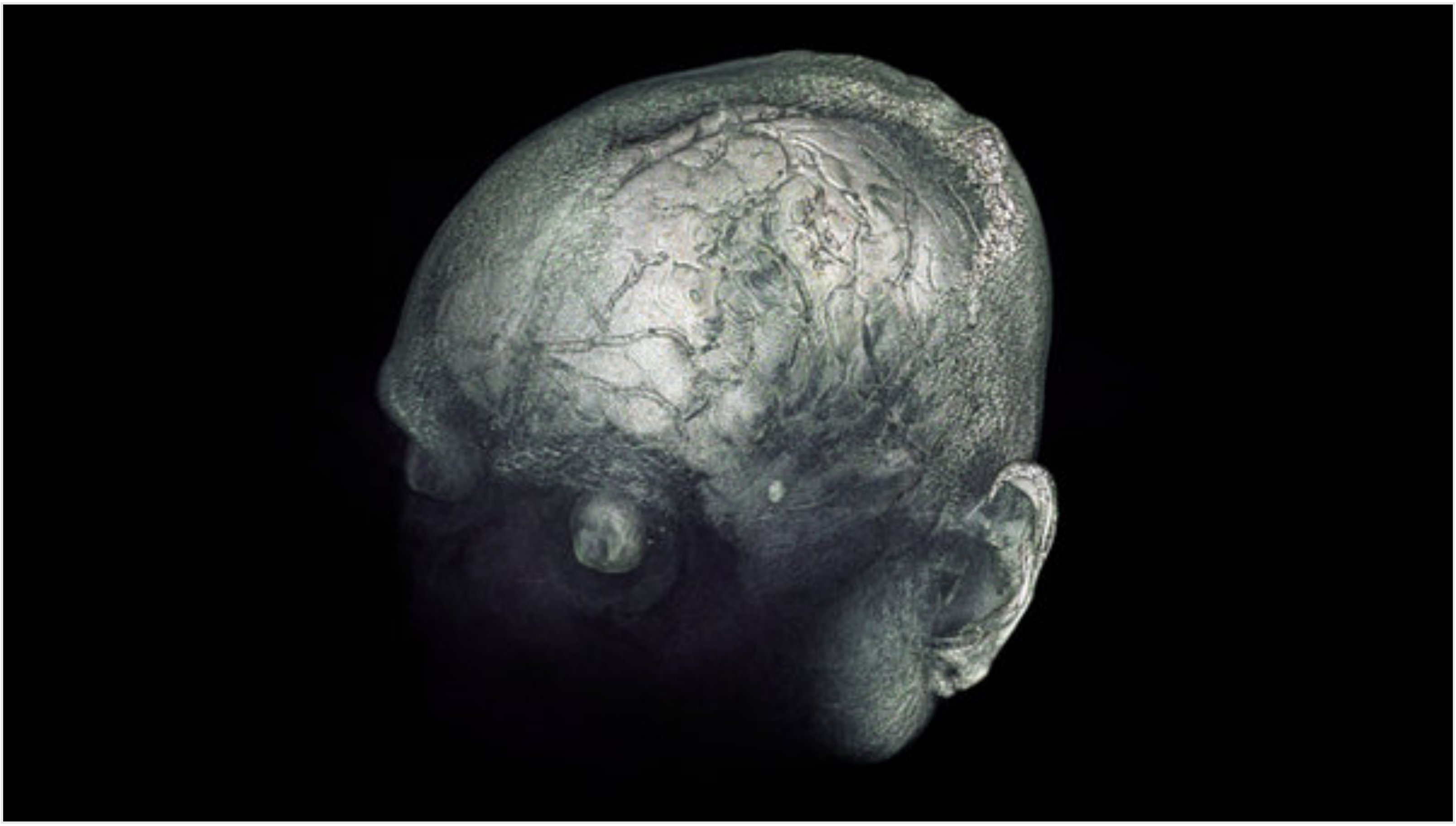
The Brain, in Exquisite Detail



ST. LOUIS — Deanna Barch talks fast, as if she doesn't want to waste any time getting to the task at hand, which is substantial. She is one of the researchers here at Washington University working on the first interactive wiring diagram of the living, working human brain.

