How Brain Scientists Forgot That Brains Have Owners

Ed Yong

Five neuroscientists argue that fancy new technologies have led the field astray.

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A rat's brain activity is recorded by sensors connected to its head. Reuters

It's a good time to be interested in the brain. Neuroscientists can now turn neurons on or off with just a flash of light, allowing them to manipulate the behavior of animals with exceptional precision. They can turn brains transparent and seed them with glowing molecules to divine their structure. They can record the activity of huge numbers of neurons at once. And those are just the tools that currently exist. In 2013, Barack Obama launched the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative—a $115 million plan to develop even better technologies for understanding the enigmatic gray blobs that sit inside our skulls.

John Krakaeur, a neuroscientist at Johns Hopkins Hospital, has been asked to BRAIN Initiative meetings before, and describes it like "Maleficent being invited to Sleeping Beauty's birthday." That's because he and four like-minded friends have become increasingly disenchanted by their colleagues' obsession with their toys. And in a new paper that's part philosophical treatise and part shot across the bow, they argue that this technological fetish is leading the field astray. "People think technology + big data + machine learning = science," says Krakauer. "And it's not."

He and his fellow curmudgeons argue that brains are special because of the *behavior* they create—everything from a predator's pounce to a baby's cry. But the study of such behavior is being de-prioritized, or studied "almost as an afterthought." Instead, neuroscientists have been focusing on using their new tools to study individual neurons, or networks of neurons. According to Krakauer, the unspoken assumption is that if we collect enough data about the parts, the workings of the whole will become clear. If we fully understand the molecules that dance across a synapse, or the electrical pulses that zoom along a neuron, or the web of connections formed by many neurons, we will eventually solve the mysteries of learning, memory, emotion, and more. "The fallacy is that more of the same kind of work in the infinitely postponed future will transform into knowing why that mother's crying or why I'm feeling this way," says Krakauer. And, as he and his colleagues argue, it will not.

That's because behavior is an *emergent* property—it arises from large groups of neurons working together, and isn't apparent from studying any single one. You can draw parallels with the flocking of birds. Biologists have long wondered how they manage to wheel about the skies in perfect coordination, as if they were a single entity. In the 1980s, computer scientists showed that this can happen if each bird obeys a few simple rules, which dictate their distance and alignment relative to their peers. From these simple individual rules, collective complexity emerges.

But you would never have been able to predict the latter from the former. No matter how thoroughly you understood the physics of feathers, you could never have predicted a murmuration of starlings without first seeing it happen. So it is with the brain. As British neuroscientist David Marr wrote in 1982, "trying to understand perception by understanding neurons is like trying to understand a bird's flight by studying only feathers. It just cannot be done."

A landmark study, published last year, beautifully illustrated his point using, of all things, retro video games. Eric Jonas and Konrad Kording examined the MOS 6502 microchip, which ran classics like *Donkey Kong* and *Space Invaders*, in the style of neuroscientists. Using the approaches that are common to brain science, they wondered if they could rediscover what they already knew about the chip—how its transistors and logic gates process information, and how they run simple games. And they utterly failed.

"What we extracted was so incredibly superficial," Jonas told me last year. And "in the real world, this would be a millions-of-dollars data set." If the kind of neuroscience that has come to dominate the field couldn't explain the workings of a simple, dated microchip, how could it hope to explain the brain—reputedly the most complex object in the universe?

This criticism misses the mark, says Rafael Yuste from Columbia University, who works on developing new tools for studying the brain. We still don't understand how the brain works, he says, "because we're still ignorant about the middle ground between single neurons and behavior, which is the function of groups of neurons—of neural circuits." And that's because of "the methodological shackles that have prevented investigators from examining the activity of entire nervous system. This is probably futile, like watching TV by examining a single pixel at a time." By developing better tools that can watch entire neural circuits in action, programs like the BRAIN Initiative are working *against* reductionism and will take us closer to capturing the emergent properties of the brain.

But Krakauer says that this viewpoint just swaps "neuron" for "neural circuit" and then makes the same conceptual mistake. "It'll be interesting to see emergent properties at the level of the circuit, but it's a fallacy to think that you get closer to the whole organism and understanding will automatically ensue," he says.

He and his colleagues aren't dismissing new technologies, either. They're not neuro-Luddites. "These new tools are amazing; I'm using them right now in my lab," says Asif Ghazanfar from Princeton University, who studies communication between pairs of marmoset monkeys. "But I spent seven years trying to understand their vocal behavior first. Now, I have some specific ideas about what the neural circuitry behind that might look like, and I'll design careful experiments to test them. Often it seems that people do the reverse: They look at the cool tech and say, 'What questions can I ask with that?' And then you get these results that you can interpret in vague ways."

