CellPress

Earl K. Miller

Earl Miller studies the neural basis of high-level cognitive functions. In an interview with Neuron, he discusses the need for a holistic approach to figure out the brain, how ideas don't happen in a vacuum, and the challenge of convincing the public that science produces facts; he also shares an open invitation to see Pavlov's Dogz.

Earl Miller is the Picower Professor of Neuroscience at the Massachusetts Institute of Technology. He received his B.A. in psychology from Kent State University in 1985 and his Ph.D. in psychology and neuroscience from Princeton University in 1990. He has academic appointments in The Picower Institute for Learning and Memory and the Department of Brain and Cognitive Sciences at MIT. Dr. Miller uses experimental and theoretical approaches to study the neural basis of the high-level cognitive functions. His main interest is in executive control, which is the higher-order processing that comes into play when our behavior has to be guided by plans, thoughts, and goals. Dr. Miller's laboratory has provided insights into how categories, concepts, and rules are learned, as well as how attention is focused and how the brain coordinates thought and action. This work has established a foundation upon which to construct more detailed, mechanistic accounts of how executive control is implemented in the brain and of its dysfunction in diseases such as autism, schizophrenia, and attention deficit disorder.

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What do you think are the big questions to be answered next in your field?

How it all fits together. The dominant paradigm from the 20th century was a piecemeal approach to brain function. The focus was on figuring out the function of the brain's individual parts: single neurons, single brain areas, single synapses. It was as if the brain was a giant clock, and if you could figure out each gear you could figure out the whole. It has become increasingly obvious that this modular view of the brain is a first approximation at best. At least in the cortex, neurons and areas have multiple functions. You can't figure out the brain one piece at a time. Many of us are now taking a more holistic approach to figuring out the brain.

To tackle your favorite research question: is there a tool that either needs to be developed or is currently available that could be implemented in a novel way?

The more holistic we get with our tools, the more we approach how the brain actually operates. The move from single-electrode recording to multiple electrodes was big because it revealed things you can't see one neuron at a time. Our analytical tools need to catch up (and they are starting to). We collect massive datasets from hundreds of simultaneous recorded signals, but our analysis is still often piecemeal (e.g., between pairs of electrodes). Also, everyone agrees that the recent advent of genetic techniques to manipulate the brain is a good thing. It would be nice to see more movement of it into non-human primates.

The Cell Symposium that you are speaking at this year covers talks ranging from cell biology to cognition and from animal models to human neuroscience. How do you view the level of crosstalk between these disciplines, and how can they profit/learn from each other?

This symposium very much helps. Getting people from different levels of analysis in the same room, and giving them exposure to other approaches and results, can be quite fertile. Ideas don't happen in a vacuum, and you can't see connections between your approach/level of analysis and others unless you are exposed to them. At the risk of tooting our own horn, the Picower Institute at MIT was founded with that idea in mind. Bring together people interested in the same questions but who answer them at different levels. It has resulted in collaborations that wouldn't have happened otherwise.

How do you view the level of crosstalk between disciplines (for example, physics, mathematics, engineering, humanities, and social science)?

The more, the better. Any field of science starts out in its own silo. As we learn more, different subfields get woven together. For example, cognitive science and computational science used to be pretty separated from neuroscience. Now they are more seamless. I used to work purely on behavioral neurophysiology. Now, I collaborate with computational modelers and have them in my lab. Not only does that approach help make sense of rich, multiple-electrode data, it also generates hypotheses that you would never get to from first principles. Sometimes people resist this weaving together of subfields, as if their field will be swallowed by another. But you risk being marginalized if you keep yourself separate from other disciplines. Also, look at Hans-Lucas Teuber, the founder of the Department of Brain and Cognitive Sciences at MIT. People thought he was nuts to bring a neuroanatomist into a department of experimental psychology. Not so much anymore.

Who were your key early influences?
Charlie Gross and Bob Desimone. They both taught me much. I was a lump of clay before I worked with them. Among other things, Charlie taught me to always have the big picture in mind. Things make the most sense and have the deepest meaning in a broader context. Both Charlie and Bob taught me how to write. Another thing they both taught me is to be open-minded and not to buy into beliefs, especially your own. Dogma is anti-science. And personal dogma is the worst because it sucks you in the deepest. Some of my favorite moments as a scientist are when I discovered something that led me to a different conclusion than one I had previously made.