To build this diagram she and her colleagues are doing brain scans and cognitive, psychological, physical and genetic assessments of 1,200 volunteers. They are more than a third of the way through collecting information. Then comes the processing of data, incorporating it into a three-dimensional, interactive map of the healthy human brain showing structure and function, with detail to one and a half cubic millimeters, or less than 0.0001 cubic inches.

Dr. Barch is explaining the dimensions of the task, and the reasons for undertaking it, as she stands in a small room, where multiple monitors are set in front of a window that looks onto an adjoining room with an M.R.I. machine, in the psychology building. She asks a research assistant to bring up an image. "It's all there," she says, reassuring a reporter who has just emerged from the machine, and whose brain is on display.

And so it is, as far as the parts are concerned: cortex, amygdala, hippocampus and all the other regions and subregions, where memories, fear, speech and calculation occur. But this is just a first go-round. It is a static image, in black and white. There are hours of scans and tests yet to do, though the reporter is doing only a demonstration and not completing the full routine.

Each of the 1,200 subjects whose brain data will form the final database will spend a good 10 hours over two days being scanned and doing other tests. The scientists and technicians will then spend at least another 10 hours analyzing and storing each person's data to build something that neuroscience does not yet have: a baseline database for structure and activity in a healthy brain that can be cross-referenced with personality traits, cognitive skills and genetics. And it will be online, in an interactive map available to all.

Dr. Helen Mayberg, a doctor and researcher at the Emory University School of Medicine, who has used M.R.I. research to guide her development of a treatment for depression with deep brain stimulation, a technique that involves surgery to implant a pacemaker-like device in the brain, is one of the many scientists who could use this sort of database to guide her research. With it, she said, she can ask, "how is this really critical node connected" to other parts of the brain, information that will inform future research and surgery.

The database and brain map are a part of the Human Connectome Project, a roughly $40 million five-year effort supported by the National Institutes of Health. It consists of two consortiums: a collaboration among Harvard, Massachusetts General Hospital and U.C.L.A. to improve M.R.I. technology and the $30 million project Dr. Barch is part of, involving Washington University, the University of Minnesota and the University of Oxford.

Dr. Barch is a psychologist by training and inclination who has concentrated on neuroscience because of the desire to understand severe mental illness. Her role in the project has been in putting together the battery of cognitive and psychological tests that go along with the scans, and overseeing their administration. This is the information that will give depth and significance to the images.

She said the central question the data might help answer was, "How do differences between you and me, and how our brains are wired up, relate to differences in our behaviors, our thoughts, our emotions, our feelings, our experiences?"

And, she added, "Does that help us understand how disorders of connectivity, or disorders of wiring, contribute to or cause neurological problems and psychiatric problems?"

The Human Connectome Project is one of a growing number of large, collaborative information-gathering efforts that signal a new level of excitement in neuroscience, as rapid technological advances seem to be bringing the dream of figuring out the human brain into the realm of reality.

Worldwide Study

In Europe, the Human Brain Project has been promised $1 billion for computer modeling of the human brain. In the United States last year, President Obama announced an initiative to push brain research forward by concentrating first on developing new technologies. This so-called Grand Challenge has been promised $100 million of financing for the first year of what is anticipated to be a decade-long push. The money appears to be real, but it may come from existing budgets, and not from any increase for the federal agencies involved.

A vast amount of research is already going on — so much that the neuroscience landscape is almost as difficult to encompass as the brain itself. The National Institutes of Health alone spends $5.5 billion a year on neuroscience, much of it directed toward research on diseases like Parkinson's and Alzheimer's.

A variety of private institutes emphasize basic research that may not have any immediate payoff. For instance, at the Allen Institute for Brain Science in Seattle, Janelia Farm in Virginia, part of the Howard Hughes Medical Institute, and at numerous universities, researchers are trying to understand how neurons compute — what the brains of mice, flies and human beings do with their information. The Allen Institute is now spending $60 million a year and Janelia Farm about $30 million a year on brain research. The Kavli Foundation has committed $4 million a year for 10 years, and the Salk Institute in San Diego plans to spend a total of $28 million on new neuroscience research. And there are others in the U.S. and abroad.

