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Brain Activation while Thinking about the Self from Another Person's Perspective after Traumatic Brain Injury in Adolescents

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Abstract

Deficits in self awareness and taking the perspective of others are often observed following traumatic brain injury (TBI). Nine adolescents (ages 12–19 years) who had sustained moderate to severe TBI after an average interval of 2.6 years and nine typically developing (TD) adolescents underwent functional magnetic resonance imaging (fMRI) while performing a perspective taking task (D'Argembeau et al., 2007). Participants made trait attributions either from their own perspective or from that of the significant other. The groups did not differ in reaction time or on a consistency criterion. When thinking of the self from a third-person perspective, adolescents with TBI demonstrated greater activation in posterior brain regions implicated in social cognition, the left lingual gyrus (BA 18) and posterior cingulate (BA 31), extending into neighboring regions not generally associated with social cognition, i.e., cuneus (BA 31) and parahippocampal gyrus, relative to TD adolescents. We postulate that adolescents with moderate to severe TBI recruited alternative neural pathways during perspective-taking because traumatic axonal injury disrupted their fronto-parietal networks mediating social cognition.

Keywords

traumatic brain injury; fMRI; social cognition; adolescents

INTRODUCTION

Hospitalizations and deaths due to traumatic brain injury (TBI) are more common in late adolescence than during any other time in childhood (Langlois, Rutland-Brown, & Thomas, 2006). Despite at least partial recovery of many cognitive abilities following moderate to severe TBI in adolescents, a limited number of studies have shown deficits in social cognitive skills and psychosocial adjustment that can persist or worsen over time (Muscara, Catroppa, Eren, & Anderson, 2008; Yeates et al., 2004). In comparison to typically developing youth, solving interpersonal problems posed in hypothetical dilemmas remains impaired in adolescents during the first year following moderate to severe TBI (Hanten, et al., 2008) with similar findings at four years post-injury (Janusz, Kirkwood, Yeates, &

Taylor, 2002; Yeates, et al., 2004). In uninjured adolescents, diminished friendships, increased loneliness, and reduced quality of life are associated with reduced social skills (Bohnert & Garber, 2007; Parker, Rubin, Erath, Wojslawowicz, & Buskirk, 2006) and are problematic because peer interactions and support are especially salient during adolescence. Difficulty in processing the intentions and emotions (Dennis & Barnes, 1990; Dennis, Barnes, Wilkinson, & Humphreys, 1998; Henry, Phillips, Crawford, Ietswaart, & Summers, 2006) and taking the perspectives (Turkstra, Dixon, & Baker, 2004) of others may contribute to the observed deficits in social problem solving and poor psychosocial adjustment that persist after moderate to severe TBI in adolescents (Max et al., 2006).

The abilities to reflect on knowledge about the self as distinct from knowledge of other people and to adopt others' perspectives are key for effective understanding of others' intentions, beliefs, and feelings necessary for guiding communication and social actions. The ability to take another person's perspective enhances social interaction when one mentally places oneself in another person's position and makes a response based from that vantage point. By approximately age eight years, typically developing children realize that their feelings or thoughts may differ from those of others, with self-awareness continuing to develop throughout adolescence (Damon & Hart, 1982). By approximately 9 years, children appreciate that their own traits can be stable over time, as opposed to being based on one instance of behavior (Damon & Hart, 1988). In uninjured populations, Choudhury et al. (2006) reported less efficient perspective taking in pre-adolescents than young adolescents, with both groups being less efficient than adults. As traumatically brain injured populations commonly show deficits in reflecting on their own post-injury abilities and changes in behavior (e.g., Bach & David, 2006), self-awareness during perspective taking may be particularly affected in adolescents after TBI.

