# Insulin deprivation leads to decreased ATP production in animal study

January 24 2019

Despite the strong association between diabetes and dementia, how insulin deficiency affects brain function remains unclear. A recent study published in *The FASEB Journal* used a mouse model to investigate this mechanism.

First, researchers induced diabetes in a group of mice by administering streptozotocin, an agent that is destructive to insulin-producing cells. They then gave the diabetic mice insulin treatments to bring their blood glucose levels close to those of non-diabetic mice. After stabilizing the body weight and blood glucose levels of the diabetic mice, the researchers withdrew the insulin treatment.

The researchers observed a decline in the production of mitochondrial adenosine triphosphate (ATP)—critical for all cellular functions—in cortical regions of the brain that are associated with memory. The decline in ATP production mirrored previous studies examining insulin deficiency in the skeletal muscle of mice.

The team then administered intranasal insulin treatment to a group of non-diabetic mice, which subsequently exhibited an increase in mitochondrial ATP production.

"Our study points to the critical role of insulin in maintaining brain mitochondrial function," stated K. Sreekumaran Nair, MD, Ph.D., a consultant in endocrinology and professor of medicine at the Mayo Clinic. "Future human studies should explore how insulin treatment

could reduce dementia and Alzheimer's disease among the millions of people living with diabetes."

Interestingly, unlike skeletal muscle and other organs in the body, the brain did not demonstrate an increase in reactive oxygen species (ROS) emission or oxidative stress. This finding suggests that, in the absence of insulin, the brain is uniquely protected from oxidative damage by enhancing anti-oxidant buffers that prevent the rapid decline of energy metabolism and cellular functions.

"Few would have anticipated these findings as regards the brain being within this overall energy balance sheet; not a frank intrusion like local hypoxia or a block in cerebral vasculature, but rather a more nuanced impact," said Thoru Pederson, Ph.D., Editor-in-Chief of *The FASEB Journal*.

Provided by Federation of American Societies for Experimental Biology