Nonmotor Symptoms in Dystonia: Pathophysiological Implications

Dystonia is a hyperkinetic movement disorder characterized by involuntary muscle contractions leading to twisting movements and abnormal posturing. This motor definition of dystonia is commonly used. However, recently increasing evidence has suggested that dystonia patients may have a series of nonmotor symptoms. In this issue of the journal, Ray *et al.* have reviewed the nonmotor symptoms in cervical dystonia patients, which included anxiety, depression, and sleep-related problems.[1]

Nonmotor symptoms help us in understanding the pathogenesis of dystonia. Subtle sensory symptoms such as throat irritation before spasmodic dysphonia, grittiness of the eyes before blepharospasm, and discomfort in the neck before developing cervical dystonia have been duly noted months before the onset of dystonia. This disease-related pain is more commonly seen in patients with cervical dystonia than other types of focal dystonia such as writer's cramp.[2] Positive correlation with significant anxiety unrelated to motor symptoms is unsupported, but the risk of recurrent major depression has been hypothesized to be an independent expression of the *DYT1* gene.[3] In addition, a family history of depression has been noted in these patients.[4] Obsessive-compulsive traits are frequently seen in DYT11 families.[5] Minimal or no impairment in cognition is reported attributable to dystonia.[6] Impaired sleep efficiency unrelated to the motor symptoms has been reported, but later it was shown to better correlate with depression and not to dystonia *per se*.[7]

Pathophysiologically, under-functioning of the normal inhibitory mechanisms of the motor and sensory networks, increased pathological neuroplasticity, decreased expression of GABA-A receptors, genetic predisposition toward functional and neurochemical imbalance of the basal ganglia along with other factors such as trauma, stress, emotional arousal, and repetitive activity have all been implicated for the development of these concomitant nonmotor symptoms in dystonia.[8] Research shows that there is a loss of topographical specificity of paired associative stimulation-induced effects that normalize after botulinum toxin and improve on Braille and transcutaneous electrical nerve stimulation, thus confirming the role of afferent input in the generation of these responses.[9] Latest voxel-based neuroimaging indicates the increased volume in the putamen, sensorimotor cortex, cerebellum, and thalamus in sporadic dystonia.[10] Diffusion tensor imaging shows increased fractional anisotropy in the fiber tracts connecting the basal ganglia, cortex, and cerebellum.[10] As an overview, the cortico-striatal-thalamic-cortical circuit seems to be most obviously involved in these cases. Nevertheless, as it is seen with almost all pathways of the human brain, this frontostriatal circuit is interconnected with the circuits that are related to sleep, cognition, perception, reward processing, and other neuropsychiatric domains.

Depression, anxiety, and pain seem to be the most common nonmotor deterrents in dystonia.[11] This highlights the importance of identification and amelioration of these very pertinent complaints along with addressing the overt motor discomfort in order to treat dystonia as a multicomponent disorder similar to Parkinson's disease for better patient satisfaction. Unfortunately, these symptoms have not yet received a necessary amount of attention, particularly in a glaringly motor disorder such as dystonia. Due to the significant impairment of the quality of life, these complaints demand respect, consideration, and development of in-depth objective assessment scales to enhance overall treatment outcomes.

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