Autism in Fruit Flies II: Behavior of Drosophila mGluR Pathway Mutants

Paietta, Elise

The study of genetic variations that cause autism and the identification of associated defects in synaptic signaling pathways may lead to more effective treatments for autism. The hypothesis that mutations in mGluR (metabotropic glutamate receptor) pathway genes will result in a common defect of autistic behavior was tested. Drosophila melanogaster strains with mutations in the dlg-1, dnl-2, shank, and tsc-1 genes were tested for defective social interaction. Initial testing of the mGluR pathway mutants showed general behavioral responses of phototaxis and chemotaxis that were essentially normal. The social interaction test was performed in a chamber where two flies were separated by a mesh screen and the total time the test subject fly was nearby the other fly was used as the measure of social interaction. The mGluR mutant strains showed impairment in the social interaction test in that they performed at less than 10% of the level seen in wild type. This finding demonstrates that genetic defects in the mGluR signaling pathway can cause a common behavioral defect of autistic behavior. R-baclofen, a potential drug for human autism treatment, was administered to wild type and the mGluR pathway mutants. The social interaction test performance in R-baclofen, but not S-baclofen (an inactive isomer), treated mutant flies improved to 64-81% of that seen in wild type. MPEP, an mGluR antagonist, was also effective in improving the level of social interaction. This shows that a common treatment approach can potentially help multiple defects in the mGluR signaling pathway.

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