

Running Head: NEURAL CORRELATES OF INHIBITION IN ADOLESCENTS WITH TBI

Neural Correlates of Inhibitory Processing in Adolescents with Traumatic Brain Injury: fMRI study of the Counting Stroop Task

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Abstract

Inhibitory deficits are common and significant sequelae of pediatric traumatic brain injury (TBI). The present study used fMRI to examine inhibitory processing in 11 adolescents, aged 12 – 16, (mean age = 15.7) with TBI who were at least 1 year postinjury and 11 age-matched typically developing control participants (TC) (mean age = 14.2). Participants completed a Counting Stroop task with 2 conditions: 1) a neutral condition requiring the counting of animal words and 2) an interference condition in which mismatched number words were counted. Both TBI and TC adolescents activated similar networks of brain regions relevant to inhibitory processing, but the TBI group showed higher levels of activation relative to the TC group in multiple brain areas within this network, including predominantly frontal and parietal regions. Higher levels of activation were correlated with more error responses during the inhibition condition. Findings of *over*-activation of the relevant inhibitory-related neural network in the TBI group are consistent with recent fMRI findings using other attention-related paradigms in TBI. In contrast, imaging studies of other clinical conditions such as attention deficit-hyperactivity disorder have documented *under*-activation of the attention network.

Keywords: childhood brain disorder, inhibition, interference, Stroop, brain imaging, children, head injury

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Traumatic brain injury (TBI) is the most common cause of acquired disability in childhood and adolescence. The highest peak in incidence of TBI is during the adolescent and young adult years (Langolis et al., 2006). Adolescence constitutes an important transitional phase during which the child is expected to assume increasing responsibility for self-management and care (Crosnoe & Trinitapoli, 2008; Wigfield & Eccles, 1994). It is also a critical time for brain development (Casey, Tottenham, Liston, & Durston, 2005) and higher-order cognitive processes often referred to as executive functioning skills (EF). Negotiating the difficult developmental transitions of adolescence may be exacerbated following a brain insult, particularly if the injury involved the frontal lobes of the brain as is often the case in TBI.

Deficits in various aspects of attention and EF, including inhibition, are commonly observed in pediatric TBI (Max et al., 2005a,b,c). In general, children with severe TBI display poorer performance on a variety of measures of attention and EF than less-severely injured or healthy control children across behavioral paradigms (e.g., Anderson et al., 1998, 2005; Catroppa & Anderson, 2005; Ewing-Cobbs et al., 1998; Yeates et al., 2005). One aspect of attention and EF, variously described as cognitive or inhibitory control, refers to the ability to withhold or suppress pre-potent responses and to resist interference. Inhibitory control may be particularly important for adolescents as they learn to navigate a rapidly changing social and academic environment. Behavioral inhibition may also lay the foundation for the development of other EF skills (Barkley, 1997). The neural network mediating inhibitory control has been referred to as the executive attention network and is hypothesized to include brain regions such as the anterior cingulate, prefrontal cortex, and basal ganglia (Rothbart & Posner, 2001).

Deficits in attention and executive function skills (EF) may help explain the discrepancy between seemingly normal performance on standard cognitive measures and observed impairments in everyday social and academic functioning (Anderson, Catroppa, Morse, Haritou, & Rosenfeld, 2005; Catroppa & Anderson, 2003; Ewing-Cobbs, Prasad, Landry, Dramer, & DeLeon, 2004). Intact attention and EF skills play an important role in interpersonal, school, and vocational success (Konrad, Gauggel, Manz, & School, 2006; Levin & Hanten 2005; Pennington, 1994; Schachar, Levin, Max, Purvis, & Chen, 2004). Thus, if we can understand how TBI affects existing and emerging attention and EF skills in adolescence we have the potential to develop EF interventions. Enhancing EF skills will likely improve both academic and vocational outcomes, as well as emotional well-being and quality of life.

A few studies have used functional magnetic resonance imaging (fMRI) to examine inhibition, working memory, and sustained attention in individuals with TBI. Scheibel and colleagues (2007, 2009) investigated inhibitory control in adults with TBI at 3 months post-injury using a stimulus response compatibility task. In this task, participants pressed keys on the side indicated by the direction of arrows on the screen (neutral) or on the side opposite to that indicated by the arrows (interference). These authors reported higher levels of and more extensive inhibition-related activation (i.e., incompatible minus compatible) in adults with TBI relative to adults with orthopedic injuries (OI) in a range of brain regions including the left precentral gyrus, midline cingulate region, medial frontal, middle frontal and superior frontal gyri bilaterally. Participants with more severe TBI had higher levels of activation than those with milder injuries or OI. Higher levels of activation were reported to be associated with higher levels of task performance in the incompatible condition in participants with TBI (e.g., Scheibel et al., 2009). FMRI studies of working memory (N-back tasks) in adults with TBI have

demonstrated over-activation in participants with TBI relative to controls following both mild (McAllister et al., 1999, 2001) and moderate to severe TBI (Christodoulou et al., 2001; Newsome et al., 2007a; Perlstein et al., 2004; Scheibel et al., 2007). During a sustained attention task, Kramer et al., 2008 found higher levels of activation in frontal and parietal regions of children with moderate to severe TBI (mean age = 9.4) relative to children with OI.

