Abnormalities of Supratentorial White Matter in Multiple System Atrophy: Diffusion Tensor Imaging Observation

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Background and Purpose

Multiple system atrophy (MSA) is a sporadic neurodegenerative disorder with poor prognosis. Pathological hallmark is accumulation of α-synuclein-positive inclusions in the oligodendroglia of the brain, associated with neuronal loss, reactive gliosis and myelin degeneration. These inclusions are mainly accumulated in the infratentorial compartment, but can also be observed in the supratentorial white matter — including bilateral cerebral white matter subjacent to the motor cortical areas, internal and external capsules[1]. MR imaging of the brain is usually performed in MSA, to non-invasively assess the pathological changes as well as to rule out other differential diagnoses. To date, reported MR imaging findings of the brain in MSA have mostly been limited to atrophy and signal abnormalities of pons, middle cerebellar peduncle, cerebellum and dorsolateral aspect of putamen[2]. Very few have been reported about the abnormalities of supratentorial white matter. Further, clinical significance of these abnormalities are not known.

Diffusion tensor imaging (DTI) is an MR imaging technique, which is capable of depicting the microstructural abnormalities of white matter associated with alterations in diffusion characteristics. It has been reported that DTI can show abnormalities that are not detectable on conventional MR imaging sequences[3]. This study sought to determine if DTI can depict abnormalities of supratentorial white matter in MSA, and evaluated the clinical significance of abnormalities depicted by DTI.

Materials and Methods

This study included 12 patients (5 men and 7 women, mean age = 60.2 ± 5.3 years) with probable MSA (MSA-C with predominant cerebellar symptoms) and 16 age and gender-matched normal healthy subjects. Conventional MR imaging sequences, including T2-weighted imaging, proton density-weighted imaging, T1-weighted imaging and fluid-attenuated inversion recovery imaging were performed for visual analysis. DTI was also performed, and fractional anisotropy (FA) and mean diffusivity (D) maps were generated. FA and D of the patients were compared voxel-by-voxel to those of normal subjects. Overlapped maps were created to distinguish areas with (i) concomitant FA and D alterations, (ii) FA alterations only, and (iii) D alterations only. FA and D alterations of the patients were correlated with overall and individual Barthel index (index to assess activity of daily living) scores, severity of postural hypotension, disease duration and age of disease onset. For statistical analysis, two-sample t-test or Spearman rank correlation analysis or Pearson's product-moment correlation analysis was used, and significance was determined as $p<0.05$.

Results and Discussion

Findings of conventional MR imaging sequences were consistent with the classical findings of MSA-C. Signal abnormalities of supratentorial white matter were not remarkable (limited to rating scale 1or 2 by Wahlund et al[4]).

Figure below illustrates the topography of FA and D alterations observed in the patients. Bilateral cerebellar white matter, superior and middle cerebellar peduncles and pontine brachium revealed concomitant FA decrease and D increase. Bilateral temporal white matter, optic radiation, splenium of corpus callosum, bilateral genu and posterior limbs of internal capsule, dorsal aspect of external capsule and centrum semiovale had alterations confined to FA decrease. Pontine tegmentum and bilateral cerebral peduncles exhibited D increase only. Areas which revealed significant correlation with overall or individual Barthel index scores and/ or severity of orthostatic hypotension are listed in the Table below. No significant correlation was observed between FA and D of these areas and disease duration or age of disease onset.

It is considered that concomitant FA decrease and D increase represent areas with significant neuronal loss or myelin degeneration[1]. Isolated FA decrease may represent neuronal loss or myelin degeneration with accumulation of α-synuclein-positive inclusions or cellular debris which restricts water diffusion[1]. In contrast, isolated D increase may denote a decline in macromolecular synaptic proteins[5]. Significant correlation of FA and D alterations with clinical parameters may suggest that DTI can be a useful tool for severity assessment of the disease.

Conclusion

DTI can demonstrate the microstructural abnormalities of supratentorial white matter, which are associated with limitation in the activity of daily living or severity of orthostatic hypotension, in probable MSA-C. DTI can be a useful imaging tool for severity assessment in MSA-C.

References

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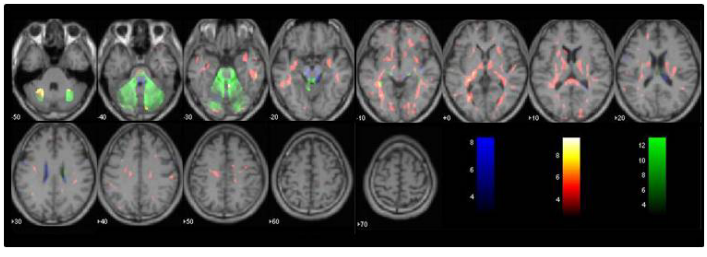
Figure

Topography of FA and D alterations in probable MSA-C patients (FDR-corrected $p<0.05$, cluster size = 200 voxels). Look-up tables represent t-values. Areas with concomitant FA decrease and D increase, areas with isolated FA decrease and areas with isolated D increase are shown in green, red and blue gradations, respectively.



Table

List of areas with FA and D alterations showing correlation with overall or individual Barthel index scores and/ or severity of orthostatic hypotension. FA correlates positively with Barthel index scores. D correlates negatively with Barthel index scores, but positively with severity of orthostatic hypotension. B denotes areas showing correlation with Barthel index scores, and H denotes those with severity of orthostatic hypotension.

FA alteration	D alteration
Cerebellar white matter [B]	Cerebellar white matter [B]
Middle cerebellar peduncle [B]	Middle cerebellar peduncle [B]
Pontine brachium [B]	Superior cerebellar peduncle [B]
Genu of internal capsule [B]	Pontine brachium [B]
Posterior limb of internal capsule [B]	Pontine tegmentum [B H]
Centrum semiovale [B]	Cerebral peduncle [B]