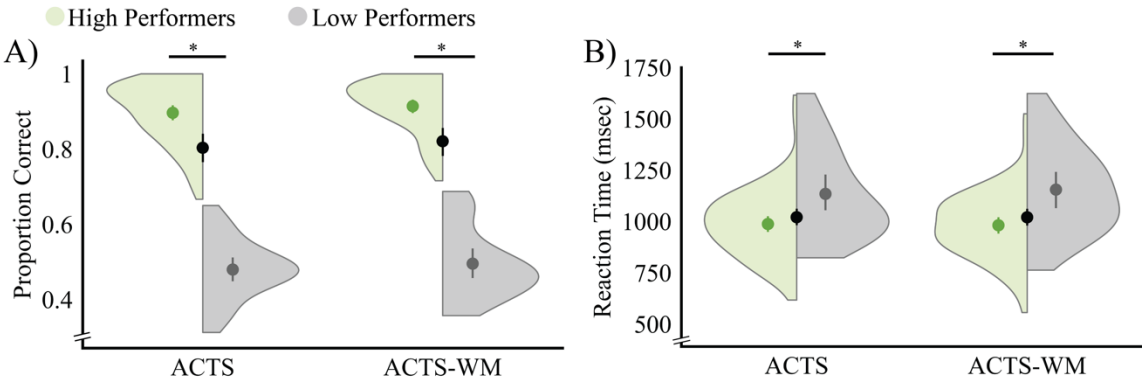

Figure 12. Dividing the participants into two subgroups. A clustering algorithm separated participants based on their accuracy in the ACTS and ACTS-WM task. A. The graph shows proportion correct across both tasks for the two subgroups: high performers (green) and low performers (gray). B. The graph shows the reaction time of each group across both tasks. There was a significant main effect of performance group, but no significant two-way interactions. * $p < 0.001$.

This analysis tested if there were subgroups within the participants based on accuracy, and, if so, did group membership interact with hmTBI status or task (Fig. 12). Participants were sorted into groups via an agglomerative clustering algorithm. Clustering performance was assessed via Silhouette Coefficient (SC). SC provides a metric of how cohesive a cluster and how separate a cluster is from another. An SC of 0 would be a low-quality cluster result with overlapping clusters. An SC of 1 is a perfect clustering result. We tested all possible linkage types and splitting the data into 2-5 groups and choose the combination with the highest SC. The best clustering used a linkage type used was ward (minimizing variance within clusters) and splitting the data into 2 groups (SC = 0.74). The algorithm used accuracy data from both ACTS and ACTS-WM. We replicated the three mixed effects MANOVAs of overall performance (*within-factor*: task; *between-factor*: group, performance group *measures*: accuracy for each position, reaction time for each position), position performance (*within-factor*: task, position; *between-factor*: group, performance

group *measures*: accuracy for each position, reaction time for each position), and trial type (*within-factor*: task, trial type; *between-factor*: group, performance group *measures*: accuracy for each position, reaction time for each position). In overall performance, there was a significant main effect of performance group in accuracy ($F(1,108) = 287.40$, $p < 0.001$, $\eta_p^2 = 0.73$) and reaction time ($F(1,108) = 7.28$, $p = 0.008$, $\eta_p^2 = 0.06$). All two-way interactions were non-significant (ps 0.05 – 0.93). In summary, we used a clustering analysis to separate the data into two groups based on behavior and found participants were either high performers (higher accuracy, faster reaction times) or low performers (lower accuracy, slower reaction times).

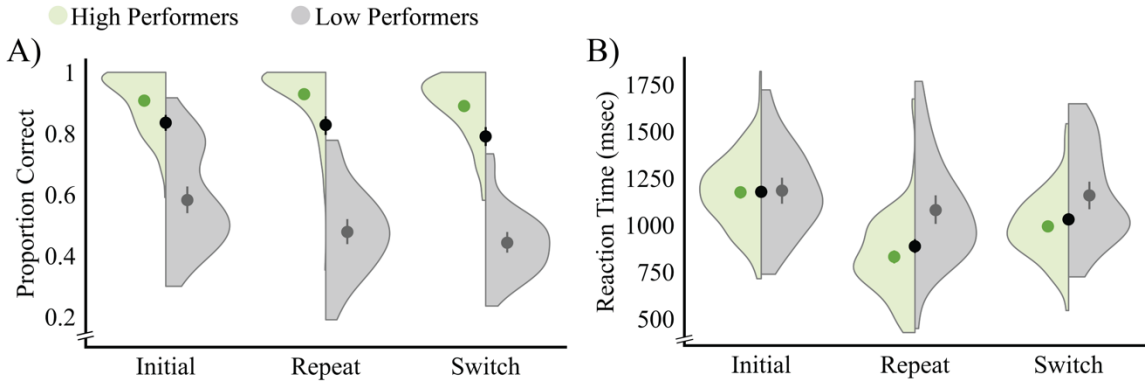

Figure 13. Performance across trial type separated by high and low performers. A. The graphs shows the accuracy for high and low performers in all trial types. B. The graph shows the reaction time for the high and low performers in all trial types. For both graphs, there is a significant two-way interaction.

In the feature-switching analysis (Fig. 13), there was a significant two-way interaction between performance group and trial type (Accuracy: $F(2, 215.55) = 10.43$, $p < 0.001$, $\eta_p^2 = 0.09$; Reaction time: $F(2, 215.55) = 12.76$, $p < 0.001$, $\eta_p^2 = 0.11$). The accuracy difference between the trial types (initial, switch, and repeat) is larger in the low performers. However, in reaction time, low performers show less change between the trial types than the high

performers. All other main effects and two-way interactions were already tested in the previous MANOVA. In summary, high performers showed a larger difference between trial type in reaction time while low performers showed a larger difference between trial type in accuracy. This may be indicating the higher performers are reaching ceiling.

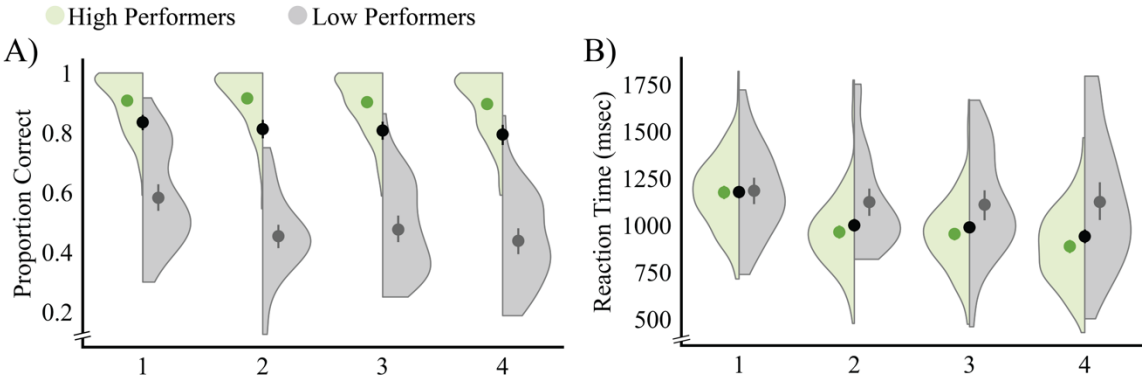

Figure 14. Performance across sequence position separated by high and low performers. A. The graphs shows the accuracy for high and low performers in sequence positions. B. The graph shows the reaction time for the high and low performers in sequence positions. For both graphs, there is a significant two-way interaction.

In the positional analysis (Fig. 14), there was a significant two-way interaction between sequence position and performance group (Accuracy: $F(2.84, 206.67) = 7.87$, $p < 0.001$, $\eta_p^2 = 0.07$; Reaction time: $F(2.82, 206.67) = 8.16$, $p < 0.001$, $\eta_p^2 = 0.07$). This analysis replicated the previous finding: low performers had wider gaps in accuracy between position, but more consistent reaction times than high performers. In short, this analysis replicated the findings of the previous and also supports the idea the higher performers are reaching ceiling.

Correlation between Tasks

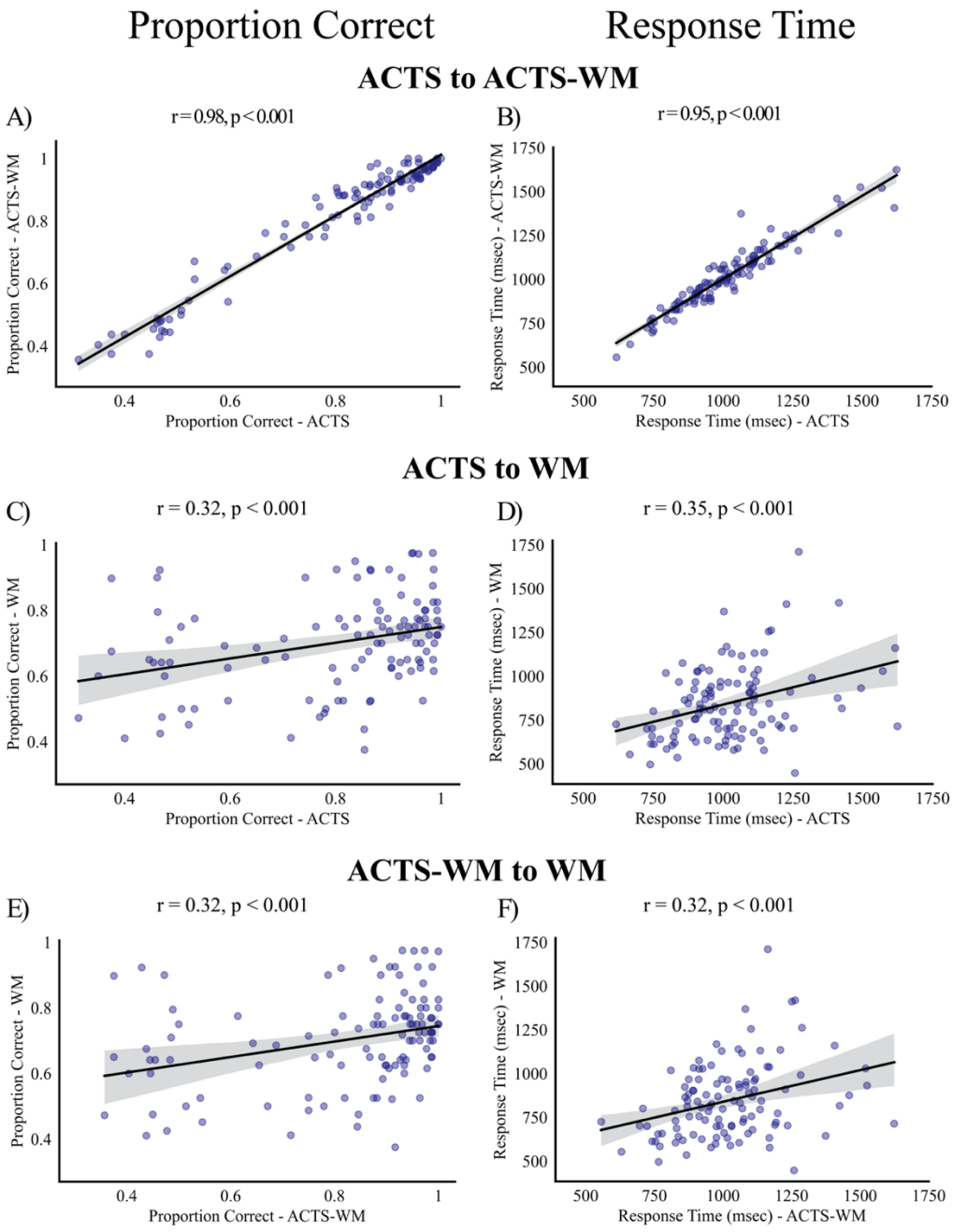

Figure 15. The correlation of performance between the three tasks in Aim 1. The left column shows correlations between tasks in proportion correct. The right column shows correlations between tasks in response time. A and B compare ACTS and ACTS-WM. C and D compare ACTS and WM. E and F compare ACTS-WM and WM.

This analysis tested how correlated accuracy and reaction time were in each task (Fig. 15). If performance is highly correlated, it would suggest similar cognitive resources are used in both tasks. Since there were no significant effects of hmTBI in the previous analyses, we collapsed across group. All correlations between the three tasks were significant in both accuracy (ACTS and ACTS-WM: $r(110) = 0.98$, $p < 0.001$; ACTS and WM: $r(110) = 0.32$, $p < 0.001$; ACTS-WM and WM: $r(110) = 0.32$, $p < 0.001$) and reaction time (ACTS and ACTS-WM: $r(110) = 0.95$, $p < 0.001$; ACTS and WM: $r(110) = 0.35$, $p < 0.001$; ACTS-WM and WM: $r(110) = 0.32$, $p < 0.001$).

Discussion

Summary

We used a novel WM task to test two questions: 1) Are lasting hmTBI deficits in WM due to *prefrontal* involvement, and 2) Are abstract and concrete items held in the *same* WM store. To succeed on the ACTS task, participants had to maintain a sequence of abstract instructions, requiring RLPFC (Desrochers et al., 2015, 2019; McKim & Desrochers, 2022). We added an additional challenge in the ACTS-WM by requiring them to maintain both the concrete visual items and the abstract sequence. To complete the comparison, we used a change detection WM paradigm used previously in hmTBI research showing a WM impairment in hmTBI. In the next sections, we will discuss the implications and interpretations of our findings.

No Group Differences between hmTBI and Controls

We predicted the hmTBI group would perform worse than the controls across tasks. However, we found no significant difference between controls and hmTBI, in either accuracy or reaction time. This contradicts previous research in our lab which found a significant difference in change detection and n-back tasks for a set size of three (Arciniega et al., 2021). The major difference between this study and the previous study is the method of data collection. In the previous study, the dataset was collected in-person. The current dataset was collected *online* using Qualtrics. Additional research would be needed to test if this difference would introduce enough extra noise to eliminate the effect of an hmTBI. By noise, we mean computer lags and poorly controlled environments.

Separate Stores for Abstract and Concrete Items in WM?

In this study, we developed a novel paradigm, ACTS-WM, to test if abstract items (e.g., a sequence of instructions) and concrete visual items (e.g., colored shapes) were maintained within the same WM store. Under the one store hypothesis, we predicted the performance on an ACTS-WM task would be worse than a WM task or an ACTS task by itself because of the added task demands. Alternatively, if there are separable pools maintaining abstract and concrete contents, then the performance would not be consistent across tasks. Surprisingly, we found the performance on ACTS-WM was significantly better than ACTS or WM. This finding supports the maintenance of abstract items does not interfere with the maintenance of concrete items. However, further analyses suggest the alternative as well.

