भारतीय भेषजी परिषद्
(स्वास्थ्य एवं परिवार कल्याण मंत्रालय के अंतर्गत सांविधिक निकाय)
भारत सरकार
आई-300, तीसरी मंजिल, टावर-1, वर्ल्ड ट्रेड सेंटर,
नौरोजी नगर, नई दिल्ली-110029
टेलीफोन नंबर 011-65218900-01
E-mail: registrar@pci.nic.in

कामये दु:खतप्तानाम् प्राणिनामार्तिनाशनम्

PHARMACY COUNCIL OF INDIA
(Statutory body under Ministry of Health & Family Welfare)
Government of India
I-300, 3rd floor, Tower-I, World Trade Centre,
Nauroji Nagar, New Delhi-110029
Telephone No. 011-65218900-01
E-mail: registrar@pci.nic.in

Ref. No. 10-1/2014-PCI Pt-I
POLICY-14011/38/2025-POLICY I/99/2025

- 4 APR 2025

All Institutions approved by PCI-

- **u/s 12 of the Pharmacy Act, 1948**
- **for conduct of course**

Sub: Seeking assistance in addressing the continueduse of a scientifically misleading and cruel animal test called the Forced Swim Test.

Ref: PCI circular Nos.1. 10-1/2002-PCI/3869-4376 dt. 3.6.2002.
2.10-1/2002-PCI-/1659-17122 dt. 7.3.2013.
3. 10-1/2002-PCI-Pt-I/2934-3490 dt. 18.5.2004.
4. 10-1/2002-PCI-Pt-I/24101-25375 dt. 25.11.2009.
5. 10-1/2002-PCI-Pt-I/13377-15229 dt.17.3.2011.
6. 10-1/2002-PCI-Pt-I/40704-42813 dt. 19.1.2012.
7. 10-1/2002-PCI-Pt-I/10845-12755 dt. 26.6.2013.
8. 10-1/2002-PCI-Pt-I/9959-11898 dt. 9.6.2014.
9. 10-1/2002-PCI-Pt-I/12904-14000 dt. 9.6.2014.
10. 10-1/2002-PCI-Pt-I/44985-47215 dt. 1.3.2016.

Sir/Madam,

With reference to the subject cited above, please find enclosed herewith a copy of letter dt. 20.1.2025 received from Science Policy Advisor People for the Ethical Treatment of Animals India, Maharashtra, which is selfexplanatory& for necessary action at your end.

Yours faithfully

ANIL MITTAL
Digitally signed by ANIL MITTAL
Date: 2025.04.04 12:34:32 +05'30'

(ANIL MITTAL)
Registrar-cum-Secretary
CC to -
Dr. Anjana Aggarwal
Science Policy Advisor
People for the Ethical Treatment of Animals India
PO Box-28260 Juhu,
Mumbai- 400049 (Maharashtra)
E.Mail: info@petaindia.org

PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS INDIA

PETA India
PO Box 28260
Juhu, Mumbai
Maharashtra 400049
022 40727382

Info@petaindia.org
PETAIndia.com

20th January 2025

Dr. Montu M.Patel
President PCI
O/o of PCI President
Pharmacy Council of India
NBCC Centre, 3rd Floor,
Plot No.2, Community Centre
Maa Anandamai Marg
Okhla Phase I
New Delhi – 110020

Via post and email: presidentpci2718@gmail.com

Dear Dr. Montu M.Patel,

On behalf of People for the Ethical Treatment of Animals (PETA) India and our more than 2 million members and supporters, I am writing to urge the Pharmacy Council of India to take leadership in modernizing and humanizing education and research practices by adopting policies that replace cruel animal experiments with advanced, non-animal methodologies. With growing awareness of animal welfare and advancements in technology, now is the perfect time for the Pharmacy Council of India to drive meaningful change in academic institutions and research settings across India.

Over the last decade, progressive decisions by other regulatory bodies—such as banning dissection and animal experimentation in undergraduate and postgraduate zoology and life sciences courses—have saved millions of animals annually while promoting compassionate education and innovation. **Inspired by these achievements, I am writing to urge the Pharmacy Council of India to adopt a policy banning the use of the forced swim test in academic institutions and research settings.**

The forced swim test, also known as the Porsolt swim test, involves dropping small animals, such as mice and rats, into inescapable tanks of water. Some experimenters claim that when animals spend more time floating (as opposed to trying to escape), they're more "depressed"—despite evidence to the contrary—and often use the test in an attempt to model human depression or test antidepressant drugs. In reality, the forced swim test is not scientifically credible and is deliberately cruel. It has already been abandoned or banned outright by most of the world's major pharmaceutical companies and a number of academic institutions and government jurisdictions (See **Annexure A** for details). Please also see the **enclosed 2022 report** titled, "**The Invalidity of the Forced Swim Test**," drafted by PETA US, for evidence detailing scientific and ethical considerations supporting a move away from this flawed experiment.