What's your favorite experiment?
Moran and Desimone (1985). It was the first example of a purely cognitive process (attention) not explicitly linked to motor output or sensory input. It is the first time we saw the "middle" of cortical processing. You know, a mistake people often make when studying cognition is that their paradigm includes a direct link between sensory input and motor output. You have to isolate the middle. If you short-circuit between the brain's inputs and outputs, you can't be really sure you are truly getting at what is happening in between.

There was also Charlie Gross and colleagues' discovery of face cells—an awesome example of "serendipity favors the prepared mind." They didn't intend to look for something like face cells. But when it happened (accidentally, by someone bending down in front of the animal), they recognized that they had something important.

What career paths did you consider other than as a scientist?
I was a pre-med major. I volunteered to work in a neuroscience lab to help get into medical school. I remember my first experiment in that lab and the first time I heard the "thunderstorm" of neural activity. Hit me like a lightning bolt (pun intended). I was hooked. I decided to go to grad school instead. My mom sat shiva, but she got over it.

Did you encounter particular difficulties? How did you overcome them?
Money to pay for college was a bit of an issue. My family was middle class, but just barely. I once considered joining the ROTC (at Kent State of all places—talk about desperation). More than a couple times, I sold plasma.

My (identical twin) brother, Harvey (a professor at Ohio State University) and I were the first in our immediate family to graduate from college. Our family was happy about that, but they didn't really understand grad school. Some of them thought we were being lazy, hiding out in school instead of getting a real job. Meanwhile, I was working 12 to 14 hours a day. Plus, not all of them were happy that we moved away from home. We had to deal with that.

Which aspect of science, your field or in general, would you wish the general public knew more about?
That science produces facts. Opinions and feelings are not just as true as facts. More Americans believe in angels than science. Our society has moved into a pre-Enlightenment phase. Sad!

What do you think are the biggest problems/challenges that science as a whole is facing today?
The biggest challenge is convincing the general public that science is worthwhile. Too many people think that their feelings and opinions are as relevant, or even more relevant, than facts.

Even scientists can be prone to some version of this. I've seen too many examples of people who think they have the answers. They dismiss some lines of investigation, even to the point of discouraging the research. Anyone who says that studying a given brain signal or phenomenon is irrelevant or a waste of time is not even wrong; no one knows enough about how the brain works to say something like that. Science is not about what you think you already know. That kind of self-reinforcing approach will lead you to run around in circles. Thomas Kuhn got it right. The people who fight the most against new ideas and approaches are the people who feel most threatened by them.

In your opinion, what are the most pressing questions for the field?
How do ensembles of neurons work? Everything seemed easier when we thought that the single neuron was the functional unit of the brain. Now, with repeated demonstrations of neurons with multiple functions and "mixed selectivity," it is becoming clear that ensembles of neurons, not individual neurons, are likely to be the functional units. This raises a whole host of questions like: how do you identify an ensemble? Part of the solution may be technical (like techniques to identify anatomically connected neurons in the working brain), but I suspect it will also be computational/analytical. Anatomy is like the road and highway system. It determines where traffic *could* go. Something else directs where traffic actually does go from moment to moment.

How do you find inspiration?
I don't. Inspiration finds you, most often when you're not trying to find it. Many times, inspiration and decision-making are the result of unconscious processes churning away at something. Your conscious mind then receives the result. In fact, your conscious mind can often get in the way by forcing you down the same well-worn paths. Inspiration often comes when your conscious mind is not engaged by the question at hand. This is why we often get ideas when we are drifting off to sleep, or walking to work in the morning, etc. One of the central ideas of my most cited paper (Miller and Cohen,

2001) came to me suddenly at a bar in Vancouver. Good thing there was a cocktail napkin nearby.

Do you have a favorite anecdote from doing science that you'd like to share (perhaps a key discovery moment?)

The bar in Vancouver (see above).

If you could ask an omniscient higher being one scientific question, what would it be and why?

Humans are clever enough to do science. Do you think we are clever enough not to use it to destroy ourselves? I know. I'm a buzz kill.

What do you do when you're not in the lab?

Think about the lab. Just kidding (kind of). I play music. Come see Pavlov's Dogz, a band of cognitive neuroscientists that gig whenever we find ourselves in the same city. We'll be playing the Sunday night (November 12th) of the Society for Neuroscience meeting at Songbyrd DC.

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