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The Neural Systems of Working Memory: The Sternberg  
Working Memory Task in a Pediatric  
Traumatic Brain Injury Sample

Jon Pertab

A dissertation submitted to the faculty of  
Brigham Young University  
in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

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August 2010

## ABSTRACT

The Neural Systems of Working Memory: The Sternberg  
Working Memory Task in a Pediatric  
Traumatic Brain Injury Sample

Jon Pertab

Department of Psychology

Doctor of Philosophy

Working memory tasks are associated with the activation of widely distributed neural networks. The Sternberg working memory task has been used to explore the neural correlates associated with changes in memory load and the resolution of interference. Preliminary research suggests that the integrity of the anterior cingulate is correlated with resolving load adjustments but not in resolving interference demands; the opposite pattern of associations have been observed with the right middle frontal gyrus.

Participants in the present study were 28 children who had sustained moderate to severe traumatic brain injuries (TBI) and 28 children who had sustained orthopedic injuries (OI). Participants were aged between 7 and 17 years at the time of injury (mean age = 13.2, *s.d.*=2.3). The groups were matched on age, gender, socioeconomic level, and pre-injury measures of behavioral and emotional functioning. Participants completed the Sternberg working memory task and structural MRI scans three months post injury. Automated brain parcellation software (Freesurfer) was used to calculate volumetric data for regions of interest. Regions of interest included the anterior cingulate and right middle frontal gyrus; additionally, the volume of the corpus callosum was used as an index of overall brain integrity.

There were no significant differences between the groups on percent errors on the Sternberg task. Participants in the TBI group had significantly longer reaction times overall than the OI group. Interference in the Sternberg task has the potential to either help or hinder performance. Participants in the OI group displayed the anticipated effects of interference on reaction time whereas the TBI group as a whole did not display this pattern (priming effect not observed). The TBI group had significantly lower volumes in the regions of interest than the OI group. Hypothesized correlations between the regions of interest and changes in load / interference demands were partially supported. Exploratory analyses identified positive correlations between the volume of the right middle frontal gyrus and reaction time measures that warrant further exploration.

Keywords: traumatic brain injury, Sternberg, working memory, priming, interference, executive functioning.

## ACKNOWLEDGEMENTS

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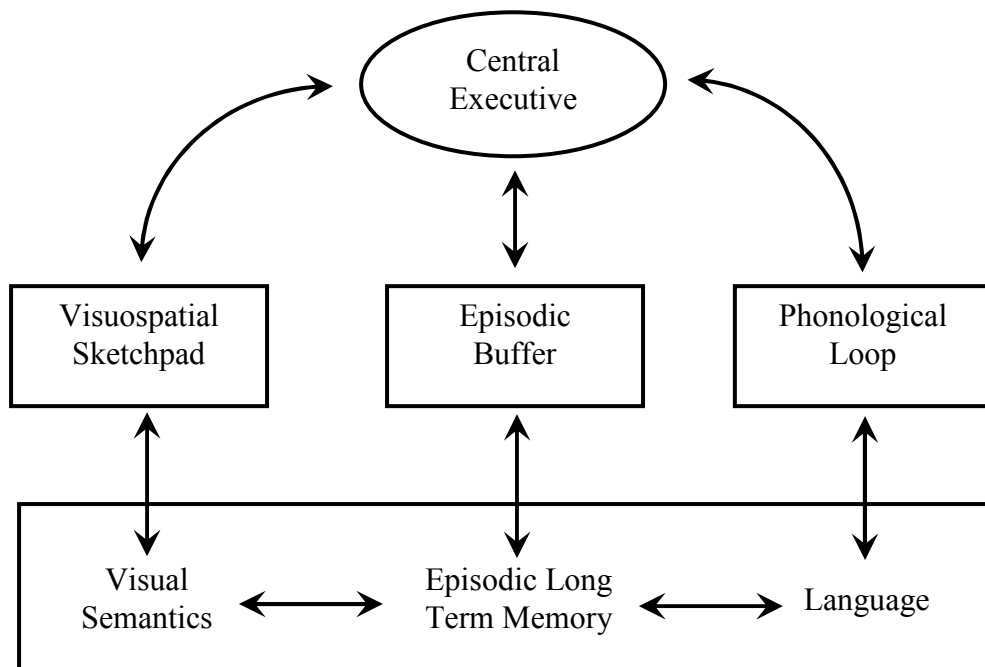
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## Introduction

### Working Memory Background Information

Working memory is a term that refers to a brain function involving the simultaneous temporary storage and processing of task relevant information (Baddeley, 1992). It has been conceptualized to comprise of storage buffers that retain information briefly, rehearsal processes that refresh the buffers, and executive processes that manipulate the contents of the buffers (Jonides, Lacey, & Nee, 2005). One of the most influential conceptual models of working memory was proposed by Baddeley and Hitch (1974) and has undergone several subsequent refinements (Baddeley, 1981, 1988, 1992, 2000, 2003a, 2003b; Baddeley & Hitch, 1994, 2000). The current version of the model (Baddeley, 2003b) is summarized in Figure 1.



*Figure 1.* Illustration of the relationships between working memory subsystems and long term memory subsystems (Baddeley, 2003b)

In this model the central executive subsystem directs the activity of the three slave systems – visuospatial sketchpad, episodic buffer, and phonological loop. The phonological loop comprises two components - a store of verbally based information that lasts a few seconds and a rehearsal system that acts to refresh items in the store by re-articulation. The visuospatial sketchpad is the parallel store for visual and spatial information. Experiments support the idea that the contents of the phonological loop and visuospatial sketchpad both contribute to, and activate, information in long term memory stores. The episodic buffer integrates information from long term memory, the phonological loop, and visuospatial sketchpad to create a cohesive episode that is perceived as conscious awareness. The workings of these three systems are under the control of the central executive. The central executive acts as an attention controller which focuses, inhibits, divides, and switches attention; directing the activities of the component subsystems to maximize functioning of the individual according to the demands of the environment.

Although the neural underpinnings of working memory components are only partially understood, the various aspects of working memory appear to be differentially localized throughout the brain. The most consistent neurological relationships in working memory research are found for the phonological loop with Brodmann's Area (BA) 40 involved in the storage component of the loop and BA 6 and 44 involved in the rehearsal component (Awh et al., 1996; Jonides et al., 1996; Vallar, Di Betta, & Silveri, 1997). Visuospatial working memory appears to be located primarily throughout the right hemisphere (Awh et al., 1996; De Renzi & Nichelli, 1975; Della Sala, Gray, Baddeley, Allamano, & Wilson, 1999; Hanley, Young, & Pearson, 1991; Jonides et al., 1996; Jonides et al., 1993; Smith, Jonides, & Koeppel, 1996; Smith, Jonides, Marshuetz, & Koeppel, 1998; Vallar et al., 1997). The central executive and its neural



correlates is considered the most complex and the least understood / elaborated component of working memory and is associated with bilateral dorsolateral prefrontal, inferior frontal, and parietal activation (Braver et al., 1997; Cohen et al., 1997; D'Esposito, Postle, Ballard, & Lease, 1999; D'Esposito, Postle, Jonides, & Smith, 1999; Jonides, Smith, Marshuetz, Koeppe, & Reuter-Lorenz, 1998).

While generalized areas of the brain have been identified as relevant in working memory tasks, relationships are complex, and conflicting results, particularly when examining processes of the central executive are not uncommon (Baddeley, 2003b). One potential reason for discrepancies is that working memory is not a unitary function but a collection of processes. Thus, in seeking to understand the neural correlates of working memory the importance of specificity in the aspect of working memory under consideration cannot be underestimated. It may be problematic to assume that brain regions involved in resolving the challenges of one working memory task such as digit span forwards are the same as those involved in another working memory task such as an n-back paradigm. Selection of a specific working memory paradigm and exploring aspects of working memory that apply to that paradigm is important if conflicting findings are to be reconciled.

### **The Sternberg Working Memory Task and its Neural Correlates**

The present study explores specific aspects of working memory that are elicited by the Sternberg working memory task. The Sternberg task (Sternberg, 1966) and its adaptations has been a popular paradigm to explore aspects of working memory since its development in the 1960s (see Figure 2 for schematic). In this task the participant is shown an array of symbols on a screen (encoding array, typically 1-6 letters or digits) which they attempt to hold in working

memory; after a short delay (maintenance) a single target symbol is presented (probe) and the subject responds by indicating whether or not the target was present in the previous array by pressing one of two buttons (or by using levers in original studies). Initial experiments using this paradigm found that the more digits in the initial array (greater load), the longer the response latency (Sternberg, 1966, 1969).

Research in adult populations has employed brain imaging in combination with the Sternberg task to identify which brain regions are associated with various aspects of the task. These studies have found that the various aspects of working memory engaged by the Sternberg task correlate with activation of both generalized and specific neural networks. For example, Manoach, Greve, Lindgren, and Dale (2003) investigated the neural correlates of a Sternberg working memory task with adult participants in an fMRI paradigm. They found the encoding stage of the task was correlated with activation of the bilateral visual and visual association cortices, including the fusiform gyrus and the ascending intraparietal sulcus (these same regions were activated during the presentation of the probe but to a lesser extent). The maintenance stage was associated with activation of the bilateral visual association areas in the occipital and temporal lobes including the lingual gyrus, and primary somatosensory cortex, and left hemisphere activation of the supplementary motor area, primary motor area, and lateral premotor area (dorsolateral prefrontal cortex activation was not identified). The probe stage of the task was associated with the most widespread activation and included bilateral activation of the motor and premotor cortex, with unique stage activation of the descending segment of the intraparietal sulcus, insula, cingulate, inferior frontal, thalamus and lenticular nucleus.

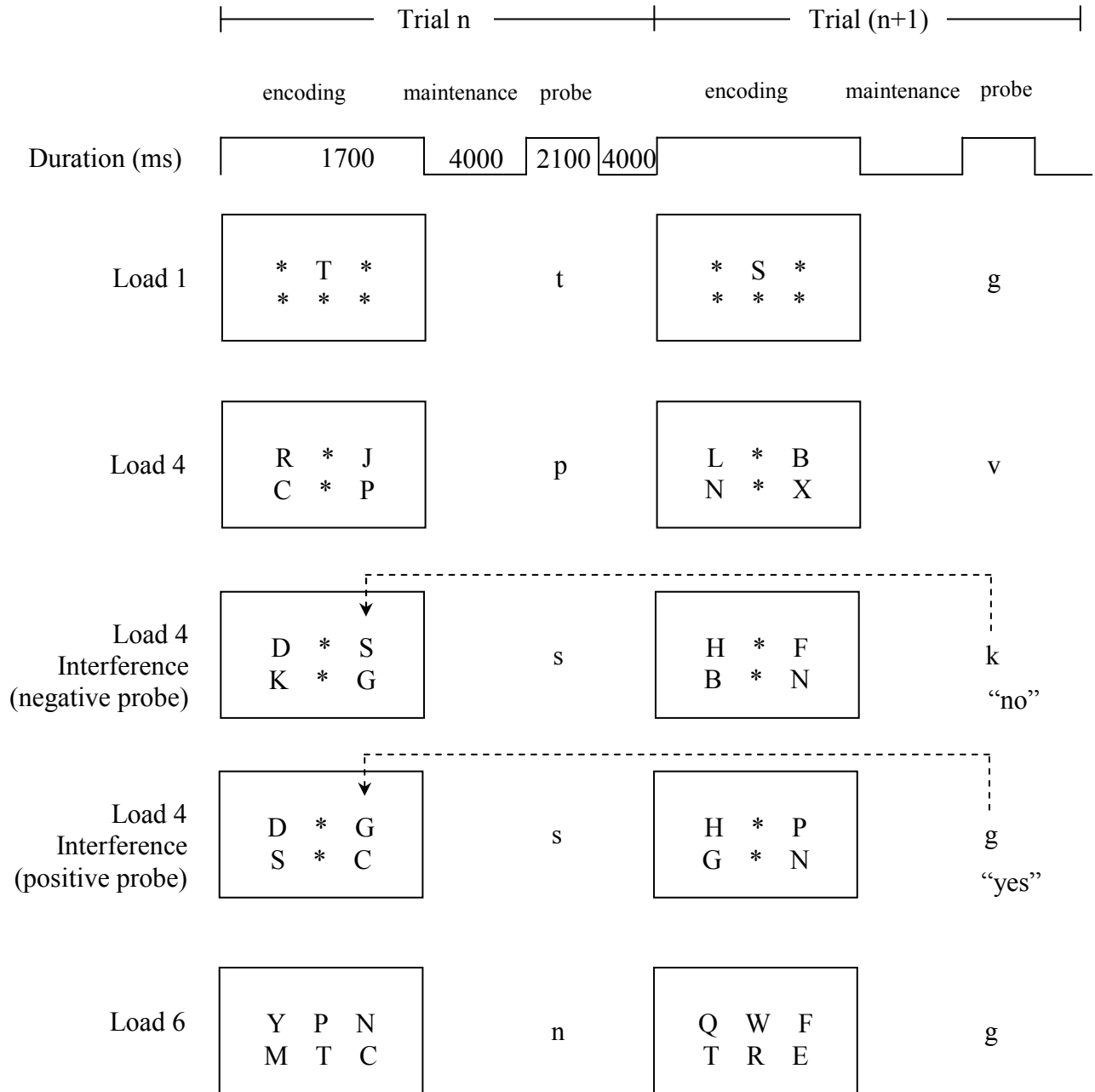


Figure 2. Schematic of the Sternberg working memory task.

By manipulating task demands during the Sternberg task researchers can identify not only which neural networks are involved at each stage, but also which networks are involved with each type of task demand. The traditional manipulation involves increasing the number of stimuli in the array to be encoded – a load manipulation (Sternberg, 1966, 1969). More recently experimenters have also added an interference manipulation. In this condition proactive interference is increased by presenting the target/probe letter of a given trial in the array of the immediately preceding trial (see Figure 2). On trials where the correct response to the probe is “no/not present,” subjects are slower to respond if the probe is recent - i.e. appeared in the array of the previous trial (Monsell, 1978).

Bunge, Ochsner, Desmond, Glover, and Gabrieli (2001) used the Sternberg task with both the load and interference manipulation in an fMRI study with adults. Regions that had increased activation when load demands increased were considered to be sensitive to working memory load. These areas were the bilateral regions of the ventrolateral prefrontal cortex, dorsolateral prefrontal cortex, anterior insula, anterior cingulate and parietal cortex, with right hemisphere activation in the frontopolar cortex, caudate nucleus and cerebellum. Regions with greater activation during trials that required resolution of interference from the previous trial were the right middle frontal gyrus, right anterior cingulate gyrus, left inferior frontal gyrus, left anterior middle frontal gyrus, bilateral anterior insula, and bilateral parietal cortex. In general, the areas activated by the interference manipulation were also activated during the load manipulation. Effective activation of these networks is correlated with Sternberg task performance; the strongest associations are summarized in Table 1.

Table 1

*Regions demonstrating the strongest linear relationships between fMRI activation intensity and performance on load or interference conditions during the Sternberg Task (from Bunge et al., 2001).*

Region Activated	Brodmann area	Z-Score	Volume (mm <sup>3</sup> )	Correlation Coefficient	
				Load (4-6 items)	Interference
<i>Load related activation and susceptibility</i>					
Anterior Cingulate	R32,24	4.65	5472	+0.78	-0.02
Medial frontal gyrus	R6	3.57	384	+0.48	+0.06
Inferior frontal gyrus	L45,46	3.14	400	+0.30	-0.34
Middle temporal gyrus	L22	3.97	416	+0.43	-0.06
Thalamus	R, L	3.27	1840	+0.56	-0.10
Posterior cerebellum	n/a	3.21	96	+0.43	+0.21
Superior temporal gyrus	L22	3.16	160	-.21	+0.16
<i>Interference related activation and susceptibility</i>					
Middle frontal gyrus	R9	3.88	128	+0.07	-0.58
Superior temporal gyrus	R22	3.41	112	+0.42	-0.48

Using regression analyses of the Bunge et al., (2001) data, subjects that had the least susceptibility to the interference manipulation had the highest activation in the right middle frontal gyrus and right superior temporal gyrus. Activation of the superior temporal gyrus correlated with trials where interference was present and the correct response to the target was “yes/present” but not in interference trials where the correct response was “no/not present.” The inverse association was found for the right middle frontal gyrus, i.e. there was unique activation where the subject was primed to respond positively but the correct response was negative “no/not present.”

This pattern of results suggests that the right middle frontal gyrus may be specifically involved in inhibiting a primed response as this region was not significantly correlated with increased demands of the load condition. Regression analyses identified positive correlations for the load manipulation in the anterior cingulate. This area was not significantly correlated with the interference manipulation suggesting that it may be specifically involved when the task demands adjustments to increases in working memory load.

The Sternberg task thus allows for examination of both generalized and specific aspects of working memory and, when combined with neuro-imaging data, associated brain regions can also be identified.

### **Elaborated Working Memory Model**

Research on executive functions suggests that the 'central' executive may not be as central as conceived in the Baddeley & Hitch model. Rather, there seem to be separate executive functions that can vary largely between individuals and can be selectively impaired or spared by brain damage (Miyake et al., 2000). In line with these findings, the current study focuses on a

few specific aspects of the cluster of abilities subsumed under the construct of the central executive as depicted in Figure 3. This figure combines core aspects of working memory, neural correlates relevant to this study, and other brain functions that are closely tied to the working memory construct (such as sensory processing).

In this model multiple streams of sensory stimulation are processed in primary sensory processing areas (labeled “A” in Figure 3). This information is fed into neural networks associated with the central executive (B). The central executive neural networks determine which streams are relevant to the task at hand and provide feedback to sensory processing areas (C) regarding which streams to filter out of storage and which to maintain for further processing. Research suggests that relevant streams are stored in the same brain regions that are involved in primary processing of sensory information (see review by Jonides et al., 2005). Information active in working memory stores triggers activation of associated long term memory stores (D). This is not surprising considering that long term memory and working memory share neural substrates (Cabeza, Dolcos, Graham, & Nyberg, 2002; Nyberg, Forkstam, Petersson, Cabeza, & Ingvar, 2002; Nyberg et al., 2003). Central executive feedback loops (E) direct resources in the brain so that only task relevant sensory and long-term memory information is maintained active for use in task related motor planning and response activation (F).

