Midbrain 'start neurons' control whether we walk or run

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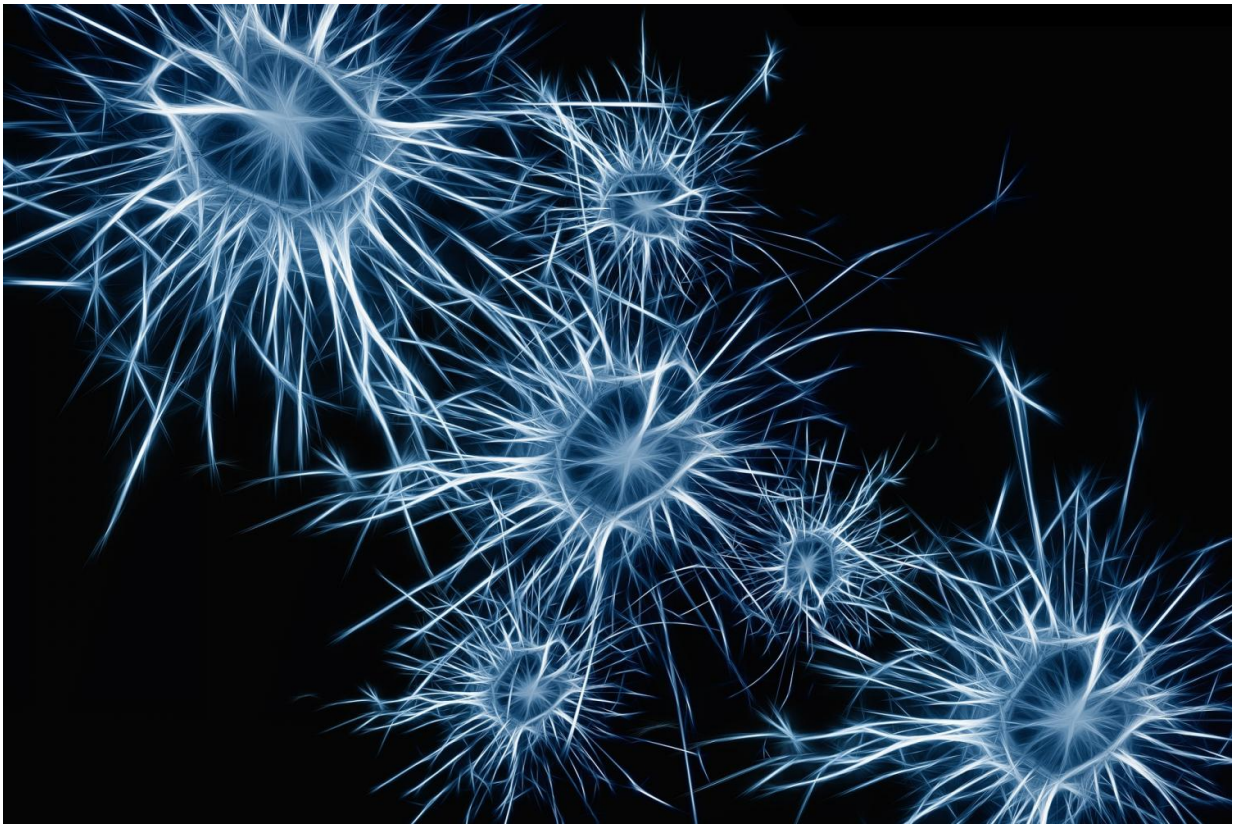

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Locomotion comprises the most fundamental movements we perform. It is a complex sequence from initiating the first step, to stopping when we reach our goal. At the same time, locomotion is executed at different

speeds to regulate how fast we travel from one place to another. Now, a new study published in the journal *Nature* shows that two regions in the midbrain, the cuneiform nucleus (CnF) and the pedunculopontine nucleus (PPN) play specific roles in controlling the start, speed and context-dependent selection of locomotion in mice.

"We find that neurons in both PPN and CnF can start locomotion and that activity in these areas contribute to the maintenance and speed regulation of slower locomotion. However, only CnF is able to elicit the high-speed escape locomotor activity. In contrast, activity in PPN neurons favours slow explorative locomotion," says Professor Ole Kiehn Department of Neuroscience, UCPH.

While the precise coordination of locomotor movements is controlled by neuronal circuits in the spinal cord, the episodic control of locomotion is attributed to descending signals from the brainstem that activate neuronal circuits in the spinal cord.

The midbrain circuits are complex and contain neurons of many different types although the main players are shown to be the so-called glutamatergic neurons. The researchers have used a number of advanced techniques, including optogenetics, to study which types of neurons are involved and the location of the neural networks. By using light and designer drugs, they have been able to activate or inactivate selected groups of nerve cells and to study how this affects the locomotor output in mice.

The researchers identify populations of "start neurons," and show, for the first time, how the two regions in the midbrain can act both in common or separately to control speed and to select context dependent locomotor behaviours.

"By identifying the midbrain 'start' neurons, we complement a previous

study where we found 'stop cells' in the brainstem that halt locomotion. Together, the start and stop cells define the episodic nature of locomotion," says Ole Kiehn.

The study breaks new ground in locomotor control, and is important for understanding the normal brain function in mice. And the authors believe that the results might benefit humans with disabled locomotion as well. "In Parkinson's disease which affect the basal ganglia—one of the main source of inputs to the PPN—gait disturbances and freezing of gait are very pronounced. By implanting fine electrodes in the brain—a technique called deep brain stimulation which is already used to treat some symptoms in Parkinson's disease—circuits in either CnF or PPN might now be targeted with new precision and used to increase the locomotor capabilities. Similar approaches may also be attempted after damage to the spinal cord, where initiation of locomotion is strongly affected," says Ole Kiehn.

More information: V. Caggiano et al, Midbrain circuits that set locomotor speed and gait selection, *Nature* (2018). DOI: 10.1038/nature25448

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