Project will map googols of brain circuits

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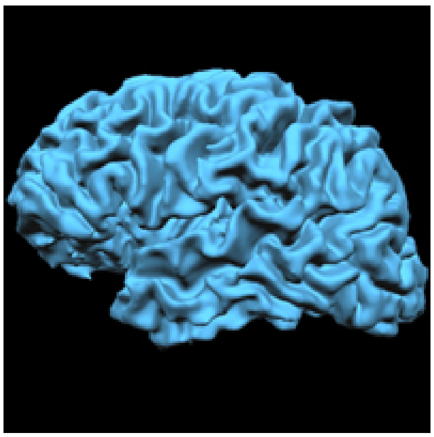

MRI brain scan

The human brain is among the most complex structures in the universe -- and researchers will try to map it in just five years.

A consortium led by scientists at the Washington University School of Medicine and the University of Minnesota has launched a project, dubbed the Human Connectome, that will diagram all the major circuits in a healthy human brain. The effort is the first of its kind and will lay the groundwork for understanding how the human brain functions -- and eventually, how it doesn't.

"This will give us a vastly better understanding of brain connectivity that is sorely lacking," said David Van Essen, head of the department of anatomy and neurobiology at Washington University. "This is the first effort to create a wiring diagram of the brain in a comprehensive way."

The task is staggering. The brain consists of 90 billion neurons, connected by 150 trillion synapses -- the connections that transmit signals from neuron to neuron. These connections make up the pathways that allow one part of the brain to "talk" to another. It is these circuits that the Connectome project will try to map. The Human Genome Project, by comparison, mapped the 3 billion base pair sequences that make up human DNA.

"It's daunting," Van Essen concedes. But promising.

Scientists have long known which parts of the brain control different functions, yet they have been unable to explore pathways from one part of the brain to another. These pathways are the key, researchers believe, to an understanding of what makes one person's brain different from another. They could lead researchers to understand brain-based disorders such as alcoholism, autism or schizophrenia.

"We know a lot about the chemistry of human brains, and the chemistry of animal brains, and quite a bit about the connectivity of animal brains," explained Michael Huerta, an associate director at the National Institutes of Mental Health, a unit of the National Institutes of Health. "But we don't know about the connectivity in the human brain."

Advances in imaging technology will allow researchers to get a better glimpse of these circuits as they work in a live human brain.

Recognizing these advances, Huerta started asking around to see whether research communities were linking research and technologies from place to place. He found they were not.

In an effort to spark a large-scale, coordinated research effort, the NIH launched the Connectome Project and asked researchers to apply for a five-year, $30 million grant.

Van Essen began gathering researchers from universities around the world. "We realized we needed to get a team together in world experts," he said, "and I tried to make it clear that this meant toil and sweat."

Van Essen said reviewers chose the Washington University consortium from a half dozen candidates. The group now includes more than 60 researchers from nine institutions. The award was announced in September, and the consortium has met to begin planning.

"Having this come to St. Louis is just a huge boon for the entire community," said Richard Bucholz, director of the division of neurosurgery at St. Louis University, which will be involved in the research. "It's the biggest neuroscience project the NIH has ever funded."

The first two to three years of the five-year project will focus on the construction of a customized magnetic resonance imaging scanner at the University of Minnesota, which has a research unit that specializes in imaging equipment. That scanner will be sent to St. Louis.

The second phase will consist of recruiting and scanning volunteers. Researchers will look for 1,200 volunteers consisting of twins and two non-twin siblings, so they can compare the brain structures of people who share the same heredity.

The recruitment process will be streamlined because Washington University's Andrew Heath has developed a registry of candidates for other research. This registry was gleaned from Missouri birth records, which means all the volunteers will be Missouri-born.

"We have lots of information on people in the registry," explained Deanna Barch, a professor at Washington University. "We know who to contact, we can hone in on the people that make sense for this project."

Volunteers will be screened on the phone, then asked to submit to a battery of behavioral tests. The idea, Barch explained, is to get a diverse group of healthy brains in the mix. "We want variability," she said. "We want to collect the data that puts us in a good position to understand what's normal."

That will give researchers a baseline for understanding how brain circuits differ in people with mental illnesses, she said.

Volunteers will undergo two days of scanning. Then two smaller groups will go to the University of Minnesota, where they will be scanned with an even more powerful machine, and to St. Louis University, where they will undergo magnetoencephalography, which measures the magnetic fields generated by brain activity. Researchers also will draw blood samples to look at genetic material.

The researchers will map the data they gather in units called voxels -- square-shaped patches of a brain's gray matter, each containing about 1 million neurons. By tracing the cells from one voxel to another, the researchers hope to understand how different regions of the brain work together.

The project is expected to produce at least 1 quadrillion bytes, or one petabyte, of data, which will be stored on a new supercomputer at Washington U. It will be available for free to qualified researchers.

"This is going to be an incredibly rich and complicated data set," Van Essen said.

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Researchers have started their planning but are still celebrating the project, which will likely have long-term impact for St. Louis beyond the five-year time frame.

"To me, this is a home run," Bucholz said. "You put all this together and you have a tremendous consortium. Once it makes these tools, it can apply them here. Our assets would be hard to replicate in other cities."

However, researchers say it could be a long time before they realize the ultimate goal of understanding brain circuitry, how it malfunctions and how disorders can be treated.

"We have to urge the public to be enthusiastic, supportive, but patient," Van Essen said. "Some of these projects will be a century in the making."

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