Brain Changes FROM CHILDHOOD TO ADULTHOOD

Researchers study shifting brain regions in children and adults

by Candace O'Connor

On his computer screen, Bradley Schlaggar, MD, PhD, can play a graphic version of changes that take place in the human brain between childhood and maturity. He has color-coded the brain regions—black, yellow, red, and blue—according to their function in performing different tasks. In an eight-year-old child, these regions are largely bound together and "talking" in one large, gregarious, clique-type network.

But as time goes on, this picture changes, as regions realign and acquire new "friends." When a child is around age 13, the red regions pull away and become an integrated unit. One important region for cognition, the dorsal anterior cingulate cortex, moves away from its yellow companions and settles at the heart of another network. By the time humans are in their twenties, the last connections break between yellow and black.

The shifting life of the brain, in which regions—like social groups—form new allegiances over the years, came as a surprise to Schlaggar and Steven Petersen, PhD, whose study results recently appeared in the scientific journal *Proceedings of the National Academy of Sciences*. Their description of brain changes not only redefines the development of normal brain structure but also may shed light on network malfunction in attention deficit hyperactivity disorder (ADHD), autism, Tourette's syndrome, and other neurological disorders.

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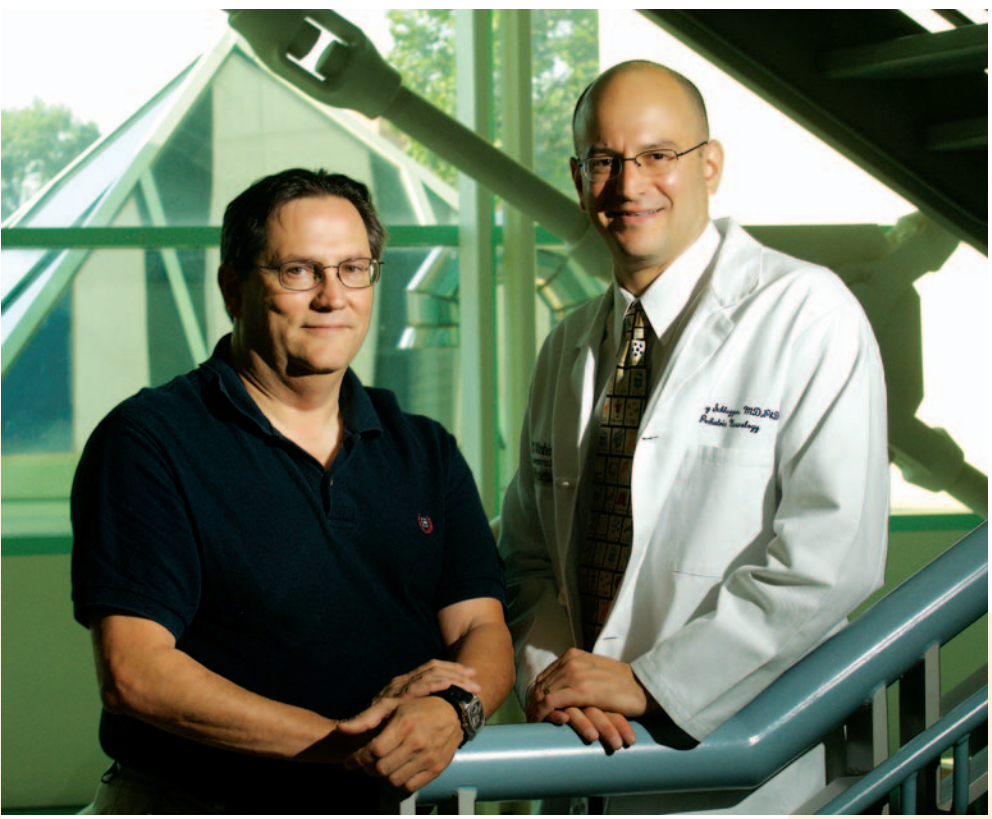
By adulthood, says Schlaggar, the brain regions have completely re-formed into two distinct, control networks—a finding they made in an earlier study also published in *Proceedings*. The cingulo-opercular (or sustaining) network is the stable player, active during sustained mental activities, while the frontoparietal network is the adaptive piece, allowing a person to change behavior in response to a problem.

