The Effect of Obesity-Related Gene can be Blunted by High Levels of Physical Activity

High levels of physical activity can help to counteract a gene that normally causes people to gain weight, according to a new study by researchers at the University of Maryland School of Medicine. They analyzed gene variants and activity levels of the Old Order Amish in Lancaster County, Pa., and found that the obesity-related FTO gene had no effect on individuals who were the most physically active.

"Our results strongly suggest that the increased risk of obesity due to genetic susceptibility can be blunted through physical activity," the authors conclude. "These findings emphasize the important role of physical activity in public health efforts to combat obesity, particularly in genetically susceptible individuals." The results of the study are being published in the Sept. 8, 2008, issue of the Archives of Internal Medicine.

Soren Snitker, M.D., Ph.D., the senior author and an assistant professor of medicine and pediatrics at the University of Maryland School of Medicine, says, "Our study shows that a high level of physical activity can 'level the playing field,' equalizing the risk of obesity between those who have copies of the FTO gene variant and those who don't."

The FTO gene recently has been linked to obesity and increased body mass index, or BMI, in several large-scale studies. More than half of all people of European descent have one or two copies of a variation of this gene, British scientists reported last year. Individuals with two copies of the gene variant are on average 7 pounds heavier and 67 percent more likely to be obese than those who don't have it.

University of Maryland researchers found this same link between variations of the FTO gene and increased risk of obesity in their study of 704 Amish men and women. But, in examining the gene in this unique group of people with a similar genetic background and active lifestyle, the researchers also found that high levels of physical activity helped to counteract the gene's effects.

"Having multiple copies of FTO gene variants had no effect on body weight for people who were the most physically active, regardless of whether they were men or women. But in less active people, the association between the gene and increased BMI was significant," says Evadnie Rampersaud, Ph.D., the lead author and a former postdoctoral fellow at the University of Maryland School of Medicine who is now at the University of Miami Institute for Human Genomics. "This provides evidence that the negative effects of the FTO variants on increasing body weight can be moderated by physical activity."

Dr. Snitker, of the University of Maryland School of Medicine, says the FTO gene is likely only one of a number of genes linked to obesity and notes that the effect of these genes may have changed over time.

"Some of the genes shown to cause obesity in our modern environment may not have had this effect a few centuries ago when most people's lives were similar to that of present-day Amish farmers," he says. He adds that environmental and lifestyle factors, such as a high-fat diet and lack of exercise, also may serve as triggers for obesity in genetically susceptible people.

"We are just starting to unravel these complex interactions between genomics and environment. It's really a new age of discovery," Dr. Snitker says. "One day, we hope to be able to provide a personally optimized prescription to prevent or treat obesity in people based on their individual genetic makeup."

In this study, which was funded by the National Institutes of Health (NIH), the researchers examined dozens of variations in the FTO gene. They gauged the participants' physical activity level with the help of a device worn on the hip called an accelerometer, which measures body movement. "We were able to get objective measurements of physical activity over seven consecutive 24-hour periods using this device, and that is a real strength of our study," says Dr. Rampersaud.

Participants were classified as having "high activity" or "low activity" levels. The more active people used 900 more kilocalories, or units of energy, a day, which translates into three to four hours of moderately intensive activity, such as brisk walking, housecleaning or gardening.

Despite an active lifestyle, 54 percent of the men in the study were considered overweight (BMI over 25) and 10.1 percent were obese (BMI over 30). Sixty-three percent of the women were overweight, and 30 percent were considered obese. The mean BMI was slightly higher in women (27.8) than in men (25.7).

These figures are in line with previous University of Maryland studies that showed that the Amish are as obese as other Caucasians in the United States. The earlier research also found that the Amish have half the incidence of Type 2 diabetes as well as favorable cholesterol levels, despite a diet high in fat and cholesterol, although the reasons for this remain unclear.

The Old Order Amish are considered ideal for genetic research because they are a genetically homogenous people who trace their ancestry back 14 generations to a small group that came to Pennsylvania from Europe in the mid-1700s. They don't drive cars or have electricity in their homes, eschewing many of the trappings of modern life. Most Amish men are farmers or work in physically demanding occupations such as blacksmithing or carpentry. Women are homemakers who work without the aid of

modern appliances and often care for many children.

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University of Maryland School of Medicine researchers, led by Alan R. Shuldiner, M.D., have conducted more than a dozen studies of the Amish in Lancaster County, Pa. since 1993, looking at various medical problems, such as diabetes, obesity, osteoporosis and high blood pressure. The latest research is an offshoot of a larger NIH-funded study, the Heredity and Phenotype Intervention (HAPI) Heart Study, examining how genes and lifestyle factors influence the Amish people's risk of developing cardiovascular disease.

Among the co-authors of the FTO gene study are Dr. Shuldiner, who is a professor of medicine, head of the Division of Endocrinology, Diabetes and Nutrition, and director of the Program in Genetics and Genomic Medicine at the School of Medicine; Toni I. Pollin, Ph.D., an assistant professor of medicine; and Braxton D. Mitchell, Ph.D., a professor of medicine.

Source: Karen Warmkessel