In the Indian context, where there is a growing awareness and concern for the ethical treatment of animals, **Pharmacy Council of India** can lead the way in adopting humane and progressive research practices under your leadership and expertise. We acknowledge the positive strides India has made in recognizing animal welfare as a significant aspect of scientific research and encourage **Pharmacy Council of India** to

Entities:
- PETA US
- PETA Asia
- PETA France
- PETA Australia
- PETA Germany
- PETA Switzerland
- PETA Netherlands
- PETA Foundation (UK)

Registered Office:
F-110, First Floor, Jagdamba Tower
Plot No 13, Community Centre
Preet Vihar, New Delhi
Delhi 110092

CIN: U74899DL2000NPL103217

be at the forefront of this ethical shift. Such a commitment not only aligns with evolving ethical norms in scientific research but also sets a positive precedent for other institutions to follow.

Given this compelling evidence, will you meet with us about this issue? Thank you, and I look forward to your reply.

Sincerely,

Dr Anjana Aggarwal
Science Policy Advisor
PETA India

Enclosures:

Annexure A

The Invalidity of the Forced Swim Test

PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS INDIA

PETA India
PO Box 28260
Juhu, Mumbai
Maharashtra 400049
022 40727382

Info@petaindia.org
PETAIndia.com

PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS INDIA

PETA India
PO Box 28260
Juhu, Mumbai
Maharashtra 400049
022 40727382

Info@petaindia.org
PETAIndia.com

Annexure A
Global Bans and Restrictions on the Forced Swim Test (FST)

- **July 2024:** Three medical research funding charities—the BMA Foundation, Medical Research Scotland, and The Dunhill Medical Trust—banned funding of future experiments involving FST.[2]
- **June 2024:** La Trobe University (Australia) prohibited FST to model human depression, anxiety disorders, and their treatment.[2]
- **March 2024:** The U.K. barred the use of FST a model of human depression and for studies of anxiety and its treatment, and explicitly stated it intends to "go further … to enable a complete ban on the use of the forced swim test in the near future."[3]
- **March 2024:** New South Wales (Australia) has enacted legislation making it illegal to conduct new FST.[4]
- **January 2024:** The Australian Research Council prohibited funding any experiments that use FST to model human depression in order to study "depression-like behaviour" or anxiety disorders and their treatment.[1]
- **December 2023:** The Australian National Health and Medical Research Council prohibited funding any experiments that use FST to model human depression in order to study "depression-like behaviour" or anxiety disorders and their treatment.[5]
- **December 2023:** The University of Western Australia confirmed it "no longer conducts" FST.[2]
- **December 2023:** AgResearch, a New Zealand government research institute that oversees the use of animals in experimentation for more than 40 other institutions in the country, revised its legally-binding code of conduct to state that its ethics committees "will not consider an application" that includes FST.[6]

