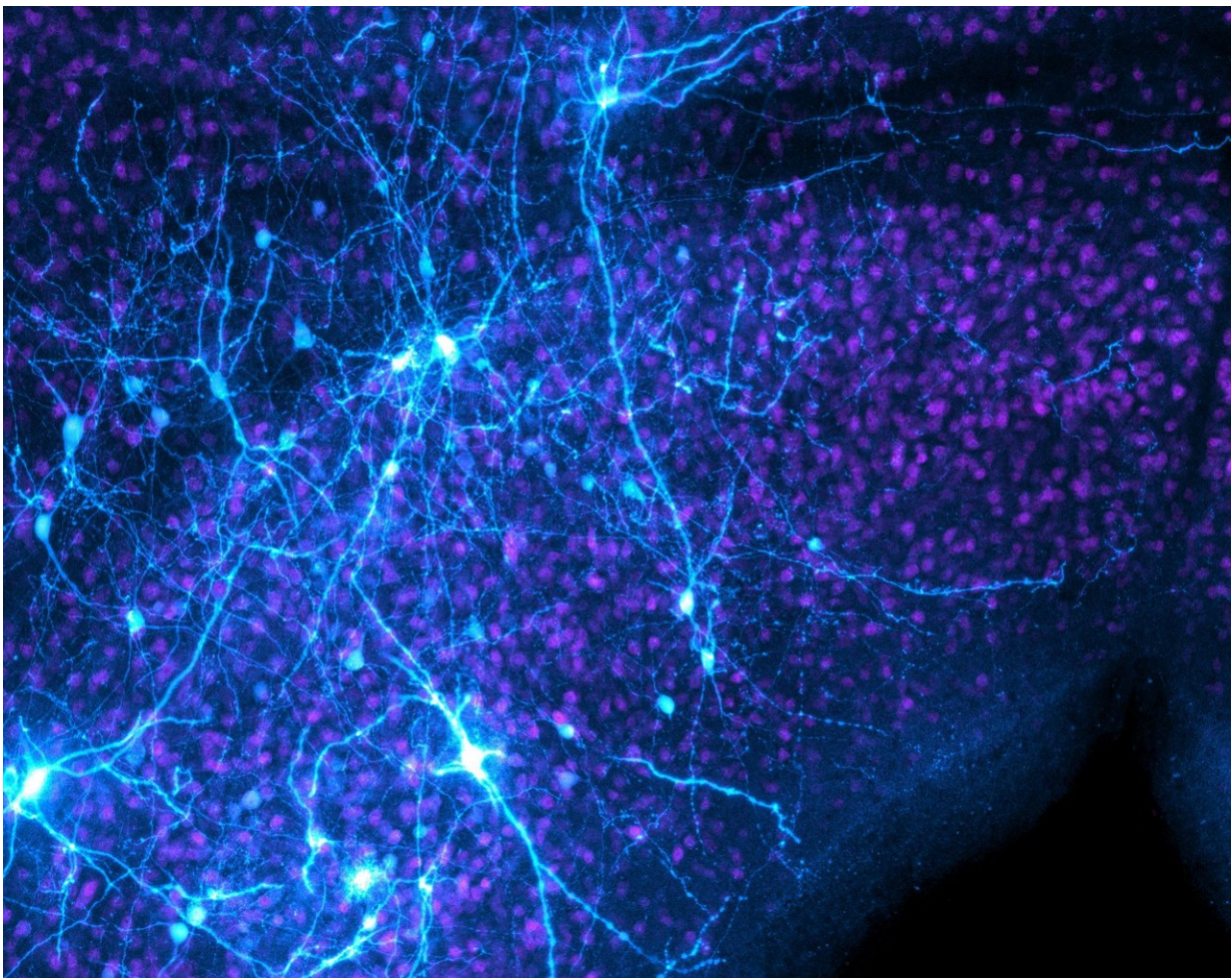


Study on instinctive behaviour elucidates a synaptic mechanism for computing escape decisions

June 21 2018



Escape decision neurons in the mouse midbrain. Credit: Sainsbury Wellcome Centre

How does your brain decide what to do in a threatening situation? A new paper published in *Nature* describes a mechanism by which the brain classifies the level of a threat and decides when to escape.

