

'Forrest Gump' mice show too much of a good thing, can be bad

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A line of genetically modified mice that Western University scientists call "Forrest Gump" because, like the movie character, they can run far but they aren't smart, is furthering the understanding of a key neurotransmitter called acetylcholine (ACh). Marco Prado and his team at Robarts Research Institute say the mice show what happens when too much of this neurotransmitter becomes available in the brain. Boosting ACh is a therapeutic target for Alzheimer's disease because it's found in reduced amounts when there's cognitive failure. Prado's research is published in the *Journal of Neuroscience*.

"We wanted to know what happens if you have more of the gene which controls how much acetylcholine is secreted by [neurons](#)," says Prado, a Robarts scientist and professor in the Departments of Physiology and [Pharmacology](#) and Anatomy and [Cell Biology](#) at Western's Schulich School of Medicine & Dentistry. "The response was the complete opposite of what we expected. It's not a good thing. Acetylcholine release was increased threefold in these mice, which seemed to disturb cognitive function. But put them on a treadmill and they can run twice as far as normal mice before tiring. They're super-athletes." In addition to its function in modulating cognitive abilities, ACh drives muscle contraction which allowed for the marked improvement in motor endurance.

One of the tests the scientists, including first author Benjamin Kolisnyk, used is called the touch screen test for mice which uses technology similar to a tablet. After initiating the test, the mice have to scan five

different spots on the touch screen to see a light flash, and then run and touch that area. If they get it right they get a reward. Compared to the control mice, the "Forrest Gump" mice failed miserably at the task. The researchers found the mice, which have the scientific name ChAT-ChR2-EYFP, had terrible attention spans, as well as dysfunction in working memory and spatial memory.

Prado interprets the research as showing ACh is very important for differentiating cues. So if your brain is presented with a lot of simultaneous information, it helps to pick what's important. But when you flood the brain with ACh, your brain loses the ability to discern what's relevant. This study was funded mainly by the Canadian Institutes of Health Research.

Provided by University of Western Ontario

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