

## http://informahealthcare.com/bij ISSN: 0269-9052 (print), 1362-301X (electronic)

Brain Inj, 2013; 27(13-14): 1528-1535 © 2013 Informa UK Ltd. DOI: 10.3109/02699052.2013.828851



ORIGINAL ARTICLE

# Emotional prosody and diffusion tensor imaging in children after traumatic brain injury

Adam T. Schmidt<sup>1</sup>, Gerri Hanten<sup>2</sup>, Xiaoqi Li<sup>2</sup>, Elisabeth A. Wilde<sup>2,3,4</sup>, Alyssa P. Ibarra<sup>2</sup>, Zili D. Chu<sup>4</sup>, Antonia R. Helbling<sup>2</sup>, Sanjeev Shah<sup>2</sup>, & Harvey S. Levin<sup>2,3</sup>

<sup>1</sup>Department of Psychology and Philosophy, Sam Houston State University, Huntsville, TX, USA, <sup>2</sup>Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, TX, USA, <sup>3</sup>Department of Neurology, Baylor College of Medicine, Houston, TX, USA, and <sup>4</sup>Department of Radiology, Baylor College of Medicine, Houston, TX, USA

#### **Abstract**

Primary objective: Brain structures and their white matter connections that may contribute to emotion processing and may be vulnerable to disruption by a traumatic brain injury (TBI) occurring in childhood have not been thoroughly explored.

Research design and methods: The current investigation examines the relationship between diffusion tensor imaging (DTI) metrics, including fractional anisotropy (FA) and apparent diffusion coefficient (ADC), and 3-month post-injury performance on a task of emotion prosody recognition and a control task of phonological discrimination in a group of 91 children who sustained either a moderate-to-severe TBI (n = 45) or orthopaedic injury (OI) (n = 46).

Main outcomes and results: Brain-behaviour findings within OI participants confirmed relationships between several significant white matter tracts in emotional prosody performance (i.e. the cingulum bundle, genu of the corpus callosum, inferior longitudinal fasciculus (ILF) and the inferior fronto-occipital fasciculus (IFOF). The cingulum and genu were also related to phonological discrimination performance. The TBI group demonstrated few strong brain behaviour relationships, with significant findings emerging only in the cingulum bundle for Emotional Prosody and the genu for Phonological Processing.

Conclusion: The lack of clear relationships in the TBI group is discussed in terms of the likely disruption to cortical networks secondary to significant brain injuries.

#### Keywords

Brain imaging, DTI, emotional prosody, paediatric, traumatic brain injury

Received 11 September 2012 Revised 22 July 2013 Accepted 22 July 2013 Published online 12 November 2013

## Introduction

Children who experience a traumatic brain injury (TBI) are at risk for a variety of long-term cognitive, behavioural and emotional impairments. Some of the most devastating impairments involve disruptions in social skills including social cognition [1-3]. Although impaired socialization is multi-factorial in nature, evidence suggests core impairments in processing of emotions may contribute to broader social functioning deficits [4,5]. Children sustaining TBI experience long-term disruptions in emotion processing in both the visual (i.e. face recognition) and auditory (i.e. emotional prosody) domains [6]. Emotional prosody in particular appears uniquely vulnerable as it is influenced by environmental factors such as socioeconomic status (SES) and family finances [7]. Emotional prosody refers to the subtle 'melodic and rhythmic' aspects of speech that convey a speaker's emotional disposition [8]. Prosodic information may have relevance to the processing of subtle social cues conveyed

verbally and may be highly vulnerable to disruption by paediatric TBI [9].

Previous research in uninjured and brain injured populations suggests processing of emotional information, regardless of mode of presentation, recruits an extensive neural network including various frontal and temporal areas [9]. Studies with children have demonstrated that these regions are particularly vulnerable to TBI [10]. Although diffuse injuries in the acute stage may resolve, especially in mild TBI, evidence indicates children with moderate and severe TBI may have focal frontal or fronto-temporal brain lesions that persist [11] and white matter anomalies that can affect functional connectivity of cortical and sub-cortical circuits [10,12]. These findings may have particular significance for complex procedures that are processed over a widely distributed network, such as the accurate interpretation of

In adults, functional neuroimaging tasks involving emotional prosody have been associated with specific brain regions including fronto-opercular, fronto-temporal and subcortical areas [13,14]. Although right hemisphere structures are involved in the processing of emotional stimuli, including perception and decoding of prosodic information, several studies, including those using transcranial magnetic

Correspondence: Adam T. Schmidt, PhD, Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, 1709 Dryden Rd., Suite 1200, Houston, TX 77030, USA. Tel: 1-713-798-7420. Fax: 1-713-798-6898. E-mail: ats013@shsu.edu



stimulation [15] and lesion studies [8], suggest that both hemispheres contribute to perception of meaning from emotional tone within speech. For example, Pell [8] found evidence that damage to either hemisphere could uniquely impact the processing of prosodic information. Specifically, results showed that participants with right hemisphere disruption tended to express more insensitivity to the emotive features of the prosodic stimuli, whereas individuals with left hemisphere damage had more trouble with prosodic processing when it was embedded in the content of the spoken language. Thus, the extent to which the right hemisphere processing advantage is relative or absolute over analogous left hemisphere structures continues to be investigated.

