

Detection of misfolded alpha-synuclein by RT-QuIC assay in olfactory mucosa brushing of subjects affected by neurodegenerative disorders

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Objectives: Real Time - Quaking-Induced Conversion (RT-QuIC) allows for highly sensitive and specific detection of misfolded α -synuclein (α -syn) in biological fluids or biomatrices, being a promising tool for early diagnosis of Parkinson's Disease (PD) [1, 2]. Olfactory mucosa (OM) can be easily sampled and efficiently analysed for this purpose. Here, we assessed RT-QuIC for α -syn diagnostic accuracy in OM samples from patients affected by parkinsonisms and isolated REM Sleep Behaviour Disorder (RBD).

Materials: we performed RT-QuIC on OM samples from 33 patients affected by PD, 12 affected by Lewy Body Dementia (LBD), 11 by Multiple System Atrophy (MSA), 15 by RBD and 19 with Alzheimer's Disease (AD; 6 subjects) and other parkinsonian syndromes (progressive supranuclear palsy, corticobasal syndrome and frontotemporal dementia).

Methods: a trained Otolaryngologist obtained two Olfactory Swabs (OS) samples from each patient using FLOQBrushes® (Copan, Italy) through a fibroscopic guide, as already described [1]. Each sample was sealed in saline solution 0.9%, frozen and sent to Neuropathology Laboratory of Verona University for RT-QuIC analysis. Clinical data were gathered through questionnaires.

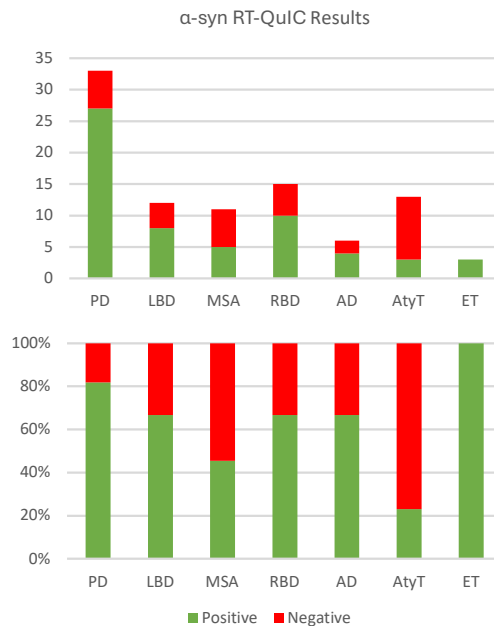


Figure 1 – Ratio of RT-QuIC positive results in different diagnostic groups. AD: Alzheimer's Disease; AtyT: atypical tauopathies; ET: Essential Tremor; LBD: Lewy Body Dementia; MSA: Multiple System Atrophy; PD: Parkinson's Disease; RBD: isolated REM Sleep Behaviour Disorder.

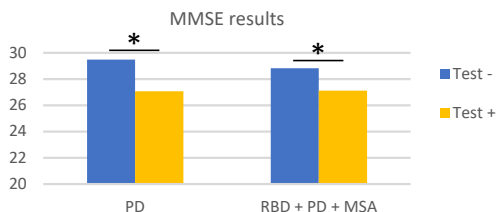


Figure 2 – Comparison of mean MMSE scores between positive- and negative-tested subjects. Negative-tested subjects performed significantly better when considering PD patients and all patients affected by PD, MSA or RBD.

Results: We obtained a positive RT-QuIC analysis for 81.8% of PD, 66.7% of RBD, 66.7% of LBD and 45.4% of MSA patients (Figure 1). Specificity yielded an overall result of 76.9%. As regards clinical aspects, we detected a borderline significant difference in MMSE scores between positive- and negative-tested patients affected by PD (U test, $p=0.050$); we obtained a similar result when considering all patients affected by PD, MSA and RBD (U test, $p=0.037$), with negative-tested subjects having higher MMSE scores (Figure 2).

Discussion: RT-QuIC efficiently detects α -syn in patients affected by α -synucleinopathies; differences in sensitivity among disease phenotypes may be related to different α -syn conformers. The extent of positive RT-QuIC assay in α -syn-related disorders may be explained by coexisting different pathologies [3]. A higher cognitive impairment in positive-tested OM samples in PD patients might reflect a more advanced involvement of olfactory areas including OM, as already described [1]. Further efforts and a higher number of OM samples are needed in evaluating the precise link between clinical characteristics and RT-QuIC results, including different clinical presentations when α -syn pathology is concomitant.

Conclusions: RT-QuIC for α -syn detection in OM is an effective diagnostic tool for identifying α -syn aggregates in patients with parkinsonisms and might help characterising different clinical disease phenotypes.

References:

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