The present study explores three features of this elaborated model; these are labeled 1-3 in Figure 3. The first feature (1) relates to the overall functioning of the central executive. The central executive manages streams of information from sensory stimulation and long term memory in a variety of different ways and is thought to comprise multiple sub-functions that enable it to effectively manage working memory resources. Research reviewed above suggests that the functioning of the central executive as a whole, involves widespread activation of

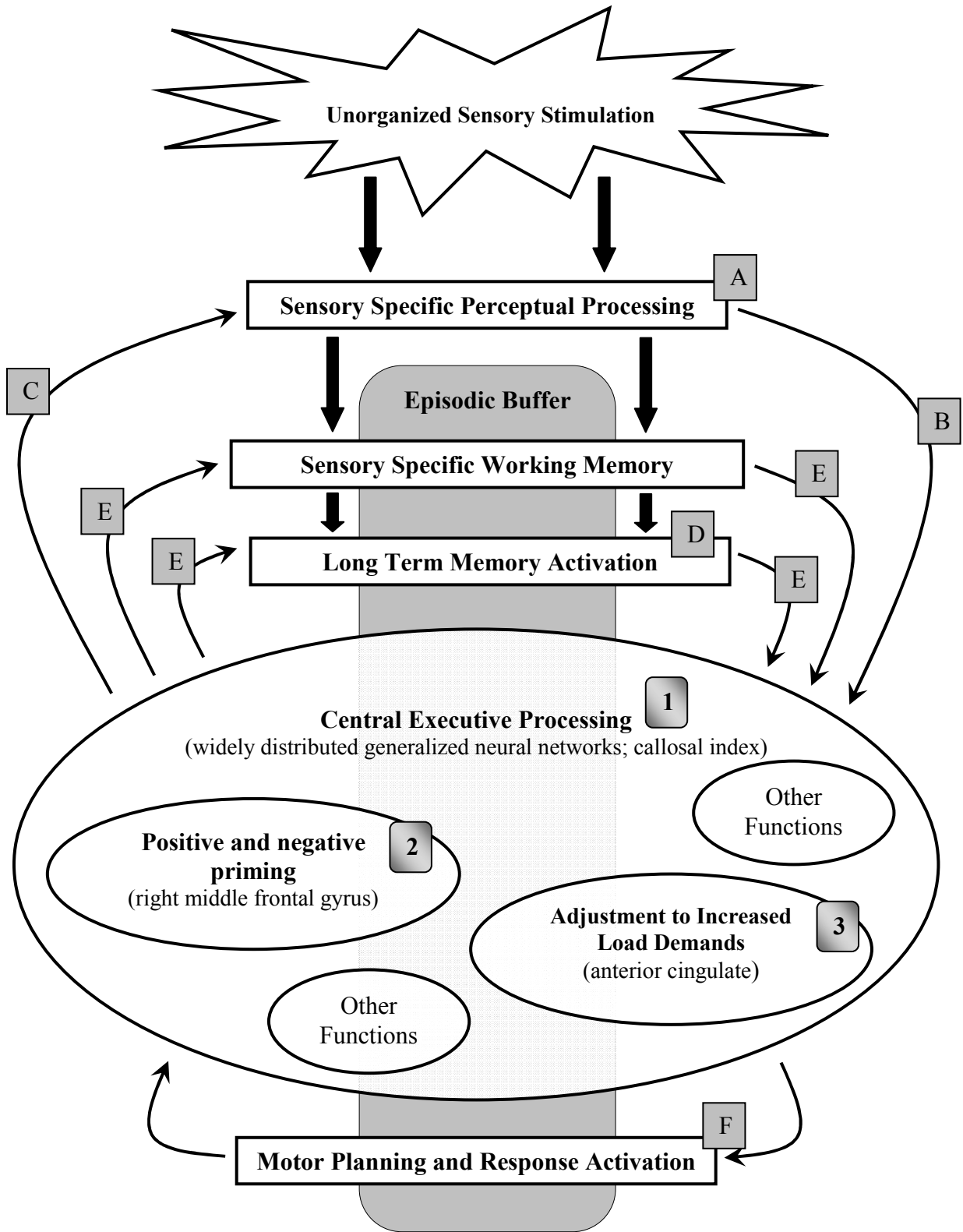


Figure 3. Schematic of neural network relationships related to working memory.



neural networks throughout the cortex and subcortex. The integrity of these networks and communication pathways between them is necessary for effective working memory performance. Efficient communication between these areas is dependent on the integrity of white matter pathways throughout the brain. Projection plots of the Corpus Callosum (CC) identify this as an important structure that provides interconnectivity of brain regions that are activated during the Sternberg working memory task (see Alexander et al., 2007). The present study is designed to answer the following question:

**Question one.** Is the integrity of widely distributed neural networks as defined by the volume of the corpus callosum corrected for total intracranial volume correlated with performance on the Sternberg working memory task?

By employing the Sternberg task we are also able to assess the influence of priming on reaction time and errors. In Figure 2, examples of negative and positive priming are illustrated. In the negative condition – interference from the encoding array of the previous trial primes the individual to respond “yes” to the probe for the subsequent trial, this must be inhibited to produce the correct “no” response. The extra inhibition demands are anticipated to result in relatively longer reaction times and increased errors. In the positive priming condition both the present and previous trial contain the probe letter – the previous trial and the current trial prime the individual to respond “yes.” In this situation the priming condition facilitates a correct response and increased accuracy and relatively shorter reaction times are anticipated.

In, addition to exploring the impact of priming / interference on performance (labeled 2 in Figure 3), the Sternberg task also enables examination of the impact of increasing load demands on reaction time and errors (labeled 3 in Figure 3). The Bunge et al. (2001) article and

others reviewed above suggest that certain brain regions may take a more dominant role in mediating these specific aspects of working memory. In particular the literature reviewed raises the following questions that are explored in this study:

**Question two.** Does the integrity of the right middle frontal gyrus have a stronger correlation with vulnerability to interference demands of working memory tasks than the anterior cingulate?

**Question three.** Does the integrity of the anterior cingulate gyrus have a stronger correlation with vulnerability to increases in load demands of working memory tasks than the right middle frontal gyrus?

### **Pediatric TBI and Impact on Working Memory**

Understanding the effects of pediatric traumatic brain injury has utility for both clinical and research applications. Clinically, impaired working memory in children has been associated with impaired reasoning, learning disabilities and developmental disabilities (Kyllonen & Christal, 1990; Russell, Jarrold, & Henry, 1996; Swanson, 1994). Understanding working memory deficits after TBI has the potential to inform rehabilitation efforts and learning accommodations. From a research perspective, studies examining the relationships between impaired aspects of working memory functioning in pediatric TBI samples and their neural correlates can help clarify the neural underpinnings associated with these functions. In the context of the present research, data from a pediatric TBI sample was utilized to explore neural correlates of aspects of the central executive as well as identify aspects of working memory that are impaired after TBI in children.

Children with TBI as a group have been found to display functional impairments in many areas of cognition and achievement (Allen et al., 2001; Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2005; Catroppa & Anderson, 1999, 2003, 2006; Fenwick & Anderson, 1999; Kinsella, Prior, Sawyer, & Murtagh, 1995; Lord-Maes & Obrzut, 1996; Slomine et al., 2002; Taylor et al., 1999; Taylor et al., 2002; Verger et al., 2000; Wozniak et al., 2007). Research has identified specific deficits in the area of working memory following pediatric TBI. For example, Levin et al. (2004) conducted a study of working memory in a Pediatric TBI sample with 144 participants ranging in severity from mild (Loss of consciousness < 15 min Glasgow Coma Score (GCS) 13-15), to severe (GCS < 9). They found that greater injury severity resulted in poorer performance on an n-back working memory task and that these effects persisted at 24 month follow-up. An earlier study demonstrated poorer n-back task performance in pediatric TBI participants in comparison to control group children (Levin et al., 2002). Mangeot, Armstrong, Colvin, Yeates, and Taylor (2002) used a parent rating form of executive functioning and assessed which neuropsychological measures predicted executive functioning outcomes. From a number of executive functioning, working memory, and memory tasks, only Consonant Trigrams (a working memory task) consistently accounted for unique variance in executive functioning. Ewing-Cobbs, Prasad, Landry, Kramer, and Deleon (2004) explored aspects of the central executive using an experimental working memory task. They found that compared to controls, pediatric TBI participants had difficulties with inhibition, but not set shifting, and that different patterns of impairment were related to the developmental stage of the child.

While it appears that impairments in aspects of working memory performance are well documented following pediatric TBI, there appears to be only one study that has employed the

Sternberg task in this population. Newsome et al., (2008) conducted an fMRI study with 8 adolescents (Mean age = 16.2,  $SD = 1.7$ ) with moderate to severe TBI (GCS 3-12) and 8 control subjects matched on age and gender. Injured participants were studied between 12 and 20 months post injury. Analysis of task accuracy and response time data revealed no significant group differences. When compared with the control participants, TBI participants demonstrated greater activation during encoding and retrieval in the dorsolateral and ventrolateral prefrontal cortex. During encoding TBI participants also demonstrated more extensive activation in the supplementary motor areas, paracentral lobule, insula, and visual cortex. The direction of activation was reversed during the maintenance stage with greater activation noted in the control group in prefrontal and parietal regions.

These patterns of activation were interpreted as indicating weaker maintenance of information in working memory following TBI with associated greater activation of neural networks during the encoding and retrieval phases to compensate for this.

Structural imaging also provides support for the feasibility of exploring working memory relationships in a pediatric TBI population. Many of the areas identified as central in working memory performance (see Table 1) have also been identified as vulnerable to the effects of TBI. Structural atrophy of the cerebellum (Spanos et al., 2007), cingulate gyrus (Yount et al., 2002), thalamus (Fearing et al., 2008), and frontal and temporal lobe structures (Wilde et al., 2007; Wilde et al., 2005) are prominent after traumatic brain injury. The volume of the corpus callosum (CC) has been shown to be related to the integrity of widely distributed neural networks and is also smaller in traumatically brain injured (TBI) samples (Mathias, Beall, & Bigler, 2004; Mathias, et al., 2004).

## Study Overview

The primary purpose of the present study is to explore working memory deficits in a group of children with traumatic brain injury (TBI). The secondary purpose is to determine whether the neural networks associated with aspects of the central executive in functional imaging studies with adults are apparent in TBI related morphological changes in a pediatric TBI sample and their matched controls. As depicted in Figure 3, there are three primary relationships reported in the literature that are to be investigated in the current study. Firstly, effective performance on the Sternberg tasks overall is correlated with efficient activation and communication between widely distributed neural networks – the volume of the corpus callosum (CC) is used as an index of the efficiency of widely distributed neural networks in the proposed study; secondly, predicted priming / interference effects of the Sternberg task is correlated with the integrity (size) of the right middle frontal gyrus (rMFG) - the literature reports that the rMFG may have a specialized role in the overall WM network in managing interference; thirdly, vulnerability to load demands on the Sternberg is correlated with the integrity (size) of the anterior cingulate gyrus (AC) – the literature reports that the AC may have a specialized role in the overall WM network in managing load demands.

The cingulate cortex demonstrates high levels of connectivity between posterior and anterior portions and the parietal and frontal regions activated in working memory tasks (van den Heuvel, Mandl, Luigjes, & Hulshoff Pol, 2008). Thus the present study also included the posterior cingulate and isthmus of the cingulate as variables and explored interactions of these variables with working memory indices.

## Methods

The data used in the present study is part of an ongoing brain injury research program coordinated by the Baylor College of Medicine. The raw imaging and Sternberg data was gleaned from an ongoing data collection network coordinated by the Baylor College of Medicine. The structural analysis (Freesurfer) and statistical analysis of results was conducted at the BYU Brain Imaging Lab.

### Participants

Data was gathered from 28 control children who were hospitalized for orthopedic injuries (OI), and 28 children who had sustained a moderate to severe traumatic brain injury (TBI), as defined by emergency department Glasgow Coma Score (GCS) between 3 and 12 (Teasdale & Jennett, 1974). Twenty-two children in the TBI group had scores in the severe range (GCS 3-9); mean for entire TBI group = 6.57,  $SD = 2.94$ . All participants were aged between 7 and 17 years at the time of injury ( $M = 13.2$ ,  $SD = 2.3$ ). Inclusion criteria for the TBI group included having a score of less than 4 on the Abbreviated Injury Scale (Association for the Advancement of Automotive Medicine, 1998) for areas of the body other than the head, and an upper limit for post resuscitation hypoxia or hypotension of 30 min. Inclusion criteria for the OI group included mild to moderate orthopedic injuries as defined by the Abbreviated Injury Scale. All participants were English-speaking, had at least a 37-week gestational period before birth, and had no previous hospitalization for head injury.

Efforts were made to ensure equivalence between TBI children and OI children on factors that impact cognitive functioning – these variables included maternal education level,

socioeconomic level, gender, and pre-injury variables including internalizing symptoms, externalizing symptoms, mood disturbance, and pre-injury indicators of executive functioning.

Operationalization of these variables included a socioeconomic index (SCI) that considers occupational status, annual family income, and years of maternal education. The SCI was calculated according to the guidelines outlined in Yeates et al. (1997); with higher scores reflecting higher socioeconomic status. This information was collected via a demographics questionnaire filled in by the parent. The BASC-2: Behavior Assessment System for Children, Second Edition was employed to assess pre-injury internalizing externalizing and mood symptoms. The BASC-2 is a 160 item parent report questionnaire that has scales for attention problems, hyperactivity, depression, and anxiety, and index scores for externalizing problems and internalizing problems (Reynolds & Kamphaus, 2004). The BRIEF: Behavior Rating Inventory of Executive Function parent form was used to quantify pre-injury behavioral indicators of executive functioning (Gioia, Isquith, Guy, & Kenworthy, 2000). The BRIEF is an 86 item parent report measure and the BRIEF scales used in the equivalence analysis provide an indication of functioning in the following areas: emotional control, shifting attention, inhibition, self-monitoring, organization of materials, planning / organization, initiation, and working memory.

All participants are currently engaged in a longitudinal multisite (San Antonio, Dallas, Miami) study of the lingering effects of TBI coordinated by Baylor College of Medicine. Institutional review board (Brigham Young University (E090145), Baylor College of Medicine (H-4373)) approval was obtained for the current study. Informed consent by each participant's parent or guardian and assent by each child prior to participation in data collection was previously obtained as part of the longitudinal study process.

## **MRI Acquisition**

All subjects underwent MRI without sedation on Philips 1.5 T Intera scanners (Philips, Best, Netherlands) at hospitals in Houston, Dallas and Miami, including Children's Medical Center Dallas (Dallas), Parkland Memorial Hospital (Dallas), Cook Children's Medical Center (Fort Worth), Baylor Institute for Rehabilitation (Dallas), Our Children's House at Baylor (Dallas), Texas Children's Hospital (Houston) and Jackson Memorial Hospital (Miami), Miami Children's Hospital (Miami). T1-weighted (15 ms TR, 4.6 ms TE, 1.0 mm slices) 3D sagittal acquisition series were used for volumetric analysis. A 256 mm field of view (FOV) was used for these series with a reconstructed voxel size of 1 x 1 x 1 mm.

