CEREBELLAR MUTISM SYNDROME: THE CEREBELLO-THALAMO-CEREBRAL PATHWAY AS A POTENTIAL NEUROANATOMICAL SUBSTRATE

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Purpose: Cerebellar mutism syndrome (CMS) has been documented in up to 25% of children following resection of posterior fossa (PF) tumors. CMS can present with diminished speech output, dysarthria, hypotonia, ataxia, emotional lability, as well as behavioural and affective disturbances. In addition to cerebellar involvement, disruption of cerebrocerebellar communication has been implicated in many of these symptoms. We investigated the structural integrity of the cerebello-thalamo-cerebral white matter pathway as a potential neuroanatomical substrate of CMS in PF tumors.

Methods: Seventeen children with PF tumors and CMS, 34 children with PF tumors without CMS, and 28 healthy control children underwent MRI at the Hospital for Sick Children, British Columbia Children's Hospital, or Alberta Children's Hospital. We used diffusion tensor imaging (DTI) and probabilistic tractography to delineate the cerebello-thalamo-cerebral pathway from each cerebellar hemisphere to contralateral dorsolateral prefrontal cortex (DLPFC) via contralateral thalamus. Means and standard deviations for anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) were calculated for the whole tract as well as each segmented anatomic region of the tract (i.e. frontal, internal capsule/thalamus/midbrain, pons, and cerebellum) to provide insight into pathway integrity.

Results: Bilateral tracts connecting the cerebellum with DLPFC were delineated in all participants (Figure 1). Multivariate analyses revealed a significant group difference in the integrity of the cerebellar regions of the tract connecting the right cerebellar hemisphere with the left DLPFC via the left thalamic region ($p=.015$). Univariate analyses showed significant differences in MD ($p=.002$), AD ($p=.01$), and RD ($p=.02$) across groups for this region (see Table 1). Post-hoc comparisons revealed the following significant differences: between patients with CMS and controls for MD ($p=.001$), AD ($p=.01$), and RD ($p=.006$); and between patients with CMS and patients without CMS for MD ($p=.003$) and AD ($p=.004$). No differences were found between groups for DTI measures of the tract connecting the left cerebellar hemisphere with the right DLPFC.

Conclusion: We have shown that the cerebello-thalamo-cerebral pathway is structurally altered in CMS – specifically in the cerebellar region. Notably, we found that the pathway connecting the right cerebellar hemisphere with the left DLPFC was selectively damaged (signified by higher MD, AD, and RD in this region of the pathway) in patients with CMS relative to patients

without CMS and healthy controls. In addition to the cerebellum, left frontal regions (i.e. DLPFC) are involved in mediating speech production, expressive language, and inhibitory control. Thus it is possible that many of the symptoms of CMS are associated with the disruption of cerebrocerebellar communication – namely the right cerebellar to left DLPFC cerebello-thalamo-cerebral pathway – following treatment for PF tumors.