"These studies provide a conceptual framework for thinking about how executive control emerges in typically developing people," says Schlaggar, an assistant professor of neurology, who holds joint appointments in radiology, pediatrics and anatomy, and neurobiology. "That framework is critical because we've been dealing with a literature that has reached a plateau in terms of new insights. This gives us a new injection of energy that I think will take us beyond where we've been previously."

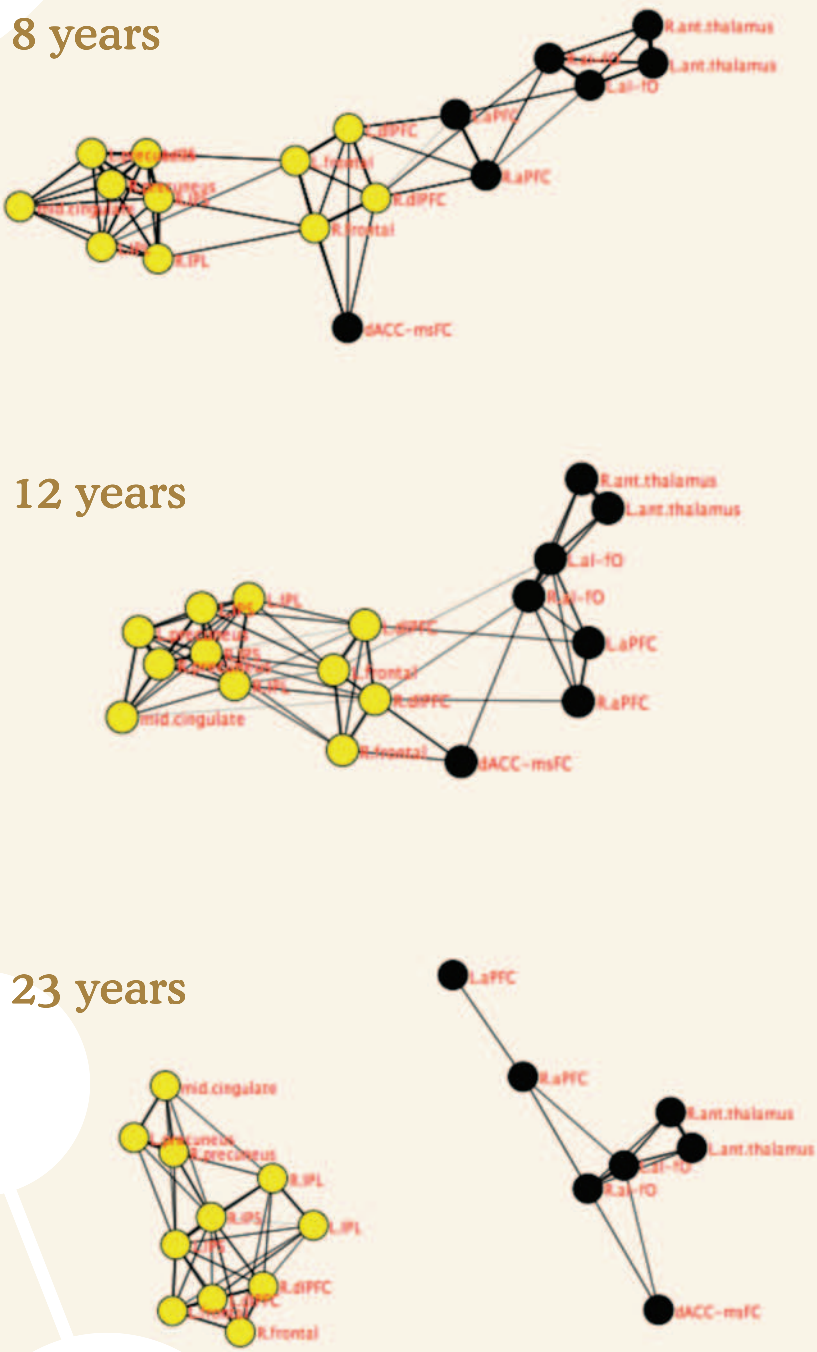
The Research Study

For his study of brain development, Schlaggar recruited three groups of participants: 49 children ages seven to nine, 43 adolescents, and 47 adults over 21 years of age. Instead of asking them to perform a certain task or to answer specific questions (often the way studies have been done in the past), he had participants relax and engage in ordinary reflection or free-ranging thought.



