

New discoveries on depression

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(Medical Xpress) -- During depression, the brain becomes less plastic and adaptable, and thus less able to perform certain tasks, like storing memories. Researchers at Karolinska Institutet have now traced the brain's lower plasticity to reduced functionality in its support cells, and believe that learning more about these cells can pave the way for radical new therapies for depression.

"We were able to cure memory dysfunction in 'depressed' rats by giving them doses of D-serine," says Mia Lindskog, biologist and Assistant Professor at Karolinska Institutet's Department of [Neuroscience](#).

Dr Lindskog and her team used FSL rats, which are rats that have been specially bred with a disposition for 'depression'. The rats were first put through two tests to confirm that they had the symptoms that are also characteristic of human depression. In the first, the rats' memories were checked by repeatedly being exposed to different objects; in the second, the team assessed their level of apathy by releasing them in a container of water and observing whether they merely stayed floating in the container or immediately tried to climb out (non of the rats had to stay in the water for more than five minutes). In both cases the FSL rats' results were compared with normal [laboratory rats](#), and [memory disorders](#) and apathy could be confirmed.

The researchers then injected the rats with D-serine. This substance improved their memories but had no effect on the [apathy](#).

"We have shown that there are two symptoms here that can be

influenced independently of one another, which means they could be treated in tandem in patients with depression," says Dr Lindskog.

The researchers also studied the synaptic activity in the [hippocampus](#) of the rats, a part of the [brain](#) which plays an important part in the memory. They found that there was a much higher degree of [synaptic activity](#) in the brains of the depressed rats than in the controls. However, when the researchers tried to increase the level of signal transmission, they found the brains of the depressed rats to be unresponsive, which indicated that they had a lower plasticity that rendered them unable to increase neuronal activity when needed - unlike the brains of the healthy rats. When the brain samples were soaked in D-serine, the plasticity of the depressed rats' brains improved.

D-serine is a substance secreted by astrocytes, which are support cells for brain neurons.

"We don't actually know very much about these glial cells, but it's very likely that they perform a very important function in the brain," says Dr Lindskog.

It is hoped that their discoveries will eventually lead to new therapies for depression.

"D-serine doesn't pass the blood-brain barrier particularly well, so it's not really a suitable candidate on which to base a drug, but the mechanism that we've identified, whereby it's possible to increase plasticity and improve the memory, is a feasible route that we might be able to reach in a way that doesn't involve D-serine," says Dr Lindskog.

More information: Marta Gómez-Galán, Dimitri De Bundel, Ann Van Eeckhaut, Ilse Smolders & Maria Lindskog, Dysfunctional Astrocytic Regulation of Glutamate Transmission in a Rat Model of Depression,

[Molecular Psychiatry](#), online 28 February 2012.

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