The current study sought to examine the neural substrates associated with inhibitory processing in adolescents with moderate to severe TBI relative to a cohort of age and sex-matched healthy controls. The Counting Stroop task developed by Bush and colleagues (1998; 1999) was used as a probe of inhibitory control. Consistent with Scheibel and colleagues (2007) and Kramer and colleagues (2008), we hypothesized that adolescents with and without TBI would activate similar frontal and parietal regions, but that the adolescents with TBI would demonstrate *over*-activation of brain regions supporting inhibition compared to controls.

Methods

Participants

Participants included 11 adolescents (mean age = 15.7, range = 12 to 16), with moderate to severe TBI (defined as GCS score of ≤ 12 or a GCS of 13-15 accompanied by abnormalities on imaging) who were identified through their participation in ongoing behavioral intervention studies. Both the intervention project and the current imaging study were approved by the Institutional Review Board. All adolescents with TBI were required to be ≥ 12 months post injury because we were interested in the longer-term effects of TBI on developing brain networks during adolescence. A total of 39 children with TBI were identified as eligible for participation based on current age and time since injury. Seventeen were successfully enrolled in the study, 3 were excluded due to metal in their bodies that would interfere with the scanning,

and 1 was unable to be scheduled during the period of the study. The remaining 17 were never contacted because sufficient numbers of participants had agreed to participate. A comparison cohort of 15 adolescents (mean age = 14.2, range = 12 to 16), matched with the TBI group on sex, handedness, and race/ethnicity, were recruited through the hospital e-mail system. Eligibility criteria for both groups included English as the primary language spoken in the home.

Adolescents were excluded if they had a diagnosis of significant developmental disability (i.e., placement in a special classroom and $IQ < 70$), significant psychiatric/behavioral disturbances (e.g., bipolar, major depression, autism), or extreme vision and hearing deficits. Additional exclusion criteria for the control group included any prior diagnosis of a neurological disorder or any indications of a history of TBI. A total of 32 children completed informed consent to participate in the study, and 20 (63%) yielded usable fMRI data. Those with usable fMRI data did not differ from those who were excluded due to unusable data in terms of age, IQ, injury severity, or self- or parent-report of EF skills.

[INSERT TABLE 1 HERE]

Procedures

After informed consent was obtained, adolescents completed a brief neuropsychological battery including an abbreviated assessment of intelligence and measures of various aspects of EF. Participants then completed four fMRI tasks including the Counting Stroop, described in the present report.

Cognitive and behavioral functioning. Receptive vocabulary was assessed using the Peabody Picture Vocabulary Test-Fourth Edition (PPVT-IV, Dunn & Dunn, 2007). Single word reading skills, which have been used as a proxy for pre-injury cognitive status (Orme et al., 2004), were measured using the Wide Range Achievement Test-Fourth Edition (WRAT-4,

Wilkinson & Robertson, 2006). The Working Memory (WM) and Processing Speed (PS) Indices from the Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV, Wechsler 2003) were administered to assess domains of EF known to be vulnerable to TBI. Verbal inhibition was assessed using the Color-Word Interference Test of the Delis-Kaplan Executive Function System (D-KEFS, Delis et al., 2001). The participant is presented with a color word that is printed in a font color that is different from the word and asked to name the color of the font. Parents and adolescents completed the Behavior Rating Inventory of Executive Function (BRIEF, Gioia et al., 2000) and BRIEF-self report (BRIEF-SR, Guy et al., 2004) respectively.

Stimuli and Behavioral Tasks used for fMRI. In the variant of the Counting Stroop Task used in the present study (Bush et al., 1998, 1999), one to four identical words were presented in a vertical column on the screen on each trial of 1.5 seconds. Participants were asked to note the number of words that appeared on the screen and press one of four corresponding response buttons on a button box. For example, if the word appeared four times on the screen, the correct response would be “4”. The Interference condition contained all number words (i.e., “one,” “two,” “three,” or “four), with each appearing 2 to 5 times in each block in a random fashion. The Neutral condition contained names of common animals (i.e., “dog,” “cat,” “mouse,” or “bird”), again each appearing 2 to 5 times in each block in a random fashion. The two conditions were balanced for the number and length of the words. There were fourteen trials in each of the two conditions. A third condition, the fixation block, was also included as a baseline condition. Participants were asked to monitor a row of “+” signs presented at the center of the screen, and the number of “+” signs on screen changed every two seconds (randomly from two to six “+” signs). This condition was not included in subsequent analyses presented here. Participants were

given one example of each condition during a pre-scan training session, and all indicated understanding of the instructions. No further training was provided.

