

**Effects of Cognitive Training on Attention and Neural Processing Following Pediatric
Traumatic Brain Injury (TBI)**

Principal Investigator: Shari Wade, PhD

Co Investigators: Peter Chiu, PhD; Weihong Yuan, PhD.

Final Report

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I. Introduction

Traumatic brain injury (TBI) is the leading cause of acquired disability in children affecting hundreds of young Ohioans each year and resulting in significant deficits in cognition, behavior, and social development (Janusz *et al.*, 2002; Langlois *et al.*, 2006; Max *et al.*, 1998). Changes in attention and executive function skills (EF) are particularly common post-TBI and may contribute to academic and social difficulties. However, few evidence-based programs exist to remediate attention difficulties following TBI. In this study, we piloted the Attention Intervention and Management Program (AIM) designed to improve attention and reduce EF deficits. Additionally, we examined whether AIM resulted in brain-based changes in the neural substrates of attention, working memory, and EF skills using fMRI in 15 adolescents who sustained a moderate to severe TBI and were experiencing persistent problems with attention and EF. We also used diffusion tensor imaging (DTI) to characterize increases in white matter integrity associated with AIM and their relationship to EF performance. Our overarching goals were to provide preliminary evidence regarding the efficacy of AIM and to establish the relationship between improvements in attention and EF and the integrity of neural substrate underlying the functional and structural network in the brain before and after receiving AIM.

II. Executive summary

Background

Traumatic brain injury (TBI) is the leading cause of disability in children (Langlois *et al.*, 2006). Each day approximately 11 Ohioans under 22 years of age suffer TBIs (Ohio Brain Injury Association Website). Impairments in attention are among the most frequently reported symptoms by parents and teachers following pediatric TBI (Max *et al.*, 2005). Further, these cognitive disabilities are responsible for a wide range of academic and adjustment issues (Fay *et*

al., 1994; Loken *et al.*, 1995). Broadly defined, attention encompasses all of the mental processes, operations, and systems requisite for acquiring and applying information. It interacts with other cognitive functions including perception, memory/learning; organization, and reasoning. In fact, attention is core to the integration of these systems (Sohlberg & Mateer, 2001). A number of different attentional subcomponents with interconnected neural systems have been identified and shown to be differentially disrupted following trauma (Posner & Rothbart, 2007; Sohlberg & Mateer, 2001) including: maintenance or sustained attention, attentional selectivity, attentional capacity, and the ability to effectively shift attention. Given the prevalence of attention difficulties and Secondary Attention Deficit Hyperactive Disorder (ADHD) following TBI, it is imperative to identify treatments to effectively address attention impairments (Levin *et al.*, 2007). The Attention Improvement Management program sought to remediate attention and EF difficulties in youth with TBI.

Participants

Participants included children with a history of TBI and healthy comparison children recruited from Cincinnati Children's Hospital Medical Center (CCHMC). Seven participants from the previous pilot were included in the current study. Children aged 9-18 years with complicated mild to severe TBI (GCS [Glasgow Coma Scale; Teasdale & Jennett, 1974] score of ≤ 12 or a GCS of 13-15 accompanied by abnormalities on imaging) were recruited from the CCHMC Trauma Registry, ongoing study participants, and hospital clinicians that identified potentially eligible participants. In order to minimize potential adherence problems, participants aged 18 were required to reside in the home for the duration of the study. Additional eligibility for the TBI group included: attentional impairments on the Vanderbilt ADHD Diagnostic Parent Rating Scale,

Attention Subscale (Wolraich et al., 2003; endorsed at least 4 out of 9 attention items with a frequency score of 2 or 3), at least 1 year post injury to ensure relatively complete neural recovery, and convenient access to a computer. A comparison cohort of children aged 9-18 years and matched with the TBI group on age and sex were recruited through CCHMC allowing us to control for practice effects and determine whether changes associated with AIM are reliable. Exclusionary criteria for the healthy comparison group included a diagnosis of ADHD or attentional impairments on the Vanderbilt ADHD Diagnostic Parent Rating Scale, Attention Subscale (endorsed at least 4 out of 9 attention items with a frequency score of 2 or 3). Exclusionary criteria for both controls and children with TBI included a diagnosis of cognitive disability or inability to operate a computer. Participants were consented in accordance with the Institutional Review Board.

A total of 22 children with TBI and 11 healthy comparison children were originally enrolled in the pilot study. Nine participants with TBI dropped out before study completion (41%) and one participant with TBI was excluded due to non-adherence with the number of required home practice sessions. There were no significant differences in age, sex, ethnicity, or GCS between completers and non-completers (all $p > .05$).

Participants who completed the study ranged in age from 9 and 15 years ($M = 13.3$, $SD = 2.2$). There were no significant differences between the TBI and healthy comparison groups in age, sex, ethnicity, or handedness (all $p > .05$; see Table 1). Of the 12 participants with TBI who completed the study, five had complicated mild injuries, two had moderate injuries, and five had severe brain injuries. Participants with TBI were

an average of 5 years post-injury ($M = 5.3$, $SD = 2.8$, range 1.1 – 9.1). See Table 2 for characteristics of the participants with TBI.

	TBI $n = 12$	Healthy Comparison $n = 11$	p
Age at pre-test (M [SD])	13.22 (2.5)	13.37 (2.1)	.882
Sex (% male)	42	38	.267
Ethnicity (% non-white)	17	15	.401
Handedness (% right)	75	77	.360

Note. TBI = traumatic brain injury

Age	Sex	Ethnicity	Mechanism of Injury	GCS	Time Since Injury (years)
14.84	M	AA	Pedestrian	13	3.52
15.58	F	C	Pedestrian	3	4.11
14.34	F	C	Recreational	9	3.67
15.59	M	C	Recreational	14	5.84
13.44	F	C	Fall	3	8.36
13.69	F	C	Recreational	3	7.77
13.71	F	C	MVA	15	7.71
9.25	F	C	MVA	7	3.50
9.17	F	C	Recreational	11	1.50
9.50	M	C	Fall	15	1.08
15.02	M	C	MVA	3	9.10
14.44	M	AA	Fall	15	8.02

Note. AA = African American; C = Caucasian; GCS = Glasgow Coma Scale; F = female; M = male; MVA = motor vehicle accident; Pedestrian = pedestrian collision with motor vehicle; TBI = traumatic brain injury

Methodology

This project provided data regarding the efficacy of a research-based intervention to remediate attention and EF deficits following pediatric TBI. It also shed light on whether cognitive remediation contributes to brain-based changes in attention, working memory, and EF, thus providing support for the theory of neural remodeling or reallocation. To our knowledge, this was among the first investigations of a cognitive remediation intervention for pediatric TBI that uses functional imaging to understand

treatment effects. The overarching objectives of the project were to provide preliminary evidence regarding the efficacy of AIM and to establish the relationship between improvements in attention and EF and the integrity of neural substrate underlying the functional and structural network in the brain before and after receiving AIM. The primary outcomes of the study were the measures of attention, behavior, and executive function skills that were completed pre-and post-intervention. Results indicated improvements in parent-reported executive function behaviors, limited aspects of attention, and patient-identified goals. Improvements in neuropsychological performance may have been limited by an absence of initial deficits on many of the measures. Changes in structural connectivity and the neural substrates of executive attention correspond to improvements in parent-reported EF, suggesting that AIM results in both neural and behavioral changes.

Conclusions

This project provides novel information about the efficacy of a computerized attention drill program for adolescents with TBI and attention impairments. Findings from this project should provide crucial evidence for subsequent large-scale investigations of the neural underpinnings of cognitive remediation interventions for children and adolescents with TBI.

III. Information/qualifications – principal and all co-investigators

Principal Investigator – *Shari Wade, PhD* – Dr. Wade is Professor of Pediatrics at CCHMC and Director of the Rehabilitation Research and Training Center for Pediatric TBI Interventions. Dr. Wade is a leader in the field of research on recovery from

pediatric TBI with particular emphasis on developing evidence-based interventions to improve long-term child and family functioning.

