

## **Drug Reverses Abnormal Brain Function in Rett Syndrome Mice**

A few weeks ago, a promising new study was published in the *Journal of Neurosciences* by Dr. David Katz and his colleagues at Case Western Reserve University that demonstrated that in a mouse model of Rett syndrome they were able to reverse abnormalities in brain activity and improve neurological function by treating animals with an FDA-approved anesthesia drug, ketamine.

The authors sought out to create the first global map of neural activity in the RTT brain to understand the brain's circuitry dysfunctions in Rett syndrome. In order to do this, they compared brains from Mecp2 mutant mice and normal mice by tracking markers of brain activity. These comparisons found that there are two regions in the brain where neural activity differed in the RTT brain. First, the forebrain, which controls nearly all processes in the Central Nervous System, was found to have less neural activity in the RTT brain compared to the normal brain. Second, the brainstem, which is responsible for basic vital life functions such as breathing, heartbeat, and blood pressure, was reported to have abnormally high neural activity in the RTT brain compared to the normal brain. By identifying that these brain structures have such different activity levels in the RTT brain, they were able to begin focusing on these areas to see if they could modify the abnormal activity.

"These studies provide new evidence that drug treatment can reverse abnormalities in brain function in Rett syndrome mice and they also provide new leads as to what kinds of drugs might be effective in individuals with Rett syndrome" says David Katz, PhD

The identification of these brain regions provided clues into specific areas to target for treatment. Based on previously published findings that ketamine activated neurons in the forebrain, the researchers gave the drug to the Rett syndrome mice and found it increased levels of brain activity in those regions and improved neurological function. Importantly, the drug was effective at a low dose that did not produce anesthesia.

Katz strongly cautioned that, because ketamine can have potent anesthetic effects and is a controlled substance; further work is needed to establish the safety of ketamine in patients with Rett syndrome. Moreover, ketamine has never been used to treat a chronic condition, and additional studies are required to determine whether or not this is feasible and safe. However, safer drugs acting in the same pathways as ketamine may be available.