Unlocking The Brain: Are We Entering A Golden Age Of Neuroscience?

"We still haven't unlocked the mystery of the three pounds of matter between our ears. That knowledge could be — will be — transformative," President Obama said in announcing the BRAIN (Brain Research through Advancing Innovative Neurotechnologies) Initiative on April 2, 2013, at the White House. (Charles Dharapak/AP)

President John F. Kennedy set the nation's sights on the moon. Fifty years later, President Obama announced his signature science project: neuroscience, the study of the brain.

"As humans," he said last April, "we can identify galaxies light years away, we can study particles smaller than an atom, but we still haven't unlocked the mystery of the three pounds of matter between our ears."

The president committed an initial $100 million to BRAIN, an acronym for Brain Research through Advancing Neurotechnologies, to fund the development of better tools for studying how the brain works. “That knowledge could be — will be — transformative,” he said.

Over the next two months, WBUR will present a weekly series about brain science advances — many happening in Boston, a major hub for neuroscience research. Today, the overview.

CommonHealth
The Sounds Of Neurons: Brandeis Neuroscientist Eve Marder Explains:
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If you click the “Play” arrow above, you'll hear the hissy, Morse-Code-on-steroids sound of neurons firing, sending signals to each other.

So is this what a thought of yours would sound like, if it were played through an audio monitor like this? No. What you're hearing is far, far simpler. These neurons belong to a crab; they make up a simple circuit of about 30 neurons that control how it chews and digests food. Their steady, rhythmic cycle is more like what your neurons do to control your breathing.

“Imagine now,” says Brandeis University neuroscientist Eve Marder, “an orchestra with billions of neurons firing in different patterns depending on what you were seeing, what you were hearing, what you were thinking and what you were feeling, so those rhythms would be changing in a tremendous symphony. If you could hear all of the neurons in your brain, it would be very hard to hear patterns, because there would be so many instruments, if you will, playing at the same time. It might sound like a cacophony.”

Making sense of that cacophonous complexity, she says, will be a lot harder than JFK's moon shot.

“Unlike putting [a] man on the moon, where you knew exactly where the goal was and the problem was largely an engineering problem,” she says, “understanding the brain is a series of engineering problems and a series of intellectually creative, imaginative understandings, and it's going to require the coordination of creativity across every scientific discipline that we know.”

But even if we give it everything we've got, can the human brain ever understand itself?

That's the monumental gamble of Obama's BRAIN initiative — and other major neuroscience efforts now getting under way around the world. They're not trying to solve philosophical questions. They're responding to the growing realization that brain disorders — from autism to mental illness to dementia — are a worldwide scourge, affecting at least a billion people.