---

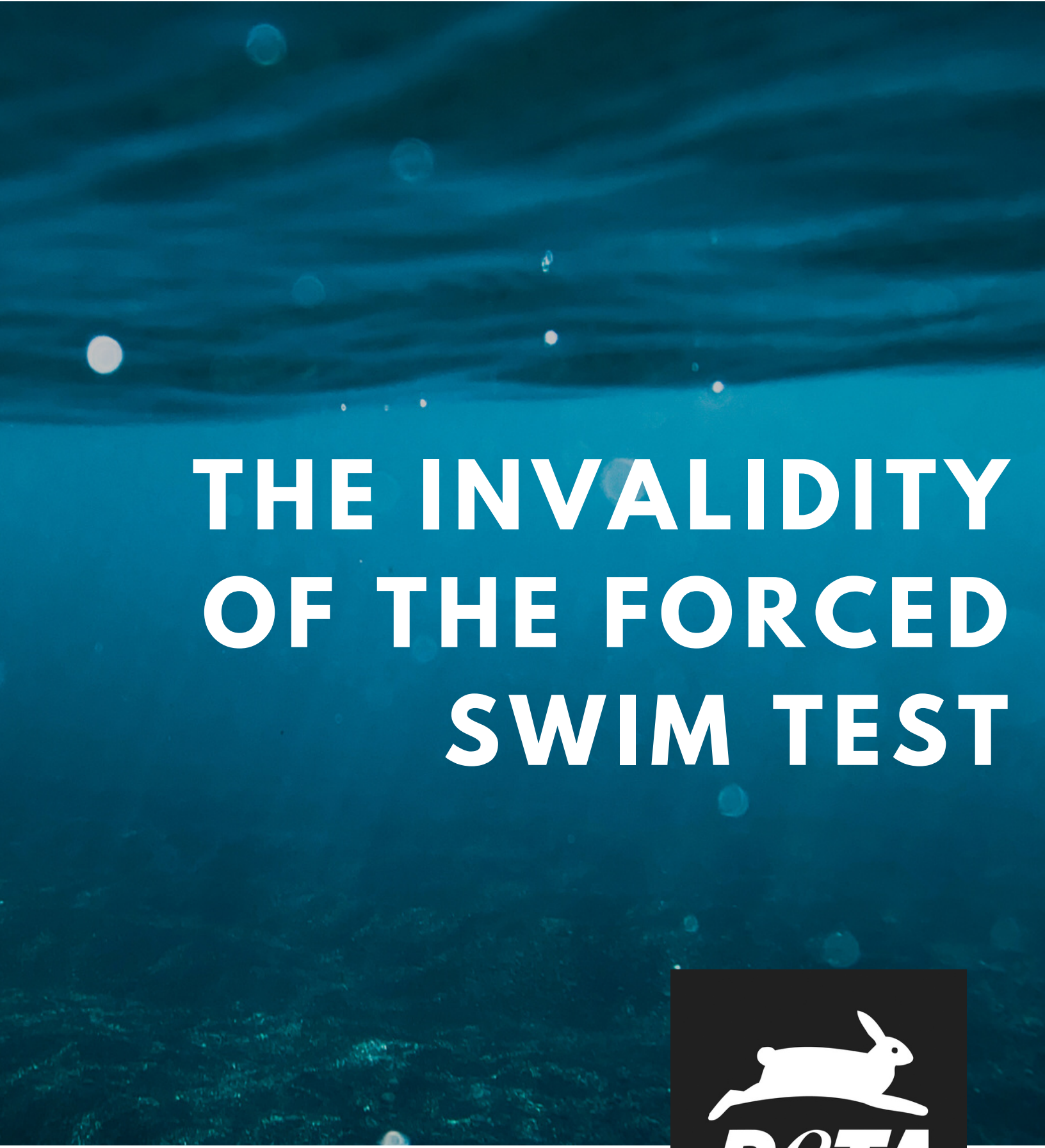
[2] People for the Ethical Treatment of Animals (PETA). (2022, September). Victories! PETA Is Ending Near-Drowning Experiments on Animals. Retrieved August 22, 2024, from https://www.peta.org/features/peta-ends-near-drowning-tests-small-animals/
[3] Sharpe, Lord. "Response to Review of the Use of the Forced Swim Test." Home Office, 01 Mar. 2024, pp. 1-8. https://www.gov.uk/government/publications/advice-on-the-use-of-the-forced-swim-test-letter-from-lord-sharpe/letter-from-lord-sharpe-of-epsom-responding-to-the-asc-forced-swim-test-report-accessible Accessed 8 Aug. 2024.
[4] Hurst, Emma. "Animal Research Amendment (Prohibition of Forced Swim Tests and Forced Smoke Inhalation Experiments) Bill 2023." New South Wales Parliament, 2023. https://www.parliament.nsw.gov.au/bill/files/18431/First%20Print.pdf Accessed 8 Aug. 2024.
[5] Statement on the forced swim test in rodent models. NHMRC. https://www.nhmrc.gov.au/research-policy/ethics/statement-forced-swim-test-rodent-models Accessed 8 Aug. 2024.
[6] NZAVS | Ending Animal Experimentation. "Huge Victory - AgResearch Bans the Use of the Forced Swim Test in NZ!" Huge Victory - AgResearch Bans the Use of the Forced Swim Test in NZ! - NZAVS | Ending Animal Experimentation Accessed August 08, 2024