Given that previous research has implicated a widely distributed network in processing emotional information, it is likely to be related to the observed deficits in prosody recognition. Diffusion tensor imaging (DTI), an advanced neuroimaging methodology that indexes the integrity of white matter microstructure, appears to be a good candidate for an initial investigation of brain-behaviour relationships in emotional prosody [10].

The principle behind DTI is derived from the observation that, when unrestricted, water molecules tend to diffuse equally in all directions. When various impediments, such as cell membranes, interfere with diffusion, the measure is called the apparent diffusion coefficient (ADC) (because the impediments are not specifically accounted for, hence are apparent). In general, higher ADC reflects the ability to diffuse randomly (i.e. the absence of organized structure); therefore, the lower the ADC, the more intact the structure. In the presence of fibres oriented in the same direction, such as in white matter structure of the brain, molecules tend to diffuse faster parallel to the long axis of a fibre bundle and slower perpendicular to it. If the fibres are disrupted, the diffusion along the length of the bundle is slower, with the degree of disruption related to the degree of slowing. The measure of fractional anisotropy (FA) is an approximation of the shape of the ellipse created by the ratio of the speed of molecules moving perpendicular to the long axis to those moving parallel to it, with more intact structures having higher values and more disrupted structures having lower values. Both ADC and FA, which range on a scale of 0-1, have proven to be sensitive to axonal injury after traumatic brain injury [10].

A previous work examined the degree of impairment and recovery of prosodic processing deficits in children with moderate-to-severe TBI in a longitudinal study over 2 years [6] and found an interaction of injury group (TBI or OI) with SES such that children with TBI and OI from low SES differed in rate of change over time, whereas children with higher SES did not. It was also reported that there are decreases in white matter integrity (as measured by DTI) in children after TBI [16]. The current investigation examines the relationship between emotion prosody recognition and brain white matter microstructure as measured by DTI, including FA and ADC in the acute stages of recovery of children who sustained either a moderate-to-severe TBI or orthopaedic injury (OI) 3-months previous. Due to the distributed nature of emotion prosody recognition, it was anticipated that one would see relationships between

performance and DTI measures in frontal and temporal regions, but that these relationships would be stronger in the right hemisphere considering the pre-eminence of this hemisphere in the processing of emotional material. It was also hypothesized that significant relationships would be observed between performance and measures of white matter integrity in specific tracts that connect frontal and temporal or frontal and sub-cortical structures, specifically the inferior longitudinal fasciculus and the uncinate.

#### Materials and methods

## **Participants**

Children and adolescents with moderate or severe TBI or an orthopaedic injury (OI) between the ages of 7-17 years at the time of injury were recruited from consecutive admissions to medical centres in Dallas and Houston, TX and in Miami, FL. As is common in the field of TBI research [12,17], an OI comparison group was included to control for risk factors pre-disposing children to injury and to equate for non-specific factors such as maturation or stress resulting from hospitalization. An attempt was made to match OI participants on demographic variables such as estimated SES, age and gender with those participants in the TBI group.

As a part of an ongoing project on the neurobehavioural outcomes following paediatric TBI, children and adolescents were assessed on cognitive and neuropsychological tests at baseline, 3, 12, 18 and 24 months and underwent structural magnetic resonance imaging (MRI) at 3 and 18 months.

Because the primary interest for the current study was the relation of white matter microstructure integrity to emotional prosody identification during acute stages of recovery, analyses were limited to data at 3 months post-injury. Data from participants who had both behavioural data and imaging data were included in the analyses for a total of 91 children (45 children with moderate-to-severe TBI and 46 children with orthopaedic injuries). Inclusion criteria for the TBI group included a lowest post-resuscitation Glasgow Coma Scale (GCS = 18) score recorded at the emergency centre consistent with moderate or severe TBI. Moderate TBI was defined as a GCS score of 9–12 or 13–15 with brain lesions (contusions, haematomas) indicated by computed tomographic (CT) scans. Severe TBI was defined by GCS scores of 3–8. The 46 hospitalized OI patients had mild-to-moderate orthopaedic injuries, as defined by the Abbreviated Injury Scale [18]. All participants in both groups were Englishspeaking; had no previous hospitalization for head injury; and no previous diagnosis of a severe psychiatric disorder (e.g. bipolar disorder or schizophrenia), mental retardation or a neurodevelopmental disorder (e.g. autism). All procedures were approved by the institutional review boards of the participating organizations and were in compliance with the National Institute of Health policies on human subjects protection. Demographic and injury characterization data, including age at injury, race, gender, SES as measured by the Socioeconomic Composite Index (SCI), Glasgow Coma Scale (GCS) scores, mechanism of injury and Abbreviated Injury Scale (AIS) scores are displayed in Table I.



Table I. Demographic and injury characteristics by group.