The neural underpinnings of making judgments about the self and adopting the perspectives of others involve several brain regions, based on results from previous fMRI studies. In an fMRI task, Pfeifer et al. (2007) reported activation in medial prefrontal cortex (MPFC) in both healthy children and adults when retrieving knowledge about the self, including traits of the self such as "I am popular" and "I am a good speller", compared to when retrieving knowledge about others, with greater activation in children than adults, suggesting that the neural networks for differentiating the self from others are in place by approximately 11 years and become more focal with age. Posterior brain regions, precuneus and posterior cingulate, were activated during retrieval of knowledge about another person. In healthy adults, D'Argembeau et al. (2007) reported activation in different locations in the MPFC when uninjured adults judged from a first or third person perspective whether they or a significant other displayed various personality traits, consistent with Schmitz & Johnson's (2007) review of dorsal-ventral MPFC regions involvement in self-appraisal. Trait judgment additionally activated precuneus, while perspective-taking also activated temporal pole, inferior parietal lobe, and precuneus. MPFC was again implicated when participants had to think about themselves from another person's perspective.

Frontal and temporal regions are the most frequently injured regions following TBI (Graham, Ford, Adams, et al., 2002; Levin, Mendelsohn, Lilly et al., 1997). The vulnerability of prefrontal and anterior temporal cortex to focal lesions and disruption of the circuitry for neural networks mediating social cognition have been implicated in reduced awareness of one's own mental state, impaired processing of the mental states of others, and inability to make social inferences (Cicerone, Levin, Malec, Stuss, & Whyte, 2006). We were interested in brain activation in adolescents with moderate to severe TBI when they had to evaluate themselves from another person's perspective, given the difficulty in self awareness and in processing the mental states of others following TBI (Henry et al., 2006). We chose to measure brain activation while thinking of the self from another's perspective

with a task that has shown reliable activation in prefrontal regions during perspective taking. As the task used by D'Argembeau et al. (2007) replicated areas of activation reported in several previous studies of trait attribution (e.g., D'Argembeau et al., 2005) and perspective taking (e.g., Ruby & Decety, 2001; 2004), suggesting reliability, we employed a similar design in the present study, which adapted the stimuli for TBI patients. Traumatically brain injured and typically developing (TD) participants were asked to think about themselves or a significant other either from their own perspective or from that of the significant other, with the trait attribution condition included solely to provide content for the perspective taking. This design allowed us to measure the brain activation associated with thinking of the self from another's perspective. We hypothesized that disruption of circuitry involving MPFC, medial parietal cortex, and temporal regions would result in more extensive activation in adolescents with moderate to severe TBI to compensate for reduced neural resources (Newsome et al., 2008).

MATERIALS AND METHODS

Patient and Comparison Groups

Nine adolescents (mean age at scanning=16.8 years, standard deviation (SD)=2.4, range=12.8–19.1 years; 6 males) who had sustained moderate to severe TBI as defined by a post-resuscitation score of 3–12 on the Glasgow Coma Scale (GCS) (Teasdale & Jennett, 1974), or a higher score associated with brain pathology on computed tomography, were selected from a cohort of pediatric moderate to severe TBI patients (Table 1). Selection criteria included severity of injury, age, availability for participation, ability to provide valid responses (see below) and restrain movement during scanning. Patients were recruited from hospitals in Dallas and Houston, Texas, and were studied between 1.9 years and 3.6 years (mean 2.6 years) post-injury. For comparison, nine TD adolescents (mean age=16.8 years, SD=1.8, range=13.9–19.3 years) served as controls. All participants were right-handed (Oldfield, 1971). No child was taking psychoactive medications and none had previous neurologic or psychiatric disorder. All TBI patients had focal frontal lobe lesions, and five patients had temporal lesions on structural MRI. Child assent and parental consent were obtained, and the study was approved by the institutional review boards at Baylor College of Medicine and The University of Texas Southwestern Medical School at Dallas.

To understand the performance of our social cognition task in the context of general social and cognitive functioning, additional measures were administered outside of the scanner (Table 2). The Functional Assessment of Verbal Reasoning and Executive Strategies (FAVRES; MacDonald & Johnson, 2005) measured social problem solving in a naturalistic setting, requiring the participant to make inferences, view the situation from another's perspective, eliminate irrelevant facts, choose a correct answer from a large number of options, and formulate a rationale to defend the option chosen. The Virtual Interpersonal Negotiations Strategy Interview (after Yeates, Schultz, & Selman, 1990), presented social dilemmas via live dialog between computer-animated characters to which the participant answered questions linked to four steps of a social problem-solving model (defining problem, generating solutions, evaluating outcome selecting solution). The Gray Oral Reading Test (GORT; Weiderholt & Bryant, 2001) provided a developmental measure of oral reading. The Keep Track Task (Friedman et al., 2006) measured working memory updating. The vocabulary and block design subtests of the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) measured verbal knowledge and spatial processing.

