TEMPORAL CORTICAL PHOSPHORYLATED A-SYNUCLEIN CONCENTRATION USEFUL FOR PREDICTING EARLY STAGES IN LEWY BODY DISORDERS


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Introduction: We have developed a Unified Lewy Body (LB) Staging scheme to characterize a variety of LB disorders, based on abundance of LB pathology in various anatomical regions. We demonstrated that LB staging correlates with clinical progression in Parkinson's disease (PD) and Dementia with Lewy Bodies (DLB).

Aims: This study was to biochemically quantify S129P α-synuclein (α-syn) concentration at different LB stages and to determine whether S129P α-syn concentration increases in the absence of histological evidence of LB pathology.

Methods: S129P α-syn concentrations were measured by immunoblotting in the brain regions affected at stages 2 (cingulate cortex) or 3 (temporal cortex) in 140 cases encompassing LB stages 0 to 4 and being clinically diagnosed as non-demented controls, PD with or without dementia, Alzheimer's disease with LB and DLB.

Results: Comparing the amounts of S129P α-syn and total α-syn, and their ratio by Unified LB stages, stage 4 was distinguished from the other stages by drastic increases in the amounts of S129P-α-syn and its ratio to t-α-syn: increased by 1.4 fold from Stage 3 to Stage 4 in cingulate and 1.2 fold in temporal cortex. The ratios increased by 1.5 fold from Stage 3 to Stage 4 in cingulate and increase 3 fold in temporal cortex. Statistical analysis indicated the potentials for such measure to predict anatomical progression of LB pathology.

Conclusion: Our results support that increasing α-syn phosphorylation is an early event preceding the detection of LB pathology; and could be a potential target for intervention (Support from MJFox Foundation).