	OI			TBI			Statistics	
	Mean	SD	Range	Mean	SD	Range	Statistic	<i>p</i> -value
Age (years)	11.85	2.40	7.05-16.28	13.48	3.03	7.10-17.22	-2.84	0.0055
SCI (score)	0.16	0.84	-1.52 - 1.89	-0.02	0.81	-1.86 - 1.41	1.05	0.2957
Interval (months)	4.10	0.89	2.70-7.11	4.20	1.28	2.50-7.70	1.44	0.0164
GCS	15	0	15-15	7.84	4.43	3	15	
Gender	13 female; 33 male			14 female; 31 male			0.0886	0.7660
AIS score	6.38	3.82	1–22	23.89	10.19	9-50	-10.66	< 0.0001
Race	15 AA; 16 Caucasian/Asian; 15 Hispanic			4 AA; 19	4 AA; 19 Caucasian/Asian; 22 Hispanic			0.0189
Mechanism of injury	High	Speed $= 6$ ; Lo	w Speed $= 40$	High Speed = $29$ ; Low Speed = $16$			25.391	0.0006

High speed mechanism of injury included motor vehicle accident or hit by a motor vehicle; Low speed mechanism of injury included accidents from construction, bicycle, falls, hit by falling object, sports or play, assault.

### Behavioural methods

Emotional prosody task [19,20]

During this task, children listened to a digital recording of the same four semantically neutral sentences (e.g. 'The trees are in the forest') spoken with eight different emotional prosodic contours, including three basic emotions (happy, sad, angry) and five complex or subtle emotions (neutral, afraid, surprised, disgusted and sleepy). The child indicated which emotion was expressed by pointing to the name of the emotion printed beneath a stylized picture of a face emotion. The 32 sentences of 3-second duration were played in fixed random order. The child proceeded at his/her own pace with a minimum of 10 seconds between sentences. Performance was evaluated in terms of the number of sentences correctly identified for both simple and complex emotions for a Total Score and, separately, for a sub-set (happy, sad, angry) for a Simple Emotion Score, easily discriminated by facial expression and by the stylized pictures. This task has been validated for use in children with head injury in this age range (please see [6,7]).

## Phonological discrimination test

Because emotional prosody depends on the ability to accurately perceive and process subtle changes in sound, this study included a basic test of phonological discrimination to rule out any perceptual-level deficits and to examine the overlap and differences between relations of prosody and phonological processing to specific brain regions. Participants listened to 16 pairs of non-words that were either identical or varied by a single phoneme and had to determine whether the non-words matched or were different. The score was the number of correct trials.

## Socioeconomic composite index (SCI) [21,22]

As used in the original study [22], this measure is a composite variable of three factors important in the determination of socioeconomic status (i.e. maternal education, coded on a 7-point scale with values representing <7 years education on one end of the scale, to attainment of a graduate degree on the other; annual family income, based on an 8-point scale ranging from <\$20000 to >\$60000 as part of the Life Stressors and Resources Scale (LISRES) [23]; and the Duncan occupational status index [24].

These three variables were transformed into z-scores and then averaged together to yield a standardized composite z-score (mean = 0, SD = 1).

#### DTI methods

MRI data was collected on unsedated participants with Philips 1.5-Tesla Intera scanners at each of the participating sites. Cross-site reliability was checked prior to subject enrolment in the project and analysis of cross-site differences in both imaging and behavioural data reliability was checked to verify that there were no systematic errors.

## DTI acquisition

Transverse multi-slice spin echo, single-shot, echo-planar imaging sequences (10 150.5 ms repetition time; 90 ms echo time; 2.7-mm-thick slices with 0-mm gap) were used to acquire 55 slices over ~6 minutes. A 256-mm field of view (FOV; receiver FOV = 100%) was used with a measured voxel size of  $2.69 \times 2.69 \times 2.7$  mm. Diffusivities were assessed in 15 directions (number of b value = 2; low b value =  $0 \text{ s mm}^{-2}$ ; high b value =  $860 \,\mathrm{s}\,\mathrm{mm}^{-2}$ ). Two acquisitions of high-b images were obtained and averaged to optimize signalto-noise ratio.

## DTI analysis

Shear and eddy current distortion and head motion artifact were corrected by using the Philips Pride registration tool [25] before FA maps were computed with the Philips fibre tracking 4.1v3 Beta 2 software. Because of the relatively small sample size, the investigation was limited to tracts that connect brain regions theoretically associated with emotional prosody, notably the inferior frontal and orbitofrontal regions, superior temporal region and the amygdala [15,26-31].

The analyses included structures that have connections with or pass through these regions:

- The inferior longitudinal fasciculus (ILF), a ventral bundle with long and short fibres that connect the occipital and temporal lobes. The long fibres are medial to the short fibres and connect visual regions to the amygdala and hippocampus [32].
- The inferior fronto-occipital fasciculus (IFOF), a long ventral bundle that transverses the brain, connecting the occipital lobe with the orbitofrontal cortex, with projections through the temporal lobe.



DOI: 10.3109/02699052.2013.828851 Prosody and DTI 1531

• The *uncinate*, which connects the anterior temporal lobe with the medial and lateral orbitofrontal cortex [33,34].

- The *cingulum bundle*, which parallels the corpus callosum connecting medial frontal, parietal, occipital and temporal lobes with different portions of the cingulate cortex [35].
- The genu of the corpus callosum, which connects the orbitofrontal and prefrontal regions of the left and right hemispheres.
- The arcuate fasciculus, which connects the perisylvian cortex of the frontal, parietal and temporal lobes [36].

