

Dystonia in Machado-Joseph disease: clinical profile, therapeutic response and anatomical substrate

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Abstract

Dystonia is a classical feature of Machado-Joseph disease, but its anatomical substrate and responsiveness to levodopa/botulinum toxin (BT) are still unclear. We have thus evaluated clinically and through MRI scans a cohort of 75 patients (21 with dystonia) to address these questions. We found in a single blind trial that dystonia is not levodopa responsive, but improves on BT. Furthermore, dystonia is associated with thalamic and precentral atrophy in the disease.

Key words: dystonia, Machado-Joseph, MRI

Introduction

Dystonia is frequent in Machado-Joseph disease, but several important aspects are not yet defined.

Objective: To determine the clinical profile, response to treatment and anatomical substrate of dystonia in Machado-Joseph disease.

Results and Discussion

Methods: We screened 75 consecutive patients and identified those with dystonia (dMJD/SCA3). The Burke-Marsden-Fahn scale was employed to quantify dystonia severity. Patients with dystonia received levodopa 600mg/day for 2 months and were videotaped before and after treatment. A blinded evaluator rated dystonia in the videos. Patients with disabling dystonia who failed levodopa treatment received botulinum toxin. Finally, volumetric T1 and diffusion tensor imaging sequences were obtained on 3T-MRI scanner to identify areas of gray and white matter that were selectively damaged in the dystonic group.

Results: There were 21 patients with dystonia (28%): 9 with generalized and 12 with focal/segmental presentations. Dystonic Patients had earlier onset and larger (CAG) expansions (28.9 ± 11.7 vs 40.6 ± 11.4 ; $p < 0.001$ and 75 vs 70 ; $p < 0.001$, respectively). Levodopa therapy fell short of reaching statistical significance towards improvement ($p = 0.07$). In addition, ten patients received botulinum toxin resulting in significant change in dystonia scores after 4 weeks ($p = 0.03$). Patients with dystonia had atrophy at pre and paracentral cortices; whereas, non-dystonic patients had essentially occipital atrophy. Basal ganglia volume was reduced in both groups, but atrophy at the thalami, cerebellar white matter and ventral diencephali was disproportionately higher in the dystonic group.

Structure	dMJD/SCA3 mean (mm)	Control mean (mm)
Left Hemisphere		
Paracentral Lobule and Sulcus	1.977±0.187	2.148±0.120
PrecentralGyrus	2.417±0.177	2.613±0.206
Temporal Superior Sulcus	2.163±0.180	2.331±0.125
ParacentralCortex	2.049±0.178	2.252±0.141
PrecentralCortex	2.221±0.138	2.380±0.142
SupramarginalCortex	2.285±0.160	2.352±0.160
Right Hemisphere		
ParacentralLobuleandSulcus	1.957±0.183	2.146±0.139
Triangular Part of the Inferior Frontal Gyrus	2.316±0.232	2.527±0.175
PrecentralGyrus	2.374±0.272	2.596±0.288
ParacentralCortex	2.074±0.176	2.263±0.152
PrecentralCortex	2.188±0.192	2.379±0.189

Table 1. Areas with cortical thinning in patients with dMJD/SCA3 compared with matched healthy controls (level of significance 0.001).

Conclusions

Dystonia in Machado-Joseph disease is frequent and often disabling, but may respond to levodopa replacement. It is associated predominantly with structural abnormalities around the motor cortices and in the thalami.

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