- **August 2023:** Universidad del Valle (Colombia) banned FST.[2]
- **April 2023:** 12 U.K. research universities—Exeter, Newcastle, Brighton, Glasgow, Leeds, Liverpool, Manchester, Nottingham, St. Andrews, Southampton, Warwick, and York—stated they neither use FST nor intend to in the future.[2]
- **September 2022:** Macquarie University (Australia) prohibited FST.[2]
- **May 2021:** Amgen confirmed it won't pursue FST.[1]
- **April 2021:** The University of South Australia stated FST will not be approved for any future research projects.[2]
- **September 2020:** The University of Adelaide (Australia) stated it will stop using FST.[2]
- **June 2020:** GlaxoSmithKline banned FST.[2]
- **January 2020:** King's College London confirmed it will no longer use FST.[2]
- **January 2020:** Bristol Myers Squibb banned FST.[1]
- **November 2019:** Bayer banned FST.[1]
- **October 2019:** Pfizer banned FST.[1]
- **September 2019:** Sage Therapeutics banned FST.[1]
- **August 2019:** Novo Nordisk A/S stated it will ban FST.[1]
- **August 2019:** AstraZeneca banned FST.[1]
- **July 2019:** Boehringer Ingelheim banned FST.[1]
- **June 2019:** Astraea Therapeutics stated it does not conduct or fund such experiments and has no intention of doing so in the future.[1]
- **June 2019:** Roche Pharma banned FST.[1]
- **May 2019:** NutriFusion confirmed it will no longer be involved with FST.[2]
- **April 2019:** DSM Nutritional Products discontinued FST.[2]
- **March 2019:** Johnson & Johnson banned FST.[1]
- **December 2018:** AbbVie banned FST.[1]

PEOPLE FOR THE ETHICAL TREATMENT OF ANIMALS INDIA

PETA India
PO Box 28260
Juhu, Mumbai
Maharashtra 400049
022 40727382

Info@petaindia.org
PETAIndia.com



THE INVALIDITY OF THE FORCED SWIM TEST

2022

PETA
People for the Ethical Treatment of Animals

Development of the Forced Swim Test

The forced swim test (FST), also called the Porsolt Swim Test, has been used since at least the 1950s but was popularized in 1977 by Roger D. Porsolt as a potential method for screening antidepressant drugs. During this test, a small animal, typically a rat or mouse, is placed in a container of water with no way to escape nor any place to rest out of the water. Naturally, the animal will spend some time swimming and trying to escape the stressful situation but will eventually become immobile and float. The experimenter records the time that the animal spends swimming and the time that they spend floating in the water. Sometimes the swimming behavior is divided into two types: climbing behavior, in which the rodent attempts to climb up the sides of a tank or beaker, and swimming behavior, in which the rodent typically swims around but doesn't try to climb out of the container.

A similar test to the FST is the tail suspension test (TST), which operates on analogous principles. An animal (typically a mouse) is held upside down by the tail, typically affixed to a stationary bar or object with a piece of tape. For a while, the mouse will struggle and try to correct this frightening and uncomfortable position but will eventually become immobile.

Porsolt and others found that when an experimenter acutely administers some commonly used antidepressant drugs to the animal prior to the FST or TST, the animal may swim (or struggle) for longer and spend less time floating (or remaining still) (1,2). This was taken to mean that longer swimming times indicate a less "depressed" animal and that the antidepressant is what caused the change in behavior. Animals who spent more time immobile were thought to be in "despair," as if they had "given up." However, this interpretation is incorrect for several reasons.

Is Immobility a Learned Behavior?

Evidence suggests that immobility in the FST may be a learned or adaptive behavior, not one representing an internal state of despair. In some FST protocols, typically ones involving rats, the same animal is made to participate in the test more than once, usually before and after administration of a particular substance, so that the animal serves as their own control. In this case, immobility becomes a learned behavior. De Pablo et al. demonstrated that rats generally show less mobility on the second day of testing than they do on the first day (3). When a group of rats was administered anisomycin, a substance known to disrupt consolidation of memories, the anisomycin-treated group stayed more active on the second day of the test than rats who had not been given the drug, meaning that disrupting the learning process affects behavior during the FST. The untreated rats may have learned that there was no way to escape their situation and that they would eventually be removed from the water by the experimenter, facts that the anisomycin-treated rats did not learn. The anisomycin had no effect on the rats' behavior during the first day of the test.

Proponents of the idea that FST immobility is a reflection of behavioral despair equate the behavior to types exhibited in learned helplessness paradigms (4). To create a state of learned helplessness, an experimenter exposes an animal to a series of inescapable shocks. At first, the animal will actively look for ways to escape the shocks—but over time, he or she will exhibit fewer types of escape behavior and sometimes won't attempt to escape the shocks, even when provided with the means to do so. Experimenters say that these animals have "given up" and resigned themselves to the fate of being shocked.