Co –Principal Investigator – *Weihong Yuan, PhD* – Dr. Yuan is trained in biomedical engineering and received his Ph.D. (2000) from Rutgers, The State University of New Jersey. In 2005, Dr. Yuan joined faculty of Imaging Research Center and Pediatric Neuroimaging Research Consortium at CCHMC. His research focuses on the application of functional MRI and diffusion tensor imaging in pediatric populations including hydrocephalus, epilepsy, traumatic brain injury, supratentorial tumors, and spina bifida.

Co- Investigator – *Peter Chiu, PhD* – Dr. Chiu is Director of the Cognitive Neuroscience Laboratory at the University of Cincinnati and Associate Professor in the Department of Psychology at University of Cincinnati. For the past decade, he has studied how the brain works in children and adolescents in domains of attention, language, memory, decision making and other areas of cognition using behavioral and brain imaging methods. He has collaborated with the Cincinnati Children’s Hospital Medical Center (CCHMC) TBI team led by Dr. Shari Wade for the past 5 years on various brain imaging studies of TBI.

Co – Investigator – *Nicolay Walz, PhD* – Dr. Walz is a Clinical Neuropsychologist and Associate Associate Professor of Behavioral Medicine at CCHMC. Dr. Walz has collaborated with Dr. Wade for the past decade on studies examining predictors of recovery following childhood TBI and interventions to improve outcomes.

Co – Investigator – *McKay Moore Sohlberg, PhD* – Dr. Sohlberg is Professor of Speech Pathology at the University of Oregon. She is an internationally recognized leader in the field of TBI rehabilitation. Dr. Sohlberg's research focuses on the development and

evaluation of therapy programs and tools to increase community reintegration for people with brain injury. In addition, Dr. Sohlberg developed the AIM intervention.

IV. A review of the literature related to the project topic

Traumatic brain injury (TBI) is the leading cause of disability in children (Langlois et al., 2006). Each day approximately 11 Ohioans under 22 years of age suffer TBIs (Ohio Brain Injury Association Website). Impairments in attention are among the most frequently reported symptoms by parents and teachers following pediatric TBI (Max et al., 2005). Further, these cognitive disabilities are responsible for a wide range of academic and adjustment issues (Fay et al., 1994; Loken et al., 1995). Broadly defined, attention encompasses all of the mental processes, operations, and systems requisite for acquiring and applying information. It interacts with other cognitive functions including perception, memory/learning; organization, and reasoning. In fact, attention is core to the integration of these systems (Sohlberg & Mateer, 2001). A number of different attentional subcomponents with interconnected neural systems have been identified and shown to be differentially disrupted following trauma (Posner & Rothbart, 2007; Sohlberg & Mateer, 2001) including: maintenance or sustained attention, attentional selectivity, attentional capacity, and the ability to effectively shift attention. Given the prevalence of attention difficulties and Secondary Attention Deficit Hyperactive Disorder (ADHD) following TBI, it is imperative to identify treatments to effectively address attention impairments (Levin et al., 2007).

Background and Rationale for the AIM Intervention

Sohlberg and Mateer (2001) described a clinical model of attention that was derived by examining cognitive theories of attention in concert with clinical observations

from the assessment and rehabilitation of individuals with traumatic brain injuries. These authors divided attention into five components: focused attention, sustained attention, selective attention, alternating attention, and divided attention. However, based on increasing evidence regarding the functional importance of executive control and working memory, these constructs have been incorporated into their revised model (Sohlberg & Mateer, 2010). This clinical model of attentional processes forms the foundation of the AIM intervention. Further rationale and description is provided below.

Although a number of different paradigms have been employed to ameliorate attention deficits in children, metacognitive strategy training and direct attention training are supported by the most extensive evidence base. Thus the proposed study will evaluate a manualized intervention integrating these two approaches for the treatment of attention deficits in children with TBI. Metacognitive strategy training refers to teaching self-monitoring, self-management, and goal-setting strategies to improve attention, behavior, and academic performance. There is considerable empirical support for the efficacy of training in reflecting on one's thoughts and actions and using that information to regulate one's learning and behavior (Kennedy et al., 2008). When paired with attention training, metacognitive strategy instruction typically emphasizes facilitating efficient allocation of cognitive resources. It often includes provision of feedback, goal setting and self-awareness enhancement. Recent reviews (Reid et al., 2005; Mooney et al., 2005) provide support for the utility of metacognitive strategy training in improving target behaviors in children with ADHD and social and emotional behavior disorders respectively. However, data regarding their efficacy for TBI are lacking.

Unlike strategy training, direct attention training aims to improve the underlying attention deficit by targeting specific attention skills such as sustained attention, working memory, and shifting from one task to another (Butler et al., 2008; Sohlberg et al., 2003). The premise is that attentional abilities can be improved by providing structured opportunities for exercising particular aspect of attention. Treatments typically involve children engaging in a series of repetitive drills or exercises that are designed to provide opportunities for practice on tasks with increasingly greater attentional demands.

Direct attention training, like metacognitive strategy training has been evaluated with positive findings in a number of pediatric groups with attention deficits, including child survivors of cancers affecting the central nervous system (Butler et al., 2008), children with ADHD (Penkman, 2004), fetal alcohol syndrome (Vernescu, 2008) and developmental learning disabilities (Stevens et al., 2008). Recent studies have investigated the efficacy of attention training and metacognitive strategy instruction to treat pediatric patients with attention deficits due to Acquired Brain Injury (ABI). Galbiati and colleagues (2009) completed a study on 65 patients (with 25 as non-treated controls) with TBI, ages 6-18 years, utilizing computerized direct attention training intervention (i.e., RehaCom and Attention and Concentration) along with their clinician-delivered cognitive rehabilitation intervention. The computerized, direct attention-training program was similar to the proposed AIM activities with tasks designed to address vigilance, attention and concentration, response and response behavior (in the RehaCom Intervention) and selective and sustained attention, attention span, divided attention, shifting, and resistance to distraction (in the Attention and Concentration intervention). After intervention, treated students showed significant improvements on

the Continuous Performance Task (CPT) Overall Index as well as reductions in impulsiveness on the task and omission errors when compared to controls. Additionally, students that received the intervention demonstrated significant improvement on measures of adaptive behavior including daily living skills, social skills, and communication (as reported by parents) both at post-testing as well as in one year follow-up compared to controls. Similar findings were reported by Butler and colleagues when treating children undergoing cancer treatments (Butler et al., 2008). van't Hooft and colleagues (2007) also examined the impact of direct attention training and strategy instruction on children (ages 9-17) with acquired brain injury. Treated students showed significant improvement in sustained and selective attention as well as verbal working memory at post-test as well as 6-months post treatment when compared to control students.

All three of the existing studies evaluating the efficacy of direct attention training and strategy instruction in children with ABI (Butler, 2008; van't Hooft, et al., 2007; Galbiati et. al, 2009) provide support for integrating both attention and behavioral/metacognitive training in working with students with TBI or ABI. However, in each of these studies, the metacognitive strategy development was delivered by a clinician. While this may be an ideal way to deliver interventions, issues related to availability of well-trained interventionists as well as access by geographic local remain a critical stumbling-block to provision of services to all that need it in a timely manner (Galbiati et. al, 2009; Kesler, Lacayo, & Jo, 2011).

Considerable evidence supports the potential utility of both Attention Process Training (APT) and strategy training to address the attention and executive functioning

difficulties arising from pediatric TBI. Given the pervasive nature of secondary attention difficulties, an intervention package integrating both process and strategy training is likely to result in greater improvements than an intervention including only one of these approaches. Direct attention training builds on the emerging literature on experience-dependent neural plasticity (i.e., repeated practice allows new pathways to be established in the brain). However, it has been criticized as decontextualized, thereby resulting in a lack of generalization to new settings and situations. In response to these concerns, the Attention Intervention and Management program (AIM) integrates attention training with the use of metacognitive strategies to ensure that the child can apply these skills across settings and situations.

The proposed AIM intervention is a fully computer-delivered intervention that provides direct attention and metacognitive strategy development. Clinicians are led through a computer-based assessment procedure to assist in the selection of attention training tasks and metacognitive strategies as well as the levels of prompting for each individual client. Additionally, the AIM is set up to facilitate home practice with its capacity to capture and send performance data remotely. The emphasis on home practice addresses the gulf between the efficacy research which emphasizes intensive, daily sessions and clinical delivery constraints.

