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Alpha-synuclein RT-QuIC seeding activity in olfactory mucosa of GBA-associated Parkinson's disease

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Introduction: RT-QuIC assay may detect abnormal α-syn seeding activity in olfactory mucosa (OM) samples of patients with Parkinson's disease (PD) with approximately 60% sensitivity. [1-2] PD patients carrying heterozygous GBA mutations (GBA-PD) present more aggressive disease course3, which might be associated with a different pattern of α-syn seeding activity.

Objective: To investigate the pattern of α-syn seeding activity by RT-QuIC in OM of GBA-PD and PD-noncarriers.

Methods: Nasal brush was performed in 24PD-GBA carriers and 24 PD-noncarriers, matched by age and disease duration. Demographic, neurological, and neuropsychological data were collected. A sample was considered to induce α-syn seeding activity (positive) when at least two of four replicates exceeded the fluorescence threshold (30,000 AU before 20 hours), and lag time was calculated by averaging the time required to reach the fluorescence threshold.

Results: No differences were found in clinical features between two groups, excepted from higher prevalence of olfactory dysfunction was found in GBA-PDs than PD-noncarriers (p=0,004). We found trend towards lower positive α-syn seeding in OM of 25% GBA-PD vs. in 50% of PD-noncarriers (p=0.074). GBA-PD with positive seeding had lower MDS-UPDRS-III (p=0.044) than those without seeding. The mean RT-QuIC lag time was significantly longer in GBA-PD (p=0.039) and correlated to (a) MDS-UPDRS parts I (p=0.013) and II (p=0.012); (b) NMSS sleep/fatigue (p=0.005) and perceptual domain (p=0.031); (c) COMPASS-31 urinary domain(p=0.042).

Conclusion: We found lower α-syn seeding activity in GBA-PD than noncarriers. This might be explained by different α-syn conformation and binding to RT-QuIC primers. Alternatively, GBA-PD might exhibit increased OM neurons degeneration, resulting in suboptimal tissue samples. Analysis of α-syn strains in OM by electronic microscopy may clarify these results.

References:

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