When the same animal is subjected to the FST more than once, it is thought by some that prior exposure to the testing situation acts as a stressor for the animal and that increased immobility on later testing days reflects a sort of learned helplessness caused by the inescapable FST. However, experiments by O'Neil and Valentino showed that prior exposure to the FST had no effect on behavior in other stress paradigms, such as inescapable shock, and that allowing rats a means of escaping from the water container during the first FST didn't affect their behavior on subsequent exposures (5). (They're still more immobile on later days—an observation that is inconsistent with learned helplessness paradigms.) This is further evidence that immobility in the FST is a learned behavior and not indicative of learned helplessness.

Is Immobility an Adaptive Behavior?

Reviews by West as well as by Molendijk and de Kloet have explained that immobility in the FST is likely a beneficial behavior for these animals (4,6). Swimming and climbing expend unnecessary energy, and animals who are quicker to realize this have a greater chance for survival in extended submerged situations. In experiments described by Nishimura et al., rats were forced to swim until they sank for as long as two hours. Experimenters found that the amount of time spent immobile within the first 15 minutes of the test predicted sinking—the rats who struggled longer were quicker to sink, while the rats who conserved their energy floated longer before sinking (7). The experimenters noticed that rats who struggled and swam longer also defecated more, potentially signifying increased fear in the "less adaptive" group.

Molendijk and de Kloet argue that the FST lacks two essential forms of validity used to assess animal models of human diseases or conditions: construct validity and face validity.6 Because the development of depression is a slow process, a test of 15 minutes or even tests conducted over a 24-hour period cannot be used to determine depression (8); therefore, the FST lacks construct validity. The FST lacks face validity because "there is no single sign or symptom of depression modeled apart from the anthropomorphic interpretation of floating behavior in terms of despair" (6) and because there is "little similarity between the clinical symptoms of depression in humans and the behaviors measured in the test" (9).

Another way to interpret the adaptive behavior of immobility during the FST is to consider that an animal's actions may represent their individual response to the stressor of being immersed in water, not knowing when or if escape will be possible. Some animals will cope with this situation actively by struggling, and some will cope passively by floating. Commons and colleagues write, "While it could be argued that passive coping strategies to stress are characteristic of depression, the connection between swimming and the human condition begs an abstraction at best. Behavior in the FST is a reaction to the acute stressful stimulus of being placed in a container without an escape route, and human depression reflects a chronic subjective emotional state rather than a reaction to an individual stimulus" (9).

Initial Interpretations of the FST Were at Odds With Biochemical Reality

The methodology by which the FST was discovered provides cause to doubt that immobility can be equated with "despair." Experimenters noted that acute administration of antidepressants decreased

immobility; however, antidepressants do not work in humans to relieve depression when administered acutely. As noted by O'Leary and Cryan, "The FST and TST have been criticised because they are sensitive to acute treatment with an antidepressant drug, whereas several weeks or months of antidepressant treatment is required before a clinical response is reported. Because the inducing factor (acute stress of swimming or suspension) is intrinsically coupled with the readout (time spent immobile), these tests also muddy the water between definitions of test versus model"(10). The acute immobility response of mice and rats to antidepressant treatment compared with repeated exposure required for humans to note antidepressant effects indicates that these drugs act on—and these types of behavior reflect—different mechanisms between species.

Some experimenters have shown that chronic treatment with the antidepressant fluoxetine also reduces time spent immobile in mice (11). However, the immobility response also occurs after treatment with drugs that are not used as antidepressants, such as antihistamines and other miscellaneous drugs (12), putting the entire premise on unstable ground.

Experimental and Strain Effects

Experimental details such as water temperature and depth can alter an animal's behavior during the FST and potentially confound results. Jeffrys and Funder conducted an experiment designed to test whether water temperature influenced a rat's mobility. They found that when the water was 20°C, rats spent less time immobile and were slower to learn immobility behavior over the course of the experiment (which included four exposures to the water tank) compared to when the water was 25 or 30°C.13 A different outcome has been observed for mice, with immobility decreasing in warmer water (12–14).

The depth of water used by experimenters also influences results in the FST. In one study, placing rats in water with a depth of 35 cm increased swimming and decreased immobility compared to situations in which rats were placed in water with a depth of 15 cm (3). Presumably, the rats could detect the bottom of the container with their tails at 15 cm.

Importantly, mice show different types of behavior in the FST depending on their strain. When comparing 11 commonly used strains of mice, Lucki and colleagues found that time spent immobile differed over tenfold between the strain that swam the most and the one that swam the least (15). Strains also differ in sensitivity to antidepressant drugs administered before the FST. Dulawa et al. noted strain differences in the response to chronic fluoxetine treatment, where the drug regimen affected swimming and immobility times in BALB/c mice but not in three other strains, including the ubiquitous C57BL/6 mouse (11).