## **Volumetric Acquisition**

Structural MRI scans were processed using Freesurfer software to glean the volume of the 7 structural variables of interest for this study:

- Anterior Cingulate (AntCin)
- Isthmus Cingulate (IstCin)
- Posterior Cingulate (PosCin)
- Total Cingulate (TotCin)
- Right Rostral Middle Frontal Gyrus (RtRosMidFro)
- Right Caudal Middle Frontal Gyrus (RtCauMidFro)
- Corpus Callosum (TotCC)

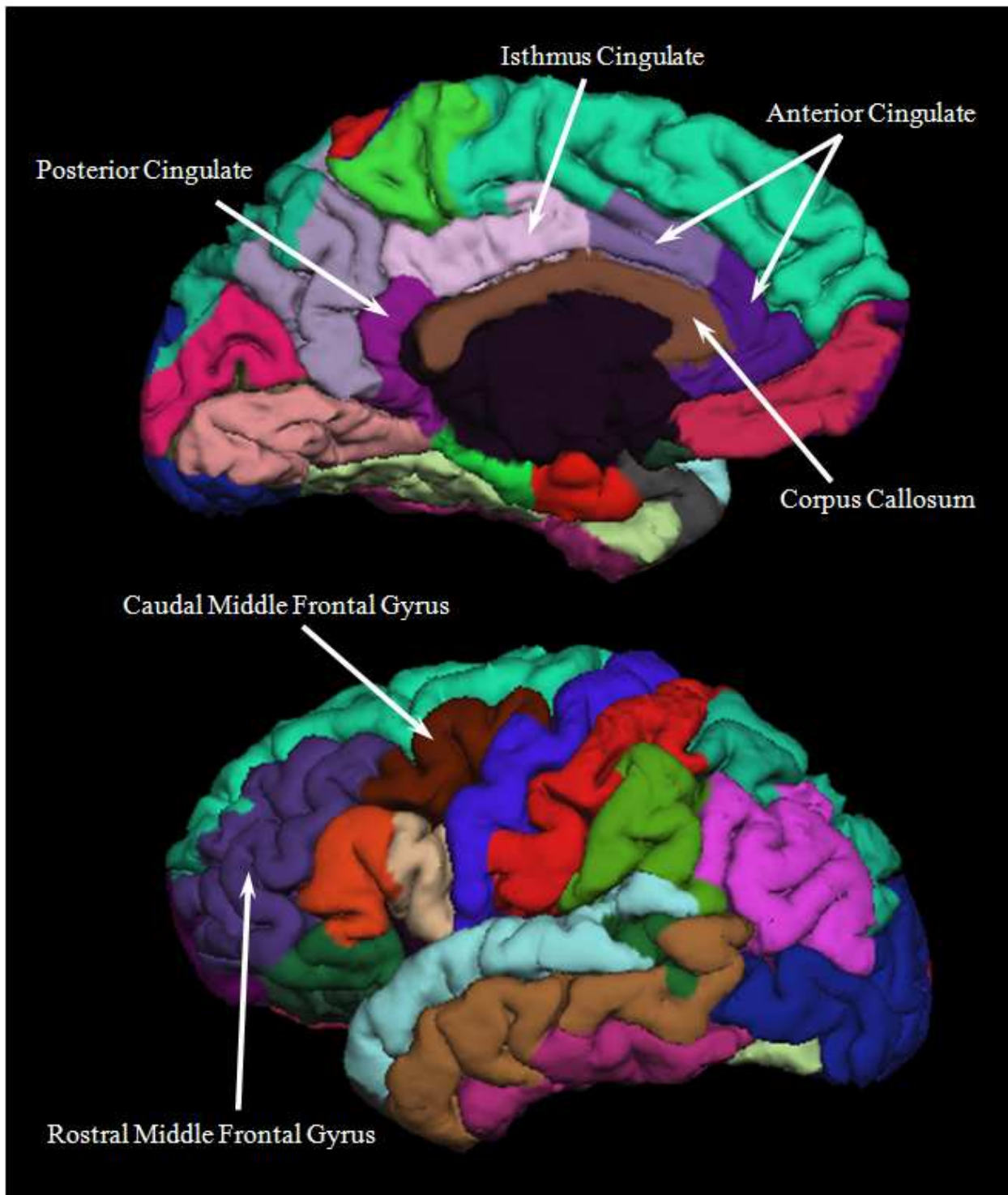


Freesurfer is an automated parcellation software program that is capable of providing volumetric and cortical thickness measures for cortical structures from a high resolution T1 weighted 3-D MRI dataset. Freesurfer first corrects for intensity variations in the original images and then removes non-cerebral voxels using a skull stripping procedure (Dale, Fischl, & Sereno, 1999; Desikan et al., 2006; Fennema-Notestine et al., 2006; Fischl & Dale, 2000; Fischl, Sereno, & Dale, 1999; Fischl, Sereno, Tootell, & Dale, 1999). The resulting image is then segmented in a variety of steps to produce several subcortical and cortical areas (see Figure 4 for a visual image of one stage of the parcellation for a participant in this study); volumetric, grey matter thickness, and curvature variables are tabulated (Fischl, Liu, & Dale, 2001; Fischl et al., 2002; Fischl et al., 2004). Several reliability and validity studies have confirmed the accuracy of this methodology (Ju et al., 2005; Lee et al., 2006; Makris et al., 2005; Tae, Kim, Lee, Nam, & Kim, 2008).

Scans from all participants in this study were processed using Freesurfer software. Parcellation results were visually examined for accuracy and any participants with errors in the automated process were re-analyzed using a standard editing procedure. For each region of interest the raw volume was corrected for total intracranial volume by dividing the raw value by the volume of the intracranial vault generated by the freesurfer parcellation software, and multiplying this value by 100. The resulting variable is the percentage of the intracranial vault that is filled by the respective structure.

### **Sternberg Memory Task**

The Sternberg memory task is depicted in Figure 2. Each child viewed a memory set of 1, 4, or 6 uppercase letters for 1700 ms on a 13" laptop computer screen and after a 4000 ms



*Figure 4.* Freesurfer cortical parcellation with indication of regions of interest for the current study.

delay identified whether a probe letter had been in the memory set. On interference trials (limited to sets with 4 letters), the probe letter was present in the memory set on the immediately preceding trial, thus introducing priming / interference. Trials from load 1, load 4 and load 6 were randomized and then trials from load 4 interference were overlaid prior to the load 4 trials. Twenty-four trials of each memory load were presented using E-prime software, there were an equal number of “yes” and “no” trials. Variables gathered from this procedure were the number of errors for each condition and reaction time for correct responses for each condition. For the load 4 and load 4-interference conditions, separate error rates and reaction times were also gathered dependent on whether the correct response was “yes” (probe present in current encoding array) or “no” (probe not present). Six types of data were created by this process:

- Percentage of errors for each memory set (1,4,6, 4interference).
- Average response time for each memory set (1,4,6, 4interference).
- Percent errors correct response “no” (4, 4 interference)
- Average response time correct response “no” (4, 4 interference)
- Percent errors correct response “yes” (4, 4 interference)
- Average response time correct response “yes” (4, 4 interference)

## **Procedure**

Parental consent and child assent were obtained in accordance with the Institutional Review Boards’ approved guidelines at each medical center. Parents were approached by a research assistant during the child’s hospital admission or within one week of discharge. Data was collected at baseline (within 1 month of injury), and at 3 months ( $\pm 1$  month). Baseline data gathering included demographic questionnaire, BASC-2, and BRIEF. Data gathered at the 3

month mark included MRI acquisition and the Sternberg assessment which were performed on the same day.

### **Summary of the Variables of Interest:**

- Group Membership:
  - Pediatric moderate to severe traumatic brain injury (TBI)
  - Orthopedic Injury Control (OI)
  
- Sternberg Data (see Figure 2):
  - Load 1
    - Average response time (L1-RT)
    - Percent Errors (L1-E)
  
  - Load 4
    - Average response time (L4-RT)
    - Percent Errors (L4-E)
    - Probe absent “no” response time (L4 probe abs-RT)
    - Probe present “yes” response time (L4 probe pres-RT)
    - Probe absent “no” errors (L4 probe abs-E)
    - Probe present “yes” errors (L4 probe pres-E)
  
  - Load 6
    - Average response time (L6-RT)
    - Percent Errors (L6-E)

- Load 4 Interference
  - Average response time (L4i-RT)
  - Percent Errors (L4i-E)
  - Probe absent “no” response time (L4i probe abs-RT)
  - Probe present “yes” response time (L4i probe pres-RT)
  - Probe absent “no” errors (L4i probe abs-E)
  - Probe present “yes” errors (L4i probe pres-E)
  
- Sternberg Vulnerability Data:
  - Vulnerability to Load Demands
    - Change in average response time (Load Inc. (6-4)-RT)
      - calculation: L6-RT minus L4-RT
    - Change in percent errors (Load Inc. (6-4)-E)
      - calculation: L6-E minus L4-E
  - Vulnerability to Interference Demands – change when moving from nonprimed to primed condition
    - Change in response time for all conditions (Int.Total (4i-4)-RT)
      - calculation: L4i-RT minus L4-RT
    - Change in percent errors for all conditions (Int.Total (4i-4)-E)
      - calculation: L4i-E minus L4-E
  - Secondary vulnerability to interference variables
    - Change in response time for probe absent “no” trials (Int. probe abs (4i-4)-RT)

- calculation: (L4int probe abs-RT) minus (L4 probe abs-RT)
  - Change in response time for probe present “yes” trials (Int. probe pres (4i-4)-RT)
    - calculation: (L4int probe pres-RT) minus (L4 probe pres-RT)
  - Change in percent errors, probe absent “no” trials (Int. probe abs (4i-4)-E)
    - calculation: (L4int probe abs-E) minus (L4 probe abs-E)
  - Change in percent errors for probe present “yes” trials (Int. probe pres (4i-4)-E)
    - calculation: (L4int probe pres-E) minus (L4 probe pres-E)
- Brain Volumes Adjusted for Intracranial Volume for regions of interest:
  - Anterior Cingulate (AntCin)
  - Isthmus Cingulate (IstCin)
  - Posterior Cingulate (PosCin)
  - Total Cingulate (TotCin)
  - Right Rostral Middle Frontal Gyrus (RtRosMidFro)
  - Right Caudal Middle Frontal Gyrus (RtCauMidFro)
  - Corpus Callosum (TotCC)

## Hypotheses and Analyses

### Preinjury Group Equivalence

A series of one way ANOVAs was used to determine whether the TBI and OI groups differed significantly on baseline demographic and psychological variables as listed in the methods section.

### Behavioral and Volumetric Comparisons

**Hypothesis one.** Participants in the OI group will outperform the TBI group on each of the load conditions of the Sternberg Task and there will be an interaction effect such that discrepancies between the groups will be more pronounced as task difficulty (load) increases.

*Analysis.* Two ANOVAs were conducted one with percent errors as the DV and the other reaction time, between subject variables being Group (OI, TBI) and Level (L1, L4, L6). Identical analyses were also performed to compare level variables L4 with L4i and to compare L4 and L4i responses split into probe absent and probe present conditions. Where main effects were identified, the location of differences was clarified using the least significant difference method where indicated.

**Hypothesis Two.** Participants in the OI group will benefit more from positive priming and be less vulnerable to the effects of negative priming than the TBI group. They will also be less vulnerable to increases in load demands. Differences will be apparent for errors and response time.

**Analysis.** Two one-way MANOVA analyses were conducted with dependent variables consisting of errors and reaction time for the primary vulnerability indexes. One MANOVA tested vulnerability to load, the other vulnerability to interference. ANOVA models were employed to determine whether percent errors or reaction times differed for secondary vulnerability to interference measures that split responses in the L4 and L4i conditions into probe present or absent conditions. Where main effects were identified, the location of differences was clarified using the least significant difference method where indicated.

**Hypothesis three.** The TBI group will have lower adjusted volume in the regions of interest than the OI group.

**Analysis.** A one-way MANOVA with group as the IV, and DVs being seven adjusted brain volume measures: AntCin, IstCin, PosCin, TotCin, RtRosMidFro, RtCauMidFro, TotCC. Univariate comparisons (ANOVAs) were employed to identify the specific variables contributing to multivariate effects.

### **Working Memory Model Comparisons**

**General hypothesis.** The overarching general hypothesis of this section is that deficits in working memory as defined by impaired performance on the Sternberg working memory task are associated with reduced integrity of the regional brain networks associated with general and specific aspects of working memory performance.

The associated specific hypotheses drawn from this general thesis are detailed below.



**Hypothesis four.** Vulnerability to increased load variables will be correlated with TotCC volume and AntCin volumes but not Rt Mid Fro volumes.

**Hypothesis five.** Vulnerability to increased interference demand variables will be correlated with TotCC, RtRosMidFro, and RtCauMidFro volume but not AntCin volumes.

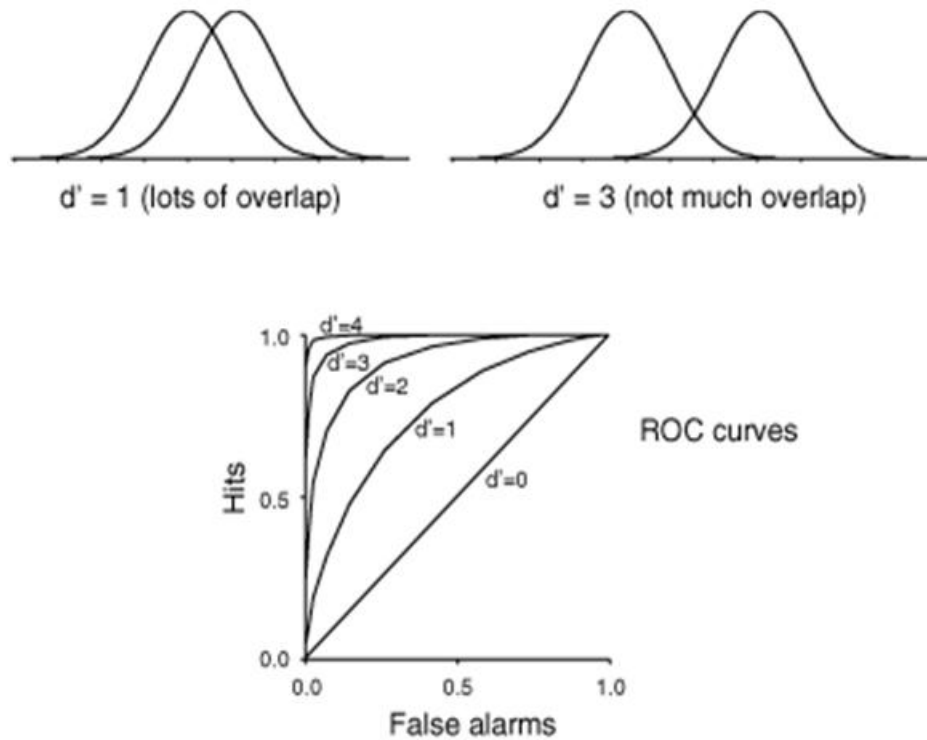
*Analysis.* This analysis involved calculating separate Pearson's correlations for the combined sample, the TBI sample, and the OI sample using a cross tabulation of the vulnerability variables and the brain region variables. Where significant relationships exist scatter plots were produced.

### **Discriminability and Response Bias**

Discriminability ( $d'$ ) is a measure of subjects' ability to discriminate between letters that were in the memory set and false alarms. Typically the range is from approximately 0 to 4, where 0 represents a random or non-discriminating response pattern and 3+ represents nearly perfect discrimination (see Figure 5). The response bias measure "criterion ( $c$ )" is an indicator of tendency to be biased to respond either "yes" or "no;" with negative scores indicating a bias to respond "yes."

**Hypothesis six.** The TBI group will have significantly lower discriminability and significantly larger response bias than the OI group.

*Analysis.* Two two-way ANOVAs were conducted one with discriminability as the DV and the other with criterion as the DV; between subject variables being Group (OI, TBI) and Level (L4, L4i).



*Figure 5.* Noise and signal + noise histograms for various levels of discriminability ( $d'$ ) with associated isosensitivity or receiver operating characteristic (ROC) curves.

### Analysis Software

Discriminability and Response bias measures were computed using Microsoft Excel according to the formulae described by MacMillan and Creelman (2005). All other data analyses for this dissertation were generated using SAS software, Version 9.13 of the SAS System for Windows. Copyright © 2003 SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA.

## Results

### Pre-injury Group Equivalence Data

Twenty-eight TBI patients (19 male, 9 female) and 28 OI patients (21 male, 7 female) participated in the study. A chi-squared analysis was used to assess gender composition equivalence; the results indicated no statistically significant difference between the groups on gender composition ( $\chi^2 = 0.35, p = \text{n.s.}$ ).

Univariate analyses to explore potential differences for pre-injury non-categorical variables are summarized in Table 2. These analyses indicate that the differences between the groups on all pre-injury variables assessed in this study were not statistically significant.

### Behavioral and Volumetric Comparisons

#### Hypothesis One Results – Errors and Reaction Time

Hypothesis One: Participants in the OC group will outperform the TBI group on each of the load conditions of the Sternberg Task and there will be an interaction effect such that discrepancies between the groups will be more pronounced as task difficulty (load) increases.

Separate analyses were conducted for the dependent variables percent errors and reaction time. Three ANOVAs were performed for each dependent variable: 1) Group (OI, TBI) x Load (L1, L4, L6), 2) Group (OI, TBI) x Load (L4, L4int), and 3) Group (OI, TBI) x Load (L4, L4int), x Probe (Absent, Present).

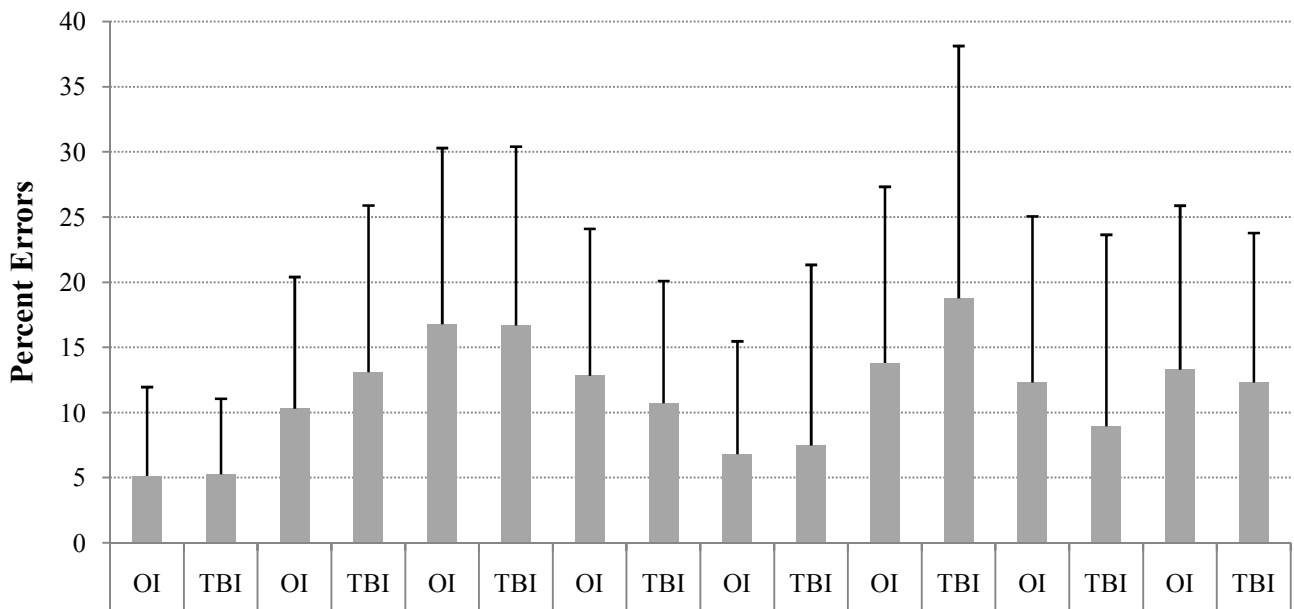
Table 2.

Descriptive Data for traumatic brain injury and orthopedic injury groups with equivalence analysis results for pre-injury variables.