BrainMATTERS

- Part 1: Unlocking The Brain: Are We Entering A Golden Age Of Neuroscience?
- Part 2: ‘I'm Not Stupid, Just Dyslexic’ — And How Brain Science Can Help
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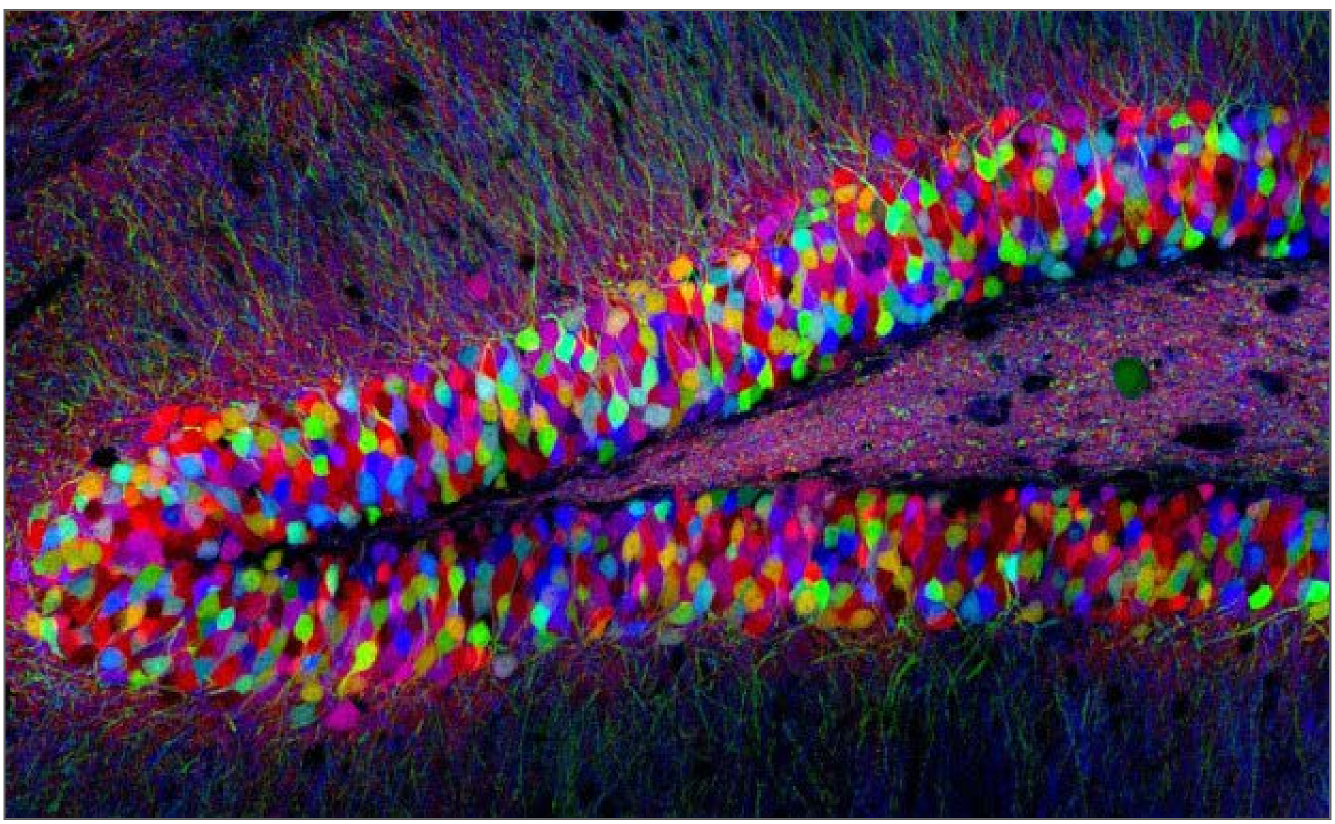
“The global cost from brain disorders is about $2.5 trillion, and will go up more than double over the next two decades,” says Tom Insel, director of the National Institute of Mental Health. “So policymakers look at these numbers and say, ‘Oh my God, we have got to begin investing to make sure we don’t incur those kinds of costs.’ ”

- Brain Images: New Techniques, Bright Colors
- WBUR Series: Brain Matters

Neuroscientists have been studying the brain for more than a century, and better treatments for brain diseases have been desperately needed for a lot longer than that. What’s different now is that for the first time, researchers say, we’re beginning to get a handle on the workings of the brain’s billions of neurons and trillions of connections. We’re starting to understand how groups of neurons interact, in smaller circuits or bigger networks — and that scale, out of reach even just a few years ago, is what we need if we ever hope to understand how we have a thought, or a memory, or a mental illness.

“This is an exciting time to be a neuroscientist. I’m not sure there’s ever been a more exciting time,” Larry Swanson, president of the Society for Neuroscience, told an audience last fall at the society’s annual conference of about 30,000 scientists. “Scientists are advancing the field in ways that we actually couldn’t even imagine say five, 10 years ago, and this is reflected in the tremendous attention that’s being paid to neuroscience not only in the White House and the European Union but really literally around the globe,” he said.

At the conference in San Diego, government science officials touted the importance of an array of new tools for analyzing the brain — much the way a microscope lets us analyze cells, or the telescope helps us understand space.



This is a part of a mouse brain called the dentate gyrus. It is located in the brain’s hippocampus, a region involved in memory formation. This mouse was genetically engineered to express fluorescent proteins of varying color combinations in its neurons. This labeling process, called Brainbow, allows scientists to more easily distinguish individual cells and connections. (Courtesy of Livet, Weissman, Sanes and Lichtman/Harvard University)

They talked up some splashy recent methods to discern brain structure — like the Brainbow, a technique that uses genetics and a rainbow of gorgeous fluorescent colors to map neurons. There's Clarity, a new chemical treatment to make brain tissue transparent, so that it's easier to study big networks of neurons. And there's the Connectome, an evolving map of the trillions of pathways that connect neurons to each other.

"We might be in a golden age of making such tools," says Ed Boyden, a neuroengineer at MIT, "because most fields of engineering had not been applied to the brain, so there's just a gold rush of possibility."

When Boyden was in grad school over a decade ago, he was told not to bother trying to develop better tools for illuminating how the brain works — it was just too complex. But then, he says, "Around 10 years ago, several groups started developing tools that allowed people to map, control and observe the brain with greater precision than before."

