Different neuronal groups govern right-left alternation when walking

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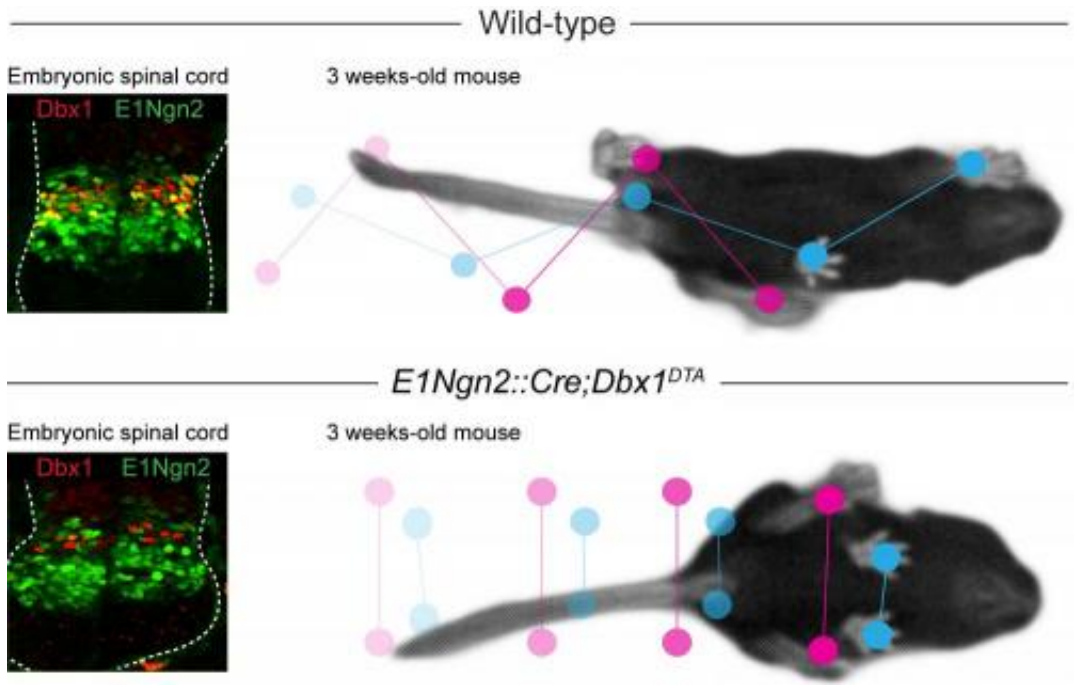


In the embryonic spinal cord, progenitor cells express various genes that determine their final cell specificity. In normal mice (top image) some nerve cells express the genes Dbx1 (red), E1Ngn2 (green), or both (yellow). When walking, animals move their left and right limbs in alternation. In contrast, when animals were genetically engineered to lack the nerve cells co-expressing Dbx1 and E1Ngn2 (bottom image, note absence of yellow cells), their walking gait was changed to a complete rabbit-like hopping, with the left and right limbs moving in synchrony. Credit: Julien Bouvier