We found a strong correlation between performance on ACTS and ACTS-WM in both accuracy and reaction time. An important implication of this is the cognitive resources or strategies used for one task are useful for the other. In other words, abstract and concrete sequences could be using similar neural mechanisms. Individuals who are good at maintaining abstract sequences are also good at maintaining *both* an abstract and visual concrete sequence in WM. The second finding, the significant correlations between both ACTS tasks and the WM task, suggest the ACTS tasks require similar demands on WM as a typical WM task. The positive relationship between performance on the WM task and the ACTS tasks suggest all three tasks are using similar cognitive resources. However, the ACTS and ACTS-WM are capturing something unique since the correlations to the WM task is weaker for both tasks. In summary, the overall performance between the ACTS and ACTS-WM task suggests separate WM resources, but the strong correlation between performance on both tasks suggests shared WM resources.

One of the surprising findings is that the ACTS-WM performance is better than ACTS when the participants are required to maintain two sequences. It may suggest participants are handling the extra load through differential strategies. For example, the responses could be encoded into a motor sequence while stimuli were presented. A sequence can be easily re-coded into button presses as the stimuli appear or just as the feature of interest. This would reduce the sequence load on WM by half. To test this, we compiled the questionnaire data we gathered from the participants after completing both ACTS and ACTS-WM.

Table 1

Reported Strategies Used During the ACTS and ACTS-WM Task

Strategy Category	Definition	Example Response
None	No strategy reported	*I had no set strategy, just played it on the fly*
Unknown	Response did not clearly state any strategy	*Because I could see the colors faster then the shape*
Chunking	Splitting up the sequence into groups.	*It was easier to split the sequence into two sections instead of four for remembrance purposes.*
Looping	Running through the sequence (no clear indication of the repetition method)	*I would just repeat to myself the pattern color shape shape color*
Both	Reported using both chunking and looping at some point or at the same time	*While doing the test I grouped them by AA and BB, but I also tried to keep them in groups of four as well.*
Verbalization	Saying a feature or the sequence out loud	*As the shapes/colors flashed I said what category*
Number Association	Connecting the response to the position number	*I remembered the pattern in groupings of 4 and associated them with the numbers 1-4*
Letter Association	Associating the response to a letter with the response	*I just tried to remember the first letters. So I kept repeating 4 letters in my head.*
Inference	Inferred the upcoming stimuli based on what was previously seen	*I inferred what would be next based off what already came up*
Motor Encoding	Associating the response with the key needed for the response	*I didn't have an exact strategy since I was more focused on what letter to be clicking when the shape and color came up.*
Feature Coding	Only remembering a list of the features required by the abstract sequence	*I built a list of what attributes were in the rules as I saw the images*
Multiple	Using a combination of multiple strategy types	*I said what each of the shapes/colors should be as they flashed on the screen, trying to remember them in pairs.*
No Response	Left the question blank	

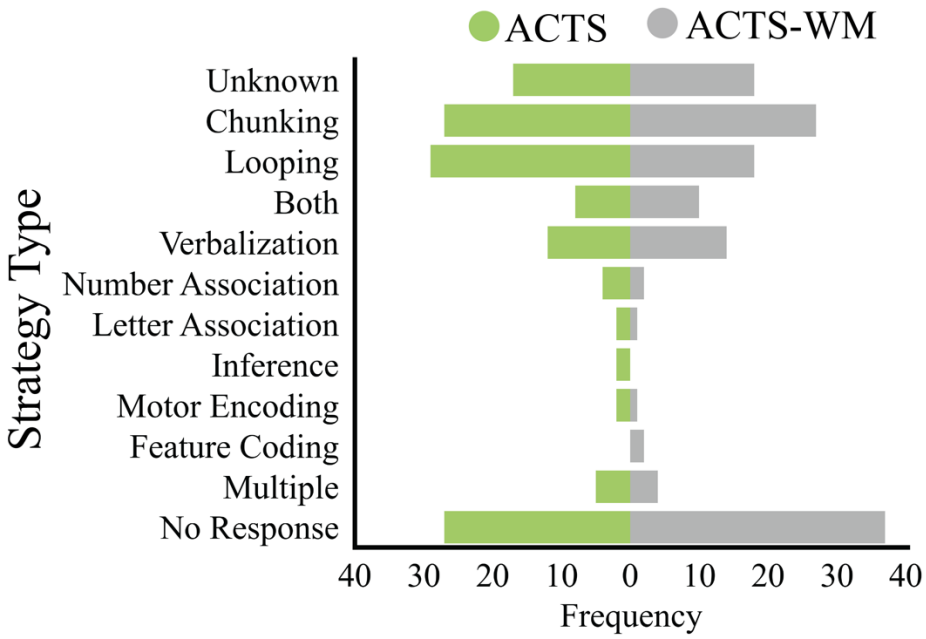

Figure 16. The strategies participants reported using during ACTS and ACTS-WM. See Table 1 for a definition and example of each strategy type. Participants reported a strategy for each sequence type (simple, complex and hyper-complex) and each task. Participants were recorded as using a strategy if they reported it once for a task. Ergo, participants may be represented multiple times depending on the number of strategies they mentioned. However, participants were never double counted. No response was considered if a participant did not report any strategy for all sequence types.

Participants reported numerous types of strategies (Fig. 16 and Table 1). For some responses, it was clear the participants struggled to describe their strategy well. Others reported confusion about the set-up of the questionnaire. While the data are very noisy, we can observe some important observations. First, participants are chunking. They report splitting the sequences into pairs. For the ABBA sequences, some reported shifting their mental positional cue and then chunking (e.g., turning 'ABBA ABBA ABBA' into 'ABB AABB AABB A…'). Second, participants use a wide variety of 'looping' methods. Since the data were collected through an online questionnaire, we could not probe them for further details about how their looped the sequence. Looping suggests they may be keeping one of the sequences as an auditory loop instead of a visual sequence. Future research

should include an auditory task to help eliminate any potential auditory, mental or otherwise, strategies. A pleasant surprise was the lack of motor encoding reported. This suggests most participants were maintaining everything in WM and not in the motor cortex. Regardless, all the strategies provide potential methods of off-loading one of the sequences onto a different cognitive resource. While at first glance our data seem to support separate WM resources, there are a few alternative explanations that need to be tested before a strong conclusion can be made.

High and Low Performing Participants

We noticed potential subgroups in the participants from the distribution of their performance. We predicted there were two groups: a high and low performing group. A clustering algorithm supported this prediction and separated the participants into the two groups based on their performance on both ACTS tasks. The two groups have significant differences in behavior across the sequences. In the high performing group, their accuracy is more stable, but their reaction time varies depending on the position within the sequence. They show a sequence initiation cost with a slower reaction time for the first position of the sequence. On the other hand, the low performing group shows variability in their accuracy across position, but a stable reaction time (Fig. 14). They show evidence of a primacy effect with a higher accuracy on the first position of a sequence. This may indicate the two groups are using different strategies or a group difference in WM capacity. Additionally, the presence of more classic findings, such as initiation cost or primacy effects, is dependent on whatever differentiates the two groups.

Sequence Types

Surprisingly, we found no significant differences between sequence types. Previous research showed significant differences in performance between the simple and complex sequence types (Desrochers et al., 2015). This study used an additional sequence pattern with three feature switches termed hyper-complex. We believe this may be due to the noise within the dataset. This dataset has a lower accuracy than previous research (Desrochers et al., 2015). Additionally, the use of different strategies may impact the findings. Some participants did report using different strategies depending on the sequence while others used the same one throughout. In short, our dataset contains more variability in performance and individuals. A stricter data cleaning processing might show findings the align with previous research.

Aim 2. Is there a common EEG signature of WM deficiency in hmTBI?

HMTBI research has been limited by the subjective measures associated with hmTBI diagnosis. In other words, clinicians diagnose hmTBI based on a patient's physical symptoms rather than by a laboratory test. A *neural signature* of hmTBI would provide a subjective measure to determine if someone has or recently had an hmTBI. This is made more difficult because MRI fails to catch the subtle neuronal changes in either animal models (Meconi et al., 2018; Palacios et al., 2017; Robinson et al., 2017) or human models (Gao & Chen, 2011; Kaltiainen et al., 2018; Palacios et al., 2017). This issue is further exacerbated by the heterogeneity in injury (Eierud et al., 2019). Post-injury damage can be detected by diffusion tensor imaging (DTI) (Braeckman et al., 2019; Churchill et al., 2017;

Raizman et al., 2020; Wu et al., 2020), EEG (Lewine et al., 2019; McNerney et al., 2019), and fMRI (Palacios et al., 2017). The DTI studies found metrics of white matter integrity predicted clinical outcomes months after injury (Braeckman et al., 2019; Wu et al., 2020), increased white matter fractional anisotropy as an adaptive response after injury (Churchill et al., 2017), and chronic hmTBI showed white matter disconnection (Raizman et al., 2020). The EEG studies found increased theta, decreased alpha, and global beta coherence were associated with the hmTBI group (Lewine et al., 2019), and EEG along with symptomatology were better predictors of hmTBI than symptomatology alone (McNerney et al., 2019). The fMRI study found changes in functional connectivity was predictive of outcome six months after initial injury (Palacios et al., 2017). In summary, damage is found in changes in white matter (Braeckman et al., 2019; Churchill et al., 2017; Raizman et al., 2020; Wu et al., 2020) and changes in connectivity (Lewine et al., 2019; McNerney et al., 2019; Palacios et al., 2017). It is important to note that some studies identify reduced cortical thickness in acute mTBI (Govindarajan et al., 2016), but this may be specific to the radiating intensity of blast-related mTBI in veteran populations (Eierud et al., 2019). Lasting mTBI effects are believed to be due to disconnection within white matter tracts that alter network connections (Raizman et al., 2020). MRI fails to detect these small changes in neural integrity and activity (for a review of MRI limitations and findings, see (Bigler, 2023)).

One of the long-term effects of mTBI can be detected most reliably by looking at measures of neural connectivity due to changes to white matter (Wu et al., 2020). Non-imaging

findings have consistently found impairments in vestibular and ocular motor function (Cochrane et al., 2021; Hac & Gold, 2022; Master et al., 2018; Murray et al., 2014, 2019, 2020). Research suggests assessments of ocular motor function can reliably diagnosis a concussion (Hossain et al., 2022). This dissertation focuses on altered networks since they are associated with mTBI and EEG, which is cheap and easy to use, can detect changes in network activity. For example, mTBI is associated with changes in connectivity patterns in the alpha, beta, and theta frequency bands (Kaltiainen et al., 2018; Lewine et al., 2019). MTBIs are associated with overall reduced power (Lewine et al., 2019). Larger neural networks, such as the default mode network and connectivity between the frontal and parietal regions, are also distributed after an injury (D'Souza et al., 2020). Frontal lobe activity has been highly predictive of mTBI status and long-term outcomes (Cavanagh et al., 2019; Hocke et al., 2018; Poltavski et al., 2019). In short, previous research suggests a disconnection between frontal and parietal regions persists in the hmTBI population long after the initial injury.

High-density EEG is well-suited to capture hmTBI given its high temporal resolution and the connectivity metrics that can be leveraged to assess altered neural function. Therefore, in this aim, we used EEG to test for a consistent mechanism underlying hmTBI. A key question is whether there is a *common* neural signature associated with poor VWM performance after hmTBI. The VWM deficit may be due to the disconnection between anterior and posterior brain regions (D'Souza et al., 2020), at any point along the tract. Support for residual disconnection comes from the observation of changes in connectivity

detected in alpha, beta, and theta frequencies after an mTBI (Kaltiainen et al., 2018; Lewine et al., 2019).

In this aim, we expanded upon the previous research by testing what metric of EEG (i.e., raw signal, phase, power, connectivity) would best classify hmTBI and controls, we subjected EEG data to machine learning classification analyses. Resting state and WM performance data were collected from control and hmTBI. In this first analysis, we predicted that classification might be used to identify participant groups, and if so, it could point toward a consistent underlying neural difference. However, hmTBI is highly heterogeneous and only a subset exhibit a WM deficit (Arciniega et al., 2021). Therefore, a second analysis went further and used classification to try to detect EEG differences between hmTBI *with* and *without* WM performance differences. In other words, to begin to identify which neural differences drove behavioral performance. Overall, the role of this aim is to shed light on potential subjective methods of detecting hmTBI and predicting hmTBI outcomes. The results of this study would help develop diagnostic tools and outcome assessments for mTBIs.

Although this past research suggests a successful application of classification using EEG data, we found our first prediction (that EEG would classify hmTBI and controls) was unsubstantiated. We had not contemplated this outcome, because we had excellent preliminary data. Unfortunately, we discovered a major software bug/data processing problem. When this was fixed, the exciting preliminary findings disappeared. In the next

few sections, we will go over everything we tried, but all models failed to classify between hmTBI and controls. Therefore, our predictions about connectivity best classifying hmTBI with and without WM impairments are no longer viable.

Method

Datasets

High Density EGI Dataset

This EEG dataset consists of 56 hmTBI resting-state recordings and 28 control resting-state recordings. Some recordings were multiple sessions of the same individual. All hmTBI were at least 3 months post-injury. There were 34 unique hmTBI participants with 5 hmTBI completing two sessions, 4 participants doing three sessions, and three participants doing four sessions of resting-state. There were 25 unique control participants with 3 participants doing two sessions of resting-state. The unusual number of participants and session was an unsuccessful attempt at creating a longitudinal database. All EEG recordings were collected using a 256 electrode HydroCel Geodesic Sensor Net. Resting-state sessions were three minutes in length. The sampling rate was 1,000 Hz. All recordings were collected with participants' eyes closed.

Low Density Sleep Profiler Dataset

We also performed the same analyzes in a low-density EEG system to test if a low-density EEG could classify between hmTBI and controls. The goal of this analysis was the application benefit. It would easier and cheaper to use a low-density system compared to the high-density system. This EEG dataset consists of 147 control resting-state recordings and 73 hmTBI resting-state recordings. All hmTBI were at least 3 months post-injury. These data had originally been collected as part of an intended longitudinal EEG study that was never completed due to participant attrition. There were 28 unique hmTBI participants completing different numbers of sessions (1 session: n=5 participants; 2 sessions: n=15, 4 sessions: n=5; 6 sessions: n=3). There were 62 unique control participants (1 session: n=13 participants; 2 sessions: n=31, 4 sessions: n=18). All EEG recordings were collected on a three-electrode wireless B-Alert Sleep Profiler (Advanced Brain Monitoring, ABM, Carlsbad, CA). The three electrodes were positioned over AF7, FpZ, and AF8. Resting-state sessions were two minutes in length, eyes-closed, twice per session. All recordings were eyes-closed.

