## **REM sleep behaviour disorder**

REM sleep behaviour disorder (RBD) occurs frequently in patients with synucleinopathies such as Parkinson's disease, dementia with Lewy bodies, or multiple system atrophy, but may also occur as a prodromal stage of those diseases; and is termed idiopathic RBD (iRBD) when not accompanied by other symptoms. Cholinergic degeneration of the mesopontine nuclei have been described in synucleinopathies with or without RBD, but this has not yet been explored in iRBD. We sought to assess cholinergic neuronal integrity in iRBD using PET neuroimaging with the 18Ffluoroethoxybenzovesamicol (FEOBV).

METHODS: The sample included 10 participants evenly divided between healthy subjects and patients with iRBD. Polysomnography and PET imaging with FEOBV were performed in all participants. Standardized uptake value ratios (SUVRs) were compared between the two groups using voxel wise t-tests. Non-parametric correlations were also computed in patients with iRBD between FEOBV uptake and muscle tonic and phasic activity during REM sleep.

RESULTS: Compared with healthy participants, significantly higher FEOBV uptakes were observed in patients with iRBD. The largest differences were observed in specific brainstem areas corresponding to the bulbar reticular formation, pontine coeruleus/subcoeruleus complex, tegmental periacqueductal grey, and mesopontine cholinergic nuclei. FEOBV uptake in iRBD was also higher than in controls in the ventromedial area of the thalamus, deep cerebellar nuclei, and some cortical territories (including the paracentral lobule, anterior cingulate, and orbitofrontal cortex). Significant correlation was found between muscle activity during REM sleep, and SUVR increases in both the mesopontine area and paracentral cortex.

CONCLUSION: We showed here for the first time the brain cholinergic alterations in patients with iRBD. As opposed to the cholinergic depletion described previously in RBD associated with clinical Parkinson's disease, increased cholinergic innervation was found in multiple areas in iRBD. The most significant changes were observed in brainstem areas containing structures involved in the promotion of REM sleep and muscle atonia. This suggests that iRBD might be a clinical condition in which compensatory cholinergic upregulation in those areas occurs in association with the initial phases of a neurodegenerative process leading to a clinically observable synucleinopathy <sup>1)</sup>.

## 1)

Bedard MA, Aghourian M, Legault-Denis C, Postuma RB, Soucy JP, Gagnon JF, Pelletier A, Montplaisir J. Brain cholinergic alterations in idiopathic REM sleep behaviour disorder: a PET imaging study with (18)F-FEOBV. Sleep Med. 2019 Jan 6;58:35-41. doi: 10.1016/j.sleep.2018.12.020. [Epub ahead of print] PubMed PMID: 31078078.

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