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**Speaking of Science** 

## Researchers just doubled what we know about the map of the human brain

## By Amy Ellis Nutt July 20

Scientists like to say the human brain is the most complex object in the universe — three pounds of fluid and tissue, about which we understand only a fraction.

That fraction just grew dramatically.

In a <u>study</u> published Wednesday online in Nature, a team of researchers more than doubled the number of distinct areas known in the human cortex, from 83 to 180. This new map of the brain combines data from four different imaging technologies to essentially bring high-definition to brain scanning for the first time.

The immediate implications, say those familiar with the results, include the possibility of identifying biological markers for a host of neurological diseases and mental illnesses, and the new knowledge may aid neurosurgeons who need to know exactly what sort of tissue they are operating on.

"We may really have within our grasp a fairly straight-forward, non-invasive technique ... of using brain imaging as a biomarker at an individual level," said Greg Farber, director of the Office of Technology Development and Coordination at the National Institute of Mental Health, who was not involved in the study. "It's like taking an X-ray of a broken arm: it doesn't take a genius to see where the break is. But in brain imaging we haven't had anything that works at all for mental illness, substance abuse, aging." An international team led by Matthew Glasser and David Van Essen at Washington University in St. Louis scanned the brains of 1,200 young adults using four techniques: magnetic resonance imaging, or MRI, which reveals the structure of the brain; functional MRI, or fMRI, which registers brain activity, when the subjects were resting; task-based fMRI, which registers activity while the subjects were engaged in mental exercises; and diffusion imaging, which reveals the paths of neurons and shows how the brain is "wired." By aligning the brain areas in those 1,200 subjects using the combined scanning protocol, the researchers achieved an extraordinary degree of precision. The work was funded by the National Institutes of Health as part of the Human "Connectome" Project, referring to the connections within the brain.

"If things aren't aligned, the features will be blurry," said Glasser, who likened the difference between the old and new cortical maps to the difference between observing the night sky with a ground telescope vs. one in space.

"Stars twinkle because of turbulence in the universe," he said, "but if you put a telescope in space, there's no atmosphere so you don't have that blurring. If you're not aligned, it's like twinkling. ... If they are, you just get a much sharper image."

The magnitude of the breakthrough can be measured against how long it took to get here. The cortical map used most frequently today by both researchers and clinicians is essentially the same one developed more than 100 years ago by anatomist Korbinian Brodmann. The German scientist delineated almost 50 basic brain regions, several of which bear his name. In the decades between then and now, the number only increased incrementally to 83.

Glasser and Van Essen's team have developed an algorithm that will now make their data collection protocol available to researchers and clinicians around the world.

"These are discrete areas that have unique fingerprints," said lead author Glasser, "meaning anybody who gets an MRI scan [the doctor or researcher] will be able to find the same cortical areas."

Accuracy was critically dependent on finding a new method of comparing brains. Up until now, that method was largely dependent on comparing the complex folding patterns in gray matter.

"But every person's brain is folded differently," Van Essen said. "You can't align [brains] by relying on a particular fold."

Instead of comparing folds, the team relied on measures that included not just cortical topography, but thickness, white matter content and activity.

"Being able to discriminate differences, say, in location and size as well as connectivity," Glasser said, "means investigators will know if we're talking about the same thing, as opposed to a neighboring area."

Both researchers cautioned that there remains much to be learned, primarily understanding the functioning of these new brain regions. One of the newly identified areas, called 55-B, is in the frontal cortex, Van Essen said, and is "very distinctive in language-related tasks, in contrast to neighboring areas of eye movement control. It's part of a language network that includes much better studied regions in the frontal lobe," including both Broca's area, known for more than a century to be involved in speech production, and Wernicke's area, which is involved in understanding language.

"So what we've done is add a new area, 55-B, to the language network that had been overlooked because it was small and essentially blurred out in previous maps," Van Essen said.

This recent breakthrough also changes the game at a more fundamental level by introducing uniformity in a discipline that sorely needs it.

"Up until now people who were doing MRI imaging tended to be a sort of a cottage industry," Farber said. "There were a lot of different ways to collect similar data and all were a little different because there was no clear gold standard."

Farber says neuroscientists are "paying attention."

"With things widely available we're seeing the research community really settle on this as the preferred method of data collection. And now their data will also be consistent."

Glasser calls this new mapping technique version 1.0, meaning there are many refinements still to come, but for Farber at least, even version 1.0 "goes to show how powerful this may end up being."