NEWS

Therapies reverse autism in mouse model

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New pharmacological and behavioral interventions can reverse characteristics of autism in a mouse model of the disorder, according to unpublished results presented in poster sessions today at the **Society for Neuroscience** meeting.

BTBR is a commercially available inbred strain of mice that displays several autism-like features, including impaired social interactions and a strange pattern of vocalization, which researchers say mimic communication deficits seen in autism. The mice also self-groom repeatedly, reminiscent of similar behaviors seen in people with autism.

Jacqueline Crawley and her colleagues at the National Institute of Mental Health have found that early exposure to a healthy mouse seems to help BTBR mice overcome their social problems.

The researchers housed BTBR mice and controls shortly after they were weaned from their mothers, with a healthy mouse. After 40 days of living with the new mouse, the researchers found, both BTBR mice and controls are more likely to be interested in other unfamiliar mice rather than in unknown objects. When the BTBR mouse is paired with another BTBR cage mate, in contrast, its social deficits do not improve.

That result is consistent with human studies showing that interacting with healthy peers early in life can help children with autism overcome difficulties in socializing, says Mu Yang, a postdoctoral fellow in Crawley's lab who conducted the study.

Unfortunately, the social deficits in BTBR eventually return: when researchers separated a BTBR mouse from its cage mate, they found that, after 40 days of isolation, the BTBR mouse shows no preference for the unfamiliar mouse over the object.

Drug therapy:

In a separate test, Crawley's group administered risperidone, an antipsychotic drug approved by the **U.S. Food and Drug Administration** to treat autism and other psychiatric conditions. Risperidone reduces repetitive behavior in BTBR mice, as it does in people, but sedates the animals at the drug's effective doses.

The group then decided to test MPEP — which blocks metabotropic glutamate receptor 5, or mGluR5 — a signaling molecule shown to be involved in fragile X syndrome. Fragile X syndrome shares genetic, cellular and clinical characteristics of autism. BTBR mice given MPEP groom for shorter periods and behave more like control mice, the researchers found.

"We were really excited about this because we got a reduction in self-grooming without the side effect of sedation," says Jill Silverman, Crawley's laboratory manager, who conducted the study. The researchers plan to assess the effects of more specific mGluR5 blockers.

The similarity between Crawley's findings and those of human studies validates the BTBR model for studying autism, says **Richard Deyo**, a professor of psychology at Winona State University in Minnesota.

Deyo's group has also found that housing a BTBR mouse with a healthy mouse reduces its tendency to over-groom.

In the past several years, Crawley and others have characterized features of autism in the BTBR mice. Crawley's group showed in one poster presented today that the BTBR mouse is interested in exploring the scent of an unfamiliar mouse — taken from its bedding — but not the mouse itself.

"There is something about a live mouse that is deterring social behavior," says graduate student Adam Katz, who conducted the study.

In another poster, the researchers showed that the strange vocalizations previously described in pups — which they compare to unusual hums, grunts and coos in babies — persist into adulthood. The distinctive calls in adults may be similar to unusual speech intonation and rhythm in adults with autism, the researchers say.

Because its behaviors are so well characterized, the BTBR mouse is a good place to develop therapies for autism, Deyo says, adding that it will be crucial to test pharmacological and behavioral therapies in animals.

"We'll want to test before the impairments begin," he says. "That's where the payoff will come."