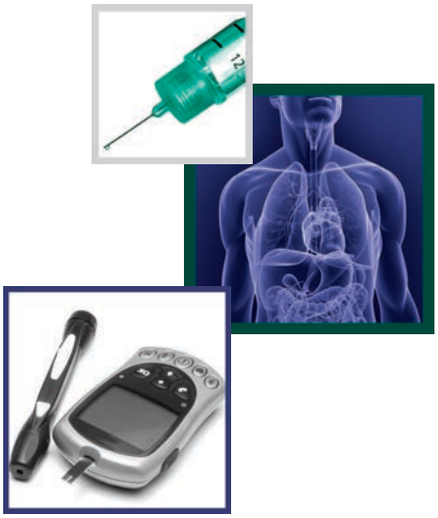
Link between post-traumatic stress disorder and Type 2 diabetes



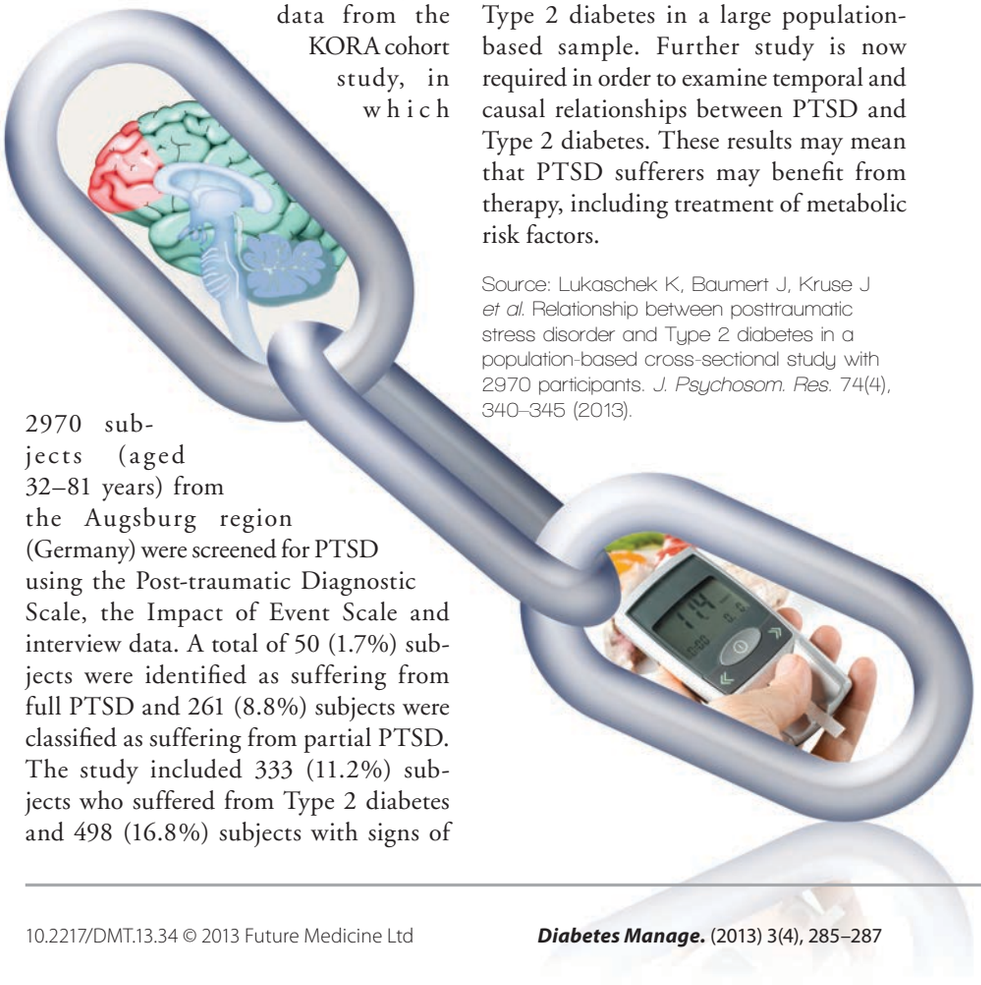
Researchers at the Helmholtz Zentrum München (Oberschleißheim, Germany) and the University Hospital Gießen and Marburg (Marburg and Gießen, Germany) have discovered a significant association between post-traumatic stress disorder (PTSD) and Type 2 diabetes. The study, published in the *Journal of Psychosomatic Research*, worked with data from the large population-based KORA cohort study.

