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Using fMRI to study brain development

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Functional magnetic resonance imaging (fMRI) is a powerful noninvasive tool for studying brain activity in both humans and experimental animals. Most fMRI studies are carried out on adults, but this technique also has great potential for studying early brain development. That potential is hampered, however, by a lack of knowledge about the basis of the fMRI signal in the developing brain.

Now, by studying rats, MIT neuroscientists show that the fMRI signal changes during first few weeks of life. By correcting for those changes, the researchers were able to monitor the development of the rat brain. Determining whether analogous changes occur in humans will be important for interpreting developmental fMRI studies in young children.

“Our study lays a foundation for using fMRI to study development,” explains senior author Alan Jasanoff, Associate Member of the McGovern Institute and Assistant Professor of Nuclear Science and Engineering . “It establishes an approach that others can apply to investigate many aspects of neurodevelopment in very young animals.” Jasanoff collaborated with the lab of developmental biologist Martha Constantine-Paton, a McGovern Institute Principal Investigator. The study was published online November 25, in the journal *Nature Neuroscience*.

A fundamental difficulty in interpreting fMRI is that it provides only an indirect readout of brain activity, based on changes in the brain’s blood supply. Increases in brain activity cause increased blood flow, but the

coupling mechanism that links these two processes is itself subject to change in early life. Thus, a weak fMRI signal in young animals could mean less neural activity, or it could simply mean that MRI cannot detect that activity because of weak neurovascular coupling.

To resolve this uncertainty, Jasanoff and colleagues compared fMRI signals with direct electrical recordings of neuronal activity as they stimulated rats' forepaws. In animals younger than 11 days, they could not detect fMRI signals, even though electrical recordings showed that the brain was responding to stimulation. The fMRI signals became both stronger and faster as the animals matured, until they approached adult levels by about 3 weeks of age. This corresponds approximately to 7-8 years in terms of human brain development.

By compensating for these age-related changes, the authors were able to track the development of connections between different touch-sensitive brain regions as the animals matured.

The researchers also investigated what molecular events might underlie the changing relationship between neural activity and the blood response. Their findings suggest that a key player is carbonic anhydrase (CA), a well-known enzyme that helps remove carbon dioxide from the blood. Age-related increases in CA activity corresponded to the changes in the fMRI signal, and drugs that block the activity of this enzyme in adult animals caused the fMRI signal to "regress" to that seen in younger animals. CA is an important target for drugs used to treat diverse conditions, including glaucoma, altitude sickness and epilepsy, so it will be interesting to determine whether such drugs alter the relationship between activity and blood flow in the adult human brain.

In the longer term, Jasanoff hopes to circumvent the difficulties of fMRI altogether, by developing new methods that will make it possible to visualize neural activity directly, rather than indirectly through its effect

on blood flow.

Source: McGovern Institute for Brain Research