

Idiopathic cervical dystonia and autonomic nervous system: expanding the non-motor symptoms list?

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Background: Non-motor symptoms in idiopathic cervical dystonia(ICD) [1] (e.g. neuropsychiatric symptoms, sleep disturbances, fatigue, cognitive impairment, sexual dysfunction, sensory abnormalities) have been widely reported. The autonomic nervous system (ANS) involvement is still poorly understood [2-3].

Objects: To investigate ANS functions by clinical and neurophysiological assessment in idiopathic cervical dystonia.

Methods: 20 ICD patients and 20 controls were enrolled to investigate ortosympathetic and parasympathetic functions by clinical and neurophysiological assessment. The Composite-Autonomic-System-Scale-31/COMPASS-31 was used to clinically assess the ANS functions. The laser doppler flowmetry quantitative spectral analysis, recorded from the indexes skin, was used to measure at rest, after parasympathetic (six deep breathing) and sympathetic (isometric handgrip and mental arithmetic calculation) activation, the power of high-frequency and low-frequency oscillations and the low-frequency/high-frequency ratio.

Results: ICD patients featured more often autonomic symptoms at COMPASS-31($p < 0.05$, 86%), mainly orthostatic intolerance (35%) and gastrointestinal manifestation (55%) compared to controls. At rest, lower high-frequency powerband was detected among cases, statistically significant in the subgroup of age³60-year-old ($p < 0.05$; 11.25 right and 10.2 left; 71% right, 86% left). The latter group showed lower low-frequency/high-frequency ratio than in the same age control subgroup at rest ($p < 0.05$; 0,64 right and 0,29 left; 86% right and left) and after mental calculation ($p < 0.05$; 1,18 right, 1,25 left; 100% right, 86% left). Cases showed lower ratio during handgrip than controls ($p < 0.05$; 1,64; 80%), and a similar increase of the low-frequency oscillatory component was observed in both groups. By contrast, high-frequency component remained unchanged among cases and decreased in controls. No differences between the two groups were detected during deep breathing, featuring a significant increase in high-frequency oscillations.

Conclusion: The present study detected ANS dysfunction in ICD patients at clinical and neurophysiologic levels. Abnormal parasympathetic-sympathetic interaction might be hypothesised. Low gamma-aminobutyric acid (GABA) concentration in ICD1 might contribute to ANS dysfunction. Indeed, in rats, injection of GABA-agonist increased sympathetic nerve activity [4-5]; in humans, low GABA levels lead to abnormal vagal efference [6].

References:

- [1] Stamelou M, Edwards MJ, Hallett M, Bhatia KP. The non-motor syndrome of primary dystonia: clinical and pathophysiological implications. *Brain*. 2012 Jun;135(Pt 6):1668-81. doi: 10.1093/brain/awr224.
- [2] Tiple D, Strano S, Colosimo C, Fabbrini G, Calcagnini G, Prencipe M, Berardelli A. Autonomic cardiovascular function and baroreflex sensitivity in patients with cervical dystonia receiving treatment with botulinum toxin type A. *J Neurol*. 2008 Jun;255(6):843-7. doi: 10.1007/s00415-008-0753-6.
- [3] Hentschel F, Dressler D, Abele M, Paus S. Impaired heart rate variability in cervical dystonia is associated to depression. *J Neural Transm (Vienna)*. 2017 Feb;124(2):245-251. doi: 10.1007/s00702-016-1639-x.

- [4] Osborne PG, Kurosawa M. Perfusion of the preoptic area with muscimol or prostaglandin E2 stimulates cardiovascular function in anesthetized rats. *J Auton Nerv Syst.* 1994 Mar;46(3):199-205. doi: 10.1016/0165-1838(94)90037-x.
- [5] Tanaka M, McKinley MJ, McAllen RM. Roles of two preoptic cell groups in tonic and febrile control of rat tail sympathetic fibers. *Am J Physiol Regul Integr Comp Physiol.* 2009 Apr;296(4): R1248-57. doi: 10.1152/ajpregu.91010.2008.
- [6] McMenamin CA, Travagli RA, Browning KN. Inhibitory neurotransmission regulates vagal efferent activity and gastric motility. *Exp Biol Med (Maywood).* 2016 Jun;241(12):1343-50. doi: 10.1177/1535370216654228.