Hope and Optimism, Improving Memory, Viewing America with Foreign Eyes
What Happens Next – 8.29.2021
Michael Kahana QA

Larry Bernstein:

Fantastic, Michael. I want to start with trying to understand how it works. First of all, the most basic questions. What is a memory? How does the brain access that memory? Why would adding an energy pulse allow for better access to that memory? And then finally, I think that once we are able to grab that memory, how do we then use that memory in thought and speech and action?

Michael Kahana:

Well, now I have to remember five things. I'm writing an article on the big questions in memory that we don't have the answer to. And the first question that I'm trying to come up with... Well, I'm articulating how hard it is to answer the question of what is a memory? What actually is a memory? Well, I'll give you my tentative answer to what is a memory. A memory is an association between the content of an experience and the situational context, including when, where, and in what cognitive state that experience occurred. It's a linking between the actual event, let's say you asked me a question and I see your face on the Zoom and then linking it into its temporal, spatial, situational, emotional context that forms a tapestry into which all memories become woven.

Now, how do we access the memory? Well, we need a way of reinstating of essentially doing a mental jump back in time. The author, HG Wells, in The Time Machine, when the time traveler is questioned by the psychologist says, "Time travel is impossible," he retorts and says, "No, in fact, we do it all the time." Whenever you have a powerful memory of a past event, you are jumping back in time, you're doing mental time travel. Now, most memories don't have that kind of powerful mental time travel, but that is the element, is that you're able to somehow navigate through the space of context that linked to the memories.

Michael Kahana:

Now, that process, both the process of weaving the memory with the context and the process of navigating the memory space depend on a circuit, on a network, like in a city that is connected by roads and other modes of transportation, subways. There's a network of communication that supports those functions. And what's fascinating is that that network of communication varies in how well it works at moment to moment. There are traffic jams. Sometimes it just gets stuck and it doesn't work. And sometimes it works fine. And even in a patient who's impaired where it never works fine, sometimes it works poorly and other times it just simply doesn't work at all. And the idea is to be able to rapidly decode the state of the network, the electrical state, and intervene in some way to alter that state.

The magic of this approach is that rather than being the external agent that is imposing the will like the will of a divine power on the actor, to call back to Marty's presentation, instead what

we're going to do is we're going to say that the brain possesses the capacity to produce good function, but right now it's not. And we're going to just give it a little nudge, a little nudge to try and get it to do what it sometimes is able to do well. I don't know if I answered all five questions. I think I only answered three.

Larry Bernstein:

It's totally fine. What I found amazing in one of your previous presentations on this topic was I asked you, how quick do we know if you're in a bad state? Sometimes I might be the bad state a whole morning. And you said, "Well, I can pretty much determine that in milliseconds," type of situations. So, this morning, which is, for me, only a few hours because I get up late, and then there is milliseconds, which I can't even distinguish in time space. And what I think is interesting is how is it that we drift in and out of good and bad memory states in milliseconds? And then how is it that an energy pulse can do some sort of a reboot, like a computer reboot? My computer takes a long time to reboot. How long does it take my brain to reboot to go from this bad state to a good state?

Michael Kahana:

Those are really great questions, and we've actually just published a paper looking at the timescale of these good and bad states. You can decode the states very rapidly. Imagine a system that can decode the weather rapidly. You have an algorithm, you're detecting the pressure, the temperature, the humidity, the air flow. You've got all these things going into a computer. You might be able to, like a thermostat, you're able to read out a rapid index of air quality or likelihood of precipitation. In our case, it would be likelihood of forgetting. That doesn't mean that that your mental state is going to change very quickly.

And you can think of it as a diffusion process. You could think of it as like stock prices. They can go up and down at different timescales. There are going to be fluctuations that are very fast and fluctuations that are medium term and fluctuations that are much slower. You can actually think of it as almost like a diffusion process. It's not as simple as a fusion process because it's bound to a range. Is it an Ornstein–Uhlenbeck? Is it something more complicated? But you can think of it as something akin to a diffusion process, something that's fluctuating, and that has fluctuations that many timescales from very slow to much faster.