Each region was manually traced on the midsagittal plane, following previously published protocols [16]. The automated Philips 3-D fibre tracking programme was used for fibre tractography. Quantitative DTI variables included the mean fractional anisotropy (FA) and mean apparent diffusion co-efficient (ADC). Fibre tracking proceeded via an algorithm for fibre assignment by continuous tracking methods [37]. Fibre tracking terminated if the FA in the voxels was <0.2 or if the angle between adjacent voxels was  $>7^{\circ}$ . Figure 1 demonstrates the tracts as represented by DTI tractography for the regions used in the analysis.

## Intra- and inter-rater reliability

DTI analysis was performed by two experienced raters (interrater reliability) supervised by a neuroradiologist (Jill Hunter) and an expert in DTI tractography analysis (Elisabeth Wilde) and following a specified protocol. Each region was analysed twice by each rater (to establish intra-rater reliability). Shrout-Fleiss intra-class correlation coefficients showed satisfactory inter-rater (range = 0.937-1.000) and intra-rater reliability (range = 0.913-0.976). All three scanners were subjected to regular quality assurance testing including American College of Radiology phantom and Weisskoff testing for echo-planar imaging sequences and were found to be consistently within an acceptable range.

## Statistical analysis

The demographic data were compared using t-tests for continuous variables (e.g. age-at-injury, mother's education)

and a Chi-Square test for categorical variables (e.g. gender and ethnicity). The emotional prosody task and phonological discrimination task were analysed with a General Linear Model including group, age at injury, socioeconomic status (SCI), interval between injury and test (Interval). Betweengroups differences in DTI variables were compared with t-tests and relations between the performance measures and brain variables were examined using Spearman correlations, with correction applied for multiple comparisons.

Analysis was conducted for each group using Pearson correlations and corrected for false discovery rate.

### Results

## Demographic variables

Preliminary analyses indicated that groups did not differ significantly on SES or gender, but the groups differed on age at injury, post-injury interval, race and mechanism of injury (high speed or low speed). Within the group of moderateto-severe TBI patients the effect of GCS on the performance measures failed to reach significance, although there was a trend for a relation to prosody in the Simple Emotion Score, r = 0.296, p = 0.067, and Total Score, r = 0.296, p = 0.067, but not Phonological Discrimination performance, r = 0.071, p = 0.673, indicating that any difference in groups on the prosody variables could not be accounted for by hearing deficits.

## **Emotional prosody task**

Total score

As compared to children with orthopaedic injury, children with TBI were not significantly impaired on emotional prosody, when all eight conditions were averaged together. Neither was age at injury a significant factor in this analysis. However, on the total score, SES was a significant factor, as children with higher SCI scores performed better than those with lower scores, t(89) = 4.85, p < 0.0001, with the relation the same for both groups. For both groups across all eight

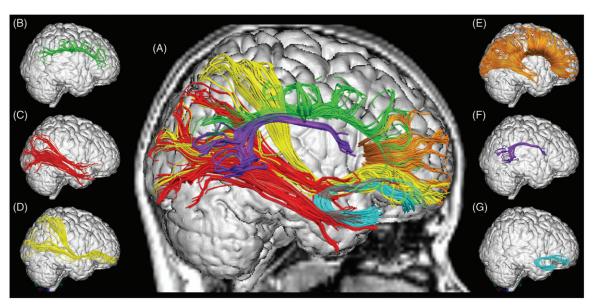


Figure 1. Simple prosody scores by group and age.



emotions, Phonological Discrimination was related to performance on the emotional prosody task, t(89) = 3.00, p = 0.004.

## Simple emotions

Children with TBI were impaired on the Simple Emotion Score as compared to children with orthopaedic injury and this was modified by age, F(1, 89) = 5.53, p = 0.021, such that within the OI group task performance depended on age, with older children showing an advantage. However, in the TBI group greater age was not associated with better performance. Thus, the group difference was larger for older children than for younger children (Ismeans = OI, 11.6; TBI, 9.47; p = 0.0052) (Ismeans = OI, 9.61; TBI, 9.75; p = 0.827), as shown in Figure 1. SCI was significantly related to the Simple Emotion Score, F(1, 89) = 4.59, p < 0.001, with higher estimated SES associated with better performance. The relation between phonological processing and emotional prosody recognition for simple emotions was not significant.

## **Brain** imaging

## Group differences on DTI variables

The hypothesis that injury to specific brain circuits is associated with performance on the emotional prosody recognition task relies on group differences in those regions. Table II displays the means, t-values, p-values and effect sizes (Cohen's f) for the group differences in DTI in the regions of interest. As can be seen from the table, the children with TBI had greater ADC values and lesser FA values in all cases, although not all differences reached statistical significance.

Relation of DTI variables to emotional prosody recognition and to phonological discrimination

In order to assess the extent to which prosody recognition relied upon the selected specific structures, this study examined the relations of Simple Emotion Score, the Total Score and Phonological Discrimination with the white matter tracts of interest for both hemispheres.