11 participants were removed from the modeling analysis due a missing electrode. The missing electrode was not due to the processing since it was an automated batch process. It is uncertain if the missing electrode was due to a complication during data collection or any type of file corruption. 5 of the participants were in the hmTBI group.

EEG Analysis

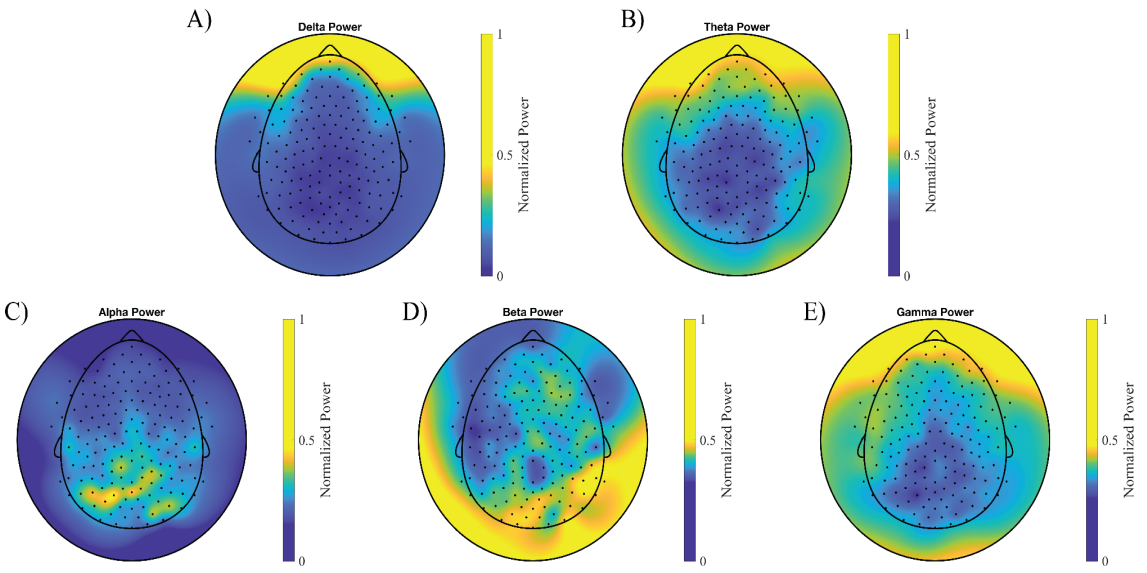

Figure 17. Five topographical graphs of the EGI dataset in each frequency band. Black dots represent electrodes kept and used in the analysis. Colors extend beyond head for aesthetic purposes only. The average power for each frequency band was normalized between 0 and 1. A) The topoplot for the delta frequency (1-3 Hz). B) The topoplot of the theta frequency (4-8 Hz). C) The topoplot of the alpha frequency (9-13 Hz). D) The topoplot of the beta frequency (13-30 Hz). E) The topoplot of the gamma frequency (> 30 Hz).

EEG datasets were lightly processed to increase real-world applicability (i.e., a fast, on-site diagnostic tool). For the EGI dataset, all electrodes located on the neck and checks were removed, leaving 174 electrodes. The EGI was down sampled to 500 Hz. The Sleep Profiler was down sampled to 250 Hz since the sampling rate was the original sampling rate was 515 Hz unlike EGI at 1,000 Hz. Datasets were filtered between 0.05 - 60 Hz. The EGI recordings were epoched into 3 trials of eyes-closed resting state of 45 seconds in the middle of the resting-state session. The choice to limit the epoch to the middle of the resting state was to reduce data size for later modeling. The middle time points were selected to reduce the chance of potential outside events (e.g., researcher leaving the room, making

noise, etc.). The Sleep Profiler recordings were one trial session and epoched in the middle 45 seconds. The epoched data were used in the model and considered the ‘raw’ EEG input.

The EGI recordings were run through a Laplacian filter to increase spatial resolution. Due to the low-density of the Sleep Profiler, this step was skipped. A Hilbert Fourier transform was performed on all the data between the frequencies 2 - 60 with a 1 Hz resolution. The phase was calculated as the angle of the transformed data. The power was calculated by taking the amplitude of the transformed data.

We attempted to run a connectivity analysis but did not find evidence of any potential connectivity (Fig. 17). While we did detect a small peak in power in the alpha band, the other frequency bands were only detected at the edge electrodes. It was not apparent on how to test for connectivity between theta-gamma (important for WM) or alpha-theta or alpha-beta (noted in both WM and default mode network).

All EEG analyses were performed using MATLAB (2024A), EEGLAB (Version 2024.0), and Fieldtrip (2024).

Modeling

A primary training value of this portion of the dissertation was to teach me to conduct different kinds of modeling. As such, each dataset trained multiple models to test if raw, power, or phase inputs would improve model performance in classifying hmTBI and

controls. The classification methods used in this analysis were: 1) Logistic Regression, 2) K-Nearest Neighbors, 3) Support Vector Modeling, 4) Random Forest Classifier, and 5) Gaussian Naive Bayes. All modeling was performed using Python (Version 3.11.5), NumPy (Version 1.24.3) and Sklearn (Version 1.3.0).

The data were normalized over each electrode across all time points before being used to train any models. For power and phase data, each frequency was isolated and then normalized across all time points per each electrode. Then, the raw EEG data were averaged across all time points.

For all models, 10 participants' data were randomly chosen to be excluded from the training process. This subset of the data will be referred to as the test data. All models used a 4-fold stratified K-Fold. In each permutation, three fourths of the data was used to train the models (the train data) and the remaining was used to assess model performance (the validation data). Performance was assessed using the mean area under the curve (AUC). AUC is more robust to random chance than model accuracy (Bradley, 1997). A model AUC below .70 is considered to be chance level. An AUC of .7 - .8 is considered acceptable and above .8 is considered excellent. Until an acceptable AUC was achieved, only the validation data was assessed (Mandrekar, 2010).

Results

EGI Dataset

The aim of this first analysis was two-fold: 1. To test if resting-state EEG could be used to objectively differentiate hmTBI from controls. 2. To test if a particular activity pattern (i.e., frequency) or region was *consistently* useful for differentiating between hmTBI and controls.

All models failed to classify hmTBI from control group membership at an acceptable level regardless of any hyperparameter tuning. Therefore, we did not get to the step where we would have had to validate the model using the test data. A total of 16 models were assessed (all 5 types listed in the methods section with slight differences in hyperparameters adding to a total of 16).

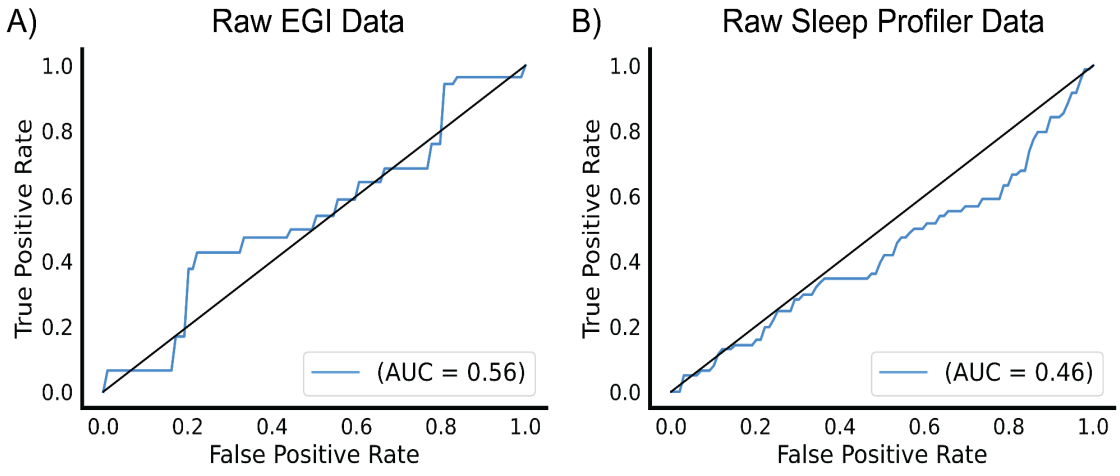

Figure 18. The performance of a Logistic Regression model for both datasets. Logistic Regression was one of the best performing models for each set. A shows the model performance when trained on raw EGI data. B shows the model performance when trained on raw Sleep Profiler data. The black line indicates chance performance for the model.

For the raw EEG input, the best performing model was the Logistic Regression with an accuracy of 0.58 and AUC of 0.56 (Fig. 18A).

For the power data, the Support Vector Model, Random Forest Classifier, and K-Nearest Neighbor initially performed at an AUC >.70. To ensure these results were due to true group discrimination and not random chance, we re-shuffled the data and performed a 4-fold cross validation 3 times. This ensured the performance of the model was not due to having a particular group of data within one of the K-Folds. Every model failed to show a consistent ability (defined as more than 50% of assessments with an AUC above .70) to discriminate hmTBI and controls. The highest AUC achieved among any of the models was a K-Nearest Neighbor model with an AUC of .73 and accuracy of 0.72.

The best performing model trained with the phase data was a Logistic Regression with an AUC of 0.66 and accuracy of 0.64.

Sleep Profiler Dataset

This analysis replicated and expanded on the previous analysis by testing a low-density could discriminate between hmTBI and controls. All models failed to achieve an acceptable AUC. All AUCs were between 0.46 - 0.55.

Discussion

In Aim 2, our goal was to find neural biomarkers of hmTBI using machine learning and EEG. HMTBI research has been limited due to the subjectivity of its diagnosis, making it difficult to understand the full impact of an hmTBI. A fast, easy, and cheap method of detecting an hmTBI would greatly improve outcomes, research, and diagnosis. We predicted that EEG would be suitable for such a test since mTBI has lasting impacts on the connectivity between neural networks (Kaltiainen et al., 2018; Lewine et al., 2019). However, EEG was not capable of discriminating between hmTBI and controls. This failure persisted across different EEG metrics (i.e., power, phase, raw signal).

Our failure to classify was very disappointing because previous research had success using machine learning to detect mTBI from controls (Luo et al., 2021; McNerney et al., 2019; Vergara et al., 2017). An important difference in participants, however, is that these authors tested *acute* mTBI who have more highly disordered neural activity. Our approach was riskier because we attempted to expand this research into chronic hmTBI (>3 months post injury). One interpretation of our findings is that the hmTBI population returns to neurotypical brain activity eventually. However, other work has shown mTBI patients exhibit cognitive defects (Chung et al., 2019; Green et al., 2018; Kumar et al., 2013; L'Ecuyer-Giguère et al., 2020; Quinn De Launay et al., 2021) and connectivity deficits in functional fMRI connectivity even years after injury (Arciniega et al., 2019, 2020, 2021). Additionally, classification has been successful with only neural data (Luo et al., 2021; Vergara et al., 2017).Thus, our conclusions can be narrowed down to two probable

possibilities. First, EEG activity returns to neurotypical levels sometime after the 3 months. This conclusion has interesting implications about differences in fMRI and EEG. The second conclusion, and most probable in our opinion, is that our EEG lacked the signal-to-noise ratio required for modeling. One choice point was that we limited the amount of data cleaning during preprocessing. The rationale for this was to maximize potential real-world application, in which a robust classification algorithm would be essential. However, when we later attempted to run the data through a more rigorous preprocessing pipeline, EEGLAB threw multiple warnings that output would not be reproducible. We stopped the pipeline before it could finish due to the lack of reproducibility. While the error was not clear what aspect of the data was the cause, it does indicate that some data were of lower quality. Taking this into account and previous research, the clear conclusion is our data lacks the quality necessary to model.

Accounting for the Preliminary Data EEG Analysis: MNE vs EEGLAB

Before this dissertation began, I conducted a preliminary study to test if EEG could classify hmTBI and controls. At that time, we found models could predict with an excellent AUC score of .85. However, our results now are vastly different. The same dataset and modeling techniques were used. The following section details the technical differences that we think explain the disparate results.

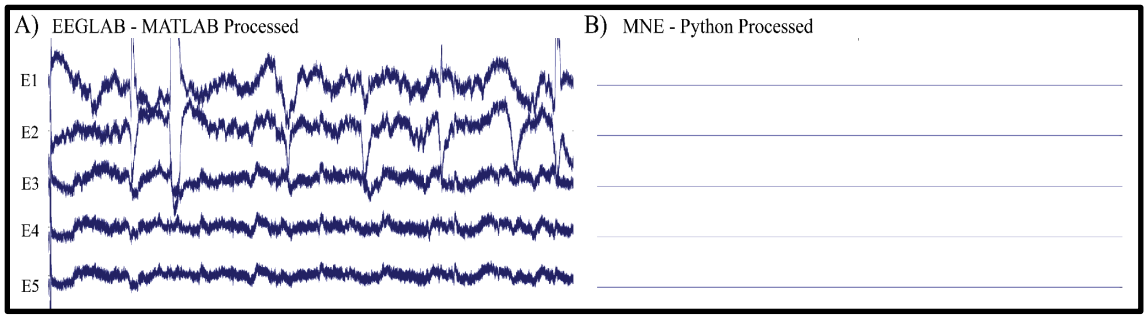

Figure 19. Two different EEG processing software: *same* participant, *same* session. Processing conducted in (A), EEGLAB/MATLAB; (B), MNE/Python. Both A and B show the same individual, the same five electrodes, and the same timeframe. We believed the same steps involving the same processing (bandpass filtering, epoch) were happening, but the processing was distinctly different. The same axes are used on the left and the right.

First, the *only* difference between now and then is the software I used to process the EEG data. During the first attempt, we used the python toolbox MNE to keep the data accessible within Python. As I began working on this aim, I discovered a method of opening and accessing MATLAB files in Python, negating the need for the MNE toolbox. I recreated a processing pipeline to be identical to the MNE pipeline but got dramatically different results. When I examined the same participant data in EEGLAB, the MNE processed data looked completely different from the EEGLAB data. The EEGLAB data (Fig. 19A), while messier, looked like a human EEG recording whereas the MNE data (Fig. 19B) did not.

