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Pediatric traumatic brain injury: Language outcomes and their relationship to the arcuate fasciculus

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ABSTRACT

Pediatric traumatic brain injury (TBI) may result in long-lasting language impairments alongside dysarthria, a motor-speech disorder. Whether this co-morbidity is due to the functional links between speech and language networks, or to widespread damage affecting both motor and language tracts, remains unknown.

Here we investigated language function and diffusion metrics (using diffusion-weighted tractography) within the arcuate fasciculus, the uncinate fasciculus, and the corpus callosum in 32 young people after TBI (approximately half with dysarthria) and age-matched healthy controls ($n = 17$). Only participants with dysarthria showed impairments in language, affecting sentence formulation and semantic association. In the whole TBI group, sentence formulation was best predicted by combined corpus callosum and left arcuate volumes, suggesting this "dual blow" seriously reduces the potential for functional reorganisation. Word comprehension was predicted by fractional anisotropy in the right arcuate. The co-morbidity between dysarthria and language deficits therefore seems to be the consequence of multiple tract damage.

1. Introduction

Traumatic brain injury (TBI) in childhood is a serious public health problem worldwide due to its high prevalence (e.g., 91 per 100,000 in Australia; Berry, Jamieson, & Harrison, 2010) and morbidity rates. Sustaining a TBI in childhood has been found to cause persistent, diverse and complex neuropsychological impairments across cognitive domains (Anderson, Godfrey, Rosenfeld, & Catroppa, 2012; Anderson, Morse, Catroppa, Haritou, & Rosenfeld, 2004; Babikian & Asarnow, 2009; Crowe, Catroppa, Babl, & Anderson, 2012; Taylor, 2004), including chronic language impairments (Anderson et al., 2004; Jordan & Murdoch, 1990), especially if the injury is severe. Given the varied and often widespread nature of brain white matter damage after TBI (Smith, Meaney, & Shull, 2003), it is not surprising that the neural correlates of persistent language impairments remain elusive.

Childhood acquired language disorders may be characterised by deficits in any or all linguistic domains of vocabulary, pragmatics, syntax, morphology or semantics (Feldman & Messick, 2008). 'Higher-order' language is particularly impaired in pediatric and adult TBI, including discourse skills (Lê, Coelho, Mozeiko, Krueger, & Grafman, 2012; Marini et al., 2011) and understanding of irony or non-literal concepts (Angeleri et al., 2008; Dennis, Purvis, Barnes, Wilkinson, & Winner, 2001). However, factors such as severity of TBI and age at injury are reported to influence outcome, and younger children with severe TBI may present with impairments in both lower- (e.g., semantic, syntactic) and higher-order levels of language (Anderson et al., 2004; see Sullivan & Riccio, 2010 for a review).

Dysarthria, a motor-speech disorder, is also a common occurrence after TBI and may affect the intelligibility of the speaker (Morgan, Mageandran, & Mei, 2010). It can result from a combination of respiratory, phonatory, articulatory, and/or resonatory impairments (Cahill, Murdoch, & Theodoros, 2002). Although distinct functions, language deficits and dysarthria can both result following pediatric TBI, with reported co-morbidity rates being as high as 55% (Morgan et al., 2010). It is well established that both long-range distance and U-shaped white matter connections exist between traditional language regions such as Broca's area and primary motor regions (Catani et al., 2011). It is therefore possible that damage to speech motor regions may have a direct impact

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on language production regions. Whether the co-morbidity between dysarthria and language impairments is due to the functional links between speech and language networks, or to widespread injury affecting both motor and language tracts, remains unknown.

TBI can result in heterogeneous neural injuries, causing both global and focal lesions (see Gaetz, 2004 for a review), with diffuse axonal injury being most commonly observed. Diffusion-weighted magnetic resonance imaging (DWI) methods are optimal for detecting changes in white matter that are assumed to reflect microstructural changes (Beaulieu, 2002; Marquez de la Plata et al., 2011; Sundgren et al., 2004) such as those seen in TBI. Tractography is one specific DWI-derived technique that permits the tracing and reconstruction of white matter tracts in vivo. This approach is proving to be clinically useful (Ciccarelli, Catani, Johansen-Berg, Clark, & Thompson, 2008), for example, in identifying neural biomarkers and improving prognostic accuracy of long-term neuropsychological functioning after TBI in adults (e.g., Huisman et al., 2004; Shenton et al., 2012; Wang et al., 2011) and in children (Johnson et al., 2011; Oni et al., 2010; Tasker, Westland, White, & Williams, 2010). Specifically, fractional anisotropy (FA) has been used to infer the structural "integrity" of the tract – which animal models have suggested may be related to demyelination and axonal degeneration (Budde, Janes, Gold, Turtzo, & Frank, 2011). FA has been shown to increase with age in most white matter tracts during normal development (Trivedi et al., 2009), including those involved in language function (Lebel & Beaulieu, 2009) and the presence of TBI is likely to affect this developmental trajectory.

