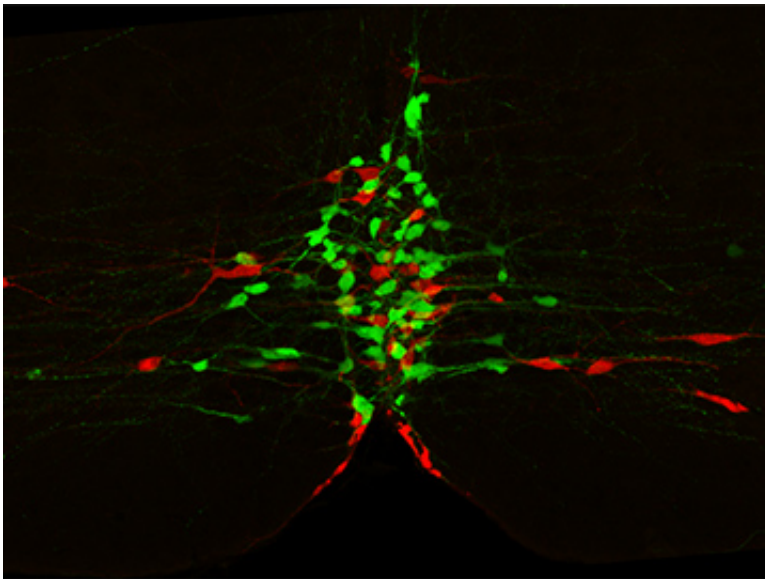


Good things come to those who wait? More serotonin, more patience

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Two subtypes of serotonergic neurons, one marked green and one marked red, intermingle in a mouse brain stem, yet have different functions. Image: Rachael Brust

In a study published today in the journal *Current Biology*, a team of scientists, led by Zachary Mainen at the Champalimaud Centre for the Unknown (CCU), found a causal link between the activation of serotonin neurons and the amount of time mice are willing to wait, and rejected a possible link between increased serotonin neuron activation and reward.

Serotonin is a neuromodulatory chemical that is targeted by

antidepressant drugs, such as Prozac, which are widely used to treat depression and other disorders such as chronic pain. Serotonin is normally released by a small set of cells in an area of the brain called the raphe nuclei. However, what naturally causes these neurons to become active and release [serotonin](#) and how this affects brain function are still poorly understood.

To investigate the role of serotonin in patience, the researchers used a task in which [mice](#) have to wait for a reward that arrives at random times. During some of the trials, they stimulated serotonin neurons using a technique called optogenetics. "We made serotonin neurons sensitive to light, so when we illuminated them, they were activated and released serotonin in the brain", said Madalena Fonseca, team member at the CCU.

The scientists observed that when they activated serotonin neurons, mice became more patient. Explained Masayoshi Murakami, also part of the CCU team, "we tested how different levels of activation influence waiting and saw that stronger activation resulted in longer waiting durations - the more serotonin neurons were activated, the longer the mice would wait."

To test whether increased waiting was a side effect of another serotonin function, the scientists performed experiments to test if stimulation of serotonin neurons could act as a reward. "If the sensation of serotonin was pleasant or rewarding for the mice, this could have explained why they waited longer", said Fonseca. To do this, they tested whether mice preferred to perform actions associated with serotonin stimulation. The results of these experiments were negative, ruling out that increased patience was a consequence of reward.

This study has implications for understanding the involvement of serotonin in depression and other diseases. "Because antidepressants are

thought to increase serotonin, people assume that more serotonin neuron firing would feel good. Our results show that the story is not so simple. That serotonin affects patience gives us an important clue that we hope will help us crack the serotonin mystery", said Zachary Mainen. The Champalimaud team is continuing to investigate other aspects of serotonin function in work funded by the European Research Council.

Provided by Champalimaud Centre for the Unknown

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