PTSD is a severe anxiety syndrome with symptoms developing after an extremely stressful life event. Previous research has linked stress from mental illness with diabetes mellitus but this is the first study to demonstrate a significant association between the two.

The team analyzed data from the KORA cohort study, in which 2970 subjects (aged 32–81 years) from the Augsburg region (Germany) were screened for PTSD using the Post-traumatic Diagnostic Scale, the Impact of Event Scale and interview data. A total of 50 (1.7%) subjects were identified as suffering from full PTSD and 261 (8.8%) subjects were classified as suffering from partial PTSD. The study included 333 (11.2%) subjects who suffered from Type 2 diabetes and 498 (16.8%) subjects with signs of a prediabetic metabolic state, as assessed by an oral glucose tolerance test and validation by a physician. The model was adjusted for sociodemographic characteristics, metabolic risk factors and psychopathological conditions. A significant association was observed between full PTSD and Type 2 diabetes, compared with subjects who had not experienced a traumatic event. This association may be attributed to the fact that chronic stress may cause changes in hormonal response patterns, leading to detrimental effects on metabolism and glucose utilization. However, no significant associations were observed between PTSD and prediabetes.

This study has demonstrated a significant association between PTSD and Type 2 diabetes in a large population-based sample. Further study is now required in order to examine temporal and causal relationships between PTSD and Type 2 diabetes. These results may mean that PTSD sufferers may benefit from therapy, including treatment of metabolic risk factors.

Source: Lukaschek K, Baumert J, Kruse J *et al.* Relationship between posttraumatic stress disorder and Type 2 diabetes in a population-based cross-sectional study with 2970 participants. *J. Psychosom. Res.* 74(4), 340–345 (2013).



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Adolescents with Type 2 diabetes may be at a greater risk of developing heart and kidney disease

Recent data from the TODAY diabetes study, led in San Antonio by pediatricians from the University of Texas Health Science Center (TX, USA), show that adolescents with Type 2 diabetes develop heart and kidney problems faster than those who acquire the disease later in life.

> "The risk for developing hypertension was linked with male sex, but the risk for developing microalbuminurea was more closely related to glycemic control."

The study aimed to observe the incidence of hypertension and microalbuminurea in youths with Type 2 diabetes and to observe the effects of treatment, glycemic control, sex and ethnicity. The study included a cohort of 699 adolescents (aged 10–17 years), who had been diagnosed with Type 2 diabetes in the last 2 years.

Participants were randomized to three treatment groups: metformin; metformin plus rosiglitazone; or metformin plus intensive lifestyle intervention. The primary outcome of the study was loss of glycemic control for 6 months or sustained metabolic decompensation requiring insulin. The average follow-up of the study was 3.9 years.

A total of 319 (45.6%) participants reached the primary study outcome, with 11.6% being hypertensive at baseline and 33.8% by the end of the study. The study demonstrated that male sex and increasing BMI were the primary factors that correlated with the development of hypertension, with obese teenage boys being 81% more likely to develop hypertension. A total of 6.3% of participants had microalbuminurea, a figure that rose to 16.6% by the end of the study. Better glycemic control reduced the risk of developing microalbuminurea, but there was no evidence that sex or ethnicity played a role.

The study demonstrated that the incidence of hypertension and microalbuminurea increased over time among adolescent subjects with Type 2 diabetes. This incidence was unaffected by the intervention in all of the treatment arms. The risk for developing hypertension was linked with male sex, but the risk for developing microalbuminurea was more closely related to glycemic control.

The study will now continue in order to monitor the long-term outcomes of the participants with a view to elucidate potential methods of preventing or predicting these secondary diseases in young patients with Type 2 diabetes.

Source: TODAY Study Group. Rapid Rise in Hypertension and Nephropathy in Youth With Type 2 Diabetes: the TODAY clinical trial. *Diabetes Care* 36(6), 1735–1741 (2013).