Larry Bernstein:

At the beginning of your talk, you remembered your grandmother coming into your bedroom and asking you to do something good in the world. I imagine the way that memory works is you don't remember exactly what she said, but you got the gist of it. The memory is the gist, do good. She may not even have said that, but that's the key essence of it. And there's other stuff. You remember her tone. You may remember her love. You may remember the smell, all these things. And there's these axions in the brain. I actually don't know how the brain works at all, but there must be these axions, love, smell, sound, the gist, all connected.

And then when it hits, all of these memories are released at once. What I don't understand is when memory is impinged or impugned in some way, is it the axion network that's compromised? And then how does it lift out all those different axions to all those different

places in the brain? Because I imagine that smell might be one part and sight in another, and the gist is in a different place as well, because I imagine that you're doing with the electric pulse is very location particular with regards to the electrical shock. You're shocking maybe into the smell area, you get the smell, but what has that got to do with the gist?

Michael Kahana:

It turns out that there are a couple of important elements here. I didn't really explain what are these signatures of good and bad memory in the brain? There are two principal signatures of good and bad memory and I finally gave them a name, TAG and TILT. TAG is increased data oscillations, which are slow frequency oscillations, diminished alpha oscillations, and increased gamma oscillations. I call it +T -A +G, TAG. And TILT is a general tilt in the power spectrum of the Fourier analysis of the brain signal. Now, I'm not going to go into Fourier analysis for all your listeners, but the idea is that there's this time series of brain activity that has two characteristic patterns that occur in multiple memory centers of the brain at moments of memory success versus memory failure. You can decode those in those centers.

Now, the precise regions where you see how much of the TAG and how much of the TILT will be different for every single person. And so that's where the machine learning algorithms are learning a patient specific formula for how one person's brain can be restored. However, on average, there are these general patterns. Now, to come back to the question about my memory of my grandmother, I think that when you have... There's a movie called Inside Out. I don't know, has anybody seen Inside Out? It's a Disney movie. Marty's raising his hand. I'm glad that I'm not the only person above the age of 50, Marty and I, and I think we're all in the over 50 club, who's watched Inside Out. It's a Disney movie. And there's this idea of these poor memories, really core memories, the core memories are maybe related to, I don't know, whether you're optimistic about something. But my grandmother is certainly a core memory for me.

And I think that the idea there is not that I'm remembering a specific episode. It's that many things over my life remind me of those events and they get reinterpreted and modified repeatedly, so that by now, the memory is more of a caricature that has been shaped by my life than any original episode. In this particular case, she was Hungarian and I can hear exactly the words that she said in Hungarian, because those don't have a lot of interference and she was the only person who ever in my life spoke to me in Hungarian. I hear only a few things in Hungarian. So that gives me a precise version of that memory. But all the rest of it is just a feeling, as you said. It's recursive. It just repeats and builds and it gains compound interest over time, so to speak, in how it influences who we are.

But in terms of the question of, how does a pulse affect the network? Well, if you have an electrical network that has different modes of oscillations, of connections, of correlations, and it knows mode... Let's just make it very simple. Let's assume that we're just a good mode and a bad mode. Then all you need to do is figure out how to press a switch that will flip it from the bad mode back to the good mode. It's more complicated than that because the brain is going to tell you how to do that. But that's the idea, that you're trying to get it to switch modes. Just like if you see in those pictures where it's a vase if you look at it one way and it's a face if you look at it the other way, and how sometimes your brain just switches between the two images. So

here, the idea is that there's a little pulse, an electrical pulse that will allow you to jump between the good and the bad state.

Martin Seligman:

Mike, this is great science that you're doing. I'm so proud of you.

Michael Kahana:

That means a lot coming from you.

Martin Seligman:

Can we get electrical control to increase the probability of good memories?

