SP25 Interrelationships among quantitative measures of brain white matter injury and locomotion in children with cerebral palsy

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Objectives

Cerebral palsy (CP) describes a group of motor-impairment syndromes secondary to disorders of early brain development. It is commonly linked to white matter injury in premature infants. Diffusion-tensor imaging (DTI) is a powerful technique to visualize brain white matter tracts, thereby providing more precise identification of white matter maldevelopment and injury. The overall goal of this case-control study was to correlate DTI derived measures of white matter (WM) integrity with sensorimotor function in children with cerebral palsy (CP). This report focuses on a comprehensive sensorimotor analysis of a small cohort of children with CP and correlated DTI measures of WM injury with treadmill walking to predict locomotor learning.

Methods

A convenience sample of children aged 6-14 years with spastic diplegia (GMFCS I-III) were recruited from the Kennedy Krieger Institute's Phelps Center for Cerebral Palsy, Baltimore, MD, USA. Fourteen children with cerebral palsy and 11 age and gender matched typically developing controls were consecutively enrolled and scanned using conventional magnetic resonance (MR) and diffusion-tensor imaging (DTI). The protocol was approved by the Johns Hopkins Institutional Review Board and informed consent was obtained from the parents.

All participants had an MRI scan and sensorimotor assessment including gait and kinematic testing. Each patient's FA map was transformed to the standardized space by using single-subject brain atlas, then probabilistic tract maps quantified the pixel intensities along the probabilistic tracts (Figure 1). The fractional anisotropy (FA) in specific regions of interest (ROIs) such as thalamus, corticospinal tract (CST), PTR (posterior thalamic radiation) and probabilistic tracts, such as thalamic radiation to precentral area and thalamic radiation to postcentral area, was compared between case-control groups by unpaired t-tests, corrected for multiple comparisons with FDR at a p-value threshold of 0.05 . To gauge capacity for motor learning, the children walked on a split-belt treadmill with one belt moving twice as fast as the other belt for 10 minutes. Upon return to normal walking, the magnitude of learning was measured by calculating the normalized difference between the step lengths of the two legs (affect-effect in step length symmetry). The size of the after-effect was correlated with the FA in the above referenced regions.

Results

Demographics: Scans from 3 children were not analyzable due to motion artifact. The final sample was composed of 11 children with spastic diplegia and 11 typically developing controls born term (Table 1). The mean age of the child participants was 9.4 years (range 6.2 to 14 years). There were 13 males and 9 females. Among children with CP, 8 children were born preterm (<37 weeks gestation) and 3 at term; birth gestational age (GA) ranged from 24-39 weeks (mean 29.9 weeks).

FA measurements in bilateral posterior thalamic radiation and in the probabilistic tract connecting right thalamic radiation to postcentral area were significantly lower in children with CP as compared to controls (p=0.0005 and 0.0004, respectively)(Figure 2). In correlations between the step symmetry aftereffect and FA data within the CP group, the only tract with a significant relationship to step symmetry was the FA CST-L (r= .83, p=.02) in ROI. Children with CP who demonstrated motor learning had significantly higher (more intact) mean FA in the probabilistic tract connecting right CST to precentral gyrus area (t=.055, df 7; p=.035).

Figure 1. MR and Diffusion-Tensor Imaging of Participant with CP (6y 6m, GA 31)

