

LRRK2 variants linked to lower age at onset of Parkinson's

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(HealthDay)—The presence of multiple *LRRK2* risk variants is

associated with a younger age at onset (AAO) of Parkinson's disease (PD), according to a research letter published online Nov. 13 in *JAMA Neurology*.

Bin Xiao, M.D., Ph.D., from the National Neuroscience Institute in Singapore, and colleagues assessed 1,284 patients with PD for the *LRRK2* risk variants S1647T, R1628P, and G2385R. The variants were genotyped by TaqMan real-time polymerase chain reaction; 10 percent of the results were checked for errors using Sanger sequencing. The AAO of carriers and noncarriers of *LRRK2* variants was compared.

The researchers found that the mean AAO was 62.3 years among all patients with PD, with women developing PD later than men (63.3 versus 61.6 years). Overall, 789 participants carried at least one of the S1647T, R1628P, and G2385R risk variants and 495 did not. The mean AAO was 62.5 years among participants with no variants, compared with 62.3 years (95 percent confidence interval, -1.35 to 1.18) for participants with one risk [variant](#), 61.3 years (95 percent confidence interval, -0.7 to 3.15) for those with two risk variants, and 52.6 years (95 percent confidence interval, 3.29 to 16.51) for those with all three risk variants. After adjustment for multiple testing, the difference between carriers with all three variants and noncarriers remained significant.

"These coding variants may contribute to PD development through distinct mechanisms and additively lower the AAO of PD," the authors write. "Our data suggest that increases in the genetic burden of *LRRK2* variants may be associated with an earlier AAO in PD."

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