

RT-QuIC DETECTION OF PATHOLOGICAL α -SYNUCLEIN IN THREE CASES OF LATE-ONSET ESSENTIAL TREMOR: A CASE SERIES

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Objectives: Essential Tremor (ET) is a common syndrome, diagnosed on clinical examination [1]. ET has a bimodal distribution of the age at onset with different phenotypic characteristics: a positive family history and alcohol sensitivity are more frequent in the early age of onset, while patients with a late age at onset show a faster progression of tremor and an early mortality [2]. ET etiology is still not completely understood and, although ET is also associated with higher rates of PD and dementia, the hypothesis of ET as a neurodegenerative disorder related to "PD with antecedent ET" or with other synucleinopathies is still debated [1]. At the same time, increasing evidence are showing that Real-time quaking-induced conversion (RT-QuIC) can efficiently detect pathological α -synuclein (α -syn) in patients affected by synucleinopathies [3], even in prodromal stage. However, evidence on RT-QuIC for α -syn in patients with ET is still lacking.

We present a series of three cases of late-onset ET with positive RT-QuIC for α -syn.

Methods: three patients with late-onset ET underwent RT-QuIC for α -syn detection in nasal mucosa (NM).

Results	Case 1 ♀	Case 2 ♀	Case 3 ♀
Age at onset	63 yo	72 yo	52 yo
Disease duration at brushing	2 years after the onset	1 year after the onset	15 years after the onset
NM RT-QuIC	α -syn +	α -syn +	α -syn +
Neurological Examination	Slight postural/kinetic tremor in R hand, later bilateral (R>L). Rest tremor present (ET plus).	Mild postural tremor UL L, slight UL R. Slight kinetic tremor UL L. Slight rest tremor UL L>R. Arm swing change (ET plus).	Mild postural/kinetic tremor R limbs, slight UL L after. Slight voice tremor (ET).
Brain MRI	Negligible leukoaraiosis	Mild leukoaraiosis (Fazekas 1)	Negligible gliotic lesions
DaT-SCAN SPECT	Mild deficit in left putamen	Negative	Negative
CSF AD markers	Negative	Negative	Negative
NMSS	None/negligible fatigue (no treated)	Mild mood impairment (no treated)	Anxious distress (treated)
Dementia	NO (3 years after brushing)	NO (3 years after brushing)	NO (3 years after brushing)

Discussion: the few data on RT-QuIC α -syn results in subjects with ET are generally negative [3]; however, the number of these studies is limited [3]. Considering the increased risk of ET to develop Lewy body diseases [1] and our RT-QuIC results, we can hypothesize that, at least in some cases, ET may represent a limited manifestation of synucleinopathy. However, further studies are needed to clarify the possible progression of late ET in alpha-synucleinopathies, its etiology, and the role of RT-QuIC as a possible predictive test for ET progression into synucleinopathies.

Conclusion:

biological evidence of pathological α -syn can be demonstrated in vivo in patients with late-onset ET.

References

- Okelberry T, Lyons KE, Pahwa R. Updates in essential tremor. *Parkinsonism Relat Disord.* 2024 May;122:106086. doi: 10.1016/j.parkreldis.2024.106086. Epub 2024 Mar 12. PMID: 38538475
- Hopfner F, Ahif A, Lorenz D, Kiebe S, Zeuner KE, Kuhlensäumer G, Deuschl G. Early- and late-onset essential tremor patients represent clinically distinct subgroups. *Mov Disord.* 2016 Oct;31(10):1560-1566. doi: 10.1002/mds.26708. PMID: 27384030.
- Bongianini M, Catalan M, Perra D, Fontana E, Janes F, Bertolotti C, Sacchetto L, Capaldi S, Tagliapietra M, Polverino P, Tommasini V, Bellavita G, Kachoei EA, Baruca R, Bernardini A, Valente M, Fiorini M, Bronzato E, Tamburin S, Bertolasi L, Brozzetti L, Cecchini MP, Gigli G, Monaco S, Manganotti P, Zanusso G. Olfactory swab sampling optimization for α -synuclein aggregate detection in patients with Parkinson's disease. *Transl Neurodegener.* 2022 Jul 28;11(1):37. doi: 10.1186/s40035-022-00311-3. Erratum in: *Transl Neurodegener.* 2022 Aug 12;11(1):38. doi: 10.1186/s40035-022-00312-2. PMID: 35902902; PMCID: PMC9330656



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