## Orthopaedic group

The Total Score was related to FA in the left cingulum bundle, r = 0.362, p = 0.013, and the right IFOF, r = 0.303, p = 0.041. Total Score showed significant relations with ADC in the right cingulum bundle, r = -0.331, p = 0.025; left cingulum bundle, r = -0.342, p = 0.020; the left ILF, r = -0.350, p = 0.019; and the IFOF on the right, r = -0.353, p = 0.016; and left, r = -0.318, p = 0.031.

There was also a relation of ADC of the genu, r = -0.297, p = 0.045.

The Simple Emotion Score was weakly related to FA of the right ILF, showing a trend, r = 0.275, p = 0.070, but failing to reach significance. Simple Emotional Prosody showed relations to ADC the left cingulum bundle, r = -0.322, p = 0.029; the left IFOF, r = -0.357, p = 0.015; and right IFOF, r = -0.306, p = 0.039.

Phonological processing in the OI group was associated with FA in the left cingulum bundle, r = 0.294, p = 0.040. As well, significant relations were seen with ADC of the genu, r = -0.302, p = 0.035; the left cingulum bundle, r = -0.294, p = 0.040; and the left arcuate, r = -0.291, p = 0.047.

## TBI group

FA was related to the Simple Emotion Score only in the left cingulum bundle, r = -0.305, p = 0.047. There were no significant relations of white matter tracts with Total Score, nor did ADC correlate with prosody, either Total or Simple within the TBI group.

On the measure of phonological processing, FA of the genu of the corpus callosum was related to performance, r = 0.407, p = 0.012. There were no correlations of phonological processing with ADC.

## Discussion

The current study aimed to examine the relationship between the DTI metrics FA and ADC and performance 3 months after injury on a task of emotion prosody recognition in a group of children who sustained either a moderate or severe TBI or OI. Due to the distributed nature of the processing of emotional prosody, it was hypothesized that one would observe relationships between performance and DTI measures in frontal and temporal regions, especially in the right hemisphere. Relationships between specific white matter tracts that connect frontal and temporal regions were also anticipated.

The findings relating performance on the Emotional Prosody task to white matter microstructure integrity confirmed the involvement of several of the structures of interest. In all cases, greater microstructure integrity was associated with better performance. Notably involved was the cingulum bundle, particularly on the left side, for which both FA and ADC were related to emotional prosody. As well, the left cingulum bundle was associated with phonological processing. The IFOF was associated bilaterally with emotional prosody, but not with Phonological Processing, and the ILF showed somewhat weaker relations with emotional Prosody,

Table II. Group differences in mean ADC and FA for white matter structures of interest.

		Left				Right			
	Mean OI	Mean TBI	t-test	Cohen D	Mean OI	Mean TBI	t-test	Cohen D	
ADC									
ILF	0.8215	0.8673	0.0001	0.8759*	0.8294	0.8539	0.0242	0.4982*	
Uncinate	0.8237	0.8550	0.0121	0.5941*	0.8129	0.851	0.0010	0.7639*	
FA									
ILF	0.4114	0.3981	0.0395	0.4545	0.40725	0.399	0.23314	0.26071	
Uncinate	0.3803	0.3490	0.0000	1.1435*	0.3789	0.3457	0.0001	1.0699*	

Prosody and DTI 1533 DOI: 10.3109/02699052.2013.828851

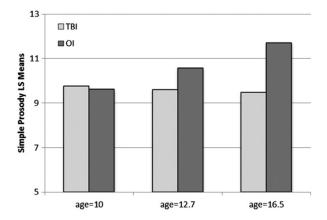


Figure 2. Pearson correlations of Total Prosody Score with ADC by specific tract and hemisphere. The dark bars represent significant

but none at all with Phonological Processing. The genu was associated with both Emotional Prosody and Phonological Processing. The left arcuate showed a relation with Phonological Processing, but not with Emotional Prosody, confirming previous studies' findings of a link between language and the arcuate. Surprisingly, the uncinate showed no relation with task performance for either group, despite its close connections among regions that are putatively related to emotional processing. Converse to expectations, the findings of significant relations between Emotional Prosody and specific white matter tracts was biased towards left lateralization, with double the number of significant relations for left hemispheric structures as for right. Notably, most of the findings were within the OI group. The TBI group showed very little, with only the cingulum related to Emotional Prosody and the genu to Phonological Processing.

The findings regarding emotional prosody performance generally concur with the previous results [6] in that older age and higher estimated SES were associated with better performance. However, the current investigation also revealed some novel group differences in that OI participants always outperformed TBI participants in the recognition of basic emotions. This is an interesting finding given that the previous study did not indicate differences between groups when all categories of emotional prosody were combined into a single performance measure. If processing of simple emotions is more perturbed in paediatric TBI, this may have repercussions for rehabilitation as these basic abilities may influence age-appropriate social interactions and peer relationships [3–7]. In both groups, phonological discrimination was related to the Total Score, but not the Simple Emotions Score, suggesting a greater role for phonology in subtle or complex emotions than in simple (angry, sad, happy) emotions.

