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Investigation of alpha-synuclein post-translational modifications in idiopathic Parkinson's disease and multiple system atrophy

Introduction: Aggregated alpha-synuclein (a-syn) is a key component of Lewy bodies (LBs) and Lewy neurites (LNs) which are the defining pathological hallmarks of Parkinson's disease (PD). The pathological filamentous oligodendroglial inclusions in multiple system atrophy (MSA) also contain aggregated a-syn. A-syn can exist in several forms from monomers to oligomers to fibrils and can also be post-translationally modified including nitration and phosphorylation. Herein we aimed to investigate the different a-syn species in PD and MSA cellular inclusions.

Material and methods: Formalin fixed human brain tissue from 15 PD, 5 MSA and 5 neurologically normal controls were obtained from the archives of Queen Square Brain Bank. Using routine protocols immunohistochemistry was performed with 4 a-syn antibodies, three of which were specific for different post-translational modifications namely, phosphorylation (Ser129 and Ser87-residues) and nitration (Tyr39-residue) in 8 different brain regions.

Results: All the a-syn antibodies recognised LBs and LNs in PD. Phospho-Ser129 and nitrated a-syn antibodies also highlighted thin neurites and dot-like structures. Phospho-Ser87a-syn was present in fewer LBs and LNs. Glial cytoplasmic inclusions (GCIs) were the dominant pathological structure recognised in MSA cases.

Conclusion: Both nitrated and phosphorylated forms of a-syn are present in pathological inclusions in PD and MSA. Phospho-Ser129a-syn highlights thin LNs and dot –like structures in addition to classical Lewy bodies. This may indicate differential phosphorylation of a-syn in different pathological inclusions in PD.