Variable	TBI Group		OI Group		<i>F</i> -value	prob.
	Mean	<i>SD</i>	Mean	<i>SD</i>		
<i>Demographics</i>						
Participant Age (years)	13.57	2.46	12.75	2.13	1.78	.19
Maternal Education (years)	12.65	3.31	13.81	2.63	2.01	.16
Social Composite Index (z)	.01	.95	.07	.78	.07	.79
<i>BASC-2 Scales (T-scores)</i>						
Attention Problems	52.67	11.39	50.40	9.02	.495	.49
Hyperactivity	50.14	8.54	49.85	6.64	.015	.90
Anxiety	47.10	13.39	43.65	8.88	.933	.34
Depression	48.33	9.11	48.30	10.77	.000	.99
Externalizing Probs. Index	50.81	7.07	49.55	6.80	.337	.57
Internalizing Probs. Index	46.71	11.17	44.85	8.55	.358	.55
<i>BRIEF Scales (raw-scores)</i>						
Inhibition	14.70	3.10	14.56	3.57	.020	.89
Shift	11.57	2.76	12.00	2.75	.298	.59
Emotional Control	13.43	3.20	13.60	2.77	.037	.85
Initiate	13.13	3.27	12.72	2.87	.215	.65
Working Memory	16.00	5.33	15.92	4.98	.003	.96
Plan/Organize	20.61	5.79	20.56	5.37	.001	.98
Organization of Materials	11.30	3.27	11.40	3.51	.009	.92
Monitor	13.83	3.95	14.08	3.59	.054	.82

Note: BASC-2 = Behavior Assessment System for Children, Second Edition, BRIEF = Behavior Rating Inventory of Executive Function, z = z-score, prob. = probability.

**Sternberg percent errors analysis results.** The analysis for L1, L4 and L6 indicated a significant effect for load level,  $F(2,162) = 15.66, p < .01$ . The group effect and group x level interaction effect were not significant. There were no significant main or interaction effects for the analysis of the L4, L4int grouping. For the L4, L4int split by probe type analysis there was a significant effect for probe type,  $F(1, 216) = 9.61, p < .01$ ; all other main and interaction effects were not significant (see Appendix 1, Table 14 for ANOVA table of the three percent error analyses). Follow-up tests were conducted to evaluate pairwise differences where main effects were apparent in these three analyses using a least significant difference procedure. Descriptive statistics and the results of follow-up tests are reported in Figure 6 and Table 3.



Note: no significant univariate differences between OI and TBI pairs evident in figure above.

*Figure 6.* Percent Errors on differing Sternberg load conditions Orthopedic Injury (OI) versus Traumatic Brain Injury (TBI) groups; mean and SD displayed.

Table 3.

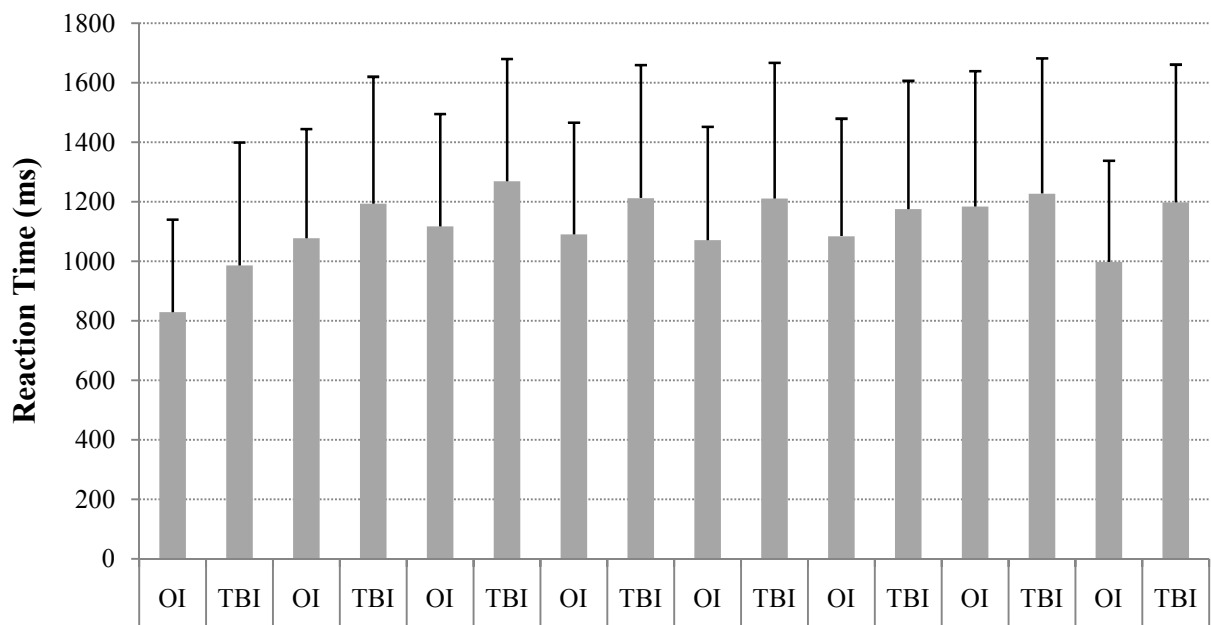
Descriptive statistics and follow-up analyses results for Percent Errors on Sternberg load conditions and participant grouping.

Level	Grp.	Mean (SD)	Level / Probe	Mean (SD)	Group	Mean (SD)
<i><u>L1,L4,L6 analysis</u></i>						
L1	OI	5.13 (6.82)	L1 <sup>a</sup>	5.20 (6.27)	OI	10.74 (11.43)
L1	TBI	5.27 (5.78)	L4 <sup>b</sup>	11.69 (11.51)	TBI	11.68 (12.17)
L4	OI	10.29 (10.10)	L6 <sup>c</sup>	16.73 (13.49)		
L4	TBI	13.10 (12.80)				
L6	OI	16.77 (13.51)				
L6	TBI	16.68 (13.71)				
<i><u>L4, L4i analysis</u></i>						
L4	OI	10.29 (10.10)	L4	11.69 (11.51)	OI	11.56 (10.67)
L4	TBI	13.10 (12.80)	L4i	11.78 (10.31)	TBI	11.90 (11.18)
L4i	OI	12.84 (11.25)				
L4i	TBI	10.71 (9.37)				
<i><u>L4 and L4int split by probe type analysis</u></i>						
L4ProAbs	OI	6.80 (8.67)	L4	11.71 (15.00)	OI	11.55 (12.19)
L4ProAbs	TBI	7.47 (13.86)	L4i	11.72 (12.85)	TBI	11.88 (15.53)
L4ProPres	OI	13.80 (13.53)				
L4ProPres	TBI	18.77 (19.35)	Absent <sup>a</sup>	8.88 (12.71)		
L4iProAbs	OI	12.32 (12.73)	Present <sup>b</sup>	14.54 (14.57)		
L4iProAbs	TBI	8.96 (14.69)				
L4iProPres	OI	13.28 (12.59)				
L4iProPres	TBI	12.31 (11.46)				

Note: descriptors with different superscripts that are in same column and same analysis group are significantly different at alpha = .05. Individual comparison and type 1 error rate = alpha. Follow-up testing is only reported where significant main or interaction effects were found.

**Sternberg reaction time analysis results.** The analysis for L1, L4 and L6 indicated a significant effect for load level,  $F(2,162) = 8.55, p < .01$ , and group,  $F(2,162) = 5.63, p < .05$ . The group x level interaction effect was not significant. There were no significant main or interaction effects for the analysis of the L4, L4int grouping. For the L4, L4int split by probe type analysis there was a significant effect for group,  $F(1, 216) = 4.39, p < .05$ ; other main effects and interaction effects were not significant (see Appendix 1, Table 15 for ANOVA table of the three reaction time analyses). Follow-up tests were conducted to evaluate pairwise differences where main effects were apparent in these three analyses using a least significant difference test.

Descriptive statistics and the results of the follow-up tests are reported in Figure 7 and Table 4.



Note: no significant univariate differences between OI and TBI pairs evident in figure above.

*Figure 7.* Reaction Time on Sternberg Load Conditions Orthopedic Injury (OI) versus Traumatic Brain Injury (TBI) groups; mean and SD displayed.

Table 4.

Descriptive statistics and follow-up analyses results for Reaction Time (ms) on Sternberg load conditions and participant grouping.

Level	Grp.	Mean (SD)	Level / Probe	Mean (SD)	Group	Mean (SD)
<i><u>L1,L4,L6 analysis</u></i>						
L1	OI	829 (310)	L1 <sup>b</sup>	908 (370)	OI <sup>a</sup>	1007 (371)
L1	TBI	986 (412)	L4 <sup>a</sup>	1135 (398)	TBI <sup>b</sup>	1149 (429)
L4	OI	1078 (366)	L6 <sup>a</sup>	1192 (398)		
L4	TBI	1193 (426)				
L6	OI	1117 (377)				
L6	TBI	1269 (411)				
<i><u>L4, L4i analysis</u></i>						
L4	OI	1077 (366)	L4	1135 (398)	OI	1084 (367)
L4	TBI	1193 (426)	L4i	1151 (413)	TBI	1202 (433)
L4i	OI	1090 (375)				
L4i	TBI	1212 (467)				
<i><u>L4 and L4int split by probe type analysis</u></i>						
L4ProAbs	OI	1070 (381)	L4	1135 (415)	OI <sup>a</sup>	1084 (395)
L4ProAbs	TBI	1211 (455)	L4i	1151 (434)	TBI <sup>b</sup>	1203 (445)
L4ProPres	OI	1084 (394)				
L4ProPres	TBI	1175 (430)	Absent	1173 (436)		
L4iProAbs	OI	1183 (455)	Present	1113 (412)		
L4iProAbs	TBI	1227 (454)				
L4iProPres	OI	997 (340)				
L4iProPres	TBI	1197 (463)				

Note: descriptors with different superscripts that are in same column and same analysis group are significantly different at alpha = .05. Individual comparison and type 1 error rate = alpha. Follow-up testing is only reported where significant main or interaction effects were found.



Results Summary for Hypothesis One: The results described above partially support the assertions of hypothesis one. Overall on the L1, L4, L6 conditions the OI participants had significantly faster reaction times than the TBI group (Cohen's effect size  $d = .35$ ). There were no identified group differences on percentage errors. More pronounced discrepancies between groups as task difficulty increased (interaction effects) were not apparent.

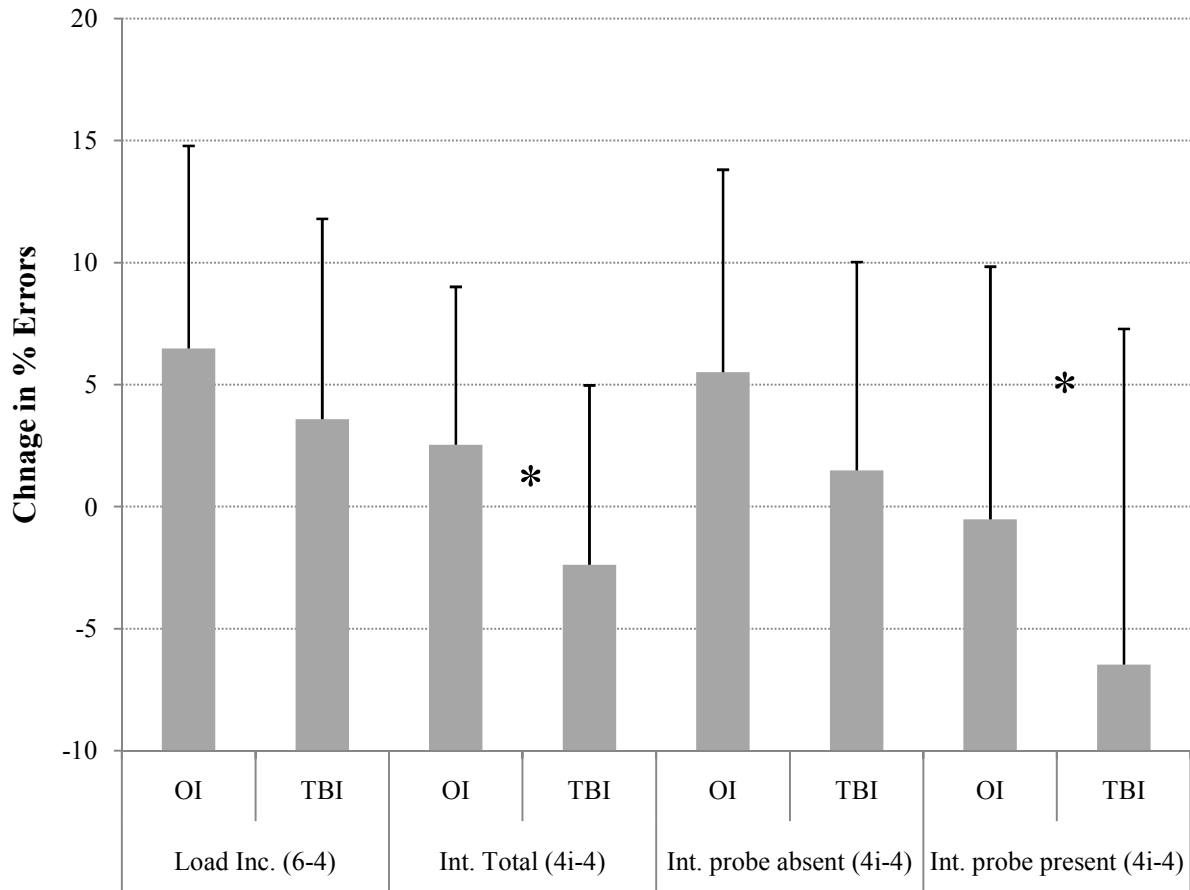
### **Hypothesis Two Results – Interference and Load Increases**

Hypothesis Two: Participants in the OI group will benefit from positive priming and be less vulnerable to the effects of negative priming than the TBI group. They will also be less vulnerable to increases in Load demands. Differences will be apparent for errors and response time.

**Vulnerability to interference and load increases results.** Changes in percent errors and reaction time due to interference and load changes are presented in Figure 8 and Figure 9 respectively. Vulnerability to Load increases was assessed using a MANOVA with DVs percent errors and reaction time (Load Inc. (6-4)-E and Load Inc. (6-4)-RT) and IV as group (OI, TBI). The multivariate analysis was not significant, Wilks' Lambda = .937,  $F(2, 53) = 1.77$ ,  $p = n.s.$ ; univariate comparisons were also not statistically significant.

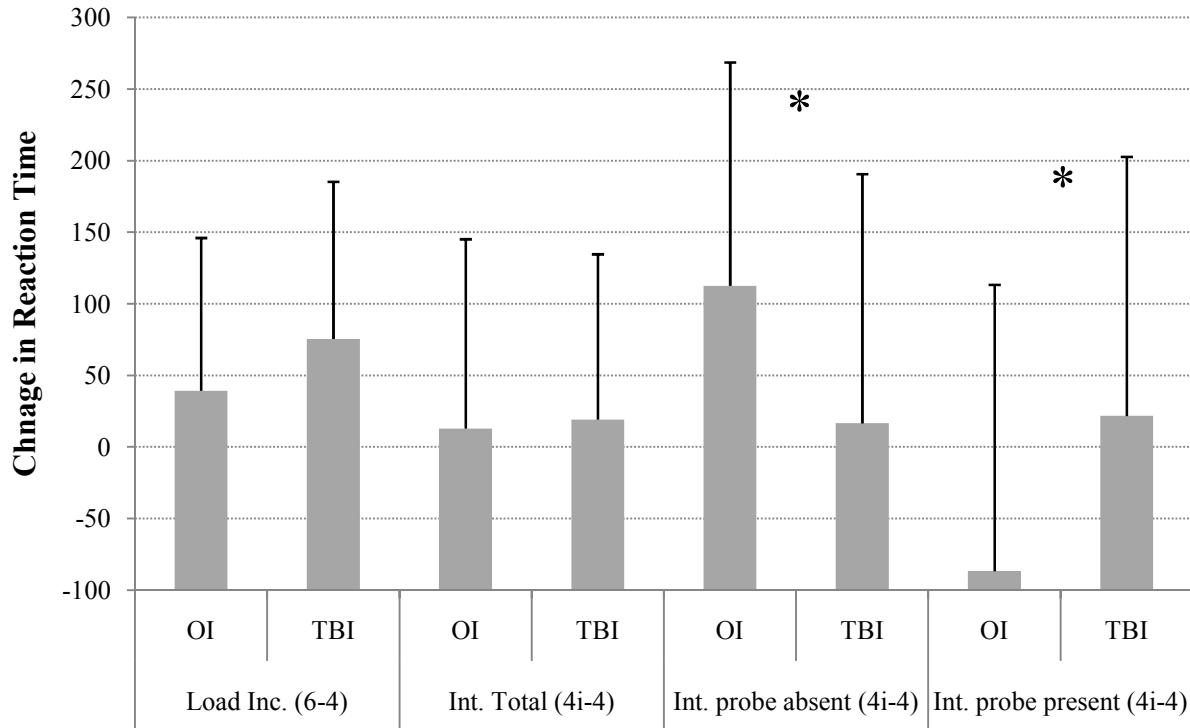
The Sternberg paradigm used in this study adds proactive interference. To determine if interference had an overall effect on performance a MANOVA was performed with DVs of percent errors and reaction time (Int.Total (4i-4)-E and Int.Total (4i-4)-RT) and IV as group (OI, TBI). The multivariate analysis was significant, Wilks' Lambda = .879,  $F(2, 53) = 1.77$ ,  $p < .05$ ;

univariate comparisons indicated that reaction time measures were not statistically significant but error differences were  $F(1,54) = 7.08, p < .05$ . Descriptive statistics and the results of the follow-up tests are reported in Table 5.



\* indicates significant difference ( $p \leq .05$ ) between OI-TBI pairing on variable listed on x-axis.

*Figure 8.* Vulnerability to load and interference increases, change in percent errors by condition and group; mean and SD displayed.



\* indicates significant difference ( $p \leq .05$ ) between OI-TBI pairing on variable listed on x-axis.