Trait Attribution Task

Procedures for presentation of the Trait Attribution Task were modified from D'Argembeau et al. (2007) to be readily understood by brain injured adolescents and to present two choices

between two response buttons rather than four. The participant was asked to make judgments about whether an adjective described himself or herself (Target=Self) or described a significant other (Target=Other) whom the participant designated prior to beginning the task. Orthogonal to the target condition, the perspective for making judgments varied as the participant was asked to take either his or her own (first-person) perspective, or the perspective of the other person (third-person). This 2×2 (Target × Perspective) design included four conditions: Self-First Person (S1P), Other-First Person (O1P), Self-Third Person (S3P), and Other-Third Person (O3P). Across the top of a computer screen, the participant viewed one of four incomplete statements that respectively described each of the four conditions: “You think you are...”, “You think (significant other) is...”, “(Significant other) thinks you are...”, and “(Significant other) thinks she is...” After 3 s, adjectives were presented below each statement for 4.5 s, during which time the participant pressed a response button held in the right hand if the adjective described the target some or all of the time, or a response button held in the left hand if the adjective did not describe the target or did so to a limited degree. These choices, presented in child/adolescent vernacular (*Kind of/ Totally* and *No way/Not really*) were presented at the bottom right and left sides of the screen, respectively, throughout the task as reminders. This was an fMRI block design, in which each block consisted of a condition that was presented for 5 trials of 22.5 s per block, followed by an interblock interval in which a fixation cross was presented for 9 to 15 s. After all 4 block conditions were presented, they were repeated during each run for a total of 8 blocks, or 40 trials, per run. Each run duration was 5 minutes and 3 s. There were 4 runs with 1 minute of rest between runs. Order of conditions was counterbalanced between runs and between subjects. Forty adjectives were selected from age of acquisition and familiarity normative data (Wilson, 1988) to be on a third to fourth grade reading level and to be high in familiarity, with a mean familiarity rating of 552 (normative data mean = 488, range 100–700). E-Prime (www.pstnet.com/eprime) was used to present stimuli and collect responses.

Pre-scan training with a practice version of the task that utilized words different from those presented in the scanner was provided. Before scanning, the participant was also asked to define the words that were to be presented during scanning. Any errors in definition were corrected to ensure that all participants understood the meaning of the adjectives to be presented during the task. To validate performance during the scan, participants were asked after the fMRI session to identify adjectives from the task that have opposite meanings by drawing lines between adjectives presented in two columns. Consistency scores were calculated for each participant by comparing the opposite words judgments to how the same words were responded to during the scan. For example, if after a scan a participant indicated that “interesting” and “boring” are opposites, then during the scan (within a condition), one of the words should have received a left button press, and the other word should have received a right button press if the participant was consistent. Agreement of 60% or higher on all 4 conditions for 8 word pairs was taken to indicate meaningful performance in the scanner, and all participants met this criterion.

MRI Scanning Procedures

Whole brain imaging data were acquired using a multi-channel SENSE headcoil on identical 3.0 T Philips Achieva scanners in Houston and in Dallas. Blood oxygen level dependent (BOLD) T2* weighted single-shot gradient-echo echoplanar images (EPI) were acquired in 32 axial slices of 3.75 mm thickness with an 1.0 mm gap, using a 240 mm × 240 mm field of view (FOV), 64 × 64 matrix, and a TR of 1700 ms, TE 30 ms, and 73 degree flip angle, and SENSE factor 2.0. After the functional scans, a set of high-resolution T1-weighted 3D-Turbo Field Echo (TFE) anatomical images was acquired in 132 axial slices of 1.0 mm thickness (no gap) with 240 mm × 240 mm FOV, 256 × 256 matrix, TR of 9.9 ms, TE of 4.6 ms, and 8.0 degree flip angle, and SENSE factor 1.2. These parameters produced 1 mm

isotropic voxels for the anatomical data. Additional anatomical series to assess neuropathology included T2-weighted gradient echo imaging, T2-weighted FLAIR, and T2-weighted GRASE. Similar ranges of values for Weisskoff stability measurements (Weisskoff, 1996) (minimum 1/SNR index, peak-to-peak and RMS stability) taken on the day of scan indicated stability of both scanners over time.

