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# Scientists find new clues to brain's wiring

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New research provides an intriguing glimpse into the processes that establish connections between nerve cells in the brain. These connections, or synapses, allow nerve cells to transmit and process information involved in thinking and moving the body.

Reporting online in *Neuron*, researchers at Washington University School of Medicine in St. Louis have identified a group of proteins that program a common type of brain nerve cell to connect with another type of nerve cell in the brain.

The finding is an important step forward in efforts to learn how the developing brain is built, an area of research essential to understanding the causes of intellectual disability and autism.

"We now are looking at how loss of this wiring affects brain function in mice," said senior author Azad Bonni, MD, PhD, the Edison Professor of Neurobiology and head of the Department of Anatomy and Neurobiology at the School of Medicine.

Bonni and his colleagues are studying synapses in the cerebellum, a region of the brain that sits in the back of the head. The cerebellum plays a central role in controlling the coordination of movement and is essential for what researchers call procedural motor learning, which makes it possible to move our muscles at an unconscious level, such as when we ride a bicycle or play the piano.

"The cerebellum also regulates mental functions," Bonni said. "So, impairment of the wiring of nerve cells in the cerebellum may contribute to movement disorders as well as cognitive problems including autism spectrum disorders."

His new results show that a complex of proteins known as NuRD (nucleosome remodeling and deacetylase) plays a fairly high supervisory role in some aspects of the cerebellum's construction. When the researchers blocked the NuRD complex, cells in the cerebellum called granule cells failed to form connections with other nerve cells, the Purkinje neurons. These circuits are important for the cerebellum's control of movement coordination and learning.

Bonni and his colleagues showed that NuRD exerts influence at the epigenetic level, which means it controls factors other than DNA that affect gene activity. For example, NuRD affects the configurations of molecules that store DNA and that can open and close the coils of DNA like an accordion, making genes less or more accessible. Changing the accessibility of genes changes their activity levels. For instance, cells can't frequently make proteins from genes in a tightly packed coil of DNA.

NuRD also alters tags on the proteins that store DNA, decreasing the chances that the gene will be used. Among the genes deactivated by NuRD are two that control the activity of other genes involved in the wiring of the cerebellum.

"This tells us that the NuRD complex is very influential—not only does it affect the activity of genes directly, it also controls other regulators of multiple genes," Bonni said.

Provided by Washington University School of Medicine