*Figure 9.* Vulnerability to load and interference increases, change in reaction time by condition and group; mean and SD displayed.

There is potential for interference in the Sternberg task to either help or hinder performance. Interference can potentially help in performance of the current trial if the person is primed to the probe letter for the current trial in both the current array and the array of the previous trial (see the second interference example in Figure 2). If the probe letter for the current trial appears in the previous trial array but not the current array the priming of the previous array must be inhibited for a correct response, potentially hindering performance (see the first interference example in Figure 2). To determine if there were differences in performance based on the nature of the probe (absent or present in current array), two two-way ANOVA analyses

Table 5.

Descriptive statistics and follow-up analyses results pertaining to MANOVAs exploring overall vulnerability to increased load and the addition of interference.

Error Variable	Grp.	Mean (SD)	Reaction Time Variable	Grp.	Mean (SD)
<i>Vulnerability to load increase analysis</i>					
Load Inc. (6-4)-E	OI	6.47 (8.30)	Load Inc. (6-4)-RT	OI	39.26 (106.77)
Load Inc. (6-4)-E	TBI	3.58 (8.21)	Load Inc. (6-4)-RT	TBI	75.43 (109.78)
<i>Vulnerability to addition of interference analysis</i>					
Int.Total (4i-4)-E	OI <sup>a</sup>	2.54 (6.47)	Int.Total (4i-4)-RT	OI	12.92 (132.16)
Int.Total (4i-4)-E	TBI <sup>b</sup>	-2.38 (7.34)	Int.Total (4i-4)-RT	TBI	19.16 (115.43)

Note: descriptors with different superscripts that are in same column and same analysis group are significantly different at  $\alpha = .05$ . Individual comparison and type 1 error rate = alpha. Follow-up testing is only reported where significant main or interaction effects were found.

were performed one with DV percent errors, the other with DV reaction time; IVs were Group (OI, TBI) and probe type (Int. probe abs (4i-4), Int. probe pres (4i-4)).

The results of the analysis with DV Percent Errors indicated a significant effect for group  $F(1,108) = 6.37, p < .05$ , and probe type,  $F(1,108) = 12.51, p < .01$ . The group x probe type interaction effect was not significant. For the Reaction Time analysis there was a significant main effect for probe type,  $F(1, 108) = 8.28, p < .01$ . The group level effect was not significant

but there was a significant group x probe type interaction,  $F(1, 108) = 9.19, p < .01$ . The results of these analyses are graphically represented in Figure 10 and Figure 11. Follow-up tests were conducted to evaluate pairwise differences where main effects were apparent in these three analyses using a least significant difference test. Descriptive statistics and the results of the follow-up tests are reported in Table 6 (ANOVA Tables are in Appendix 1, Table 16).

Table 6.

Descriptive statistics and follow-up analyses results for vulnerability to interference split by probe condition and participant group analyses.

Probe	Grp.	Mean (SD)	Probe (all groups)	Mean (SD)	Group (all levels)	Mean (SD)
<i>Vulnerability to interference Percent Errors analysis</i>						
absent	OI	5.51 (8.29)	absent <sup>a</sup>	3.50 (8.58)	OI <sup>a</sup>	2.50 (9.78)
absent	TBI	1.48 (8.53)	present <sup>b</sup>	-3.49 (12.42)	TBI <sup>b</sup>	-2.48 (12.02)
present	OI	-0.51 (10.34)				
present	TBI	-6.46 (13.75)				
<i>Vulnerability to interference Reaction Time analysis</i>						
absent	OI <sup>a</sup>	112.52 (156.02)	absent <sup>a</sup>	64.55 (170.79)	OI	12.91 (204.18)
absent	TBI <sup>c</sup>	16.56 (174.07)	present <sup>b</sup>	-32.46 (196.67)	TBI	19.16 (175.87)
present	OI <sup>b</sup>	-86.69 (200.01)				
present	TBI <sup>c</sup>	21.76 (180.80)				

Note: descriptors with different superscripts that are in same column and same analysis group are significantly different at  $\alpha = .05$ . Individual comparison and type 1 error rate =  $\alpha$ . Follow-up testing is only reported where significant main or interaction effects were found.

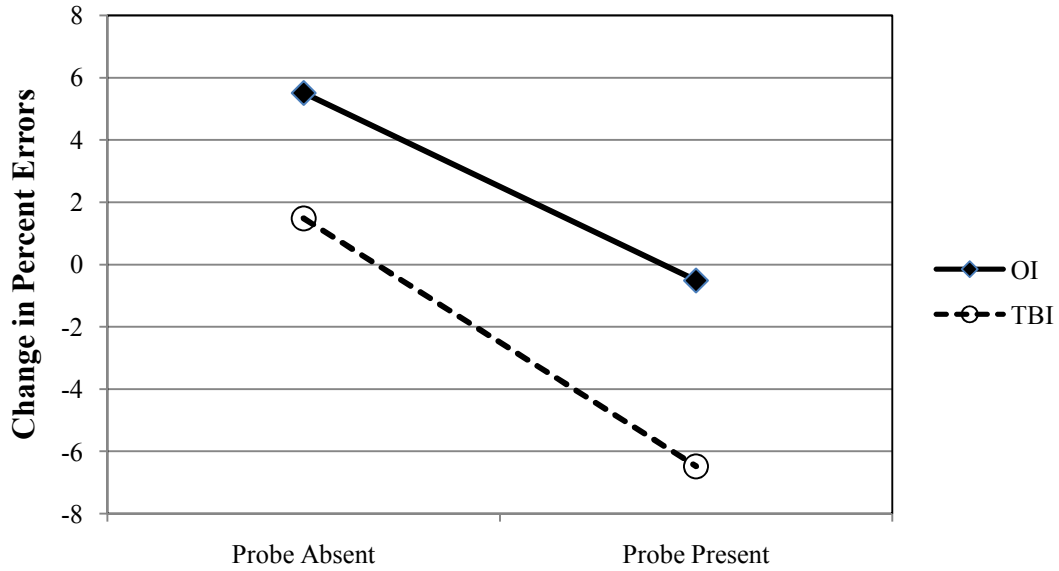


Figure 10. Change in Percent Errors when moving from Load 4 to Load 4 interference condition for probe absent or probe present trials.

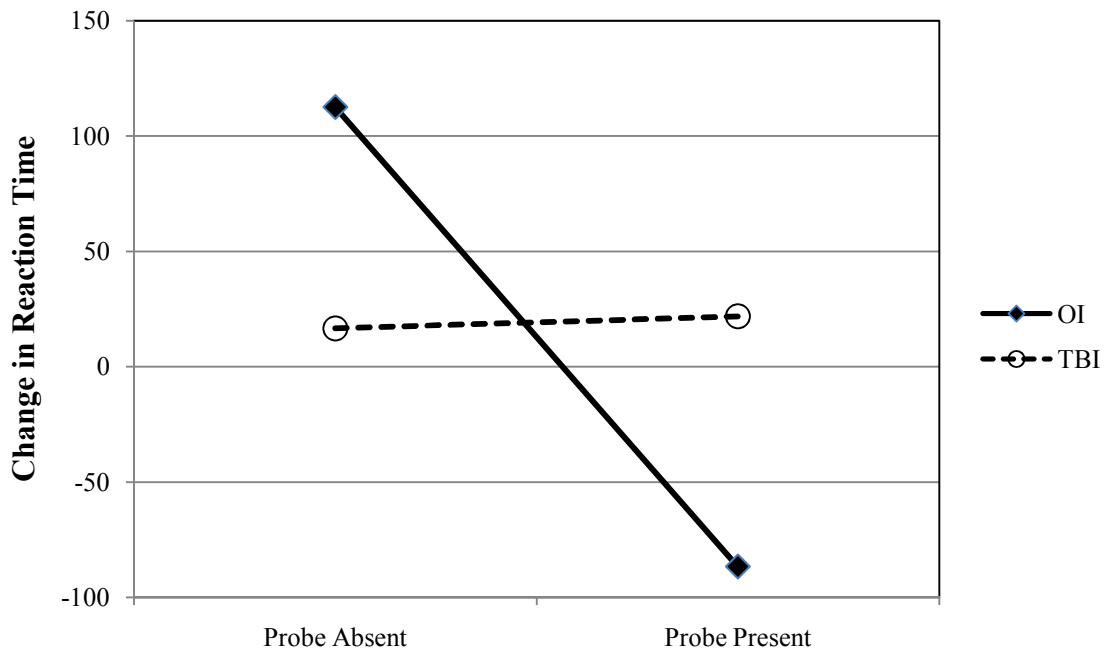


Figure 11. Change in Reaction Time when moving from Load 4 to Load 4 interference condition for probe absent or probe present trials.

Results Summary for Hypothesis Two: The results only partially supported the assertion of hypothesis two. No significant effects were found between groups for changes in load demands. Consistent with hypothesis two, OI participants did benefit from positive priming in terms of reduced reaction time when compared to TBI participants (Cohen's  $d = 0.57$ ). None of the other assertions of hypothesis two were supported.

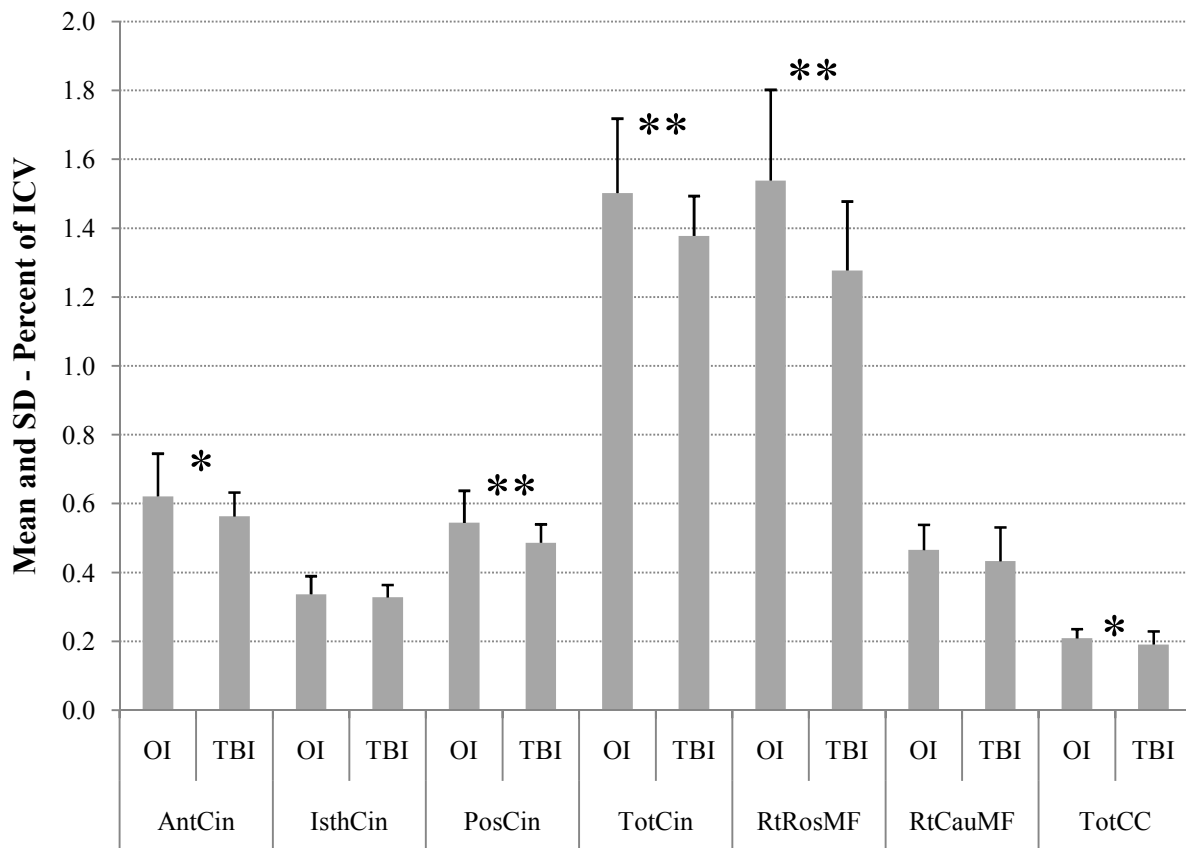
In contradiction to hypothesis two, OI participants were more vulnerable to the effects of negative priming (in terms of increased reaction time) than the TBI group ( $d = -0.58$ ). In terms of the reaction time data for the probe absent / probe present analysis (see Figure 11) the OI group benefitted and was hampered by positive and negative priming as anticipated (positive-negative priming contrast:  $d = 1.11$ ), but priming appeared to have minimal effect on the reaction times of the TBI group (positive-negative priming contrast:  $d = 0.03$ ).

In terms of errors and negative and positive priming there was a significant finding suggesting that priming overall led to a slight reduction in percent errors for the TBI group and a slight increase for the OI group,  $d = -0.45$  (see Figure 10). No interaction effects were apparent and both the OI and the TBI group demonstrated a pattern of increased errors for negative priming conditions and reduced errors for positive priming conditions,  $d = 0.65$ .

### **Hypothesis Three Results – Brain Volume**

Hypothesis Three: The TBI group will have lower adjusted volume in the regions of interest than the OI group.

**Brain volume analysis results.** A MANOVA was performed on corrected brain volumes to determine if there were significant differences in the regions of interest for this study. Results indicate significant differences between the groups, Wilks' Lambda = .687,  $F(6, 49)=3.71$ ,  $p < .01$ . Descriptive statistics for brain variables and univariate analyses are presented in Figure 12 and Table 7 (ANOVA tables for univariate analyses can be found in Appendix 1, Table 17).



\* indicates significant difference between OI-TBI pairing on variable, pairwise Type 1 error rate alpha = .05.

\*\* indicates significant difference between OI-TBI pairing on variable, pairwise Type 1 error rate alpha = .01.

*Figure 12.* Percent of intra-cranial volume occupied by regions of interest for OI and TBI groups.



Table 7.

Descriptive statistics and univariate analyses results for regions of interest by group (OI, TBI).

Area of Interest		Raw volume (mm <sup>3</sup> )		% of intracranial volume		<i>F</i> -value
		Mean	<i>SD</i>	Mean	<i>SD</i>	
Anterior Cingulate	OI	8861.8	2058.6	0.621	0.124	4.63*
	TBI	8359.8	1187.6	0.563	0.069	
Isthmus Cingulate	OI	4777.9	727.6	0.337	0.053	0.51
	TBI	4867.0	628.4	0.328	0.036	
Posterior Cingulate	OI	7738.9	1377.0	0.544	0.093	8.19**
	TBI	7209.2	876.7	0.486	0.054	
Total Cingulate	OI	21378.6	3433.5	1.502	0.216	7.32**
	TBI	20436.0	2130.3	1.377	0.116	
Right Rostral Middle Frontal Gyrus	OI	21938.5	4307.3	1.538	0.264	17.42**
	TBI	18853.4	2325.9	1.277	0.201	
Right Caudal Middle Frontal Gyrus	OI	6632.0	1193.3	0.465	0.073	1.96
	TBI	6399.5	1427.3	0.433	0.098	
Corpus Callosum	OI	2971.7	453.4	0.209	0.027	4.06*
	TBI	2838.6	624.5	0.191	0.038	

\* =  $p < 0.05$ , \*\* =  $p < 0.01$

Results Summary for Hypothesis Three: The results indicated that 5 of the 7 regions of interest demonstrated smaller corrected volumes in the TBI group compared to the OI group as predicted (see Table 7).

#### **Hypothesis Four Results – Load Vulnerability and Regions of Interest**

Hypothesis Four – Vulnerability to increased load variables will be correlated with corpus callosum (TotCC) volume and anterior cingulate (AC) volumes but not right middle frontal (Rt Mid Fro) volumes.

**Correlation of load vulnerability with regions of interest results.** The results of the analysis of load vulnerability and regions of interest are summarized in Table 8. Scatter plots for significant correlations in the combined sample are presented in Figure 13, Figure 14, and Figure 15; scatter plots for the OI and TBI group separately are presented in Appendix 2.

Results Summary for Hypothesis Four: Consistent with hypothesized relationships – vulnerability to load errors was correlated with the anterior cingulate and total cingulate volume. The larger these regions, the greater the increase in errors. In contrast to the hypothesis, the volume of the right rostral middle frontal gyrus was also positively correlated with increased errors. Reaction time change correlations and all other correlations as listed in Table 8 were not significant.

Table 8.

Correlation between vulnerability to load errors (Err) and reaction time (RT) and regions of interest for combined, OI, and TBI participants; Pearson's  $r$  over probability; significant relationships in bold.

Variable	Regions of Interest						
	AntCin	IstCin	PosCin	TotCin	RtRosMFG	RtCauMFG	TotCC
<i>Vulnerability to Load - Combined Sample n=56</i>							
Err	<b>.363</b>	.024	.131	<b>.270</b>	<b>.335</b>	.030	-.010
	<b>.006</b>	.861	.334	<b>.044</b>	<b>.011</b>	.825	.943
RT	-.103	.198	.038	.007	.021	.033	-.075
	.450	.143	.780	.958	.880	.808	.581
<i>Vulnerability to Load – OI participants n=28</i>							
Err	.355	.117	-.039	.216	.336	.087	-.061
	.063	.554	.845	.269	.080	.660	.757
RT	-.066	.241	.154	.088	.113	.057	.010
	.740	.217	.432	.656	.567	.771	.960
<i>Vulnerability to Load – TBI participants n=28</i>							
Err	.324	-.156	.278	.275	.233	-.071	-.059
	.092	.427	.152	.156	.233	.721	.765
RT	-.055	.198	.041	.047	.133	.074	-.062
	.783	.314	.837	.810	.498	.707	.754

Note: AntCin = anterior cingulate, IstCin – Isthmus Cingulate, PosCin = posterior cingulate, TotCin = total cingulate, RtRosMFG = right rostral middle frontal gyrus, RtCauMFG = right caudal middle frontal gyrus, TotCC = total corpus callosum.