fMRI Processing

Functional MRI data were processed and analyzed using Statistical Parametric Mapping software (Friston et al., 1995) (SPM2, Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab (Mathworks Inc. Sherborn MA, USA). Spikes greater than 2.5 standard deviations above the mean voxel intensity across time series were replaced with the median voxel intensity for that time series using Analysis of Functional Neuroimages software (AFNI) (Cox, 1996). Thereafter all processing and analyses were completed in SPM2. After slice-timing correction, the fMRI time series was realigned and corrected for head motion and susceptibility-by-movement interactions. Series with head motion component on any axis greater than 2.0 mm translational or 2.0 degrees rotational were eliminated from analysis. The high-resolution anatomical scan was co-registered to the fMRI images and was transformed to the stereotactic coordinates of the Montreal Neurologic Institute using the SPM2 Normalise procedure. The same transformation was applied to the functional images, which were then resliced to 2 mm isotropic voxels, and spatially smoothed with a 6 mm isotropic full width at half maximum Gaussian filter. The cluster-defining (height) threshold was voxel-level $p=0.05$, uncorrected. All reported clusters were statistically significant ($p<0.05$) at the cluster level of inference, using Random Field Theory correction for multiple comparisons over the whole brain volume. When cluster sizes exceeded 2000 voxels, a more stringent voxel-level (height) threshold was used to reduce cluster sizes to 2000 voxels or less. Significant coordinates were converted to the coordinates of the Talairach Atlas (Talairach & Tournoux, 1988) using the mni2tal script (Brett, 1999). The Talairach Daemon (Lancaster et al., 2000) and the Talairach Atlas were then used to determine the anatomical locations and approximate Brodmann's Areas (BA) (when available) of the Talairach coordinates.

RESULTS

Trait Attribution Performance

Table 3 reports mean reaction time (ms) by group for each condition. Because there are no correct or incorrect answers for the trait attribution task, accuracy analyses are not reported. Average consistency scores were similar between groups (TD $M = 0.80$, $SD = 0.10$; TBI $M = 0.78$, $SD = 0.15$), $t(16) = -0.36$, $p = 0.72$, Cohen's $d = 0.174$. Significant main effects of response time (RT) for Target, $F(1,16) = 8.14$, $p = 0.01$, Cohen's $f = 0.71$, and Perspective, $F(1,16) = 5.79$, $p = 0.03$, Cohen's $f = 0.60$, indicate that judgments about the Self were made more quickly than judgments about the Other (1360 msec vs. 1434 msec), and that judgments from the First Person perspective were made more quickly than those from a Third Person perspective (1373 msec vs. 1431 msec), replicating D'Argembeau et al. (2007). There were no significant interactions of group with Target, $F(1,16) = 2.02$, $p = 0.17$, Cohen's $f = 0.36$, Perspective, $F(1,16) = 0.01$, $p = 0.93$, Cohen's $f = 0.025$, or Target and Perspective, $F(1,16) = 0.07$, $p = 0.80$, Cohen's $f = 0.07$.

Trait Attribution Related Brain Activation

Table 4 presents the coordinates, cluster sizes, and probability levels of significant clusters of activation observed for between-groups differences.

Main Effect of Target (Self vs. Other)—There were no significant between groups differences for the main effect of target.

Main Effect of Perspective (First-Person vs. Third-Person)—There were no significant between groups differences for the main effect of perspective.