Michael Kahana:

That's hard. That's hard, because what I've done focuses on the system's ability to retrieve memories. So that means that if you're better at retrieving memories, you're going to retrieve all kinds of memories. So now you're talking about something that would bias the system toward good or away from negative memories. It would be a different kind of technology. So yes, I think you could. It would be a different approach. What you would do is instead of looking for the pattern associated with memory success versus memory failure, you'd look for the pattern of good memory versus bad, or maybe two patterns, good, bad pattern and the success failure pattern. And now you're trying to jointly modulate that. You want to drive the system toward good memory when the memory is positive, drive the system toward bad memory when the memory is negative. And that is theoretically possible.

I think that your question opens a much broader set of ideas, which is once you can decode all kinds of cognitive states and you can manipulate the brain to make it do more of what it would normally do, but biased either one way or the other, then you could imagine an assistive device, kind of like a better version of my eyeglasses that help me see, this device would help me use my brain more effectively, but in many ways, it could address anxiety or depression. You would just need a good machine learning model for anxiety, for depression, for positive affect, or for OCD behaviors or for anything else. And memory is, in a way, easier. Because with memory, there's very clear-cut moments of success and failure, and I can trigger them very easily, whereas with those emotional states, it's maybe a little bit less straightforward how you measure it at a moment-to-moment basis.

Martin Seligman:

Particularly important for me, since optimism and good memories are tied to agency. If there's a way of producing more good memories, very important for increasing agentic behavior. One more question, Mike. I think of memory as being in service of the future, that is, I think, the past and how we represent the past has evolved to be in service of an adoptive future. And indeed, I think we distort memory or select from memory for that purpose. Is there a

neuroscience-electrical tank on the relationship of a memory, stimulating memory, and preparing for the future?

Michael Kahana:

Well, Marty, I'm glad you brought that up, because the future is what memory is really for. We can play this trick of going to visit the past, but the reason it's so valuable for me to my grandmother's memories is that it directs me to a more functional, adaptive, and productive future. And for some people, they have bad memories that direct them to future behavior that is less functional, less adaptive, et cetera. So, yes, I completely resonate with that idea. And I agree that when we imagine the future, we're doing it using the Lego blocks of our memory system. We are imagining the future with the past. As you were talking, I could imagine that the therapy that I'm developing, it could be standalone, but it could be combined with other therapies. Imagine a positive therapy intervention, coupled with a memory therapy where you turn on good memory at the moments when you applied positive psychology interventions. Then that would serve the role, not of specifically improving memory per se, but improving positive memories, creating strong, positive memories that can direct future behavior.

And if you have somebody who had early life negative memories, which then they reminisced and reincarnated and consolidated over a long period of time, those will color and flavor all neutral experiences with a tone of negativity. You could imagine a positive psychology intervention that would work better if it were combined, especially if a person, because we know depressed individuals have impaired memory, so it's hard for them to learn. And there may be reasons for that that we can't get into right now. But if you could improve their memory during an intervention, that could really be very helpful, I think.

Larry Bernstein:

Michael, when I first met you, I think it was five years ago or so, I asked you what a memory was, and you said something like 164K. And I said, "What are you talking about?" And you said, "It's the amount of memory. You've seen an amount of memory on your computer when you get an email, how many bytes it is." And I said, "Well, what is 164K?" And you said, "It's a bad Polaroid. That's about what a memory is." And then I said to you, "How do you know that?" And you said, "Well, in one of my epilepsy patients, we put an electrode in someone's head and we put some power on it and out came a memory."

Larry Bernstein:

And it was, "Oh my God, I'm in seventh grade history. I haven't thought about that girl, it must be 50 years. Do it again. Oh, there she is. I love it." How do you think about that memory in seventh grade history with the embellished characteristic of your grandmothers telling you to do good, which was a false memory, it was a caricature of the memory? How do you think of the specificity of a moment verses of this other of the gist?

