Abstract

Etiological data on Parkinson's disease (PD) which is a common neurodegenerative disorder is lacking. In this study the roles of genes, lifestyle and environmental factors that may influence dopamine levels and function were investigated in the Maltese Geoparkinson samples and dataset after testing for PD-causing mutations known to be common in the Mediterranean. The data was analysed with respect to PD and addiction. Addiction is related to dopaminergic systems and thus may shed light on PD etiology and treatment.

Samples consisted of 200 cases with PD or parkinsonism (PS) and 400 controls collected as part of the EU FP5-funded Geoparkinson project. Common mutations in the Mediterranean Leucine-Rich Repeat Kinase 2 (LRRK2) G2019S, LRRK2 R1441G and Alpha-Synuclein (SNCA) G209A were tested by restriction fragment length polymorphism (RFLP). RFLP was also used to genotype two mutations in the dopamine synthesis pathway reported to be common in the Maltese population the Quinoid Dihydrobiopterine Reductase (QDPR) G23D and Sepiapterin Reductase (SPR) IVS2-2A>G mutations. Genotyping of two polymorphisms in Methylenetetrahydrofolate reductase (MTHFR) C677T and MTHFR A1298C polymorphisms will be done by real-time PCR. Some DNA changes were confirmed by DNA sequencing. The effect of tea, coffee, chocolate and alcohol consumption, smoking and use of specific medications are being analysed using logistic regression with respect to (i) PD and PS and (ii) addiction.

Allele frequencies were found to be 1.4% in cases for LRRK2 G2019S, 0.3% in controls for QDPR and 0.7% in controls for SPR mutations. Tobacco was found to be protective for PD whilst certain medications showed an increased Odds Ratio. Interesting associations were obtained for substance use, some of which were confirmed in other countries that participated in the Geoparkinson project. Data analysis and further genetic testing is still underway.