Scientists identify brain region in mice that keeps the body from losing its balance

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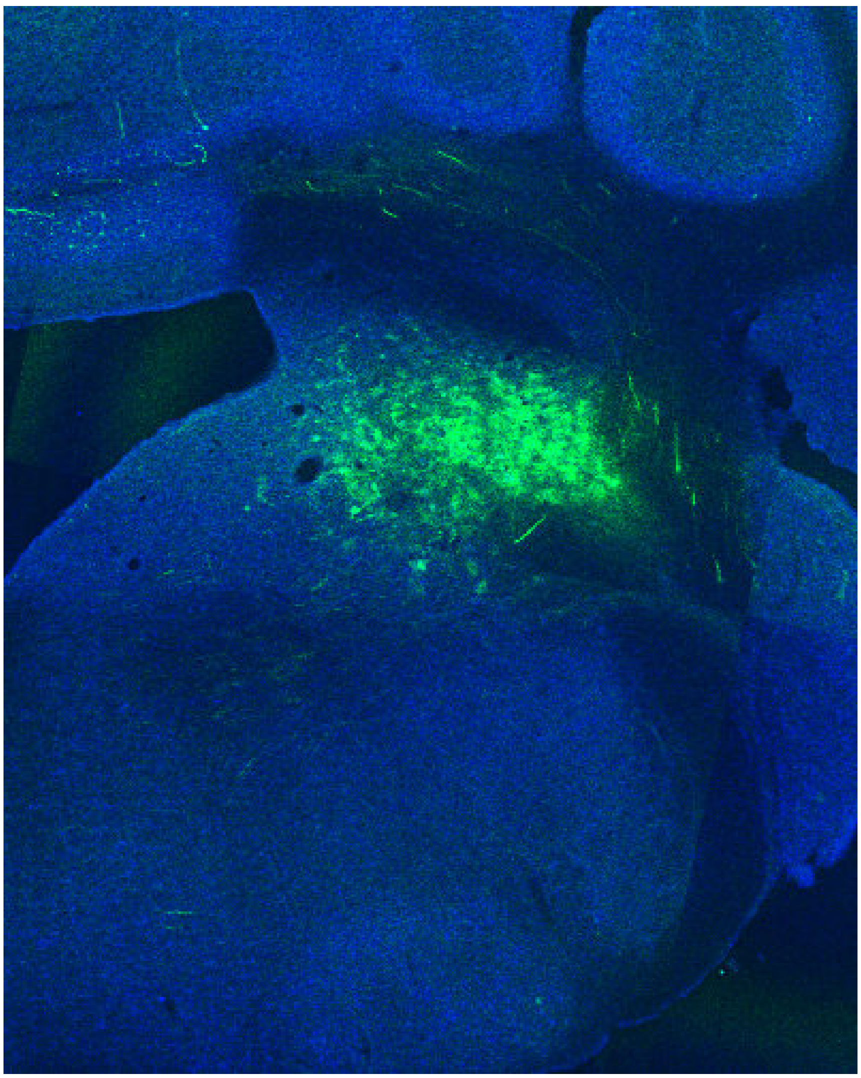

A mouse brain that has received an injection of an adeno-associated virus (green) into the LVN. The virus makes a synaptic protein that is tagged with green fluorescent protein, this allows us to follow the projections coming from the LVN through the brain and spinal cord. Credit: Andrew Murray/Jessell

Lab/Columbia's Zuckerman Institute

New scientific research has revealed how a small part of the brain singlehandedly steadies the body if it is thrown off balance. The study in mice found that a brain region called the lateral vestibular nucleus, or LVN, accomplishes this feat by moving muscles in a two-step, kneejerk response that first widens the animal's center of gravity, and then strengthens and stabilizes its limb muscles and joints. These findings provide powerful evidence that the LVN is the key to animals' ability to maintain balance, while also offering insight into the mechanics of how animals stay upright when unexpected changes occur beneath their feet.

The study was published today in *Cell Reports*.

"Whether it's tripping on an uneven patch of sidewalk or negotiating a wobbly balance beam, we can all recall times when we've nearly lost our balance—only to be saved by some quick reflexes," said Thomas M. Jessell, PhD, codirector of Columbia's Mortimer B. Zuckerman Mind Brain Behavior Institute and the paper's senior author. "Today's findings in mice suggest that reflexes like these may be driven by a predictable process guided by the LVN, a brain region that appears to be dedicated to one thing: keeping the body on its feet."

Decades of research has shown that multiple brain regions are involved in different aspects of balance. But which regions were involved in the reactive parts of balance—how an animal maintains its stance after experiencing a disturbance—remained unclear.

To get to the root of balance in the brain, the researchers first trained mice to walk across a balance beam, while the beam was nudged at specific intervals. After being momentarily thrown off balance, the mice almost always steadied themselves and continued on their way. Throughout this activity, researchers monitored muscle activity in the animals' limbs.

"Every time we nudged the beam, we observed a predictable pattern of muscle activity that helped the mice to regain their balance," said Andrew Murray, PhD, the paper's first author who completed the majority of this research while a postdoctoral researcher at Columbia in the Jessell Lab.

That pattern consisted of two movements in sequence: first, the mouse extended its paw, which widened the animal's base of support. Second, the muscles around the animal's limb joints become strong and rigid, which helped the mouse propel itself back over the center of the balance beam. Once they've righted themselves, they continued to walk down the length of the beam.

This reflexive action is something to which nearly everyone can relate.

"If you've ever been standing on a subway train when it moved suddenly, your body may have performed a similar sequence of movements to keep you upright," said Dr. Jessell, who is also the Claire Tow Professor of Motor Neuron Disorders at Columbia University Irving Medical Center and an investigator at the Howard Hughes Medical Institute. "First, you extend your hands or feet outward to widen your base of support. And if you find yourself falling to one side, you may push yourself in the opposite direction to regain your balance."

In a second set of experiments, the researchers sought to identify how the animals' brains made all this possible. By using advanced molecular tools, they traced which brain region directed these specific movements. The data pointed to a tiny region in the brain called the LVN.

To confirm that the LVN was indeed responsible for maintaining balance, the researchers then silenced it. When the mice walked on the ground, they appeared normal. They could even walk on the beam—but when the scientists again nudged the beam, this time they could not steady themselves; they'd lost their ability to regain their balance.

"Intriguingly, the brain had no backup plan; no other part of the brain stepped in to compensate for the LVN," said Dr. Murray, now a Group Leader at the Sainsbury Wellcome Centre, University College London. "This points to the fact that the LVN is orchestrating the movements that keep the body balanced."

Moving forward, the researchers are delving deeper into the brain science of balance. For example, preliminary research in mice has shown that the LVN appears to perk up when the animal begins walking on something unsteady, such as a balance beam. But when it is walking on a more stable surface, such as a treadmill, it remains dormant.

"The brain seems to know that it's about to embark upon a potentially dangerous journey, and therefore needs to be extra aware of its surroundings," said Dr. Jessell. "The precise mechanisms that guide this process are likely complex, involving multiple brain regions. But the LVN may very well be at the center of it all."

This paper is titled "Balance control mediated by vestibular circuits during limb extension or antagonist muscle co-activation."

More information: Balance control mediated by vestibular circuits during limb extension or antagonist muscle co-activation, *Cell Reports* (2018).

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