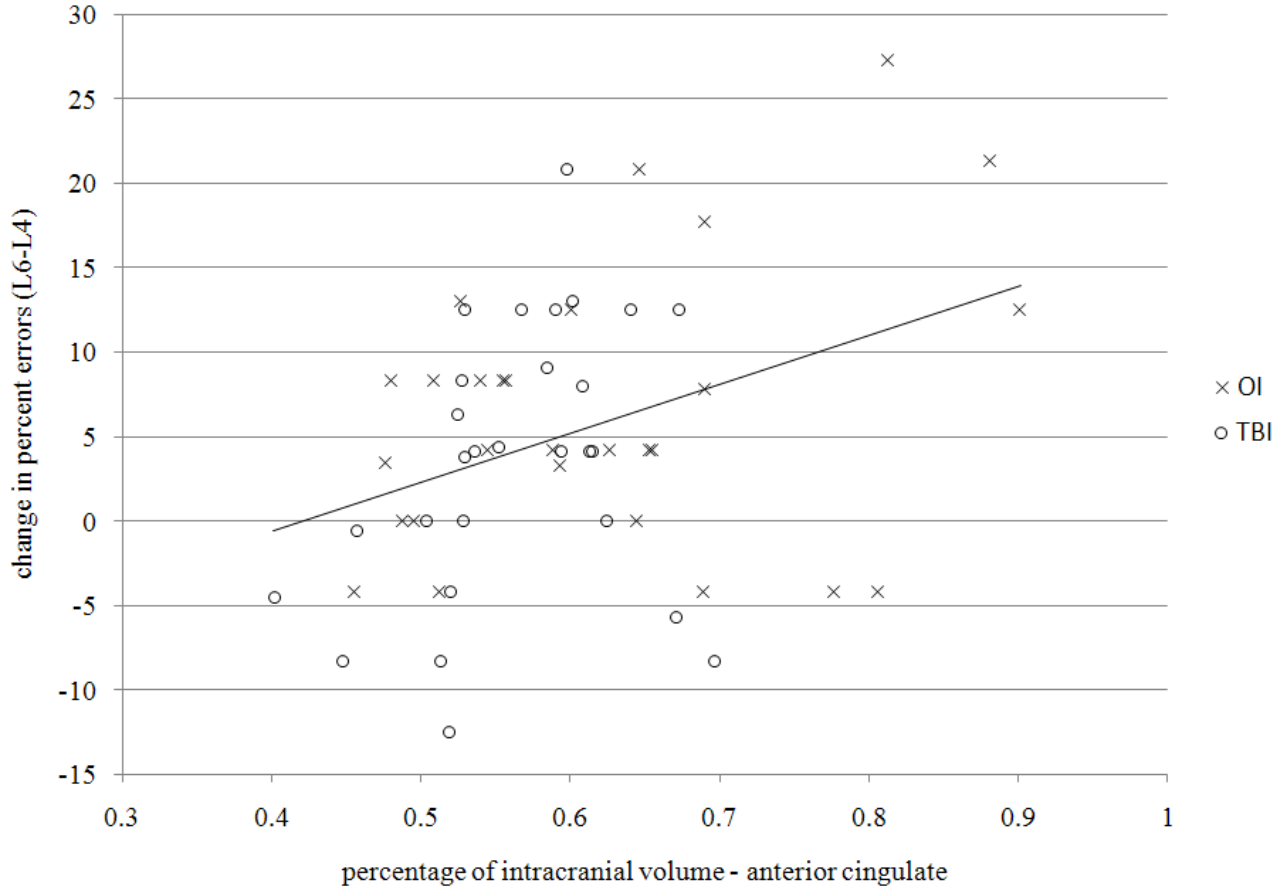


Figure 13. Scatter plot – anterior cingulate volume v. vulnerability to load – error change; combined sample ( $r = .363$ ).

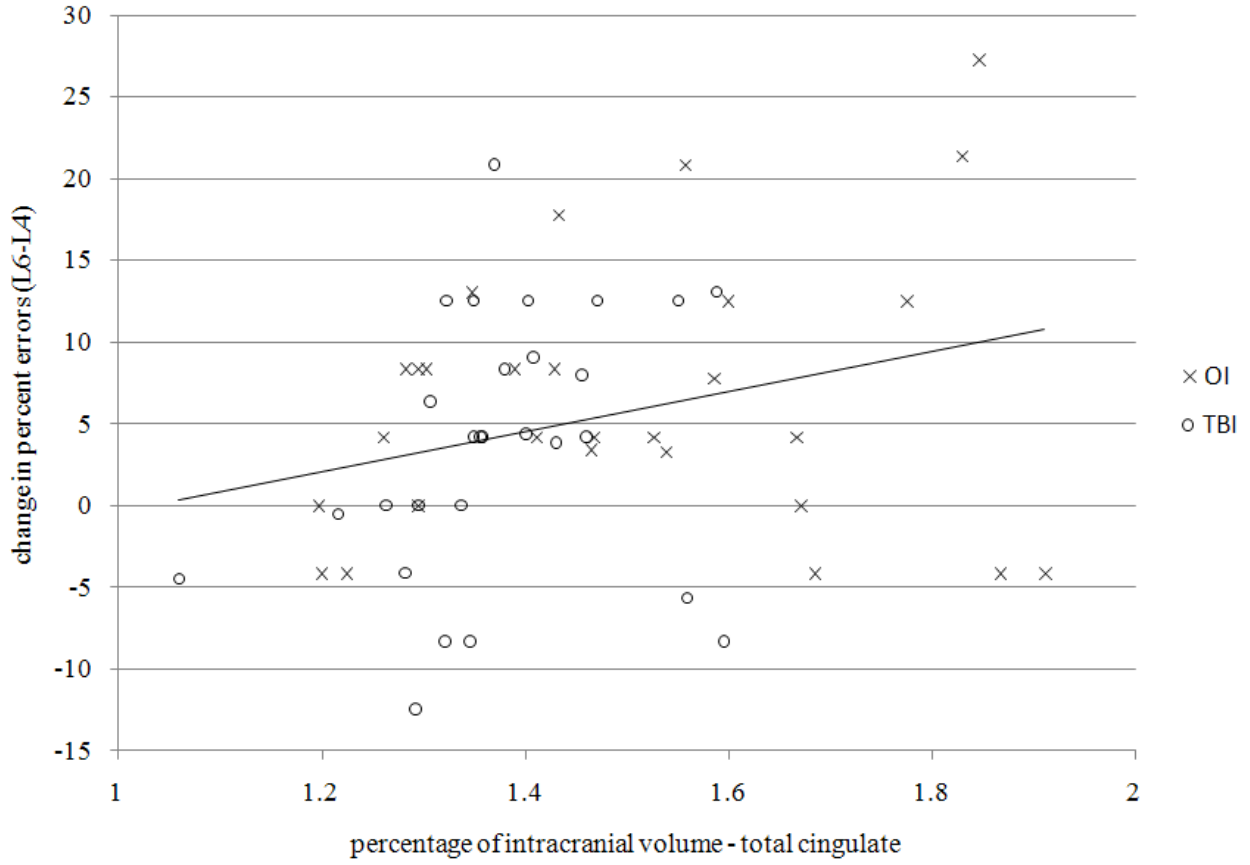


Figure 14. Scatter plot – total cingulate volume v. vulnerability to load – error change; combined sample ( $r = .270$ ).

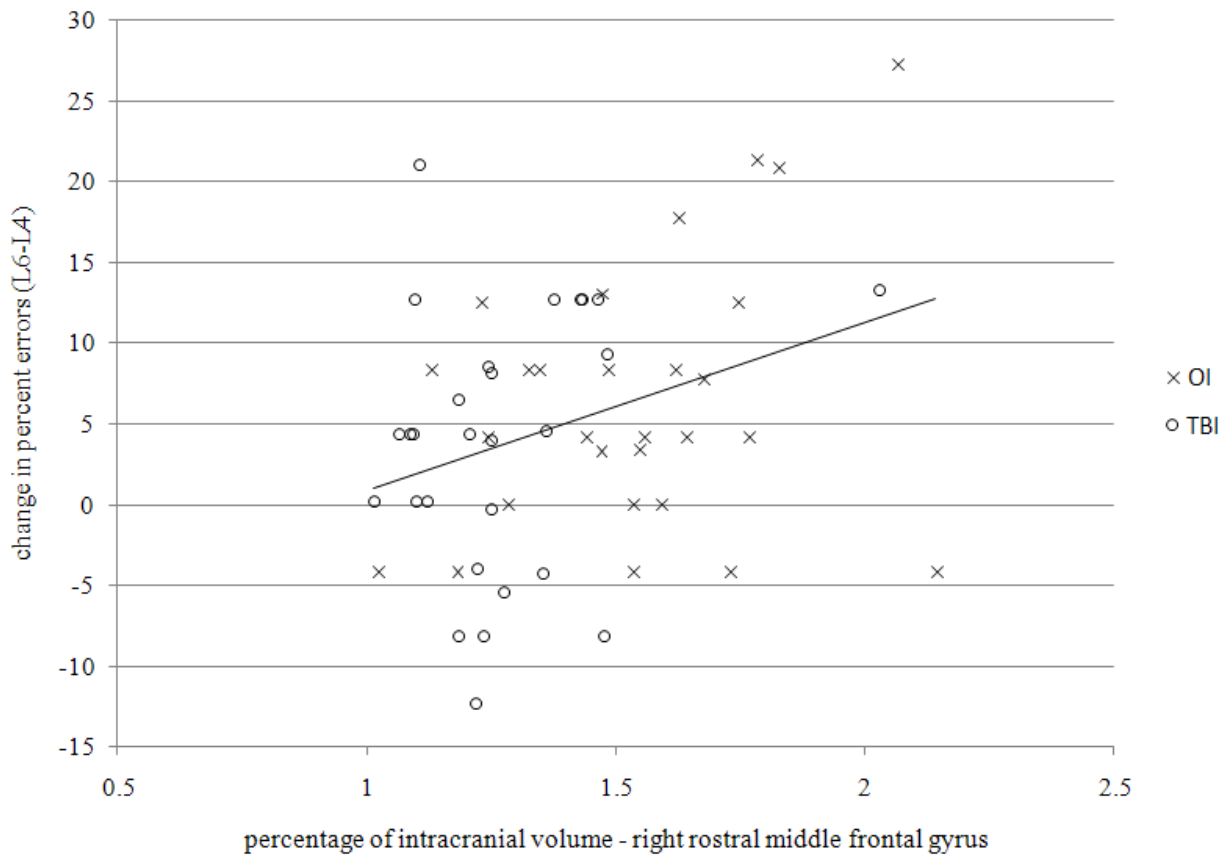


Figure 15. Scatter plot – right rostral middle frontal gyrus volume v. vulnerability to load – error change; combined sample ( $r = .335$ ).

## **Hypothesis Five Results – Interference Vulnerability and Regions of Interest**

Hypothesis Five – Vulnerability to increased interference demand variables will be correlated with TotCC, RtRosMidFro, and RtCauMidFro volume but not AC volumes.

**Correlation of interference vulnerability with regions of interest results.** The results of the analysis of interference vulnerability and regions of interest is summarized in Table 9. Scatter plots for significant correlations for the combined sample are presented in Figure 16 and Figure 17.

Results Summary for Hypothesis Five: There were no relationships consistent with the predictions of hypothesis five. Contrary to hypotheses, for the combined sample there were significant relationships between the anterior cingulate and vulnerability to interference errors; there was also a significant correlation between the total cingulate and vulnerability to interference reaction time. In both cases increases in errors and increases in reaction time was correlated with larger corrected volumes in these areas. For the TBI group there were several significant correlations between vulnerability to interference reaction time and regions of interest – all other relationships, as depicted in Table 9, were not significant.

Table 9.

Correlation between vulnerability to interference errors (Err) and reaction time (RT) and regions of interest for combined, OI, and TBI participants; Pearson's  $r$  over probability; significant relationships in bold.

Variable	Regions of Interest						
	AntCin	IstCin	PosCin	TotCin	RtRosMFG	RtCauMFG	TotCC
<i>Vulnerability to interference - Combined Sample n=56</i>							
Err	<b>.268</b>	-.030	.068	.175	.113	-.031	-.040
	<b>.046</b>	.827	.618	.197	.407	.823	.768
RT	.248	.085	.243	<b>.269</b>	.103	.257	-.030
	.066	.534	.071	<b>.045</b>	.448	.056	.826
<i>Vulnerability to interference – OI participants n=28</i>							
Err	.186	-.080	-.090	.049	-.032	-.015	-.144
	.342	.684	.650	.805	.873	.939	.464
RT	.297	.011	.173	.248	-.002	.086	.007
	.125	.955	.378	.203	.993	.662	.970
<i>Vulnerability to interference – TBI participants n=28</i>							
Err	.228	-.055	-.032	.105	-.112	-.160	-.145
	.244	.783	.872	.595	.571	.418	.462
RT	.220	.219	<b>.480</b>	<b>.423</b>	.338	<b>.431</b>	-.051
	.261	.263	<b>.010</b>	<b>.025</b>	.079	<b>.022</b>	.798

Note: AntCin = anterior cingulate, IstCin – Isthmus Cingulate, PosCin = posterior cingulate, TotCin = total cingulate, RtRosMFG = right rostral middle frontal gyrus, RtCauMFG = right caudal middle frontal gyrus, TotCC = total corpus callosum.



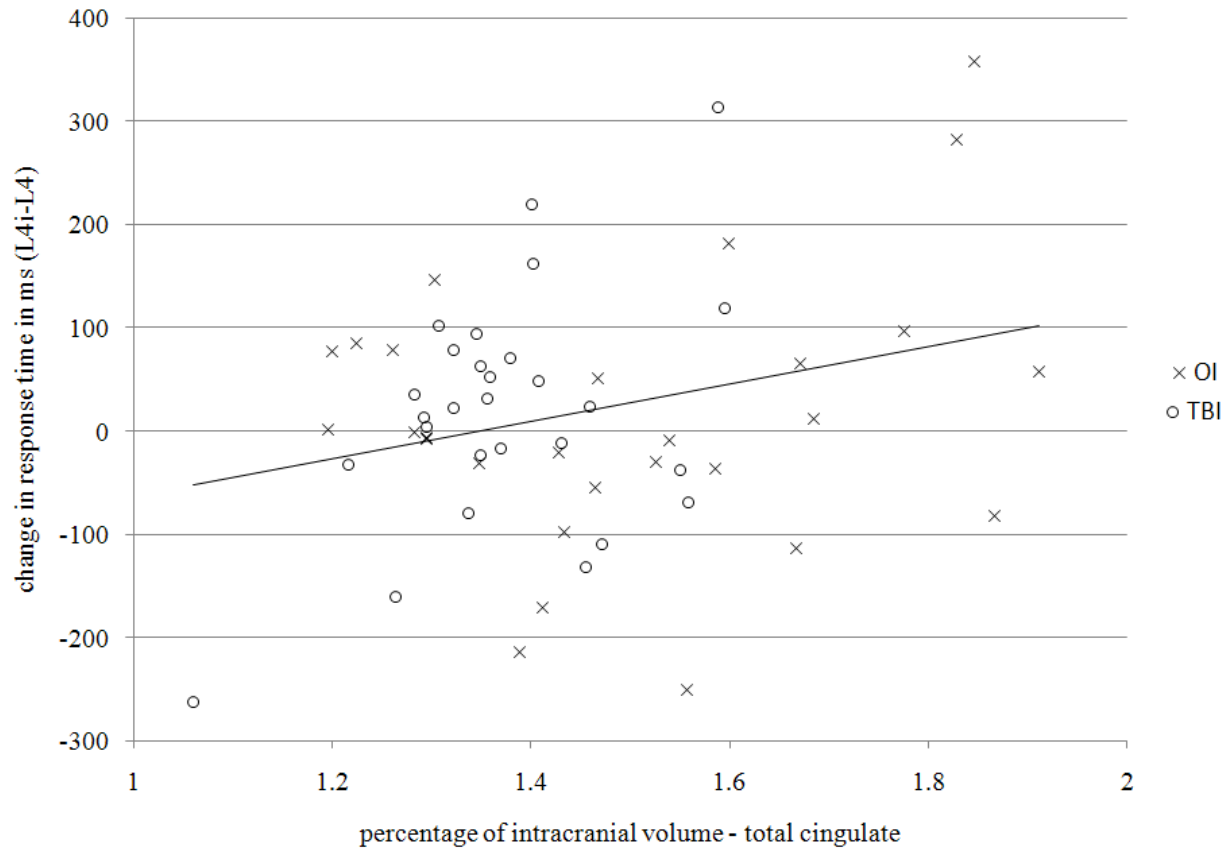


Figure 16. Scatter plot – total cingulate volume v. vulnerability to addition of interference – response time change ( $r = .269$ ).

