Disruption of natural motion perception in dystonia patients with DYT1 mutation

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Introduction

Dystonia is characterized by the involuntary concomitant contraction of agonist and antagonist muscles resulting in repetitive movements and abnormal posture. Some dystonia patients have a causative gene mutation in TOR1A gene which is known as DYT1 [1]. There are other known gene mutations in dystonia. Despite of the gene mutations, no apparent structural abnormalities of primary dystonia were found in conventional magnetic resonance imaging (MRI) or autopsy [2]. Nonetheless, novel abnormalities were detected by functional imaging including positron emission tomography (PET) and diffusion tensor imaging (DTI) [3]. We used a speed-dependent motion perception fMRI task to discover movement processing abnormalities in the brains of dystonia patients. The task consists of displaying natural and unnatural motion [4] of a ball over an elliptic trajectory. The subjects just observe the movement of the ball, but do not move themselves.

Subjects and Methods

We studied 10 healthy controls (7M, 3W, 42.3 ± 9.0 yrs old) and 10 dystonia patients with symptoms, carrying DYT1 mutation (4M, 6W, age 43.5 ± 17.7 yrs old). Images were acquired in a 3T GE whole-body MR scanner with an eight-channel head coil. The fMRI protocol included FOV of 240 mm, 40 slices with 3 mm thickness, imaging matrix of 64 × 64, flip angle 77 degrees, TR of 2 sec, TE of 27.2 ms and scan time 320 sec. A high resolution T1-weighted structural image was also acquired for each subject with resolution of 0.9 × 0.9 × 1 mm^3. The T1-weighted structural image protocol included FOV of 240 mm, 176 slices with 1 mm thickness, imaging matrix of 256 × 256, flip angle 8 degrees, TR of 7.6 ms, TE of 2.9 ms, TI of 650ms. Image pre-processing, first- and second-level analyses were performed using FEAT in FMRIB software [5]. The activation map was created for each individual according to general linear model (GLM) in first-level analysis. Second-level analysis was conducted through the results of first-level analysis. Comparison of each condition were analyzed at the threshold of corrected voxel P = 0.01 with an extent threshold of 100 voxels according to GRF-theory-based maximum height threshold. The concept of task employed in this study was summarized in Figure 1.

Results

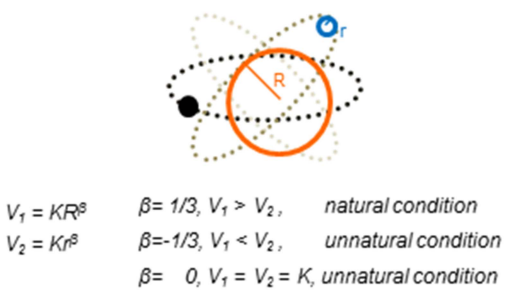

Figure 1: A black ball moves on the elliptic trajectory. The speed of the ball is governed by $V = KR^\beta$, where K is a constant, and the instantaneous velocity V depends on the radius of the curvature R of the trajectory. $\beta = 1/3$ always produces faster speed in almost straight path than curved path, which interpreted as natural motion. In contrast, other two conditions provide unnatural motion.

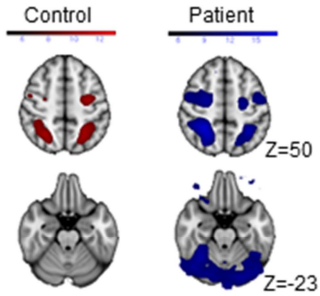

Figure 2: Activation map of controls and patients during observing an unnatural motion of the ball. Patients have more activated regions in primary motor cortex, premotor cortex and cerebellum than controls. This finding might indicate a loss of inhibition in dystonia patients during motion processing. The color scale represents Z-values thresholded at 4.78 (P=0.01, corrected).

Significant brain activation during observing unnatural motion was present in primary motor cortex (M1) and premotor cortex (PMC) in both groups (Figure 2). The range of increased area in M1 and PMC in patients, however, was larger than controls. Additionally, only the patients showed activation in cerebellum which is important in motor control. These results suggest that inappropriate and excessive brain activity associated with patients carrying DYT1 mutation and manifesting dystonia.

Discussion/Conclusions

We investigated the extent of neural activity of dystonia patients even during motion perception without actual limb movement relative to controls using fMRI motion perception task. Excessive activations were observed in M1, PMC and cerebellum under unnatural motion. Our results support the notion that hyper-activation of cerebellum in dystonia is involved in the disease, and could lead to novel method of diagnosis and treatment strategy [3].

Acknowledgments

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