Stress hormones accelerate obesity and diabetes upon aging

More than 600.000 people suffer from diabetes in Austria and every third person is not yet aware of that metabolic disease. Even a greater number of the population is seriously overweight, which underlies many age-related diseases including development of type II diabetes. Preventive medications and detailed understanding to avert these diseases are therefore an important health issue.

Glucocorticoids are stress hormones which act on each cell in the body. Glucocorticoids are also used clinically as successful anti-inflammatory drugs that can also block autoimmune diseases or chronic allergies. Glucocorticoids also play a major role in the metabolism. They are important for the mobilization of energy, which is crucial in hazardous situations, such as during infections or during long periods of food shortage. The hormones coordinate the complex interaction between the brain, glands, fat deposits, liver or muscle tissue. Hormones can affect metabolism, for example, the typical age-related gain of weight with concomitant fatty liver disease or diabetes result from changed hormonal levels to a significant extend. These health problems develop due to complex interactions between different organs and hormones and the purpose of the current study was to improve our understanding of these disease mechanisms. This might result in drugs modulating stress hormone signaling to treat obesity or diabetes.

Now a research team led by Richard Moriggl at the Ludwig Boltzmann Institute for Cancer Research (LBI-CR), the Veterinary and Medical University of Vienna in cooperation with the universities in Ulm, Graz and Munich, has investigated how reduced stress hormone signaling affects fat cells. The central observation was that an attenuated glucocorticoid signaling in fat cells leads to leaner old mice and prevents onset of age-related diabetes. The hormone action is mediated through receptors that sit at the cell surface and triggers signals inside the cell when stress hormone is secreted. To interfere with the signal transmission, the researchers studied mice whose fat cells could not exert any stress hormone response by virtue of a genetic deletion of the glucocorticoid receptor. Their results are now published in the renowned journal Diabetes.

The lack of a stress hormone response leads to loss of energy reserves from fat cells and fat cells remain with a huge seize and a huge fat droplet after a period of enforced starvation, because the fat could not be mobilized. In compensation other sources of energy in the body were accessed and thus the loss of the glucocorticoid receptor in fat cells results in a fundamental readjustment of the metabolism in mice. A surprising result was that the animals were less overweight when fed a diet rich in fat compared to control animals. Also aged mice showed a significantly reduced body weight without stress hormone response. "The fact that a reduced mobilization of fat in the long term leads to less fat in the body has surprised us," says Moriggl. So it is not the lack of stress, but too much stress, which makes at least old or malnourished mice obese. The scientists propose that the stress hormone levels in later life are more prone to typical signs of aging such as obesity or diabetes. It was interesting to observe that genetically modified mice without stress hormone response had improved glucose balance. Whether this can be exploited therapeutically with diabetes must be seen.

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Mueller KM, Hartmann K, Kaltenecker D, Vettorazzi S, Bauer M, Mauser L, Amann S, Jall S, Fischer K, Esterbauer H, Müller TD, Tschöp MH, Magnes C, Haybaeck J, Scherer T, Bordag N, Tuckermann JP, Moriggl R.

"Adipocyte Glucocorticoid Receptor Deficiency Attenuates Aging- and Hfd-Induced Obesity, and Impairs the Feeding-Fasting Transition"

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