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CREDIT: CHRISTOPHER NEUGEBAUER
Stainless steel sculpture "Neuron" by Roxy Paine. Outside the Museum of Contemporary Art, Sydney

NOT EXACTLY ROCKET SCIENCE: 14 hours ago

Neurons Could Outlive the Bodies That Contain Them

by Ed Yong

Most of your body is younger than you are. The cells on the topmost layer of your skin are around two weeks old, and soon to die. Your oldest red blood cells are around four months old. Your liver's cells will live for around 10 to 17 months old before being replaced. All across your organs, cells are being produced and destroyed. They have an expiry date.

In your brain, it's a different story. New neurons are made in just two parts of the brain—the hippocampus, involved in memory and navigation, and the olfactory bulb, involved in smell (and even then only until 18 months of age). Aside from that, your neurons are as old as you are and will last you for the rest of your life. They don't divide, and there's no turnover.

But do neurons have a maximum lifespan, just like skin, blood or liver cells? Yes, obviously, they die when you die, but what if you kept on living? That's not a far-fetched question at a time when medical and technological advances promise to prolong our lives well past their usual boundaries. Would we reach a point when our neurons give up before our bodies do?

Lorenzo Magrassi, a neurosurgeon at the University of Pavia, thinks not. He recently transplanted neuron-making cells from mouse embryos into the developing brains of longer-lived rats. These cells matured into neurons that looked like mouse neurons… but with rat lifespans. They survived for up to 36 months, around twice as long as they normally do in their native mouse brains.

"Neurons do not have a fixed lifespan," says Magrassi. "They may survive forever. It's the body that contains them that die. If you put them in a longer-living body, they survive as long as the new body allows them to. It increases our hope that extending lifespan will not necessarily result in brain depleted of neurons."

Magrassi worked with genetically modified mouse embryos whose cells all produce a glowing green protein, and could be easily tracked. From these embryos, he removed the precursors of brain cells, and transplanted them into rat embryos. In their new hosts, the green glow of these foreign cells gave away their presence, and that of any of their descendants.

The transplanted cells survived in around a third of the rats. They produced many types of mature brain cells, including several classes of neurons and supportive cells called glia. The neurons hooked up with their rat counterparts while staying true to their mouse origins in terms of size and shape.

Their lifespans, however, shot up. Magrassi focused on Purkinje cells—a class of large, bushy, many-branching neurons that are involved in controlling movements. These cells spontaneously die during ageing, in both humans and rodents. But while their donor mice live for around 18 months, and 26 at the most, the transplanted Purkinje cells lived for as long as their new rat hosts did—around 30 months, and 36 at the most. Their maximum lifespan went up by 38 percent. Their branches thinned with time, but they didn't die.

For perspective, while some exceptional mice lead very long lives, there is no artificial way of extending an entire mouse's life by 38 percent—not through good diets, drug treatments, or genetic engineering.

Diana Woodruff-Pak, a neuroscientist from Temple University, is certainly impressed.

"Purkinje neurons are the most vulnerable of neurons and one of the few kinds lost in normal ageing," she says. "To extend the life of mouse Purkinje neurons is remarkable."

But Judith Campisi, who studies ageing at the Buck Institute in California, is not surprised by the study's results. "The idea that an organism dies when its cells die is not mainline thought in ageing research," she says. "If you take a neuron from a mouse and put it in an elephant, would you really expect that neuron to live for2.5 years?" She thinks not. "Most people die with most of their neurons intact. If you live to 123, you'll die with much of the cells you were born with."

But Magrassi says that the idea that extending lifespan would lead to a neuronally impoverished brain was a "generalised belief until quite recently". And the evidence to the contrary—like the fact that very old people still have most of their neurons—has been indirect. His experiments provide more direct confirmation that neurons don't have some fixed lifespan, set by their genes. Instead, it's their environment that determines when they die.

Magrassi doesn't think that the rat brain provides anything special that the mouse brain lacks. It's the same proteins at work in both rodents, but presumably deployed to different rhythms. (And Woodruff-Pak suspects that the rats' own glia are working to support the mouse Purkinje neurons and extend their lives.)

The team are now dissecting the transplanted cells to understand why they live longer in rats. "If we discover what factor or factors are responsible, we may hope to use them in those diseases when neurons start to die much earlier," says Magrassi. "Of course, there is still a long way to go."

Reference: Magrassi, Leto & Rossi. 2013. Lifespan of neurons is uncoupled from organismal lifespan. PNAS http://dx.doi.org/10.1073/pnas.1217505110

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