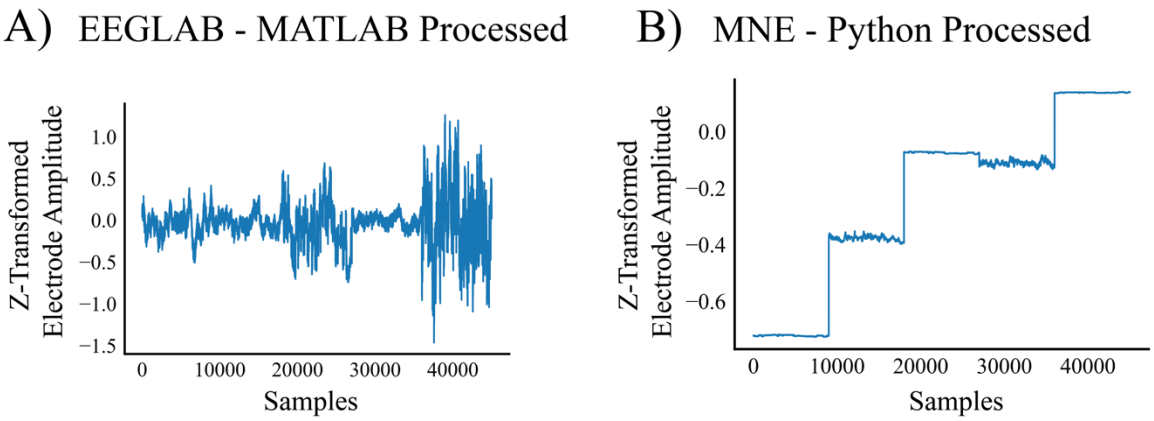

Figure 20. Z-Transformed EEG data after EEGLAB and MNE Processing. X-axis is the samples (total: 45,000). Y-axis is the z-transformation for a single electrode averaged across participants. A. The data after undergoing band-pass filtering and being split into epochs through EEGLAB. B. The data after undergoing the same process in MNE.

We probed the differences between the different processing toolboxes further. First, we tested if the same electrodes in the EEGLAB dataset were highly correlated with the MNE dataset. The correlation was low between the two datasets (Average: 0.19, STD: 0.13). Second, we wanted to examine the data on the same scale and used a z-transformation to directly compare the two datasets. The z-transformation was applied across an electrode and then averaged across all participants. While the EGI data looked correct (Fig. 20A), the data processed through MNE showed a clear stepwise pattern (Fig. 20B). Our next step was to determine at which processing step the stepwise appear in the MNE processed data.

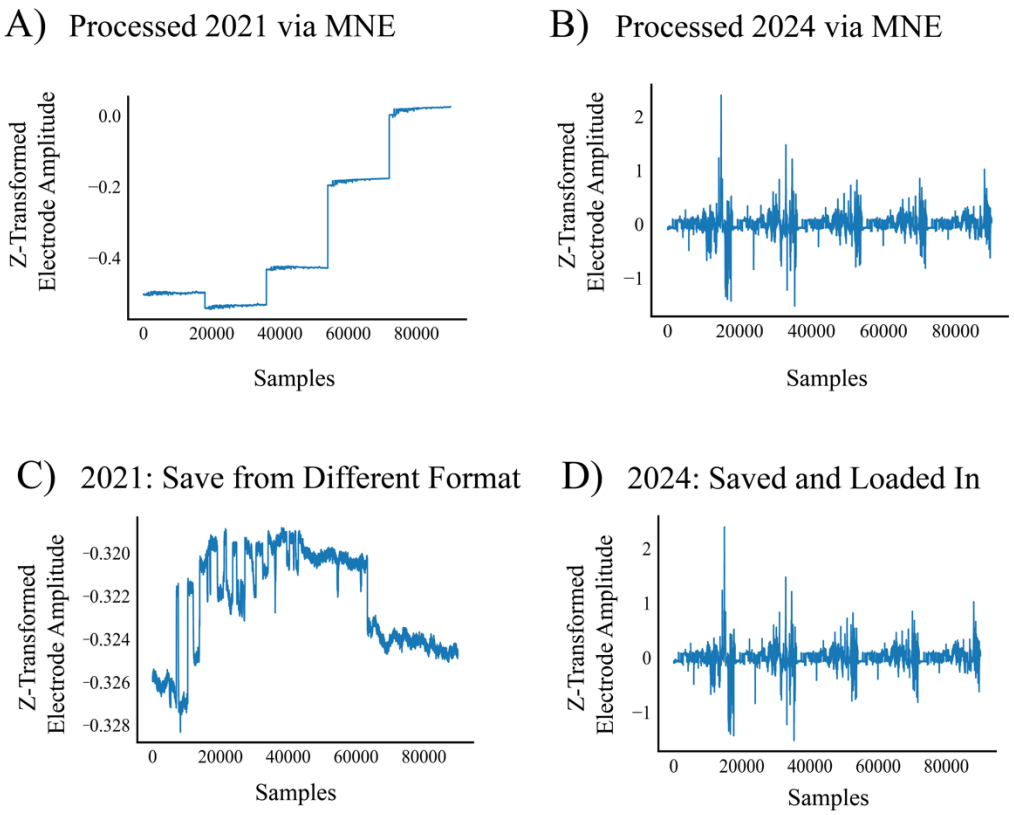

Figure 21. Multiple attempts to recreate issues in MNE data. All graphs have the same participant and same electrode. A. Graph shows the subject's data after z-transformation. B. Graphs shows the subject's data if the same processing steps are recreated in the same version of MNE (0.23.0) from the raw EGI data. C. Graph shows the data processed in 2021 but saved in a different file format. D. Graph shows the data after saving and reloading the results from B in the same file format as C.

For simplicity, the old MNE dataset will be referred to as the 2021 dataset and the recreated MNE dataset will be called the 2024 dataset. All the recreations were done in the same version of MNE (0.23.0) as the 2021 dataset. The stepwise did not appear in the 2024 dataset at any point during the processing (Fig. 21A and B). The 2021 dataset was saved in two file formats: '.fif' used by MNE and '.npy' used by the toolbox, NumPy. We loaded in the back-up file format, NumPy, to see if the data in the MNE format was corrupted (Fig. 21C). There were some signs of the stepwise function, but surprisingly the NumPy format looked like neither the 2021 nor 2024 MNE formats. Finally, we

tested if the issue was loading of the data by saving and reloading the 2024 data (Fig. 21D). This also failed to replicate the stepwise. In short, we tested several possible causes of the differences between MNE and EEGLAB and found only more questions. At some point, the 2021 dataset became strangely warped without any clear cause.

Aim 3. Can tDCS restore hmTBI cognitive impairments?

In Aim 3, the goal was to develop a non-invasive intervention that would restore WM in the hmTBI and/or those with a low WM capacity. Neurostimulation has shown promising results in improving WM performance in both older (Stephens & Berryhill, 2016) and young adults (Gözenman & Berryhill, 2016; Jones et al., 2017, 2020). Stimulation helped improve cognitive function in other special populations such as bipolar, depression, and schizophrenia (Berryhill & Martin, 2018; Martin et al., 2023). Transcranial direct current stimulation (tDCS) can strengthen connectivity between neuronal regions (Jones et al., 2017). A consistent finding is that the mTBI population has reduced connectivity strength, even years after injury (Arciniega et al., 2021; D'Souza et al., 2020; Hocke et al., 2018; Maleki et al., 2021). The neuronal changes can have a lasting behavioral impact. Findings revealing increased aggression and anxiety in adolescents who experience an mTBI (Dailey et al., 2018; Veliz & Berryhill, 2023). The impact of a *midlife* mTBI is now considered to increase dementia risk (Livingston et al., 2020). Our goal is to develop interventions to prevent these behavioral outcomes. Here, we expanded on both the previous stimulation and connectivity work by testing if hmTBI can see WM improvement from HD-tDCS.

Our choice to use HD-tDCS over tDCS was to provide stronger stimulation at the cost of broader spatial coverage. Additionally, HD-tDCS can remediate performance in participants with *lower* WM capacity. Gözenman et al. (2016) found HD-tDCS improved WM in those with a lower WM capacity while tDCS helped those with a higher WM capacity. Participants received HD-tDCS or tDCS during a WM retro-cue task. Participants with a lower WM capacity had a greater retro-cue benefit in the HD-tDCS condition compared to tDCS (Gözenman & Berryhill, 2016). It is important to note that Gözenman et al. found no significant difference between HD-tDCS and the control group. However, numerous studies show a WM improvement and neuronal changes after HD-tDCS (Left DLPFC: Dong et al., 2020; Centered at F3: Liu et al., 2020; Wang et al., 2019). When compared directly to HD-tDCS during the same WM task, HD-tDCS showed greater improvement in WM performance than tDCS (Gözenman & Berryhill, 2016). Thus, we choose HD-tDCS to test if stimulation can help hmTBI and/or those with a lower WM capacity.

Methods

Participants

39 (Female = 24, Age = 19.5; 1 hmTBI participant refused to complete the demographics) undergraduate students from the University of Reno participated in the study. Every participant read and signed a consent form. Participants had no history of neurological diseases or disorders. 19 (Female = 11, Age = 19.5) of the participants self-reported a previous concussion with the most recent occurring at least more than three months. The

hmTBI reported an average 2.4 of concussions (2 participants did not report the number of hmTBI). The hmTBI data collection in particular has been slow since the stimulation techniques add multiple exclusion criteria. The 20th hmTBI participant has not been collected despite 13 hmTBI participants arriving. All 13 were excluded from the study due to medical exclusion criteria.

Task Design

Participants completed two sessions separated by 48-hours. The 48-hour wash-out period between sessions ensured the effects of stimulation had dissipated. During one session, participants received active HD-tDCS and the other session a sham control HD-tDCS. The order of the active and sham sessions were counterbalanced across participants. At the end of the second session, participants filled out a short survey about their previous mTBIs.

Stimulation: HD-tDCS implemented a 4 x 1 montage style with four cathodal electrodes and one anodal electrode (Soterix Medical Inc., New York). Cathodal electrodes are equidistant from each other and the center anodal. Cathodal electrodes were placed at Pz, C4, P8, and O2. The anodal electrode was placed at P4 over the right parietal cortex. Stimulation lasted for 20 mins at 1.5 mA. Previous research using this montage successfully improved WM performance in HD-tDCS compared to tDCS (Gözenman & Berryhill, 2016).

Sham experiences 30s of ramp up (0 mA - 1.5 mA) and 30s of ramp down (1.5 mA to 0mA) at the beginning and end of the session. Between the ramp up/down, there is no stimulation. The ramp up/down blinds participants.

The HD-tDCS montage, timings, and intensity replicate Gözenman, et al. (2016). This study found HD-tDCS improved WM performance in low WM capacity individuals whereas tDCS improved performance in high WM capacity individuals (Gözenman & Berryhill, 2016).

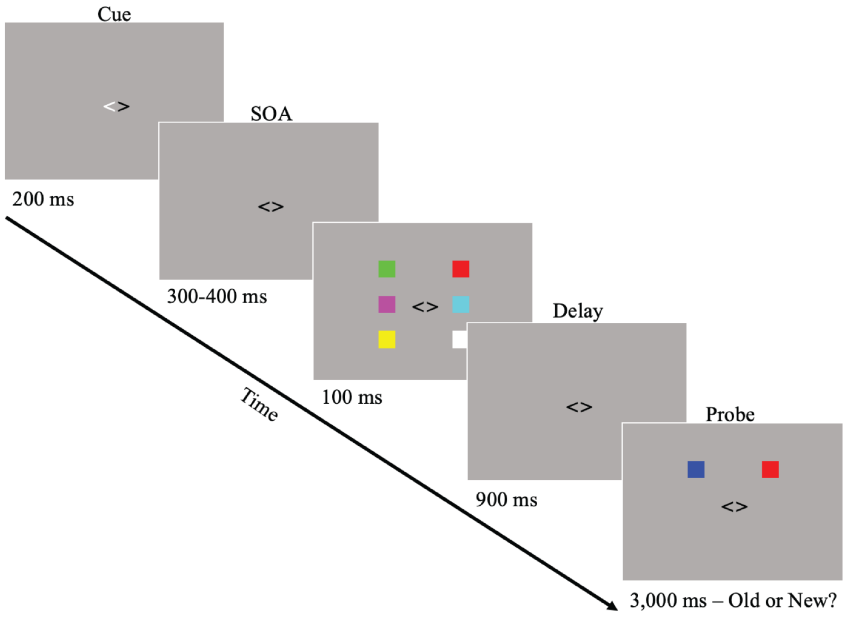

Figure 22. The WM change detection task used in Aim 3 to test if online HD-tDCS improved performance. Participants were cued to the left or right and answered if the probe on the cued sided was among the three presented on the cued side.

WM Task: We used the change detection VWM task previously used (Arciniega et al., 2019). In short, participants are cued (white arrowhead) to attend to the stimuli presented either to the left or right of a fixation cross. Afterwards, an array of three-color patches appear on each side of the fixation cross and are briefly presented (100 ms). The three

attended squares were then maintained for 900 ms. Next, two probes appeared on either side of fixation. The participants made a judgment if the probe on the cued side was present among the three (Fig. 22).

Results

For the following analyses (Fig. 23 and Fig. 24), we used a Bonferroni correction to reset alpha to 0.01, accounting for five separate statistical tests (4 correlations, 1 MANOVA) since we were testing if HD-tDCS had an effect on WM performance. The other analyses (Fig. 17) used the typical alpha of 0.05 since the tests were for a unique question. The MANOVA performs a correction for both metrics. All statistical testing was performed using SPSS (Version 29).

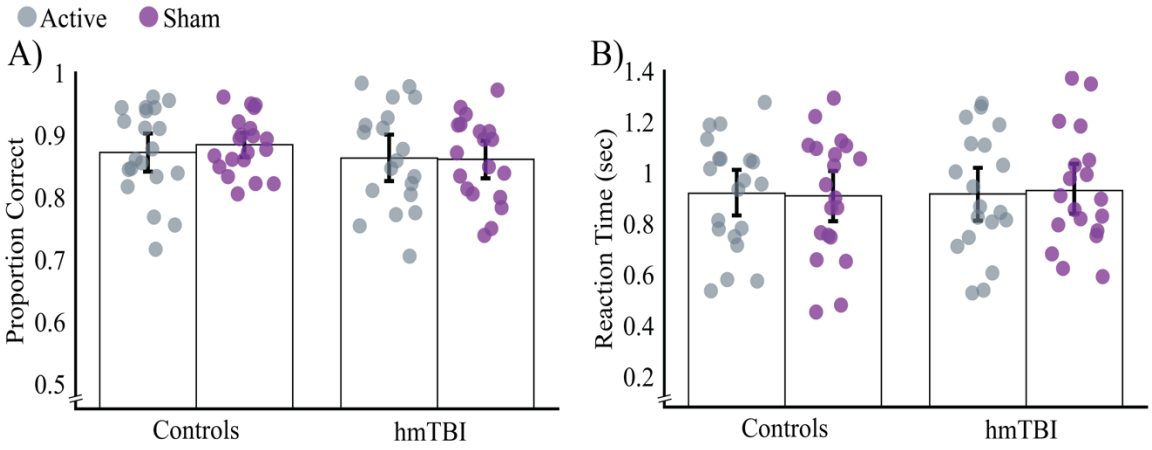

Figure 23. Performance of the controls and hmTBI group on a change detection WM task during active (gray) and sham (blue) HD-tDCS. There was no main effect of group (hmTBI or controls) or stimulation (active or sham).