The reality that variables such as water temperature, water depth, and strain can alter FST results so dramatically and have the potential to confound interpretation further invalidates it as a reliable measure of despair or behavior in general.

FST Is Used to Draw False Conclusions

The problem with misinterpretation of the FST is that it has led to a false assumption that it can be

used to measure depression in animals. Frighteningly, it has sometimes led to the assumption that the FST can serve as the sole measure used in a study to describe an animal's mood and thus to make inferences about human mood.

In a commentary in Psychoneuroendocrinology, Molendijk and de Kloet estimate that in the 4,300 papers reporting use of the FST at the time of publication, "[n]o less than [2,020] papers label the phenotype of the floating rodent as depression-like behavior—sometimes with a remark that the validity of the test is debated but often without discussion" (6). Additionally, 7.5% of these (320 papers) had "used the FST to monitor the outcome of genetic manipulations of signaling pathways suspected to be involved in the precipitation of depression-like symptoms. Most of these studies (we estimate 70%) indeed infer a depression phenotype from the immobility response displayed by the rodent" (6).

In a 2019 follow-up to this analysis, Molendijk and de Kloet found that in the three years prior, "the popularity of the FST [was] still increasing" (16). Of the papers they analyzed, 72% qualified the behavior of a floating mouse or rat as "depressive-like, but without evidence for face, predictive, or construct validity" (16).

The FST in Stress Research

The use of the FST in stress research is on the rise (17). It's clear that the FST is stressful. You can view a compilation video of the test here. When an experimenter places an animal into the water, the animal's stress is clearly visible and they sometimes defecate in the water. However, the FST should not be used to make inferences about stress in humans.

According to Mental Health First Aid England, humans typically experience stress because of troubling changes at home or work, financial pressures, relationship issues, emotional dilemmas, or poor health habits (18). These types of stressors, which are typically chronic in nature, stand in stark contrast with the acute stress of potential drowning—something that, thankfully, few humans are forced to cope with in their lifetime. When acute, life-altering stressors do occur, they can result in post-traumatic stress disorder, which is difficult to assess in animals since many of the psychological symptoms, such as flashbacks, emotional numbness, and detachment, are not measurable and many of the symptoms that experimenters can observe could be attributed to other types of mood disturbances (19) or to species-specific factors that are entirely unrelated to stress or emotion.

The increased levels of baseline stress experienced by animals held and used in laboratories further undermine the relevance of the FST for human stress research. Unnatural laboratory settings inherently do not meet the ethological needs of any animal and introduce confounding variables stemming from confinement-induced stress, undermining the value of the data collected from these animals.

Several specific factors contribute to baseline stress in the experimental setting:

- Experimenters keep mice and rats in unnaturally cold temperatures for the duration of their lives (20).
- Experimenters force animals to live in solitary confinement (21) inside small cages devoid of any meaningful enrichment (22), which, along with feeding them an unnatural and unvaried diet, has a negative impact on their metabolic health (23).
- Experimenters make animals perform complicated and distressing behavioral tasks at times that are biologically irrelevant to when they would normally be active (24-25).
- Abnormal behavior is common in animals in laboratories and considered a direct result of living in a laboratory environment. Abnormal behavioral patterns have even been linked to long-term effects in abnormal physiological development and brain functioning, with some abnormal behavior patterns thought to reflect permanent brain dysfunction (26).

These factors increase stress-related morbidity and mortality (27) and result in experiments being conducted on animals who are fundamentally different from their wild counterparts and even further removed from humans.

Industry and Academia Abandon the FST

In 2021, PETA scientist Emily Trunnell and psychologist Constança Carvalho published their analysis of publicly available data on pharmaceutical companies' use of the FST to test novel compounds for their potential value as human antidepressants. The data showed that the FST did not reliably predict whether experimental compounds would be effective in treating human depression or ultimately be marketed successfully as antidepressants. Of the 109 compounds identified as having been used in FST experiments by the top 15 most profitable pharmaceutical companies, less than a third were also explored in humans with depression and, of these, there were only three compounds for which the FST appeared to positively predict antidepressant efficacy (28). However, not one of the 109 compounds is currently approved to treat any form of depression.

After being presented with their own data and asked by PETA to reconsider their position on the use of this test, 15 companies have committed not to conduct, commission, or fund the FST any longer: AbbVie, Amgen, Astraea Therapeutics, AstraZeneca, Bayer, Boehringer Ingelheim, Bristol Myers Squibb, DSM Nutritional Products, GSK (formerly GlaxoSmithKline), Johnson & Johnson, Novo Nordisk A/S, NutriFusion LLC, Pfizer, Roche, and Sage Therapeutics (29).

