A NOVEL ELISA IMMUNOASSAY FOR THE DETECTION OF N-TERMINAL ?-SYNUCLEIN IN CSF OF PATIENTS WITH DIFFERENT SYNUCLEINOPATHIES (0800)

Topic
Theme C: ?-Synucleinopathies

Authors
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Aims
Alpha-synuclein (?-Syn) is the hallmark protein in Parkinson disease (PD), PD with dementia (PDD), Dementia with Lewy bodies (DLB) and Multiple System Atrophy (MSA) collectively called “synucleinopathies”. The clinical use of measuring ?-Syn into CSF as a diagnostic biomarker for these disorders is limited so far, due to significant overlap. However, most relevant studies, use immunoassay methods targeting the C-terminal ?-Syn. We developed a novel immunoassay targeting N-terminal region and explored the clinical performance in a cohort of patients with different synucleinopathies vs. controls.

Methods
A novel prototype N-terminal ?-Syn ELISA was used using monoclonal antibody (mAb) 16A6 (aa 1-60; detector) and mAb 24G6 (aa 91-110; capture). The C-terminal ?-synuclein fragment was additionally measured using the commercial Euroimmun ?-Syn ELISA (Cat#EQ6545-9601-L). A total of 52 CSF samples (13 PD, 6 PDD, 10 DLB, 12 MSA and 11 control subjects) were included in the study.

Results
The detection range of the novel N-terminal ?-Syn ELISA was between 25 and 400 pg/mL, while the inter-run precision was between 1.1 and 3.1%. The assay is specific for ?-Syn, without cross-reactivity with ? or ? synuclein up to a concentration of 10^4 pg/mL. All clinical samples were detected within the measuring range as shown in the Figure. Statistical significant difference was found for the PDD (p=0.0416) and marginal for DLB (p=0.0656) groups compared to controls, while this was not evident with the commercial ELISA.

Conclusions
N-terminal ?-synuclein measured into CSF may be a promising potential biomarker for synucleinpathies. Further confirmation is needed.

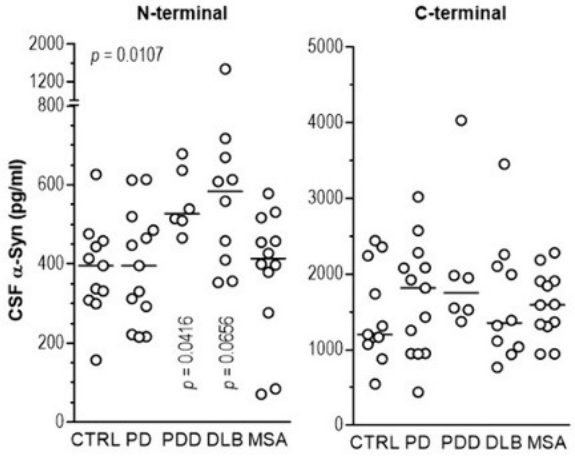
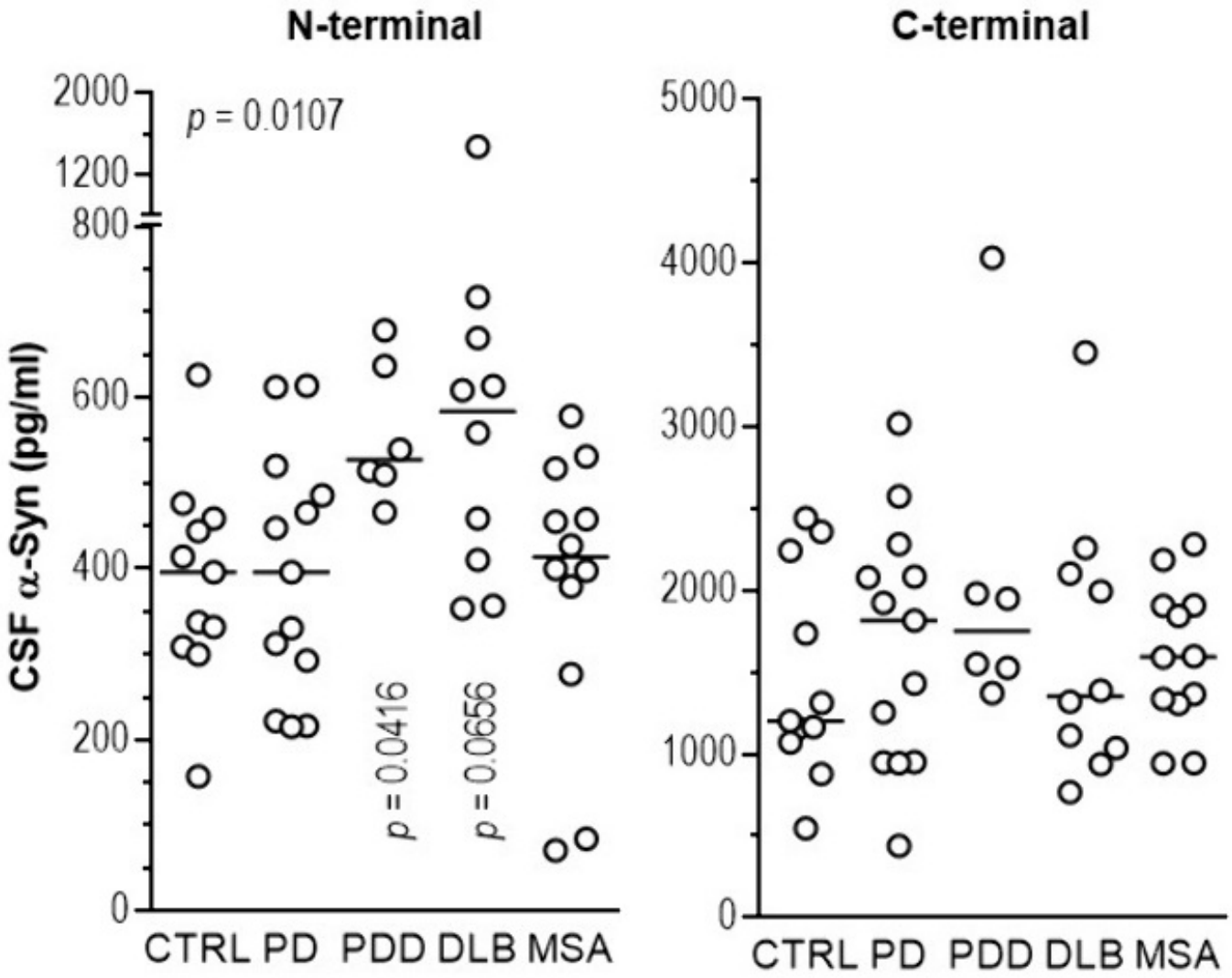


Figure: Scatterplot of CSF α-Syn levels in the studied groups, measured by the two ELISAs. Significant results were observed only in measurements performed by the N-terminal ELISA. The horizontally placed p value is the result of the Kruskal-Wallis test. The vertically placed p values are the results of Dunn's post-hoc tests for comparison between patient groups and controls (CTRL) (significant 0.0416 for PDD vs CTRL and marginally significant 0.0656 for DLB vs CTRL; all others non-significant)



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