Michael Kahana:

Well, I love that you have such a great memory of the presentation I gave at the Penn Book Club. I don't know if that number is exactly the number, but I did have a number that I had

calculated based on the number of neurons that are recurrent in one of the main memory centers of the brain. That number was really just saying theoretically this number of neurons in an average brain could store this number of bytes of information. And you could store many of these things. You could store potentially millions of these memories of that size, that Polaroid size. That's where that calculation came from.

You're absolutely right that I described a study that I didn't personally conduct, a former student of mine, Josh Jacobs is a professor at Columbia Bioengineering did this study where he was able to stimulate the brain and reliably evoke in a patient memories of that patient's junior high school experience, and consistently did it over and over and over again with this stimulation, which was a more compelling version of what was more anecdotally described by neurosurgeons in early years. Those are two related findings.

I think that this is a really fascinating question about why some memories can be evoked so precisely and other memories are more schematized or more generic. Obviously, I've seen Marty many times, I've seen you a number of times, Larry, and so it would make sense for my brain to create a composite and not try to hold onto every precise detail. But on the other hand, you can imagine an experience, a salient experience that does not have other competing similar memories.

We can all come up with examples. I do have some very specific memories that I can access from my childhood, but not so many. Most of them are more gist based, and only a few of them are very precise memories. And even the precise ones I don't even know how accurate they really are. But I think it's all about the issue of using those memories over time is that it will make it harder to remember the original memory.

Now, you're raising the possibility of would it be conceivable that we could somehow stimulate the brain so that all of our memories could be called back precisely? That's an open question. I don't know the answer to that question. I somehow think it's unlikely, but it's probably the case that we could evoke many more memories than those that we can call up with our own volition.

Larry Bernstein:

What am I going to remember from your talk? In real time, I'm engaged with you 100%. I'm giving you my all, Michael. And I'm listening and I'm trying to take it in. I got the visual of you, I got the background because this is a Zoom call for me, and yet, in a few hours I'm going to send this file to Rev.com and I'm going to get a transcript. And when I read the transcript, I'm going to be awestruck, and I always am, how much I missed. I'm telling you, I'm giving it to you, 100% but I'm going to miss tons of it. I'm going to go, "Oh my God, how did I miss that? What a fool. I really should focus more."

Larry Bernstein:

And then my mother's going to say to me, "Larry, how did Michael perform today?" I say, "Well, he did great. Here's what he said." And I will distill your half hour presentation into something like a 60 or 90 second gist of what you said. And then if you ask me a year from now what I remember from this incident, it will basically come down to the 60 or 90 seconds that I distill

for my mother. Why is it that I miss so much? Why is it that looking over the written words is almost like a completely new experience for which I can now remember? And why is it that the story I tell is the one that will have the greatest recall?

Michael Kahana:

Let me start out by trying to answer the last of those questions. What I say will be much more easily remembered if it resonates with something that you previously thought. Your internal thoughts become part of the memory. There is no memory of me by myself. That does not exist. Your memory of me is filtered through your internal thoughts, and now your internal thoughts, in between my words when I'm hemming and hawing and trying to remember what was your other question, going to reconstruct your own version of what I was saying, and you're now going to think about your thoughts and your questions. That's a big part of the memory.

It's not correct to say that there's the original memory, which was perfect, then somehow you recode it your way and then you remember the recoded version. What I'm saying is that the recoding is happening as part of the original memory, and it's the decoded version that you will be able to more easily access later.

Larry Bernstein:

Marty, in your book you talk about that as you've gotten older, one of your best functions is to help your colleagues and your students do their best work. As you see Michael's dream of what he wants to accomplish, what are your thoughts on what he's trying to do? How can he improve upon it? As the elder statesman, what do you make of all this?

Martin Seligman:

Well, I'm very enthused about Mike's work. And for me, what Mike said about the therapeutic aspects for depressed people, but also, I'm very interested in normal people increasing their productivity, increasing their success. Since I know that success and agency depend on memories and thoughts, what Mike was saying about coupling of the right electrical stimulation to the right psychological interventions to produce more positivity, more success in life seemed like a possibility for a future. I hope Mike will be taking some post-docs to go in that direction.