Interaction of Target and Perspective (S3P – S1P) – (O3P – O1P)—Figure 1 is an SPM activation map of between group differences for the interaction of Target (Self vs. Other) and Perspective (First-Person vs. Third-Person) when thinking about the self from a third person perspective. There were no areas where the interaction of target and perspective was significantly greater in the TD group, relative to the TBI group. However, there was one large cluster in which the interaction was significantly greater in the TBI patients than in the TD adolescents (mean difference across all voxels within the cluster = 2.3 percent of whole brain BOLD signal; 90% confidence interval = 1.2 – 3.4), and this cluster included the *left* posterior cingulate (Talairach x y z [mm] = -16 -52 6 BA 30; -14 -64 14 BA 31), cuneus (-8 -60 8 BA 31), lingual gyrus (-14 -52 4 BA 18; -12 -52 0 BA 19), parahippocampal gyrus (-16 -48 4), inferior parietal lobule white matter (-36 -44 26), supramarginal gyrus white matter (-34 -48 26), posterior cingulate white matter (-14 -48 18); *bilateral* thalamus (-4 -18 4; 6 -20 4), brainstem (-8 -24 -26; 2 -38 -26), and cerebellum (-10 -52 -42; 8 -64 -40).

DISCUSSION

To investigate the effects of moderate to severe TBI on neural mechanisms mediating social cognition in youths, we performed fMRI during a trait-attribution and perspective-taking task (D'Argembeau et al., 2007) in adolescents an average of 2.6 years post-injury and in TD adolescents. With traumatic axonal injury (TAI) putatively disrupting interconnectivity of prefrontal subregions involved in trait attribution and other social cognition tasks, including medial prefrontal cortex (MPFC), anterior cingulate cortex (ACC), and their connections to posterior cortical regions (e.g., medial parietal and temporal cortex), we anticipated that adolescents with TBI would exhibit more extensive activation to compensate for fewer available resources.

We were interested in brain activation in adolescents with moderate to severe TBI when they had to evaluate themselves from another person's perspective, given difficulty in self awareness and processing mental states of others following TBI (Henry et al., 2006). Measurement of how consistently the participants defined adjectives during and after the task indicated good consistency in both groups, suggesting that activation in the TBI group reflected processes they were able to perform (Price & Friston, 1999). We did not find group differences in frontal regions. As compared with TD adolescents, attribution of traits to the self while taking a third-person perspective in adolescents with moderate to severe TBI resulted in widespread brain activation in posterior and subcortical regions. The greater activation found in left lingual gyrus (BA 18), which is reported to be activated during perspective-taking in adults (D'Argembeau et al., 2007), and in left posterior cingulate (BA 31), which is reported to be activated in children while attributing traits to other people (Pfeifer et al., 2007), may indicate greater reliance on nonfrontal regions when frontal areas and their connections have been disrupted (Price & Friston, 1999). Neighboring regions not generally associated with social cognition (i.e., parahippocampal gyrus and cuneus (BA 31)) were also recruited more by TBI adolescents, suggesting reorganization. The cuneus has been suggested to provide compensatory activation in aging and patient populations during different cognitive tasks, such as category monitoring (Léonard, de Partz, Grandin, & Pillon, 2009), recognition memory (Eliassen, Holland, & Szaflarski, 2008; Scarmeas et al., 2003) and response inhibition (Haldane, Cunningham, Androutsos, & Frangou, 2008).

Additionally, activation in the cuneus has been reported in several studies of cognition when it had not been hypothesized, suggesting the cuneus may have nonspecific effects. For example, in addition to expected frontal and temporal areas, activation in the cuneus was seen in a sentence completion task (Allen et al., 2008). Greater activation in the parahippocampal gyrus may also be a result of less efficient access to long term memory representations when judging whether the other person has experienced a particular trait in the subject. As TAI alters projections from the frontal lobes (Wilde et al., 2006), increased thalamic activation in the TBI group may indicate reliance on a more intact area in the fronto-thalamic network.

Given damage to frontal lobes following TBI, one might expect reduced frontal activation in the TBI group to be evident in a group difference. BOLD signal in damaged areas has frequently been associated with increased activation (Turner & Levine, 2008), possibly due to compensation from other frontal areas; in such situations, any group effects where increased activation is normally expected in uninjured populations would be cancelled out. Further it is possible that frontal activation might be reduced in some sub-processes of thinking of the self from another person's perspective, but not in others, as seen in working memory with TBI patients (Newsome et al., 2008). Future studies delineating such sub-processes and associated activation with event-related fMRI are needed to further characterize this possibility.