Does stimulation improve WM performance? Does it help the hmTBI group more?

The first prediction was that there would be a significant main effect of HD-tDCS on WM performance. The second prediction was that there would be an interaction such that the

hmTBI group would demonstrate a greater benefit from HD-tDCS than controls. We tested this using a MANOVA (within-subjects: active or sham stimulation, between-subjects: hmTBI or control). We found there was no significant difference of stimulation type ($F(2, 36) = 0.31$, $p = 0.74$, $\eta_p^2 = 0.2$), group difference ($F(2, 36) = 0.31$, $p = 0.74$, $\eta_p^2 = 0.02$) or two-way interaction ($F(2, 36) = 0.54$, $p = 0.59$, $\eta_p^2 = 0.03$).

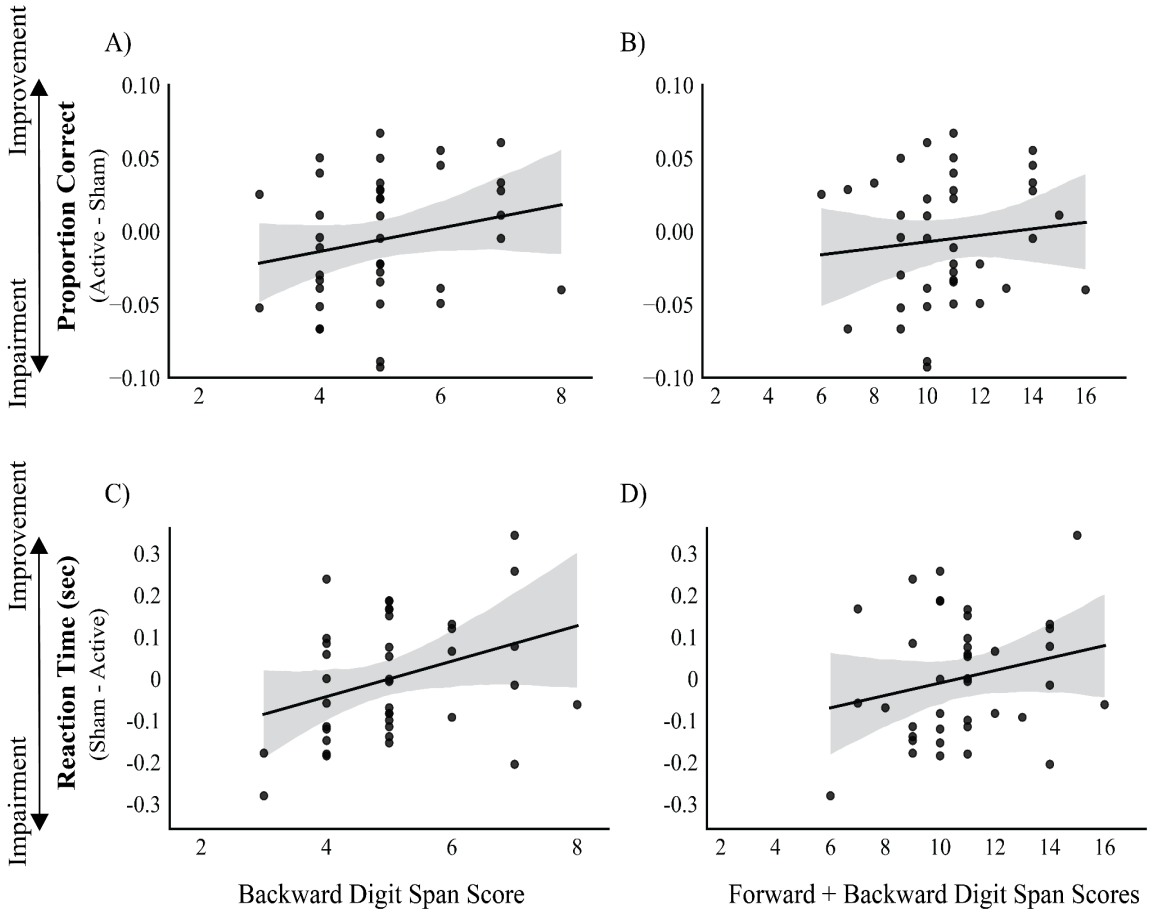

Figure 24. Four correlations testing if low WM capacity is correlated with HD-tDCS benefit. None of the correlations were significant when accounting for multiple comparisons. The top row is correlations with proportion correct change (active - sham). The bottom row is response time change (sham - active). The Backward Digit Span is the X-axis for A and C. Forward plus Backward Digit Span scores is the X-axis for B and D.

Do we replicate previous benefits of HD-tDCS?

To test if we replicated our previous findings that HD-tDCS benefits those with a low WM capacity, we performed six two-tailed correlations. WM capacity was assessed in three ways: backward digit span (BD), and the combination of forward and backward digit span scores (CD). We tested each of these assessments with the difference between the sham and active HD-tDCS session for both accuracy and reaction time. No correlation was statistically significant (Accuracy and BD: $r(39) = 0.22$, $p = 0.19$; Accuracy and CD: $r(39) = 0.11$, $p = 0.50$; RT and BD: $r(39) = 0.34$, $p = 0.04$; RT and CD: $r(39) = .23$, $p = 0.17$).

Is the current hmTBI group different from the current hmTBI group?

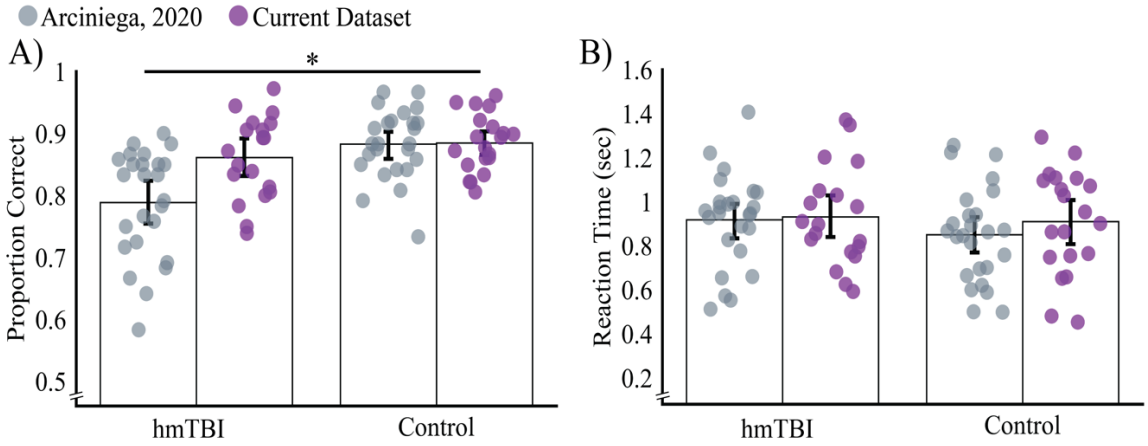

Figure 25. A comparison of the hmTBI and control group between the current dataset and the data collected by Dr. Arciniega (Arciniega et al., 2020). There was a significant two-way interaction between group and dataset in proportion correct, but not in reaction time. While the controls have nearly the same average, the hmTBI groups differ between Dr. Arciniega's dataset and the current dataset. The black line indicates a significant two-way interaction between group and dataset. * - $p = 0.01$

To test if our hmTBI group was different from previously collected hmTBI, we compared a previously collected dataset (Arciniega et al., 2020) and current dataset (Fig. 25). We used a two-way between-subjects MANOVA (between-subject factors: group, dataset; dependent variables: proportion correct, reaction time) to answer this question. There was

a significant two-way interaction in proportion correct between group and dataset ($F(1,85) = 6.23$, $p = 0.01$, $\eta_p^2 = 0.07$), but not in reaction time ($F(1,85) = 0.24$, $p = 0.62$, $\eta_p^2 = 0.003$). In sum, the hmTBI group we tested performed significantly better than the hmTBI group tested by Arciniega et al., just a few years ago.

Discussion

These results were not consistent with our predictions. Firstly, we failed to replicate the WM deficit found in the mTBI group across multiple research studies (Arciniega et al., 2019, 2020, 2021; Chung et al., 2019; Green et al., 2018; Kumar et al., 2013; L'Ecuyer-Giguère et al., 2020; Quinn De Launay et al., 2021). There was no difference in WM capacity or WM task performance between neurotypicals and hmTBI, in contrast to the previous WM deficit in the hmTBI group. Importantly, there appears to be a major shift in undergraduates with hmTBI at UNR, and this may be a consequence of the COVID-19 pandemic. Evidence supporting this possibility comes from a direct comparison of earlier data (pre-COVID) with our current hmTBI group on the *exact same task* (Fig. 17). The group means and measures of spread reveal significant group differences between the earlier and current hmTBI groups. We can speculate that those poor-performing hmTBI students with low WM struggled more academically and they may have left college after the pandemic at a higher rate. Alternatively, low-performing people with hmTBI may have switched majors *away* from Psychology, as the Department switched from the College of Liberal Arts to the College of Science and was widely believed to have increased academic

standards. Another possibility is, due to chance, we managed to collect a group of high-performing hmTBI, perhaps those more highly motivated to receive course bonus credit.

The second surprising finding was a failure to replicate our previous findings in HD-tDCS. However, the results of tDCS and HD-tDCS suffer from low-consistency. Some find benefits of tDCS (WM: Gözenman & Berryhill, 2016 (left and right PPC); Jones et al., 2015 (left PFC), 2017 (PPC & PFC), 2020 (PPC & PFC); Stephens & Berryhill, 2016 (right PFC)), but others do not (WM: Hill et al., 2018 (left DLPFC or left DLPFC and PC), 2019 (left DLPFC); Nikolin et al., 2019 (left IPS or LDPLC); Shires et al., 2020 (PC, FC, or both)). Sometimes HD-tDCS can provide a greater benefit than tDCS (Gözenman & Berryhill, 2016) and other studies have found no difference between the two (Breitling et al., 2020; D. Müller et al., 2022). The effect of stimulation likely depends on many factors, including age, education, cognitive strategy, and motivation (Jones et al., 2017; Shires et al., 2020; Stephens & Berryhill, 2016).

Our failure to replicate may be due to a difference in how we measured WM capacity. To save time, we used the direct capacity measure of the Backward Digit Span, instead of the OSPAN as in Gözenman & Berryhill (2016). Additionally, we used a different WM task, one emphasizing attention more heavily. The benefit of HD-tDCS and tDCS may be task dependent since Gözenman et al. used a retro-cue WM task whereas we used a change detection WM task. Our choice of the change detection task was to replicate the previously

found hmTBI deficit. Although our current findings did not improve WM performance, the findings may contribute to future research to develop these kinds of interventions.

Overall Results Summary

Aim 1. Are Abstract and Concrete Stimuli Held in Separate WM Stores?

In Aim 1, we used a new paradigm, ACTS, to test if abstract stimuli, such as instructions, were held in the same store as concrete visual stimuli. We predicted that the two stimuli types were held in the same store. Thus, when we add WM components to ACTS, we predict a lower performance than only ACTS or only WM tasks. We secondarily tested if the hmTBI population would perform worse the greater the frontal load in the ACTS tasks versus a WM task. Our prediction for this test was hmTBI would perform worse as the load on the frontal regions increased. Research has found a persistent disconnection in the mTBI group between the frontal and parietal regions, both important for WM tasks (D'Souza et al., 2020; Maleki et al., 2021). This study tested if the reduced connectivity is due to neuronal changes in the frontal region. We tested both of these predictions by having both controls and hmTBI do an ACTS, ACTS-WM and WM task.

Our findings supported the view that the abstract and concrete demands on WM are maintained separately, because performance on the ACTS-WM was significantly better than ACTS. The second prediction was that if low performing hmTBI participants experience executive function deficits due to frontal disconnection, we should see significantly worse performance in the ACTS and ACTS-WM tasks. We did not observe

any significant difference between hmTBI and controls on any task. We think this is due to testing a sample of highly performing hmTBI. Unlike previous studies showing a highly heterogeneous hmTBI group with some showing WM impairment and some without an impairment (Arciniega et al., 2020), our sample was much more homogeneous. In summary, the current results provide evidence for separate WM stores for abstract and concrete stimuli and no evidence for a differential deficit in the hmTBI group.

Aim 2. Is there a common EEG signature of WM deficiency in the impaired hmTBI?

In Aim 2, we tested if resting state EEG could classify between hmTBI and controls. This was to extend a successful set of preliminary analyses. However, we found these results relied on a 'black box' software program that we detected midway through the project. The fixed EEG analysis did not show any classification success. We tested multiple models with multiple hyperparameters, but none of these models could discriminate between the two groups. Previous research suggests that neural activity can classify mTBI and controls successfully (Luo et al., 2021; McNerney et al., 2019; Vergara et al., 2017), but the current datasets may lack the current quality necessary for modeling.

Aim 3. Can tDCS restore hmTBI cognitive impairments?

In Aim 3, we tested if HD-tDCS could improve WM performance generally, and if it could provide added benefit to the hmTBI group. The mTBI group has a WM impairment (Arciniega et al., 2019, 2020, 2021; Chung et al., 2019; Green et al., 2018; Kumar et al., 2013; L'Ecuyer-Giguère et al., 2020; Quinn De Launay et al., 2021). Previous research

shows HD-tDCS can benefit those with low WM capacity (Gözenman & Berryhill, 2016). We merged these findings in this experiment. We predicted a main effect of group, such that the hmTBI would perform worse than controls on a WM task. We predicted a main effect of right parietal HD-tDCS, such that WM would generally improve. Finally, we predicted an interaction such that the hmTBI group would show greater WM improvement in the active HD-tDCS session. Instead, we observed no main effects of group or HD-tDCS and no interaction. We did find a significant difference between the current hmTBI group and previously collected hmTBI dataset (Arciniega et al., 2020). The current hmTBI group performs significantly better than earlier hmTBI participants in the same task. This may explain while we have not replicated an WM impairment in the hmTBI. The change in the hmTBI samples may be due to changes in the student population after the COVID-19 pandemic.

