Human cerebellum, cortex age in different ways

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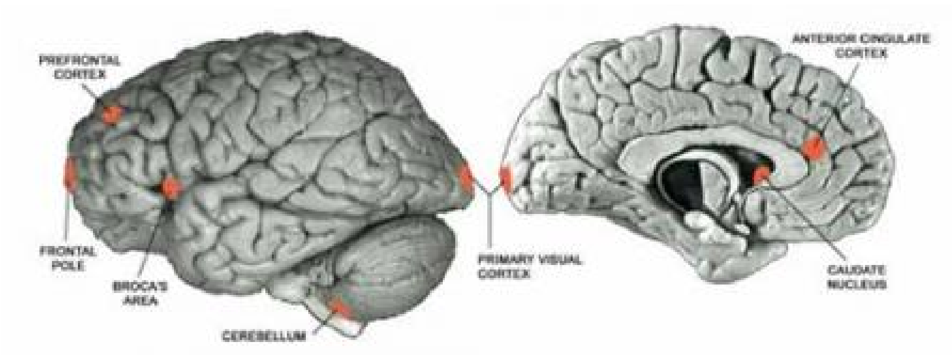
Researchers have found that the two primary areas of the human brain appear to age in radically different ways. The cortex used in higher-level thought undergoes more extensive changes with age than the cerebellum, which regulates basic processes such as heartbeat, breathing and balance.

Their work, based on an analysis of gene expression in various areas of human and chimpanzee brains, also shows that the two species' brains age very differently, despite their close evolutionary relationship.

The research, by scientists at the University of California, Berkeley, Lawrence Berkeley National Laboratory, Harvard University and the Max-Planck-Institute for Evolutionary Anthropology, will be reported this week in the open-access journal PLoS Biology.

"Much remains to be learned about how the brain ages and how changes in gene expression over time are related to brain activity," said Michael B. Eisen, assistant professor of molecular and cell biology at UC Berkeley. "Our analyses suggest that the different functions of different regions of the brain influence how they age, and that we can learn about functional variation and evolution by studying gene expression changes with age."

"We were surprised both by the homogeneity of aging within the cortex and by the dramatic differences in aging between cortex and cerebellum," said Joshua B. Plotkin, a junior fellow in the Harvard Society of Fellows. "The fact that gene activity levels in the cerebellum remain more stable as a person ages suggests that this region of the brain experiences less oxidative stress and damage as part of normal aging."



Scientists compared gene expression in the brains of humans of different ages and of a chimpanzee, focusing on seven regions (red): the anterior cingulate cortex, Broca's area, the caudate nucleus, the cerebellum, the frontal pole, the prefrontal cortex, and the primary visual cortex. (Michael Eisen/UC Berkeley & LBNL)

The researchers used data from gene chips to look at gene expression - the degree to which various genes are turned "on" and "off" - in five different regions of the brain's cortex. They found that in all five cortical areas, brain changes with aging were pronounced and consistent. Changes in gene expression in the cerebellum were smaller and less coordinated.

The study by Eisen, Plotkin, UC Berkeley graduate student Hunter B. Fraser, and Philipp Khaitovich and Svante Paabo from the Max-Planck-Institute in Leipzig, Germany, is one of many conducted to date on the question of how gene expression changes across the human lifespan, but the first to examine how the two major brain areas age differently. Scientists had also not previously compared the effects of aging on the brains of humans and other primates.

"The fact that chimpanzees' brains age so differently from our own suggests that our closest evolutionary relatives may use their brains very differently than we do," Plotkin said. "It appears that genome-wide patterns of aging evolve very rapidly."

The scientists say their results may cast some doubt on the effectiveness of mice and other species to model various types of neurodegenerative disease. If human and chimpanzee brains age in markedly dissimilar ways, the difference between humans and more distantly related species is likely greater yet.

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Source: UC Berkeley