

# Diabetes drug metformin makes brain cells grow

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The widely used diabetes drug metformin comes with a rather unexpected and alluring side effect: it encourages the growth of new neurons in the brain. The study reported in the July 6th issue of *Cell Stem Cell* also finds that those neural effects of the drug also make mice smarter.

The discovery is an important step toward therapies that aim to repair the brain not by introducing new stem cells but rather by spurring those that are already present into action, says the study's lead author Freda Miller of the University of Toronto-affiliated Hospital for Sick Children. The fact that it's a drug that is so widely used and so safe makes the news all that much better.

Earlier work by Miller's team highlighted a pathway known as aPKC-CBP for its essential role in telling [neural stem cells](#) where and when to differentiate into mature neurons. As it happened, others had found before them that the same pathway is important for the metabolic effects of the drug metformin, but in [liver cells](#).

"We put two and two together," Miller says. If metformin activates the CBP pathway in the liver, they thought, maybe it could also do that in neural stem cells of the brain to encourage brain repair.

The new evidence lends support to that promising idea in both mouse brains and [human cells](#). Mice taking metformin not only showed an increase in the birth of new neurons, but they were also better able to

learn the location of a hidden platform in a standard maze test of spatial learning.

While it remains to be seen whether the very popular [diabetes drug](#) might already be serving as a brain booster for those who are now taking it, there are already some early hints that it may have [cognitive benefits](#) for people with Alzheimer's disease. It had been thought those improvements were the result of better [diabetes control](#), Miller says, but it now appears that metformin may improve Alzheimer's symptoms by enhancing brain repair.

Miller says they now hope to test whether metformin might help repair the brains of those who have suffered brain injury due to trauma or radiation therapies for cancer.

**More information:** Wang et al.: "Metformin activates an atypical PKC-CBP pathway to promote neurogenesis and enhance spatial memory formation." *Cell Stem Cell*, DOI:10.1016/j.stem.2012.03.016

### **Abstract**

Although endogenous recruitment of adult neural stem cells has been proposed as a therapeutic strategy, clinical approaches for achieving this are lacking. Here, we show that metformin, a widely used drug, promotes neurogenesis and enhances spatial memory formation. Specifically, we show that an atypical PKC-CBP pathway is essential for the normal genesis of neurons from neural precursors and that metformin activates this pathway to promote rodent and human neurogenesis in culture. Metformin also enhances neurogenesis in the adult mouse brain in a CBP-dependent fashion, and in so doing enhances spatial reversal learning in the water maze. Thus, metformin, by activating an aPKC-CBP pathway, recruits neural stem cells and enhances neural function, thereby providing a candidate pharmacological approach for nervous system therapy.

Provided by Cell Press

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