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Obesity gene, carried by more than a third of the US population, leads to brain tissue loss

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Three years ago, geneticists reported the startling discovery that nearly half of all people in the U.S. with European ancestry carry a variant of the fat mass and obesity associated (FTO) gene, which causes them to gain weight — from three to seven pounds, on average — but worse, puts them at risk for obesity.

Now, UCLA researchers have found that the same gene allele, which is also carried by roughly one-quarter of U.S. Hispanics, 15 percent of African Americans and 15 percent of Asian Americans, may have another deleterious effect.

Reporting in the early online edition of the journal Proceedings of the National Academy of Sciences, senior study author Paul Thompson, a UCLA professor of neurology; lead authors April Ho and Jason Stein, graduate students in Thompson's lab; and colleagues found that the FTO variant is also associated with a loss of brain tissue. This puts more than a third of the U.S. population at risk for a variety of diseases, such as Alzheimer's.

Using magnetic resonance imaging, the researchers generated three-dimensional "maps" of brain volume differences in 206 healthy elderly subjects drawn from 58 sites in the U.S. as part of the Alzheimer's Disease Neuroimaging Initiative, a large, five-year study aimed at better understanding factors that help the brain resist disease as it ages.

They found that there was consistently less tissue in the brains of those

who carry the FTO allele, compared with non-carriers. Individuals with the "bad" version of the FTO gene had an average of 8 percent less tissue in the frontal lobes, the "command center" of the brain, and 12 percent less in the occipital lobes, areas in the back of the brain responsible for vision and perception. Further, the brain differences could not be directly attributed to other obesity-related factors such as cholesterol levels, diabetes or high blood pressure.

Thompson called the findings worrying and mysterious.

"The results are curious. If you have the bad FTO gene, your weight affects your brain adversely in terms of tissue loss," he said. "If you don't carry FTO, higher body weight doesn't translate into brain deficits; in fact, it has nothing to do with it. This is a very mysterious, widespread gene."

People who carry this specific DNA sequence are heavier on average, and their waist circumference is half an inch bigger.

This is a large percentage of the population, said Thompson, who is also a member of UCLA's Brain Research Institute and the UCLA Laboratory of Neuro Imaging.

"This is a shocking finding. Any loss of brain tissue puts you at greater risk for functional decline," he said. "The risk gene divides the world into two camps — those who have the FTO allele and those who don't."

But the news is not necessarily completely negative, Thompson said, because "carriers of the risk gene can exercise and eat healthily to resist both obesity and brain decline."

Thompson sees both a public health message and a science message in this finding.

"Half of the world carries this dangerous gene. But a healthy lifestyle will counteract the risk of brain loss, whether you carry the gene or not. So it's vital to boost your brain health by being physically active and eating a balanced diet," he said.

And from a scientific standpoint, he said, "the gene discovery will help to develop and fine tune the anti-dementia drugs being developed to combat brain aging."

Provided by University of California - Los Angeles