BRAIN SCIENCE PODCAST

With Ginger Campbell, MD

Episode #78

Discussion of *Beyond Boundaries: The New Neuroscience of Connecting Brains with Machines—and How It Will Change Our Lives*, by Miguel Nicolelis, MD, PhD

[music]

The *Brain Science Podcast* is part of sciencepodcasters.org, the website where you can find high-quality science podcasts from a wide variety of fields.

[music]

INTRODUCTION

Welcome to the *Brain Science Podcast*. I'm your host Dr. Ginger Campbell, and this is Episode 78. Today we're going to be talking about how brain-machine interfaces are changing our understanding of how the brain works.

Today's discussion is based on the book, *Beyond Boundaries: The New Neuroscience of Connecting Brains with Machines—and How It Will Change Our Lives*, by Miguel Nicolelis. Now, over the last month or so I've been trying to schedule an interview with Dr. Nicolelis, and, in fact, he has had to postpone this several times. So, I've decided to go ahead and tell you a little bit about his book.

But first I want to mention that the *Brain Science Podcast* is sponsored by Audible.com, the world's leading provider of downloadable audio content, including over 70,000 books. This includes Dr. Nicolelis's book, *Beyond Boundaries*. If you aren't already a member you can get this book, or any book you want, for free, by going to audiblepodcast.com/brainscience.

[music]

DISCUSSION

Now, you might be wondering, who is Miguel Nicolelis, and why should I care about his work? Well, even though you might not recognize his name, you have probably heard about his work, because it has received quite a bit of attention from the mainstream press. Dr. Nicolelis leads a team at Duke University that has demonstrated that it is possible for a monkey to control a robot arm using only its brain. In fact, working with researchers in Japan, they were able to show that the monkey's brain could control the robot arm from thousands of miles away.

My goal today is to explain why this work has implications for how we understand the brain's function. The style of *Beyond Boundaries* is somewhat reminiscent of Eric Kandel's autobiography, *In Search of Memory*, which we talked about way back in Episode 3. Three threads weave through both books: autobiography, the history of neuroscience, and a description of key experiments. But there is surprisingly little overlap between the books, because neuroscience is a huge field, and the two writers come at it from very different perspectives.

In fact, in *Beyond Boundaries*, Dr. Nicolelis challenges two longstanding assumptions from twentieth-century neuroscience: one is the primacy of the single neuron, and the other is strict localization—the idea that each part of the cortex has a relatively fixed function. Connected with that, he also challenges the idea that time is not important in describing brain function—but I'll get more into that as we go along.

Before we talk about Dr. Nicolelis's experiments, I need to talk a little bit about why earlier work seemed to support the ideas that he challenges. It had to do with the way experiments were done in the early days. Early on, electrodes were very large, and it was only possible to make single-cell recordings, and usually from either very large neurons, or ones that were almost chosen at random. Secondly, the experiments were done on anesthetized animals, because, again, these electrodes were very large, and it wasn't possible to allow the animal to move around.

Both of these features are obviously the result of technical limitations. And these technical limitations had to be overcome; which meant developing extremely small, flexible electrodes that could be left in animals, and then let them wake up, and let them go about their lives.

Now, much of this early work—especially in developing these small electrodes—was done in rats. And in his book, Dr. Nicolelis chronicles the achievements of the many people working in this field, including how the small electrodes were developed, and how they were then able to implant large arrays of electrodes—which is very important to understanding the difference between his work and the previous work.

One of the experiments that he does describe in detail involves rat whiskers. The hair follicle of each facial whisker of a rat contains a high density of mechanoreceptors. It's similar to the face of a primate; that is, that they really can have very detailed feeling of their whiskers, and the signals go to the trigeminal system—just like signals from the face do in a primate. These signals go to the thalamus before being sent to the cortex.

The prevailing theory was that the signals were purely feed-forward. This was called the "labeled line theory." And it was supported by the early work, which was, as I mentioned before, done in deeply anesthetized animals. That is to say, they were able to show that single neurons responded to movement of specific whiskers. It was only when it became possible to put electrodes in a large number of neurons that it became clear that, in reality, neurons can respond to multiple whiskers. Some neurons actually responded to nearly every whisker on the face.

The other thing they discovered was that the receptive field for any given neuron was not fixed, but changed over time. This is a big deal, because it overturns the longstanding assumption that both receptive fields and somatosensory fields are static, or fixed. Of course, now the plasticity of these fields is well established, but this was not the case in the early '90s, when these experiments were first conducted.