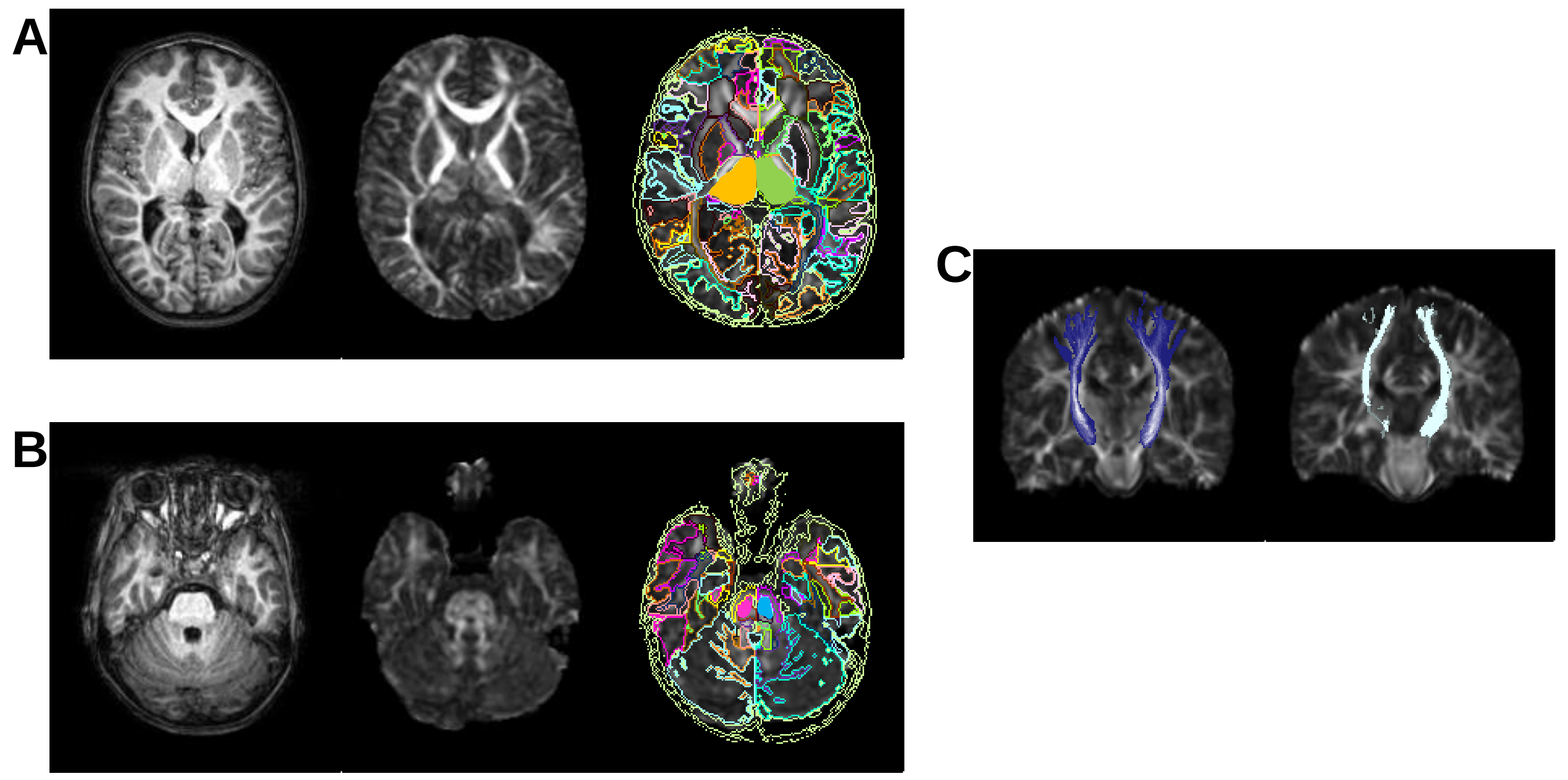


Figure 1. **A** and **B** show axial conventional MR images (left), fractional anisotropy (FA) map of diffusion tensor imaging (middle), and parcellated ROI map superimposed on FA map (right). **A** shows bilateral thalamus (yellow and light green) and **B** shows bilateral CST at the pons level (pink and light blue). **C** shows the coronal image of probabilistic tracts, superimposed to the normalized FA images of the same patient. (Left: thalamic radiation to precentral area, Right: thalamic radiation to postcentral area)