Since January 2020, a number of research universities in Australia, New Zealand, and the U.K. have also stopped using the test (29).

The FST Is Discouraged by Regulators

In 2021, scientists from the U.K. Medicines and Healthcare products Regulatory Agency published a paper discouraging companies from including FST data in their submissions to the agency, citing its irrelevancy to drug efficacy, the danger that its use could erroneously filter out potentially effective antidepressants, and the simple fact that it is not required (30). The issue was covered by the news outlet STAT. In the article, a U.S. Food & Drug Administration official confirms that the agency also does not require the FST for regulatory submissions (31).

In 2019, the European Medicines Agency's Committee for Medicinal Products for Human Use issued its public assessment report on Spravato (esketamine), a recently approved antidepressant. The assessment revealed that no "animal models of depression" (a category including the FST) were performed by Janssen, the applicant, and that the agency agreed that "animal models of depression or antidepressant-sensitive behavioural tests are poorly predictive for the human situation" and "would not add further value to the overall assessment" (32).

Similarly, officials in New Zealand have a low opinion of the FST and support a transition away from its use. In a report from a meeting in which the FST was reviewed, the New Zealand government's Economic Development, Science and Innovation Committee discussed the disadvantages of the test and called an expert witness who commented on the FST's "ethical cost" and "lack of utility" (33).

Conclusion

For decades, experimenters have been subjecting mice and rats to a stressful procedure in which these animals are forced to swim in deep water with no way to escape. Experimenters have been using this procedure to make uninformed determinations about an animal's mood and to use these determinations to make potentially false inferences about biology related to human health.

Use of the FST has wasted much in public funds, animal lives, and research hours. The onus to correct this poor science is on several major players: Regulators, institutions, and funders can prevent these experiments before they occur by evaluating proposals for the FST or TST and rejecting their use. Additionally, journals can prevent spurious conclusions based on the FST or TST from being reported and circulated in the literature by more closely scrutinizing manuscripts including animal behavioral protocols.

When there is such a poor translation of studies on animals to therapies for humans (34), something is clearly wrong with current methodologies. Animal experimentation has been cited as the primary source for attrition, or drug failure, in human neurobehavioral clinical trials (34). It is time for experimenters to follow the evidence and focus their efforts on human-based experimental models, such as computational modeling, the use of human cells in advanced in vitro experiments such as those using human brain organoids, the use of patient-specific stem cells for personalized medicine, human neuroimaging, and human genomics.