fMRI Data Acquisition and Analyses. MR scanning was performed on a 3 Tesla Philips Achieva MR scanner. A T2*-weighted, spin-echo EPI sequence was used for fMRI scans (TR/TE = 2000/30 ms, FOV = 24 x 24 cm, matrix = 80 x 80, slice thickness = 4mm, flip angle = 90 degree). Forty-one slices were acquired at 210 time points for a total imaging time of 432 seconds, beginning with a 12 second (6 volumes) fixation period to allow for T1 relaxation effects. The initial 6 volumes were subsequently discarded prior to statistical post-processing of the fMRI data. Functional imaging time consisted of six cycles, each 66 seconds long with fixation periods of 12 seconds and condition periods of 21 seconds alternating with one another (i.e., fixation-neutral-fixation-interference). A T1-weighted, 3D MP-RAGE whole brain scan was also obtained for anatomical co-registration (TR/TE = 8.2/3.7ms, FOV = 25.2cm x 25.0cm, matrix = 252x250, slice thickness = 1mm, scan time = 355 s) prior to the functional scans.

fMRI image post-processing was done using in-house software written in IDL[™] (ITT visual information solutions). The reconstructed EPI data were corrected for drift using quadratic baseline correction on a pixel-by-pixel basis (Hu et al., 1995; Le & Hu, 1996), co-registered to reduce the effects of motion artifacts (Thevenaz & Unser, 1998), and transformed into Talairach coordinates (Talairach & Tournoux, 1988) using a linear affine transformation shown previously to be valid for individuals 5 to 18 years of age (Muzik & Chugani, 2000; Wilke et al. 2002).

For each participant, Pearson's correlation maps were computed on a voxel-wise basis between MR data and task reference function corresponding to the Neutral (21s) and the Interference (21s) conditions. A 6s delay was applied to the reference function to allow for the canonical hemodynamic response to peak. Correlation coefficients were transformed into z-score

maps using Fisher's z-transformation. Group analyses were performed on these z-maps from individual participants in the context of the random-effects General Linear Model (GLM). A post-processing filter (4mm FWHM) was then applied before significant regions of activation on a voxel-by-voxel basis were identified (Worsley & Friston, 2002), generating a statistical parameter map. A clustering threshold of 30 contiguous voxels was also used (Xiong et al., 1995) to improve visualization of the parameter maps and to reduce the severity of the corrections that were made for multiple comparisons. Monte-Carlo simulation was performed to assure $p < 0.0001$ after adjusting for multiple comparisons. For each cluster, the Talairach coordinates of the pixel that showed the maximum Z value before filtering (i.e., the maxima) is reported here.

Results

Group comparisons on demographic, cognitive, and behavioral data

Table 1 provides the demographic, cognitive, and behavioral data for the adolescents with TBI and the TC groups. The mean Glasgow Coma Scale score for the TBI group was 12.6 (SD = 3.6) with one adolescent having sustained a severe TBI. Eight of 11 children had GCS scores of 13-15 with abnormal imaging. The remaining three children had GCS scores of < 13 with no abnormalities on clinical CT or MRI at the time of injury. The average time since injury was 1.8 years (SD = .45). The groups were comparable with respect to age, family income, race/ethnicity, sex and handedness. There were no group differences on any of the cognitive measures, all $ps > 0.14$. Adolescents with TBI had significantly higher levels of parent-rated executive dysfunction (BRIEF) than did the TC group; although means in both groups were within the normal range. The groups did not differ on self-report (BRIEF-SR) ratings of executive functioning.

Counting Stroop: Behavioral and fMRI results

Performance data for the Counting Stroop task were recorded during the fMRI scan. All but one participant showed higher accuracy and faster median reaction time in the Neutral condition than the Interference condition. Mean accuracy for participants with TBI did not differ from those for participants in the TC group, all $ps > 0.11$. Median reaction time (RT) calculated for each participant, excluding data from all error trials, showed that adolescents with TBI were slower than those in the TC group in the Neutral condition, $t(20) = 2.08$, $p = 0.05$, while the groups were not significantly different in the Interference condition, $p > 0.13$. Focusing on the magnitude of interference in behavioral performance, defined as the difference between the Neutral and the Interference conditions, the two groups were well matched and not different *in RT* (79 ms for the TBI group and 86ms for the TC group) or *in accuracy* (10.4% for the TBI group and 9.3% for the TC group), both $ps > 0.7$. The magnitude of the behavioral interference effects in RT and accuracy were larger than has been demonstrated in studies of adults (RT range = 29 to 46ms, see Bush et al., 2003; accuracy = 0 to 3%, see Bush et al., 1998, 1999).

