00475 Evidence of Lifestyle-gene Interactions in Parkinson's Disease: A Study of 4488 Subjects

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Aims: Current information on lifestyle-gene interactions in Parkinson's disease (PD) is limited. Caffeine intake reduces PD risk, but its potential interaction with genes is unclear. We have previously identified leucine-rich-repeat-kinase-2 (LRRK2) risk (G2385R) and protective (R1398H) variants in PD population, with healthy-population-frequencies of 5-15%. No studies have investigated caffeine-consumption-LRRK2 interactions in PD. We investigated the gene-environment interaction between caffeine and genetic susceptibility to PD at LRRK2 risk and protective variants.

Methodology: A prospective case-control study of 4488 subjects (1790 PD, 2698 controls) was conducted. Patients who satisfied the UK PD Brain Bank criteria and controls without neurological disorders were recruited. Caffeine intake was assessed using a validated evaluation tool. LRRK2 risk variant G2385R and protective variant R1398H were genotyped. Statistical analysis was conducted with logistic regression models. Gene-caffeine interactions were evaluated using an additive statistical model. Interactions were quantified using attributable proportion (AP) due to interaction (AP>0 shows positive interaction).

Result: G2385R risk mutant carriers who were non-caffeine-drinkers have 8 times increased PD risk compared to wildtype caffeine-drinkers [OR 8.58 (2.62, 28.06) p<0.001; AP=0.71]. R1398H protective variant non-carriers who were non-caffeine-drinkers had a 2.6 times higher PD risk than wildtype caffeine-drinkers [OR 2.63 (1.93, 3.59) p<0.001; AP=0.63].

Conclusion: We demonstrated novel significant interactions between LRRK2 gene and caffeine intake in PD. G2385R risk variant carrier non-caffeine-drinkers have more than 8 times PD risk compared to non-carrier caffeine-drinkers. R1398H protective variant non-carriers have more than 2 times PD risk. Our findings have important clinical implications. Personalised lifestyle modifications minimising PD risk in asymptomatic carriers may form the new management paradigm.