P45

Oligomeric α-Synuclein and SNARE complex proteins in peripheral neural-derived extravesicles (NDEs) differentiate Parkinson's disease from healthy controls

Mario Meloni[1], C. Agliardi[1], F.R. Guerini[1], M. Zanzottera[1], F.L. Saibene[1], A.V. Milner[1], J. Navarro[1], M. Clerici[1,2]

[1]IRCCS Fondazione Don Carlo Gnocchi ONLUS, Milan, Italy
[2]Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

Introduction: Blood-based biomarkers are needed to be used as easy, reproducible, and non-invasive tools for the diagnosis and prognosis of chronic neurodegenerative disorders including Parkinson's Disease (PD). In PD, aggregated toxic forms of α-Synuclein (α-Syn) accumulate within neurons in the brain and cause neurodegeneration; α-Syn interaction with SNARE proteins also results in synaptic disfunction [1].

Objective: The objective of this study was to measure oligomeric α-Syn and presinaptic SNARE complex proteins (STX-1A; VAMP-2 and SNAP-25) levels in peripheral neural derived extravesicles (NDEs) in a group of PD patients and sex- and age-matched healthy controls (HC).

Methods: NDEs were isolated from peripheral serum samples of 32 PD patients and 40 HC by immunocapture with L1CAM antibody. Oligomeric α-Syn, SNAP-25, VAMP-2 and STX-1A levels were measured in NDEs protein extracts by sandwich enzyme-linked immunosorbent assay (ELISA).

Results: Oligomeric α-Syn was significantly augmented whereas STX-1A and VAMP-2 were significantly reduced in NDEs of PD patients compared to HC ($p < 0.001$ in all cases). ROC curve analyses confirmed the discriminatory ability of NDEs oligomeric α-Syn, STX-1A and VAMP-2 levels to distinguish between PD patients and HC. Oligomeric α-Syn NDEs concentration also positively correlated with disease duration and severity of PD.

Conclusions: These results are promising and confirm that NDEs cargoes likely reflect core pathogenic intracellular processes in their originating brain cells and could serve as novel easily accessible biomarkers. Further studies are needed to confirm these results and eventually for testing drug treatments and rehabilitation programs.

References

[1] Bong-Kyu Choi et al. Proc Natl Acad Sci U S A. 2013 Mar 5; 110(10): 4087–4092.