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Orthostatic hypotension in Parkinson's disease: is there a role for the locus coeruleus?

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Introduction: Orthostatic hypotension (OH) is a common and debilitating non-motor symptom in Parkinson's disease (PD) but the mechanisms underlying its development remain largely elusive. Peripheral and central noradrenergic denervation are both likely to play a key role[1]. Locus coeruleus (LC) is the main noradrenergic nucleus of the brain and its early degeneration in PD has been put in relation with a variety of non-motor symptoms, including OH, but with inconsistent results[2-4].

Objective: To test whether degeneration of the LC is associated with OH in PD.

Methods: A total of 21 cognitively intact PD patients and 52 age matched healthy volunteers (HC) underwent 3T magnetic resonance (MRI) with specific neuromelanin-sensitive FSE T1-weighted sequences for LC. For each subject, a template space-based LC-MRI was used to calculate LC signal intensity (LC ratio) and the estimated number of voxels (nVOX) belonging to LC[5,6]. In a case-control study we compared the two MRI-LC parameters in 11 PD patients with OH (OH+) versus 10 without OH (OH-) (matched for sex, age and disease duration) using Kruskal Wallis test. We also tested for correlations between subject's LC-MRI parameters and orthostatic drop in systolic blood pressure.

Results: PD with and without OH did not differ significantly based on demographics and clinical characteristics (LEDD, UPDRS-III, MoCA, HAM-A, HDRS, RBD and SCOPA-AUT scales), except for blood pressure measurements. Both LC ratio and nVOX were significantly lower in PD compared to HC, while no differences were observed between PD OH+ and PD OH-. Additionally, no correlation was found between the MRI-LC parameters and the orthostatic drop in systolic blood pressure or the clinical severity of autonomic symptoms (SCOPA-AUT score).

Conclusions: Our results failed to indicate that the LC MRI parameters were associated with the presence of OH in PD but confirmed a marked alteration of LC signal in PD patients.

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