

Promising drug candidate reverses age-related memory loss in mice

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Researchers at the University of Edinburgh today report a new experimental compound that can improve memory and cognitive function in ageing mice. The compound is being investigated with a view to developing a drug that could slow the natural decline in memory associated with ageing.

With support from a Wellcome Trust Seeding [Drug Discovery](#) award, the team has identified a preclinical candidate that they hope to take into human trials within a year.

Many people find they become more forgetful as they get older and we generally accept it as a natural part of the [ageing process](#). Absent mindedness and a difficulty to concentrate are not uncommon, it takes longer to recall a person's name, and we can't remember where we left the car keys. These can all be early signs of the onset of dementia, but for most of us it's just part of getting old.

Such [memory loss](#) has been linked with high levels of 'stress' [steroid hormones](#) known as glucocorticoids which have a deleterious effect on the part of the brain that helps us to remember. An enzyme called 11beta-HSD1 is involved in making these hormones and has been shown to be more active in the brain during ageing.

In a study published today in the [Journal of Neuroscience](#), the team reports the effects of a new [synthetic compound](#) that selectively blocks 11beta-HSD1 on the ability of mice to complete a memory task, called

the Y maze.

Professor Jonathan Seckl from the University of Edinburgh, who discovered the role of 11beta-HSD1 in the brain, described the findings: "Normal old mice often have marked deficits in learning and memory just like some elderly people. We found that life-long partial deficiency of 11beta-HSD1 prevented [memory decline](#) with ageing. But we were very surprised to find that the blocking compound works quickly over a few days to improve memory in old mice suggesting it might be a good treatment for the already elderly."

The effects were seen after only 10 days of treatment.

Professor Brian Walker and Dr Scott Webster from the University of Edinburgh are leading the drug development programme. Professor Walker added: "These results provide proof-of-concept that this class of drugs could be useful to treat age-related decline in memory. We previously showed that carbenoxolone, an old drug that blocks multiple enzymes including 11beta-HSD1, improves memory in healthy elderly men and in patients with type 2 diabetes after just a month of treatment, so we are optimistic that our new compounds will be effective in humans. The next step is to conduct further studies with our preclinical candidate to prove that the compound is safe to take into clinical trials, hopefully within a year."

The 11beta-HSD1 enzyme has also been implicated in metabolic diseases including diabetes and obesity by the Edinburgh team, and similar drugs that block its activity outside of the brain are already under investigation.

This study was supported by the Wellcome Trust and the Medical Research Council (MRC). The drug development programme in Edinburgh is supported by a Seeding Drug Discovery award from the

Wellcome Trust.

Dr Rick Davis of the Wellcome Trust commented: "Developing drugs that can selectively inhibit this enzyme has been a challenge to the pharmaceutical industry for nearly 10 years. Advancing this compound towards clinical trials takes us a step closer to finding a drug that could have far reaching implications as the population ages."

Provided by Wellcome Trust

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