Rationale for fMRI Study to Examine Neural Remodeling Associated with AIM

Repeated activation and stimulation of attentional systems are hypothesized to facilitate changes in cognitive capacity through underlying changes in neural circuitry (Posner & Rothbart, 2007). Knowledge of the mechanisms believed to underlie neural plasticity or experience-dependent recovery such as the modification of synaptic

connectivity is mounting (Posner & Rothbart, 2005), and provides a brain-based explanation for improvements seen following attention training. Biological mechanisms have been identified that could account for the changes observed following attention training. We know that the brain is a dynamic organ capable of reorganization following neurological impairment. When we provide attention training combined with the metacognitive training, our goal is to positively influence that neural reorganization and encourage connections that will boost attention and executive functions. The research evaluating neuroplasticity while nascent is growing with the advent of different technologies that allow us to measure activity in different neural networks. Several studies have particular relevance to identifying possible mechanisms responsible for benefits with direct attention training. Recently, Kessler and colleagues (2011) evaluated the effects of a computerized cognitive program with attention and executive function drills on children with cancer-related brain injury. Their results suggested that the exercises were effective for improving executive attention with corresponding neurobiologic changes documented with fMRI. Similarly, Kim and colleagues (2009) used fMRI to explore possible neural remodeling following attention training in adult patients with traumatic brain injury. Ten patients completed attention training three times per week for 4 consecutive weeks using tasks designed to train sustained and divided attention in both visual and auditory modes. Participants then received follow-up fMRI studies using a visuospatial attention task and were compared to healthy individuals. Following the cognitive training, the patients with TBI demonstrated improved performance on attention tasks accompanied by changes in attention network activation including a decrease in frontal lobe activity and an increase in the anterior cingulate

cortex activity. The authors suggested that the results demonstrate the plasticity of the neural networks, and the ability for attention training to induce redistribution of the visuospatial attention network in patients with TBI. The AIM program incorporates attention and executive function drills similar to these two studies and has the added metacognitive training component. These studies provide the foundation for the second aim of our study-to examine neural correlates of improvements in attention and related abilities.

Previous Research on Neural Changes following Pediatric TBI

We previously shed light on the utility of using DTI and fMRI in characterizing underlying neural changes following TBI in young children (Karunanayaka et al., 2007; Kramer et al., 2008; Kurowski et al., 2009; Walz et al., 2008; Yuan et al., 2007) and adolescents (Tlustos et al., 2011). In the initial study, families of 23 children consented to participate and imaging data were successfully obtained on > 90% of participants. DTI images were acquired on a 3.0 Tesla Siemens Trio Magnetic Resonance Imaging (MRI) scanner using 12-direction diffusion-weighted spin-echo-planar imaging (EPI) scan. Results revealed a significant decrease of fractional anisotropy (FA) values in several white matter regions correlating strongly with injury severity in the children with TBI (Yuan et al., 2007). These findings provided initial evidence that that DTI is a sensitive and predictive index of white matter injuries following TBI in young children. Given that only two of the TBI group had severe injuries (i.e, Glasgow Coma Scale (GCS) scores < 8), they also support the notion that mild/moderate TBI in young children may result in persistent white matter alteration.

Children also completed an fMRI task assessing sustained attention (Continuous Performance Task: CPT; Kramer et al., 2008). In this task, single digits (“0”, “9” etc.) appeared one at a time centrally on the screen at the rate of one per second and participants had to press a button if a number was repeated on two consecutive trials. Examination of group differences revealed several areas of significantly greater activation in the TBI group relative to the orthopedic injuries (OI) group, including bilateral frontal cortex, right fusiform gyrus, bilateral occipital areas (BA 18,19), bilateral parietal cortex, and posterior cingulate. Thus, we found over-activation of the relevant attention network in the parietal and frontal regions in children with TBI relative to controls. These findings contrast with those obtained in studies of Attention Deficit Hyperactivity Disorder where under-activation of the attention network has been documented. These results provided the first evidence that children’s brains function differently following TBI and that these differences in activation can be reflected in task performance, thereby providing a critical first step in understanding the neural underpinnings of the cognitive and behavioral deficits commonly observed following TBI in children.

In a subsequent study, supported by a grant from the Ohio Department of Public Safety, we examined the neural substrates of executive function skills following TBI in adolescents. Two of the fMRI tasks assessed aspects of attention relevant to the AIM intervention and the current proposal. As described in a recently published paper (Tlustos et al., 2011), we used fMRI to examine one aspect of attention, interference control, in 11 adolescents, aged 12–16 years, (mean age, 15.7 years) with TBI who were at least 1 year post-injury and 11 age-matched typically developing control participants (TC)

(mean age, 15.2 years). Participants completed a Counting Stroop task with 2 main conditions: (1) a neutral condition requiring the counting of animal words and (2) an interference condition in which mismatched number words were counted. Both TBI and TC adolescents activated similar networks of brain regions relevant to interference control, but the TBI group showed higher levels of activation relative to the TC group in multiple brain areas within this network, including predominantly right frontal and parietal regions. Findings of greater activation of the relevant neural network in the TBI group are consistent with recent fMRI findings using other interference control paradigms with individuals with a history of TBI.

As part of the same Ohio Department of Public Safety/Emergency Medical Services- (ODPS/EMS) funded study, we investigated the neural basis of emotionally-mediated response inhibition in adolescents with TBI compared to typically-developing adolescents using fMRI. While undergoing fMRI, 10 participants with TBI and 9 healthy controls saw faces with varying emotional expressions and were instructed to “go” (press a button) on pictures displaying happy, sad, or fearful, and “no-go” (withhold pressing) on angry pictures. Groups showed similar performance on the Emotion Go/No-Go task during “Go” trials, with a trend towards higher accuracy among the healthy controls on “No-Go” trials. There were no group differences on the Interference score. A group comparison revealed that participants in the control group demonstrated greater inhibition-related activation than participants in the TBI group in superior medial frontal lobe, right precentral gyrus, medial precuneus, and left postcentral gyrus and inferior parietal lobe. The study provides preliminary evidence that adolescents with TBI show differential patterns of neural activation than their typically-developing counterparts

during an emotionally-mediated inhibition task, particularly within regions known to be related to inhibition, perspective-taking, and self-monitoring. Together these studies provide foundation for the current study.

V. Historical perspectives

In the United States, it is estimated that approximately 4 million TBIs occur annually. In children aged 0-19 years, there are approximately 600,000 emergency department visits, 40,000 hospitalizations, and 3,000 deaths annually in the United States related to TBI (Faul, Xu, Wald, & Coronado, 2010). Children aged 0-4 years have the highest rate of TBI (1,256 per 100,000) and teens aged 15-19 years also have an increased incidence (757 per 100,000) (Faul et al., 2010). It is estimated that more than 50% of TBIs in children are due to falls, approximately 25% are due to being struck by/against an object (e.g., colliding with a moving or stationary object), and around 7% are due to motor vehicle accidents. TBI in children is also associated with a large economic and societal cost. Hospital charges associated with pediatric TBI are over \$2.56 billion annually in the United States (Shi et al., 2009). Further, it is estimated that pediatric TBIs results in \$60 billion direct and indirect medical costs in the United States (Finkelstein, Corso, & Miller, 2006).

VI. A brief review of the current status of the topic in Ohio, the surrounding states, and nationally

Each day approximately 11 Ohioans under 22 years of age suffer TBIs (Ohio Brain Injury Association Website). There has been a spike in recent media attention highlighting the short-and long-term effects of concussion. These reports may lead to heighten public awareness regarding the health and behavioral sequelae associated with

TBIs in general. Investigators in Ohio are recognized both nationally and internationally as the source of some of the most important findings regarding TBI outcomes and intervention in the past two decades (Yeates et al., 2004; Taylor et al., 2004; DePompei ref; Wade et al 2006; 2014). The University of Pittsburgh is also conducting important research on management and recovery following mild TBI or concussion (references to Collins and Lovell papers). Nationally, both the Institute of Medicine and The American Congress of Rehabilitation Medicine issued recent reports regarding the efficacy of cognitive remediation for attention problems following TBI in adults. However, data regarding attention training/cognitive remediation following TBI in children is still limited (Sohlberg, Harn, MacPherson, & Wade, 2014).

