DETECTION OF A-SYNUCLEIN AGGREGATES BY FLUORESCENCE MICROSCOPY

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Introduction: The accumulation of α-synuclein as aggregates is a critical step in the progression of Parkinson’s disease (PD). PD is caused by the degeneration of dopaminergic neurons in the brain, which in turn causes the typical symptoms. Currently the diagnosis of PD is based heavily on clinical symptoms, which appear only after a massive loss of dopaminergic neurons. The validation of biomarkers showing the onset of disease prior to clinical symptoms is of major importance.

Aims: We established a method to specify and count single α-synuclein aggregates called surface-FIDA (Fluorescence-Intensity-Distribution-Analysis). The aim of this work is to establish a diagnostic tool based on detection of α-synuclein aggregates in human body fluids.

Methods: Surface-FIDA is based on the binding of α-synuclein aggregates by capture antibodies on a surface. As probes different antibodies conjugated with fluorescent dyes bind to α-synuclein aggregates and are detected by laser scanning microscopy. α-synuclein aggregates can be detected as fluorescence bursts, because only in case of aggregates many fluorescence labeled antibodies are able to bind to one aggregate.

Results: First results show a significantly higher number of fluorescence bursts in samples with aggregated α-synuclein compared to samples containing the same amount of α-synuclein monomers.

Conclusion: With our method we are able to specifically detect α-synuclein aggregates and to differentiate them from monomers. Therefore we present the proof of principle that surface-FIDA has the potential as a diagnostic tool.