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Depressed mice have excitable neurons

Study pinpoints cells involved in coping with stress.

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A group of neurons was much more excitable in depressed mice compared with more resilient ones.

Most people handle stress well, but some find it difficult to cope and as a result develop depression and other mood disorders. Researchers have previously been able to identify the part of the brain that controls this response, but not exactly how it does so. Now, a study in mice identifies a small group of neurons that could be responsible. The research might also help elucidate the mechanism of deep brain stimulation, a therapy that uses electrical impulses to treat depression and other neurological disorders.

How an animal deals with stress is controlled by a part of the brain known as the prefrontal cortex, and the neurons in this part of the brain are known to change in structure and function in response to stressful situations[1]. To look at the cellular basis of the responses, neuroscientist Bo Li of Cold Spring Harbor Laboratory in New York and his colleagues subjected mice to small electric shocks at random intervals to produce stress. Most of the mice tried to avoid the shocks, but just over one-fifth did not. They also started to avoid other animals or failed to choose tasty foods over plain ones — typical signs of depressive behaviour.

The researchers then looked at the animals' brains and found that a specific set of neurons in the prefrontal cortex were easily excitable in depressed mice, but much harder to excite in those resilient to the stress. Furthermore, artificially increasing the activity of these neurons caused mice that were once resilient to become susceptible to depressive behaviours. “We were surprised that we were able to see a difference between depressed and resilient animals at the level of synaptic transmission,” says Li.

The results, published today in the *Journal of Neuroscience*[2], suggest that these cells are responsible for responses to stress, although why they respond differently in some animals than in others remains a mystery. “The mechanism is unlikely to be as simple as enhancing or decreasing activity,” Li says. “It’s about specific neuronal elements in the circuit, and looking at these might be more meaningful for better treatments.”

Pathway to treatment

The researchers have identified a “critical pathway and brain area that seems to be important in resilience”, says neurologist Helen Mayberg of Emory University in Atlanta, Georgia. If the same pathway is relevant in people, then the findings could point to ways to treat major depression, which affects around 7% of US adults in any one year.

For instance, a technique known as deep brain stimulation — the delivery of electrical impulses to specific brain regions through implants — has shown promise in the treatment of depression and can inhibit the activity of neurons[3]. But its precise mechanism of action is still unclear. By identifying the specific neurons linked to depression-like behaviour in mice, this study could help point to the underlying mechanism. The therapy is approved by the US Food and Drug Administration for Parkinson's disease and a few other conditions, but not yet for depression.

"This is the first time we have differentiated behaviour using an electrophysiological method," says Li. "If we do this more and more with different types of cells, we can put these pieces together to understand how deep brain stimulation might work."

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References

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