Zebrafish behavior monitoring system could boost drug discovery (w/ Video)

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Researchers from the University of British Columbia and Harvard University have co-developed a system that captures on video and barcodes the behavioral responses of zebrafish to chemical compounds on a large scale. The approach could dramatically speed up the discovery of new psychiatric drugs.

The discovery in the 1950s of drugs that act in the nervous system has been important both for the understanding of neurobiology and the treatment of neurological diseases. Since then, very few new drugs have been developed.

The new system, detailed in today's edition of *Nature Chemical Biology*, was developed by UBC statisticians Jennifer Bryan and Rick White and Harvard's Randall Peterson and David Kokel. It can track the behavioral effects of up to 14,000 chemicals at a time and has already identified new chemicals that affect behaviour in fish.

"The capacity of this approach is quite distinctive," says Bryan, an associate professor in the Department of Statistics and the Michael Smith Laboratories. "Most pharmacological studies of behaviour have been relatively small scale, involving a few small molecules at most."

"New psychoactive drugs represent new windows into how the brain works," says Randall Peterson of Harvard. "We hope that behavioral screens with zebrafish will lead to many new compounds that help us understand and ultimately treat nervous system disorders."

Zebrafish models have increasingly been used to assess drug toxicity and safety, largely because they are transparent, genetically tractable, and have organ systems that are very similar to those of humans. Zebrafish embryos are permeable to drugs.

Capable of screening approximately 5,000 zebrafish embryos per day, the new platform monitors the motion of embryos in response to two strong light pulses after exposure to chemicals, and compares that to untreated, controls. In total, the study evaluated the behavioral effects of compounds on more than a quarter million embryos.

"The UBC team was able to help devise ways to turn these behavioral observations into more manageable barcodes that capture how the behavior in a treated group differs from that in an untreated, control," says Bryan, co-author of the study. "This makes it possible to generate visualizations of the massive screening datasets generated by this powerful tool, and to group compounds based on the similarity of their associated barcodes."

The new tool may also make it possible to generate genetic models of nervous system disorders and screen for chemical modifiers of the associated behavioral defects.

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