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Screening of SNCA p.A53T mutation in the Sele river Valley: the Contursi Kindred 2.0

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Introduction: Parkinson disease (PD) is a common progressive neurodegenerative condition with unknow etiology. The majority of cases of PD are sporadic, however, also rare familial forms exist. The first identified mutation was a missense mutation resulting in an alanine to threonine substitution at position 53 (A53T) in the alpha-synuclein gene (SNCA) in the Contursi Kindred.

Objectives: The aim of the study is to describe the prevalence of p.A53T mutation in individuals with Parkinson and/or Dementia in the Sele River Valley and the clinical differences between patients with and without this mutation.

Methods: We tracked the prevalence of individuals with parkinsonism and dementia in the Sele river Valley through the National Health System Electronic Database (NHSED). Neurological examination and blood sampling were proposed to all the individuals in such lists and their relatives as well as to affected and unaffected subjects belonging to families known to harbor the p.A53T mutation. Genetic testing was performed using real-time polymerase chain reaction.

Results: The Sele Valley includes 13 villages for a total of 34.114 inhabitants (16.944 ≤44 years; 9.391 45-64 years; 7.626≥65 years). Exploration of the NHSDED disclosed 185 cases affected by Parkinsonism (0,54% total prevalence; 0,01% ≤44 years; 0,12% 45-64 years; 2,09% ≥65 years) and 124 cases affected by Dementia (0,36% prevalence, all ≥65 years). A total of 179 subjects were visited, 150 subjects performed genetic analysis. The 89% of subjects were p.A53T^{-}, 16 were p.A53T^{+} of which 11 affected and 5 unaffected. Subjects with p.A53T^{+} showed autosomal dominant inheritance pattern and presented heterogeneous manifestations with bradykinesia and rigidity (100%), tremor (62%), pyramidal signs (12.5%), dystonia (25%) and RBD (37%). Conversely, p.A53T^{-} have more frequent myoclonus (3.1%) and apraxia (5.2%).

Conclusions: All subjects with parkinsonism and positive family history from the Sele river Valley should be investigated for SNCA p.A53T.