Lifespan maturation of the human brain

Properties of human brain tissue change across the lifespan. In a recent research, ELSC scientist model these changes in the living human brain by quantitative magnetic resonance imaging (MRI) measurements.

We are born and die with brains not working at full capacity. Throughout our early lives protective layers of fat wrap nerves and help them fire more efficiently. That maturation reaches a peak at around age 40, then begins to unravel. By the end of life, our brain’s fat levels return to about where they were at age 7.

So finds a team of Stanford psychologists who have for the first time shown how brain composition changes throughout life. Knowing what’s normal at different ages, doctors can now image a patient’s brain, compare it to this standard curve and be able to tell if a person is out of the normal range, much like the way a growth chart can help identify kids who have fallen below their growth curve. They’ve already used the technique to identify previously overlooked changes in the brain in people with multiple sclerosis.

“This allows us to look at people who have come into the clinic, compare them to the norm and potentially diagnose or monitor abnormalities due to different diseases or changes due to medications,” said Jason Yeatman, a graduate student in psychology and first author on a September 17th paper in Nature Communications. Aviv Mezer, a research associate, was senior author on the paper. Both collaborated with Professor Wandell and his team of researchers in the Department of Psychology.

For decades scientists have been able to image the brain using magnetic resonance imaging (MRI) and detect tumors, brain activity, or abnormalities in people with some diseases, but those measurements were all subjective. A scientist measuring some aspect of the brain in one lab couldn’t directly compare findings.
with someone in another lab. And because no two scans could be compared, there was no way to look at a patient’s image and know whether it fell outside the normal range.

“A big problem in MRI is variation between instruments,” Mezer said. Last year Mezer and Wandell led an interdisciplinary team to develop a technique that can be compared quantitatively between labs, published in Nature Medicine. “Now with that method we found a way to measure the underlying tissue and not the instrumental bias. So that means that we can measure 100 subjects here and Jason can measure another 100 in Seattle (where he is now a postdoctoral fellow) and we can put them all in a database for the community.”

The technique the team had developed measures the amount of fat, or white matter, in the brain. That white matter comes primarily from an insulating covering called myelin that allows nerves to fire most efficiently and is a hallmark of brain maturation, though the white matter can also be composed of other types of cells in the brain.

White matter plays a critical role in brain development and decline, and several diseases including schizophrenia and autism are associated with white matter abnormalities. Despite its importance in normal development and disease, no metric existed for determining whether any person’s white matter fell within a normal range, particularly if the people were imaged on different machines.

Mezer and Yeatman decided to use the newly developed quantitative technique to develop a normal curve for white matter levels throughout life. They imaged 24 regions within the brains of 102 people aged seven to 85 and from that established a set of curves showing the increase and then eventual decrease in white matter in each of the 24 regions throughout life.

What they found is that the normal curve for brain composition is rainbow-shaped. It starts and ends with roughly the same amount of white matter and peaks between ages 30 to 50. But each of the 24 regions changes a different amount. Some parts of the brain like those that control movement are long, flat arcs, staying relatively stable throughout life.

Others, like the areas involved in thinking and learning are steep arches, maturing dramatically and then falling off quickly. (The group did point out that their samples started at age seven and a lot of brain development had already occurred).

“Regions of the brain supporting high level cognitive functions develop longer and have more degradation,” Yeatman said. “Understanding how that relates to cognition will be really important and interesting.” Yeatman is now a postdoctoral scholar at the University of Washington, and Mezer is now assistant professor at the Hebrew University of Jerusalem. They plan to continue collaborating with each other and with other members of the Wandell lab, looking at how brain composition correlates with learning and how it could be used to diagnose diseases, learning disabilities or mental health issues.

Wandell has had a particular interest in studying the changes that happen in the brain as a child learns to read. Until now, if a family brought a child into the clinic with learning disabilities, Wandell and other scientists had no way to diagnose whether the child’s brain was developing normally, or to determine the relationship between learning delays and white matter abnormalities.

“Now that we know what the normal distribution is, when a single person comes in you can ask how their child compares to the normal distribution. That’s where this is headed,” said Wandell, who is also Isaac and Madeline Stein family professor and a Bio-X affiliate. Wandell runs the Center for Cognitive and Neurobiological Imaging, where the Mezer and the team developed the MRI technique to quantify white matter, and where the scans for this study were conducted.
The group has already shown that they can identify people with multiple sclerosis as falling outside the normal curve. People with MS develop what are known as lesions—regions in the brain or spinal cord where myelin is missing. In this paper, the team showed that they could identify people with MS as being off the normal curve throughout regions of the brain, including places where there are no visible lesions. This could provide an alternate method of monitoring and diagnosing MS, they say.
