

NEWS

Brain's motor hub plays unsung role in social skills, cognition

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A handshake, a casual high-five, a polite and efficient end to a phone call: Such behaviors are among the building blocks of social interactions.

These interactions also require retooling behaviors on the fly — retracting an outstretched hand when the other person moves in for a hug or changing the subject when a conversation partner has lost interest.

All of these skills can be challenging for autistic people. And they all depend on the brain's hub for prediction, error correction and routine learning: the cerebellum.

The main job of the cerebellum, a butterfly-shaped structure at the base of the skull, was long thought to be coordinating movement — a function that has only peripheral ties to autism.

“If you go to the traditional view of the cerebellum, nothing about autism should at all jump out at you,” says **Peter Tsai**, assistant professor of neurology at the University of Texas Southwestern in Dallas.

But mounting evidence over the past decade has pointed to a role for the cerebellum in cognition and social skills. There is also increasing support for the idea that problems with the cerebellum contribute to autism.

“There's now more and more evidence to say that actually it's not just an innocent bystander, that suggests there is causation here,” Tsai says.

Researchers have traced connections between the cerebellum and social brain circuits — and have linked disruption of those circuits to autism or its traits. Meanwhile, behavioral data hint that the cerebellum calibrates social skills in a way that is analogous to its role in movement.

Knowledge of the region's importance in autism is inspiring a search for new treatments, too. Ideas range from electrical stimulation of the region to shaping cerebellar circuits through video games.

Moving target:

For more than 20 years, researchers have known that postmortem autism brains show a loss of **neurons called Purkinje cells**, which carry signals out of the cerebellum¹. This pattern is one of the most consistently identified features in these brains. Many imaging studies have also shown differences in the **size of the cerebellum**, or in parts of the structure, between autistic and neurotypical people².

For a long time, researchers did not know what to make of these findings. It was hard to square the notion of autism as a condition affecting communication and social skills with the cerebellum's role as a motor hub.

Still, evidence pointing to a **role for the cerebellum** in autism kept accumulating. Some of the findings suggested that **motor problems** "are actually a bigger part of autism than initially we recognized," says **Matthew Mosconi**, associate professor of clinical child psychology at the University of Kansas in Lawrence.

Mosconi and others have found that autistic people often have impairments in eye movements, grip strength and other functions linked to the cerebellum. And in 2018, a European analysis of brain scans from almost 500 people showed that people with autism have altered connectivity between the cerebellum and **sensory and motor networks** of the brain.

Other research links the cerebellum to autism's core traits. For example, disrupting certain genes associated with autism, such as **TSC1** and **PTEN**, only in Purkinje cells is enough to **trigger social problems in mice**. And infants born prematurely who have injuries to the cerebellum from bleeding or lack of oxygen around the time of birth have dramatically **increased odds of having autism**.

Consistent computation:

In the 2000s, researchers learned that the cerebellum has a topography of functional areas akin to those of the cerebral cortex, and that different parts of the cerebellum are active during different tasks³.

These findings expanded researchers' view of the cerebellum's role beyond the fine tuning of movement to predicting and correcting errors in other domains: Just as the cerebellum prevents

people from tripping on an uneven sidewalk, it might also alert them when they sit too close to a conversation partner, or help them laugh or sympathize at appropriate times.

“The principal idea is that whatever the cerebellum is doing for movement — of which there is a massive literature — the cerebellum might be doing something similar for cognition,” says **Catherine Stoodley**, associate professor of psychology at American University in Washington, D.C.

With that logic in mind, some researchers are studying movement problems in autism to uncover mechanisms that might also underlie the social and other cognitive difficulties that characterize autism.

For example, Mosconi’s team has found that people with autism have trouble **controlling the position** of a line on a computer screen by pressing a sensor between their thumb and forefinger with just the right amount of force⁴. “They either overcorrect or they undercorrect or they do it in a variable and unpredictable way,” Mosconi says.

Another group has found evidence that people with autism tend to rely more on **internal than visual feedback** when learning new movements⁵. This tendency could contribute to social difficulties in autism because most people learn social skills primarily through visual feedback, says **Stewart Mostofsky**, director of the Center for Neurodevelopmental and Imaging Research at the Kennedy Krieger Institute in Baltimore, Maryland, and the study’s lead researcher.

Social station:

Researchers are also probing specific regions of the cerebellum that appear to have strong links to autism, especially one known as the **right crus I** (RCrusI).

A 2017 study showed that disrupting RCrusI in mice produces social behavior, **repetitive behaviors** and mental inflexibility **reminiscent of autism**. But these mice do not have motor difficulties. “There’s something about this region that is divorced from the cerebellar motor coordination role,” says Tsai, who co-led the study.

The team also showed that RCrusI connects to two networks implicated in autism: the **default mode network**, which is active during daydreaming and sleeping, and the frontoparietal network, which is involved in high-level cognitive processes.

Disrupting connections between the cerebellum and another region — the ventral tegmental area, which is involved in reward — **diminishes mice’s interest in socializing**.

Adults who sustain damage to the cerebellum from tumors or strokes may also develop subtle social and emotional problems — but they do not acquire autism. This is “evidence that there was

something special that was happening that required the cerebellum early in life but not in adulthood,” says **Sam Wang**, professor of neuroscience at Princeton University. In other words, there may be a so-called ‘critical period’ for the cerebellum’s link to social behavior.

In line with this idea, Wang and his colleagues showed last year that **inactivating parts of the cerebellum** early in life, but not later on, leads to autism-like traits in mice.

“What this shows is that the cerebellum appears to be necessary for the normal development of these cognitive and social capacities,” Wang says.

In support of a critical period, Tsai and his colleagues have shown that a drug called rapamycin can prevent Purkinje cell loss and **reverse some autism traits** in mice lacking TSC1 in this cell type — but only when the mice are younger than 10 weeks. It’s unclear whether a similar window of opportunity exists in people.

Stoodley is investigating the use of **transcranial direct current stimulation**, which delivers current to the brain via electrodes placed on the scalp, to alter activity in parts of the cerebellum. And Mostofsky and his colleagues are trying to train the visual motor systems in autistic children using a video game in which players try to imitate dance movements. The training is designed to fine tune ties between RCrus1 and other brain regions in a bid to improve social behavior.

Meanwhile, researchers continue to explore the workings of the cerebellum, and their relationship to autism. Cutting-edge techniques such as advanced microscopy are contributing to a new understanding of this brain structure’s functions.

“People have really started grooving to the idea that it’s possible to study these non-motor functions of the cerebellum in ways that were just not possible even five years ago,” Wang says.

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