NEWS

Molecular mechanisms: Autism gene linked to fragile X traits

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Memory loss: Mice lacking one copy of CYFIP1 tend to forget that they receive shocks in a dark area of their cage.

Deleting CYFIP1, a gene in a region linked to **Angelman syndrome** and autism, in mice leads to symptoms reminiscent of **fragile X syndrome**, according to a study published 10 August in *PLoS One*[1].

CYFIP1 binds to FMRP, the protein lacking in individuals with fragile X syndrome. It is located in the 15q11-13 chromosomal region, which is linked to autism, developmental delay and **Angelman syndrome**[2].

In the new study, researchers engineered mice lacking one copy of CYFIP1. (Missing both copies of the gene is lethal.) Neurons from mice missing one copy show deficits similar to those seen in mouse models of fragile X syndrome, the researchers found.

After neurons fire, their ability to fire again is temporarily repressed, a phenomenon called long-term depression. In fragile X mice, this delay is longer for signals transmitted through a protein called mGluR5. The researchers saw the same delay in mice lacking one copy of CYFIP1.

As in the fragile X mice, compounds that dampen mGluR5 activity restore normal neuronal firing in mice lacking a copy of CYFIP1. These compounds are being tested as **treatments for fragile X**

syndrome in people with the disorder.

Like the fragile X models, mice lacking CYFIP1 also have memory deficits. Like controls, they learn to stay away from a darkened area in their cage where they are given shocks. But they return to the area sooner after the shocks stop than controls do.

Mutations or deletions of CYFIP1 are likely to affect the same pathway affected in fragile X syndrome, the researchers say. The gene may also play a role in symptoms associated with duplications and deletions of the 15q11-13 region.

References:

1: Bozdagi O. *et al. PLoS One* Epub ahead of print (2012) **PubMed**

2: Cooper G.M. *et al. Nat. Genet.* **43**, 838-846 (2011) **PubMed**