To test the idea that the maps were plastic, they actually took the same rat, anesthetized a patch of its face, and re-did their measurements. And, amazingly, the entire map was reorganized, almost instantly. This was published in *Nature* in 1993[1]. It was the first time an entire neural circuit was visualized and measured in a free-behaving mammal.

I can't emphasize enough how important this was—"freely awake and whisking," is how Dr. Nicolelis describes the rat. For one thing, it turns out that when it's awake, the rat's whiskers are always moving with a small-amplitude oscillation that corresponds to an oscillating signal in the brain. And this signal actually goes in the opposite direction of the feed-forward signals in the trigeminal pathway.

It also has been shown that the receptiveness of the neurons in the thalamus depend on what the animal is doing. This brings us back to an idea I've talked about several times in the past: the brain is not a passive receiver of sensory

---

[1] Nicolelis, Miguel A.L., Rick C. S. Lin, et al. "Peripheral block of ascending cutaneous information induces immediate spatiotemporal changes in thalamic networks.: Nature 361 (1993): 533-536. (ABSTRACT)

information from the world; active interaction with the world changes perception. In the case of the rat, it needs not only the baseline oscillation of its whiskers, but also the ability to move its head, so it can judge things, like whether it can fit through a hole to escape from a cat.

When Nicolelis and his postdoc, David Krupa, took measurements from awake, freely-behaving rats, they discovered that many more neurons became involved in tasks than what had been traditionally assumed. In fact, neurons in different cortical layers responded differently; which challenged the accepted view championed by Vernon Mountcastle.

It appears that the functional unit of thinking is not a column of neurons, but populations of neurons distributed across the entire 3D volume of the S1 cortex—that's the main somatosensory area of the cortex. In retrospect, the significance of this work might seem obvious, but at the time, they had a difficult time getting the larger neurophysiological community to appreciate that their work represented a credible challenge.

[music]

So, the brain-machine interface was actually conceived as a new experimental paradigm. Working with his colleague, John Chapin, the goal was to, "… demonstrate that populations of neurons, working together as a part of widespread neural circuits, could encode enough information, using dynamic spaciotemporal patterns of activity, to sustain a motor activity." They wanted to show that populations of neurons, rather than a single brain cell, should be considered the functional unit of the central nervous system.

They started with training a rat to push a lever to get water. After recording from the motor cortex of the rat, they were able to create a circuit that produced a brain-derived signal capable of predicting the rat's forepaw activity. And then they used that to actuate the release of the water. Once it appeared that the rats were going back and forth between using their brain or their paws, they disconnected the actual lever, but turned on the brain-machine interface. Eventually the rats actually figured out how to get the water with just their brains. Most of them quit pressing the bar completely.

Now, as you might expect, working with monkeys was more complex. It involved taking measurements from the motor cortex, and then developing algorithms for predicting motion. These then had to be converted into signals for controlling the robot arm.

But the basic principle is this: A large number of neurons are involved in any given motor activity. If a sufficient number are sampled, the motor activity can be predicted and modeled. In the case of the famous monkey, Aurora, she spent many hours playing a videogame with a joystick; and these signals were what was used to move the robot arm. However, the coolest part was that she showed that she could move the robot arm without using the joystick.

Now, when we talk with Dr. Nicolelis, we will get him to describe these experiments in more detail; but what I want to emphasize today is what these experiments tell us about how the brain works. They demonstrate what he calls the "distributed coding principle;" which is that any type of information processed in the brain involves a recruitment of widely-distributed populations of neurons. It was only by sampling from vast areas of Aurora's brain that it became possible to, "…mathematically translate the probabilistic nature of her neurons into deterministic motor behavior."

Early in his book, Dr. Nicolelis demonstrated this idea in a very memorable way. He described a mass protest that occurred in his homeland, Brazil, in 1984. More than a million people were chanting. I'm not sure how long it went on, but the point that he made was the effectiveness of the chant was based on a large number of people. No one person could be heard; and, no doubt, over time, some dropped out as others joined in. As he says on Page 13, "The same is true for the brain. It does not pay attention to the electrical screaming of a single noisy neuron. It needs many more cells singing together, to know what to do next."

Before I review the key ideas, I want to mention one other interesting finding that came out of the monkey robot experiments. This is something that surprised even the experimenters. It was that neuronal firing can be decoupled from motor output. They discovered three different neuronal populations: some that fired only when the arm moved; some that fired when both the arm and the robot arm were moving; and some that fired only when the robot arm, alone, was moving. Amazing!

