Mechanism explains complications associated with diabetes

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New research uncovers a molecular mechanism that links diabetes with an increased risk of cardiovascular problems and sudden cardiac death. The study, published by Cell Press in the June 24 issue of the journal *Neuron*, finds that high blood sugar prevents vital communication between the brain and the autonomic nervous system, which controls many involuntary activities in the body.

"Diseases, such as diabetes, that disturb the function of the autonomic nervous system cause a wide range of abnormalities that include poor control of blood pressure, cardiac arrhythmias, and digestive problems," explains senior study author Dr. Ellis Cooper from McGill University in Montreal. "In most people with diabetes, the malfunction of the autonomic nervous system adversely affects their quality of life and shortens life expectancy."

To investigate why the autonomic nervous system malfunctions in diabetics, Dr. Cooper and colleagues examined the transmission of electrical signals from the brain to autonomic neurons. The brain communicates with autonomic neurons at synapses, a small gap between two nerve cells where electrical signals from one nerve cell are sent to the next by chemical neurotransmitters. "In healthy individuals, synaptic transmission in the autonomic nervous system is strong and stable; however, if synapses on these neurons malfunction due to some disease process, the link between the nervous system and the periphery becomes disrupted," says Dr. Cooper.

Using a mouse model of diabetes, the researchers discovered that high blood sugar elevates reactive oxygen species in autonomic neurons and causes a disruption in synaptic transmission between the brain and the autonomic neurons. The researchers went on to show that this elevation in reactive oxygen species inactivates the neurotransmitter receptors at these synapses causing synaptic transmission to fail.

"Our work provides a new explanation for diabetic-induced disruptions of the autonomic nervous system," concludes Dr. Cooper. "We show that an early step leading to autonomic abnormalities in diabetes is a depression in synaptic transmission triggered by events downstream of high blood sugar and reactive oxygen species. This synaptic depression is apparent as early as 1 week after the onset of diabetes and becomes more severe over time."

More information: Campanucci et al.: “Report: Diabetes Depresses Synaptic Transmission in Sympathetic Ganglia by Inactivating nAChRs through a Conserved Intracellular Cysteine Residue.” Publishing in Neuron 66, 827-834, June 24, 2010. DOI:10.1016/j.neuron.2010.06.010

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