

The different faces of the p.A53T alpha-synuclein mutation: a screening of Greek patients with Parkinsonism and/or dementia

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Introduction: The p.A53T mutation in the alpha-synuclein (*SNCA*) gene is a rare cause of autosomal dominant Parkinson's disease (PD). Although generally rare, it is particularly common in the Greek population due to a founder effect. A53T-positive PD patients often develop dementia during disease course and may very rarely present with dementia. **Methods:** We screened for the p. A53T *SNCA* mutation a total of 347 cases of Greek origin with parkinsonism and/or dementia, collected over 15 years at the Neurogenetics Unit, Eginition Hospital, University of Athens. Cases were classified into: "pure parkinsonism" (PD, atypical parkinsonism), "pure dementia" (frontotemporal dementia, Alzheimer disease, "other") and "parkinsonism plus dementia" (frontotemporal dementia with parkinsonism, PD dementia, Lewy Body disease, atypical parkinsonism). **Results:** In total, 4 p. A53T *SNCA* mutation carriers were identified. All had autosomal dominant family history and early onset. Screening of the "pure parkinsonism" category (137 cases) revealed 2 cases with typical PD. The other two mutation carriers were identified in the "parkinsonism plus dementia" category (89 cases). One had a diagnosis of PD dementia and the other of behavioral variant frontotemporal dementia. Screening of patients with "pure dementia" (121 cases) failed to identify any further A53T-positive cases. **Conclusion:** Our results confirm that the p.A53T *SNCA* mutation is relatively common in Greek patients with PD or PD plus dementia, particularly in cases with early onset and autosomal dominant family history. However, routine screening of patients with "pure dementia" is unlikely to be clinically useful even in the Greek population.