Language functions rely on an extensive network of short- and long-range connections, both ventral and dorsal to the sylvian fissure (e.g., Glasser & Rilling, 2008; Saur et al., 2008). The arcuate fasciculus (AF) is part of the "dorsal pathway" and corresponds to the long segment of the superior longitudinal fasciculus that connects Broca's and Wernicke's areas (Catani, Jones, & Ffytche, 2005). The AF is considered a major language tract, and studies of healthy adults have demonstrated a relationship between its symmetry and performance on a word list recall task (Catani et al., 2007). AF abnormalities have been documented in pediatric populations that exhibit language impairments of varying severity, as part of a more globally affected profile including cognitive involvement, such as Angelman syndrome (Wilson et al., 2011), bilateral perisylvian syndrome (Saporta, Kumar, Govindan, Sundaram, & Chugani, 2011), autism (Fletcher et al., 2010) and in developmental populations with a primary or specific language impairment (SLI children, who have language deficits despite adequate development, typical intelligence and language learning opportunity, Verhoeven et al., 2011). Whether persisting language impairments after childhood TBI can be predicted by examining the diffusion properties of the AF remains to be investigated.

In contrast to the arcuate fasciculus, the uncinate fasciculus is part of the "ventral" language pathway (Parker et al., 2005) and connects the anterior temporal lobe to the orbitofrontal cortex. This tract has recently been the focus of renewed interest in the language literature (Axer, Klingner, & Prescher, in press; Weiller, Bormann, Saur, Musso, & Rijntjes, 2011), and together with the extreme capsule system, is an integral part of the semantic network (Friederici, 2012; Saur et al., 2008; Vigneau et al., 2006). Because it runs through the extreme capsule and goes through the temporal stem, the uncinate fasciculus is vulnerable to TBI (Bigler et al., 2010). Changes in the diffusion properties of this tract may therefore explain a significant proportion of language outcome, especially semantic deficits, in young people who have suffered a TBI in childhood.

Finally, we have recently reported that corpus callosum integrity (especially the splenium) was the main predictor of language impairments in adolescents born very preterm (Northam et al., 2012). Another study in a small group of children with idiopathic language impairment reported a significant FA reduction in the genu of the corpus callosum relative to healthy controls (Kim et al., 2006). These results point towards a crucial role of inter-hemispheric connections (between the temporal lobes in Northam et al. (2012)) in language development and processing. The role of inter-hemispheric connections may be particularly important during language development where a shift from inter- to intra-hemispheric connectivity has been suggested between childhood and adulthood (Friederici, Brauer, & Lohmann, 2011). Given that the corpus callosum is particularly vulnerable to shearing and stretching during TBI (both acutely and chronically, Ewing-Cobbs et al., 2008; Wang et al., 2011; Wu et al., 2011), we also investigated whether damage to this tract could explain some of the language variance in our sample.

Here we sought to examine the relationship between white matter integrity and persistent language impairment after pediatric TBI, with and without concomitant dysarthria. First we aimed to investigate whether poor language outcome long-term following a TBI in childhood can be predicted by changes in tractography-derived properties that are measured within the arcuate fasciculus, the uncinate fasciculus, and the corpus callosum. We hypothesised that language impairments would be found in children with TBI regardless of dysarthria, with variance in language ability being partially explained by cumulative effects of tract abnormalities. Secondly, we examined which MRI measure was the best predictor of language outcome after childhood TBI. Finally, we explored whether age at injury and injury severity affect outcomes in our sample (Anderson, Brown, Newitt, & Hoile, 2011).

2. Materials and methods

2.1. Participants

Data were collected as part of a wider study investigating neural correlates of speech and language outcomes after pediatric TBI. Forty-nine young people (22 males) who completed both the neuropsychological assessment and MRI scanning sessions participated in this study. Thirty-two (14 males) had sustained a traumatic brain injury (TBI) in childhood (3–16 years, see Table 1, and also Table 1 in Morgan, Masterton, Pigdon, Connelly, and Liégeois (2013), for individual data) at least 1 year earlier and were recruited from the medical records of the Royal Children's Hospital Melbourne (RCH), in Australia. A subset of this sample had been diagnosed with dysarthria as a result of their traumatic brain injury (TBI+ group), while the remainder did not (TBI− group, see Table 1). Breakdown of injury severity ranged from mild to moderate–severe using the Mayo injury severity scale (Malec et al., 2007), sustained in various accidents (see Table 1, and also Table 1 in Morgan et al. (2013), for individual injury characteristics). We also collected GCS scores for each participant, coded as Mild (scores >12), Moderate (scores were between 9 and 12), or Severe (scores <9). The GCS is limited in being a single indicator of injury severity, where scores may be influenced by factors such as whether or not early sedation was utilised and the timing of when the score was taken post-injury (see Malec et al., 2007 for further review and discussion). GCS scores were recoded categorically as severe (3), moderate (2) or mild (1) for statistical analyses.

A typically developing group ('Control' group) was also recruited from the community. Each control participant was individually age- and sex-matched to two TBI participants, one of whom had dysarthria and one who did not. The majority of participants were right handed (14/17 in the TBI+ and TD group, 13/15 in the TBI− group).