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Reduced integrity of sensorimotor projections traversing the posterior limb of the internal capsule in children with congenital hemiparesis

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ABSTRACT

There is reduced integrity of corticospinal projections that traverse the posterior limb of the internal capsule (PLIC) in children with unilateral cerebral palsy (CP). It remains unclear whether there are changes in integrity of other projections traversing the PLIC. Forty children with congenital hemiparesis and 15 typically developing children underwent structural and diffusion-weighted MRI. All children with congenital hemiparesis showed lesions to the periventricular white matter. Structural images were parcellated into 34 cortical regions per hemisphere and posterior limb of the internal capsule was identified. PLIC connections to each cortical region were extracted using probabilistic tractography. Differences between hemispheres for each cortical projection (asymmetry index (AI)) and tract microstructure (fractional anisotropy (FA), mean diffusivity (MD)) were assessed. The results showed that 17 children (42.5%) with congenital hemiparesis showed bilateral lesions on structural MRI. Projections to the primary motor cortex (precentral gyrus and paracentral lobule) showed greater asymmetry in unilateral CP group compared to typically developing children and indicate reduced projections on the hemisphere contralateral to the impaired limb (i.e., contralateral hemisphere). Reduced FA and increased MD were also observed for connections with the primary motor cortex, primary sensory cortex (postcentral gyrus) and precuneus on the contralateral hemisphere in children with congenital hemiparesis. Similar changes were observed between children with unilateral and bilateral lesions on structural MRI. Notably, microstructural changes were associated with deficits in both sensory and motor function. The findings further unravel the underlying neuroanatomical correlates of sensorimotor deficits in children with congenital hemiparesis.

1. Introduction

Cerebral palsy (CP) is the most common cause of physical disability in children in Western society and is associated with non-progressive lesion(s) to the developing brain (Bax et al., 2005). Motor dysfunction is the hallmark of CP, although sensory deficits can also be present (Odding, Roebroceck, & Stam, 2006). Structural MRI (i.e., T1- and T2-weighted MRI)

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remains the gold standard for the investigation of brain lesions associated with CP (Ashwal et al., 2004). The most common lesion identified is that to the periventricular white matter, which occurs during the early parts of the third trimester and is most commonly observed in children with spastic motor type (Krageloh-Mann & Horber, 2007; Towsley, Shevell, Dagenais, & Consortium, 2011). However, structural MRI is unable to examine white matter connectivity and microstructure. One method to examine the integrity of white matter projections in vivo is diffusion-weighted MRI, which measures the diffusion of water molecules within tissue as a surrogate of white matter orientation and integrity (Jones, 2008). Studies have focused on the descending corticospinal connections and show that loss in the integrity of these projections is associated with deficits in motor function (see reviews Scheck, Boyd, & Rose, 2012; Staudt, 2010). Anatomically, the corticospinal projections traverse the posterior limb of the internal capsule (PLIC), which is situated between the thalamus and lentiform nucleus of the basal ganglia. The PLIC contains other ascending and descending white matter projections, but little is known about the potential for changes in the organisation and microstructure of white matter projections that traverse the PLIC in children with CP.

A common application of diffusion-weighted imaging is diffusion tensor imaging. Diffusion tensor imaging allows assessment of the microstructure of white matter projections via two common measures: fractional anisotropy (FA) and mean diffusivity (MD). FA measures the degree of uniformity in the diffusion direction in a given voxel and ranges from 0 to 1, with a higher FA value indicative of more coherent fibre organisation. MD measures overall water diffusion where a high MD value suggests reduced fibre density (Jones, 2008). In addition, tractography of diffusion tensor imaging in healthy adults showed that white matter projections traversing the PLIC were arranged topographically based on cortical connectivity with some overlap (Zarei et al., 2007). The arrangement involved connections with the premotor cortex, primary sensorimotor cortex, posterior parietal cortex, temporal lobe and occipital cortex arranged approximately from anterior to posterior. However, a limitation with diffusion tensor imaging is that it only allows for a single fibre orientation within a voxel. This shortfall can be overcome using high angular resolution diffusion imaging (HARDI) parameters, which permits multiple fibre orientations within a voxel. No study has applied the HARDI parameters of diffusion-weighted imaging to investigate organisation and microstructure of white matter projections traversing the PLIC in unilateral CP.

The current study aims to investigate the organisation and microstructure (FA and MD) of white matter projections that traverse the PLIC in typically developing children (TDC), and to compare these with children with congenital hemiparesis. A second aim of the study was to explore whether changes, if present, were associated with deficits in sensorimotor function.

2. Material and methods

2.1. Participants

Fifty-four children aged between 5 and 16 years with confirmed clinical diagnosis of congenital spastic hemiparesis were initially recruited. To minimise heterogeneity in the CP group, only subjects with lesions to the periventricular white matter on structural MRI were included as this is the most common lesions in children with spastic motor type (Krageloh-Mann & Horber, 2007). This was assessed by an independent and experienced clinical neurologist (S.F.; see Section 2.3). Eight children with grey matter lesions were therefore excluded. In addition, six children showed enlarged ventricles that prevented automated anatomical parcellation and were also excluded. Thus data from 40 children with congenital hemiparesis were included in the CP group (Table 1). Children with CP showed mild to moderate deficits in motor function classified on the Gross Motor Function Classification System (GMFCS; I: $n = 29$, II: $n = 11$) and Manual Ability Classification System (MACS; I: $n = 20$; II: $n = 20$). Fifteen typically developing children (TDC) were also recruited and acted as controls (Table 1).

Written informed consent was obtained from all parents of children prior to study participation, and assent was also obtained for children 14 years or older. All children were checked for MRI safety and a mock MRI scanner was used to familiarise each child with the imaging procedure. This optimised compliance in the scanner and minimised movement

Table 1
Subject demographics for typically developing children and children with unilateral cerebral palsy (CP).

	CP ($n = 40$)	Healthy ($n = 15$)
Age (years)	11.5 ± 3.1	11.2 ± 2.8
Gender	21 F 19 M	9 F 6 M
Side of lesion/dominance	20 left hemiplegia 20 right hemiplegia	6 left-handed 9 right-handed
JTTHF (s)	Dominant: 45.8 ± 20.1 Impaired: 246.0 ± 214.4[a]	–
AHA (0–100 score)	62.1 ± 13.2	–
MUUL (%)	92.9 ± 21.9	–
Two-point discrimination (mm)	Dominant: 2.2 ± 0.1 Impaired: 4.2 ± 2.3[a]	–
Stereognosis (/9)	Dominant: 8.3 ± 0.4 Impaired: 6.8 ± 2.3[a]	–

JTTHF – Jebsen–Taylor Test of Hand Function; MUUL – Melbourne unilateral upper limb assessment; AHA – assisting hand assessment.
[a] $P < 0.05$ between dominant and impaired limbs.