Questions about quiet group of brain cells lead to new discovery

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What started as a project investigating the role of memories in Parkinson's disease patients took Hotchkiss Brain Institute (HBI) researchers Dr. Bin Hu and Taylor Chomiak, PhD, down a ten-year path towards what Hu calls the most significant discovery in his career.

And it has nothing to do with Parkinson's disease.

Their discovery, which was published in the in the flagship general-interest biology journal *BMC Biology*, is the first to explore a cellular mechanism by which the brain deactivates a group of neurons and then gradually reactivates them when the time is right.

Hu, who is also an associate member of the Alberta Children's Hospital Research Institute and Chomiak, in the Cumming School of Medicine's Department of Clinical Neurosciences, began their work looking at a region of the brain that is responsible for learning and memory and is known to be implicated in Parkinson's disease. The region is called the temporal association cortex (TeA) and one day Chomiak was looking at some neurons from young rats when he saw something unusual.

"Really the cells were just very quiet. Boring even," says Chomiak. "So I continued on with my other experiments and assumed it was maybe a technical limitation, or a different type of cell that we were seeing."

However hard he tried to ignore it though, the phenomenon persisted. The researchers moved labs, changed equipment, and still there was this quiet group of cells sitting in the periphery that they just couldn't explain.

"Finally I couldn't ignore it anymore - it became so profound and was so robust that we decided it was time to figure out what was going on."

The development of learning and memory: Starting small

In the context of learning and memory, there are several models to explain how the brain develops. One of the models that is supported by experimental data, states that there is a hierarchical mechanism of maturation - in essence, basic functions such as vision develop first and once those foundations are fully established, then the more complex functions such as learning and long term memory follow.

Starting small, the brain gradually builds on itself and increases in complexity as it grows and develops. Hu thinks this makes sense when you think about language acquisition in children, or infantile amnesia - the inability to remember things that happened to us when we were babies.

He explains, "As infants, we don't have the cognitive ability to correctly understand and judge the context for our experiences, so there are no evolutionary benefits for us to store them in our long term memory."

Previous research has shown on a macroscopic level that there are changes going on in the TeA as the brain develops. For example, MRI data has been able to show that there are changes in activity in the TeA at different points in neural development. Until now however, nobody has looked at what's going on at the cellular level.

Neurons are functionally decoupled and then gradually brought online

Hu is clearly excited by the discovery. "We are exploring this for the first time, showing that there are neurons in the brain that are present at birth, but remain dormant and are slowly activated as the brain matures."

Their work challenges the dogma that all neurons in the brain are present and fully active from birth.

Normally, information comes into the dendrites of a neuron and converges in the soma, or cell body. The soma then integrates all of this information and sends it down the axon where it goes out to be picked up by the dendrites of other neurons.

What Hu and Chomiak have discovered, is that there is a temporary lipid and protein layer that exists between the dendrites and the soma in neurons located in the TeA.

"The cell is still there and it's fully intact, but it is functionally disconnected," explains Chomiak. The message comes in to the dendrites, but then it hits the barrier and can't be passed on to the other cells in the network."

Over time, the barrier gradually disappears and slowly the cells 'wake up' and begin communicating with one another.

The scientists believe it is at this point that long term memories start to form.

Understanding the mechanism and how it could influence normal and abnormal neurodevelopment

Hu and Chomiak believe that this discovery is important for understanding how we learn and that it might have implications for certain neurodevelopmental disorders. They have started to look at what might be facilitating the decoupling and whether or not it can be manipulated.

When they added a growth factor that is known to be important in normal neurodevelopment, the scientists found that they could wake these cells up prematurely.

"This has led us to ask all kinds of new questions," says Chomiak. "Clearly this growth factor is important, so now we want to know how it is regulated and how or if it might be signalling this decoupling process."

The researchers have also observed certain neurodevelopmental disorders where there is an abnormal level of activity in this brain region at certain times.

"I think that this mechanism could be related to certain disorders where we have observed cells in the TeA coming online either too early, or too late," says Chomiak. "There seems to be a window of time for normal neurodevelopment and if we can understand this mechanism, I believe it could lead to interventions that could normalize these abnormal growth trajectories."

What started as an almost accidental observation has now become a major research focus for Hu and Chomiak, and one with a lot of potential impact. Perhaps that's the most interesting part of research - you never know what you might discover when you're busy looking for something else.

More information: Taylor Chomiak et al, Somato-dendritic decoupling as a novel mechanism for protracted cortical maturation,

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