Figure 1 presents the composite Z-score map of brain regions that were significantly more active during the Interference condition compared to the Neutral condition in the entire sample of 22 participants. Predominantly bilateral activation with a leftward bias was seen in broad extent of the brain. These include dorsal as well as ventrolateral prefrontal cortices, anterior cingulate, posterior parietal cortex, lingual and fusiform gyrus, cerebellum and other occipital regions. With respect to group-related differences (Figure 2, Table 4), participants in the TBI group had higher levels of inhibition-related activation in frontal areas including broad extent of the right superior frontal gyrus (SFG, BA 6), medial frontal areas including dorsal anterior cingulate (BA 32) and frontal cortex (BA 8), dorsolateral prefrontal cortex bilaterally

(BA 9), left dorsolateral prefrontal cortex (BA 10, 46), right ventrolateral prefrontal cortex (BA 10, 11), and right insula. Activation differences were also seen in the parietal cortices, including right superior parietal lobule including the precuneus (BA 7) and bilateral inferior parietal lobule including the supramarginal gyrus (BA 40), temporal cortices, including the middle / inferior temporal gyrus and fusiform gyrus (BA 20, 21), as well as bilateral cerebellum and right putamen. The brain areas in which participants in the TC group demonstrated greater inhibition-related activation than participants in the TBI group were much more restricted and included left frontal cortex (BA 10/46), left posterior cingulate (BA 31) and left inferior / middle temporal gyrus (MTG/ITG).

[INSERT Figure 1, Figure 2, TABLE 2 HERE]

We also examined the correlation between task performance and brain activation for all 22 participants as a group. For each participant, an accuracy difference score (Accuracy Neutral minus Accuracy Interference) was calculated and served as an index of interference susceptibility (i.e., in theory, participants who showed poor inhibition would show a high difference score). Within all brain regions that showed inhibition-related activation in either participant group, interference susceptibility was *positively* correlated with levels of activation differences in a variety of regions (Figure 3). Many of these areas correspond to those that showed higher levels of activation in TBI participants (Figure 2), including multiple regions in the prefrontal (right BA 6, BA 8 / dorsal anterior cingulate, BA 9 bilaterally, left BA 46) and parietal cortex (BA 40 bilaterally, BA 7 and 40 on the right). However, additional areas in the cerebellum bilaterally, left BA 6 and broad extent of BA 7 and BA 40 in the left posterior parietal cortex also showed interference-susceptibility related correlation. Notably, no areas showed negative correlation that survived the same threshold.

[INSERT Figure 3 HERE]

Finally, we examined whether the relationship between brain activation and performance was different across groups in regions showing over-activation in TBI. We first identified regions of interest (ROIs) that showed more inhibition-related activation in the TBI group than the TC group. Within these ROIs, we tested to see if any showed a significant correlation between inhibition-related brain activation and the interaction between group and task performance. None of the regions exhibit such a correlation. This finding suggests that the relationship between task performance and brain activation level was not significantly different across groups in the over-activated brain regions relevant for inhibition in the TBI group.

Discussion

The findings from this study are consistent with our hypotheses that adolescents with TBI would activate similar networks of brain regions during the Counting Stroop task relative to typically developing controls, but would demonstrate an *over*-activation of brain regions supporting inhibitory processing. Many of these over-activated regions in the frontal and parietal cortices, including BA 6, 8, 9, and 46 were also associated with interference susceptibility. Specifically, participants who had higher levels of differential brain activation in the interference minus neutral contrast tended to be more susceptible to interference behaviorally (i.e., poorer in interference trials relative to neutral trials). The positive association between brain activation level and worse performance (in RT) in interference trials has been observed in previous studies using this paradigm. Specifically, both brain activation and RT declined with practice in interference trials in the anterior cingulate and other regions (Bush et al., 1998, 1999). In our study, however, regions showing interference susceptibility characteristics across participants tend to be more bilaterally distributed dorsally and did not include the anterior cingulate,

whereas over-activation in TBI participants tend to be more right lateralized dorsally (BA 6 and BA 7/40). Our findings are broadly consistent with other fMRI studies that observed altered, specifically higher levels of and more extensive, neural activation patterns in individuals with TBI (Christodoulou et al., 2001; McAllister et al., 1999, 2001; Newsome et al., 2007a, b; Perlstein et al., 2004; Scheibel et al., 2003, 2007, 2009). Notably, the finding of over-activation in tasks probing cognitive control, attention, or working memory in populations with TBI relative to controls contrasts with those using similar behavioral paradigms in populations with Attention Deficit Hyperactivity Disorders (ADHD) (as noted by Kramer et al., 2008; for review see Epstein, in press). Finally, in this study a few brain regions confined to the left hemisphere (BA 10, 37, & 31) were noted to have higher levels of inhibition-related activation in healthy adolescents relative to adolescents with TBI. These regions do not show an inhibition-related response profile and their precise role remains to be determined in future investigations.