VII. Future trends, both regionally and nationally

There is a need to develop effective treatment protocols for children and adolescents with TBI and attention deficits. Currently, there is a paucity of strong evidence-based interventions available for management of attention problems in children with TBI. Future research will continue to examine the efficacy of various treatment options that may alleviate attention deficits in children and adolescents with TBI, the utility of combined interventions (attention training and medication), and the optimal timing and intensity of treatments. Developing effective treatment of attention problems may lead to improved functioning after injury.

VIII. Financial issues and considerations

Not applicable for this research

IX. Education and training issues and considerations

Not applicable for this research

X. Legislative and regulatory issues and considerations

Not applicable for this research

XI. Data and information issues and considerations

The following standardized measures were administered pre- and post-treatment to assess changes in attention, working memory, and executive function skills. Each of these measures has substantial evidence documenting the reliability and validity for this population and are regularly used in these types of studies.

The Behavior Rating Inventory of Executive Function (BRIEF; Gioia et al., 2000). The BRIEF is a well-validated self- and parent/teacher- measure of daily behaviors associated with executive functioning that are often affected following TBI. The Global Executive Composite (GEC) of the parent- and adolescent self-report versions of the BRIEF served as a summary measure of problems with behavior regulation and metacognition. The BRIEF also assesses executive function abilities across eight clinical scales (Inhibition, Shift, Emotional Control, Plan/Organize, Organization of Materials, Monitor) thereby providing information regarding patterns of improvement.

The Test of Everyday Attention-for Children (TEA-Ch; Manly, Anderson, Nimmo-Smith, Turner, Watson, & Robertson, 2001). Subtests from the TEA-Ch were administered to assess aspects of working memory and attention. Specifically, the Code Transmission task provided a measure of working memory and sustained attention, the Walk/Don't Walk task provided a measure of inhibition, the Sky Search task provided a measure of selective/focused attention and the Score! task provided a measure of sustained attention.

Delis–Kaplan Executive Function System (D-KEFS; Delis, Kaplan, & Kramer, 2001).

Specific subtests from the D-KEFS were administered to assess executive functions such as flexibility of thinking, inhibition, problem solving, planning, impulse control, concept formation, abstract thinking, and creativity in both verbal and spatial modalities. The Trail Making (flexibility of thinking on a motor task); Color-word Interference (verbal inhibition); and Tower (planning and reasoning, impulsivity) subtests were administered to assess improvements on laboratory measures of inhibition and EF.

AIM Program Gathered Data. Because the program is computer delivered, it gathers a range of data related to the frequency of practice across a week, the types of attention and working memory tasks utilized (sustained, selective, working memory, suppression, or alternating attention tasks), types of strategies (see Table 2) and task accuracy. During the weekly clinic visit, the clinician also recorded reasons for modifying tasks or strategies (e.g., criteria met, too difficult; participant appeared bored, limited progress; set off somatic symptoms) and hypothesized reasons for lack of compliance or engagement (e.g., seemed bored, lacked self-confidence, technology issues, family stressors or competing activities).

Goal Attainment Scale (GAS; Malec, 1999). AIM uses an automated process to structure Goal Attainment Scaling (GAS), a criterion-referenced measure of a person’s goal achievement using a collaborative interview process involving the clinician, participant and parent. GAS quantifies summary outcomes across participants receiving the same intervention, but who have different individual goals (Ottenbacher & Cusick, 1990; Trombly, Radomski, Trexel, & Burnet-Smith, 2002). For direct cognitive interventions, GAS provides an ecological measure of generalization to activities that are meaningful to

participants and their families. Consistent with previous research, goal attainment was rated on a 5-point scale (-2 to +2). The midpoint of 0 was established as the predicted expected level of performance, with -1 and +1 indicating somewhat less than and somewhat greater than expected performance, respectively.

XII. An analysis of the researcher findings

Feasibility & Dose

As noted earlier, nine of 22 participants with TBI (41%) dropped out of the study before completion. Of the participants who dropped out, four completed no intervention sessions, three completed a single intervention session, and two dropped out after two and four sessions, respectively. One additional participant completed the minimum number of in-clinic intervention sessions but did not complete the minimum number of home practice sessions and was, therefore, excluded. Reasons cited for discontinuation included health or family factors ($n = 1$); too time-consuming ($n = 2$); dissatisfaction with the program or clinician ($n = 3$); or the family was lost to follow-up ($n = 3$). Treatment dosage for participants who completed the study varied. The number of in-clinic 60-90 minute sessions ranged from 10 to 13 (more clinic sessions were added for participants who had not completed at least two home practice sessions), and the number of self-initiated 20 to 40 minute home practice sessions ranged from 11-44 ($M = 22.2$, $SD = 9.5$).

Neuropsychological Test Performance

Pre- and post-test means and standard deviations for each group are reported in Table 3, along with results of t-tests for pre-test group differences and the mixed model Group x Time interaction and their respective effect sizes. The TBI group showed

significantly poorer performance at pre-test relative to the healthy comparison group on the TEA-Ch Code Transmission subtest and the D-KEFS TMT Combined Sequencing score, both with large effect sizes. Group differences at pre-test for the TEA-Ch Walk/Don't Walk subtest and the D-KEFS CWIT Inhibition/Switching and TT Total Achievement did not reach statistical significance in our small sample; however, effect sizes were medium and large, respectively, for the former two measures.

Table 3. Results of Mixed Model Analysis										
Measure	Pre-Test		Effect of Group at Pre-Test			Post-Test		Group x Time Interaction		
	TBI	Comparison	<i>t</i>	<i>p</i>	effect size	TBI	Comparison	<i>F</i>	<i>p</i>	effect size
Neuropsychological Tests										
TEA-Ch Code Transmission	6.83 (3.9)	10.45 (2.3)	2.70	.013	1.02	8.50 (3.9)	9.00 (3.2)	6.85	.016	0.88
TEA-Ch Walk/Don't Walk*	5.54 (3.8)	7.00 (2.4)	1.08	.292	0.40	8.18 (4.2)	8.00 (3.9)	1.07	.314	0.45
D-KEFS TMT Combined Sequencing	8.42 (5.4)	12.36 (2.1)	2.25	.035	0.93	9.33 (4.5)	11.64 (3.2)	1.18	.289	0.39
D-KEFS CWIT Inhibition/Switching	8.67 (3.6)	11.00 (1.9)	1.92	.069	0.73	9.50 (4.3)	10.82 (1.7)	1.42	.246	0.32
D-KEFS TT Total Achievement	9.58 (2.5)	10.82 (1.7)	1.35	.191	0.52	10.45 (2.6)	12.36 (1.9)	0.34	.564	-0.26
Parent BRIEF										
BRI	64.50 (9.2)	45.27 (6.7)	-5.68	<.001	-1.74	55.92 (8.8)	47.91 (8.0)	13.98	.001	-1.02
MI	71.92 (9.3)	47.55 (7.9)	-6.75	<.001	-1.82	65.17 (8.4)	49.45 (8.9)	21.46	<.001	-0.65
GEC	70.25 (7.9)	46.55 (7.6)	-7.32	<.001	-1.87	62.67 (7.8)	48.36 (8.8)	17.92	<.001	-0.74
Child BRIEF										
BRI	62.33 (10.9)	44.56 (12.7)	-3.19	.006	-1.23	59.00 (10.1)	45.56 (15.9)	0.81	.382	-0.30
MI	64.44 (7.6)	44.67 (12.4)	-4.07	<.001	-1.40	61.00 (9.6)	46.00 (15.0)	2.19	.158	-0.35
GEC	64.78 (9.2)	44.22 (13.3)	-3.82	.002	-1.38	60.44 (9.1)	45.44 (16.0)	1.88	.190	-0.37
<p><i>Note.</i> Values are means and standard deviations; scores are scaled scores for neuropsychological tests and <i>T</i> scores for the BRIEF</p> <p>*TEA-Ch Walk/Don't Walk score is missing for one child with TBI due to motor impairment; BRI = Behavioral Regulation Index; BRIEF = Behavior Rating Inventory of Executive Function; D-KEFS = Delis-Kaplan Executive Function System; CWIT = Color-Word Interference Test; GEC = Global Executive Composite; MI = Metacognitive Index; TBI = traumatic brain injury; TEA-Ch = Test of Everyday Attention for Children; TMT = Trail Making Test; TT = Tower Test</p>										

Mixed model analyses revealed a significant Group x Time interaction for the TEA-Ch Code Transmission subtest, with a large effect size. As illustrated in Figure 1, simple main effects revealed that the TBI group's scores showed marginally significant improvement from pre- to post-test, $t(21) = -2.02$, $p = .056$, medium effect size = -0.47 , whereas the scores of the healthy comparison group who did not receive the AIM intervention remained relatively unchanged, $t(21) = 1.69$, $p = .106$, small effect size = 0.41 . The Group x Time interactions for the other neuropsychological test measures were not statistically significant and effect sizes were small to medium in magnitude. After trimming the non-significant interaction from the models, the only significant main effect was for the effect of Time on the TEA-Ch Walk/Don't Walk subtest, $F(1, 20) = 4.24$, $p = .033$, medium effect size = -0.50 , and the D-KEFS TT Total Achievement, $F(1, 21) = 5.45$, $p = .030$, medium effect size = -0.52 , suggesting practice effects across groups on these measures.

