Study IDs gene variants that speed progression of Parkinson's disease

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UCLA researchers may have found a key to determining which Parkinson's disease patients will experience a more rapid decline in motor function, sparking hopes for the development of new therapies and helping identify those who could benefit most from early intervention.

In a study published May 15 in the peer-reviewed online journal PLoS ONE, the researchers found that Parkinson's sufferers who possess two specific variants of a gene known to be a risk factor for the disease had a significantly speedier progression toward motor decline than patients without these variants.

"This is a relatively small study, with 233 patients, but the effects we're seeing are actually quite large," said Dr. Beate Ritz, vice chair of the department of epidemiology at the UCLA Fielding School of Public Health and the study's primary investigator.

The SNCA gene is a well-known risk factor for Parkinson's disease, and higher levels of the α-synuclein protein made from this gene are associated with greater disease severity in familial cases of Parkinson's. The researchers examined two risk variants, the REP1 263bp promoter and rs356165. They recruited Parkinson's disease patients shortly after they were diagnosed from three Central California counties and followed 233 of those patients for an average of 5.1 years.

They found that carriers of the Rep1 263bp variant had a four-fold

higher risk of faster motor decline. They observed an even stronger trend in progression toward motor decline when both the Rep1 263bp and rs356165 variants were present in patients.

When doctors currently see Parkinson's disease patients, they can't predict how rapidly their motor function will deteriorate — how quickly, for instance, they will reach a point when they need a wheelchair or other aids, said Dr. Jeff Bronstein, professor of neurology at the David Geffen School of Medicine at UCLA. "But if our results are confirmed," Bronstein said, "these gene variants can now identify patients who are likely to have faster progression."

And because of these differences in the rate of disease progression, researchers can test potential therapies in individuals carrying the genetic variations, obtaining faster results on the efficacy of those drugs, said co-author Shannon Rhodes, a researcher in epidemiology at the UCLA Fielding School of Public Health. "Plus," she said, "you're helping the people who are the most affected."

Ritz, who is also a professor of neurology at the David Geffen School of Medicine at UCLA, said there are probably other markers that need to be identified, because not all patients with the variants in question become fast progressors. In addition, the results need to be replicated, so future studies with many more subjects are needed.

"Since motor symptom severity predicts increased mortality (in Parkinson's disease) independent of age and disease duration, identifying genetic predictors of faster motor decline is critical to pinpointing biological mechanisms as targets for therapies and identifying patients who will most benefit from early interventions," the authors write. "While replication of our results in similarly well-characterized population-based incidence PD cohorts that have been longitudinally followed is still needed, our findings strongly suggest that α-synuclein

and related pathogenic pathways have great promise as potential disease modifying and therapeutic targets."

Provided by University of California, Los Angeles

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