So, let's emphasize the key lessons from these experiments: First, single neurons can't do anything—ensembles do. And single neurons can participate in multiple ensembles simultaneously. In the monkey experiments, neurons fired from all over the cortex; and some of the ones that fired only when the robot arm was moving were right next to the ones that fired when the monkey moved her arm. That seems pretty amazing to me!

Now, I started out by saying that the work of Nicolelis and his colleagues challenges two longstanding assumptions. In the last few minutes I think we have seen why he argues against the primacy of the single neuron: the functional unit of the brain is made up of a population of neurons recruited from all over the brain. The other dogma that he challenges is what he calls "strict localization;" which is the idea that each part of the cortex has a relatively fixed function. The fact that neurons across the cortex may be recruited for wildly divergent tasks challenges this view.

But, let's consider how this relates to discussions we've had in the past about how our brain maps the body. We've talked about the fact that these maps are plastic;

and Dr. Nicolelis's work has confirmed this conclusion. We've also talked about how our brain can incorporate tools and other objects into its body map. The monkey's ability to control the robot arm seems to be an extension of that concept. It also demonstrates an important principle, which is that in order to incorporate an object into our body map, we have to actively engage with it.

Before I close, I want to address a question that I am sure many of you may be asking: how do you explain all the data that appears to support the old way of looking at the brain—the one that maps single functions to each area? Dr. Nicolelis addresses this in his book, and he comments that it probably represents genetics and early development. That is to say, we start out with, you might say, a starting blueprint, or what our brain expects the various parts to do. But as we also know from what we've talked about before, experience is necessary in order for these areas to function properly.

Remember, early on we talked about—and this is true for people, too—how a cat's visual cortex will not develop the proper connections for seeing properly, if they have their eye sewn shut during the critical period. So, we might start out with a certain blueprint of what the parts of the brain are going to do, but then we have to have the actual sensory input to get the connections fully developed.

On the other hand, experiments like the one that shows that the visual cortex can begin to process tactile stimulus when a normal-sighted person is blindfolded—for as little as six hours—shows that those other capabilities are already there; because you can't grow any new connections or synapses in six hours.

What about Broca's aphasia? This refers to the fact that when people have a stroke in a certain area of the brain, they lose the ability to speak. This is important, because this is the first area that was established, and really got 'localization' going. Well, we now know that this is also an area that involves many connections to other parts of the brain; so, it is highly likely that one of the reasons why this area leads to aphasia is because of loss of connections, as much as to loss of that one particular area.

So, it's not that studying single neurons, or even older experiments about localization, are totally invalid. But they do provide an incomplete picture. And if we are trying to understand the brain as a complex system, they are insufficient. For those of you who have been listening to the *Brain Science Podcast* for the last several years, these ideas may not seem particularly new, because they dovetail so nicely with many of the topics we have discussed.

One of the things that I really appreciate about *Beyond Boundaries* is the way that it puts this work into an historical context, and helps one appreciate the subtle ways that assumptions affect what questions we ask. It also demonstrates the ongoing interaction between science and technology. When funding is tight, there is a tendency to push basic science to justify itself by pointing to its practical benefits. But I think such an attitude is shortsighted.

The work of Dr. Nicolelis and his colleagues has the potential to bring very real benefits to people with disabilities. But consider this: he was driven by scientific curiosity about how the brain works. If he had not challenged old ideas, we would not be on the threshold of these exciting new technologies.

Here again, we have a wonderful example of the power of the interdisciplinary approach that combines both technological and scientific creativity. It's one of the things that makes neuroscience such an exciting field to follow.

I really do hope that I can get Dr. Nicolelis on a future episode of the *Brain Science Podcast*. If you have any questions you would like me to ask when he comes on the show, you can send me email at docartemis@gmail.com. Or post it in our discussion forum at goodreads.com. I will post a link to that in the show notes at brainsciencepodcast.com; which is where you also can find a free transcript for this episode, and every other episode of the *Brain Science Podcast*.

Don't forget that the *Brain Science Podcast* is made possible by donations from listeners like you. Just visit brainsciencepodcast.com to learn more. And if you can't afford to donate, remember you can help by posting a review on iTunes, or by telling your friends to listen.

I will be back next month with a new episode; but in the meantime, don't forget to check out the latest episode of my other podcast, *Books and Ideas*.

Also, I am looking forward to attending Science Online 2012 in January. If you are interested in that, you'll want to check out ScienceOnline2012.com.

Thanks again for listening. I look forward to talking again with you very soon.

[music]

[music]

Transcribed by Lori Wolfson
All errors or omissions responsibility of the transcriber