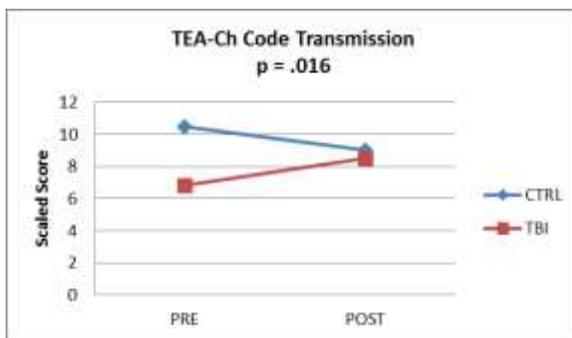


Figure 1. Group x Time interaction effect on the Test of Everyday Attention for Children (TEA-Ch) Code Transmission subtest.

Parent- and Child-Report Measures

Pre- and post-test means and standard deviations for each group are also reported in Table 3, along with results of t-tests for pre-test group differences and the mixed model Group x Time interaction and their respective effect sizes. The TBI group showed significantly more parent- and child-reported behaviors associated with executive dysfunction at pre-test relative to the healthy comparison group on all three examined BRIEF scores, all with large effect sizes.

Mixed model analyses revealed significant Group x Time interactions for all three parent-reported BRIEF scores, with medium to large effect sizes. As illustrated in Figure 2, simple main effects revealed that the TBI group's scores improved significantly from pre- to post-test, (BRI: $t(21) = 4.14, p < .001$, large effect size = 0.78; MI: $t(21) = 5.22, p < .001$, medium effect size = 0.51; GEC: $t(21) = 4.94, p < .001$, medium effect size = 0.60), whereas the scores of the healthy comparison group who did not receive the AIM intervention remained relatively unchanged, (BRI: $t(21) = -1.22, p = .237$, small effect size = -0.24; MI: $t(21) = -1.41, p = .172$, trivial effect size = -0.14; GEC: $t(21) = -1.13, p = .270$, trivial effect size = -0.14). The Group x Time interactions for all three child-reported BRIEF scores were not statistically significant and effect sizes were small in magnitude. After trimming the non-significant interactions from the child-report BRIEF models, there were significant main effect of Group on each measure (BRI: $F(1, 16) = 9.37, p = .008$, large effect size = -1.13; MI: $F(1, 16) = 17.13, p < .001$, large effect size = -1.42; GEC: $F(1, 16) = 13.21, p = .002$, large effect size = -1.30), indicating poorer self-reported EF in the TBI group across time.

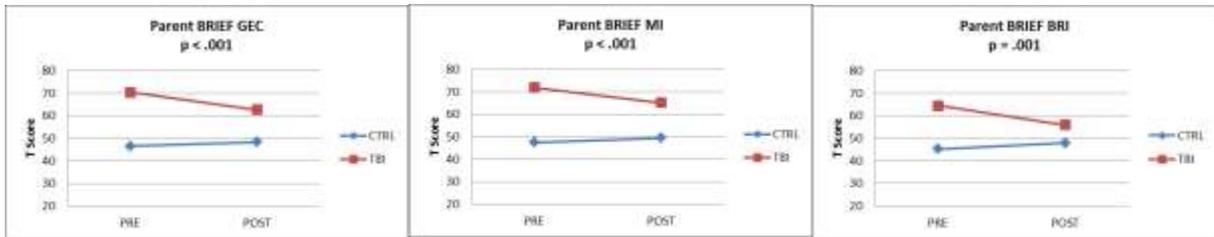


Figure 2. Group x Time interaction effect on the Behavioral Regulation Index (BRI), the Metacognition Index (MI), and the Global Executive Composite (GEC) from the parent-report of the Behavior Rating Inventory of Executive Function (BRIEF).

Goal Attainment

Across the 12 participants, six reported improvement as somewhat greater than expected, one reported expected progress, three reported somewhat less than expected progress, and two participants did not complete the GAS.

Abnormal Network Connectivity in Children with TBI & their Response to AIM

Training

Structural connectivity based on DTI & Graph Theory. The goal was to investigate changes in structural network connectivity, at both global and regional level, in the brains in children with chronic moderate to severe TBI from pre- to post-AIM using graph theoretical and diffusion tensor tractography. DTI data were acquired from 17 children with chronic TBI at baseline. Among these children, 10 also had post-AIM DTI data. The control group included 10 normally developing children who had both pre- and post-AIM DTI data. Graph theory analysis was applied to calculate the global network measures including small-worldness, normalized clustering coefficients, normalized characteristic path length, global efficiency, and modularity. Regional network parameters, including nodal degree, local efficiency, clustering coefficient, and betweenness centrality, were also calculated. Group difference was tested cross-sectionally at baseline and also longitudinally between pre- and post-AIM results. In addition, we also explored the

correlation between the changes in network connectivity and the changes in behavioral outcomes (Walk-. Code- , pMI, pBRI,GEC) in response to the AIM training.

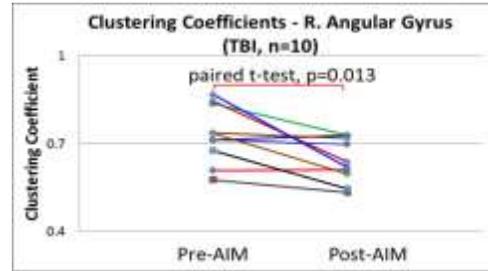
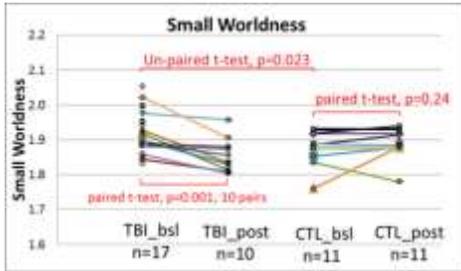


Figure 3. Comparison of Global network measures. **Figure 4.** Comparison of local network measures

Global network Measures: At baseline, children with chronic TBI were found to have significantly higher small-worldness than the controls (two-tailed t-test, $p=0.023$, Figure 1). No significant group difference was found at baseline in other global network measures. Longitudinally, significant decrease in the small-worldness was found in children with chronic TBI after AIM training ($n=10$, two-tailed paired t-test, $p=0.001$).

No significant longitudinal change was found in the small-worldness in the control group.

Most importantly, changes in connectivity between the initial and follow-up scans differed significantly between the groups ($\Delta\sigma = -0.056 \pm 0.037$ in TBI vs. $\Delta\sigma = 0.017 \pm 0.044$ in control, $t=4.07$, $df = 19$, $p = 0.0007$).

Regional network Measures: A series of brain regions showed significant group differences at baseline in various regional network measures. However, among these regions, only the angular gyrus in TBI group showed significant pre- vs. post-AIM change in nodal clustering coefficient and local efficiency (both $p<0.05$, see Figure 4 for clustering coefficient result).