The hypotheses regarding the brain behaviour relationships for findings on DTI and performance on the emotional prosody task were partly supported. That is, findings revealed a widely distributed network of relationships across both hemispheres and various white matter tracts. However, this pattern was observed only in the OI group. Counter to expectation, associations were more prevalent in left hemispheric structures than in right, which suggests the possibility

of a greater role for language in emotional prosody recognition than has previously been assumed.

The left cingulum bundle and the genu of the corpus callosum were associated with both emotional prosody and phonological processing. This suggests that one or both of these structures is involved in basic language processing and/or task demands non-specific to emotional processing (e.g. attention or performance monitoring). The cingulum, in particular through its connections with the cingulate cortex, has been linked to attention and learning processes in a variety of cognitive tasks [35].

Conversely, the IFOF and the ILF were specifically related to processing of emotional prosodic information. Both of these tracts traverse frontal and temporal structures and connect regions that may contribute to various aspects of emotional processing. For example, the IFOF is a long tract that connects the occipital lobe with the orbitofrontal cortex while passing through the temporal lobe [33,34]. The fact that this long tract was specifically related to emotional prosody recognition re-enforces the conjecture that this skill requires integration of a number of brain structures for optimal performance [8]. Likewise, although the ILF broadly connects occipital and temporal structures, it contains fibres connecting medial temporal regions (i.e. hippocampus and amygdala) to a wider brain network of regions also hypothesized to play a role in emotion processing. Finally, results from the left arcuate fasciculus show the reverse pattern of findings in that this structure was related only to the processing of phonological information and not to emotional prosody recognition. This observation is in keeping with this structure's wellvalidated role in language processing [38].

The uncinate connects the anterior temporal lobe with the medial and lateral orbitofrontal cortex, both structures strongly implicated in emotional processing. Despite its location, this study did not find significant brain behaviour relationships involving this structure and emotional prosody. It is possible the uncinate is more closely tied to emotion regulation as opposed to basic emotion recognition. The anterior location of the uncinate combined with most of the participants being scanned prior to the age of 12 leaves open the possibility that this structure could become a more significant contributor to emotion processing as frontal structures continue to develop throughout adolescence and early adulthood.

Notably, most of the findings were within the OI group. The TBI group showed few correlations, with only the cingulum related to emotional prosody and the genu to phonological processing. This finding was not due to small between-groups differences on measures of white matter integrity in specific brain areas, as the structures with the greatest between-group differences in FA, the genu, the uncinate and the IFOF, were not significantly associated with emotional prosody scores.

Although the precise reason for the persistent lack of significant relationships in the TBI group is not known, it is possible that the severity of injuries and/or the relatively acute stage of recovery included in the present study played a role. Because the current investigation included participants who had moderate-to-severe injuries, the disruption to typically-developing brain networks significant.



Therefore, within the TBI group, the lack of correlations may be a consequence of profound, wide-scale damage to a number of critical neuro-networks. Wide-scale disruption would perturb the functioning of the networks in general and may obscure any significant relationships with task performance, especially if these findings are somewhat subtle. Likewise, because the current investigation was focused on the relatively acute stage of recovery, short-term disruptions secondary to inflammation and/or continued presence of cellular debris may have also obscured clear brain behaviour relationships from emerging within the TBI group. Additionally, significant damage may have nearly obliterated certain structures, leaving only a few tracts intact and artificially inflating DTI metrics. However, the weak relations between the performance measures and the GCS scores do not support this argument. Nevertheless, this was a study of moderate-to-severe TBI and a restricted range of GCS scores could have weakened this relationship.

Another potential cause for the present findings relates to the issue of plasticity. That is, following a moderate or severe injury, networks may re-organize to compensate for damaged areas or to bypass regions that are no longer fully functional. Thus, the same tracts recruited in OI controls may not be as involved in individuals sustaining a TBI, even though behavioural performance may not yield dramatic differences between the groups. This may result in a very diffuse collection of networks/pathways being recruited to compensate for the functioning of more focal regions/tracts that may have been disrupted by the injury. Some evidence for this pattern comes from other studies by the research group demonstrating that children sustaining a TBI exhibit a more diffuse pattern of activation during a functional MRI task [39].

## Limitations and future directions

The current study has several important limitations. First, the findings involve a single measure of emotional prosody. More robust results may have emerged if additional experimental tasks were used. Second, the current findings are restricted to participants in a relatively acute stage of recovery (i.e. 3 months following their brain injury). This was a necessary restriction given the interests in the acute phase of recovery, sample limitations and the desire to integrate DTI with cognitive performance, but future research examining these constructs longitudinally or at a later stage after injury would help to determine if additional relationships emerge within the TBI group as recovery progresses and cortical networks heal. Third, because of the range of type of TBIs represented in the current study, this study was not able to take into account mechanism of injury. This is an important caveat to consider because mechanism of injury may contribute to the pattern of findings within the TBI group (e.g. injuries secondary to motor vehicle crashes may be more vulnerable to diffuse axonal injury) and may alter the brain behaviour relationships. Finally, the lack of relations between DTI metrics and emotional prosody performance within the TBI group suggests that, in children at this stage in recovery, fibre tracts within the TBI group may be too disrupted to reveal meaningful information regarding the reorganization/ reallocation of cortical networks following moderate or severe brain injury. This situation may be exacerbated in tracts that

project over a long distance and may make behavioural correlations with cognitive procedures that also involve a very distributed network very difficult. Therefore, future investigations that employ other imaging strategies such as quantitative volumetrics and/or magnetic transfer imaging (MTI) may yield more information regarding the state of brain areas involved in emotional processing, especially at this relatively early stage in recovery.

