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THE EFFECT OF NOREPINEPHRINE ON GLUTAMATE RELEASE IN THE VMH DURING HYPOGLYCEMIA

Awais Ahmad, Owen Chan, Daniel Appadurai
University Of Utah, Department of Internal Medicine, Division of Endocrinology, Metabolism and Diabetes

Diabetes is a prevalent worldwide disease. Intensive treatment of type 1 diabetic (T1D) patients with insulin can minimize the development of long-term complications such as blindness, kidney failure, nerve damage and cardiovascular disease, but a common side effect is hypoglycemia or low blood sugars. About 3-4% of deaths in T1D patients are the direct result of hypoglycemia and therefore, it is important to understand the pathways that regulate the hormonal responses which protect against hypoglycemia - the “counterregulatory” responses. The brain and specifically, the ventromedial hypothalamus (VMH), plays an important role in detecting hypoglycemia and initiating the hormonal responses that counter the fall in blood glucose. Our research identified two brain signals, norepinephrine and glutamate, that initiate the counterregulatory responses to hypoglycemia, but it is unclear whether these two signals communicate with one another, and this was the focus of the current study. To test this hypothesis, we infused either artificial extracellular fluid (Controls; n=4) or 400nM NE (n=4) into the VMH under normal glucose levels and evaluated its effects on the release of glutamate using microdialysis and the counterregulatory hormones in the plasma. The infusion of norepinephrine into the VMH caused a significant rise in plasma glucagon (Controls: 32.3±8.4 pg/mL, NE: 93.7±5.0 pg/mL; $P<0.001$) and epinephrine (Controls: 1195±313 pg/mL, NE: 8022±1873 pg/mL; $P<0.01$) levels. The increase in these hormones was associated with a slight increase in plasma glucose concentrations. Our data shows that the infusion of norepinephrine into the VMH triggers an increase in the counterregulatory hormone response and in turn, a rise in plasma glucose levels, suggesting norepinephrine is likely a major part of the central glucose sensing circuit that is involved in the initiation of the counterregulatory response to hypoglycemia.