Association between changes in structural connectivity and changes in behavioral outcomes: Significant correlations were found between longitudinal changes in

behavioral outcomes and changes in structural connectivity at both global and regional level. Specifically, we found that the change in parent-reported metacognitive functioning increased with mean local efficiency ($p=0.008$, Fig 3A) and the change in parent-reported behavioral regulation was inversely correlated with the change in network modularity ($p=0.046$, Fig 3B). It was also found that changes in parent-reported behavior regulation decreased with the change in nodal clustering coefficient in angular gyrus at trend level ($p=0.07$, Fig 3C).

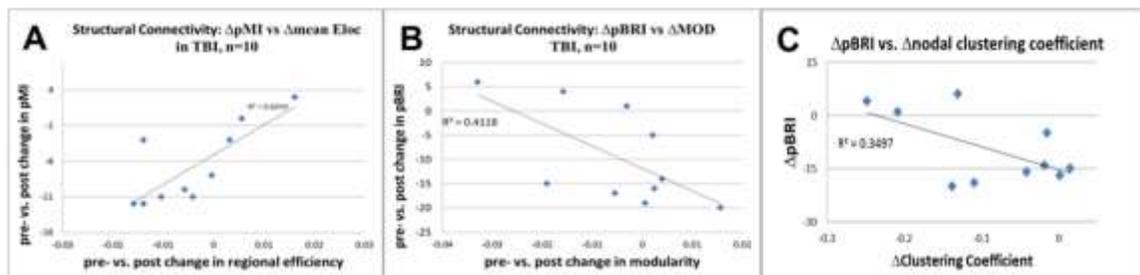


Figure 5. Correlation between behavioral outcome with global (A, B) and local (C) structural connectivity.

Functional connectivity based on resting state fMRI & Graph Theory: We also employed functional connectivity analysis based on resting state fMRI (rs-fMRI) and graph theory to investigate changes in functional connectivity in response to AIM training. The network connectivity parameters and statistical analyses used in the functional connectivity analysis were similar to those used in the analysis of structural connectivity. Among the 17 children with TBI recruited for imaging at baseline, 2 were excluded for compliance reasons. Eight of the remaining 15 children with TBI had both pre- and post-AIM rs-fMRI data. Among the 11 normal children recruited for imaging, 4 were excluded for motion artifact. Therefore, only 7 controls with both pre- and post-AIM refMRI data were available in the final analysis.

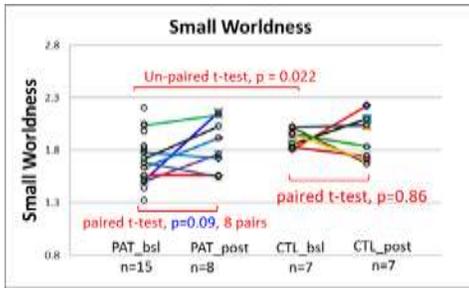


Figure 6. Comparison of global functional connectivity

Global network Measures: At baseline, children with chronic TBI were found to have significantly lower small-worldness than the controls (two-tailed t-test, $p=0.022$, Figure 4). Longitudinally, small-worldness increased at trend level in children with chronic TBI after AIM training ($n=8$, two-tailed paired t-test, $p=0.09$). No significant longitudinal change was found in the small-worldness in the control group. The two groups were found to have a trend level difference in their response to the AIM training ($\Delta\sigma = 0.17\pm 0.25$ in TBI vs. $\Delta\sigma = -0.055\pm 0.27$ in control, $t=1.77$, $df = 14$, $p = 0.099$).

Regional network Measures: A series of brain regions showed significant group differences at baseline in various regional network measures ($p<0.05$). Among these regions, middle occipital gyrus in TBI pts showed significant decrease in local efficiency ($p<0.03$) and nodal clustering coefficient ($p<0.03$) after the AIM. Superior frontal gyrus in TBI pts showed trend level decrease ($p=0.08$) in nodal clustering coefficient after AIM.

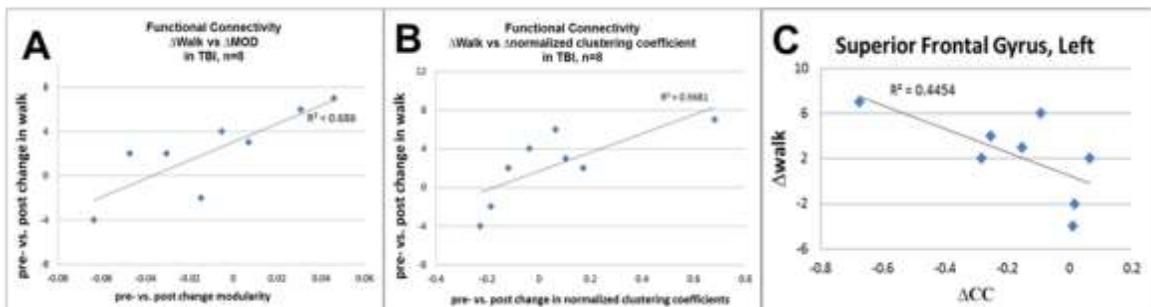


Figure 7. Correlation between behavioral outcome with global (A, B) and local (C) functional connectivity.

Association between changes in functional connectivity and changes in behavioral outcomes: Significant correlations were found between longitudinal changes in behavioral outcomes and changes in functional connectivity at both global and regional level. Specifically, we found that the change in WALK subtest increased with both network modularity ($p=0.011$, Fig 5A) and normalized clustering coefficient ($p=0.031$, Fig 5B). It was also found the change in WALK subtest decreased with the change in nodal clustering coefficient in superior frontal gyrus at trend level ($p=0.071$, Fig 5C).

Overall Summary for graph analysis of network connectivity: Our data showed both structural and functional connectivity based on graph theory were sensitive to detect abnormalities of brain network associated with TBI at both global and regional level. Using both approaches, we found significant changes in network measures in response to the AIM training. In addition, we found that the changes in some of the network measures were correlated, either significantly or at trend level, with the changes observed in the behavioral outcomes. These results strongly suggest that the network connectivity approach will provide a new avenue for potential diagnosis and prognosis for children with TBI as well as a monitoring tool to quantify response to AIM training.

Counting Stroop as an Attentional Probe: Behavioral and Functional Neuroimaging

Results: One of the goals of the current project is to recruit participants with TBI who show signs of attentional impairments. As a result, there are multiple challenges for securing usable fMRI data from these participants, including heightened susceptibility to movement artifacts in image acquisition, non-compliance to task directions, and suboptimal task performance. Of the 12 participants with TBI who completed the AIM training, only 6 contributed usable fMRI and behavioral data for both fMRI sessions

whereas 8 from the control group did so. Total performance for groups improved from time1 to time2 for participants with TBI (from 79% at time1 to 87% at time2) as well as for control participants (from 87% at time1 to 90% at time2), but neither the group effect nor the interaction effect was significant. Performance was not different between groups at time1 or time2.

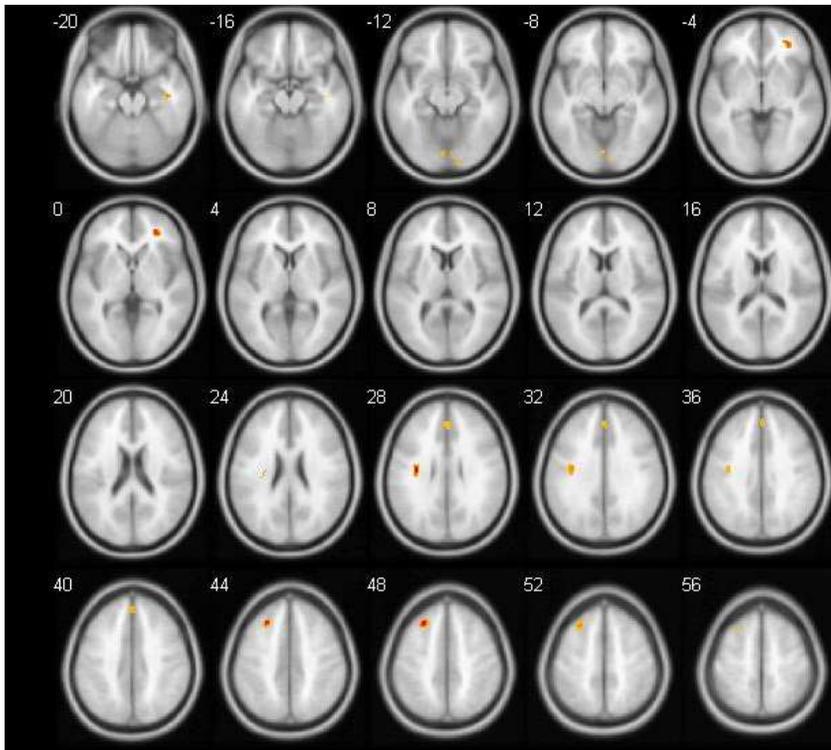


Figure 8. The dominant pattern of the preliminary findings on training effects for participants with TBI shows areas with *higher* levels of inhibition-related activation at time1 than at time2 ($p = 0.05$ uncorrected, cluster size = 25; slice location $z = -20$ to $+56$). Such areas overlap with network areas typically activated in the Counting Stroop task, including right medial temporal lobe, right lingual gyrus, right middle frontal gyrus, left post-central gyrus, medial frontal gyrus, and left middle frontal gyrus.