Child on Split-Belt Treadmilll

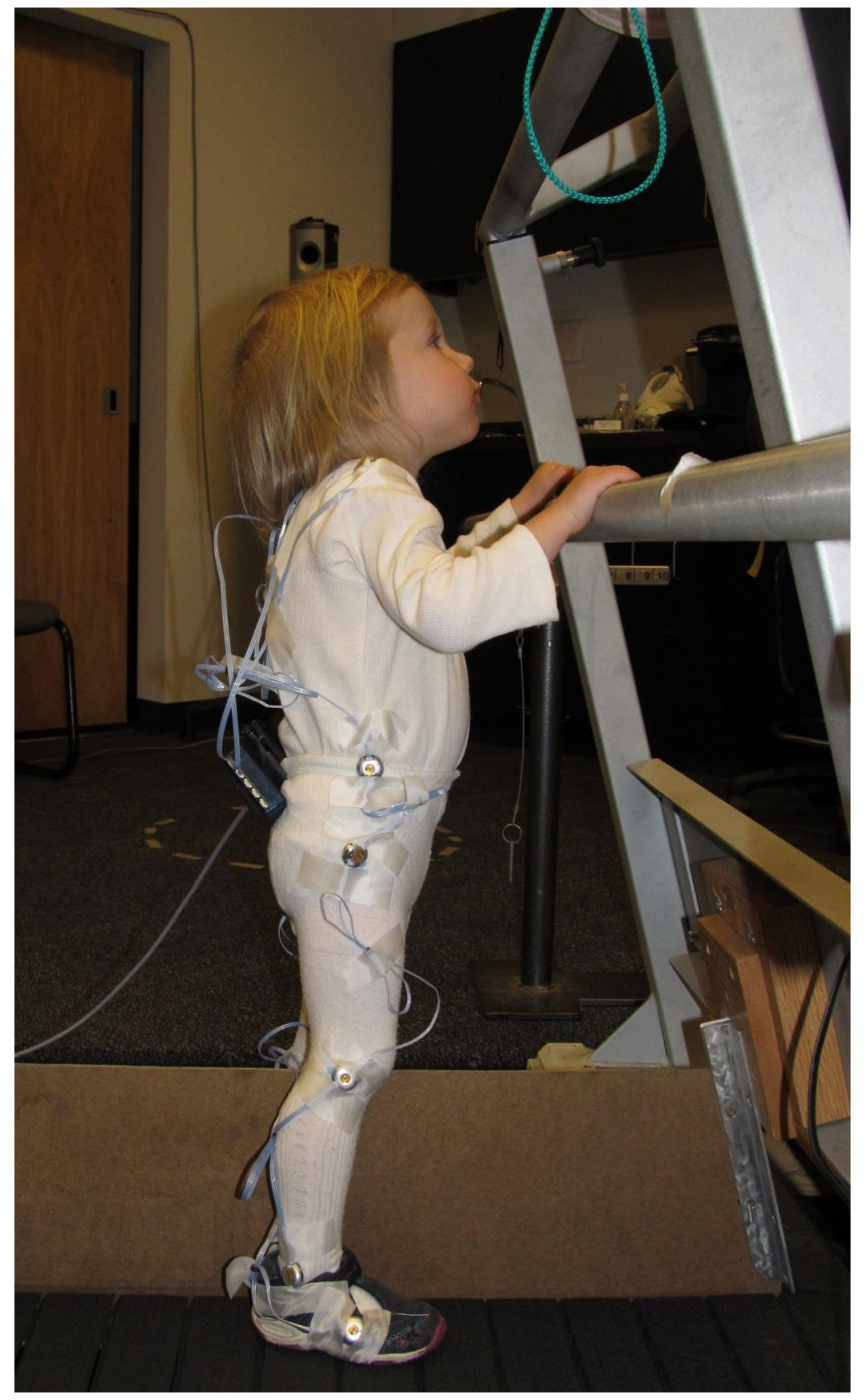
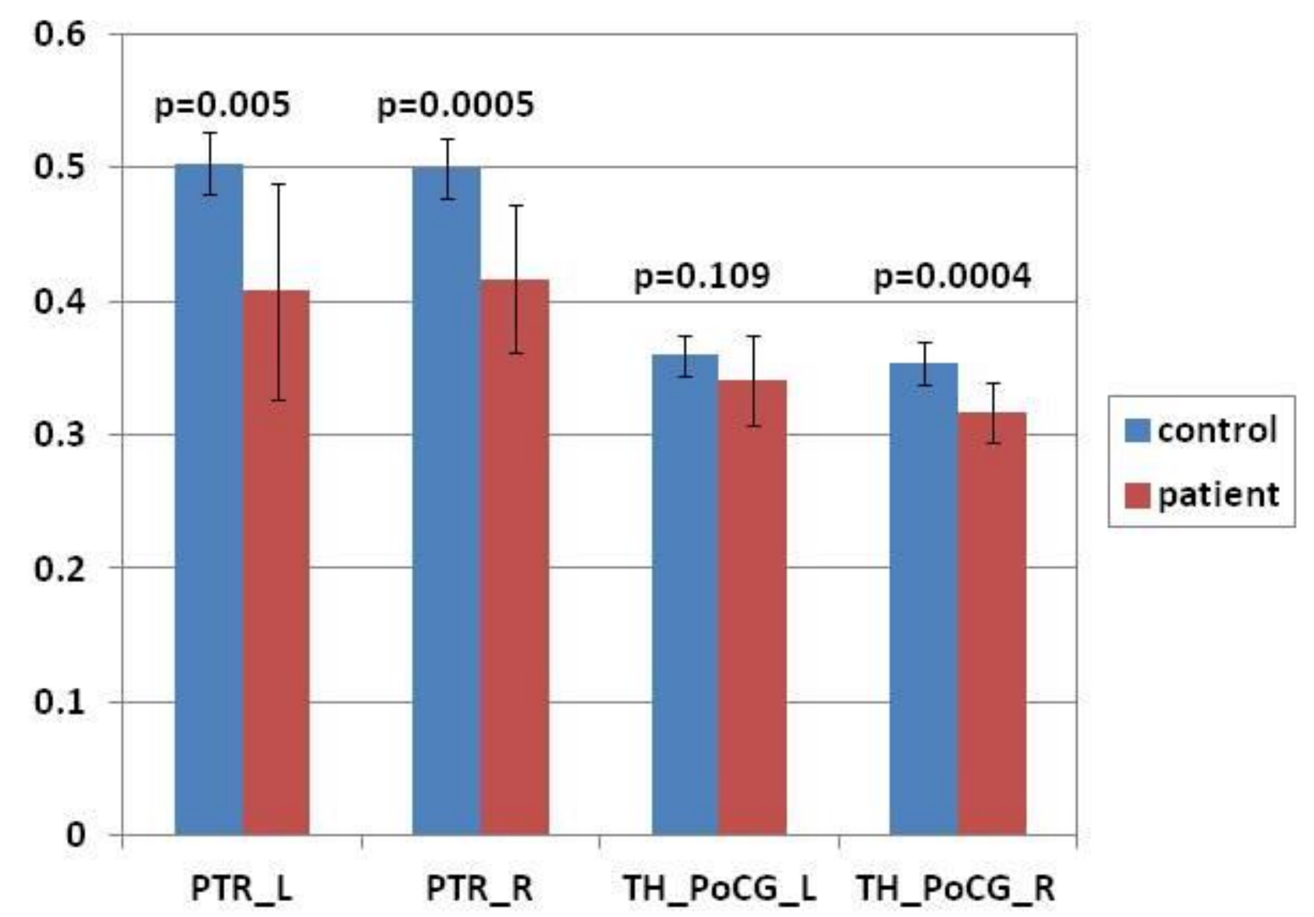


