Diffusion Tensor Imaging Provides Evidence of Brain Involvement in "Pure" Adrenomyeloneuropathy Patients

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Background: Adrenomyeloneuropathy (AMN), a phenotypic variant of X-linked Adrenoleukodystrophy (X-ALD) is believed to be restricted to spinal cord in 80% of cases, commonly referred to as Pure Adrenomyeloneuropathy. Histopathologic reports have shown brain changes in Pure AMN (1), however these results have not been adequately evaluated. Diffusion tensor imaging measures the proton diffusivity, which enables a quantitative assessment of white matter integrity. We utilized diffusion tensor imaging to detect early microstructural white matter changes in the brain of AMN patients who had normal conventional MRI. We further investigate a possible cerebral extension of the spinal cord tract involvement in the corresponding anatomic sites in the brain.

Methods: The cerebral involvement was evaluated by signal intensity assessment in axial T1- and T2-weighted brain MRI Conventional MR imaging consisted of acquisition of sagittal T1- (repetition time [TR] msec/echo time [TE] msec, 587/20) and transverse T2- (3,000/30–100) weighted). DTI (2) [Single shot-EPI; TR/TE of 7622/80 ms ; max b value=700 s/mm^2; 30 different gradient directions; 2.5 mm resolution; 50 axial slices; 5min 24s scan time per sequence; 3 repetitions] was performed at 1.5 Tesla scanner combined with SENSE (3) technique - sense factor (R) of 2.5. Study population consisted of 8 male patients with AMN (39±15 years) who had normal conventional MRI and 8 age-matched normal control subjects. For DTI processing, six independent variables (D_{xx}, D_{yy}, D_{zz}, D_{xy}, D_{yz}, D_{xz}) in the DT were calculated from the DT images, where D represents diffusion coefficient. Using color-coded orientation map as anatomical guidance (Fig. 1), four anatomical locations were identified and ROIs were manually delineated. Mean apparent diffusion coefficient (mADC) and fractional anisotropy (FA) parameters were obtained from four ROIs. The posterior limb of the internal capsule and the projection fibers in the corona radiata were chosen as the cerebral representation of spinal cord long tracts (figure1). The frontal and periventricular parietoccipital white matter (figure1) were selected for their known correspondence to the brain regions typically involved in demyelination in 20% of AMN patients and in other phenotypes of X-ALD. Statistical analyses were done using Unpaired Student's t-test and significance was set at p values < 0.05

Results and Discussion: Detailed description of results in Table 1. A significant reduction in FA compared to controls was observed in all four ROIs. A significant difference in mADC between the two groups was seen only in the corona radiata (p=0.0002), whereas the differences for other regions did not achieve statistical significance. Our results indicate early signs of white matter involvement in the brain of AMN patients with normal conventional MRI suggesting that the AMN disease process may not be limited to the spinal cord. Also, these findings demonstrate diffuse involvement in all regions, suggesting a cerebral disease process, which could be either an extension of spinal cord involvement or a precursor stage of impending demyelination. FA was a more sensitive measure than mADC in detecting white matter integrity. Follow-up studies will elucidate the exact role of these changes in predicting the progression towards demyelinating brain lesions, which is crucial for therapeutic decision making in X-ALD. In future DTI may serve as a sensitive marker for monitoring progress and therapeutic evaluation.

Table 1. Comparison of FA and Mean ADC values in four brain regions of interest in AMN patients and Controls.

Region of Interest	**Fractional Anisotropy**			**Mean Apparent Diffusion Coefficient (10^{-3}mm^2/s)**		
	AMN (Mean±SD)	Control (Mean±SD)	p value	AMN (Mean±SD)	Control (Mean±SD)	p value
R1	0.59±0.03	0.64±0.05	0.03	0.59±0.02	0.56±0.03	0.09
R2	0.45±0.05	0.54±0.036	0.001	0.63±0.02	0.62±0.02	0.60
R3	0.41±0.05	0.56±0.03	<0.0001	0.59±0.03	0.53±0.01	0.0002
R4	0.4±0.05	0.46±0.05	0.03	0.56±0.02	0.54±0.03	0.35

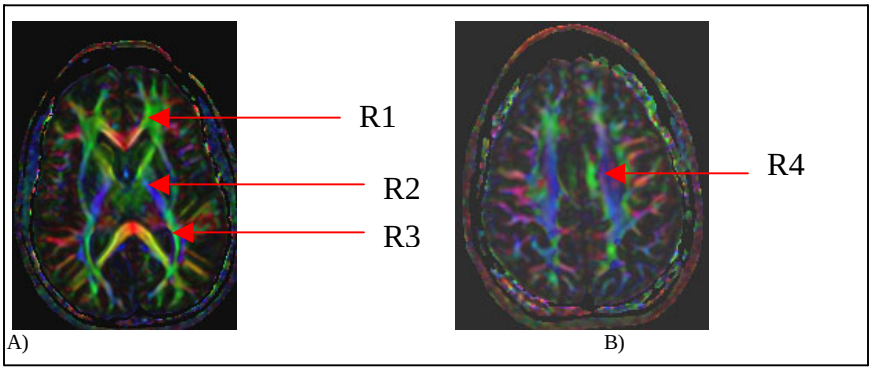

Figure1. Color Map of 36-year old normal control showing the four regions of interest manually selected for obtaining the mADC and FA values. R1- Frontal White Matter, R2- Posterior Limb Internal Capsule, R3- Periventricular Parietoccipital White Matter, R4-Corona Radiata.

References:

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