Scientists Find Gene that Ties Stress to Obesity and Diabetes

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Newswise — The constant stress that many are exposed to in our modern society may be taking a heavy toll: Anxiety disorders and depression, as well as metabolic (substance exchange) disorders, including obesity, type 2 diabetes, and arteriosclerosis, have all been linked to stress. These problems are reaching epidemic proportions: Diabetes alone is expected to affect some 360 million people worldwide by the year 2030. While anyone who has ever gorged on chocolate before an important exam recognizes the tie between stress, changes in appetite, and anxiety-related behavior, the connection has lately been borne out by science, although the exact reasons for the connection aren't crystal clear. Dr. Alon Chen of the Weizmann Institute's Department of Neurobiology and his research team have now discovered that changes in the activity of a single gene in the brain not only cause mice to exhibit anxious behavior, but also lead to metabolic changes.

All of the body's systems are involved in the stress response, which evolved to deal with threats and danger. Behavioral changes tied to stress include heightened anxiety and concentration, while changes in the body include heat generation, changes in the metabolism of various substances, and even changes in food preferences. What ties all of these things together? The Weizmann team suspected that a protein known as Urocortin-3 (Ucn3) was involved. This protein is produced in certain brain cells – especially in times of stress – and it's known to play a role in regulating the body's stress response. These nerve cells have extensions that act as "highways" that speed Ucn3 on to two other sites in the brain: One, in the hypothalamus – the brain's center for hormonal regulation of basic bodily functions – oversees, among other things, substance exchange and feelings of hunger and satiety; the other is involved in regulating behavior, including levels of anxiety. Nerve cells in both these areas have special receptors for Ucn3 on their surfaces, and the protein binds to these receptors to initiate the stress response.

The researchers developed a new, finely tuned method for influencing the activity of a single gene in one area in the brain, using it to increase the amounts of Ucn3 produced in just that location. They found that heightened levels of the protein produced two different effects: The anxiety-related behavior of the mice increased, and their bodies underwent metabolic changes. With excess Ucn3, their bodies burned more sugar and fewer fatty acids, and their metabolic rates sped up. These mice began to show signs of the first stages of type 2 diabetes: A drop in muscle sensitivity to insulin delayed sugar uptake by the cells, resulting in raised sugar levels in the blood. Their
pancreases then produced extra insulin to make up for the perceived deficit.

“We showed that the actions of a single gene in just one part of the brain can have profound effects on the metabolism of the whole body,” says Dr. Chen. This mechanism, which appears to be a smoking gun tying stress levels to metabolic disease, might, in the future, point the way toward the treatment or prevention of a number of stress-related diseases.

Participating in the research were research students Yael Kuperman, Orna Issler, Limor Regev, Ifat Musseri, Inbal Navon, and Adi Neufeld-Cohen, along with Shosh Gil, all of the Weizmann Institute’s Department of Neurobiology.

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The Weizmann Institute of Science in Rehovot, Israel, is one of the world’s top-ranking multidisciplinary research institutions. Noted for its wide-ranging exploration of the natural and exact sciences, the Institute is home to 2,600 scientists, students, technicians, and supporting staff. Institute research efforts include the search for new ways of fighting disease and hunger, examining leading questions in mathematics and computer science, probing the physics of matter and the universe, creating novel materials, and developing new strategies for protecting the environment.