

Intellectual disabilities share disease mechanisms, study suggests

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Brain disorders that cause intellectual disabilities and autism spectrum disorders may share common defects despite having different genetic causes, a study has found.

A study of two models of intellectual disability in mice has found that they share similar disease mechanisms.

Researchers found that treatment with a statin drug called Lovastatin - commonly used to treat high cholesterol - can correct high levels of <u>protein production</u> in the brain linked to the conditions.

The findings suggest that different types of <u>intellectual disabilities</u> may benefit from common therapeutic approaches, the researchers say.

Studies of people with learning disabilities have identified a wide range of genetic causes. Around a third of people affected also have symptoms of <u>autism spectrum disorders</u>, suggesting that the mechanisms underlying these conditions may be shared.

Researchers at the University of Edinburgh studied mice with a genetic mutation that means they produce lower levels of a protein called SynGAP. The mice show learning and behavioural difficulties and act as a model system to understand why people with mutations in the human version of the gene suffer from intellectual disability.

The team from the University's Patrick Wild Centre and Centre for



Integrative Physiology found that treatment with Lovastatin normalised levels of protein production in the brains of the mice. Their results suggest that Lovastatin acts by reducing levels of the active form of a protein called ERK1/2.

They compared their findings with mice that lack a protein called FMRP, which also causes cellular and behavioural changes that can be rescued with Lovastatin. Loss of FMRP in people leads to Fragile X Syndrome, the most common inherited form of intellectual disability and autism.

Further research is needed to determine whether the treatment can restore learning and development in people.

The study is published in the *Journal of Neuroscience*. It was funded by the Medical Research Council, the Biotechnology and Biological Sciences Research Council and the Patrick Wild Centre.

Professor David Wyllie, Director of the University of Edinburgh's Centre for Integrative Physiology, said: "This study shows that the core deficits associated with two very different causes of intellectual disability are shared. This is important because it means that people with diverse types of intellectual disability or autism may benefit from the same treatment."

Professor Peter Kind, Director of the University of Edinburgh's Patrick Wild Centre for Research into Autism, Fragile X Syndrome and Intellectual Disabilities, said: "Statins, such as <u>lovastatin</u>, are already used widely for treating people, including children, for <u>high cholesterol</u> with minimal side effects. Further studies are needed to determine whether these existing medications could also help people with intellectual disabilities."



More information: S.A. Barnes et al. Convergence of Hippocampal Pathophysiology in Syngap+/- and Fmr1-/y Mice. *Journal of Neuroscience*, 2015. dx.doi.org/10.1523/JNEUROSCI.1087-15.2015

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