Next: Functional connections at a different level. Dr. R. Clay Reid investigates the mouse visual cortex.

To be sure, this is not the first time such a focus has been placed on brain research. The 1990s were anointed the decade of the brain by President George H. W. Bush. Strides were made, but many aspects of the brain have remained mysterious.

There is, however, a good reason for the current excitement, and that is accelerating technological change that the most sanguine of brain mappers compare to the growing ability to sequence DNA that led to the Human Genome Project.

Optogenetics is one new technique that has been transformative. It uses light to turn on different parts of the brain in laboratory animals to open and shut modified genes. Powerful developments in microscopy made possible movies of brain activity in living animals. A modified rabies virus can target one brain cell and mark every other cell that is connected to it.

"There is an explosion of new techniques," said Dr. R. Clay Reid, a senior investigator at the Allen Institute, who recently moved there from Harvard Medical School. "And the end isn't really in sight," said Dr. Reid, who is taking advantage of just about every new technology imaginable in his quest to decipher the part of the mouse brain devoted to vision.

Charting the Brain

Of the many metaphors used for exploring and understanding the brain, mapping is probably the most durable, perhaps because maps are so familiar and understandable. "A century ago, brain maps were like 16th-century maps of the Earth's surface," said David Van Essen, who is in charge of the Connectome effort at Washington University, where Dr. Barch works. Much was unknown or mislabeled. "Now our characterizations are more like an 18th-century map."

The continents, mountain ranges and rivers are getting more clearly defined. His hope, he said, is that the Human Connectome Project will be a step toward vaulting through the 19th and 20th centuries and reaching something more like Google Maps, which is interactive and has many layers.

Researchers may not be looking for the best sushi restaurants or how to get from one side of Los Angeles to the other while avoiding traffic, but they will eventually be looking for traffic flow, particularly popular routes for information, and matching traffic patterns to the tasks the brain is doing. They will also be asking how differences in the construction of the pathways that make up the brain's roads relate to differences in behavior, intelligence, emotion and genetics.

The power of computers and mathematical tools devised for analyzing vast amounts of data made such maps possible. The gathering tool of choice at Washington University is an M.R.I. machine customized at the University of Minnesota.

An M.R.I. machine creates a magnetic field surrounding the body part to be scanned, and sends radio waves into the body. Unlike X-rays, which are known to pose some dangers, M.R.I. scans are considered to be safe. It is one of the few methods of noninvasive scanning that can survey a whole human brain.

There are a variety of ways to gather and interpret information in an M.R.I. machine. And different types of scans can show both basic structure and activity. When a volunteer is trying to solve a memory problem, the hippocampus, the amygdala and the prefrontal cortex are all going to be involved. An M.R.I. machine can detect the direction of information flow, in a technique called diffusion imaging. In that kind of scan, the movement of water molecules shows not only activity, but which way the traffic is headed.

A Path to Research

For Dr. Barch, 48, another kind of interest in the human brain put her on the path to Washington University. "I always knew I wanted to be a psychologist," she said — specifically, a school psychologist. But as an undergraduate at Northwestern, she excelled in an abnormal psychology class, and the professor recruited her to do research.

"When I graduated from college, I decided to become a case manager for the chronically mentally ill for a year to kind of suss out, 'Do I want to do more clinical work or research?' " she said. "That was a great experience, but it really made me realize that research is the only way you're going to have an impact on many lives, rather than sort of individual lives."

She obtained her Ph.D. in clinical psychology at the University of Illinois at Urbana-Champaign. but then did postdoctoral study in cognitive neuroscience at the University of Pittsburgh and Carnegie Mellon University. Her years in graduate school in the 1990s coincided with the development and use of the so-called functional M.R.I., which can show not just static structure, but the brain in action.

"I got into the field when functional imaging was just at its very beginning, so I was able to learn on the ground floor," she said.

