

Genetic factors can predict the progression of Parkinson's disease

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Parkinson's disease is marked by the abnormal accumulation of α -synuclein and the early loss of dopamine neurons in the substantia nigra region of the brain. A polymorphism in the promotor of α -synuclein gene known as NACP-Rep1 has been implicated as a risk factor for the disease. Now, researchers have found that different variants of NACP-Rep1 and its interaction with the microtubule-associated protein tau (MAPT) H1 haplotype can influence the speed of clinical deterioration in patients with Parkinson's disease.

"Our data are the first to show that polymorphisms of NACP and MAPT interact to influence the rate of progression of Parkinson's disease, a finding with clinical utility," says lead author Yue Huang of Neuroscience Research Australia and the University of New South Wales, Sydney, Australia. "Our study shows that genotypes for NACP and MAPT can be used as a surrogate marker for the estimated rate of Parkinson's disease progression, with positive predictive values of 94-100% for certain genotypes."

123 patients with Parkinson's disease underwent genetic testing to determine NACP-Rep 1 and MAPT H1 allele or genotype. The patient's disease severity was measured using the Unified Parkinson's Disease Rating Scale (UPDRS), and a measurement of disease progression was calculated based on detailed information about disease and symptom onset.

Three common variations, or alleles, of NACP-Rep1 were detected.



Patients with one '0' NACP-Rep1 allele had significantly slower disease progression compared to two or no '0' carriers. This may partially reflect the known protective influence of '0' allele on Parkinson's disease. There was a high variation in the estimated rate of disease progression for the '0' allele group due to an interactive effect with the MAPT genotype. The results showed a low relative risk for rapid clinical progression in patients with one NACP-1 '0' allele, or those carrying MAPT non-H1H1 genotype with two NACP-Rep1 '0's. In contrast there was a high risk of a fast clinical progression in patients carrying MAPT H1H1 genotype with two or no NACP-Rep1 '0's.

"Based on current knowledge, it is perhaps not surprising that genetic variation predisposing to high a-synuclein expression gives rise to more rapid progression of PD," notes Dr. Huang. "However, our results suggest that low α -synuclein expression may also be as detrimental in people with high tau expression levels, calling into question the concept that reducing neuronal α -synuclein in all PD patients may be therapeutically advantageous."

More information: The article is "Interaction between α-Synuclein and Tau Genotypes and the Progression of Parkinson's Disease," by Yue Huang, Dominc B. Rowe, and Glenda M. Halliday. *Journal of Parkinson's Disease*. 1(2011) 271-276. DOI 10.3233/JPD-2011-11027

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