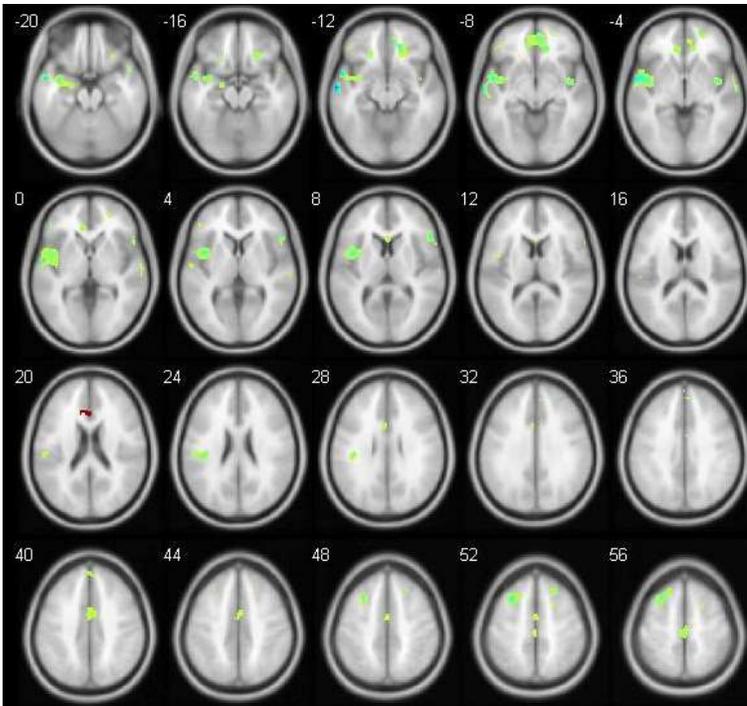


Figure 9. Preliminary findings on time effects for control participants. The *only* area that shows *higher* levels of activation at time1 than at time2 is anterior cingulate (slice $z=+20$, region shown in red). All other areas show *lower* level of attention at time1 than at time2. Convention as in Figure 8.

Our preliminary findings suggest that there is a differential effect of time for the two groups. While participants with TBI showed mostly a *drop* in levels of inhibition-related activation across a number of areas, mostly in the frontal lobes, from pre-training to post-training, control participants showed mostly an *increase* in levels of inhibition-related activation across a number of areas, including medial and superior temporal cortices, subgenual anterior cingulate, left insular cortex, and superior frontal areas, when performing Counting Stroop the first time versus a second time. The findings with the participants with TBI are consistent with the idea that there is an improvement in task performance accompanied by a drop in related brain activation level following AIMS training.

XIII. Conclusions

The results of this study are consistent with previous intervention studies suggesting that broad based training that includes both domain-general and domain specific approaches holds promise as an intervention to remediate attention, WM and EF deficits in the pediatric acquired brain injury population. Effects were greatest on parent reported executive dysfunction which improved significantly from pre- to post-treatment; whereas effects on neuropsychological performance were more limited. Improvements in parent-reported executive dysfunction corresponded to changes in both structural and functional connectivity on neuroimaging suggesting that changes in parent-reported behavior were reflected in corresponding neural changes. Structural and functional connectivity analyses appear to provide a viable approach for quantifying neural changes associated with attention training in children.

XIV. Recommendations

Despite its apparent utility, relatively high levels of attrition suggest that attention should be given to making the intervention more engaging and doable for participants. As delivered, the intervention required 10 or more weekly face to face visits as well as 2 or more independent practice sessions. Although intensity is considered to be an important treatment component, many participants had difficulty committing to this level of practice. Future research is needed to identify both the optimal timing and intensity of interventions such as AIM as well as strategies for making it more user-friendly.

XV. References

- Butler RW, Fairclough DL, Katz ER, *et al.* A multicenter, randomized clinical trial of a cognitive remediation program for childhood survivors of a pediatric malignancy. *Journal of Consulting & Clinical Psychology*. 2008; 76(3): 367-378.
- Collins, M.W., Lovell, M.R., Iverson, G.L., Cantu, R.C., Maroon, J.C., Field, M. Cumulative effects of concussion in high school athletes. *Neurosurgery*. 2002; 51: 1175-1181.
- Delis DC, Kaplan E, Kramer JH. 2001. *The Delis-Kaplan Executive Function System*. San Antonio: The Psychological Corporation.
- DePompei, R. & Williams, J. Working with families after TBI- A family centered approach. *Topics in Language Disorders*. 1994; 15: 68-81.
- Faul, M., Xu, L., Wald, M. M., & Coronado, V. G. (2010). Traumatic brain injury in the United States: emergency department visits, hospitalizations and deaths 2002-2006 Retrieved from http://www.cdc.gov/traumaticbraininjury/pdf/blue_book.pdf
- Fay GC, Jaffe KM, Polissar NL, Liao S, Rivara JB, Martin KM. Outcome of pediatric traumatic brain injury at 3 years: a cohort study. *Archives of Physical Medicine and Rehabilitation*. 1994; 75: 733-741.
- Finkelstein, E., Corso, P., & Miller, T. R. (2006). *The Incidence and Economic Burden of Injuries in the United States* The Incidence and Economic Burden of Injuries in the United States. New York, NY: Oxford University Press

- Friston KJ, Holmes AP, Price CJ, Buchel C, Worsley KJ. Multisubject fMRI studies and conjunction analyses. *Neuroimage*. 1999; 10(4): 385-396.
- Galbiati S, Recla M, Pastore V, Liscio M, Bardoni A, Castelli E, Strazzer S. Attention remediation following traumatic brain injury in childhood and adolescence. *Neuropsychology*. 2009; 23: 40-49.
- Gioia GA, Isquith PK, Guy SC. Behavior rating of executive function. *Child Neuropsychology*. 2000; 6: 235-238.
- Janusz JA, Kirkwood MW, Yeates KO, Taylor HG. Social problem-solving skills in children with traumatic brain injury: Long-term outcomes and prediction of social competence. *Child Neuropsychology*. 2002; 8: 179-194.
- Karunanayaka P, Holland S, Yuan W, *et al*. Abnormalities in language circuitry in children with traumatic brain injury, an fMRI study. *Neurorehabilitation and Neural Repair*. 2007; 22: 355-369.
- Kennedy MRT, Coelho C, Turkstra L, Ylvisaker M, Sohlberg MM, Yorkston K, Chiou H-H, Kan P-F. Intervention for executive functions after traumatic brain injury: A systematic review, meta-analysis and clinical recommendations. *Neuropsychological Rehabilitation*. 2008; 18(3): 257-299.
- Kesler SR, Lacayo NJ, Jo B. A pilot study of an online cognitive rehabilitation program for executive function skills in children with cancer-related brain injury. *Brain Injury*. 2011; 25(1): 101-112.

