DTI in Leukoencephalopathy with Brainstem and Spinal cord involvement and elevated Lactate (LBSL): Local strongly increased FA and reduced diffusivity as well as globally reduced FA and increased diffusivity.

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Introduction. Leukoencephalopathy with brainstem and spinal cord involvement and lactate elevation (LBSL) is an inherited white matter disorder first recognized in 2003 by its distinct pattern of MRI abnormalities, including involvement of cerebral white matter, pyramidal and sensory tracts over their entire extent (including the spinal cord), and specific brain stem structures [1]. The disease gene was shown to be DARS2, which encodes mitochondrial aspartyl-tRNA synthetase [2]. The pathological basis of the disease has remained unknown until now. To gain insight into tissue microstructure, the emphasis of this study was on high-resolution DTI in LBSL.

Material and methods. Seven patients diagnosed with LBSL by genetic analysis (2M/5F; aged 17-49 y, mean 28 y) and seven age- and gender-matched controls were included. The MRI protocol included conventional and DTI imaging at 1.5T (Siemens Sonata). High-resolution DTI used EPI, TR/TE=5400/103ms, 99 directions, b=900s/mm², 10 b0 volumes, matrix 160x160, 29 slices centered onto corpus callosum, resolution 1.45 x 1.45 x 2.0 mm). The diffusion tensor was calculated with FSL, resulting in MD, FA, axial diffusivity (D⊥) and radial diffusivity (D//). Voxelwise statistical analysis of the DTI metrics was carried out using TBSS (Tract-Based Spatial Statistics, v1.2). TBSS projects all subjects’ FA data after non-linear registration onto a group-mean FA tract skeleton, before applying voxel-wise cross-subject statistics [3]. In addition, ROIs were selected in individual patients in areas that showed a combination of abnormally high and low MD (fig 1B); in the controls homologous ROIs were placed, which was facilitated by all FA maps having been registered to the same coordinate space.

Results. TBSS showed an overall highly significant (corrected p< 0.01) increase in MD and decrease in FA (Fig 2A,C) in LBSL patients as compared to controls. Areas with significantly increased MD coincided with areas with higher D// (B), whereas decreased FA was mainly co-localized with D⊥ (D). Green is the tract skeleton, yellow indicates an increase, red a decrease.

Discussion and Conclusions. TBSS analysis revealed that the normal-appearing white matter in LBSL on T2-weighted images can display diffusion-based abnormalities, which is evidence that the white matter is more extensively affected than would be assumed based on T2-weighted images alone. Detailed ROI analysis showed, besides the anticipated MD increase and FA decrease, a striking FA elevation combined with a decrease of MD, D//, and D⊥ on the border of regions with high MD and low FA. Restricted diffusion has been described in leukoencephalopathies caused by myelin vacuolation [4,5], which can be a reversible process. Myelin vacuolation might also play a role in LBSL, especially in the early stages of white matter alteration, which would explain the regional distribution of the restricted diffusion at the contour of lesions.

References.