Scientists

Memories

Sheena Josselyn

Associate Professor, Senior Scientist, Neurosciences & Mental Health, Department of Physiology, University of Toronto, Ontario, Canada

Sheena Josselyn's research on learning and memory caught our attention. Curious to know more, *BioTechniques* contacted her to find out about the ambitions, character, and motivations that led to her success.

Why did you decide to study learning and memory?

I have always been interested in why a memory from last week seems to fade away, but I can still picture an older and less important memory exactly as it happened. For example, I'm constantly amazed that I can remember song lyrics I haven't heard in years. It's not as if these lyrics were important to me; I didn't write them or make any investment in learning them. But I can still remember them. How is that possible?

To try to answer those questions, I trained as a clinical psychologist and worked in that field during my Ph.D. and as a postdoctoral fellow. My interests often led me to work with sex offenders in jail, but once I heard one story, other stories were similar and I found that work to be routine. I was much more inspired by basic research where I could be creative and come up with my own hypotheses. That was always more challenging and I naturally gravitated toward that.

What are you working on now?

My lab studies how the brain encodes and stores memories. During my postdoc with Mike Davis at Yale University, we overex-

pressed a transcription factor, CREB, in a very tiny portion of neurons in the lateral amygdala of rats and found that it enhanced fear learning. Initially, we couldn't understand how affecting such a small portion of neurons would have such a large behavioral effect; it seemed that the effect should get washed out. But we were really excited by this because it's easy to knockdown learning, but enhancing it was special.

Later, during a post-doc in Alcino Silva's lab at UCLA and in my own lab, my colleagues and I discovered that neurons with higher CREB expression became part of the memory trace by out-competing their neighbors; this is why affecting such a small portion of neurons results in such a large behavioral effect. This idea was inspired by the competition among neurons during development to see which survive and which don't, which get to innervate an area and which don't. I believe that a lot of what happens during development is recapitulated during learning. Evolution is smart; it doesn't reinvent the wheel.

Now we want to see if this sort of competition occurs in neurons in other parts of the brain. We are looking at the memory of an addictive drug, spatial memories, and more complex memories to see if this competition is a general principle or specific to simple fear learning.

How do you approach that question?

We look at learning using water mazes, seeing if mice can remember where they put things, or conditioning with aversive events such as a shock or a taste that makes them feel sick. Now we are trying to get into more complex types of memory, so we are developing a touch-screen tool similar to those used in ATM machines. We teach mice to nose-poke at different pictures for a strawberry milkshake reward, which they love. To get this milkshake, they learn to differentiate between slightly different visual stimuli.

Since I work at a children's hospital, our ultimate goal is to be able to test a person and a mouse on exactly the same behavior so we can use mice to model a disorder afflicting a child and then look for treatments that we can publish to expand the clinical literature.

Do you have any pet projects outside your main area of research?

My husband, Paul Frankland, is also a neuroscientist. We recently had a daughter and watching her grow has really sparked our interest in development. She's two years old now and it's amazing that she learns so much, yet doesn't seem to remember very much. When we think back to our own childhoods, we only have vague notions of when we were 3 or 4; my first memory is probably when I started kindergarten at age 5. We see our daughter learning so much, but realize that she is unlikely to remember anything from this time. Why isn't this information stored? Or is it stored, but can't be accessed? So our new pet project is looking for a biological mechanism that explains this infantile amnesia.

In order to remember something, of course you have to learn something. But obviously there are times when you learn something but don't remember it. What is the switch? Are they parallel processes or does one follow the other? The separations and connections between learning and memory are interesting open questions in my field, and something we are still trying to tease out at the molecular level.

Interviewed by Kristie Nybo, Ph.D. Image courtesy of Paul Frankland.

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