Brain Grey Matter Changes in Young Patients with Mild Type of Essential Arms Tremor: a Voxel-based Morphometry MRI study

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Introduction: Essential tremor (ET) is common neurological movement disorders and may be related to cerebella dysregulation. Recent research on pathology of ET enhanced the concept that cerebellum plays a major role in ET [1]. Earlier studies examined ET patients using voxel-based morphometry (VBM) by magnetic resonance imaging (MRI) and the results were inconsistent [2-3]. The conflicting results may be due to the different subtypes and phase of ET patient selection. In this study, young patients with kinetic and posture tremor only in arms and hands (a-ET) were recruited to investigate the early stage of this disease, and quantitative morphology was explored by MRI VBM.

Method: In this prospective study, 8 a-ET patients and 8 healthy volunteers were recruited (see Table 1). All patients fulfilled the criteria for the diagnosis of ET as defined by the Consensus Statement of the Movement Disorder Society on Tremor[4]. Each patient was examined using the Washington Heights-Inwood Genetic Study of ET (WHIGET) tremor rating scale to rate the severity of tremor (range=0–3 for each test). This examination included one test of postural tremor and five tests of kinetic tremor (pouring water, drinking water, using spoon, finger to nose maneuver, and drawing spirals) performed with each hand (12 tests total,) And total tremor score range is 0-36 [5]. Only those whose score<30 were included in our study as mild ET [5].Healthy controls were strictly one-to-one matched to the patients in age, gender and education. Both patients and controls were right-handed. All individuals signed written informed consent before participation in the study. MRI data were acquired using a 3.0T GE Signa HDxt scanner with an 8-channel head coil. An axial T_1-weighted 3-dimensional fast spoiled gradient echo sequence (TR/TE=6.6 /2.8 ms, FOV = 256×256 mm^2, acquisition matrix = 256×256, slice thickness=1mm, flip angle=15°) resulted in an isometric resolution of 1×1×1 mm^3. The morphological changes of the gray matter were analyzed using VBM technique implemented by FSL (version 4.1). A two-sample t-test was applied through the general linear model and for TFCE based analysis ($p_{\text{uncorrected}}$ <0.01) .

Table 1 Summary of group characteristics

	ET Patients(n=8)	Control(n=8)	Two-sample *t*-test	
	Mean (SD)	Mean (SD)	t-values	p-values
Age(y)	32.88 (5.74)	34.38 (6.55)	-0.49	0.45
Education(y)	12.88 (2.80)	15.38 (4.97)	1.08	0.32
Sex, F/M	2:6	2:6		
Onset Age (y)	16.63(6.09)	-		
ET Time (y)	16.13 (8.03)	-		
Tremor Score	15.13 (4.79)	-		

Result: All patients were with arms and/or hands tremor and without intention tremor. The symptoms were symmetrical. With respect to 8 healthy controls, mild a-ET patients showed the decrease of GM density in bilateral parietal lobes and right temporal lobe ($p_{\text{uncorrected}}$ <0.01). On the contrary, the bilateral grey metter expansions in cerebellum, occipital lobe and temporal occipital fusiform cortex were seen in Fig.1.

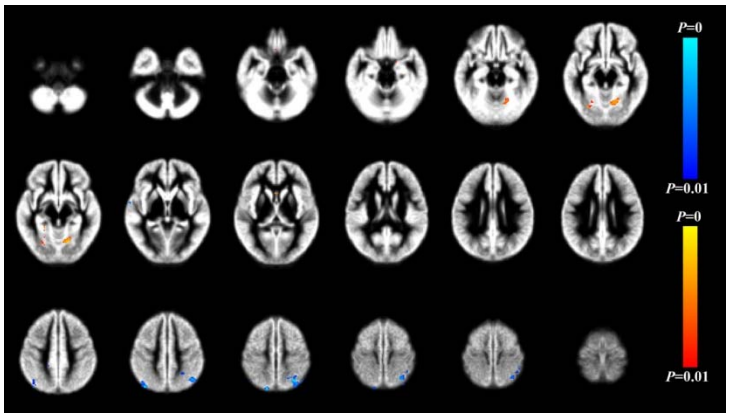

Fig. 1 Areas changes of grey matter in mild a-ET patients compared to controls. The red color showed expansion while blue color showed decrease in morphology. ($p_{\text{uncorrected}}$ <0.01)

Discussion and conclusion: Previous studies including pathology and neuroimaging studies reported atrophy of cerebellum and Purkinje cell loss in old, severe and/or head ET patients [1-3]. In this study, VBM method was used to detect the morphological change of mild a-ET patients. But there was no decrease of volume in cerebellar grey matter in our study. On the contrary, some expansion areas in grey matter related to higher order visuospatial processing were found. The cerebellum has been considered as a neural organ specialized in the regulation of somatic motor function and anterior cerebellum represented the upper limbs [6]. All a-ET patients recruited in this study had arms and/or hands tremor. In order to coordinate the corresponding movement in the a-ET, the function of cerebellum has to be enhanced to fulfill the precise action when arms and/or hands tremor occurred. The atrophy of grey matter in bilateral posterior parietal lobe might represent the diminished capacity of spatial erientation and proprioceptive sensibility in a-ET patients [7]. Moreover, mild a-ET patients show a relative expansion of grey matter areas involved in higher order visuospatial processing, which might represent the adaptive reorganizational compensation through increased demands on the visuospatial control of skilled movements in the early stage of a-ET. These findings may be closely associated with the network changes of cerebelo-thalamo-cortical loop in mild a-ET and morphological changes might help to understand and assess early stage and distinguish subtype of ET.

Reference:

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