Abnormal Microstructure of the Thalamus in Childhood Survivors of Prematurity: Assessment with Diffusion Tensor Imaging

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Purpose: Preterm infants are highly vulnerable to brain injury resulting in subsequent cognitive and motor disability. Our goal was to demonstrate both volumetric and diffusion tensor metric abnormalities of complete thalamus as well as specific subdivisions in early childhood survivors of prematurity with Periventricular Leukomalacia (PVL).

Methods: Medical records and Diffusion Tensor (DTI) data were retrospectively reviewed in this IRB approved study. 17 patients with PVL on MRI were included and compared against 74 controls. Clinical information concerning cerebral palsy, seizures and developmental delay were recorded. DTI protocol consisted of echo planar imaging (EPI) sequence using neonatal head coil with 25 directions and b=1000 s/mm^2 on a 1.5T GE Scanner. Complete thalamus as well as thalamic subdivisions such as anterior, reticular (lateral), medial dorsal and pulvinar were manually traced **(Fig. A)** on maps generated by DTIStudio (John Hopkins, MD, USA). Student's t-test, test of 2 binomial proportions and ANOVA were used for comparison purposes.

Results: PVL patients were at gestational ages of 24-36 wks. 100% PVL patients demonstrated developmental disability, 75% cerebral palsy, 67% seizure and 86% visual function abnormalities **(Table)**. Thalamic volume was lower than in controls (p<0.0001) **(Fig. B,C,D).** PVL patients had significantly reduced fractional anisotropy (FA) (p=0.003) and increased radial diffusivity (RD) (p=0.02) in the thalamus when compared to controls. The subdivision analysis showed a selective increase in axial diffusivity of the pulvinar nucleus (p=0.001) in PVL cases.

Discussion: Our study is one of the first to show combined volumetric and DTI data within the parenchyma of the thalamus in childhood survivors of prematurity with PVL. Three major patterns of damage found: (1) overall decrease in volume of the thalamus which may be related to loss of neurons; (2) global decrease in FA and increased radial diffusivity in the thalamic parenchyma which might reflect loss of myelinated efferent/afferent fibers; this could be related to disruption of the cortical-thalamic connections postulated to occur in PVL; (3) possible preferential damage to the pulvinar which also demonstrated a decrease in axial diffusivity, suggesting axonal injury.

Conclusion: PVL patients demonstrate microstructural injury to the thalamus as detected by DTI.

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References: 1. Ligam P et al, Pediatr Res 2008; 2. Leviton et al, Ann Neurol. 1984.

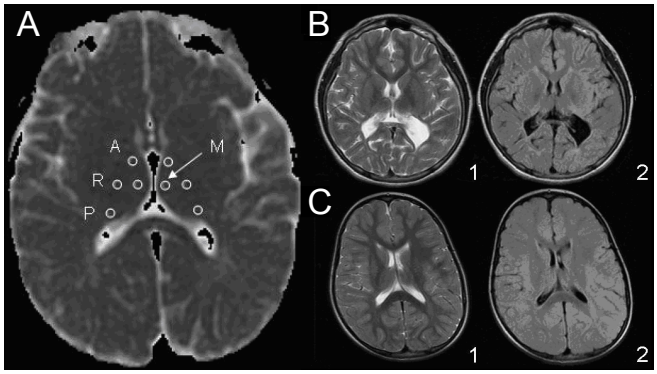

Fig. A: *Manual Traces of Anterior(A), Reticular(R), Pulvinar(P) and Medial Dorsal(M) thalamic nuclei are shown.* ***B,C:*** *T2 (1) and FLAIR (2) images for severe PVL (B) and mild PVL (C). The severity of each case is evident from the degree of periventricular white matter volume loss.*

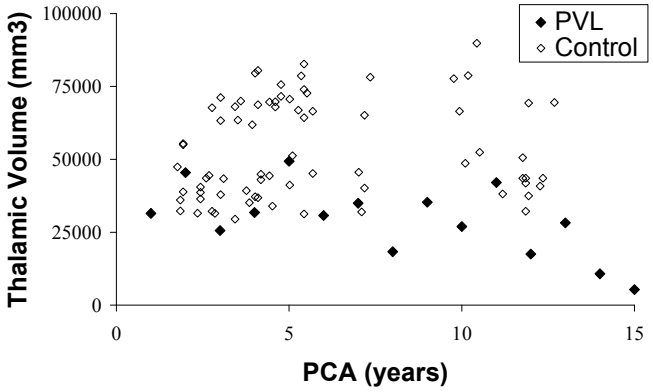

Fig. D: *Volume of the thalamus is significantly decreased in PVL cases when compared to controls. PCA – Post Conceptional Age.*

Table: *Comparison of PVL vs. Controls.*

	PVL (n=17)	Control (n=74)	P
Seizure Activity	10 (67%)	19 (26%)	0.002
Epilepsy	10 (100%)	4 (22%)	0.000
Developmental Disability	15 (100%)	5 (7%)	0.000
Volume (mm^3)	26486 (13399)	53629 (16722)	<0.0001
Complete Th FA	0.24 (0.02)	0.26 (0.02)	0.003
Complete Th Radial Diff (x10^{-3} mm^2/s)	0.73 (0.10)	0.69 (0.05)	0.02
Pulvinar FA	0.27 (0.06)	0.24 (0.04)	0.054
Pulvinar Axial Diff (x10^{-3} mm^2/s)	1.06 (0.14)	0.98 (0.07)	0.001