NEWS

High-resolution model showcases brain anatomy

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Researchers have sliced a human brain into more than 7,400 slivers, and stained and scanned them to create '**BigBrain**,' the most detailed three-dimensional (3D) map of a human brain to date, they reported 21 June in *Science*[1].

"Before, we could look at the level of cities and now we can look at the level of houses," says the study's co-lead investigator **Alan Evans**, professor of neurology and psychiatry at McGill University in Montreal, Canada. "We can't look at the level of the people in the house — the individual neurons — but we can look at the organization of streets and houses."

German neurologist Korbinian Brodmann may have launched the field of modern brain mapping at the start of the 20th century, when he divided the outer layer of the brain, the cerebral cortex, into 52 regions by structure and cell type.

People still refer to Brodmann areas today, but data from BigBrain may help create a better, more finely tuned labeling system, Evans says.

"This dataset will allow us to completely overhaul our understanding of cortical anatomy," he says.

BigBrain can serve as a reference for how a typical brain looks, but it may be several years before the autism community finds it useful.

In order to take advantage of the reference brain, researchers would need to analyze a brain from a person with autism using the same technique — and not just one brain, either.

"One would immediately need multiple individuals so one could get a sense of variance that occurs in autism," says **John Allman**, professor of neurobiology at the California Institute of Technology in Pasadena, who was not involved with the study.

In the meantime, Evans and his colleagues invite researchers to study the anatomy of BigBrain online and annotate the characteristics, cells and structures found in each slice. The more shared annotations it generates, the more useful it is likely to be, they say.

Brain assembly:

The researchers took four years to create BigBrain. They began by scanning the brain of a living 65-year-old woman using magnetic resonance imaging (MRI). After her death they preserved her brain, then embedded it in wax and sliced it into thousands of 20-micron thick sections.

The view that results for each section provides 50 times greater detail than that of an MRI scan, Evans says.

Some of the slices became crumpled or torn during handling, but researchers scanned them into a computer and reconstructed them based on the woman's MRI scans.

"The real advance is that they collected all of these sections and they dealt with all of the distortions and problems that occur in them," says **Mike Hawrylycz**, director of modeling, analysis and theory at the Seattle-based Allen Institute for Brain Science. "And they were able to reassemble them into a 3D object using a computer technique."

The **Allen Institute for Brain Science** has produced a **gene expression map** of the human brain based on 15- and 50-micron-thick slices. The BigBrain model, in contrast, looks only at anatomy.

The two models are complementary, however.

"The human brain data that we've generated from a molecular point of view can certainly be overlaid on top of this atlas," says **Ed Lein**, director of human cell types at the Allen Institute.

The new model is likely to be of limited application in the autism field, however.

Locating brains from individuals with autism and preparing them using the BigBrain technique would be time-consuming and expensive, notes Allman, who studies autism characteristics in postmortem brains.

Researchers would need to **collect brains from people** who had no medical conditions, aside from autism, that affect brain structure. They would need information about the donors' genetics, physical features and behaviors to understand how these might correlate with the characteristics of the brains postmortem.

"The sad reality is when an individual with autism dies, right now the most likely thing is that the brain will just be lost, because a very small fraction of them go to autopsy," Allman says.

In any case, assembling a 3D model of a brain from an individual with autism may not be the best way to advance research on the disorder, says **Ricardo Dolmetsch**, associate professor of neurobiology at Stanford University in California.

"You would need to have a whole bunch of brains, because autism is very heterogeneous," he says.

Still, BigBrain may help autism researchers with their work, Evans says. The functional MRIs that many researchers use produce hazy images that are difficult to interpret, he says.

"You can look at brain function with something like functional MRI, but you want to know what is the underlying architecture of the brain that gives rise to those functional changes that you can see," he says.

REFERENCES:

1. Amunts K. *et al. Science* **340**, 1472-1475 (2013) **PubMed**