Table 1. Demographics and Step Symmetry Results

Age	Gender	DX	GMFCS	GA	Step Symmetry Learner (Y/No)
8y10m	M	IVH	I	32	Learner
8y5m	F	IVH	III	27	Poor Kinematic data
6y8m	M	IVH	II	24	Learner
9y11m	M	PVL	III	30	Poor Kinematic data
9y2m	F	PVL	I	26	Learner
12y3m	M	PVL	III	28	No
12y6m	F	PVL	III	26	Learner
6y6m	M	PVL	III	31	Learner
14y3m	M	PVL	III	28	Learner
12y11m	M	PVL	III	38	No
6y6m	M	PVL	I	39	No

Figure 2. Mean fractional anisotropy (FA) in the posterior thalamic radiation (PTR) and in the pathway connecting thalamus and postcentral gyrus.



Legend The bar-graph shows differences in the mean FA in selected white matter sensory areas of cases and controls (ROIs of left- and right-posterior thalamic radiation (PTR) and probabilistic tracts connecting left and right thalamic radiation to postcentral area (Th-PoCG)).

Conclusions

As demonstrated in previous studies, sensory tract injury distinguished children with CP (cases) from controls.

However, this injury did not affect their ability to learn a new locomotor pattern, suggesting that children with intact CST motor pathways have the learning mechanisms to adapt and potentially improve gait.

Acknowledgements

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