NEWS

Molecular mechanisms: Fragile X mutation worsens memory loss

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Remembering rejection: An assay based on mating shows dramatic memory loss in fruit flies with mutations in both the presenilin and fragile X genes.

Genes responsible for Alzheimer's disease and fragile X syndrome — a form of mental retardation linked to autism — may **operate through the same pathway**, according to a study published in July in *The Journal of Neuroscience*.

Fruit flies with a mutation in presenilin, a gene linked to inherited Alzheimer's disease, show long- and short-term memory loss at an earlier age than do controls, the study shows. This effect is even more dramatic — cutting the fly's age from 30 to 5 days — when the mutation is combined with a second one in the fly fragile X gene, dFMR1.

In this case, each of the mutations was heterozygous — meaning that only one copy of each gene was flawed. Given that, a synergistic effect is rare, notes lead investigator **Thomas Jongens** associate professor of genetics at the University of Pennsylvania. "This generally indicates that

these genes are acting close to one another, more often than not in a complex."

Drugs that improve cognitive defects in the fly model of fragile X syndrome also delay age-related memory loss in the presenilin mutant flies, further linking the two genes. These drugs reduce the activity of dmGLuRA, a receptor for glutamate whose levels are elevated in both fly and mouse models of fragile X syndrome.

Jongens' group is investigating whether the shared pathway between fragile X syndrome and Alzheimer's is also involved in other autism-linked diseases.