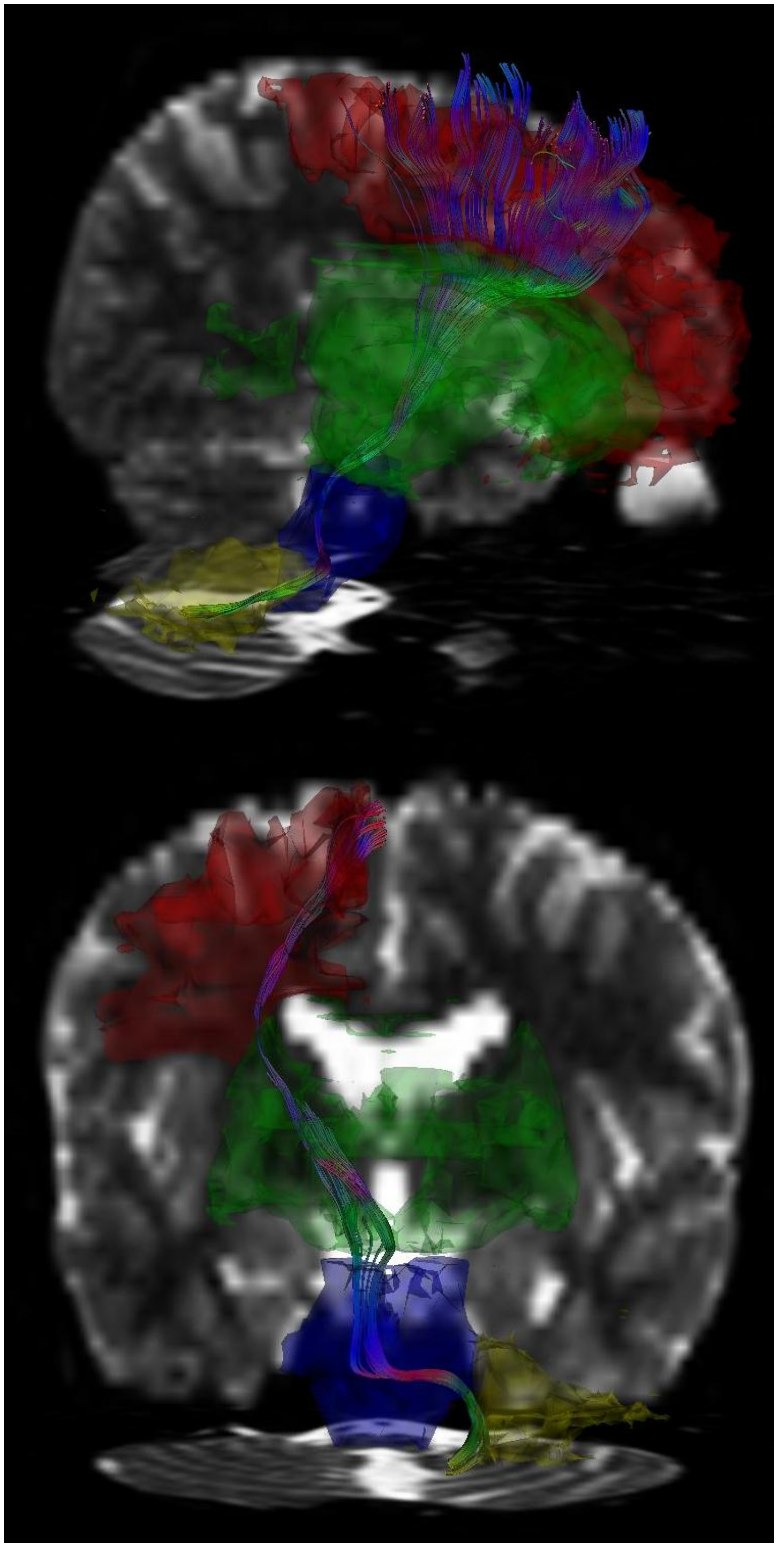

Figure 1. The cerebello-thalamo-cerebral tract connecting the right cerebellar hemisphere with left DLPFC via left thalamus. Top: A sagittal view of the pathway. Bottom: A coronal view of the pathway.

Table 1. Means and standard deviations (in parentheses) for regional DTI indices of the cerebello-thalamo-cerebral tract connecting the right cerebellar hemisphere with left DLPFC via left thalamic nuclei for patients with CMS, patients without CMS, and healthy controls.

Cerebello-Thalamo-Cerebral tract Anatomical Region	CMS (n = 17)				No CMS (n = 34)				Controls (n = 28)			
	FA	**MD**	**AD**	**RD**	**FA**	**MD**	**AD**	**RD**	**FA**	**MD**	**AD**	**RD**
Left Frontal	.451479 (.082381)	.000768 (.000037)	.001171 (.000067)	.000564 (.00007)	.425143 (.052818)	.000777 (.000038)	.001156 (.000067)	.000576 (.000123)	.42279 (.052313)	.000777 (.000035)	.001154 (.000078)	.000588 (.000044)
Left Mid	.516119 (.059816)	.000762 (.000045)	.001237 (.000064)	.000524 (.000064)	.539004 (.06707)	.000746 (.000036)	.001251 (.000106)	.000487 (.000121)	.509122 (.038224)	.000751 (.000036)	.001215 (.000063)	.000519 (.000033)
Left Pons	.456797 (.055917)	.000903 (.000133)	.001346 (.00015)	.000682 (.000132)	.490845 (.067371)	.000809 (.000105)	.001264 (.000169)	.000571 (.000144)	.474089 (.026002)	.000846 (.000131)	.001285 (.00018)	.000627 (.000109)
Right Cerebellum	.466036 (.0625)	.000775[ab] (.000101)	.001191[ab] (.000135)	.000568[b] (.000099)	.461372 (.110181)	.000712[a] (.000056)	.001119[a] (.000089)	.0005 (.000128)	.484553 (.055107)	.000696[b] (.000061)	.001103[b] (.00009)	.000492[b] (.00006)

[a, b] Different superscripts indicate significant mean difference across groups at $p < 0.02$ (i.e. [a] signifies a significant difference between patients with CMS and patients without CMS for the labelled category, while [b] signifies a significant difference between patients with CMS and controls for the labelled category).