TBSS analysis in MSA
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Introduction:
Multiple System Atrophy (MSA) is a sporadic, progressive disease characterized by autonomic dysfunction with varying degrees of parkinsonian and/or cerebellar features. Two forms of MSA are currently recognized: a parkinsonian form (MSA-P, formerly striatonigral degeneration), and a cerebellar form (MSA-C, formerly olivopontocerebellar atrophy). Overlap between these two divisions may be evident, both clinically and pathologically, with designation to one group determined by the predominant features at evaluation. Although the precise pathogenesis of the disease remains elusive, early and widespread oligodendrocyte involvement characterized by GCI accumulation and demyelination has been well documented. As these events correlate topographically and temporally with neuronal degeneration, it has been postulated that MSA is a primary oligodendrogliopathy. Previous DTI studies in MSA have primarily used ROI, tractography, and VBM-based approaches. TBSS is a method that is better suited to examine global white matter changes. We therefore elected to perform TBSS analysis in MSA to investigate global white matter changes.

Subjects and Methods:
Twenty patients with probable MSA (10 male, 10 female, mean age 60.9 Y, ± 7 SD, 10 MSA-P, 10 MSA-C) and twenty healthy volunteers (9 male, 11 female, mean age 61.2 Y, ± 7 SD) were included. All patients and volunteers provided signed, informed consent. DWI was performed on a Siemens Avanto 1.5T scanner in 12 non-collinear gradient directions using a standard SS-EPI sequence (b=1100; TR=8839 ms, TE=95 ms; NEX=2; 2.2 mm isotropic). Diffusion data were processed offline in FSL and subjected to eddy-current and motion correction, and brain extraction. DTIFit was used to calculate the scalar invariants of the tensor, and FA, MD, axial (AD) and radial (RD) diffusivity maps were generated. Further analysis was carried out in TBSS. The white matter skeleton was thresholded at FA>0.3 and statistical tests were performed using 5,000 permutations. The results were thresholded using Threshold-Free Cluster Enhancement at a p<0.01 level of significance.

Results:
No differences were observed between the MSA-C and MSA-P subgroups. In comparing MSA and health volunteers, the most striking finding was the widespread increase of RD (Fig.1). FA was reduced and MD/RD increased in the superior (SCP), middle (MCP) and inferior cerebellar peduncles (ICP) bilaterally, with changes in RD being more conspicuous. No changes in AD were detected in any infratentorial fibers. Changes in RD were also more widespread supratentorially, being increased throughout the corona radiata (CR) bilaterally, in the body and genu of the corpus callosum (CC), the internal capsule (IC) and external capsule (EC) bilaterally, and in the bilateral frontal white matter (Fig.1). Supratentorially, FA was reduced in the body and genu of the corpus callosum to a lesser extent, the right IC, and the frontal and occipital white matter (Fig.2). No FA changes in the external capsule were seen. Changes in MD followed FA supratentorially, with the addition of changes in the bilateral external capsule, where AD were observed to be increased as well (Fig.3). AD was not significantly changed in other voxels.

Conclusion:
White matter changes in MSA are widespread and not limited to discrete regions. Dramatic changes in RD with nearly unaltered AD support previous studies reporting oligodendrocytes are primarily affected in MSA. Further studies examining white matter changes in diverse regions may extend the utility of DTI in the diagnosis of MSA.

Fig.1: RD=red-yellow
Fig.2: FA=blue-lightblue
Fig.3: AD

References: