Brain white matter abnormalities in paediatric Gaucher Type I and Type III using diffusion tensor imaging

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Introduction:

Gaucher disease is a lysosomal storage disorder (LSD). Functional deficiency of glucocerebrosidase leads to accumulation of glucosylceramide. Neurological manifestations include horizontal gaze palsy, epilepsy and ataxia, and is classified as Type III. Patients without neurological involvements are traditionally classified as Type I. The 'Neuronopathic' forms are the rarest variant with an estimated incidence of <1:100,000 live births.

Diffusion Tensor Imaging (DTI) is the modality of choice for investigating the structural properties of white matter tracts[1] which are commonly expressed in terms of the fractional anisotropy (FA), mean diffusivity (MD)[2] and axial (λ_{axial}) and radial (λ_{radial}) diffusivity. High diffusion levels in white matter are indicative of poorly developed, immature, or structurally compromised white matter[3].

Methods:

Tract-based spatial statistics (TBSS)[4] was used to examine DTI parameters in Gaucher patients compared to age-sex matched controls. Imaging data was acquired using a Siemens 1.5T Avanto clinical scanner. Echo-planar diffusion-weighted images were acquired in 20 directions at b=1000 s mm^{-1}. This protocol was repeated three times to improve SNR. Three b=0 s mm^{-1} images were also acquired for normalisation. The study was approved by the local ethics committee and informed consent obtained for all participants.

Participants: Four Type III and three Type I children with Gaucher disease were recruited. Data was compared to an age-sex matched control group. To improve power for this study the control groups were made 2:1 to the Gaucher groups.

Results: A decrease in FA and an increase in MD was observed in the Type III cohort, with a significant difference observed in the middle cerebellar peduncle (Figures 1 and 2). An increase in λ_{axial} and λ_{radial} was also seen, (data not shown) which suggests that the increase in MD and decrease in FA is driven by an increase in radial diffusivity, as opposed to a change in axial diffusivity. Despite small, diffuse changes in FA and MD throughout the Type I brain the increased λ_{axial} observed in the Type III group is not observed, furthermore there were no significant differences observed in the cerebellar peduncles.

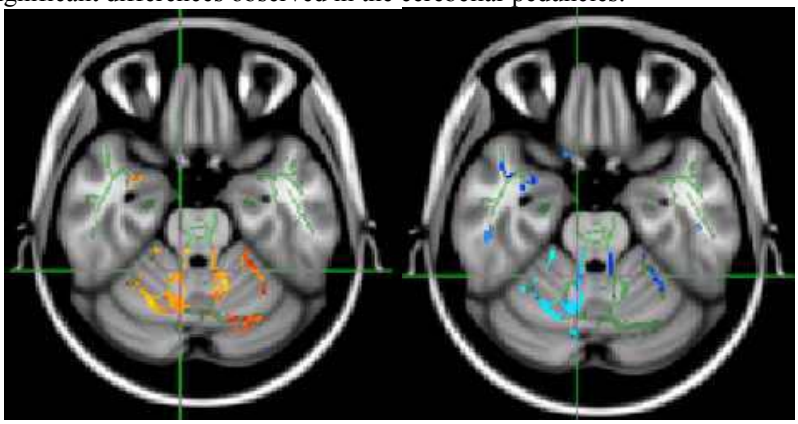

Figure 1: TBSS results (p<0.05, uncorrected) for MD (left) where red voxels correspond to higher MD and FA (right) where blue voxels correspond to lower FA in Type III patients compared to controls.

Conclusion:

This is the first TBSS study to examine brain white matter in Gaucher patients and showed a pattern of decreased FA and increased MD primarily in the middle cerebellar peduncles in the Type III patients. These findings are consistent with the clinical presentation of ataxia seen in Type III patients, which is not characteristically seen in Type I Gaucher patients. Further research is now warranted to determine the relation between the observed structural changes and clinical deficits in a larger cohort of Gaucher patients.

References: 1. LeBihan, D., *et al* (2001) Diffusion tensor imaging: concepts and applications. 13(4):534-46. 2 Pierpaoli, C., Basser, PJ (1997);36(6):893-906. 3. Cascio, CJ., *et al* (2007);46(2):213-23. 4. Smith, SM., *et al* (2006) 15;31(4):1487-505