

Genes linked to brain size may help explain some neurological diseases

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Credit: Rice University

In one of the largest research undertakings of its kind, a team of geneticists and neuroscientists has uncovered a number of genetic variations that influence the size of some key brain structures, including the hippocampus and the putamen. The result may advance understanding of such devastating neurodegenerative diseases as Alzheimer's, Parkinson's and Huntington's.

To link genes and [brain structure](#), a consortium of 290 scientists from 30 different countries conducted scans of the brains and genomes of roughly 31,000 people - "a computationally extraordinary task," according to University of Southern California neuroscientist Paul Thompson, one of the effort's leading investigators.

Their findings, reported Wednesday in the journal *Nature*, identify five novel genetic variants that appear to influence the size of two structures in the brain's basal ganglia - the putamen and caudate nucleus - that help govern the initiation and control of learned movement.

The study also confirmed earlier research locating a site on the genome that affects the brain's overall volume, and another that influences the size of the hippocampus, a key [structure](#) in the formation and retrieval of memories.

The findings provide insight "into the causes of variability in human [brain development](#), and may help to determine mechanisms of neuropsychiatric dysfunction," the authors wrote. Such massive collaborations might help uncover the forces that drive normal brain development as well, they wrote.

The work was done by a consortium called the Enhancing Neuro-Imaging Genetics through Meta-Analysis, or ENIGMA. Two-thirds of the 30,717 individuals they studied in their analysis were healthy, and the remaining one-third had a range of neuropsychiatric diseases. The

subjects ranged in age from 9 to 97.

"It is truly remarkable that you can see something as subtle as a single letter-change" in the genome's 25,000 protein-coding genes, and link it to variations in the size of a distinct brain region, Thompson said in an interview.

The volume of certain brain structures is likely to be an important measure of those structures' ability to function properly and fight off disease, said Thompson. With aging, for instance, many of the structures found to be influenced by genes lose volume, and that appears to make them vulnerable to disease, he added.

If genes contribute to make one individual's [hippocampus](#) smaller than another's, said Thompson, that person's brain might essentially be aging faster and therefore may be more at risk for neuropsychiatric disease.

"If my mental bank account is depleted, am I more at risk?" asked Thompson. "It's not far-fetched" to believe so, he added.

The eight gene sites uncovered were found in populations across a broad geographic range. The genetic variations that influenced [brain](#) volume in East Asians were the same those found to do so in Europeans, Africans and Americans.

More information: Hibar, D. P., Stein, J. L., Renteria, M. E., Arias-Vasquez, A., Desrivieres, S., Jahanshad, N, Thompson, P. M., Medland, S. E. (2015). Common genetic variants influence human subcortical brain structures. *Nature*, Published online Jan. 21, 2015; [DOI: 10.1038/nature14101](#)

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