New alterations found in young adults with type 2 diabetes

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Diet and aerobic exercise are highly effective for the treatment of type 2 diabetes, but not for obese subjects that have developed the disease when very young.

A study at the Institute for Research in Biomedicine (IRB Barcelona) and Trinity College in Dublin demonstrates that obese subjects between 18 and 25 years of age carry mitochondrial proteins and genes that work abnormally and that these anomalies contribute to generating insulin resistance and a reduced response to physical exercise. Produced by the American Diabetes Association, the journal *Diabetes Care*, which disseminates the clinical studies of greatest relevance, will publish the results of this research in its March issue.

Diabetes type 2 is the most common form of diabetes worldwide and in Europe it accounts for almost 90% of the cases of this disease. In Spain, diabetes affects 6.5% of the population between the ages of 30 and 65. In type 2 diabetes tissues don't respond properly to insulin, a hormone produced by the pancreas, and the pancreas is not able to produce the abnormal amount required by the organism. Insulin serves to help tissues take up glucose carried by blood. Experts associate the appearance of diabetes type 2 with overweight, diet, and lack of exercise. "Until now most cases were registered in subjects over 50 years of age, but young people are increasingly developing the disease", explains Antonio Zorzano, co-author of the study and head of the Molecular Medicine programme at IRB Barcelona.

Zorzano goes on to explain that the results of the clinical study are relevant for two reasons. "We are starting to observe that there are special forms of diabetes type 2 that behave in a different way to the classical form, and these differences require specific treatments for each kind of patient." In another study published in Diabetologia in 2009, Zorzano's group demonstrated that morbidly obese diabetic subjects —with a body mass index over 40— also suffer from specific mitochondrial alterations that are differentiated from classical diabetes patients.

Anomalies in mitochondria

A group of young obese adults with diabetes and another group of young obese adults without this disease followed an exercise plan four times a week for three months. The muscle biopsies of the two groups showed considerable differences in a series of mitochondrial activity proteins. "After these sessions a sedentary person shows an increase in mitochondrial proteins because the exercise increases mitochondrial biogenesis, that is to say, more mitochondria are produced". It has been demonstrated that both diet and continuous exercise stimulate greater mitochondrial activity, which in turn has a positive effect on sensitivity to insulin. In contrast, in young obese diabetic subjects some key proteins do not increase, such as the mitochondrial gene regulatory factor PGC-1α, and the protein Mitofusin-2.

"These results imply that we must classify patients with diabetes type 2, identify the differences between the distinct phenotypes and consider specific treatments", concludes Zorzano. The group of researchers at Trinity College and IRB Barcelona plan to perform a clinical study to detect more mitochondrial factors that are affected in these patients. One of the final objectives of the group is to achieve the capacity to manipulate some to the deteriorated components of young obese diabetic subjects so that they can also respond to the beneficial effects of

exercise.

More information: Subjects with early-onset type 2 diabetes show defective activation of the skeletal muscle PGC-1α /mitofusin-2 regulatory pathway in response to physical activity. *Diabetes Care* March 2010 33:652-657; published ahead of print December 23, 2009; doi:10.2337/dc09-1305

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