- Kim Y-H, Yoo W-K, Ko M-H, Park C-H, Kim ST, Na DL. Plasticity of the attentional network after brain injury and cognitive rehabilitation. *Neurorehabilitation and Neural Repair*. 2009; 23(5): 468-477.
- Kramer ME, Chiu CY, Walz NC, *et al*. Long-term neural processing of attention following early childhood traumatic brain injury: fMRI and neurobehavioral outcomes. *Journal of the International Neuropsychological Society*. 2008; 14(3): 424-435.
- Kurowski B, Wade S, Cecil K, Walz N, Weihong Y, Rajagopal R, Holland S. Correlation of Diffusion Tensor Imaging with Executive Function Measures after Early Childhood Traumatic Brain Injury. *Journal of Pediatric Rehabilitation Medicine*. 2009; 2 (4): 273-283.
- Langlois JA, Rutland-Brown W, Thomas KE. 2006. *Traumatic brain injury in the United States: emergency department visits, hospitalizations, and deaths*. Atlanta: Centers for Disease Control and Prevention.
- Levin H, Hanten G, Max J, *et al*. Symptoms of attention-deficit/hyperactivity disorder following traumatic brain injury in children. *Journal of Developmental and Behavioral Pediatrics*. 2007; 28(2): 108-118.
- Loken WJ, Thornton AE, Otto RL, Long CJ. Sustained attention after severe closed head injury. *Neuropsychology*. 1995; 9: 592-598.
- Lovell, M.R., Iverson, G.L., Collins, G.L., Podell, K., Johnston, K.M., Pardini, D., Pardini, J., Norwig, J., & Maroon, J. Measurement of symptoms following sports-

related concussion: reliability and normative data for the post-concussion scale. 2006; 13(3): 166-174.

Malec J. Goal attainment scaling in rehabilitation. *Neuropsychological Rehabilitation*. 1999; 9(3/4): 253-275.

Manly T, Robertson I H, Anderson V, Nimmo-Smith I. 1999. *TEA-Ch: The Test of Everyday Attention for Children Manual*. Bury St. Edmunds, UK: Thames Valley Test Company Limited.

Max JE, Koele SL, Smith WL, Sato Y, Lindgren SD, Robin DA, Arndt S. Psychiatric disorders in children and adolescents after severe traumatic brain injury: A controlled study. *Journal of the American Academy of Child and Adolescent Psychiatry*. 1998; 37: 832-840.

Max JE, Schachar RJ, Levin HS, Ewing-Cobbs L, Chapman SB, Maureen Dennis M, Ann Saunders A, Landis J. Predictors of attention-deficit/hyperactivity disorder within 6 months after pediatric traumatic brain injury. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2005; 44(10): 1032-1040.

Mooney P, Ryan JB, Uhing BM, Reid R, Epstein MH. A review of self-management interventions targeting academic outcomes for students with emotional and behavioral disorders. *Journal of Behavioral Education*. 2005; 14(3): 203-221.

Ohio Brain Injury Association. Retrieved March 8, 2011 from <http://www.biaoh.org/om>.

Ottensbacher, K. J., & Cusick, A. Goal attainment scaling as a method of clinical service

- evaluation. *American Journal of Occupational Therapy*. 1990; 44, 519–525.
- Penkman L. Remediation of attention deficits in children: a focus on childhood cancer, traumatic brain injury and attention deficit disorder. *Pediatric Rehabilitation*. 2004; 7(2): 111-123.
- Posner MI. Rothbart MK. Influencing brain networks: implications for education. *Trends in Cognitive Sciences*. 2005; 9(3): 99-103.
- Posner MI. Rothbart MK. Research on attention networks as a model for the integration of psychological science. *Annual Review of Psychology*. 2007; 58: 1-23.
- Reid R, Trout A L, Schartz M. Self-regulation interventions for children with attention deficit/hyperactivity disorder. *Exceptional Children*. 2005; 71(4): 361-377.
- Schmithorst V, Holland, SK. Dardzinski BJ. 2000. *CCHIPS: Cincinnati Children's Hospital Imaging Processing Software* .<http://www.irc.chmcc.org/chips.htm>.
- Shi, J., Xiang, H., Wheeler, K., Smith, G. A., Stallones, L., Groner, J., & Wang, Z. Costs, mortality likelihood and outcomes of hospitalized US children with traumatic brain injuries. *Brain Injury*. 2009; 23(7): 602-611.
- Smith SM, Jenkinson M, Johansen-Berg H, *et al*. Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. *Neuroimage*. 2006; 31(4): 1487-1505.
- Sohlberg, MM, Harn, B., MacPherson, H., Wade, S.L. A pilot study evaluation attention and strategy training following pediatric traumatic brain injury. *Clinical Practice in Pediatric Psychology*. 2014; 2 (3): 263-280.

- Sohlberg MM, Avery J, Kennedy M, *et al.* Practice guidelines for direct attention training. *Journal of Medical Speech Language Pathology*. 2003; 11(3): xix-xxxix.
- Sohlberg MM, Mateer C. 2001. *Cognitive Rehabilitation: An Integrated Neuropsychological Approach*. New York: Guilford Publications.
- Sohlberg MM, Mateer CA. 2010. *Attention Process Training III: A direct attention training program for persons with acquired brain injury*. Lash & Associates Publishing/Training Inc.
- Stevens C, Fanning J, Coch D, Sanders L, Neville H. Neural mechanisms of selective auditory attention are enhanced by computerized training: Electrophysiological evidence from language-impaired and typically developing children. *Brain Research*. 2008; 1205: 55-69.
- Taylor, H. G. (2004). Research on outcomes of pediatric traumatic brain injury: current advances and future directions. *Dev Neuropsychol*, 25(1-2), 199-225
- Teasdale, G., Jennett, B. Assessment of coma and impaired consciousness: a practical scale. *The Lancet*. 1974; 2:81-84
- Tlustos SJ, Chiu C-YP, Walz NC, Holland SK, Bernard L, Wade SL. Neural correlates of interference control in adolescents with traumatic brain injury: functional magnetic resonance imaging study of the Counting Stroop Task. *Journal of the International Neuropsychological Society*. 2011;17:181-189.
- Trombly, C. A., Radomski, M. V., Trexel, C., Burnett-Smith, S. E. Occupational therapy and achievement of self-identified goals by adults with acquired brain injury:

Phase II. *The American Journal of Occupational Therapy*. 2002; 56, 489–498.

van't Hooft I, Andersson K, Sejersen T, Bartfai B, von Wendt L. Attention and memory training in children with acquired brain injuries. *Acta Paediatrica*. 2003; 92(8): 935-940.

van't Hooft I, Andersson K, Bergman B, Sejersen T, von Wendt L, Bartfai A. Sustained favorable effects of cognitive training in children with acquired brain injuries. *Neurorehabilitation*. 2007; 22(2): 109-116.

Vernescu R. 2008. Sustained attention training in children with fetal alcohol spectrum disorder. Unpublished doctoral dissertation, Department of Psychology, Memorial University, St. John's Newfoundland.

Wade, S.L., Carey, J., Wolfe, C.R. An online family intervention to reduce parental distress following pediatric brain injury. *Journal of Consulting and Clinical Psychology*. 2006; 74(3): 445-454.

Wade SL, Karver CL, Taylor HG, et al. Counselor-assisted problem solving improves caregiver efficacy following adolescent brain injury. *Rehabilitation Psychology*. 2014; 59(1):1

Walz NC, Cecil K, Wade SL, Michaud L. Late proton MR spectroscopy following traumatic brain injury during early childhood: relationship with neurobehavioral outcomes. *Journal of Neurotrauma*. 2008; 25: 94-103.

Wolraich ML, Lambert W, Doffing MA, Bickman L, Simmons T, Worley K.

Psychometric properties of the Vanderbilt ADHD Diagnostic Parent Rating Scale in a referred population. *J Pediatr Psychol.* 2003; 28: 559– 568.

Worsley KJ, Liao CH, Aston J, Petre V, Duncan GH, Morales F, Evans AC. A general statistical analysis for fMRI data. *Neuroimage.* 2002; 15(1): 1-15.

Yeates, K. O., Swift, E., Taylor, H. G., Wade, S. L., Drotar, D., Stancin, T., & Minich, N. (2004). Short- and long-term social outcomes following pediatric traumatic brain injury. *J Int Neuropsychol Soc*, 10(3), 412-426.

Yuan W, Holland SK, Schmithorst VJ, *et al.* Diffusion tensor MR imaging reveals persistent white matter alteration after traumatic brain injury experienced during early childhood. *American Journal of Neuroradiology.* 2007; 28: 1919-1925.