Steven Petersen, PhD, and (right) Bradley Schlaggar, MD, PhD

Resting state functional connectivity MRI reveals the developmental dynamics of the brain's control networks. The fast/adaptive (yellow) network and the slow/maintenance (black) network segregate and integrate over the course of development.



"When you are in any sort of active situation, the parts of your brain that are doing the work are contingent upon the situation," says Petersen, a professor of neurology and psychology with a joint appointment in radiology. "But when you let the system relax to its free-ranging state, we think that the regions that talk to each other at rest are the ones that talk to each other most over time."

To study the brains of these research participants and to identify the control networks, Schlaggar used functional magnetic resonance imaging (fMRI), which measures, indirectly, regional brain activity. If activity in two regions of the brain correlate during this resting state, they likely are functionally connected.

"Here are two brain regions, on opposite sides from each other—activity for one is shown in yellow and the other in blue," says Schlaggar. "These are two highly correlated regions. The yellow trace is almost entirely mimicked by the blue trace."

When Schlaggar and Petersen looked closely at these correlations, what they found was a shock. Their first study, postulating that there were two control networks in adults, had shown no connectivity between the two. But in children there is marked connectivity. In fact, the two networks, which have not yet differentiated, are in active conversation as a single amalgam of regions. In adolescents, the brain regions are in an intermediate state.

Further, within this single clique in children, the cingulo-opercular network is buried within the frontoparietal network What could that mean? While any answer is speculative, it may mean that the sustaining network is simply less well-developed than is the adaptive—a possible explanation for the short attention span and distractibility of young children.

Reflections on the Study

When they began this experiment, the scientists had no fixed hypothesis, and their research approach was strictly observational. In fact, they were even uncertain about the value of the experiment. "But the result popped out," says Schlaggar, "and it alleviated our skepticism."

"We think these networks are real, they are important, and if we are going to understand the complex processing that is going on in the brain, that's going to require not just focusing on one region but on networks of regions and on how they change in response to development or disease," says Schlaggar.

They have adopted metaphors, such as "cliques," to describe the brain's alignment because they borrowed the applications they use to investigate these networks from scientists who study social networking. "We're using software, visualization tools, and mathematics that come from investigators who have been studying social systems in trade networks, economic systems, even Internet connections," says Petersen.

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What distinguishes their work from studies by earlier investigators, they say, is that they are not looking at activity in individual regions but at *networks* of regions. For example, scientists have previously examined brain activity in children with ADHD and without it, with each group given tasks that require close attention. Researchers then compared differing activity in a small number of brain regions.

Earlier work by Mallinckrodt Institute researchers, particularly Marcus Raichle, MD, a professor of radiology and an internationally acclaimed neuroscientist, has also informed Petersen's and Schlaggar's efforts. Raichle's pioneering use of functional imaging to look at brain function while the patient is at rest has driven a new wave of scientific inquiry nationally, says Schlaggar and Petersen. The interdisciplinary nature of research at Mallinckrodt Institute—locating radiologists next to neurologists, psychiatrists, neurobiologists, and anatomists—also is vitally important.

"At the Cognitive Neuroscience Society meeting last May, the buzz about the approach we are using was the most focused attention I have seen," says Schlaggar. "It has a lot of advantages. For one thing, studying the brain (that is, without an overt task) unburdens you from having research participants—some who have ADHD or dyslexia—from performing tasks in the magnetic resonance scanner, which is difficult for them and makes it difficult to interpret the imaging results in comparison to participants who find the same tasks easy."

Still, more questions remain. What about the sleeping brain? Is it in a free-ranging state similar to its waking mode? Does gender make any difference to brain changes? So far Schlaggar and Petersen have looked at only three dozen or so regions of the brain. What about other regions involved in memory and language?

Schlaggar also is undertaking a follow-up study of teen-agers with Tourette's syndrome, to see whether their networks and the relationships between them differ from those of teens without Tourette's. Half of the Tourette's-afflicted teens also have ADHD, and Schlaggar will study their brains to see whether the control networks are impaired.

"What's more, there is no reason to think that young adulthood is a stable place," says Petersen. "In humans from age twenty seven to ninety, we could still continue to see these dynamics and perhaps the degradation of some networks. There is not going to be any epoch in which the brain is not dynamic." MIR