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Finding psychiatric drugs in the movements of mice

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Developing psychiatric medications is a long and complex process. Candidate drugs are evaluated and assessed based on their effects on the behavior of animals, usually rats or mice. Each class of drugs, from antidepressants to antipsychotics, is tested differently—often in a labor-intensive process that leaves plenty of room for human error. And there is a growing consensus that current procedures fail to effectively produce new medications.

Now, using a computational method called data mining, Dr. Neri Kafkafi of Tel Aviv University's Department of Zoology has discovered a small number of mouse behaviors that can be used to categorize psychiatric drugs more quickly and easily than standard tests. The research, conducted in collaboration with Greg Elmer of the University of Maryland and published in *Psychopharmacology*, could improve the drug-testing process and identify new uses for existing medications.

"For pharma companies, psychiatric drugs carry the highest risk. Some are getting out of the business because so few drugs make it through the development process," says Dr. Kafkafi. "Our data-mining algorithm can quickly predict which drugs are most effective for which disorders—schizophrenia, psychosis, or depression, for example—and eliminate the need for a lot of testing, potentially saving significant time and money."

Staking a new claim

Data mining—which involves using computers to identify patterns in large amounts of information—has already provided valuable insights into the human body. In recent years, it has been used to find gene expressions that predict cancer and drug responses, and to classify drugs. Behavior, though, has proven a less fertile ground for data mining. The problem is that the data has not yet been divided into meaningful units of analysis that can serve a role similar to genes in physiology.

To address this problem, Dr. Kafkafi recorded the movements of mice in a small ring and analyzed them using a data-mining algorithm called Pattern Array. By comparing the movements of sober mice and mice on various drugs, he was able to find a handful of complex behaviors that he could use to classify drugs into one of six classes – like antidepressants or antipsychotics. The percentage of time a mouse performs a behavior in the ring is used to classify the drug it is on.

One of the behaviors – which Dr. Kafkafi named "universal drug detector" – is accelerating quickly when starting to move and decelerating quickly when stopping. Forty out of 41 of the drugs in the study decreased the use of this behavior by the mice, making it the broadest known test for identifying drug effect. Several other behavioral tests then served to divide the drugs into their respective classes. When tested on 11 unidentified drugs, the algorithm classified nine of them correctly. And in the two cases where the algorithm was wrong, it identified possible alternative uses, suggesting that the procedure could be used to repurpose drugs already on the market.

A powerful paradigm

In addition to its broad scope and potential for repurposing drugs, Pattern Array has the advantage that it can improve itself over time. Every time data from an additional drug or behavior is added to the database, the algorithm gains predictive ability.

"The more information you add to the database, the more you increase its power, because you discover more patterns that you can now test for," says Dr. Kafkafi. "And you can even go back and reevaluate animal tests that you ran five years ago."

Dr. Kafkafi has already expanded the algorithm to work with additional psychiatric drugs and classes. But he says it may have even more potential in detecting the effects of genetic disorders—something hinted at in a previous study, in which he diagnosed Lou Gehrig's disease in rats at a much younger age than any standard test could. He is looking into applying the algorithm to the study of children with autism.

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