Similar to the current results, previous studies using the current paradigm (Bush et al., 1998, 1999) have also reported that *lower* levels of brain activation differences between the Interference and the Neutral condition was associated with *better* performance in the interference condition (i.e., increase in accuracy or reduction in RT due to practice). This pattern of association may be characterized as *inhibition effort* (lower effort associated with better performance). In other paradigms, however, higher levels of brain activation differences between the incompatible and the neutral condition were associated with *better* performance in conditions involving interference, apparently reflecting *inhibition success*. For example, Bunge and colleagues (2002) used a flanker task with an event-related design and compared brain activation patterns in healthy adults and healthy children (aged 8 to 12). They found that participants who were *more* successful behaviorally in the incongruent condition (i.e., a shorter RT and less

interference susceptibility) showed higher levels of activation in the incompatible condition relative to the neutral condition. Participants in the Bunge et al., (2002) study, however, had excellent performance (accuracy > 98% in the incompatible condition for children and adults) compared with poorer performance of participants in the current study (accuracy = 83% and 87% for the TBI and TC groups respectively). Similarly, Scheibel and colleagues (2007, 2009) used a stimulus-response incompatibility paradigm in a blocked design with adults with TBI or with orthopedic injuries; the correlation between accuracy in the incompatible condition and the level of brain activation differences between the Incompatible condition and the Compatible condition was either positive (Scheibel 2009) or absent (Scheibel et al., 2007). In contrast to the current study, participants in both of these studies were given extensive training and behavioral performance in the incompatible condition was not significantly different from the compatible condition. In sum, it is unclear exactly how the observed differences in directional relationship between inhibition-related brain activation and level of performance relate to paradigm-specific task demands. The distinction between inhibition success and inhibition effort may parallel a distinction in the memory literature between *retrieval success* and *retrieval effort* (e.g., Buckner et al., 1998). Further studies are needed to tease apart the likely complicated relationship between task demands, task performance, and brain activation.

The current study demonstrates the feasibility of assessing inhibitory processing with fMRI in adolescents following TBI using healthy children as controls. The adolescents with TBI successfully completed the scanning protocol and were equivalent to healthy controls on task performance with minimal training prior to scanning, as well as on most demographic measures. These results suggest that the pattern of over-activation in individuals with TBI may be a general finding and is not limited to cases where OI participants were used as a comparison standard. In

the current study, we focused on examining inhibition in adolescents with TBI within a relatively restricted range of age and IQ that could be matched to the healthy controls. Future investigations using a more diverse sample with a broad GCS range could examine the relationship between GCS and brain activation in children as has been done for adults with TBI (Scheibel et al., 2009).

Care must be taken in generalizing from the current findings given the small and homogenous nature of the sample of adolescents with TBI. All but one of the children had moderate TBI and cognitive performance was within the average range. Future research is needed to determine the neural substrates of inhibition in children with more significant cognitive and behavioral impairment following TBI. Additionally, the current study examined only one aspect of the attention network at a single point in time during the chronic phase of recovery. Additional studies will be required to understand the neural substrates of other aspects of attention and executive functions, whether the process of recovery results in neural remodeling over time, and how neural functioning relates to functional outcomes. Nonetheless, this study provides important new information about neural differences in the network subserving inhibition following TBI in adolescence.

The finding that neural activation is altered following pediatric TBI during tasks requiring inhibitory processing has important clinical implications. Given the important role of inhibitory control and EF in adolescence, EF skills may warrant targeted interventions. Investigations with both acquired (e.g., brain tumor) and traumatic brain injury populations have provided preliminary evidence that training in metacognitive strategies that encourage the child to “stop and think” may improve behavioral and academic functioning (Butler et al., 2008; Wade, Walz, Carey, & Williams, 2008). However, specific interventions to alter the neural

underpinnings of inhibition deficits have not been developed, and the linkages between neural activation and treatment response remain to be elucidated. Future integration of functional imaging into intervention research may further our understanding of the recovery process.

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Table 1. Demographic Characteristics and Neuropsychological Performance by Group

<u>Measure</u>	<u>TBI</u>	<u>Control</u>	<u>t/Chi Square</u>	<u>p value</u>
Age	15.7 (1.01)	14.2 (1.54)	.77	.45
Family Income	6.64 (4.78)	8.00 (2.79)	-.82	.42
Male Sex	7 (64%)	6 (55%)	.19	.67
Right Handed	11 (100%)	9 (82%)	2.20	.14
Race				
Caucasian	9 (82%)	10 (91%)	.39	.53
African American	2 (18%)	1 (9%)		
PPVT-4	102.6 (14.5)	107.7 (9.9)	-.98	.34
WRAT-4	101.91 (18.74)	114.64 (18.58)	-1.60	.13
WISC-IV PSI	107.6 (15.2)	105.5 (17.0)	.32	.75
WISC-IV WM	98.9 (10.2)	107.7 (15.2)	-1.55	.14
BRIEF GEC	53.1 (13.3)	42.7 (8.7)	2.16	.05
BRIEF-SR GEC	53.2 (11.6)	48.7 (10.1)	.96	.35
D-KEFS CW Inhibit	10.55 (2.5)	9.82 (1.5)	.83	.42
Counting Stroop				
% Correct Neutral	93.7 (4.9)	96.55 (2.5)	-1.7	.11
% Correct Interference	83.3 (8.6)	87.27 (11.5)	-.92	.39
RT Neutral	813 (73)	746 (79)	2.08	.05
RT Interference	892 (78)	832 (98)	1.59	.13
Difference in Accuracy	10.45 (8.82)	9.27 (9.89)	.30	.77
<u>Difference in RT</u>	<u>78.91 (35.33)</u>	<u>86.27 (51.58)</u>	<u>-.39</u>	<u>.70</u>

PPVT = Peabody Picture Vocabulary Test, WISC = Weschler Intelligence Scale for Children 4th Edition, PSI = Processing Speed Index, WMI = Working Memory Index, BRIEF = Behavior Rating Inventory of Executive Function, GEC = Global Executive Composite, DKEF CW = Delis-Kaplan Executive Function System Color Word Interference Task, RT = reaction time

Table 2. Regions of interest (ROIs) showing significantly different levels of activation between children with TBI (TBI) and typically developing controls (TC) in the Interference (I) minus Neutral (NoI) contrast during the Counting Stroop task.

