NEWS

Screening zebrafish autism models: A quick take at SfN with Ellen Hoffman

BY **SPECTRUM**

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Spectrum caught up with **Ellen Hoffman**, associate professor in the Child Study Center at Yale University, to learn about the zebrafish work she presented in a **minisymposium** at **Neuroscience 2022** on Monday, 14 November. In this video, Hoffman describes how her lab screened 10 different zebrafish models with mutations in autism-linked genes using a high-throughput behavioral assay and looked at the animals' brain structure and activity as well in search of convergence.

Transcript:

Ellen Hoffman: So we did a screen where we generated zebrafish mutants of 10 different autism risk genes. And we analyzed their behavior using a high-throughput assay, and we looked at their brain structure and their brain activity. And we were interested in identifying potential convergent pathways across these different genes. We found that at a behavioral level, disrupting autism risk genes does lead to alterations in sensory processing and sleep behaviors, but not necessarily in the same direction or to the same extent. So we saw a number of divergent phenotypes at the behavioral level. At a structural level and a brain activity level, we also saw evidence for unique and shared phenotypes across the different mutants.

But interestingly, we were able to identify some points of convergence. So, for example, we found that the forebrain, or telencephalon, represents a point of vulnerability to autism risk genes in terms of brain size or brain growth at early developmental stages, whereas we found that the thalamus was one of the most significant contributors to altered baseline brain activity across the different mutants that we studied.

So we see very robust phenotypes in our zebrafish mutants of the gene DYRK1A, which has a very conserved effect on brain size all the way down to *Drosophila*. So it's a *Drosophila* mini-brain gene, and, in fact, in zebrafish we also see a gene dose-dependent effect on brain size, consistent with microcephaly in humans who have DYRK1A mutations. We also see very robust phenotypes

associated with a gene called SCN1lab, which is the zebrafish gene, the equivalent of SCN1A and 2A in mammals.

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