Our study did not reveal group differences in the activation main effects of target type or perspective. The fact that the TBI group showed more activation only for the interaction, i.e., when they considered themselves from another person's perspective, may reflect that this type of social thought is more demanding than the other conditions examined in the study. Effects of TBI are often observed during performance of more complex tasks (Gronwall & Wrightson, 1981), and thinking of the self from another's perspective may be more challenging than thinking of the self from one's own perspective (Dennis, Purvis, Barnes, Wilkinson, & Winner, 2001), or involve integration between more areas that had sustained damage. The TBI group performed worse than the TD group on all cognitive and social cognitive measures, including reading (GORT), working memory updating (Keep Track Task, (Friedman et al., 2006)), everyday living executive function skills (FAVRES), and judging social situations while holding information in working memory (INS, (Yeates et al., 1990)). It is possible that the increased activation observed when patients in the TBI group thought of themselves from a third-person perspective is related to impaired cognition. Impaired self-awareness and theory of mind have been linked to deficits in executive functions in patients with TBI (Bibby & McDonald, 2005; Bivona et al., 2008; Henry et al., 2006). In severe TBI adult patients an average of seven years post-injury, Bibby and McDonald (2005) reported that impairment in thinking about what one fictional person thinks about another person (second-order TOM task) could be accounted for by deficits in inference making and executive function. However, deficits in a task that involved thinking about one person only were attributed to apparent deficits in TOM. Our task of thinking of the self from another's perspective is not the same as a first or second-order task as it involves potentially overriding information that may be accessed about the self. However, it is similar, and because it may potentially involve additional retrieval and inhibitory processing, additional executive function may be implicated.

Relative to uninjured matched controls, TBI patients with poor self-evaluative accuracy on socio-cognitive functioning demonstrated increased activation in some areas involved in social cognition (anterior cingulate, precuneus, and temporal pole), when judging personality traits about themselves (Schmitz, Rowley, Karhara, & Johnson, 2006), suggesting increased activation in areas potentially involved in the inaccurate self-assessment outside of the scanner. Although similar to our task, this task did not involve

thinking from a third-person perspective. However, it is interesting that greater activation in a frontal area was observed. One potential explanation is that our sample size was smaller ($n=9$ vs. $n=20$); however, there was no hint of a group difference in frontal activation in our results. The patients of Schmitz et al. were an average of 81 days post-injury, while ours were an average of 2.6 years, and potentially differences in activation may in part be due to neural recruitment that may not yet have stabilized.

Milders et al. (2006) found impairment in a TBI group both one month and one year after injury in two theory of mind (TOM) tasks, the Faux Pas Task (Stone et al., 1998), in which subjects identify inappropriate actions in social settings, and the Cartoon Test (Happé et al., 1999), which involved the comprehension of jokes involving the false beliefs of others. When relating performance on these tasks to external measures of social functioning (Milders et al., 2008), they found no relationship, questioning whether the link between TOM and behavior exists. Taking another person's perspective did not reveal a significant group difference in activation in the present study; behavior that neurally distinguished groups involved relating another person's perspective to themselves. Tasks in the Milders' studies did not include a condition in which subjects relate social mistakes or false beliefs to themselves; possibly a TOM task which incorporates subjects into settings personalized to them may find a relationship between TOM and behavior.

It is possible that the IQ of the TBI group (mean=95; 37th percentile of the WASI) may be unexpectedly high, which could account for the lack of group differences. Low IQ is associated with severe TBI in very young children (mean age 5 years, Anderson et al. 2004), although children injured at older ages (8–12 years, Anderson et al., 2000) show better intellectual recovery. The TBI patients in our study sustained their injuries during early adolescence (mean age 14.2 years), and had IQ scores consistent with that of severe TBI patients reported in Anderson et al., (2000).

