

Research uncovers how antidepressants actually work

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(PhysOrg.com) -- Australian researchers at UQ's Queensland Brain Institute have uncovered how antidepressants stimulate the brain to improve a person's mood.

They have discovered the class of drugs that increase levels of a neurotransmitter known as 'norepinephrine' triggers neurogenesis - the growth of new neurons - in a [brain](#) region called the [hippocampus](#).

“If you block hippocampus neurogenesis, [antidepressants](#) no longer work,” lead researcher Dr Dhanisha Jhaveri said.

“That suggests antidepressants must up-regulate neurogenesis in order for them to actually have any affect on behaviour.”

However, the neuroscientists also found not all antidepressants worked in the same way.

Dr Jhaveri said surprisingly, the class of antidepressants that increase levels of the [neurotransmitter](#) called serotonin - Prozac is a common example - fails to stimulate neurogenesis.

“[Norepinephrine](#) is basically binding directly onto the precursors which then initiate a signal which leads to the production of more neurons,” she said.

“Serotonin just doesn't do that. Prozac doesn't work by regulating the

precursor activity - it may work outside that region, but it isn't regulating the hippocampus directly. More research is needed to find out what [serotonin](#) actually does.”

Using rodent models the research, published today in the [Journal of Neuroscience](#), established that selectively blocking the re-uptake of norepinephrine directly activated hippocampal stem cells thereby discovering a much larger pool of dormant precursors in the hippocampus than previously thought to exist.

The researchers also improved their understanding of the mechanisms by which norepinephrine activated the precursors in the hippocampus and found the expression of beta3 adrenergic receptors is critical in mediating the effect.

Fellow researcher and team leader Professor Perry Bartlett said armed with this information, the team would be able to explore improved treatments for depression as well as dementia.

“Since dementia, especially in the ageing population, appears to be related to a decrease in neurogenesis this discovery opens up exciting new ways to stimulate the production of new [neurons](#) to alleviate the devastating effects of dementia in our society,” Professor Bartlett said.

Dr Jhaveri said the findings would also allow researchers to develop specific and more effective antidepressants.

“Depression is such a complex disorder, so we are going to test different behavioural outcomes to see whether the compounds that increase norepinephrine levels or stimulate beta3 adrenergic receptors work only for certain aspects of depression. We just don't know yet but it may, for example, improve learning and memory, or reduce anxiety,” Dr Jhaveri said.

More information: Journal of Neuroscience -- www.jneurosci.org/

Provided by University of Queensland

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