

NEWS

Deer mouse model suggests combination therapy for autism

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A combination approach may hold promise for treating repetitive motor behaviors, such as those seen in people with autism, according to research presented yesterday at the **Society for Neuroscience annual meeting**.

The insight comes from studies in an unusual animal model, the deer mouse, *Peromyscus maniculatus*. “These mice exhibit restricted, repetitive behaviors when raised in standard laboratory conditions,” explains Amber Van Matre, a postdoctoral researcher at the University of Florida, who presented the findings. The mice jump vertically up the walls of their cage and do backward somersaults over and over.

There are few treatments available for managing repetitive behaviors, which affect people with autism, as well as those with schizophrenia and other neuropsychiatric disorders. The results in the deer mice suggest that using combinations of drugs may offer more effective therapy for these behaviors, Van Matre says.

In the brain, two neural pathways in the basal ganglia control motor activity. The direct pathway stimulates motor behavior, whereas the indirect one lowers it. The researchers suggest that repetitive behaviors arise when these two pathways are imbalanced — most likely due to the lack of inhibitory, indirect pathway activity.

On the surface of neurons in that pathway, triads of receptors for signaling molecules determine cell activation. These receptors — A2A for adenosine, mGluR5 for glutamate and D2 for dopamine — are arranged together in complexes that have a push-me-pull-you kind of function. For example, activating the adenosine and glutamate receptors decreases the function of the dopamine receptor.

In turn, decreasing the activity of the dopamine receptors turns up adenylyl cyclase, a so-called second messenger that sets off a cascade of activity and activates the neuron.

The researchers tested three drugs, each acting on a different receptor on these neurons. Each drug alone had no effect on mouse behavior. “But when we started to cocktail these drugs together and combine them,” says Van Matre, “they were effective at significantly reducing repetitive behavior.”

The team also tested the reverse: they used a different set of drugs to increase D2 receptor function and decrease neuron activity. Again, each of the drugs acting alone had no effect, but combinations of drugs increased repetitive behavior in the mice.

John Neill, associate professor of psychology at Long Island University, cautions that other drugs that act against dopamine receptors, such as the antipsychotic medication haloperidol, can have devastating motor side effects, particularly when used long term.

Van Matre says this may be another advantage of the combination approach: using multiple drugs at the same time may enable doctors to minimize the dose of each, reducing side effects.

For more reports from the 2010 Society for Neuroscience meeting, please [click here](#).