Boyden now leads neuroengineering at MIT, and he's the co-creator of one of the hottest of these new technologies: optogenetics. As he explains it, "Optogenetics allows us to activate or shut down cells in the brain with light. That's important because if we can turn on cells in the brain, we can figure out what kinds of behaviors or diseases they contribute to, and by shutting off neurons we can figure out what they're necessary for."

For example, researchers found a small cluster of cells in the mouse brain that, when activated with laser light, caused the mouse to behave so aggressively that it even attacked a nearby rubber glove. Another optogenetics experiment in mice turned on a cluster of cells that triggered a sense of pleasurable reward, a sort of "I want to keep doing that" feeling.

There are a host of other methods in the new brain toolbox: stem cells, computer science for manipulating big data, new ways to engineer and "edit" genes, better brain imaging and microscopy.

And, there's DNA. In 2001, sequencing one person's genome cost about $100 million. Now it's getting close to about $1,000. Researchers are sequencing DNA from tens of thousands of people with mental illnesses, and pinpointing hundreds of genes that raise a person's risk.

"This is absolutely hot-off-the-presses genetic information," says Robert Desimone, director of the McGovern Institute for Brain Research at MIT. "So, many labs — including labs here at MIT — are rushing in to try and understand these mutations."

Because genes are only a beginning. Scientists need to understand how they translate into brain disorders. And at this point, "The bridges are not complete," he says. "You can't walk from a genetic mutation to how it changes our neural circuits that lead us to abnormal behavior. It can't be done yet."

But Desimone sees "extraordinary" progress in recent years, and more on the way. Where might those bridges lead?

Imagine I'm a psychiatrist of the future, and instead of just telling you that you have bipolar disorder, I say, "Your genes and brain scans tell us that some of your neural connections are acting abnormally. We have a targeted drug for just that problem."

Or I say, “You have a severe form of major depression. We can use stem cell technologies to turn some of your skin cells into specific brain cells, edit out the disease genes in those cells, and implant them to fix your faulty circuit.”

That’s the dream, says Steven E. Hyman, director of the Stanley Institute for Psychiatric Research at the Broad Institute in Cambridge (see a full Q&A), and a champion of the idea of using scientific “biomarkers” like genes and brain scans in psychiatry.

“It’s not science fiction, though,” he says.

For example, “With enough funds, and the tools we have, and with the right kind of collaboration, I would say in the next three to five years we should be nearing the end of our genetic catalogue for schizophrenia, for autism. for bipolar disorder,” he says. “And we’re not going to get every rare variant in every human being that might contribute but if we do this well, we’ll have the parts list.”

For now, Obama’s BRAIN initiative is developing tools to meet specific challenges. One is to catalogue the thousands of different kinds of neurons in the brain. Another is to get better at mapping and manipulating circuits — groups of neurons that work together. Brandeis’ Eve Marder, who’s on the committee of scientists guiding BRAIN, says now could be “the time of the circuit” — when we fill in the gap between molecules and large ensembles of neurons.

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>
> – Neurosurgeon Emad Eskandar

“That’s what’s starting to happen now,” she says, “and it’s happening precisely because the tools to do that are starting to become available.”

Last month, the Department of Defense announced a $30 million program based at Massachusetts General Hospital to try to build brain implants for veterans with post-traumatic stress and other disorders. One of the project’s leaders, neurosurgeon Emad Eskandar, says the goal is a device about the size of a matchbox with electrodes that could detect patterns of pathological brain activity in real-time.

“When it detects those patterns, it then delivers stimulation to try and remedy that pattern of activity and restore it to something more normal,” Eskandar says.

Some neuroscientists point out that Obama’s $100 million actually isn’t very much — the National Institutes of Health already spends about $5 billion a year on neuroscience, and the BRAIN initiative’s $100 million doesn’t make up for painful recent cuts in federal research money.

But it’s a start. And it further reinforces the sense that we’re at the dawn of a new era of the brain: We’ve gone from the Freudian thinking of the 20th century to an emphasis on brain biology, and now we’re starting to figure out how that biology works — and even how to use that knowledge for fixes.

“I think we’re literally on the cusp of a complete revolution both in how we understand the brain and how we treat brain disorders,” Eskandar says.

So if we can find a way to fix brain disorders with implants, can we find a way to make normal brains even better?

At this point, that's just not the priority. "We're really just trying to help the people who are suffering the most. And it's not just the people, it's their families, it's their communities," he says. "So that's what this is really all about."

Next week in our series, "Brain Matters," we'll look at how advances in brain imaging can help to diagnose and even predict learning disabilities like the reading disorder dyslexia.