Escaping from a dangerous situation is crucial for survival, but it is also important to only escape from settings that really are dangerous. This is because decisions to escape are almost always trade-offs between safety and access to things of value. For example, animals need to forage, but when they are scared and hiding in their shelter, they are missing out on vital opportunities of finding food and mates.

This dynamic can be completely debilitating in humans with [post-traumatic stress disorder](#) (PTSD) or severe anxiety, as such individuals can become confined to their homes due to pathological fear. Thus it is important for [brain](#) circuitry to correctly classify and act on threats in the environment.

Dr. Tiago Branco, Senior Research Fellow at Sainsbury Wellcome Centre, commented: "We are excited to have found a subcellular mechanism for computing the very important [decision](#) of running away from threats. This level of detailed understanding not only advances our knowledge of how the brain makes fundamental computations, but also gives us an entry point to figure out what goes wrong in conditions that cause abnormally frequent defensive behaviours, and potentially, how to treat them."

Previous research identified parts of the brain important for escape behaviour, but up until now it wasn't known whether these regions were also involved in evaluating threat level and implementing decisions to escape. A team of neuroscientists led by Dr. Branco working first at the MRC Laboratory of Molecular Biology (LMB) and recently at the Sainsbury Wellcome Centre, systematically tested the innate reactions of mice to looming shadows, as would occur from a bird of prey, an

evolutionarily conserved behaviour that is not learnt. Using this approach they have deciphered how escape decisions are implemented in the brain at the algorithmic and mechanistic level, describing the process as a 'threshold computation' of threat level.

The work demonstrated that these decisions are made at the connections between two different parts of the brain: the superior colliculus (SC), which is responsible for integrating information about the threat and estimating the threat level, and the periaqueductal gray (PAG), which represents the activity above the threshold and causes the animal to escape.

The threshold mechanism arises because the SC-PAG connection is very weak and unreliable, so it fails most of the time. It is only when the [threat](#) level rises and is sustained that there is sufficient activity to overcome this weak connection and initiate escape. In this way the decision is computed at the level of the synaptic connection between the SC and PAG.

The study makes use of a wide range of techniques, including quantitative behaviour assays that manipulate the probability of whether the animal escapes to threats, and neural activity recordings with head-mounted microscopes and high-density Neuropixels silicon probes. In addition, a special form of chemogenetics was used to specifically inactivate the SC-PAG synapse and thereby prove that the computation of this threshold is implemented by this synaptic connection. Furthermore a computational model was developed that describes the observed behaviour.

The next piece of the puzzle will be to understand how the threshold for the decision is modulated based on past experience and the current conditions of the environment. "Successfully escaping from threats can be a very complicated process that relies on your particular

representation of the environment you are in, and what to expect from it. This is at the core of how the brain generates behaviour, and now that we have figured out a critical part of the brain neural circuitry that controls the decision to escape, we can start to explore the computation of complex variables that influence escape decisions, such as how likely it is that safety can be reached, and what are the fastest routes to possible shelters," Dr. Branco concluded.

More information: A synaptic threshold mechanism for computing escape decisions, *Nature* (2018). DOI: [10.1038/s41586-018-0244-6](https://doi.org/10.1038/s41586-018-0244-6) , www.nature.com/articles/s41586-018-0244-6

Provided by University College London

Citation: Study on instinctive behaviour elucidates a synaptic mechanism for computing escape decisions (2018, June 21) retrieved 2 May 2024 from <https://medicalxpress.com/news/2018-06-instinctive-behaviour-elucidates-synaptic-mechanism.html>

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