General Discussion

Abstract and Concrete Stimuli

In Aim 1, we tested if abstract (e.g., instructions) and concrete (e.g., colors) stimuli were maintained in the same WM store. Participants completed an ACTS, ACTS-WM, and WM task. Importantly, the ACTS and the WM only required the maintenance of abstract and concrete stimuli, respectively. ACTS-WM required a participant to hold both the abstract sequence and the concrete stimuli simultaneously. While participants did a WM task, participants saw three concrete visual stimuli presented at the same time. We did this to replicate previous hmTBI findings (Arciniega et al., 2021), but unintentionally made a

paradigm ill-suited for comparison with the ACTS. For the rest of the discussion, we will only be discussing the implications of comparing ACTS and ACTS-WM.

We had two possible predictions for results of Aim 1: one WM store or separate WM store. Some of our findings (performance significantly higher on ACTS-WM than ACTS) supported a separate WM store for abstract and concrete stimuli. There are multiple interpretations of this finding. The more traditional interpretation would be separate representations, such as the separation between long-term (LTM) and short-term memory (STM). This would require an interaction between the abstract and concrete stores in order to successfully complete an ACTS task. While this fits our current findings, we believe the findings could have more interesting implications in the emerging theoretical framework of the WM pointer system. Recent work has found that representations held in WM may work as a pointer to a representation held by sensory regions. This pointer represented the number of items in WM and the number of features of the stimuli, but not the stimuli itself (Thyer et al., 2022). There are multiple ways the current ACTS finding could fit into the pointer framework. First, a pointer could act as an indexing system, keeping track of the sequence order for the abstract and concrete stimuli. Alternatively, the abstract instruction could have a more top-down role. In other words, an abstract instruction could impose a top-down filter to the pointer. For example, it could indicate that only the task-relevant feature needs to be maintained. However, this is only considering the difference in behavior between ACTS-WM and ACTS.

Our findings also supported the alternative hypothesis: one WM store. ACTS-WM and ACTS were highly correlated suggesting the use of similar mechanisms. This may seem to disagree with the fact performance was better in ACTS-WM than ACTS. We would argue that these two pieces of evidence are not mutually exclusive. When taking considering both findings, we concluded participants are using successful strategies for both ACTS tasks. Our current post-task questionnaire was insufficient in determining a common theme in participant's strategies. We suspect there may be a strategy that favors the ACTS-WM more than the ACTS explaining the difference in performance. Ultimately, our findings are do not conclusively support either the same or separate stores hypothesis.

Other Implications

The goal of Aim 2 was to create a model to classify between hmTBI and controls in the hopes of furthering development of an objective diagnostic metric of hmTBI. We had additional goals, but those goals relied on the first being successful. The results of Aim 2 are not useful for scientific interpretation, but an important lesson for future studies. New processing software needs to be carefully tested. Ideally, one would use previous methods to ensure the software is producing the same results.

The goal of Aim 3 was to test if neurostimulation would benefit the hmTBI population. While we did not find any benefit of HD-tDCS, we did have some interesting results. First, we found that the hmTBI population collected for this dissertation is significantly different from the hmTBI sample collected pre-COVID at the same university (Arciniega et al.,

2020). This finding has implications about the shifting of special populations. The mTBI population is highly heterogeneous with only a subset showing long-term cognitive effects (Dailey et al., 2018; Keatley et al., 2023; Mollica et al., 2022; Skjeldal et al., 2022; Sterr et al., 2006). We suspect that COVID is largely responsible for the shift in the samples. The hmTBI with long-term cognitive effects may have had a harder time during COVID or returning to college after COVID. For future research, it is important to consider how neurotypicals and special populations change over time (Berryhill, 2024). Another finding of Aim 3 is the lack of HD-tDCS benefit to any participant. This finding adds to the growing amount of research with null effects of neurostimulation (WM: Hill et al., 2018 (left DLPFC or left DLPFC and PC), 2019 (left DLPFC); Nikolin et al., 2019 (left IPS or LDPLC); Shires et al., 2020 (PC, FC, or both)). The findings and methods of tDCS and HD-tDCS studies vary in montage, online or offline, session, and stimulation strength. Naturally, it is not entirely unsurprising that results vary. However, Aim 3 was a near replication of a previous study (Gözenman & Berryhill, 2016) at the same university. In fact, this is the second study (Shires et al., 2020) to fail to replicate a previously successful neurostimulation design (Jones et al., 2015, 2017). Overall, the emerging finding in neurostimulation research is that any benefit of tDCS or HD-tDCS relies on too many outside factors to expand the walls of a research lab.

Future Directions

ACTS

ACTS taps into an interesting real-world phenomenon. In the future, I would like to explore how the ACTS fits into the pointer system theory of WM (Thyer et al., 2022). In particular, I would be interested in testing if the abstract instruction acted as a pointer itself, or if a pointer held in WM represents the neuronal location of both an instruction representation and sensory representation or if the abstract stimuli require its own pointer. The finding would have implications on how multiple memory systems interact and the role of the WM in overarching theory of memory.

hmTBI

I failed to detect any long-term cognitive effects in the hmTBI population in this dissertation. This does not lessen my interest in the population. Given all the resources required, I believe it would be both extremely beneficial and interesting to do a large-scale, longitudinal DTI and EEG study on the hmTBI population. DTI and EEG are well-suited for tracking the microstructural changes after an mTBI (Churchill et al., 2017; Hocke et al., 2018; Wu et al., 2020). I suspect there are numerous subtle outcomes across multiple cognitive domains and functions after an hmTBI. A more rigorous testing of the hmTBI at time of testing may be necessary to bridge the gaps between the *hmTBI* and *mTBI* research. For example, several tests of balance, eye movements, and other motor and cognitive functions would provide a finer grain understanding of the individual differences. These differences could be a factor into the differing outcomes within the hmTBI population. If

we could understand the neuronal underpinnings of these outcomes, it would further our understanding of the cognitive functions themselves. I would especially be interested in the network connections underlying high-order cognitive functions such as working memory and attention. Beyond academic interest, it would help those who suffer after an mTBI. It would help develop interventions (using neuromodulation or other techniques) for them.

References:

Arciniega, H., Kilgore-Gomez, A., Harris, A., Peterson, D. J., McBride, J., Fox, E., & Berryhill, M. E. (2019). Visual working memory deficits in undergraduates with a history of mild traumatic brain injury. *Attention, Perception, & Psychophysics*, *81*(8), 2597–2603. https://doi.org/10.3758/s13414-019-01774-9

Arciniega, H., Kilgore-Gomez, A., McNerney, M. W., Lane, S., & Berryhill, M. E. (2020). Loss of consciousness, but not etiology, predicts better working memory performance years after concussion. *Journal of Clinical and Translational Research*. https://doi.org/10.18053/jctres.05.2020S4.003

Arciniega, H., Shires, J., Furlong, S., Kilgore-Gomez, A., Cerreta, A., Murray, N. G., & Berryhill, M. E. (2021). Impaired visual working memory and reduced connectivity in undergraduates with a history of mild traumatic brain injury. *Scientific Reports*, *11*(1), 2789. https://doi.org/10.1038/s41598-021-80995-1

Atkinson, R. C., & Shiffrin, R. M. (1968). Human Memory: A Proposed System and its Control Processes. In *Psychology of Learning and Motivation* (Vol. 2, pp. 89–195). Elsevier. https://doi.org/10.1016/S0079-7421(08)60422-3

Baddeley, A. D., & Hitch, G. (1974). Working Memory. In *Psychology of Learning and Motivation* (Vol. 8, pp. 47–89). Elsevier. https://doi.org/10.1016/S0079-7421(08)60452-1

Balaban, H., Drew, T., & Luria, R. (2019). Neural evidence for an object-based pointer system underlying working memory. *Cortex*, *119*, 362–372. https://doi.org/10.1016/j.cortex.2019.05.008

Bender, M., Romei, V., & Sauseng, P. (2019). Slow Theta tACS of the Right Parietal Cortex Enhances Contralateral Visual Working Memory Capacity. *Brain Topography*, *32*(3), 477–481. https://doi.org/10.1007/s10548-019-00702-2

Berryhill, M. E. (2024). Capturing postpandemic changes in research participants. *Trends in Neurosciences*, *47*(2), 85–86. https://doi.org/10.1016/j.tins.2023.10.005

Berryhill, M. E., & Hughes, H. C. (2009). On the minimization of task switch costs following long-term training. *Attention, Perception & Psychophysics*, *71*(3), 503–514. https://doi.org/10.3758/APP.71.3.503

Berryhill, M. E., & Martin, D. (2018). Cognitive Effects of Transcranial Direct Current Stimulation in Healthy and Clinical Populations: An Overview. *The Journal of ECT*, *34*(3), e25–e35. https://doi.org/10.1097/YCT.0000000000000534

Bigler, E. D. (2023). Volumetric MRI Findings in Mild Traumatic Brain Injury (mTBI) and Neuropsychological Outcome. *Neuropsychology Review*, *33*(1), 5–41. https://doi.org/10.1007/s11065-020-09474-0

Bradley, A. P. (1997). The use of the area under the ROC curve in the evaluation of machine learning algorithms. *Pattern Recognition*, *30*(7), 1145–1159. https://doi.org/10.1016/S0031-3203(96)00142-2

Braeckman, K., Descamps, B., Pieters, L., Vral, A., Caeyenberghs, K., & Vanhove, C. (2019). Dynamic changes in hippocampal diffusion and kurtosis metrics following experimental mTBI correlate with glial reactivity. *NeuroImage: Clinical*, *21*, 101669. https://doi.org/10.1016/j.nicl.2019.101669

Braun, U., Harneit, A., Pergola, G., Menara, T., Schäfer, A., Betzel, R. F., Zang, Z.,

Schweiger, J. I., Zhang, X., Schwarz, K., Chen, J., Blasi, G., Bertolino, A., Durstewitz, D., Pasqualetti, F., Schwarz, E., Meyer-Lindenberg, A., Bassett, D. S., & Tost, H. (2021). Brain network dynamics during working memory are modulated by dopamine and diminished in schizophrenia. *Nature Communications*, *12*(1), 3478. https://doi.org/10.1038/s41467-021-23694-9

Breitling, C., Zaehle, T., Dannhauer, M., Tegelbeckers, J., Flechtner, H.-H., & Krauel, K. (2020). Comparison between conventional and HD-tDCS of the right inferior frontal gyrus in children and adolescents with ADHD. *Clinical Neurophysiology*, *131*(5), 1146–1154. https://doi.org/10.1016/j.clinph.2019.12.412

Canolty, R. T., Edwards, E., Dalal, S. S., Soltani, M., Nagarajan, S. S., Kirsch, H. E., Berger, M. S., Barbaro, N. M., & Knight, R. T. (2006). High Gamma Power Is Phase-Locked to Theta Oscillations in Human Neocortex. *Science*, *313*(5793), 1626–1628. https://doi.org/10.1126/science.1128115

Cavanagh, J. F., Wilson, J. K., Rieger, R. E., Gill, D., Broadway, J. M., Story Remer, J. H., Fratzke, V., Mayer, A. R., & Quinn, D. K. (2019). ERPs predict symptomatic distress and recovery in sub-acute mild traumatic brain injury. *Neuropsychologia*, *132*, 107125. https://doi.org/10.1016/j.neuropsychologia.2019.107125

Che, X., Zheng, Y., Chen, X., Song, S., & Li, S. (2022). Decoding Color Visual Working Memory from EEG Signals Using Graph Convolutional Neural Networks. *International Journal of Neural Systems*, *32*(02), 2250003. https://doi.org/10.1142/S0129065722500034

Chen, Y.-C., Chen, Y.-L., Kuo, D.-P., Li, Y.-T., Chiang, Y.-H., Chang, J.-J., Tseng, S.-

H., & Chen, C.-Y. (2022). Personalized Prediction of Postconcussive Working Memory Decline: A Feasibility Study. *Journal of Personalized Medicine*, *12*(2), 196. https://doi.org/10.3390/jpm12020196

Chung, S., Wang, X., Fieremans, E., Rath, J. F., Amorapanth, P., Foo, F.-Y. A., Morton, C. J., Novikov, D. S., Flanagan, S. R., & Lui, Y. W. (2019). Altered Relationship between Working Memory and Brain Microstructure after Mild Traumatic Brain Injury. *American Journal of Neuroradiology*, ajnr;ajnr.A6146v1. https://doi.org/10.3174/ajnr.A6146

Churchill, N. W., Caverzasi, E., Graham, S. J., Hutchison, M. G., & Schweizer, T. A. (2017). White matter microstructure in athletes with a history of concussion: Comparing diffusion tensor imaging (DTI) and neurite orientation dispersion and density imaging (NODDI): DTI and NODDI of Chronic Concussion. *Human Brain Mapping*, *38*(8), 4201–4211. https://doi.org/10.1002/hbm.23658

Cochrane, G. D., Christy, J. B., Almutairi, A., Busettini, C., Van Heyningen, H. K. K., Weise, K. K., Swanson, M. W., & Gould, S. J. (2021). Vestibular, Oculomotor, and Balance Functions in Children With and Without Concussion. *Journal of Head Trauma Rehabilitation*, *36*(4), 264–273. https://doi.org/10.1097/HTR.0000000000000651

Cohen, J. D., Perlstein, W. M., Braver, T. S., Nystrom, L. E., Noll, D. C., Jonides, J., & Smith, E. E. (1997). Temporal dynamics of brain activation during a working memory task. *Nature*, *386*(6625), 604–608. https://doi.org/10.1038/386604a0

Constantinidis, C., & Steinmetz, M. A. (1996). Neuronal activity in posterior parietal area

7a during the delay periods of a spatial memory task. *Journal of Neurophysiology*, *76*(2), 1352–1355. https://doi.org/10.1152/jn.1996.76.2.1352

Cowan, N. (2010). The Magical Mystery Four: How Is Working Memory Capacity Limited, and Why? *Current Directions in Psychological Science*, *19*(1), 51–57. https://doi.org/10.1177/0963721409359277

Curtis, C. E., & D'Esposito, M. (2003). Persistent activity in the prefrontal cortex during working memory. *Trends in Cognitive Sciences*, *7*(9), 415–423. https://doi.org/10.1016/S1364-6613(03)00197-9

