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Hypothalamic involvement in multiple system atrophy: a structural MRI study

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Introduction: MSA is characterized by autonomic dysfunction and cerebellar/parkinsonian manifestations. The hypothalamus regulates autonomic and homeostatic functions and may also be involved in memory and learning. Pathological studies have identified hypothalamic neuronal loss and alpha synuclein glial and neuronal inclusions in MSA [1,2,3,4,5].

Objective: To investigate hypothalamic atrophy and its clinical correlates in multiple system atrophy (MSA) through MRI.

Methods: 11 MSA, 18 Parkinson's disease (PD) and 18 Healthy Controls (HC) were included. T1-weighted images were acquired on a 3T-MRI scanner. Images were pre-processed prior to applying a previously validated automated hypothalamic segmentation tool (https://github.com/BBillot/hypothalamus_seg). Whole hypothalamus volumes and 5 subregions were generated and adjusted for total intracranial volume. Hypothalamic volumes in MSA were compared with HC and PD volumes. Associations with clinical scales of autonomic dysfunction, depression, sleep problems and cognitive function were also tested.

Results: Age and sex were not different across groups. Total hypothalamus showed a trend towards a significant reduction in MSA vs HC ($t=1.937$, $p=0.065$) and posterior hypothalamus was significantly lower in MSA ($t=2.578$, $p=0.016$). A trend toward reduced posterior hypothalamus was also found in MSA compared to PD ($t=1.768$, $p=0.088$). Total hypothalamus volume was not associated with age or disease duration. In the parkinsonism (MSA+PD) group, total hypothalamus volume was associated with MoCA scores ($rho=0.425$, $p=0.022$), but not with autonomic (SCOPA-AUT), sleep (SCOPA-SLEEP), or depression (HADS-D) scores. Among hypothalamic subregions, only posterior hypothalamus volume was associated with MoCA scores ($rho=0.718$, $p<0.001$).

Conclusions: Total hypothalamus and posterior hypothalamus volumes are reduced in MSA compared with HCs. General cognitive functioning scores are associated with total hypothalamus and posterior hypothalamus volumes. The posterior hypothalamus volume includes the mammillary bodies and the lateral hypothalamus, regions associated with memory and learning functions. Further studies are needed to characterize the central correlates of autonomic dysfunction in MSA.

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