There are several limitations in this study. Due to small sample sizes, results should be considered tentative and pending confirmation. Although the groups were chosen to be similar in socioeconomic status, the TD group's WASI score was higher than that of the TBI group, which could have contributed to differences in activation (Perfetti et al., 2009). Larger studies which manipulate IQ would elucidate the role of intelligence in social perspective taking. Potential confounds in this study include poor comprehension of the adjectives by adolescents with TBI. However, consistency rates did not differ between the groups, suggesting that the adolescents with TBI accurately processed the meaning of the adjectives presented during the task. While our subjects appeared to have been able to complete the task successfully, TBI patients who have stronger impairments in thinking of the self from another perspective may be less adept in recruiting additional brain regions. Future studies in which patients receive training in perspective taking (Grizenko et al., 2000) and demonstrate improved ability may also show increased activation in posterior brain regions. In addition, while the TBI adolescents in our sample may have been able to take another person's perspective about themselves upon demand, an open question is how adeptly they do so in naturalistic settings, which often have a strong visual component not present in our task. In both types of real-life tasks administered outside the scanner (FAVRES and the virtual INS), the children with TBI performed less well than typically developing controls. Although we might surmise the pattern of activation may show differences in relation to performance on these tasks, sample size prohibits meaningful correlational analyses. Future studies presenting simulations of social interactions in a virtual reality environment during fMRI would further elucidate behavioral and neural alterations during perspective taking in patients following TBI.

Conclusions

Patients with TBI frequently demonstrate impairments in self awareness and in taking the perspectives of others. Because of the roles of frontal, parietal, and temporal regions in perspective-taking and trait attribution (D'Argembeau, et al., 2007; Pfeifer et al., 2007), and given alterations in fronto-parietal and fronto-temporal neural networks (Newsome et al., 2008; Wilde, et al., 2005), and reduced social problem solving skills (Hanten et al., 2008; Parker et al., 2006; Yeates et al., 2004) in adolescents with moderate to severe TBI, we predicted that their brain activation would be altered during a social perspective task. Brain activation when taking another person's perspective to think about the self was altered in adolescents after an average interval of 2.6 years post moderate to severe TBI. Relative to typically developing, uninjured peers, adolescents with TBI had greater activation in left lingual gyrus (BA 18), a posterior brain region associated with perspective-taking (D'Argembeau et al., 2007), and left posterior cingulate (BA 31), a region associated with attribution of traits to another person, (Pfeifer et al., 2007), as well as in subcortical areas.

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Figure 1.

Maximum intensity projection map of the between group contrast, TBI > TD, for the Target $\times$ Perspective interaction when judgments about the self were made from a third person perspective ((S3P – S1P) – (O3P – O1P)). TD > TBI was nonsignificant. The right hemisphere of the brain is displayed on the right side of the figure. Regions that showed significant t-test results are displayed in black.

Table 1

Features of Nine Traumatically Brain Injured Patients.

	Age at Test	Age at Injury	Post-injury Interval	Mother's Education	Gender	Mechanism of Injury	GCS score	Lesion Sites
TBI1	18.33	16.01	2.32	14	F	Fall	15 (+complications)	R OrbG, B IFG, R MFG, R MedFG, B SFG, R Temp Pole
TBI2	16.03	13.07	2.96	12	M	Fall	3	L GyrRect, B OrbG, B IFG, L MFG, B Temp Pole, L Thal
TBI3	12.83	9.36	3.47	6	F	Fall	9	B OrbG, R IFG, R MFG, L Cblm
TBI4	18.42	14.79	3.63	9	M	ATV	3	L OrbG, R IFG, R MFG, B SFG, L MidCC, L Cblm, L OccLobe
TBI5	18.66	16.67	1.99	16	M	MVA	10	R MFG, L MedFG, B SFG, B MTG, B Temp Pole, L Operculum
TBI6	19.13	17.03	2.10	12	F	MVA	7	L OrbG, B ITG
TBI7	14.42	12.37	2.06	9	M	MVA	8	L MFG, L SFG
TBI8	18.70	15.90	2.81	14	M	ATV	3	L IFG, B MFG, R SFG, B SPC, R Thal, R Putamen
TBI9	14.62	12.71	1.92	16	F	Fall	7	B OrbG, L MFG, B SFG, L STG, R MTG, R ITG, R Temp Pole, B Ant Temp Pole, Midline Ant CC