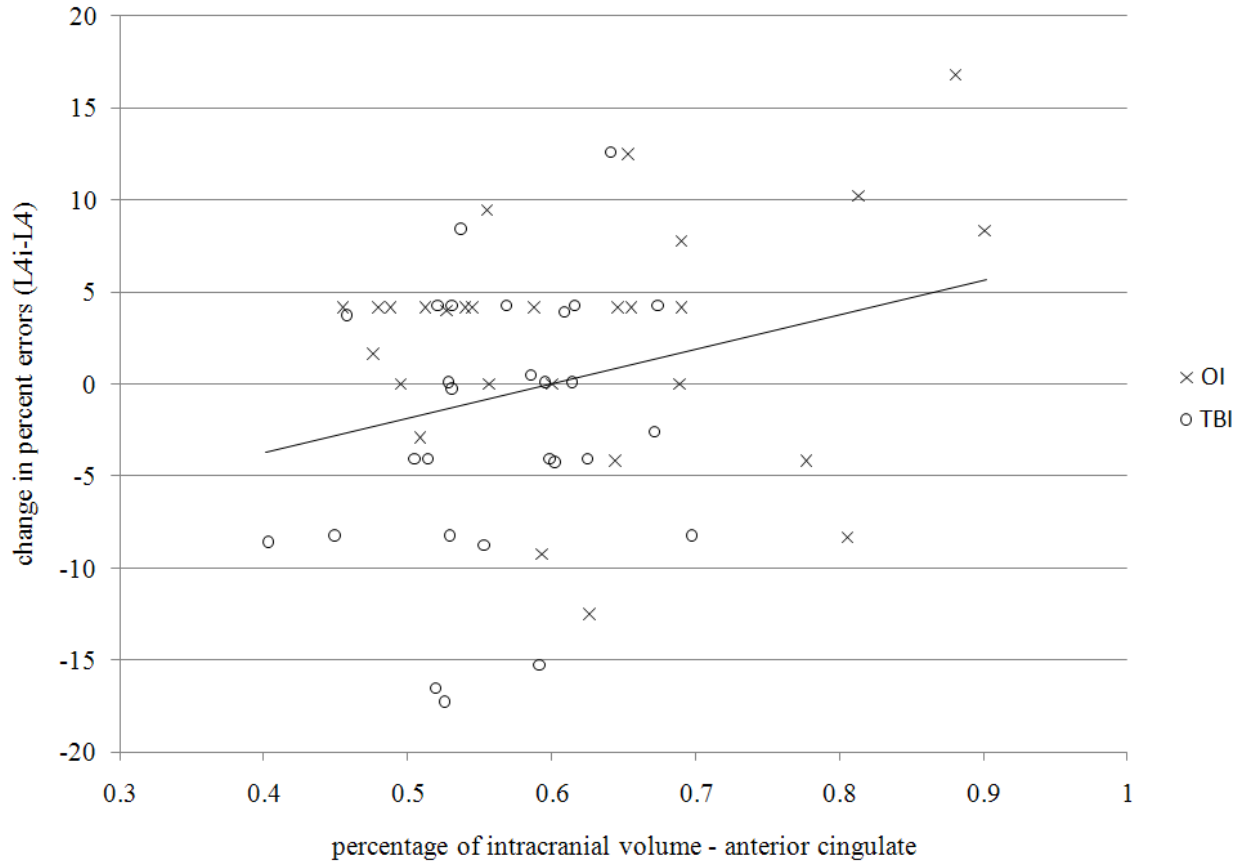


Figure 17. Scatter plot – anterior cingulate volume v. vulnerability to addition of interference – error change ( $r = .268$ ).

**Correlation of secondary interference vulnerability variables with regions of interest.** Given the strong differences between the groups on probe absent – probe present analyses described in hypothesis two results, a correlation analysis was performed using a probe absent and probe present split of the L4 and L4i vulnerability data – results are presented in Table 10.

Table 10.

Correlation between secondary vulnerability to interference errors (Err) and reaction time (RT) variables, and regions of interest for combined, OI, and TBI participants; Pearson's  $r$  over probability; significant relationships in bold.

Variable	Regions of Interest						
	AntCin	IstCin	PosCin	TotCin	RtRosMFG	RtCauMFG	TotCC
<i>Vulnerability to Interference Probe Absent- Combined Sample n=56</i>							
Err	-0.000	0.054	0.126	0.069	-0.047	-0.117	0.173
	0.998	0.689	0.352	0.612	0.730	0.387	0.200
RT	<b>0.283</b>	0.195	0.240	<b>0.315</b>	<b>0.322</b>	<b>0.300</b>	-0.018
	<b>0.034</b>	0.149	0.073	<b>0.018</b>	<b>0.015</b>	<b>0.024</b>	0.889
<i>Vulnerability to interference Probe Absent – OI participants n=28</i>							
Err	-0.068	-0.009	0.105	0.003	-0.326	-0.043	0.078
	0.729	0.962	0.591	0.984	0.089	0.827	0.689
RT	0.283	0.289	0.174	0.309	0.217	0.085	-0.142
	0.143	0.135	0.375	0.109	0.265	0.664	0.468

Continued next page . . .

Table 10. (continued)

Variable	Regions of Interest						
	AntCin	Variable	AntCin	Variable	AntCin	Variable	AntCin
<i>Vulnerability to Interference Probe Absent – TBI participants n=28</i>							
Err	-0.086	0.095	-0.053	-0.047	-0.030	-0.264	0.148
	0.665	0.630	0.788	0.814	0.881	0.175	0.451
RT	0.153	0.038	0.144	0.171	0.229	<b>0.383</b>	-0.077
	0.437	0.848	0.464	0.385	0.241	<b>0.045</b>	0.697
<i>Vulnerability to Interference Probe Present - Combined Sample n=56</i>							
Err	<b>0.308</b>	-0.066	-0.017	0.150	0.053	-0.168	0.163
	<b>0.020</b>	0.626	0.896	0.267	0.228	0.694	0.215
RT	0.063	-0.063	0.094	0.062	-0.150	0.060	-0.021
	0.639	0.642	0.486	0.646	0.267	0.659	0.877
<i>Vulnerability to interference Probe Present – OI participants n=28</i>							
Err	0.284	-0.088	-0.200	0.055	0.220	0.010	-0.254
	0.142	0.654	0.306	0.779	0.260	0.957	0.190
RT	0.170	-0.210	0.093	0.086	-0.172	0.047	0.121
	0.385	0.281	0.637	0.661	0.380	0.811	0.539
<i>Vulnerability to Interference Probe Present – TBI participants n=28</i>							
Err	0.278	-0.109	-0.030	0.119	-0.109	0.007	-0.244
	0.150	0.580	0.876	0.545	0.580	0.968	0.209
RT	0.133	0.242	<b>0.474</b>	<b>0.375</b>	0.211	<b>0.182</b>	0.009
	0.498	0.213	<b>0.010</b>	<b>0.048</b>	0.280	<b>0.352</b>	0.961

Note: AntCin = anterior cingulate, IstCin – Isthmus Cingulate, PosCin = posterior cingulate, TotCin = total cingulate, RtRosMFG = right rostral middle frontal gyrus, RtCauMFG = right caudal middle frontal gyrus, TotCC = total corpus callosum.

While there are several significant relationships apparent – there does not appear to be any clear pattern to the data – particularly considering the high likelihood of type 1 errors for this table.

### **Exploratory Correlation Analysis Results**

The region of interest variables were correlated with the error and reaction time variables for L1, L4, L6, L4i, L4 probe absent, L4 probe pres, L4i probe absent, L4i probe pres. This resulted in 112 comparisons for each sample (combined, TBI and OI) each comparison with a type 1 error rate of  $\alpha = .05$ . There were 38 significant results in the entire dataset – we would expect approximately 17 by chance with an alpha of .05; see Table 11.

There was a prominent pattern, in that 18 of the 38 significant relationships were between the right rostral middle frontal gyrus (RtRosMFG) and measures of reaction time. The correlations between all reaction time variables and the RtRosMFG are presented in Table 12. The results suggest that for the sample under consideration, longer reaction times tend to be associated with a larger volume of the RtRosMFG.

Table 11.

Number of significant correlations for all correlation analyses for percent errors (Err) and reaction time (RT) variables, with regions of interest for combined, OI, and TBI participants.

Variable	Regions of Interest						
	AntCin	IstCin	PosCin	TotCin	RtRosMFG	RtCauMFG	TotCC
<i>Percent errors variables – number of significant correlations</i>							
Combined	-	-	3	3	-	-	-
OI	-	1	6	4	1	-	-
TBI	-	-	-	-	-	-	-
<i>Reaction time variables – number of significant correlations</i>							
Combined	-	-	-	-	5	-	-
OI	2	-	-	-	6	-	-
TBI	-	-	-	-	7	-	-

Note: AntCin = anterior cingulate, IstCin – Isthmus Cingulate, PosCin = posterior cingulate, TotCin = total cingulate, RtRosMFG = right rostral middle frontal gyrus, RtCauMFG = right caudal middle frontal gyrus, TotCC = total corpus callosum.

Table 12.

Correlation between reaction time measures and right rostral middle frontal gyrus (RtRosMFG) for combined, OI, and TBI participants; Pearson's  $r$  over probability; significant relationships in bold.

Group	Reaction Time Measures							
	L1	L4	L6	L4i	L4 Probe Absent	L4 Probe Present	L4i Probe Absent	L4i Probe Present
<i>Correlation with RtRosMFG</i>								
Combined	.233	<b>.265</b>	<b>.271</b>	<b>.286</b>	.222	<b>.285</b>	<b>.330</b>	.212
	.084	<b>.048</b>	<b>.044</b>	<b>.032</b>	.099	<b>.033</b>	<b>.013</b>	.117
OI	<b>.422</b>	<b>.407</b>	<b>.427</b>	<b>.398</b>	<b>.405</b>	.367	<b>.414</b>	.324
	<b>.025</b>	<b>.031</b>	<b>.023</b>	<b>.036</b>	<b>.032</b>	.055	<b>.023</b>	.093
TBI	<b>.407</b>	<b>.394</b>	<b>.444</b>	<b>.463</b>	.320	<b>.442</b>	<b>.409</b>	<b>.493</b>
	<b>.032</b>	<b>.038</b>	<b>.018</b>	<b>.013</b>	.097	<b>.019</b>	<b>.031</b>	<b>.008</b>

Note: OI = orthopedic injury, TBI = traumatic brain injury, L1 = Sternberg Load 1, L4 = Sternberg Load 4, L6 = Sternberg Load 6, L4i = Sternberg Load 4 interference.

### Hypothesis Six Results – Discriminability and Response Bias

Hypothesis Six – The TBI group will have significantly lower discriminability and significantly larger response bias than the OI group.

**Discriminability and response bias results.** Data was available to calculate discriminability and response bias results for L4 and L4i. In the analysis for discriminability main effects for load, group, and group x load interaction were not significant. In the analysis for response bias there was a main effect for load  $F(1,108) = 5.65, p < .05$ ; the group and group

x load interaction were not significant (see Table 13 for descriptive statistics, and Appendix 1, Table 18 for ANOVA tables).

Table 13.

Descriptive statistics and follow-up analyses results for discriminability and criterion on Sternberg load conditions and participant group.

Level	Group	Mean ( <i>SD</i> )	Level (all groups)	Mean ( <i>SD</i> )	Group (all levels)	Mean ( <i>SD</i> )
<i>Discriminability analysis</i>						
L4	OI	2.61 (.78)	L4	2.52 (.83)	OI	2.51 (.82)
L4	TBI	2.42 (.87)	L4i	2.50 (.77)	TBI	2.51 (.77)
L4i	OI	2.40 (.86)				
L4i	TBI	2.59 (.67)				
<i>Criterion analysis</i>						
L4	OI	.137 (.199)	L4 <sup>a</sup>	.178 (.294)	OI	.078 (.223)
L4	TBI	.220 (.365)	L4i <sup>b</sup>	.047 (.292)	TBI	.148 (.359)
L4i	OI	.018 (.232)				
L4i	TBI	.076 (.344)				

Note: descriptors with different superscripts that are in same column and same section are significantly different at alpha = .05, individual comparison and type 1 error rate = alpha. Follow-up testing is only reported where significant main or interaction effects were found.

Results Summary for Hypothesis Six – There were no significant differences between the TBI group and the OI group on response bias or discriminability thus hypothesis six was not supported.



## Discussion

The comparison of the OI and TBI groups on the primary Sternberg task variables suggests that overall the Sternberg task is only moderately sensitive to the effects of traumatic brain injury in children: There were no differences between the groups on percent errors; for reaction time there was a significant overall difference for the L1, L4, L6 analysis with the OI group having faster times; effect size  $d=.35$ .

The hypothesis that load vulnerability is correlated with cingulate volume and not with right middle frontal volume was not supported by the results. The results of this study suggest that both of these areas are correlated with load vulnerability in terms of errors – there were no significant relationships with reaction time measures. The hypothesis that interference vulnerability is correlated with right middle frontal volume and not cingulate volume was also not supported by this study. Both of these areas were correlated with impact of interference.

As expected, the TBI group displayed evidence of atrophy in regions of interest for this study. Of the seven regions of interest, only the cingulate isthmus and right caudal middle frontal gyrus did not demonstrate significant group differences in volume when intracranial volume was controlled for.

An exploratory analysis indicated that the right rostral middle frontal gyrus was correlated with most reaction time measures. Contrary to expectations all significant correlations in the analysis were positive suggesting that where significant effects were apparent, more errors and longer reaction times were associated with larger volumes of the regions of interest. Most imaging studies in a variety of populations suggest the opposite relationship – larger ROI correlates with better functioning (Schmitz, Daly, & Murphy, 2007; Schretlen et al., 2000; Schwartz et al., 2007; Verger et al., 2001). However, the bigger is better relationship that is

found in many of these adult studies has had scant research attention for child populations. The effects of ageing, pruning, and the interaction of these variables with injury characteristics remain largely unexplored.

The most striking result of this study was found when considering interference variables when split by probe absent – probe present conditions. The results are more consistent with a priming interpretation of the L4i condition rather than solely an interference interpretation. The OI group demonstrated decrease in reaction time when the probe letter appeared in both the current and previous memory array (positive priming) and an increase in reaction time relative to the nonprime condition when the probe letter appeared in the previous but not the current memory array (negative priming). This pattern of results is consistent with those found in an early Sternberg study with non-injured adults (Monsell, 1978) but not a more recent one (Bunge et al., 2001) where negative priming resulted in a stronger increase in reaction time and positive priming a relatively smaller increase (mean 88ms v 23ms). Again, previous relationships are based on studies with adult populations and further research with children is needed to establish reliable conclusions regarding injury effects on responsiveness to priming.

The present study indicates that in contrast to the OI participants, the TBI participants group performance on the priming conditions did not appear to be significantly affected by the priming manipulation, i.e. OI children showed the expected pattern of performance benefits and decrements from positive and negative priming whereas the TBI group's performance suggests that priming is relatively non-influential on performance in this context.

If this finding is replicated in further studies it would be instructive to know if a lack of priming susceptibility in TBI groups correlates with behavioral functioning such as performance in social, academic, or workplace situations. Lack of inhibition is a common complaint after TBI

(Konrad, Gauggel, Manz, & Schall, 2000; Leblanc et al., 2005; Levin & Hanten, 2005) and the results raise the possibility that TBI patients may not be responsive to cues in the environment that prime them toward a particular behavioral direction. Thus the behavioral deficit may not represent an inhibition deficit but a lack of cue responsiveness.

The strengths of this study include well defined, highly comparable TBI and control samples and reliable measures. The methodology might be criticized for the large numbers of analyses that were performed. Alpha inflation and thus increase in the likelihood of type 1 error is a consequence of the decision to control for alpha only within the areas of analysis and not between them. While this is a valid concern it should be recognized that the present study explores relationships that have only fledgling support in the literature. The study should be considered primarily exploratory in nature, one that is more targeted at generating hypotheses for future testing with more rigorous designs rather than one that seeks to replicate, refine, and confirm well supported relationships. This is the first study that could be identified that explores volumetric correlations with the Sternberg task. Most studies employ functional brain imaging technology when exploring the brain behavior relationships with the Sternberg. These considerations would appear to counterbalance concerns over type 1 error rate.

Another consideration for interpreting the results of this study relates to the nature of the variables gathered as indicators of brain functioning. The relationship between volumetric anatomy, functional anatomy measures, and cognitive efficiency, is complex. Our findings indicate that only a small number of the volumetric correlations were significant and this is consistent with other studies exploring executive functioning and brain volume correlations (see Fine et al., 2009). It is possible that other imaging technology including diffusion tensor imaging and functional imaging methods may be more sensitive to the cognitive manipulation employed.

The results of the volumetric analysis of this study highlight the need for research that employs multiple measures of brain integrity – functional and volumetric so that relationships between cognitive capacity and brain variables, and between volumetric and functional brain measures, can be clarified. Further complicating the picture is the observation that developmental changes in the brain may mean that relationships that are robust in healthy adults do not generalize, to pediatric, or neurologically compromised populations.

The research results generate several questions that could be investigated in future research:

1) Is the slower performance in subjects with larger volume of the right middle frontal gyrus reflective of a more highly developed region and thus more cautious (and slower) response pattern; or does larger volume represent a less highly developed region (i.e. larger because cortical pruning has taken place to a lesser extent) that correlates with a less efficient speed of response processing.

2) Does lack of responsiveness to priming in the Sternberg task correlate with behavioral measures of social, academic, or behavioral inhibition?

3) In considering the Sternberg task it may be advantageous to increase sensitivity to working memory impairment in future studies so that exploring speed and accuracy using the paradigm has more power. Currently on many trials accuracy is at 100% which creates a ceiling effect that limits variability and thus power to detect impairment and group differences; i.e. the task appears to be too easy if the researcher is interested in application to naturalistic situations where both speed and accuracy are important. Increased task difficulty could easily be introduced by increasing the number of items in the memory array, reducing the presentation interval, or increasing the delay interval. One question that has not been addressed in the

literature is – which of the many variants of the Sternberg task is most sensitive to the various aspects of impaired working memory?

4) The present study explored brain volume - behavioral relationships for only 7 structures. The strongest results in this area were derived from an exploratory analysis that was outside the main hypotheses of this study. Given that the correlation of volumetric brain data and functions such as working memory is at a nascent stage of development, further exploratory analyses might help generate questions (such as question 1 above) for scientific exploration.

5) The hypotheses for this study were generated primarily from functional imaging studies but employed solely structural brain measures. While a correlation between functional and volumetric measures would appear to be logical, there appears to have been little examination of this using joint methodology in studies of working memory. Given that volumetric parcellation software has become increasingly automated, the burden of using joint methodology in future functional studies would appear minimal. The question “for the brain areas identified as highly active in working memory, does a larger (or smaller) volume in these structures result in more efficiency in performance?” appears to be one that could be readily answered by reanalysis of archival datasets.

In conclusion, the results of this study indicate that children who have sustained pediatric traumatic brain injury may have difficulty responding to priming cues in their environment. There is initial evidence that volumetric measures are sensitive to measures of working memory performance and further research exploring these relationships with cognitive measures that are tuned for sensitivity is indicated.