ROI	Brodmann Areas	Talairach Coordinates			Peak Z
		x	y	z	
TBI > TC					
R Superior Frontal Gyrus	6	22	0	51	1.7
R Superior Frontal Gyrus	6	26	-3	59	2.1
Anterior Cingulate Cortex	32	4	21	39	2.3
Medial Superior / Middle Frontal Gyrus	8	4	21	43	2.2
L Middle Frontal Gyrus	9	-28	39	31	2.9
R Middle Frontal Gyrus	9	32	24	31	2.6
L Middle Frontal Gyrus	9/10	-28	39	31	2.9
L Middle Frontal Gyrus	46	-41	30	15	2.1
R Middle Frontal Gyrus	10	31	51	-1	2.6
R Superior Frontal Gyrus	10/11	28	51	-5	2.6
R Insula	13	32	15	11	2.2
R Middle Temporal Lobe	21	56	-21	-9	2.9
R Inferior Temporal Gyrus / Fusiform	20	40	-21	-21	2.7

Thustos – Neural correlates of inhibition in adolescents with TBI 30

R Superior Parietal Lobule	7	38	-57	55	2.5
R Precuneus	7	26	-75	43	2.0
R Inferior Parietal Lobule	40	38	-54	43	2.3
L Inferior Parietal Lobule	40	-38	-45	39	2.0
L Supramarginal Gyrus	40	-38	-42	35	2.0
R Claustrum / Putamen		34	12	7	2.5
R Cerebellum		34	-51	-17	2.5
L Cerebellum		-20	-63	-21	2.3

TC > TBI

L Middle Frontal Gyrus	10/46	-44	48	7	-2.3
L Posterior Cingulate	31	-14	-51	27	-2.3
L Inferior/Mid Temporal Gyrus	37/21	-56	-54	-1	-2.6

Figure 1.

