Slide 1:

Hi my name is John Harkness and I am a neuroscientist at Oregon health and science University and Washington State university in Vancouver, where I conduct research on the neurobiology of behavior. We want to understand how our brains learn and remember, but also how these systems maintain flexibility.

We change a lot throughout our lives. Our brains are like little business, constantly receiving input, and producing product; and just like a business, it is always adapting to the pressures of the environment.

In fact, the brain's ability to respond to the environment is so important we have a word for it. "Plasticity."

—

Slide 2:

Here you can see a neurons, and some neighbors making synaptic connections. Our neurons receive input from these connections, and also send output to downstream connection. What is essential to our ability to adapt is that our brain cells make new connections with neurons all the time.

This happens following new experiences and new environmental pressures. When faced with a new challenge, our neurons will retool to better serve the need.

This happens for a couple of reasons. One is because the neuron is receiving new input; the supply chain has changed. Another is that the neuron is performing a slightly different function; for example, it might be helping remember part of a learned memory.

But once the neuron has retooled and responded to the new pressure, it needs to solidify the systems it has built and connections it has made.

—

Slide 3:

That is, we want some memories or adaptations to be long lasting. We are studying structures called perineuronal nets that help solidify these neural connections. I'm showing you a couple images here. On the right we are flying through some neurons that I photographed on our confocal microscope. We can see the PNN in green surrounding some neurons like a mesh net. On the left is another photograph of these nets. You can see the neuron in green and the PNN in red.

Illustrated below, you can see the pores that form around synaptic connections from other neurons, and acts to reduced plasticity of the connections. That is, the PNNs help to cement a habit or function.

So you can see that our brains are performing a balancing act. On one hand, we want to be plastic and agile in our ability to respond to the environment. On the other, we need to remember what we have learned and protect the systems we have in place.

Unfortunately, sometime a system becomes locked in place that is detrimental to the greater function of the brain and organism. One place that we see this is in behavioral like drug addiction.

—

Slide 4:

We use drug addiction to model behavioral agility and habit formation. Addiction is like a system that has become stuck in a way of doing things despite the loss of productivity. Addictions is the result of a neural circuit that has lost its ability to be plastic and adapt, which causes the brain and the organism to be less productive and could even risk its survival.

If we can induce plasticity in a brain that has locked in a system or habit, we think it will be able to retool and readapt to the pressures it faces. We will make the brain agile again.

To do that, we are eliminating PNNs in certain regions of the brain. We are allowing the neurons to be flexible, make new connections, and cut connections that are holding back adaptation. To do this, we introduce an enzyme that digests the PNNs to specific parts of the brain implicated in addiction. When we do this, we can see PNNs become less pronounced in the images we capture. More striking is that cocaine addicted rats will relearn to stop pressing a lever to receive cocaine.

That is, by shifting the balance away from maintaining stale connections and detrimental functions,and toward greater neural plasticity, we can re-introduce agility and help a brain retool for more productive functions. We think that treatment approaches that consider PNNs in brain plasticity can help individuals heal from drug use disorders, like cocaine addiction, and relearn more productive behaviors.

I worked with artist, Kindra Crick, the grand daughter of Francis Crick, one of the scientists that described the structure of DNA, to help us understand these PNNs. And I'm going to let Kindra tell you about this work.