Depression researchers rethink mouse swim test

Animal-rights group campaigns to end test that some scientists say is overused.

BY SARA REARDON

Nearly every scientist who has used mice or rats to study depression is familiar with the forced-swim test. The animal is dropped into a tank of water while researchers watch to see how long it tries to stay afloat. In theory, a depressed rodent will give up more quickly than a happy one — an assumption that has guided decades of research on antidepressants and genetic modifications intended to induce depression in lab mice.

But mental-health researchers have become increasingly sceptical in recent years about whether the forced-swim test is a good model for depression in people. It is not clear whether mice stop swimming because they are despondent or because they have learnt that a lab technician will scoop them out of the tank when they stop moving. Factors such as water temperature also seem to affect the results.

“We don’t know what depression looks like in a mouse,” says Eric Nestler, a neuroscientist at the Icahn School of Medicine at Mount Sinai in New York City.

Now, the animal-rights group People for the Ethical Treatment of Animals (PETA) is jumping into the fray. The group wants the US National Institute of Mental Health (NIMH) in Bethesda, Maryland, to stop supporting the use of the forced-swim test and similar behavioural assessments by its employees and grant recipients. The tests “create intense fear, anxiety, terror, and depression in small animals” without providing useful data, PETA said in a letter to the agency on 12 July.

The animal-rights group also singled out NIMH director Joshua Gordon for using the forced-swim test in the early 2000s at Columbia University in New York City.

“The National Institute of Mental Health has for some time been discouraging the use of certain behavioral assays, including the forced swim and tail suspension test, as models of depression,” Gordon said in a statement. But he added that the tests are still “crucial” for some specific scientific questions, and that the NIMH will continue to fund such studies.

The PETA campaign dovetails with scientists’ growing concern about the quality of data produced by forced-swim tests, says Hanno Würbel, a behavioural biologist at the University of Bern. “The point is that scientists shouldn’t use these tests anymore,” he says. “In my opinion it’s just bad science.”

Scientists developed the forced-swim test in the 1970s. One of its earliest applications was in studying the efficacy of drugs known as selective serotonin reuptake inhibitors (SSRIs) — a class of antidepressants that includes Prozac (fluoxetine). Mice and rats that received SSRIs swam for longer periods than animals that did not.

The test’s popularity grew in the early 2000s, when scientists began modifying mouse genomes to mimic mutations linked to depression in people. Many of these researchers adopted the forced-swim test as a “quick and dirty” way to assess their ability to induce depression, even though it was not designed for that purpose, says Trevor Robbins, a neuroscientist at the University of Cambridge, UK.

By 2015, mental-health researchers were publishing an average of one paper a day that used the procedure, according to an analysis by the IUCN.
Researchers at Leiden University in the Netherlands. Yet the swim test’s track record is mixed. It has accurately predicted whether various SSRIs are effective treatments for depression, but yields inconsistent results when used with other types of antidepressant.

Concerns about the forced-swim test’s accuracy have prompted major drug companies such as Roche, Janssen and AbbVie to abandon the procedure in recent years.

Many researchers feel obligated to use the test, says Ron de Kloet, a neuroendocrinologist at Leiden University Medical Center and a co-author of the 2015 study. “People get their grants based on this test, they write papers based on the test, they make careers,” he says. “Most of them will admit that the tests are not showing what they are supposed to do.”

Todd Gould, a neurobiologist at the University of Maryland School of Medicine in Baltimore, acknowledges the test’s poor track record, but says the procedure has proved useful for his research into whether the ‘party drug’ ketamine and related substances are effective antidepressants. Gould finds it ironic that an animal-rights group is attacking the agency’s prominence in mental-health research. “If NIMH took a stand, it would set a strong precedent,” she says.

She argues that emerging technologies, such as ‘mini-brains’ grown from human stem cells, could eliminate the need to use rodents in depression studies. Researchers are already using these clumps of human tissue to study the genetics and brain wiring that underlie various mental-health disorders.

But some scientists say that the best replacement for the forced-swim test might be more sophisticated tests that involve rodents or other animals. Robbins says that one approach could include developing animal tests that accurately measure specific symptoms, such as lack of interest in a favourite food.

And Nestler says that modelling individual signs of depression might produce better data than do attempts to mimic the full complexity of the human disorder in animals. The symptoms and underlying genetics of depression seem to vary widely between people, and the same treatments don’t work for everyone.

“We know human depression is not one disease,” he says.


**EU chief makes bold climate pledges**

Newly elected European Commission president Ursula von der Leyen plans to strengthen carbon-cutting goals.

BY QUIRIN SCHIERMEIER

German defence minister Ursula von der Leyen was elected as the next president of the European Commission on 16 July — and she has put climate change at the top of her agenda. Von der Leyen was narrowly voted in by Members of the European Parliament (MEPs), and will be the first woman to take the top job in Brussels, where she will lead the European Union’s executive branch and guide its policy agenda. She takes office in November.

In a speech to parliament before her election, von der Leyen said that she intends to make climate and the environment priorities in all policy areas. She pledged to strengthen the EU’s short-term goal on greenhouse-gas emissions from a 40% reduction by 2030 to at least a 50% cut, relative to 1990 levels. The EU will also take the lead in international climate negotiations, and will encourage other major economies to increase their ambitions by 2021, she said.

From a scientific perspective, the more ambitious carbon-reduction target is a crucial step, says Ottmar Edenhofer, director of the Potsdam Institute for Climate Impact Research in Germany. “Now she will have to deliver on those promises.”

Von der Leyen is also set to announce a ‘Green Deal for Europe’ in her first 100 days in office, which would include a law to make Europe carbon neutral by 2050. “I want Europe to become the first climate-neutral continent in the world,” she said.

The proposed deal, outlined in a political agenda she released last week, includes a biodiversity strategy for Europe, an extended emissions-trading system and a tax to avoid carbon ‘leakage’ — when companies transfer the production of goods to countries with more relaxed emission limits. She also pledged to:  

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