Curtis, C. E., & Sprague, T. C. (2021). *Persistent Activity during Working Memory from Front to Back* [Preprint]. Neuroscience. https://doi.org/10.1101/2021.04.24.441274

Czoschke, S., Fischer, C., Bahador, T., Bledowski, C., & Kaiser, J. (2021). Decoding Concurrent Representations of Pitch and Location in Auditory Working Memory. *The Journal of Neuroscience*, *41*(21), 4658–4666. https://doi.org/10.1523/JNEUROSCI.2999-20.2021

Daigle, K. M., Pietrzykowski, M. O., Waters, A. B., Swenson, L. P., & Gansler, D. A. (2022). Central Executive Network and Executive Function in Patients With Alzheimer's Disease and Healthy Individuals: Meta-Analysis of Structural and Functional MRI. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *34*(3), 204–213. https://doi.org/10.1176/appi.neuropsych.20110279

Dailey, N. S., Smith, R., Bajaj, S., Alkozei, A., Gottschlich, M. K., Raikes, A. C., Satterfield, B. C., & Killgore, W. D. S. (2018). Elevated Aggression and Reduced

White Matter Integrity in Mild Traumatic Brain Injury: A DTI Study. *Frontiers in Behavioral Neuroscience*, *12*, 118. https://doi.org/10.3389/fnbeh.2018.00118

D'Esposito, M., & Postle, B. R. (2015). The Cognitive Neuroscience of Working Memory. *Annual Review of Psychology*, *66*(1), 115–142. https://doi.org/10.1146/annurev-psych-010814-015031

Desrochers, T. M., Chatham, C. H., & Badre, D. (2015). The Necessity of Rostrolateral Prefrontal Cortex for Higher-Level Sequential Behavior. *Neuron*, *87*(6), 1357–1368. https://doi.org/10.1016/j.neuron.2015.08.026

Desrochers, T. M., Collins, A. G. E., & Badre, D. (2019). Sequential Control Underlies Robust Ramping Dynamics in the Rostrolateral Prefrontal Cortex. *The Journal of Neuroscience*, *39*(8), 1471–1483. https://doi.org/10.1523/JNEUROSCI.1060-18.2018

Dong, L., Ke, Y., Liu, S., Song, X., & Ming, D. (2020). Effects of HD-tDCS combined with working memory training on event-related potentials. *2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC)*, 3553–3556. https://doi.org/10.1109/EMBC44109.2020.9176063

D'Souza, M. M., Kumar, M., Choudhary, A., Kaur, P., Kumar, P., Rana, P., Trivedi, R., Sekhri, T., & Singh, A. K. (2020). Alterations of connectivity patterns in functional brain networks in patients with mild traumatic brain injury: A longitudinal resting-state functional magnetic resonance imaging study. *The Neuroradiology Journal*, *33*(2), 186–197. https://doi.org/10.1177/1971400920901706

Eierud, C., Nathan, D. E., Bonavia, G. H., Ollinger, J., & Riedy, G. (2019). Cortical thinning in military blast compared to non-blast persistent mild traumatic brain injuries. *NeuroImage: Clinical*, *22*, 101793. https://doi.org/10.1016/j.nicl.2019.101793

Erhart, M., Czoschke, S., Fischer, C., Bledowski, C., & Kaiser, J. (2021). Decoding Spatial Versus Non-spatial Processing in Auditory Working Memory. *Frontiers in Neuroscience*, *15*, 637877. https://doi.org/10.3389/fnins.2021.637877

Foxe, D., Irish, M., Roquet, D., Scharfenberg, A., Bradshaw, N., Hodges, J. R., Burrell, J. R., & Piguet, O. (2020). Visuospatial short-term and working memory disturbance in the primary progressive aphasias: Neuroanatomical and clinical implications. *Cortex*, *132*, 223–237. https://doi.org/10.1016/j.cortex.2020.08.018

Funahashi, S., Bruce, C. J., & Goldman-Rakic, P. S. (1989). Mnemonic coding of visual space in the monkey's dorsolateral prefrontal cortex. *Journal of Neurophysiology*, *61*(2), 331–349. https://doi.org/10.1152/jn.1989.61.2.331

Gao, X., & Chen, J. (2011). Mild traumatic brain injury results in extensive neuronal degeneration in the cerebral cortex. *Journal of Neuropathology and Experimental Neurology*, *70*(3), 183–191. https://doi.org/10.1097/NEN.0b013e31820c6878

Gilchrist, A. L., Cowan, N., & Naveh-Benjamin, M. (2008). Working memory capacity for spoken sentences decreases with adult ageing: Recall of fewer but not smaller chunks in older adults. *Memory*, *16*(7), 773–787. https://doi.org/10.1080/09658210802261124

Goldman-Rakic, P. S. (1995). Cellular basis of working memory. *Neuron*, *14*(3), 477–

485. https://doi.org/10.1016/0896-6273(95)90304-6

Govindarajan, K. A., Narayana, P. A., Hasan, K. M., Wilde, E. A., Levin, H. S., Hunter, J. V., Miller, E. R., Patel, V. K. S., Robertson, C. S., & McCarthy, J. J. (2016). Cortical Thickness in Mild Traumatic Brain Injury. *Journal of Neurotrauma*, *33*(20), 1809–1817. https://doi.org/10.1089/neu.2015.4253

Gözenman, F., & Berryhill, M. E. (2016). Working memory capacity differentially influences responses to tDCS and HD-tDCS in a retro-cue task. *Neuroscience Letters*, *629*, 105–109. https://doi.org/10.1016/j.neulet.2016.06.056

Green, S. L., Keightley, M. L., Lobaugh, N. J., Dawson, D. R., & Mihailidis, A. (2018). Changes in working memory performance in youth following concussion. *Brain Injury*, *32*(2), 182–190. https://doi.org/10.1080/02699052.2017.1358396

Hac, N. E. F., & Gold, D. R. (2022). Neuro-Visual and Vestibular Manifestations of Concussion and Mild TBI. *Current Neurology and Neuroscience Reports*, *22*(3), 219–228. https://doi.org/10.1007/s11910-022-01184-9

Hill, A. T., Rogasch, N. C., Fitzgerald, P. B., & Hoy, K. E. (2018). Effects of single versus dual-site High-Definition transcranial direct current stimulation (HD-tDCS) on cortical reactivity and working memory performance in healthy subjects. *Brain Stimulation*, *11*(5), 1033–1043. https://doi.org/10.1016/j.brs.2018.06.005

Hill, A. T., Rogasch, N. C., Fitzgerald, P. B., & Hoy, K. E. (2019). Impact of concurrent task performance on transcranial direct current stimulation (tDCS)-Induced changes in cortical physiology and working memory. *Cortex*, *113*, 37–57.

https://doi.org/10.1016/j.cortex.2018.11.022

Hocke, L. M., Duszynski, C. C., Debert, C. T., Dleikan, D., & Dunn, J. F. (2018). Reduced Functional Connectivity in Adults with Persistent Post-Concussion Symptoms: A Functional Near-Infrared Spectroscopy Study. *Journal of Neurotrauma*, *35*(11), 1224–1232. https://doi.org/10.1089/neu.2017.5365

Hossain, K. F., Kamran, S. A., Sarker, P., Pavilionis, P., Adhanom, I., Murray, N., & Tavakkoli, A. (2022). *Virtual-Reality based Vestibular Ocular Motor Screening for Concussion Detection using Machine-Learning*. https://doi.org/10.48550/ARXIV.2210.09295

Jones, K. T., Gözenman, F., & Berryhill, M. E. (2015). The strategy and motivational influences on the beneficial effect of neurostimulation: A tDCS and fNIRS study. *NeuroImage*, *105*, 238–247. https://doi.org/10.1016/j.neuroimage.2014.11.012

Jones, K. T., Johnson, E. L., & Berryhill, M. E. (2020). Frontoparietal theta-gamma interactions track working memory enhancement with training and tDCS. *NeuroImage*, *211*, 116615. https://doi.org/10.1016/j.neuroimage.2020.116615

Jones, K. T., Peterson, D. J., Blacker, K. J., & Berryhill, M. E. (2017). Frontoparietal neurostimulation modulates working memory training benefits and oscillatory synchronization. *Brain Research*, *1667*, 28–40. https://doi.org/10.1016/j.brainres.2017.05.005

Kaltiainen, H., Helle, L., Liljeström, M., Renvall, H., & Forss, N. (2018). Theta-Band Oscillations as an Indicator of Mild Traumatic Brain Injury. *Brain Topography*, *31*(6), 1037–1046. https://doi.org/10.1007/s10548-018-0667-2

Kamitani, Y., & Tong, F. (2005). Decoding the visual and subjective contents of the human brain. *Nature Neuroscience*, *8*(5), 679–685. https://doi.org/10.1038/nn1444

Katsuki, F., & Constantinidis, C. (2013). Time Course of Functional Connectivity in Primate Dorsolateral Prefrontal and Posterior Parietal Cortex during Working Memory. *PLoS ONE*, *8*(11), e81601. https://doi.org/10.1371/journal.pone.0081601

Keatley, E., Bechtold, K., Psoter, K., Peters, M. E., Everett, A., Rao, V., Van Meter, T. E., Falk, H., Korley, F. K., & Roy, D. (2023). Longitudinal Trajectories of Post-Concussive Symptoms Following Mild Traumatic Brain Injury. *Brain Injury*, *37*(8), 737–745. https://doi.org/10.1080/02699052.2023.2172612

Koch, I., Poljac, E., Müller, H., & Kiesel, A. (2018). Cognitive structure, flexibility, and plasticity in human multitasking—An integrative review of dual-task and task-switching research. *Psychological Bulletin*, *144*(6), 557–583. https://doi.org/10.1037/bul0000144

Kolb, B., Sutherland, R. J., & Whishaw, I. Q. (1983). A comparison of the contributions of the frontal and parietal association cortex to spatial localization in rats. *Behavioral Neuroscience*, *97*(1), 13–27. https://doi.org/10.1037/0735-7044.97.1.13

Kumar, S., Rao, S. L., Chandramouli, B. A., & Pillai, S. (2013). Reduced contribution of executive functions in impaired working memory performance in mild traumatic brain injury patients. *Clinical Neurology and Neurosurgery*, *115*(8), 1326–1332.

https://doi.org/10.1016/j.clineuro.2012.12.038

Lawton, T., & Huang, M.-X. (2019). Dynamic cognitive remediation for a Traumatic Brain Injury (TBI) significantly improves attention, working memory, processing speed, and reading fluency. *Restorative Neurology and Neuroscience*, *37*(1), 71–86. https://doi.org/10.3233/RNN-180856

L'Ecuyer-Giguère, F., Greffou, S., Tabet, S., Frenette, L. C., Tinawi, S., Feyz, M., & De Guise, E. (2020). Visual memory performance following mild traumatic brain injury and its relationship with intellectual functioning. *Applied Neuropsychology: Adult*, *27*(3), 219–231. https://doi.org/10.1080/23279095.2018.1528263

Lefevre-Dognin, C., Cogné, M., Perdrieau, V., Granger, A., Heslot, C., & Azouvi, P. (2021). Definition and epidemiology of mild traumatic brain injury. *Neurochirurgie*, *67*(3), 218–221. https://doi.org/10.1016/j.neuchi.2020.02.002

Levin, H. S., & Diaz-Arrastia, R. R. (2015). Diagnosis, prognosis, and clinical management of mild traumatic brain injury. *The Lancet Neurology*, *14*(5), 506–517. https://doi.org/10.1016/S1474-4422(15)00002-2

Lewine, J. D., Plis, S., Ulloa, A., Williams, C., Spitz, M., Foley, J., Paulson, K., Davis, J., Bangera, N., Snyder, T., & Weaver, L. (2019). Quantitative EEG Biomarkers for Mild Traumatic Brain Injury. *Journal of Clinical Neurophysiology*, *36*(4), 298–305. https://doi.org/10.1097/WNP.0000000000000588

Li, X., O'Sullivan, M. J., & Mattingley, J. B. (2022). Delay activity during visual working memory: A meta-analysis of 30 fMRI experiments. *NeuroImage*, *255*,

119204. https://doi.org/10.1016/j.neuroimage.2022.119204

Lisman, J. E., & Idiart, M. A. P. (1995). Storage of 7 ± 2 Short-Term Memories in Oscillatory Subcycles. *Science*, *267*(5203), 1512–1515. https://doi.org/10.1126/science.7878473

Liu, M., Ke, Y., Liu, S., Song, X., & Ming, D. (2020). Effect of HD-tDCS combined with working memory training on brain network. *2020 42nd Annual International Conference of the IEEE Engineering in Medicine & Biology Society (EMBC)*, 3594–3597. https://doi.org/10.1109/EMBC44109.2020.9176717

Livingston, G., Huntley, J., Sommerlad, A., Ames, D., Ballard, C., Banerjee, S., Brayne, C., Burns, A., Cohen-Mansfield, J., Cooper, C., Costafreda, S. G., Dias, A., Fox, N., Gitlin, L. N., Howard, R., Kales, H. C., Kivimäki, M., Larson, E. B., Ogunniyi, A., … Mukadam, N. (2020). Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. *The Lancet*, *396*(10248), 413–446. https://doi.org/10.1016/S0140-6736(20)30367-6

Lumba-Brown, A., Yeates, K. O., Sarmiento, K., Breiding, M. J., Haegerich, T. M., Gioia, G. A., Turner, M., Benzel, E. C., Suskauer, S. J., Giza, C. C., Joseph, M., Broomand, C., Weissman, B., Gordon, W., Wright, D. W., Moser, R. S., McAvoy, K., Ewing-Cobbs, L., Duhaime, A.-C., … Timmons, S. D. (2018). Centers for Disease Control and Prevention Guideline on the Diagnosis and Management of Mild Traumatic Brain Injury Among Children. *JAMA Pediatrics*, *172*(11), e182853. https://doi.org/10.1001/jamapediatrics.2018.2853

Luo, X., Lin, D., Xia, S., Wang, D., Weng, X., Huang, W., & Ye, H. (2021). Machine

Learning Classification of Mild Traumatic Brain Injury Using Whole-Brain Functional Activity: A Radiomics Analysis. *Disease Markers*, *2021*, 1–7. https://doi.org/10.1155/2021/3015238

