Can a miniscule worm hold the secret to genetically reversing brain damage?

February 5 2021

C. elegans. Credit: Hebrew University of Jerusalem

A team of Hebrew University researchers have successfully used genetic engineering as a first step to what one day may allow scientists to genetically repair damaged brain circuits. The process, which was performed in tiny translucent C. elegans worms, saw the introduction of synthetically engineered connections (or synapses), as a means for bypassing missing connections between neurons in an impaired brain.

The team, led by Dr. Ithai Rabinowitch, a Neurobiologist in the Faculty of Medicine at Hebrew University, applied the genetically engineered bypass to repair a failed odor response in the worms due to neuronal loss. With the synthetic bypass network in place, the worms successfully responded to the odor stimuli, a behavior that was diminished in the absence of the genetically engineered "fix." The study, published in *Cell Systems* was jointly led by Dr. Jihong Bai of the Fred Hutchinson Cancer Research Center in Seattle, Washington.

"While this is a discovery that has so far been limited to a tiny worm, it opens the door for potential applications that may be relevant down the road to humans," Dr. Rabinowitch said. "At present, various approaches are used for addressing human brain damage, including brain-computer interfaces that are based on external electronics rerouting information flow between intact brain regions. This research indicates a new potential route for addressing brain damage, whether caused by direct physical trauma or stroke or other neurological disease, through genetically engineered changes in brain connectivity that can serve as biological neural bypasses."

The researchers say that the species chosen, C. elegans, measuring about a millimeter long, is very beneficial for biological research. Compared to us, the worm has a very simple nervous system, and yet it is a multi-cellular animal sharing many similarities with us. According to Dr. Rabinowitch the next steps will involve deeper testing of the broader biological impact of genetically inserted neuronal connections and also applying the approach to other neural circuits and other organisms.

"In studying this tiny worm, we were able to advance our theory in an organism that has only several hundred neurons as opposed to the tens of billions neurons in the human brain," he says. "Our great hope is that as this study advances and is applied more broadly in the worm's nervous system and in other organisms, we will one day be looking at genetic therapies based on synthetic brain rewiring as possible treatments for devastating brain disease and damage."

More information: Ithai Rabinowitch et al. Circumventing Neural Damage in a C. elegans Chemosensory Circuit Using Genetically Engineered Synapses, *Cell Systems* (2021). DOI: 10.1016/j.cels.2020.12.003

Provided by Hebrew University of Jerusalem