The overarching goal of this investigation was to elucidate brain behaviour relationships in the processing of prosodic emotional information in the acute stage following moderateto-severe paediatric closed head injury. The processing of prosodic emotional information is perturbed in paediatric TBI and may have relevance to higher-level social skill deficits. The finding that simple emotional prosody appeared more sensitive to disruption than other forms of emotional processing is interesting and somewhat unexpected. This suggests that efforts to rehabilitate basic emotional processes may be beneficial, especially in the initial months after a moderate or severe TBI. Disturbances in these basic cognitive abilities may exacerbate other difficulties in selfregulation and/or social cognition [4,5]. The lack of a relation between imaging data and performance measures in the TBI group is perplexing and suggests a more significant disruption of cortical networks resulting from these types of injuries than initially anticipated. Although the possibility of such severe disruption appears disheartening regarding the long-term prognosis following paediatric TBI, the short-term follow-up time of the current investigation is far from predicting a final poor outcome for these children and opens the doors for future studies endeavouring to investigate mechanisms of cortical plasticity. Understanding brain behaviour relationships is critical for designing and tracking novel therapeutic interventions, eventually leading to more successful rehabilitation and overall better outcomes for these children.

## **Acknowledgements**

The authors wish to express gratitude to Dr Trevor Wu and Ms Ragini Yallampalli for their technical expertise in imaging and Ms Beth Herlin and Ms Charisma Kaushik for their assistance in the preparation of this manuscript.

## **Declaration of interest**

The authors report no conflicts of interest. This research was supported by Grant Number R01NS021889 from the National Institute of Neurological Disorders and Stroke to H.S. Levin.

## References

- 1. Hanten G, Cook L, Orsten K, Chapman SB, Li X, Wilde EA, Schnelle KP, Levin HS. Effects of traumatic brain injury on a virtual reality social problem solving task and relations to cortical thickness in adolescence. Neuropsychologia 2011;49:486-497.
- 2. Hanten G, Wilde EA, Menefee DS, Li X, Lane S, Vasquez C Chu Z, Ramos MA, Yallampalli R, Swank P, et al. Correlates of social problem solving during the first year after traumatic brain injury in children. Neuropsychology 2008;22:357-370.
- Yeates KO, Bigler ED, Dennis M, Gerhardt CA, Rubin KH, Stancin T, Taylor HG, Vannatta K. Social outcomes in childhood brain disorder: a heuristic integration of social neuroscience and



- developmental psychology. Psychological Bulletin 2007;133: 535-556.
- 4. Bornhofen C, McDonald S. Comparing strategies for treating emotion perception deficits in traumatic brain injury. Journal of Head Trauma Rehabilitation 2008;23:103-115.
- Bornhofen C, McDonald S. Emotion perception deficits following traumatic brain injury: a review of the evidence and rationale for intervention. Journal of the International Neuropsychological Society 2008;14:511-525.
- Schmidt AT, Hanten GR, Li X, Orsten KD, Levin HS. Emotion recognition following pediatric traumatic brain injury: longitudinal analysis of emotional prosody and facial emotion recognition. Neuropsychologia 2010;48:2869-2877.
- 7. Schmidt AT, Orsten KD, Hanten GR, Li X, Levin HS. Family environment influences emotion recognition following paediatric traumatic brain injury. Brain Injury 2010;24:1550-1560
- Pell MD. Cerebral mechanisms for understanding emotional prosody in speech. Brain and Language 2006;96:221-234.
- Ethofer T, Van De Ville D, Scherer K, Vuilleumier P. Decoding of emotional information in voice-sensitive cortices. Current Biology 2009;19:1028-1033
- 10. Wilde EA, Hunter JV, Newsome MR, Scheibel RS, Bigler ED, Johnson JL, Fearing MA, Cleavinger HB, Li X, Swank PR, et al. Frontal and temporal morphometric findings on MRI in children after moderate to severe traumatic brain injury. Journal of Neurotrauma 2005;22:333-344.
- 11. Levin HS, Mendelsohn D, Lilly MA, Yeakley J, Song J, Scheibel RS, Harward H, Fletcher JM, Kufera JA, Davidson KC, et al. Magnetic Resonance Imaging in relation to functional outcome of pediatric closed head injury: a test of the Ommaya-Gennarelli Model. Neurosurgery Issue 1997;40: 432-441.
- 12. Levin HS, Wilde EA, Hanten G, Li X, Chu Z, Vasquez AC, Cook L, Yallampalli R, Hunter JV. Mental state attribution and diffusion tensor imaging after traumatic brain injury in children. Development Neuropsychology 2011;36:273-287.
- 13. Buchanan TW, Lutz K, Mirzazade S, Specht K, Shah NJ, Zilles K, Jancke L. Recognition of emotional prosody and verbal components of spoken language: an fMRI study. Brain Research Cognitive Brain Research 2000;9:227-238.
- Kotz SA, Meyer M, Alter K, Besson M, von Cramon DY, Friederici AD. On the lateralization of emotional prosody: an event-related functional MR investigation. Brain and Language 2003;86: 366-376.
- 15. Hoekert M, Vingerhoets G, Aleman A. Results of a pilot study on the involvement of bilateral inferior frontal gyri in emotional prosody perception: an rTMS study. BMC Neuroscience 2010;11: 93.
- 16. Wilde EA, Chu Z, Bigler ED, Hunter JV, Fearing MA, Hanten G, Newsome MR, Scheibel RS, Li X, Levin HS. Diffusion tensor imaging in the corpus callosum in children after moderate to severe traumatic brain injury. Journal of Neurotrauma 2006;23: 1412-1426.
- 17. Yeates KO, Swift E, Taylor HG, Wade SL, Drotar D, Stancin T, Minich N. Short- and long-term social outcomes following pediatric traumatic brain injury. Journal of the International Neuropsychological Society 2004;10:412-426.
- 18. Copes WS, Lawnick M, Champion HR, Sacco WJ. A comparison of Abbreviated Injury Scale 1980 and 1985 versions. Journal of Trauma 1988;28:78-86.
- Adolphs R, Tranel D. Intact recognition of emotional prosody following amygdala damage. Neuropsychologia 1999;37: 1285-1292.