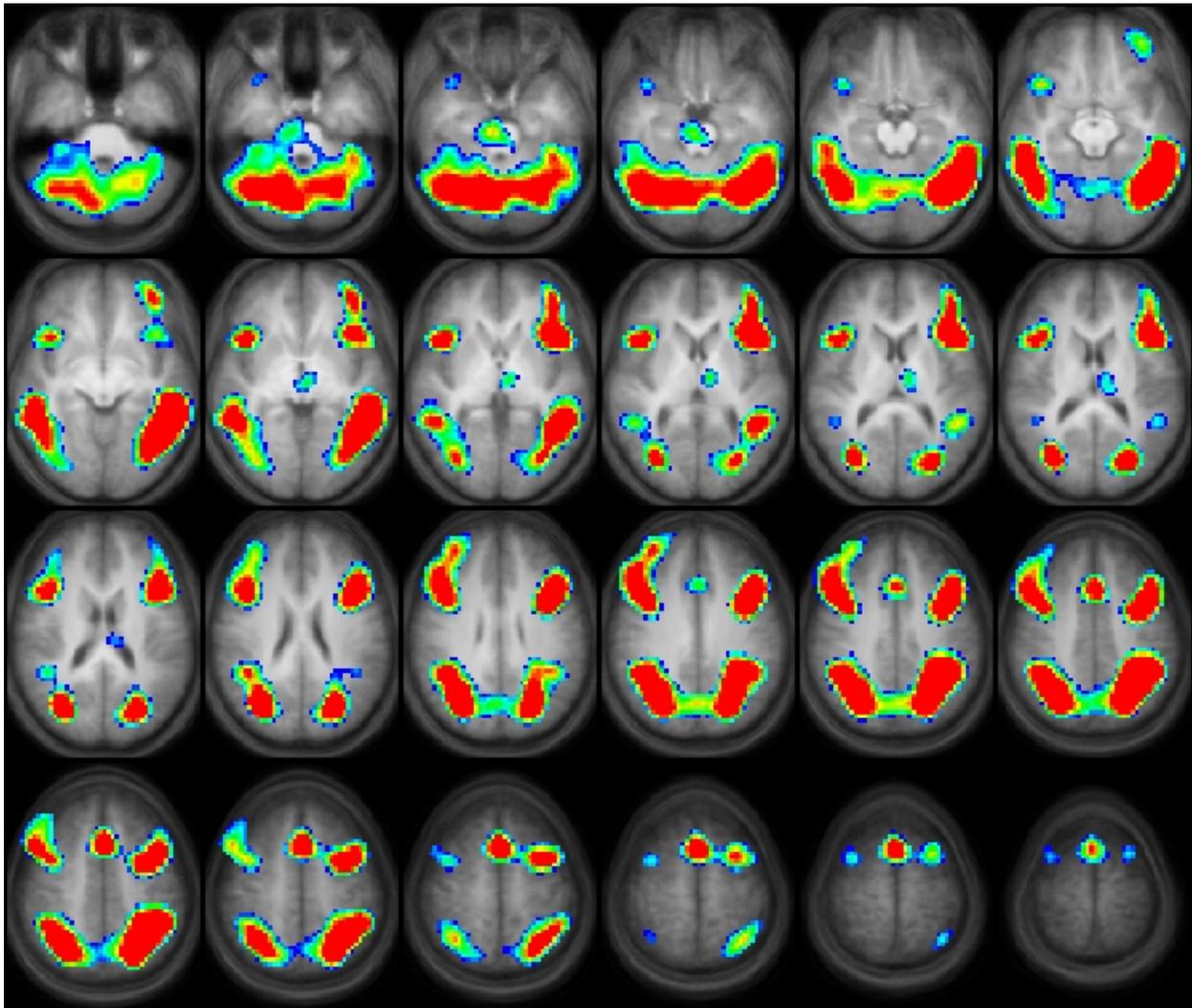


Figure 2.

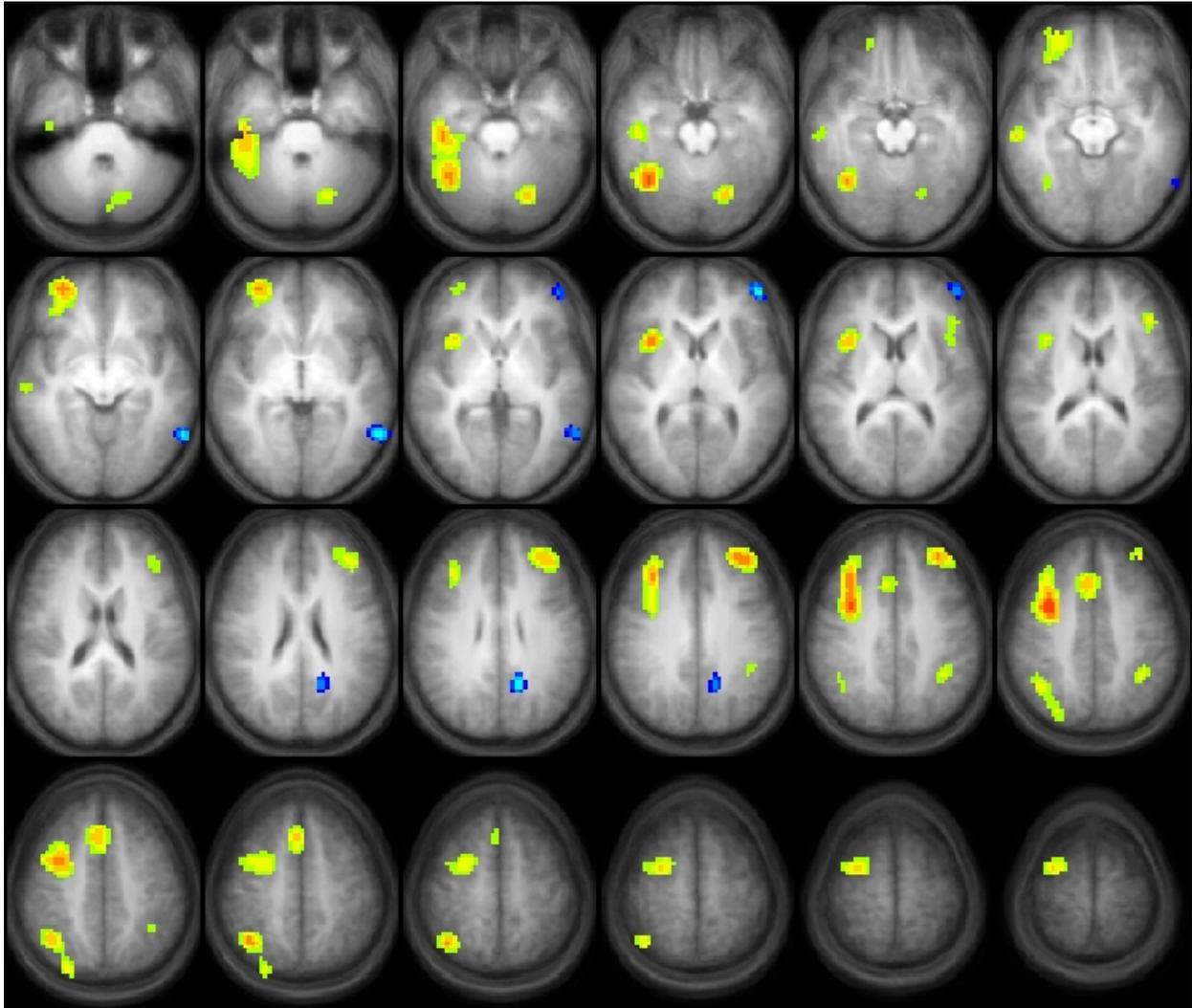


Figure 3.