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She moved to Washington University after her postdoctoral research partly because of the number of people there working on imaging, including Dr. Marcus E. Raichle, a pioneer in developing ways of watching the brain at work.

As a professor at Washington University and a leader of one of five teams there working on the Human Connectome Project, Dr. Barch focuses her research on the way individual differences in the brains of healthy people are related to differences in personality or thinking.

For instance she said, people doing memory tasks in the M.R.I. machine may differ in competitiveness and commitment to doing well. That ought to show up in activity in the parts of the brain that involve emotion, like the amygdala. However, she points out that the object of the Connectome Project is not to find the answers to these questions, but to provide the database for others to try to do so.

'Pretty Close'

The project at Washington University requires exhaustive scans of 1,200 healthy people, age 22 to 35, each of whom spends about four hours over two days lying in the noisy, claustrophobia-inducing cylinder of a customized M.R.I. machine. Sometimes they stare at one spot, curl their toes or move their fingers. They might play gambling games, or try memory tests that can flummox even the sharpest minds.

"In an ideal world, we would have enough tasks to activate every part of the brain," she said. "We got pretty close. We're not perfect, but pretty close."

Over the two days, the research subjects spend another six hours taking other tests designed to measure intelligence, basic physical fitness, tasting ability and their emotional state.

The volunteers (and they are all volunteers, paid a flat $400 for their time and effort) can also be seen in street clothes, doing a kind of race around two traffic cones in the sunlit corridor of the glass-walled psychology building, with data collected on how quickly they complete the course.

Or they can be glimpsed padding down a hallway in their stocking feet from the M.R.I. machine to an office where a technician dabs their tongues with a swab dipped in a mystery liquid, then asks them to identify the intensity and quality of the taste.

In the same office, they type in answers to cognitive tests, and to a psychological survey, for which they are left in solitude because of the personal nature of some of the questions: how they feel about life, how often they are sad. The results are confidential, as are all the test results.

So far almost 500 subjects have gone through the full range of tests, which amounts to about 5,000 hours of work for Dr. Barch and others in the program.

So far, data has been released for 238 subjects, and it is available to everyone for free through a web-based database and software program called Workbench.

The sharing of data is characteristic of most of the new brain research efforts, and particularly important to Dr. Barch.

"The amount of time and energy we're spending collecting this data, there's no possible way any one research group could ever use it to the extent that justifies the cost," she said. "But letting everybody use it — great!"

The Elusive Brain

No one expects the brain to yield its secrets quickly or easily. Neuroscientists are fond of deflecting hope even as they point to potential success. Science may come to understand neurons, brain regions, connections, make progress on Parkinson's. Alzheimer's or depression, and even decipher the code or codes the brain uses to send and store information. But, as any neuroscientist sooner or later cautions in discussing the prospects for breakthroughs, we are not going to "solve the brain" anytime soon — not going to explain consciousness, the self, the precise mechanisms that produce a poem.

Perhaps the greatest challenge is that the brain functions and can be viewed at so many levels, from a detail of a synapse to brain regions trillions of times larger. There are electrical impulses to study, biochemistry, physical structure, networks at every level and between levels. And there are more than 40,000 scientists worldwide trying to figure it out.

This is not a case of an elephant examined by 40,000 blindfolded experts, each of whom comes to a different conclusion about what it is they are touching. Everyone knows the object of study is the brain. The difficulty of comprehending the brain may be more aptly compared to a poem by Wallace Stevens, "13 Ways of Looking at a Blackbird."

Each way of looking, not looking, or just being in the presence of the blackbird reveals something about it, but only something. Each way of looking at the brain reveals ever more astonishing secrets, but the full and complete picture of the human brain is still out of reach.

There is no need, no intention and perhaps no chance, of ever "solving" a poet's blackbird. It is hard to imagine a poet wanting such a thing. But science, by its nature, pursues synthesis, diagrams, maps — a grip on the mechanism of the thing. We may not solve the brain any time soon, but someday achieving such a solution, at least in scientific terms, is the fervent hope of neuroscience.

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