Every action has a beginning and an end (and it's all in you brain)

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Rui Costa, Principal Investigator of the Champalimaud Neuroscience Programme at the Instituto Gulbenkian de Ciencia (Portugal), and Xin Jin, of the National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health (USA), describe in the latest issue of the journal *Nature*, that the activity of certain neurons in the brain can signal the initiation and termination of behavioural sequences we learn anew. Furthermore, they found that this brain activity is essential for learning and executing novel action sequences, many times compromised in patients suffering from disorders such as Parkinson's or Huntington's.

Animal behaviour, including our own, is very complex and is many times seen as a sequence of particular actions or movements, each with a precise start and stop step. This is evident in a wide range of abilities, from escaping a predator to playing the piano. In all of them there is a first initial step and one that signals the end. In this latest work, the researchers explored the role of certain brain circuits located in the basal ganglia in this process. They looked at the striatum, its dopaminergic input (dopamine-producing neurons that project into the striatum) and its output to the substantia nigra, another area in the basal ganglia, and found that both play an essential role in the initiation and termination of newly learnt behavioural sequences.

Rui Costa and Xin Jin show that when mice are learning to perform a particular behavioural sequence there is a specific neuronal activity that emerges in those brain circuits and signals the initiation and termination steps. Interestingly these are the circuits that degenerate in patients

suffering from Parkinson's and Huntington's diseases, who also display impairments both in sequence learning, and in the initiation and termination of voluntary movements. Furthermore, the researchers were able to genetically manipulate those circuits in mice, and showed that this leads to deficits in sequence learning by the mice - again, a feature shared with human patients affected with basal ganglia disorders.

Rui Costa explains the implications of these results: "For the execution of learned skills, like playing a piano or driving a car, it is essential to know when to start and stop each particular sequence of movements, and we found the neuronal circuits that are involved in the initiation and termination of action sequences that are learnt. This can be of particular relevance for patients suffering from Huntington's and Parkinson's disease, but also for people suffering from other disorders like compulsivity".

Xin Jun adds: "This start/stop activity appears during learning and disrupting it genetically severely impairs the learning of new action sequences. These findings may provide a possible insight into the mechanism underlying the sequence learning and execution impairments observed in Parkinson's and Huntington's patients who have lost basal ganglia neurons which may be important in generating initiation and termination activity in their brain".

More information: Xin Jin & Rui M. Costa; 'Start/stop signals emerge in nigrostriatal circuits during sequence learning'; Nature, volume 466, issue 7305, pp 457-462. DOI: 10.1038/nature09263

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