- 20. Adolphs R, Tranel D, Damasio H. Emotion recognition from faces and prosody following temporal lobectomy. Neuropsychology 2001;15:396-404.
- 21. Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. Lancet 1974;2:81-84.
- Yeates KO, Taylor HG, Drotar D, Wade SL, Klein S, Stancin T, Schatschneider C. Preinjury family environment as a determinant of recovery from traumatic brain injuries in school-age children. Journal of the International Neuropsychological Society 1997;3: 617 - 630
- 23. Moos RH, Moos BS. LISRES-A: Life Stressors and Social Resources Inventory - Adult Form Manual. Odessa, FL: Psychological Assessment Resources, Inc; 1994.
- 24. Stevens G, Featherman D. A revised socioeconomic index of occupational status. Social Science Research 1981;10:364-395.
- Netsch T. Towards real-time multi-modality 3-d medical image registration. International Conference on Computer Vision, Vancouver; 2001. p 718-725.
- 26. Leitman DI, Wolf DH, Ragland JD, Laukka P, Loughead J, Valdez JN, Javitt DC, Turetsky BI, Gur RC. 'It's Not What You Say, But How You Say it': a reciprocal temporo-frontal network for affective prosody. Frontiers in Human Neuroscience 2010;4:19.
- Rota G, Handjaras G, Sitaram R, Birbaumer N. Dogil G. Reorganization of functional and effective connectivity during real-time fMRI-BCI modulation of prosody processing. Brain and Language 2010;117:123-132.
- 28. Wiethoff S, Wildgruber D, Grodd W, Ethofer T. Response and habituation of the amygdala during processing of emotional prosody. Neuroreport 2009;20:1356-1360.
- Wildgruber D, Ackermann H, Kreifelts B, Ethofer T. Cerebral processing of linguistic and emotional prosody: fMRI studies. Progress in Brain Research 2006;156:249-268.
- Wildgruber D, Hertrich I, Riecker A, Erb M, Anders S, Grodd W, Ackermann H. Distinct frontal regions subserve evaluation of linguistic and emotional aspects of speech intonation. Cerebral Cortex 2004;14:1384-1389.
- 31. Wildgruber D, Riecker A, Hertrich I, Erb M, Grodd W, Ethofer T, Ackermann H. Identification of emotional intonation evaluated by fMRI. Neuroimage 2005;24:1233-1241.
- Catani M, Jones DK, Donato R, Ffytche DH. Occipito-temporal connections in the human brain. Brain 2003;126:2093-2107.
- Gaffan D, Wilson CR. Medial temporal and prefrontal function: recent behavioural disconnection studies in the macaque monkey. Cortex 2008;44:928–935.
- 34. Catani M, Mesulam M. The arcuate fasciculus and the disconnection theme in language and aphasia: history and current state. Cortex 2008;44:953-961.
- 35. Koch K, Wagner G, Dahnke R, Schachtzabel C, Gullmar D, Reichenbach JR, Schlosser RG. Structure-function relationships in the context of reinforcement-related learning: a combined diffusion tensor imaging-functional magnetic resonance imaging study. Neuroscience 2010;168:190-199.
- Catani M, Thiebaut de Schotten M. A diffusion tensor imaging tractography atlas for virtual in vivo dissections. Cortex 2008;44: 1105-1132.
- 37. Mori S, Barker PB. Diffusion magnetic resonance imaging: its principle and applications. Anatomical Record 1999;257:102–109.
- Brauer J, Anwander A, Friederici AD. Neuroanatomical prerequisites for language functions in the maturing brain. Cerebral Cortex 2011;21:459-466.
- Newsome MR, Scheibel RS, Steinberg JL, Troyanskaya M, Sharma RG, Raunch RA, Levin HS. Working memory brain activation following severe traumatic brain injury. Cortex 2007;43:95-111.

