Genetic changes can affect collective behavior

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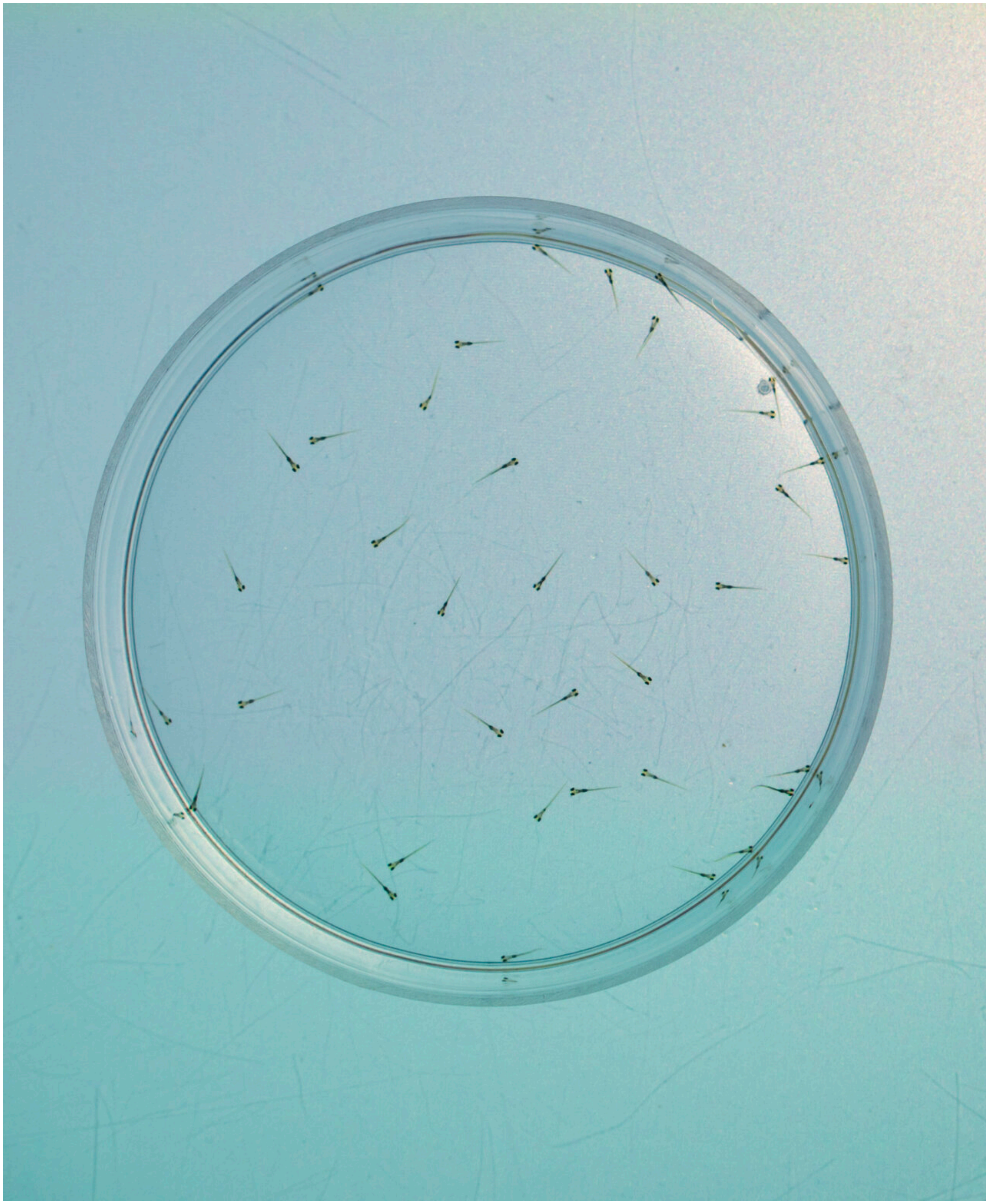

A group of wild-type zebrafish larvae. One question of the current study was to what extent the larvae keep their distance from each other or actively move towards each other, and whether the "silenced" genes play a role in this. Credit:

Pradeep Krishna Chintapalli

Individual zebrafish (Danio rerio) exhibit predictable behavioral responses to certain visual stimuli that are sufficient to explain the collective behavior of the animals—even in their larval stage. Genetic mutations associated with neurological disorders in humans alter these behavioral responses and, as a consequence, the group behavior of the larvae. These are the results of a study conducted by Konstanz neurobiologist Dr. Armin Bahl and his collaborators at Harvard University that was recently published in *Science Advances*. The research shows that genetic changes in individuals can not only alter the behavior of groups, but can also provide a methodological approach for testing existing models of collective behavior experimentally.

