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Hippocampal Neurogenesis in Mice Key to New Brain Research



Scientists have found that antidepressants (sertraline and tofranil) can boost the growth of new neurons in the hippocampus of mice. This finding is important for treatment of depression, dementia, and brain trauma.

one of the ways that antidepressants work is by boosting neurogenesis in the hippocampus. Christoph Anacker and his colleagues at King's College London have now worked out how they do so.

Previous research has shown a link between some antidepressants and stress hormones called glucocorticoids. So Anacker's team decided to test whether the antidepressant sertraline acts on the glucocorticoid receptors of brain cells. They grew human hippocampal progenitor cells in a dish and added sertraline. Ten days later, the cultures showed a 25 per cent greater than expected increase in the number of new neurons.

When the researchers added a drug to block the glucocorticoid receptors before adding the antidepressant, the number of new neurons produced after 10 days was similar to that expected from natural growth. This suggests that the antidepressant does indeed exert its effect through this receptor (Molecular Psychiatry, DOI: 10.1038/mp.2011.26). _NewScientist

US researchers suspect that this neurogenic effect of antidepressants may prove useful in the treatment of brain injury.

Jason Huang, M.D., and colleagues undertook the study after noticing that patients with brain injuries who had been prescribed anti-depressants were doing better in unexpected ways than their counterparts who were not taking such medications. <u>Not only did their depression ease:</u> their memory also seemed improved compared to patients not on the medication.

"We saw these patients improving in multiple ways – their depression was improved, but so were their memory and cognitive functioning. We wanted to look at the issue more, so we went back to the laboratory to investigate it further," said Huang, associate professor of Neurosurgery and chief of Neurosurgery at Highland Hospital, an affiliate of the University of Rochester Medical Center.

The team's findings were published online recently in the Journal of Neurotrauma.

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Huang said many patients who have a traumatic brain injury also experience depression – by some estimates, half of such patients are depressed. Doctors aren't sure whether the depression is a byproduct of the sudden, unfortunate change in circumstances that patients find themselves in, or whether the depression is a direct consequence of brain damage.

Previous research by other groups indicated that anti-depressants help generate new brain cells and keep them healthy in healthy animals. That, together with the experience of his patients, led Huang to study the effects of the anti-depressant imipramine (also known as Tofranil) on mice that had injuries to their brains.

Scientists found that imipramine boosted the number of neurons in the hippocampus, the part of the brain primarily responsible for memory. By one measure, mice treated with imipramine had approximately 70 percent more neurons after four weeks than mice that did not receive the medication.

That change was borne out on behavioral tests as well. The team tested mice by using what scientists call a novel object recognition test. Like human infants, mice tend to spend more time sizing up objects that they haven't encountered before – or don't remember encountering – than they do objects that they've seen before. This gives scientists a way to measure a mouse's memory.

The team found that mice that had been treated with imipramine had a better memory. They were more likely to remember objects they had seen previously and so spent more time exploring truly novel objects, compared to mice that did not receive the compound._PO

Improvement of memory in mice follows naturally from the boost in neurogenesis within the hippocampus -- a part of the brain which is key to laying down new memories, among other things.

The fact that brain damaged humans also show cognitive improvement after treatment with antidepressants, points the way to new research to augment neurogenesis after brain trauma, stroke, tumour, and other forms of brain damage.

It is interesting that both tofranil -- one of the oldest antidepressants -- and sertraline, a newer antidepressant, were found to be effective in growing new hippocampal neurons. This approach may be used as a screening tool for antidepressant research, as well as a means to rank to likely effectiveness of antidepressants already on the market.

More: This PDF research article from research teams in France and the US, describes a new approach to antidepressant and anti-anxiety treatment which may take a paradoxical approach to nerve growth when compared to the antidepressants described in the above studies. Anyone who is significantly interested in understanding possible deep brain mechanisms for effective antidepressant therapy should take a look. Keep in mind that it is a research article, using mice as subjects.

Labels: brain research, depression, neurons

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