Maleki, N., Finkel, A., Cai, G., Ross, A., Moore, R. D., Feng, X., & Androulakis, X. M. (2021). Post-traumatic Headache and Mild Traumatic Brain Injury: Brain Networks and Connectivity. *Current Pain and Headache Reports*, *25*(3), 20. https://doi.org/10.1007/s11916-020-00935-y

Mandrekar, J. N. (2010). Receiver Operating Characteristic Curve in Diagnostic Test Assessment. *Journal of Thoracic Oncology*, *5*(9), 1315–1316. https://doi.org/10.1097/JTO.0b013e3181ec173d

Martin, D. M., Berryhill, M. E., & Dielenberg, V. (2023). Can brain stimulation enhance cognition in clinical populations? A critical review. *Restorative Neurology and Neuroscience*, *40*(4–6), 241–259. https://doi.org/10.3233/RNN-211230

Master, C. L., Master, S. R., Wiebe, D. J., Storey, E. P., Lockyer, J. E., Podolak, O. E., & Grady, M. F. (2018). Vision and Vestibular System Dysfunction Predicts Prolonged Concussion Recovery in Children. *Clinical Journal of Sport Medicine*, *28*(2), 139–145. https://doi.org/10.1097/JSM.0000000000000507

McKim, T. H., & Desrochers, T. M. (2022). Reward Value Enhances Sequence Monitoring Ramping Dynamics as Ending Rewards Approach in the Rostrolateral Prefrontal Cortex. *Eneuro*, *9*(2), ENEURO.0003-22.2022. https://doi.org/10.1523/ENEURO.0003-22.2022

McNerney, M. W., Hobday, T., Cole, B., Ganong, R., Winans, N., Matthews, D., Hood,

J., & Lane, S. (2019). Objective Classification of mTBI Using Machine Learning on a Combination of Frontopolar Electroencephalography Measurements and Self-reported Symptoms. *Sports Medicine - Open*, *5*(1), 14. https://doi.org/10.1186/s40798-019-0187-y

Meconi, A., Wortman, R. C., Wright, D. K., Neale, K. J., Clarkson, M., Shultz, S. R., & Christie, B. R. (2018). Repeated mild traumatic brain injury can cause acute neurologic impairment without overt structural damage in juvenile rats. *PLOS ONE*, *13*(5), e0197187. https://doi.org/10.1371/journal.pone.0197187

Menon, V. (2011). Large-scale brain networks and psychopathology: A unifying triple network model. *Trends in Cognitive Sciences*, *15*(10), 483–506. https://doi.org/10.1016/j.tics.2011.08.003

Miller, E. K., Erickson, C. A., & Desimone, R. (1996). Neural Mechanisms of Visual Working Memory in Prefrontal Cortex of the Macaque. *The Journal of Neuroscience*, *16*(16), 5154–5167. https://doi.org/10.1523/JNEUROSCI.16-16-05154.1996

Mollica, A., Greben, R., Oriuwa, C., Siddiqi, S. H., & Burke, M. J. (2022). Neuromodulation Treatments for Mild Traumatic Brain Injury and Post-concussive Symptoms. *Current Neurology and Neuroscience Reports*, *22*(3), 171–181. https://doi.org/10.1007/s11910-022-01183-w

Muhle-Karbe, P. S., Myers, N. E., & Stokes, M. G. (2021). A Hierarchy of Functional States in Working Memory. *The Journal of Neuroscience*, *41*(20), 4461–4475. https://doi.org/10.1523/JNEUROSCI.3104-20.2021

Müller, D., Habel, U., Brodkin, E. S., & Weidler, C. (2022). High-definition transcranial direct current stimulation (HD-tDCS) for the enhancement of working memory – A systematic review and meta-analysis of healthy adults. *Brain Stimulation*, *15*(6), 1475–1485. https://doi.org/10.1016/j.brs.2022.11.001

Müller, N. G., & Knight, R. T. (2006). The functional neuroanatomy of working memory: Contributions of human brain lesion studies. *Neuroscience*, *139*(1), 51–58. https://doi.org/10.1016/j.neuroscience.2005.09.018

Murray, N. G., Ambati, V. N. P., Contreras, M. M., Salvatore, A. P., & Reed-Jones, R. J. (2014). Assessment of oculomotor control and balance post-concussion: A preliminary study for a novel approach to concussion management. *Brain Injury*, *28*(4), 496–503. https://doi.org/10.3109/02699052.2014.887144

Murray, N. G., Szekely, B., Islas, A., Munkasy, B., Gore, R., Berryhill, M., & Reed-Jones, R. J. (2020). Smooth Pursuit and Saccades after Sport-Related Concussion. *Journal of Neurotrauma*, *37*(2), 340–346. https://doi.org/10.1089/neu.2019.6595

Murray, N. G., Szekely, B., Moran, R., Ryan, G., Powell, D., Munkasy, B. A., Buckley, T. A., & Guskiewicz, K. (2019). Concussion history associated with increased postural control deficits after subsequent injury. *Physiological Measurement*, *40*(2), 024001. https://doi.org/10.1088/1361-6579/aafcd8

Nikolin, S., Lauf, S., Loo, C. K., & Martin, D. (2019). Effects of High-Definition Transcranial Direct Current Stimulation (HD-tDCS) of the Intraparietal Sulcus and Dorsolateral Prefrontal Cortex on Working Memory and Divided Attention. *Frontiers in Integrative Neuroscience*, *12*, 64.

https://doi.org/10.3389/fnint.2018.00064

Owen, A. M., McMillan, K. M., Laird, A. R., & Bullmore, E. (2005). N-back working memory paradigm: A meta-analysis of normative functional neuroimaging studies. *Human Brain Mapping*, *25*(1), 46–59. https://doi.org/10.1002/hbm.20131

Page, M. P. A., & Norris, D. (2009). A model linking immediate serial recall, the Hebb repetition effect and the learning of phonological word forms. *Philosophical Transactions of the Royal Society B: Biological Sciences*, *364*(1536), 3737–3753. https://doi.org/10.1098/rstb.2009.0173

Palacios, E. M., Yuh, E. L., Chang, Y.-S., Yue, J. K., Schnyer, D. M., Okonkwo, D. O., Valadka, A. B., Gordon, W. A., Maas, A. I. R., Vassar, M., Manley, G. T., & Mukherjee, P. (2017). Resting-State Functional Connectivity Alterations Associated with Six-Month Outcomes in Mild Traumatic Brain Injury. *Journal of Neurotrauma*, *34*(8), 1546–1557. https://doi.org/10.1089/neu.2016.4752

Paulraj, S. R., Schendel, K., Curran, B., Dronkers, N. F., & Baldo, J. V. (2018). Role of the left hemisphere in visuospatial working memory. *Journal of Neurolinguistics*, *48*, 133–141. https://doi.org/10.1016/j.jneuroling.2018.04.006

Polanía, R., Nitsche, M. A., Korman, C., Batsikadze, G., & Paulus, W. (2012). The Importance of Timing in Segregated Theta Phase-Coupling for Cognitive Performance. *Current Biology*, *22*(14), 1314–1318. https://doi.org/10.1016/j.cub.2012.05.021

Poltavski, D., Bernhardt, K., Mark, C., & Biberdorf, D. (2019). Frontal theta-gamma ratio is a sensitive index of concussion history in athletes on tasks of visuo-motor

control. *Scientific Reports*, *9*(1), 17565. https://doi.org/10.1038/s41598-019-54054-9

Quinn De Launay, K., Martino, A., Riggs, L., Reed, N., & Beal, D. S. (2021). Pediatric concussion working memory outcomes: A scoping review. *Brain Injury*, *35*(10), 1121–1133. https://doi.org/10.1080/02699052.2021.1972148

Raizman, R., Tavor, I., Biegon, A., Harnof, S., Hoffmann, C., Tsarfaty, G., Fruchter, E., Tatsa-Laur, L., Weiser, M., & Livny, A. (2020). Traumatic Brain Injury Severity in a Network Perspective: A Diffusion MRI Based Connectome Study. *Scientific Reports*, *10*(1), 9121. https://doi.org/10.1038/s41598-020-65948-4

Ramirez-Cardenas, A., & Nieder, A. (2019). Working memory representation of empty sets in the primate parietal and prefrontal cortices. *Cortex*, *114*, 102–114. https://doi.org/10.1016/j.cortex.2019.02.028

Robinson, S., Berglass, J. B., Denson, J. L., Berkner, J., Anstine, C. V., Winer, J. L., Maxwell, J. R., Qiu, J., Yang, Y., Sillerud, L. O., Meehan, W. P., Mannix, R., & Jantzie, L. L. (2017). Microstructural and microglial changes after repetitive mild traumatic brain injury in mice: Microstructure in Repetitive Mild Brain Injury. *Journal of Neuroscience Research*, *95*(4), 1025–1035. https://doi.org/10.1002/jnr.23848

Rose, N. S., LaRocque, J. J., Riggall, A. C., Gosseries, O., Starrett, M. J., Meyering, E. E., & Postle, B. R. (2016). Reactivation of latent working memories with transcranial magnetic stimulation. *Science*, *354*(6316), 1136–1139. https://doi.org/10.1126/science.aah7011

Serino, A., Ciaramelli, E., Di Santantonio, A., Malagù, S., Servadei, F., & Làdavas, E. (2006). Central executive system impairment in traumatic brain injury. *Brain Injury*, *20*(1), 23–32. https://doi.org/10.1080/02699050500309627

Shires, J., Carrasco, C., & Berryhill, M. E. (2020). No tDCS augmented working memory training benefit in undergraduates rewarded with course credit. *Brain Stimulation*, *13*(6), 1524–1526. https://doi.org/10.1016/j.brs.2020.08.015

Silverberg, N. D., Duhaime, A.-C., & Iaccarino, M. A. (2019). Mild Traumatic Brain Injury in 2019-2020. *JAMA*. https://doi.org/10.1001/jama.2019.18134

Skjeldal, O. H., Skandsen, T., Kinge, E., Glott, T., & Solbakk, A.-K. (2022). Long-term post-concussion symptoms. *Tidsskrift for Den norske legeforening*. https://doi.org/10.4045/tidsskr.21.0713

Sreenivasan, K. K., Curtis, C. E., & D'Esposito, M. (2014). Revisiting the role of persistent neural activity during working memory. *Trends in Cognitive Sciences*, *18*(2), 82–89. https://doi.org/10.1016/j.tics.2013.12.001

Stephens, J. A., & Berryhill, M. E. (2016). Older Adults Improve on Everyday Tasks after Working Memory Training and Neurostimulation. *Brain Stimulation*, *9*(4), 553–559. https://doi.org/10.1016/j.brs.2016.04.001

Sterr, A., Herron, K. A., Hayward, C., & Montaldi, D. (2006). Are mild head injuries as mild as we think? Neurobehavioral concomitants of chronic post-concussion syndrome. *BMC Neurology*, *6*(1), 7. https://doi.org/10.1186/1471-2377-6-7

Thyer, W., Adam, K. C. S., Diaz, G. K., Velázquez Sánchez, I. N., Vogel, E. K., & Awh, E. (2022). Storage in Visual Working Memory Recruits a Content-Independent

Pointer System. *Psychological Science*, *33*(10), 1680–1694. https://doi.org/10.1177/09567976221090923

Tseng, P., Iu, K.-C., & Juan, C.-H. (2018). The critical role of phase difference in theta oscillation between bilateral parietal cortices for visuospatial working memory. *Scientific Reports*, *8*(1), 349. https://doi.org/10.1038/s41598-017-18449-w

Veliz, P. T., & Berryhill, M. E. (2023). Gender Differences in Adolescents' Affective Symptoms and Behavioral Disorders After Mild Traumatic Brain Injury. *Journal of Head Trauma Rehabilitation*, *38*(4), 308–318. https://doi.org/10.1097/HTR.0000000000000851

Vergara, V. M., Mayer, A. R., Damaraju, E., Kiehl, K. A., & Calhoun, V. (2017). Detection of Mild Traumatic Brain Injury by Machine Learning Classification Using Resting State Functional Network Connectivity and Fractional Anisotropy. *Journal of Neurotrauma*, *34*(5), 1045–1053. https://doi.org/10.1089/neu.2016.4526

Vosskuhl, J., Huster, R. J., & Herrmann, C. S. (2015). Increase in short-term memory capacity induced by down-regulating individual theta frequency via transcranial alternating current stimulation. *Frontiers in Human Neuroscience*, *9*. https://doi.org/10.3389/fnhum.2015.00257

Wang, N., Ming, D., Ke, Y., Du, J., Liu, W., Kong, L., Zhao, X., Liu, S., Xu, M., & An, X. (2019). High-Definition Transcranial Direct Current Stimulation (HD-tDCS) enhances working memory training. *2019 41st Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, 329–332.

https://doi.org/10.1109/EMBC.2019.8856976

Wolinski, N., Cooper, N. R., Sauseng, P., & Romei, V. (2018). The speed of parietal theta frequency drives visuospatial working memory capacity. *PLOS Biology*, *16*(3), e2005348. https://doi.org/10.1371/journal.pbio.2005348

Wu, Y.-C., Harezlak, J., Elsaid, N. M. H., Lin, Z., Wen, Q., Mustafi, S. M., Riggen, L. D., Koch, K. M., Nencka, A. S., Meier, T. B., Mayer, A. R., Wang, Y., Giza, C. C., DiFiori, J. P., Guskiewicz, K. M., Mihalik, J. P., LaConte, S. M., Duma, S. M., Broglio, S. P., … McAllister, T. W. (2020). Longitudinal white-matter abnormalities in sports-related concussion: A diffusion MRI study. *Neurology*, *95*(7), e781–e792. https://doi.org/10.1212/WNL.0000000000009930

Yang, J., Pu, W., Wu, G., Chen, E., Lee, E., Liu, Z., & Palaniyappan, L. (2020). Connectomic Underpinnings of Working Memory Deficits in Schizophrenia: Evidence From a replication fMRI study. *Schizophrenia Bulletin*, *46*(4), 916–926. https://doi.org/10.1093/schbul/sbz137

Yu, R., Han, B., Wu, X., Wei, G., Zhang, J., Ding, M., & Wen, X. (2023). Dual-functional Network Regulation Underlies the Central Executive System in Working Memory. *Neuroscience*, *524*, 158–180. https://doi.org/10.1016/j.neuroscience.2023.05.025

Zokaei, N., & Husain, M. (2019). Working Memory in Alzheimer's Disease and Parkinson's Disease. In T. Hodgson (Ed.), *Processes of Visuospatial Attention and Working Memory* (Vol. 41, pp. 325–344). Springer International Publishing. https://doi.org/10.1007/7854_2019_103