

NEWS

Clinical research: Two compounds treat Rett syndrome in mice

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1 FEBRUARY 2012

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Two compounds that enhance the activity of **brain-derived neurotrophic factor** (BDNF), a protein needed for the growth of neurons, improve motor skills in mouse models of Rett syndrome and increase the mice's lifespan^{1,2}.

Rett syndrome is an autism-related disorder characterized by intellectual disability, repetitive hand movements and deficits in motor skills. It is caused by the loss of one copy of the **MeCP2 gene**.

MeCP2 regulates the expression of **thousands of other genes**, including BDNF³. Apart from its role in neuron growth, BDNF also directs the formation of **synapses**, the junctions between neurons, and is important for learning and memory. MeCP2-deficient mice have **lower-than-typical levels of BDNF** in the brain⁴.

A new study published in the February issue of *Neurobiology of Disease* shows that male mice lacking MeCP2 have low levels of two proteins — huntingtin protein and huntingtin-associated protein 1 — that help transport BDNF to synapses. BDNF transport is impaired in neurons that don't express MeCP2, but recovers when MeCP2 expression is restored, the study found¹.

MeCP2-deficient mice treated with cysteamine, a molecule that stimulates BDNF production, live longer and are more active compared with controls, the study also found.

In another study, published 22 December in the *Journal of Applied Physiology*, researchers treated MeCP2 mutant mice with 7,8-dihydroxyflavone, or 7,8-DHF, a molecule that activates a signaling receptor to which BDNF binds².

These mice also live longer and run more on a wheel placed in their cage than their untreated siblings do. In addition, 7,8-DHF alleviates breathing difficulties, another feature of Rett syndrome in both mouse models and people with the disorder.

Although MeCP2 affects a **number of important cellular pathways**, the two studies suggest that compounds targeting BDNF are promising as treatments for Rett syndrome.

References:

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2: Johnson R.A. et al. *J. Appl. Physiol.* Epub ahead of print (2011) [PubMed](#)

3: Chen W.G. et al. *Science* **302**, 885-889 (2003) [PubMed](#)

4: Chang Q. et al. *Neuron* **49**, 341-348 (2006) [PubMed](#)