Potential for regulating blood sugar levels by targeting the brain

In a recent study, published in *Nature Medicine*, researchers from the Toronto General Research Institute (ON, Canada) have shown that diabetes could potentially be managed by targeting glucagon action in the brain. The team has demonstrated how glucagon mediates the mediobasal hypothalamus' control over blood sugar levels.

> "...mediobasal hypothalamus infusion of glucagon activated PKA and inhibited hepatic glucose production."

Glucagon activates hepatic PKA to cause an increase in glucose production when blood sugar levels fall. This increase is transient and blood sugar levels soon return to normal, and this is thought to occur through the actions of glucagon in the hypothalamus. In diabetes, this transient increase is flawed so glucose levels remain high. The most common method of regulating blood sugar levels in diabetic patients is through the use of insulin, which inhibits glucose production.

The team used experimental models of obesity and diabetes to demonstrate this mechanism. In rats with a pancreatic clamp, mediobasal hypothalamus infusion of glucagon activated PKA and inhibited hepatic glucose production. This was also observed in mice given central glucagon infusion. The effect of mediobasal hypothalamus glucagon infusion in rats was negated when glucagon receptor–PKA signaling was inhibited. In control rats, a continued rise in plasma glucagon levels transiently increased hepatic glucose production, an

Potential role for adult stem cells in the treatment of Type 1 diabetes

A team investigating potential stem cell treatments for Type 1 diabetes has demonstrated the important role of immune modulation and vascular repair.

A recent study by researchers at the University of Missouri (MO, USA) has highlighted a potential treatment for Type 1 diabetes, which combines adult stem cells with a new drug.

The team made the discovery that in patients with Type 1 diabetes, as well as attacking insulin-producing β cells, the body's immune system destroys the blood vessels that supply them. In previous studies, the team developed a drug called Ig-GAD2 containing glutamic acid decarboxylase 206–220 peptide, which was able to control pancreatic inflammation, stimulate β-cell regeneration and prevent the progression of Type 1 diabetes in hyperglycemic mice. However, too few β cells remained. In this study, published in *Diabetes*, the team used Ig-GAD in combination with the injection of adult stem cells from bone marrow into mice.

The team observed a sustained recovery from Type 1 diabetes in these mice. However, instead of the bone marrow stem cells differentiating into β cells as expected, the new β cells were found to be of host origin. In fact, the donor cells differentiated into new endothelial cells. When purified endothelial progenitors were transplanted instead of whole bone marrow cells, β-cell and endothelial cell formation was sustained and the diabetic phenotype was reversed.

The conclusion of this study was, therefore, that in order to combat Type 1 diabetes, both immune modulation and vascular repair are required. This finding holds great promise for the treatment of diabetes and potentially for the treatment of other autoimmune diseases.

Source: Wan X, Guloglu F, Vanmorlan A *et al.* Recovery from overt Type 1 diabetes ensues when immune tolerance and cell formation are coupled with regeneration of endothelial cells in the pancreatic islets. *Diabetes* doi:10.2337/db12–1281 (2013) (Epub ahead of print).

– All stories written by Caroline Telfer

> "...in order to combat Type 1 diabetes, both immune modulation and vascular repair are required."

effect which was eliminated when hypothalamic glucagon action was negated. The team observed that in rats without a pancreatic clamp, mediobasal hypothalamus glucose infusion advanced glucose tolerance and inhibition of glucagon receptor–PKA signaling enhanced the increase in plasma glucose concentrations seen during intravenous glucagon injection.

> "In control rats, a continued rise in plasma glucagon levels transiently increased hepatic glucose production..."

The team demonstrated that hypothalamic glucagon signaling inhibits hepatic glucose production. This raises the possibility that therapeutics that aim to increase glucagon action in the hypothalamus and/or inhibit glucagon action in the liver could regulate blood sugar levels in diabetic patients.

Source: Mighiu P, Yue J, Filippi B *et al.* Hypothalamic glucagon signaling inhibits hepatic glucose production. *Nat. Med.* doi:10.1038/nm.3115 (2013) (Epub ahead of print).

About the News

The News highlights some of the most important events and research.
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