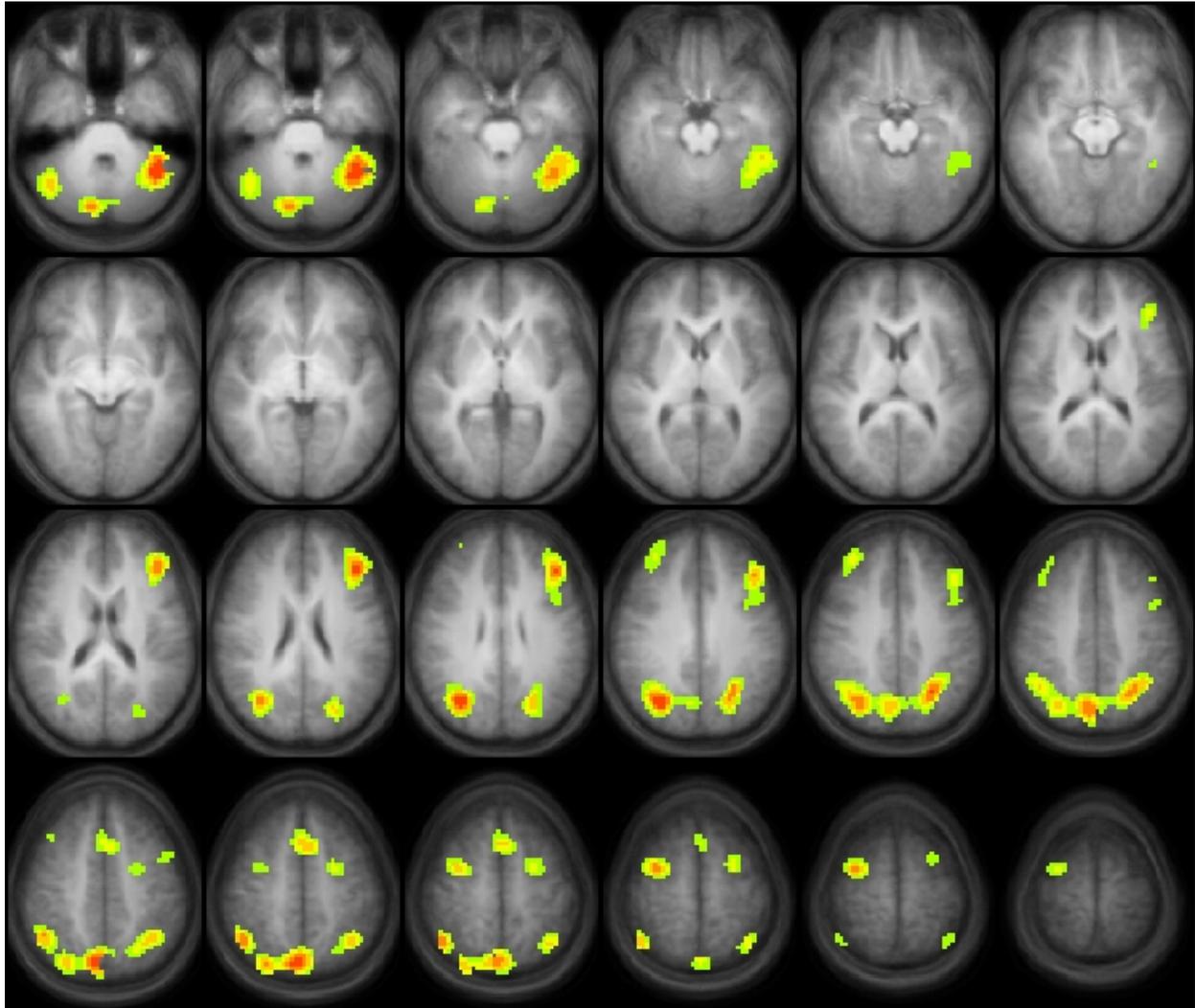


Figure Captions

Figure 1. Brain activation map for the entire group of participants. Only positive activation foci (Interference > Neutral) are shown here. Images are horizontal slices 4 mm apart and start at $z = -29$ mm (top left) to $z = +63$ mm (bottom right). Images are in radiological convention: left side of the images corresponds to the right hemisphere. Image parameters are as follows: nominal z threshold = 10.0, cluster = 30, corrected $p < 0.0001$ for multiple comparisons.

Figure 2. Group difference map in brain activation related to the Counting Stroop task. The TBI group had significantly higher levels of activation in multiple brain regions relative to the TC group (warm color). In contrast, the TC group had higher levels of activation only in 3 confined regions (cool color). Image conventions and parameters are as in Figure 1.

Figure 3. Statistical parametric map showing brain regions in which activation level was correlated with task performance (Accuracy Neutral minus Accuracy Interference) across all participants. No regions showed a significant negative correlation. Image conventions and parameters are as in Figure 1.