'Noisiest' neurons persist in the adult brain

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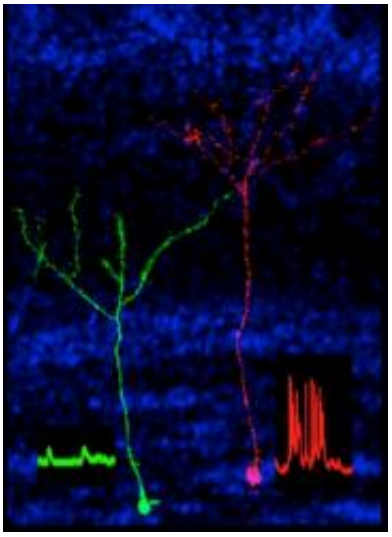

Neurons genetically rendered hyperactive (red) survive better than normal neurons (green). Traces at bottom of the image show the electrical activity of genetically-manipulated neurons (red trace) and normal neurons (green trace). Photo - Image courtesy of Carlos Lois

(PhysOrg.com) -- MIT neuroscientists have discovered that when it comes to new neurons in the adult brain, the squeakiest wheels get the grease.

"Before, scientists believed the cells with the most accurate performance were selected and the others were rejected," said Picower Institute for Learning and Memory researcher Carlos Lois. "Our study shows that it doesn't matter what the cells are doing, as long as they are doing something, even if it is wrong. It's like musicians being chosen in an

audition based not on how well they play, but how loudly."

Neuronal survival is a key component to the success of cell replacement therapies in the brain. Current therapies have hit a roadblock because the vast majority of grafted cells do not survive and do not integrate into adult brain circuits. "Our discovery of a survival-determining mechanism in new neurons is likely to have a significant influence on such treatments," said Lois, Edward J. Poitras Assistant Professor in Human Biology and Experimental Medicine at the Picower Institute.

In addition, the observation that the "noisiest" neurons have a survival advantage helps explain the prevalence of epilepsy, in which some neurons become hyperactive and fire in an uncontrollable fashion. "Our work suggests that any perturbation that increases the activity of neurons will enhance the likelihood of their survival. Thus, during childhood, when many neurons are still being added to the brain, it is likely that neurons that become pathologically hyperactive will be preferentially selected for survival, and these abnormal neurons will be the trigger for epilepsy," Lois said.

To investigate whether activity levels—and the source and pattern of activity—are crucial in governing whether an individual new neuron survives or dies, the researchers used new technology to genetically enhance or dampen the electrical excitability of single adult-generated neurons. An important technological advance, the methods used in this study allow for single-cell genetic manipulation of electrical activity in living animals.

Investigating the molecular signals launched by neuronal activity will potentially lead to new drugs that bolster the survival of new neurons. These drugs could be used to increase the efficacy of treatments that depend on grafting stem cell-derived neurons into the adult brain to treat neurological diseases such as Parkinson's and Alzheimer's.

More information: "Genetically increased cell-intrinsic excitability enhances neuronal integration into adult brain circuits," by Chiawei Lin, Shuyin Sim, Masayoshi Okada, Alice Ainsworth, Wolfgang Kelsch and Carlos Lois in Neuron, published Jan. 14, 2010.

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