Larry Bernstein:

Marty, as a follow-up to what you just said, my grandfather was a psychoanalyst. He studied at the University of Vienna in Freud's department. He was very disappointed when he came to the United States that Freud had gone out of fashion in the sense that drugs and other pharmaceutical solutions to depression had taken over. What's interesting here is that Michael is offering another path; not talking to somebody, not taking a drug but to use electrical impulses to improve cognitive ability. How do you think about those three avenues of pursuits?

Martin Seligman:

As a psychotherapist, I'm sad to say that I think psychotherapy in its usual form, psychoanalytic supportive, even cognitive behavioral has arrived at a 60% barrier. Basically, I've written five editions of abnormal psychology once every five years, and I had to revise it every five years, but there were essentially no changes in the effectiveness of therapy or the effectiveness of pharmacology over the last 25 years. I think we need something new here. Basically, the talk therapies in all their forms and the drug therapies have approached at about 60% effectiveness against a placebo.

Mike, I think, is telling us there's a different way of doing things. The psilocybin people are telling us there's a different way of doing things. The genetic people are telling us there's a different way of doing things. And I think it's time we took those methods and ideas seriously.

Larry Bernstein:

Michael, going to a more recent presentation that you gave on this topic, I asked you what improvements you can make in a patient, and you said, "12 years." And I said, "What does that mean?" And you said, "I can turn a 70-year-old into a 58-year-old memory person." To my audience, earlier you mentioned 15%, 20% - I forgot the number you said now - improvement. How should we think about what we can accomplish here in terms of an improved memory state?

Michael Kahana:

I've actually thought a lot about this because this is one of the hardest things to convey to people. What does it mean? What are you doing? In normal aging, memory declines, say, between 50 and 70, and we can basically remediate about a little more than half of that decline, from 50 to 70, meaning... That doesn't mean that we've tested that on 70-year-olds and made them look like 58-year-olds. It's just trying to quantify the benefit that we've seen in our hospital studies at the bedside of these patients.

I think a much better way of thinking about the benefit is as follows: In patients who have memory loss due to brain injury, 1/3rd of those patients, based on our data in traumatic brain injury patients in the hospital who got brain stimulation, 1/3rd of that deficit should be fully remediated, and that means they should be back to normal, 1/3rd should show 50% return to normal and 1/3rd would show no benefit. On average, we're remediating about half of the devastating loss of memory caused by a moderate to severe traumatic brain injury.

That's, I think, probably from a physician's point of view, the best way to think about it is you have a patient who's lost a certain amount of function that caused major disability in that patient, and now, on average, you can restore about half of that function, but in reality, what you're doing is you're restoring different degrees for different people, with some people benefiting enormously and others maybe not benefiting so much at all.

One of the goals of an early clinical study with a device that's implanted is to see whether we can create a kind of a virtuous cycle with the technology where the technology can learn to get better. And I believe it can. The technology can learn over time to get better. We can't do that in the epilepsy situation or in a hospital situation where we have a short-term implant, but in a

device trial, you could do that. The system will learn to get better as you amass greater and greater amounts of data.

Larry Bernstein:

I want to allow my listeners at home to understand what you just said, so I'm going to give a more layman analysis. What Mike was going to do is he's going to put these wires all over inside your brain, and he's going to be gathering information, and that's going to go into that hearing aid-like contraption in the back of your ear. It's going to gather all this information, all these impulses, good state, bad state, whatever; just data. And then Mike is going to download it at the end of the day when you go to bed, you're going to download all the information from your brain from that day, and then that information is going to be used to say, "Oh, we can do better than yesterday's software. We're going to have a T plus one software. The next morning, we install the new software, and let's do it again and see if I can do a better job. And you can experiment with one software versus another in terms of improving your memory state or not, you can do some experiments, and each day you can get better and better and better and better at that.

