NEWS

Molecular mechanisms: Fragile X mice resistant to change

BY **JESSICA WRIGHT**

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Preferred peek: Mice that model fragile X syndrome are more likely to poke their noses into a favorite hole, despite cues directing them to one with a reward.

Mice that model fragile X syndrome have **trouble changing their minds**, according to a study published in the *Proceedings of the National Academy of Sciences* in February. This behavior is accompanied by fewer connections between neurons in the prefrontal cortex — a brain region involved in higher-level cognition, such as decision-making.

Fragile X syndrome is a disorder that has some overlap with autism and includes defects in mental flexibility, such as the inability to respond to changing conditions or to shift attention. The prefrontal cortex regulates these processes and is likely to play an important role in the disorder.

Mice lacking the fragile X mental retardation gene **FMR1** show deficits in behaviors controlled by the prefrontal cortex, according to the study. These mice learn easily that poking their noses into any of five holes leads to a food reward, but they take much longer than control mice do to adjust when only the hole accompanied by a blinking light gives out a reward.

Fragile X mice also appear to have a favorite hole: they show a strong preference for a certain hole even once it stops giving out food.

The same mice also have lower levels in the prefrontal cortex of several proteins that help transmit neuronal signals — including those encoded by the autism-associated gene NR2A, also known as **GRIN2A**, and the Williams syndrome gene **PSD-95**.

Levels of NR2A are lower in the prefrontal cortex of mice that take longer to adjust in the hole test, suggesting a direct correlation between this protein and the behavioral deficits.