

2018 Talent Development Competition Awardees

Title: Disruptions in hypothalamic fuel sensing as a mechanism of antipsychotic-induced glucose dysregulation

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Abstract: Antipsychotic medications, such as olanzapine, are the main treatment for schizophrenia, and are widely used for other conditions such as anxiety, anorexia, sleep disorders, and dementia. However, antipsychotics cause serious metabolic side-effects, including blood sugar (glucose) problems which can result in type 2 diabetes and cardiovascular disease leading to a reduced lifespan of 20 years. However, we do not understand how antipsychotics cause these side-effects. Insulin, a hormone essential to regulating blood sugars, has recently been discovered to act through the brain to tell the liver to stop making glucose (to prevent high glucose levels like those seen in diabetes). Our recent research shows that antipsychotics block the ability of insulin in the brain to regulate blood sugars, which may contribute to the development of type 2 diabetes. To find out why this is happening, we will use rats to investigate exactly how antipsychotic medications (like olanzapine) block the ability of the brain to respond to insulin. We will also look at ways to reverse antipsychotic-related problems in blood sugars by using brain injections of compounds to reset the energy balance, or to block some of the components of antipsychotic medication action which we think may be involved. Results from this study can then be moved into the clinical setting to help to develop effective medications without metabolic side-effects and to treat antipsychotic-related metabolic problems, with the goal to improve our patients' quality of life.