This point is crucial. Unlike others who have levied charges of reductionism against neuroscience, Ghazanfar and his peers aren't dualists—they aren't saying there's a mind that sits separate from the brain and resists explanation. They're saying that explanations exist. It's just that we're looking for them in the wrong way. Worse, we're arriving at the wrong explanations.

Consider mirror neurons. These cells, first discovered in monkeys, fire in the same way when an animal performs an action *and* when it sees another individual doing the same. To some scientists, these shared firing patterns imply understanding: Since the monkey knows its intentions when it moves its own body, based on the firing of the mirror neurons, it should be able to infer similar intentions upon whomever it watches. And so, these neurons have been mooted as the basis of empathy, language, autism, jazz, and even human civilization—not for nothing have they been called the "most hyped concept in neuroscience."

Here's the problem: In the monkey experiments, scientists almost never check the animals' *behavior* to confirm that they genuinely actually understand what they're seeing in their peers. As Krakauer and colleagues write, "An interpretation is being mistaken for a result; namely, that the mirror neurons understand the other individual." As others have written, there's little strong evidence for this—or even for the existence of mirror neurons in humans. This is the kind of logical trap that you fall into when you ignore behavior.

By contrast, Krakauer points to his own work on Parkinson's disease. People with the disease tend to move slowly—a symptom that's been linked to a lack of dopamine. Increase the levels of that chemical, and you can hasten a person's movements. That's could lead to new treatments, which is no small victory. But it doesn't tell a neuroscientist *why* or *how* the loss of dopamine leads to the behavior.

Krakauer found a clue in 2007 by asking Parkinson's patients to reach for objects at varying speeds. These experiments revealed that they're just as capable of moving quickly as healthy people; they're just unconsciously reluctant to do so. They suggested that dopamine-producing neurons that connect two parts of the brain—the substantia nigra and the striatum—determine our motivation to move. Deplete that dopamine, and we opt for less energetic movements for a given task. Hence the slowness. Later experiments in mice, in which modern techniques were used to raise or lower dopamine levels, confirmed this idea.

There are many other examples where behavior led the way. By studying how owls listen out for scurrying prey, neuroscientists discovered how their brains—and later, those of mammals—localize sound. By studying how marmosets call to each other, Ghazanfar has learned more about the rules that govern turn-taking in human conversation. Critically, these cases began with studying behaviors that the animals naturally do, not those that they had been trained to perform. Likewise, bats, sea slugs, and electric fish have all told us a lot about how brains work, because each has its own specialized skills. "If you pick a species that does one or two behaviors super-well, you can identify the underlying circuits more clearly," Ghazanfar says. "Instead, mice are treated as if they're this generic mammal that have smaller versions of human brains—and that's preposterous."

"I am thrilled to see this paper emphasize the importance of carefully studied behavior," says Anne Churchland, who studies decision-making at the Cold Spring Harbor Laboratory. "I've seen in neuroscience that behavior is often an afterthought, studied with insufficient understanding of the animal's strategy." But she adds that such studies are hard. It's difficult to get animals to behave naturally in a lab, because you might need to recreate aspects of their world that aren't obvious to us.

Ghazanfar agrees. "If your goal is to understand the brain, you have to understand behavior, and that's not trivial. I think a lot of neuroscientists think it is," he says. "Perhaps one way forward would be to develop tools to help address the complexity of behavior" suggests Ed Boyden from MIT, who pioneered the breakthrough technique called optogenetics. "Behavioral investigation has a strong tradition in neuroscience and I hope it grows even stronger."

For the moment, the problem is that it's getting harder to publish such studies in flagship neuroscience journals. Behavioral studies get rejected for "not having enough neuro", says Ghazanfar, and "it's as if every paper needs to be a methodological decathlon in order to be considered important."

Marina Picciotto from Yale University, who is editor in chief of the *Journal of Neuroscience*, says it boils down to how studies are framed. If they're just describing behavior, they're probably more appropriate for a journal that, say, focuses on psychology. But if behavioral experiments explicitly lead to hypotheses about circuits in the brain, or something of that kind, they're more relevant for the neuroscience field. But "the line between 'pure' behavior and neuroscience is fluid," she admits, and she's both appreciative of the new paper and open to discussions about the issues it raises.

To Krakauer, the current line demeans behavioral work, deeming it valuable "as long as it tells us where to stick the electrodes." But it's important in itself. "My fear is that people will say: Yes, of course, we should continue to do everything we've been doing, but also do better behavior studies. I'm trying to say: You've got to do the behavior first. You can't fly the plane while building it."

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