Altered functional connectivity of the motor network in multiple system atrophy

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Backgrounds and Purpose:

Multiple system atrophy (MSA) is mainly a sporadic progressive neurodegenerative disease of unknown etiology. Typical histological findings of MSA are observed in the striatum, substantianigra, olivopontocerebellar pathways, the intermediolateral cell columns of the spinal cord, and the cerebellum. Similar findings have also been described in motor and supplementary motor cortex[1, 2]. The purpose of this study is to test the hypothesis that there is associated disturbance of functional connectivity of the motor cortex in MSA patients.

Subjects and Methods:

Nineteen clinically probable MSA patients[3] (8 with MSA-P subtype and 11 with MSA-C; 16 males and 3 females; mean age =59.3 years) and 11 age- and gender-matched health controls (9 males and 2 females; mean age = 53.8 years) were studied. Eight of the MSA patients had signs of pyramidal tract dysfunction. Each subject underwent resting-state functional magnetic resonance imaging (fMRI) with blood oxygenation level-dependent (BOLD) contrast. All imaging data were collected on a 3T GE Signa Excitell VH/*i* MR scanner, with a protocol consisting of an axial gradient-echo echo-planar sequence sensitive to BOLD contrast (TR=500ms, TE=30ms, flip angle=30°, field of view =24×24cm^2, matrix=64×64, slice thickness=6mm, gap=1mm, volume =960, and scan time=8min), an axial 3D spoiled gradient recalled sequence, an axial 2D T1-weigted sequence to generate the base images for fMRI, as well as other routine sequences. For fMRI, 9 slices were acquired covering the upper part of the brain just inferior to vertex. fMRI data were processed with SPM 5. Preprocessing included slice-timing, realignment and re-slicing with re-sampled 3mm isotropic voxels . A temporal filter (0.01Hz< f <0.08Hz) was applied and any linear trend was removed. A within-subject analysis was performed using the regional homogeneity (ReHo) approach[4] (www.restfmri.net) , producing individual ReHo maps. The 9 2D anatomical images were co-registered to each subject's respective whole brain 3D images. The whole brain anatomical images were segmented and normalized to the template. The resultant segmentation and normalization parameters were then applied to the co-registered functional images. The intracranial voxels for all subjects were extracted to produce a mask, followed by data smoothing using a Gaussian filter of 6mm full width at half maximum. Finally, second-level random-effect two-sample *t* test was applied to compare the ReHo results between the MSA patients and the controls with a threshold correction determined by an AlphaSim program. The threshold was set as a corrected significance level of P<0.01 and clusters with minimum volume of 34 voxels (918mm^3).

Results:

As shown in table 1 and figure 1, significant ReHo decreased in the left precentral gyrus, and increased in the right precuneus, supramarginal gyrus and middle frontal gyrus between the MSA patients and the controls.

Table 1 Regions showing ReHo changes in MSA patients

Brain regions	BA	Volume (mm^3)	Talaraich coordinates			*t* value
			X	Y	Z	
L precentral gyrus	4	1080	-32	-23	56	-3.45
R precuneus and supramarginal gyrus	7	1215	24	-42	54	4.21
	40		9	-51	60	3.05
R middle frontal gyrus	9	999	51	18	30	4.93

L, left; R, right; BA, Brodmann's area.

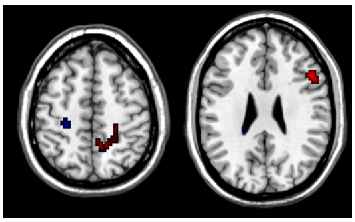

Fig 1 The MSA patients showed significant ReHo changes when compared with the health controls in the left precentral, right precuneus, supramarginal gyrus, and middle frontal gyrus (two-sample *t* test; P < 0.01, corrected). Red and blue colors indicate disease related ReHo increase and decrease, respectively.

Discussion and Conclusions:

Our results showed functional connectivity disturbances of motor-related circuits in the MSA patients, in agreement with the pathological findings[2]. The left-sided dominance of primary motor cortex involvement has also been reported using other methods, which is possibility due to the higher severity of akinesia on the right side for the MSA patients. This finding indicates that resting-state fMRI can be an important tool in imaging studies of MSA and will likely yield valuable information for diagnosis and follow-ups.

References:

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