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## Appendix 1

### ANOVA Tables

Table 14.

Two way ANOVA results for three analyses, DV – percent errors, between subject factors – group (OI, TBI) and load level (as indicated in table).

Source	<i>df</i>	Sum of Squares	Mean Square	<i>F</i> Value	Pr > <i>F</i>
<u><i>L1, L4, L6 analysis</i></u>					
Model	5	3849.91	769.98	6.45	<.001
Group	1	37.72	37.72	.32	.575
Level	2	3740.04	1870.02	15.66	<.001
Group x Level	2	72.15	36.07	0.30	.740
Error	162	19342.93	119.40		
Total	167	23192.83			
<u><i>L4, L4int analysis</i></u>					
Model	3	172.79	57.60	0.48	.697
Group	1	3.16	3.16	0.03	.871
Level	1	0.18	0.18	0.00	.970
Group x Level	1	169.45	169.45	1.41	.237
Error	108	12961.72	120.02		
Total	111	13134.52			
<u><i>L4 and L4int split by probe type analysis</i></u>					
Model	7	3001.25	428.75	2.30	.028
Group	1	6.00	6.00	0.03	.858
Probe	1	1792.39	1792.39	9.61	.002
Load	1	0.00	0.00	0.00	.998
Group x Probe	1	157.07	157.07	0.84	.359
Group x Load	1	348.48	348.48	1.87	.173
Probe x Load	1	684.30	684.30	3.67	.057
G. x P. x L	1	12.99	12.99	0.07	.792
Error	216	40283.47	186.50		
Total	223	43284.71			

Table 15.

Two way ANOVA results for three analyses, DV – reaction time, between subject factors – group (OI, TBI) and load level (as indicated in table).

Source	<i>df</i>	Sum of Squares	Mean Square	<i>F</i> Value	Pr > <i>F</i>
<u><i>L1, L4, L6 analysis</i></u>					
Model	5	3402584	680516	4.57	<.001
Group	1	838540	838540	5.63	.019
Level	2	2549900	1274950	8.55	<.001
Group x Level	2	14143	7071		.954
Error	162	24149640	149071.86		
Total	167	27552225			
<u><i>L4, L4int analysis</i></u>					
Model	3	401544	133848	.82	.488
Group	1	394066	394066	2.40	.124
Level	1	7205	7205	0.04	.834
Group x Level	1	273	273	0.00	.9675
Error	108	17731986	164185		
Total	111	18133530			
<u><i>L4 and L4int split by probe type analysis</i></u>					
Model	7	1318973	188425	1.05	.398
Group	1	788132	788132	4.39	.037
Probe	1	197557	197557	1.10	.295
Load	1	14410	14410	0.08	.777
Group x Probe	1	40330	40330	0.22	.636
Group x Load	1	546	546	0.00	.956
Probe x Load	1	131750	131750	0.73	.393
G. x P. x L	1	146246	146246	0.81	.368
Error	216	38781380	188425		
Total	223	40100353			

Table 16.

ANOVA results for Vulnerability to interference split by probe condition DV as indicated in table, IVs Group (OI, TBI) and probe condition (Int. probe abs (4i-4), Int. probe pres (4i-4)).

Source	<i>df</i>	Sum of Squares	Mean Square	<i>F</i> Value	Pr > <i>F</i>
<i>Percent Errors analysis</i>					
Model	3	2091.55	697.19	6.37	<.001
Group	1	696.97	696.97	6.37	.013
Level	1	1368.61	1368.61	12.51	<.001
Group x Level	1	25.98	25.98	0.24	.627
Error	108	11818.91	109.43		
Total	111	13910.46			
<i>Reaction Time analysis</i>					
Model	3	557086	185695	5.83	.001
Group	1	1093	1093	0.03	.853
Level	1	263502	263502	8.28	.005
Group x Level	1	292493	292493	9.19	.003
Error	108	3438110	31834		
Total	111	3995197			

Table 17.

Univariate ANOVA results for regions of interest by group (OI, TBI).

Source	<i>df</i>	Sum of Squares	Mean Square	<i>F</i> Value	Pr > <i>F</i>
<u><i>Anterior Cingulate</i></u>					
Group	1	.04695	.04695	4.63	.036
Error	54	.54740	.01014		
Total	55	.59435			
<u><i>Isthmus Cingulate</i></u>					
Group	1	.00103	.00103	0.50	.480
Error	54	.11075	.00205		
Total	55	.11179			
<u><i>Posterior Cingulate</i></u>					
Group	1	.04731	.04731	8.20	.006
Error	54	.31178	.00577		
Total	55	.35910			
<u><i>Total Cingulate</i></u>					
Group	1	.21752	.21752	7.24	.010
Error	54	1.62254	.03004		
Total	55	1.84006			
<u><i>Right Rostral Middle Frontal Gyrus</i></u>					
Group	1	.95628	.95628	17.42	<.001
Error	54	2.96367	.05488		
Total	55	3.91995			
<u><i>Right Caudal Middle Frontal Gyrus</i></u>					
Group	1	.01464	.01464	1.96	.167
Error	54	.40300	.00746		
Total	55	.41764			
<u><i>Total Corpus Callosum</i></u>					
Group	1	.00448	.00448	4.06	.048
Error	54	.05949	.00110		
Total	55	.06396			

Table 18.

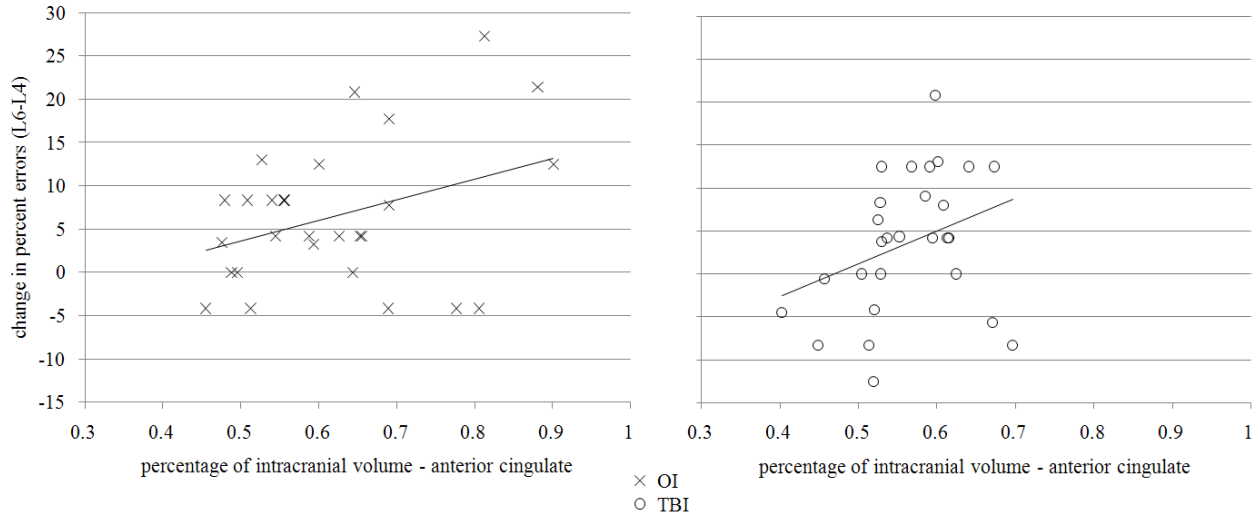
Two way ANOVA results for two analyses, DV – discriminability and criterion, between subject factors – group (OI, TBI) and load level (L4,L4i).

Source	<i>df</i>	Sum of Squares	Mean Square	<i>F</i> Value	Pr > <i>F</i>
<i><u>Discriminability analysis</u></i>					
Model	3	.9997	.3332	.52	.672
Group	1	.0000	.0000	.00	.995
Level	1	.0104	.0104	.02	.899
Group x Level	1	.9892	.9892	1.53	.218
Error	108	69.6547	.6450		
Total	111	70.6543			
<i><u>Criterion analysis</u></i>					
Model	3	.6242	.2081	2.41	.071
Group	1	.1389	.1389	1.61	.208
Level	1	.4810	.4810	5.56	.020
Group x Level	1	.0043	.0043	.05	.823
Error	108	9.3414	.0865		
Total	111	9.9656			

## Appendix 2

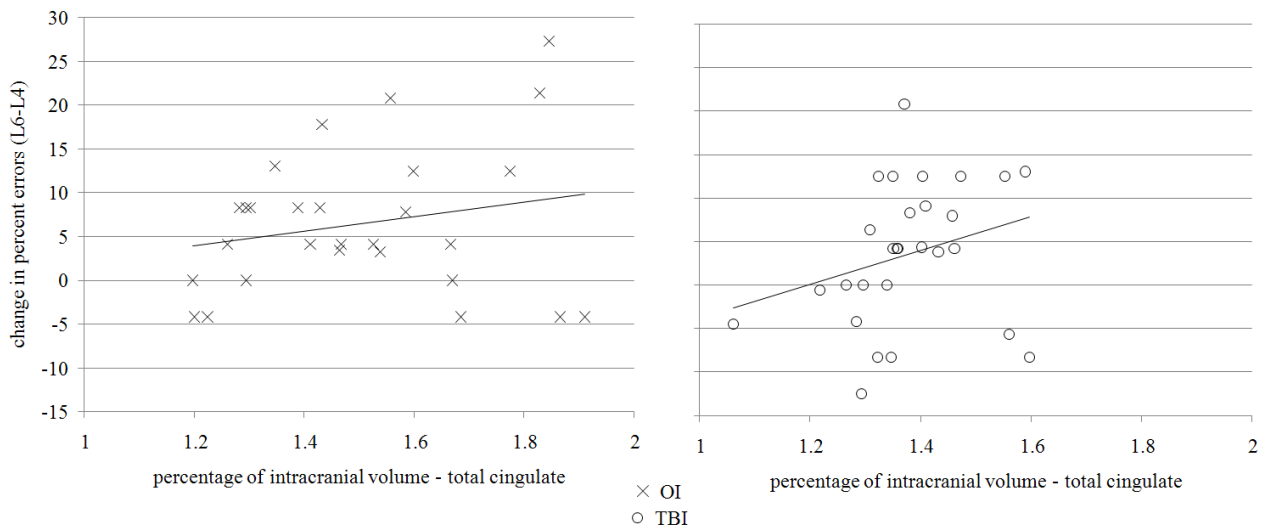
### Scatter Plots for OI and TBI groups





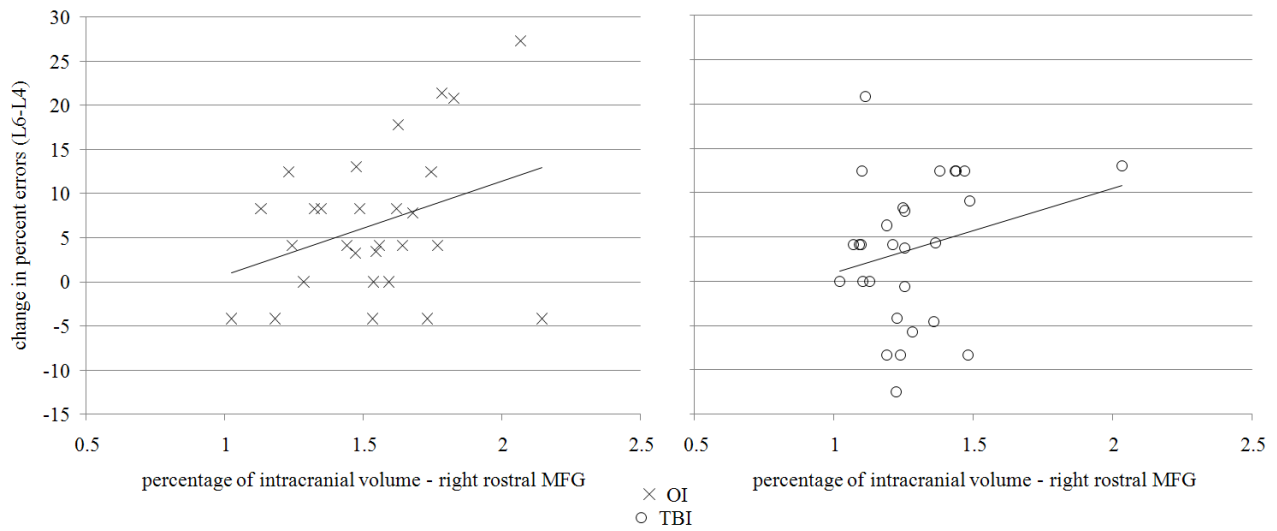
Note: regression lines in this figure are not statistically significant

Figure 18. Scatter plot – anterior cingulate volume v. vulnerability to load – error change; orthopedic injury (OI) and traumatic brain injury (TBI) groups.



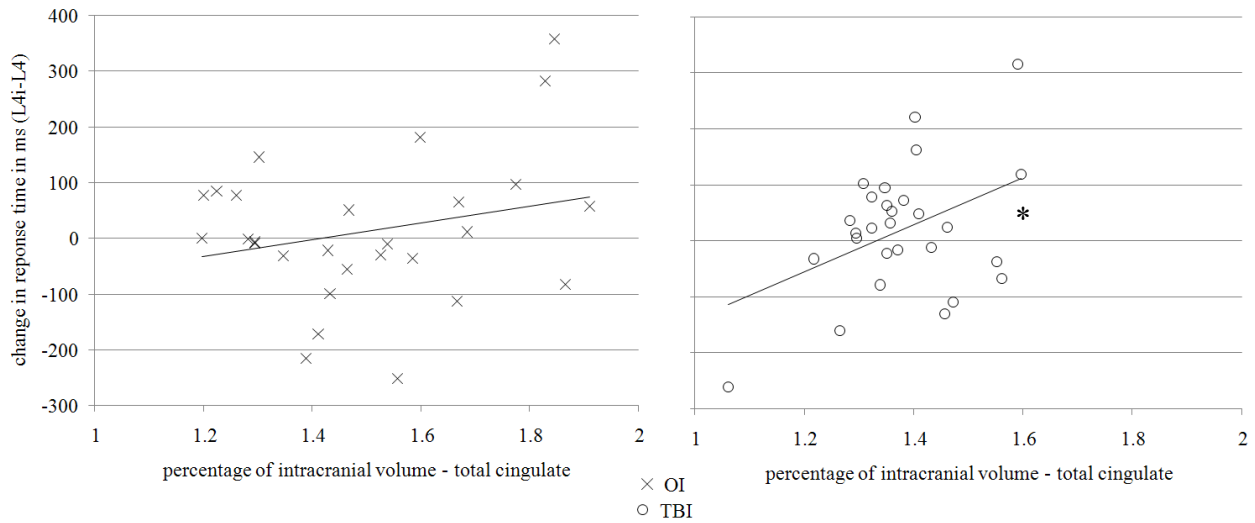
Note: regression lines in this figure are not statistically significant

Figure 19. Scatter plot – total cingulate volume v. vulnerability to load – error change; orthopedic injury (OI) and traumatic brain injury (TBI) groups.



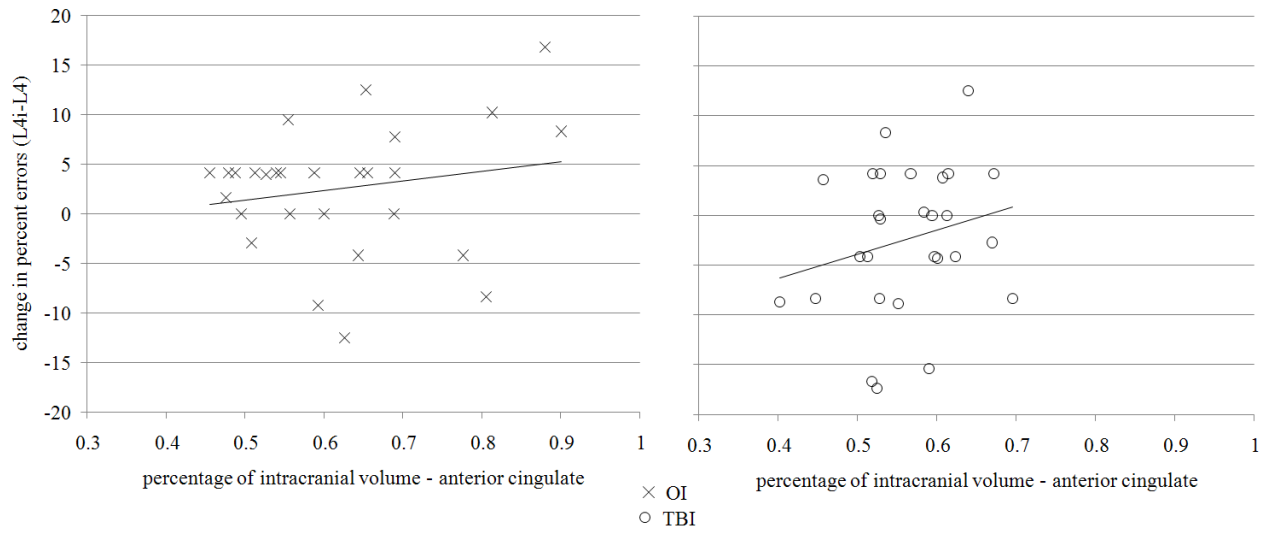
Note: regression lines in this figure are not statistically significant

Figure 20. Scatter plot – right rostral middle frontal gyrus (MFG) v. vulnerability to load – error change; orthopedic injury (OI) and traumatic brain injury (TBI) groups.



\* = significant correlation  $p \leq .05$

Figure 21. Scatter plot – total cingulate volume v. vulnerability to interference – response time change; orthopedic injury (OI) and traumatic brain injury (TBI) groups.



Note: regression lines in this figure are not statistically significant

Figure 22. Scatter plot – anterior cingulate volume v. vulnerability to interference – error change; orthopedic injury (OI) and traumatic brain injury (TBI) groups.