Primary dystonia

Primary dystonia is a neurological disease with the characteristics of abnormal, involuntary twisting and turning movements, which greatly affects the life quality of patients.

Primary dystonia is suspected when the dystonia is the only sign and there is no identifiable cause or structural abnormality in the central nervous system.

Etiology

Primary Dystonia Etiology.

Pathophysiology

The dystonia pathophysiology is poorly understood. As opposed to secondary forms of dystonia, primary dystonia has long been believed to lack any neuroanatomical substrate. During trajectory planning for DBS, however, conspicuous T2-hyperintense signal alterations (SA) were registered within the target region, even in young patients, where ischemia is rare.

Fifty MRIs of primary dystonia patients scheduled for DBS were analyzed. Total basal ganglia (BG) volumes, as well as proportionate SA volumes, were measured and compared to 50 age-matched control patients.

There was a 10-fold preponderance of percentaged SA within the globus pallidus (GP) in dystonia patients. The greatest disparity was in young patients <25 years. Also, total BG volume differences were observed with larger GP and markedly smaller putamen and caudate in the dystonia group.

BG morphology in primary dystonia differed from a control population. Volume reductions of the putamen and caudate may reflect functional degeneration, while volume increases of the GP may indicate overactivity. T2-hyperintensive SA in the GP of young primary dystonia patients, where microvascular lesions are highly unlikely, are striking. Their pathogenic role remains unclear [1].

Treatment

Pallidal Deep Brain Stimulation is the primary surgical treatment for dystonia [2]. The response is better for primary dystonias, e.g. tardive dystonias than for secondary dystonias such as postanoxic, postencephalitic, perinatal, and post-stroke dystonia [3] (other targets need to be assessed). For primary dystonias, the globus pallidus internus (GPi) is the most common primary target. Good results have also been reported with STN DBS. Dyskinetic cerebral palsy in children may also be treated with pallidal stimulation [4].

Treatments for dystonia consist of oral medications, botulinum neurotoxin injections, physical therapy

and surgeries. For medication-refractory dystonia, surgeries, especially deep brain stimulation (DBS), are the optimal option.

Treatment response is better for primary dystonias than for secondary dystonias. [5].

Case series

A strategy based on targeted gene panel sequencing identifies possibly pathogenic variants in fewer than 20% of cases in the early-onset and familial form of dystonia. By using Whole Exome Sequencing (WES), Wirth et al. aimed to identify the missing genetic causes in dystonic patients without a diagnosis despite gene panel sequencing.

WES was applied to DNA samples from 32 patients with early-onset or familial dystonia investigated by sequencing of a 127 movement disorders-associated gene panel. Dystonia was described according to the familial history, body distribution, evolution pattern, age of onset, associated symptoms and associated movement disorders. Rate of diagnoses was evaluated for each clinical feature.

They identified causative variants for 11 patients from 9 families in CTNNB1, SUCLG1, NUS1, CNTNAP1, KCNB1, RELN, GNAO1, HIBCH, ADCK3 genes, yielding an overall diagnostic rate of 34.4%. Diagnostic yield was higher in complex dystonia compared to non-complex dystonia (66.7%-5.9%; $p < 0.002$), especially in patients showing intellectual disability compared to the patients without intellectual disability (87.5%-16.7%; $p < 0.002$).

This approach suggests WES as an efficient tool to improve the diagnostic yield after gene panel sequencing in dystonia. Larger study are warranted to confirm a potential genetic overlap between neurodevelopmental diseases and dystonia [6].

Case reports

A 13-year-old boy suffering from extremely severe primary dystonia, with a BFMDRS-M score of 118 and a TWSTRS-S score of 29. The examination of 173 genes including DYT failed to identify any abnormality. He responded ineffectively to medications. After both bilateral subthalamic nucleus DBS and unilateral Vim-Vo thalamotomy (combined thalamic lesion in ventralis intermedius nucleus and ventralis oralis nucleus), his movement disorder improved dramatically. Four months and seven months after the operation, the scores of two rating scales sharply decreased. And potential brain structural changes were reflected in sensorimotor-related cortical thickness, surface area and gray matter volume from MRI, which revealed a valid method to evaluate surgical effect on the brain with enough patients.

DBS and thalamotomy is potentially an effective combination of treatments for severe medication-refractory dystonia [7].

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