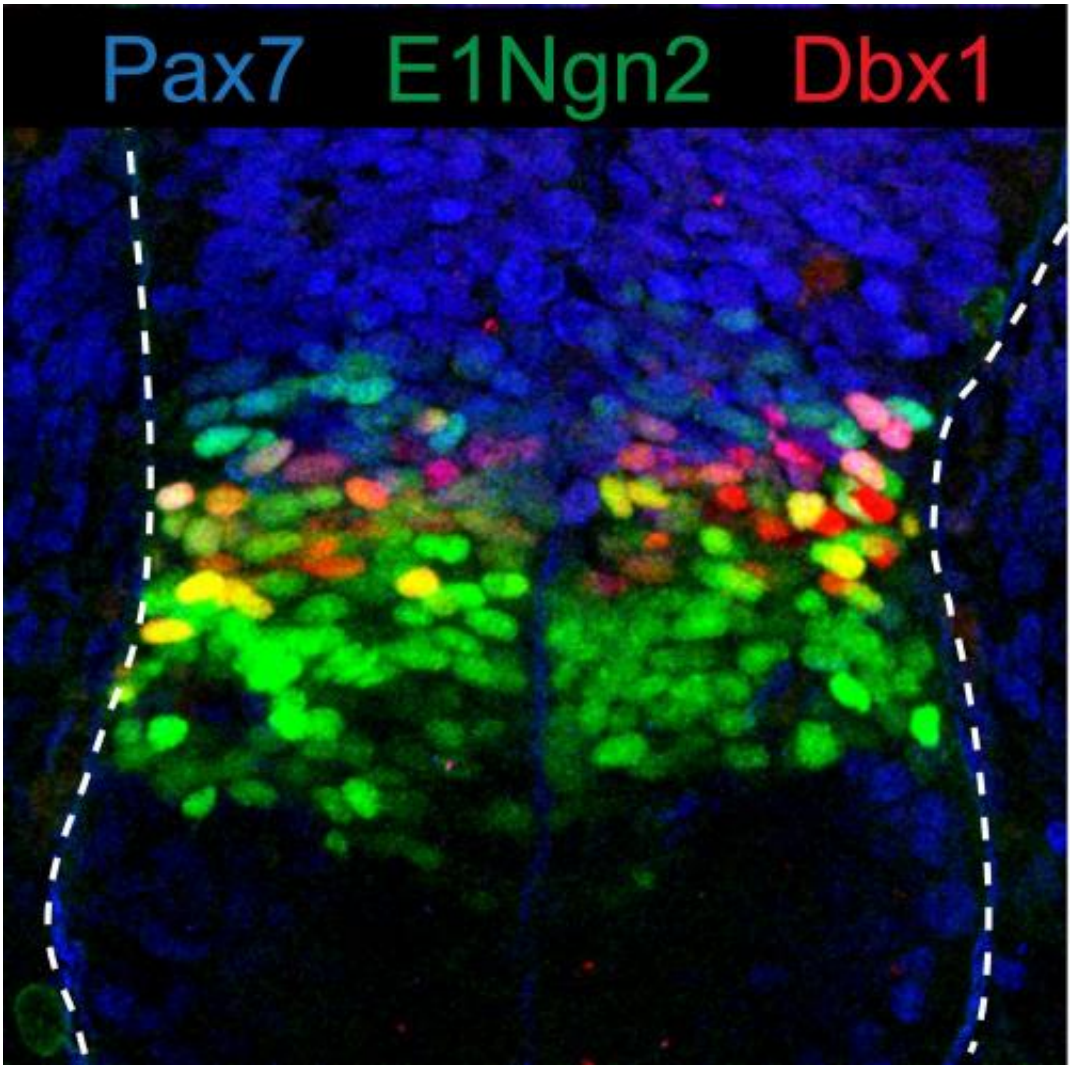
Scientists at Karolinska Institutet in Sweden have identified the neuronal

circuits in the spinal cord of mice that control the ability to produce the alternating movements of the legs during walking. The study, published in the journal *Nature*, demonstrates that two genetically-defined groups of nerve cells are in control of limb alternation at different speeds of locomotion, and thus that the animals' gait is disturbed when these cell populations are missing.

Most land animals can walk or run by alternating their left and right legs in different coordinated patterns. Some animals, such as rabbits, move both leg pairs simultaneously to obtain a hopping motion. In the present study, the researchers Adolfo Talpalar and Julien Bouvier together with professor Ole Kiehn and colleagues, have studied the spinal networks that control these movement patterns in mice. By using advanced genetic methods that allow the elimination of discrete groups of neurons from the spinal cord, they were able to remove a type of neurons characterized by the expression of the gene Dbx1.

"It was classically thought that only one group of nerve cells controls left right alternation", says Ole Kiehn who leads the laboratory behind the study at the Department of Neuroscience. "It was then very interesting to find that there are actually two specific neuronal populations involved, and on top of that that they each control different aspect of the limb coordination."

Indeed, the researchers found that the gene Dbx1 is expressed in two different groups of nerve cells, one of which is inhibitory and one that is excitatory. The new study shows that the two cellular populations control different forms of the behaviour. Just like when we change gear to accelerate in a car, one part of the neuronal circuit controls the mouse's alternating gait at low speeds, while the other population is engaged when the animal moves faster. Accordingly, the study also show that when the two populations are removed altogether in the same animal, the mice were unable to alternate at all, and hopped like rabbits instead.



The generation of the many different types of nerve cells is controlled early during embryogenesis, where distinct pools of precursor cells express distinct combinations of genes that control neuronal fate. In this illustration from an embryonic mice spinal cord, precursor cells were labeled by a different color depending on the gene they express. Using modern mice genetics, the authors have ablated specific subgroups of those precursors cells and unveiled the neuronal circuitries that control left-right hindlimb coordination during walking. Credit: Ole Kiehn, *Nature* June 2013

There are some animals, such as desert mice and kangaroos, which only

hop. The researchers behind the study speculate that the locomotive pattern of these animals could be attributable to the lack of the Dbx1 controlled alternating system.

More information: "Dual-mode operation of neuronal networks Involved in left-right alternation", Adolfo E Talpalar, Julien Bouvier, Lotta Borgius, Gilles Fortin, Alessandra Pierani, and Ole Kiehn, *Nature*, AOP 30 June 2013. DOI: 10.1038/nature12286

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