Figuring out fetal alcohol syndrome in fruit flies

February 8 2011

Drinking excess alcohol during pregnancy can cause fetal alcohol syndrome (FAS) due to the damaging effects of alcohol on a developing baby's brain. Despite its harmful effects, pregnant mothers continue to drink alcohol – up to 3 in every 1000 babies are born with FAS, which causes intellectual disabilities, behavioural problems, growth defects and abnormal facial features. How alcohol causes these effects is unclear, but researching the problem is difficult because of ethical barriers to studying human fetuses.

Ulrike Heberlein and colleagues from the University of California San Francisco decided to study FAS using the fruit fly, a commonly used organism in biological research. Their results establish a new system for studying how alcohol causes harmful effects during development and open the door to further genetic and molecular studies of FAS. Heberlein and colleagues publish their results in *Disease Models & Mechanisms* on February 8, 2011.

When Heberlein and colleagues exposed fruit flies to alcohol during development, they found that the flies grew more slowly, had smaller brains, abnormal behaviour and were more sensitive to the effects of alcohol as adults. They also confirmed previous findings that the problems were caused in part because alcohol interferes with the function of insulin – a molecule essential for normal fetal development – in the developing brain. Heberlein commented, "It was pretty surprising that so many features of FAS were recapitulated in this model, including some of the molecular mechanisms."

The issue of how much alcohol, if any, a pregnant woman can safely drink – and during which trimester – has been hotly debated. As expected, Heberlein and colleagues found that greater amounts of alcohol had more severe effects on fly development and behaviour. More surprisingly, they found that exposure to alcohol later during a fly's development was more harmful than at early stages. Fruit flies are only distantly related to humans, so it is not yet possible to draw direct parallels between this study and the effects of alcohol on human pregnancy. Heberlein says, "We can't truly draw analogies before we know exactly which biological processes are being affected at these different stages of development. But it's very clear that exposure to alcohol early, during a rapid phase of growth, has different effects than later, when the brain is getting put together."

An important aspect of this new model system is that fruit flies provide a research advantage that is not available in humans – they can be used to very rapidly find the genes that might increase FAS risk. Heberlein and colleagues are undertaking this task now: their hope is that by studying FAS at the genetic level using fruit flies, they can generate results that will guide FAS research in humans and facilitate a more targeted approach to developing new therapies.

This study establishes the fruit fly as a model to study FAS that can be used to find genes and environmental factors that could influence FAS severity in humans. Combined with complementary approaches and follow-up studies in humans, the fruit fly will be a valuable tool for identifying drug candidates that could prevent or treat FAS in at-risk fetuses.

More information: McClure, K. D., French, R. L. and Heberlein, U. (2011). A Drosophila model for fetal alcohol syndrome disorders: role for the insulin pathway. Dis. Model. Mech. doi:10.1242/dmm.006411

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