Collective behavior of zebrafish

A large proportion of today's fish species display collective behaviors, at least in certain stages of their lives. This is when a large number of individuals remain in close proximity to each other for social reasons or swim together in the same direction. The potential advantages of these behaviors are many and range from simplifying the search for partners to providing greater protection for individual fish from predation and making the search for food more effective.

Zebrafish, too, are known for these forms of collective behavior. The species has long been used as a model organism in genetic, evolutionary biology and neurobiology research. Until now, however, it has never been systematically examined when zebrafish start exhibiting such collective behavior, which genes play a role in the process and which sensory information the fish use for this purpose.

"Especially to neuroscientists like me, these questions are of importance. Since the bodies and brains of zebrafish larvae are almost entirely transparent, my group can use high-resolution, non-invasive microscopy techniques to observe in real time how nerve cells react to different stimuli and how the behavior of the zebrafish changes in response to them. Since the wiring of the larvae's brains is less complex than in adult animals, these techniques make it possible for us to investigate the neural basis of collective behavior with high precision," Armin Bahl explains the advantage of zebrafish larvae for his research. Since September of last year, Armin Bahl has led the Emmy Noether research team "Neural Circuit Computation and Behavior" in Konstanz. In the summer of this year, he was offered the professorship of zoology/neurobiology at the University of Konstanz.

Even zebrafish larvae react to each other

The research team thus examined the group behavior of zebrafish during different stages of their development—seven days and 21 days after egg fertilization. The researchers showed that even seven-day old larvae respond to their peers by orienting their movements in the same direction while, at the same time, actively avoiding close proximity to others. The 21-day old zebrafish oriented their movements even more strongly in the same direction as their peers but, instead of avoiding each other, the animals in this stage sought close proximity to each other, like in swarm formation.

Based on further behavioral experiments in this study as well as existing knowledge, the researchers suspected that the behavior observed in zebrafish larvae is based on two relatively simply behavioral responses: One system in the larval brain measures the general amount of objects in its surroundings, while a second system analyzes motion stimuli. "Both behavioral responses are visuomotor reflexes. This means that, in the animals, a certain type of visual information causes a set behavioral reaction in the form of a movement," Armin Bahl states.

To test their assumption, the researchers used a computer model to simulate the movements of small groups of fish. The model used only the two stated visuomotor reflexes as "decision rules" to determine the behavior of individual virtual fish. "The simulated groups of fish behaved exactly like the real zebrafish larvae. This clearly indicates that the collective behavior of the animals can indeed be explained using these relatively simple behavioral responses," says Armin Bahl.

Targeted mutations change the group behavior of the larvae

In order to also find out which role the individual genetic make-up plays in the group behavior of zebrafish, the researchers used the CRISPR-Cas9 technique to edit specific genes in individual larvae. In doing so, they were able to show that mutations of the genes scn1lab and disc1 altered the individual behavioral responses of the mutated animals to visual stimuli and, consequentially, the behavior of the group. These genetic mutations are respectively linked to specific forms of epilepsy and autism in children or to schizophrenia. The zebrafish larvae with the scn1lab mutation kept a greater distance between themselves and others than their peers without the mutation. By contrast, the zebrafish larvae with the disc1 mutation stayed closer together than their wild-type peers.

As before, the behavior of the mutated animals could be simulated and reproduced by the computer model. "Our approach of using modern genetic techniques and behavioral experiments with zebrafish in combination with computer simulations gives us the unique opportunity to specifically influence social behavior and then test models of the collective animal behavior. With the various molecular-genetic and microscope tools that already exist for zebrafish and that we are currently establishing in Konstanz, we will soon be able to also analyze the neural foundations for this fascinating behavior in great detail," Armin Bahl concludes.

More information: Roy Harpaz et al, Collective behavior emerges from genetically controlled simple behavioral motifs in zebrafish, *Science Advances* (2021). DOI: 10.1126/sciadv.abi7460. www.science.org/doi/10.1126/sciadv.abi7460

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