Michael Kahana:

Right. That's pretty good at explaining that. I should've explained that better, but the... Absolutely. The algorithms can learn; they can learn to decode better and they can learn which stimulation parameters work better. And the key is that without a device in a trial, there's no way to learn that. There's no dollar amount of National Institutes of Health, of National Science Foundation grant funding that, unless you can build a device and get it FDA approved put in humans in a trial, there's no way that we could actually determine how much better it can get over time. But I believe that the data we have already indicates that it could get much better.

This raises a fascinating question, which is am I going to be... What is research in cognitive neuroscience going to look like in 10 years? Because right now, we have to jump through all these hoops to try to figure out how to ethically obtain neural data, but in 10 years, probably thousands of us, 10s of thousands, maybe hundreds of thousands will have devices recording our brains. And that will be an incredible source of data. I can't even imagine. All the work I've done the last 25 years, once these devices are actually used to help people, they will become an incredible source of data that will teach us so much that we don't know about the human brain and maybe help us figure out how to cure other disorders.

Larry Bernstein:

I want to try one last question on you. It's a play that I saw. This is a play that I saw at the Writers Theater here in Glencoe Illinois. It was a new play, and it was about a woman with dementia. They had a robot which was a younger version of her dead husband. And the woman was lonely, she was a little bit demented, and what the robot would do is it would tell her stories that the husband had told her previously that she loved. Is that what we're talking about? Reinstalling those memories? Or the use of pleasant memories?

Michael Kahana:

It's a very powerful idea that somehow, yes, in a sense that play is capturing an idea, and that idea is that although we think we've forgotten so many of the things that we once knew, it's actually still in there, it's just hard to get it, it's hard to access it. And I think that that is the big theme of this type of research, which is... I'm not trying to create a superman, superwoman, superhero, I'm just trying to let the brain be the best it can be given its capability.

I was talking to a friend of mine who had a spouse who suffered for many years with dementia, and this friend told me his spouse was able to do this incredible thing. How did that happen? If the physical substrate of the brain was simply unable to do it, if it was just broken, how come that day it did it? What was it that happened that day? And can we somehow make that day happen over and over and over again? That's the idea. Now, whether it's about telling the stories, but it's reinstating the context. Coming back to what you asked what is a memory? A memory is linking this information to some kind of a tapestry. And in that play, what you're hearing is how this woman's husband, when he was alive, created a tapestry, and if you could somehow recapture the tapestry, all of a sudden it would create these little sparks that would evoke memories that were otherwise inaccessible. And yeah, I think that that's... It's a very powerful idea.

Since you brought up that play and I was telling everybody about my grandmother, I'll just say one more story about my grandmother. When my grandmother had a series of massive strokes and she was in a nursing home, and the nurse’s aids could not communicate with her because she was no longer able to speak English. She could still speak Hungarian. I don't speak Hungarian, but we would try to communicate with one another, and I understood a little bit of Hungarian. One of the things that was fascinating to me was her higher intellectual functions were preserved much, much longer, or long after she had lost some more basic abilities that almost they make it hard to see what she could do, what she did know, what she did understand. Of course, at a certain point in any disease process, it may be that at a certain point nothing you can do. But that's a very long road into the future. There's a long, long period of many years when people probably retain far greater functions than we can observe or that they can show us that they have, and so maybe we can help those abilities come to the fore.

Larry Bernstein:

What note of optimism do you want to end on, Michael?

Michael Kahana:

During this difficult time, we've all been through so much the last year and a half, and this show has been a bright point in my weekly schedule. Every Sunday afternoon I'll usually go for a jog and listen to the program, and it's been a pleasure. I guess all I want to say to everybody on the call is try to make some good memories because those good memories will recursively reactivate and will flavor and imbue all the neutral memories that surround them with the positivity of the good memories, and that in turn will evoke more and more positivity. Flavor your cognitive context with positive memories. And whenever you can, relish those positive

memories because you never know when they'll pop back up to help you when you need a little lift.

Larry Bernstein:

That's beautiful. Thank you so much, Michael.

Michael Kahana:

Thanks so much.