Ant=Anterior, B=Bilateral, L=Left, Mid=Middle, R=Right

Cblm=Cerebellum, GyrRect=Gyrus Rectus, IFG=Inferior Frontal Gyrus, ITG=Inferior Temporal Gyrus, MedFG=Medial Frontal Gyrus, CC=Corpus Callosum, MFG=Middle Frontal Gyrus, OccLobe=Occipital Lobe, OrbG=Orbital Gyrus, SFG=Superior Frontal Gyrus, Thal=Thalamus

ATV = All-Terrain Vehicle accident, MVA = Motor Vehicle Accident

Table 2
Demographic and Outcome Data (Means and Standard Deviations) for TBI and TD Groups*

Group	Age	Gender	Ethnicity	SCI	Mother's Education
TBI	16.8 years (2.4) range=12.8–19.1	4 Female 5 Male	1 African American 3 Hispanic 5 Caucasian	−0.49 (1.06)	12.00 years (3.43)
TD	16.8 years (1.8) range=13.9–19.3	4 Female 5 Male	1 African American 4 Hispanic 4 Caucasian	0.17 (0.68)	12.56 years (2.35)
	WASI ⁺	Keep Track ⁺	GORT ⁺⁺	FAVRES ⁺	Virtual INS ⁺⁺
TBI	95.0 (12.9) range=79–113	69.34 (11.9)	15.6 (5.6)	9.63 (1.18)	9.2 (1.0)
TD	109.3 (11.3) range = 96–129	85.31 (9.23)	24.7 (3.6)	10.81 (0.75)	10.7 (0.82)

* Data were not available for one TBI participant for the WASI, two TBI and two TD participants for the Keep Track Task, one TBI and two TD participants for the GORT, and two TD participants for the virtual INS task.

⁺ p<.05,

⁺⁺ p<.01

GORT = Gray Oral Reading Test

FAVRES = Functional Assessment of Verbal Reasoning and Executive Strategies

INS = Interpersonal Negotiations Strategy Interview

SCI = Socioeconomic Composite Index

WASI = Wechsler Abbreviated Scale of Intelligence

Table 3
Reaction times (msec) by condition for the typically developing (TD) and moderate to severe TBI groups.

Condition	TD		TBI		95% CI for group mean difference
	Mean	SD	Mean	SD	
Self-First Person	1330	294	1273	231	(-321.7, 207.6)
Other-First Person	1424	303	1424	342	(-323.4, 322.86)
Self-Third Person	1458	385	1380	322	(-348, 369.49)
Other-Third Person	1437	351	1448	365	(-433.1, 276.92)

SD=standard deviation CI = confidence interval

Table 4

Talairach Coordinates [x y z] mm, cluster sizes, and probability levels of significant clusters of activation observed for between-groups differences for the Target $\times$ Perspective interaction when judgments about the self were made from a third person perspective (S3P – S1P) – (O3P – O1P)), local maxima greater than 16 mm apart.

Corrected Cluster p	Number of voxels per cluster	Region	x	y	z
TD > TBI					
NS	1633	L Cblm (Tonsil)	-8	-48	-35
		L S-L Extra- nuclear WM	-20	-47	24
		R Cblm (Uvula)	4	-64	-29
		L Midbrain	-4	-26	-9
		L Cblm	-2	-79	-26
		L Cblm (Culmen)	-8	-41	-6
		L Pons	-4	-22	-22
		L S-L Extra-nuclear WM	-16	-46	8
		R Cblm (Inferior Semi-Lunar Lobule)	16	-66	-40
		L Post Cing WM	-12	-59	16
TBI > TD					

Height threshold $p=0.037$ ($T=1.90$), smoothness FWHM = 4.7 5.0 5.1 [voxels], search volume = 164642 voxels = 1262.1 resolution elements (resels)

NS = Not statistically significant

L = Left; R = Right, S-L = Sub-lobar, WM = White matter

Cblm = Cerebellum; Post Cing =Posterior Cingulate