References

1. Porsolt RD, Le Pichon M, Jalfre M. Depression: a new animal model sensitive to antidepressant treatments. Nature. 1977;266(5604):730-732. doi:10.1038/266730a0
2. Porsolt RD, Anton G, Blavet N, Jalfre M. Behavioural despair in rats: A new model sensitive to antidepressant treatments. Eur J Pharmacol. 1978;47(4):379-391. doi:10.1016/0014-2999(78)90118-8
3. De Pablo JM, Parra A, Segovia S, Guillamón A. Learned immobility explains the behavior of rats in the forced swimming test. Physiol Behav. 1989;46:229-237. doi:10.1016/0031-9384(89)90261-8
4. West AP. Neurobehavioral studies of forced swimming: The role of learning and memory in the forced swim test. Prog Neuro-Psychopharmacology Biol Psychiatry. 1990;14(6):863-IN4. doi:10.1016/0278-5846(90)90073-P
5. O'Neill KA, Valentino D. Escapability and generalization: Effect on "behavioral despair." Eur J Pharmacol. 1982;78:379-380. doi:10.1016/0014-2999(82)90043-7
6. Molendijk ML, de Kloet ER. Immobility in the forced swim test is adaptive and does not reflect depression. Psychoneuroendocrinology. 2015;62:389-391. doi:10.1016/j.psyneuen.2015.08.028
7. Nishimura H, Tsuda A, Oguchi M, Ida Y, Tanaka M. Is immobility of rats in the forced swim test "behavioral despair?" Physiol Behav. 1988;42:93-95. doi:10.1016/0031-9384(88)90266-1
8. Belmaker RH, Agam G. Major Depressive Disorder. N Engl J Med. 2008;358(1):55-68. doi:10.1056/NEJMRA073096
9. Commons KG, Cholanians AB, Babb JA, Ehlinger DG. The Rodent Forced Swim Test Measures Stress-Coping Strategy, Not Depression-like Behavior. ACS Chem Neurosci. 2017;8(5):955-960. doi:10.1021/acschemneuro.7b00042
10. O'Leary OF, Cryan JF. Towards translational rodent models of depression. Cell Tissue Res. 2013;354:141-153. doi:10.1007/s00441-013-1587-9
11. Dulawa SC, Holick KA, Gundersen B, Hen R. Effects of Chronic Fluoxetine in Animal Models of Anxiety and Depression. Neuropsychopharmacology. 2004;29(7):1321-1330. doi:10.1038/sj.npp.1300433
12. Arai I, Tsuyuki Y, Shiomoto H, Satoh M, Otomo S. Decreased body temperature dependent appearance of behavioral despair in the forced swimming test in mice. Pharmacol Res. 2000;42:171-176. doi:10.1006/phrs.2000.0672
13. Jeffrys D, Funder J. The effect of water temperature on immobility in the forced swimming test in rats. Eur J Pharmacol. 1994;253:91-94.
14. Peeters BWMM, Smets RJM, Broekkamp CLE. The involvement of glucocorticoids in the acquired immobility response is dependent on the water temperature. Physiol Behav. 1992;51(1):127-129. doi:10.1016/0031-9384(92)90213-L
15. Lucki I, Dalvi A, Mayorga AJ. Sensitivity to the effects of pharmacologically selective antidepressants in different strains of mice. Psychopharmacology (Berl). 2001;155:315-322. doi:10.1007/s002130100694
16. Molendijk ML, de Kloet ER. Coping with the forced swim stressor: current state-of-the-art. Behav Brain Res. 2019;364(February):1-10. doi:10.1016/j.bbr.2019.02.005
17. Molendijk ML, de Kloet ER. Forced swim stressor: Trends in usage and mechanistic consideration. Eur J Neurosci. 2021;2021:1-19.
18. Mental Health First Aid England. Sources of Stress. luton.gov.uk. https://www.luton.gov.uk/Health_and_social_care/Lists/LutonDocuments/PDF/sources-of-stress.pdf. Accessed June 9, 2022.
19. Flandreau EI, Toth M. Animal Models of PTSD: A Critical Review. In: Vermetten E, Baker D, Risbrough V, eds. Behavioral Neurobiology of PTSD. Current Topics in Behavioral Neurosciences. Vol 38. Springer, Cham; 2017:47-68. doi:10.1007/7854_2016_65
20. Hankenson FC, Marx JO, Gordon CJ, David JM. Effects of Rodent Thermoregulation on Animal Models in the Research Environment. Comp Med. 2018;68(6):425. doi:10.30802/AALAS-CM-18-000049
21. Arakawa H. Ethological approach to social isolation effects in behavioral studies of laboratory rodents. Behav Brain Res. 2018;341:98-108. doi:10.1016/J.BBR.2017.12.022
22. Lahvis GP. Point of view: Unbridle biomedical research from the laboratory cage. Elife. 2017;6. doi:10.7554/ELIFE.27438
23. Cressey D. Fat rats skew research results. Nature. 2010;464(7285):19. doi:10.1038/464019A
24. Hawkins P, Golledge HDR. The 9 to 5 Rodent − Time for Change? Scientific and animal welfare implications of circadian and light effects on laboratory mice and rats. J Neurosci Methods. 2018;300:20-25. doi:10.1016/J.JNEUMETH.2017.05.014
25. Nelson RJ, Bumgarner JR, Walker WH, DeVries AC. Time-of-day as a critical biological variable. Neurosci Biobehav Rev. 2021;127:740-746. doi:10.1016/J.NEUBIOREV.2021.05.017
26. Mason G, Rushen J, eds. Stereotypic Animal Behaviour: Fundamentals and Applications to Welfare. 2nd ed. Wallingford: CABI; 2006. doi:10.1079/9780851990040.0000
27. Cait J, Cait A, Scott RW, Winder CB, Mason GJ. Conventional laboratory housing increases morbidity and mortality in research rodents: results of a meta-analysis. BMC Biol. 2022;20(1):1-22. doi:10.1186/S12915-021-01184-0/TABLES/2
28. Trunnell ER, Carvalho C. The forced swim test has poor accuracy for identifying novel antidepressants. Drug Discov Today. 2021;26(12):2898-2904. doi:10.1016/J.DRUDIS.2021.08.003
29. People for the Ethical Treatment of Animals. Victories! PETA Is Ending Near-Drowning Experiments on Animals. PETA.org. https://www.peta.org/blog/astrazeneca-novo-nordisk-as-save-animals-ban-forced-swim-test/. Published 2022. Accessed June 9, 2020.
30. Sewell F, Waterson I, Jones D, Tricklebank MD, Ragan I. Preclinical screening for antidepressant activity – shifting focus away from the Forced Swim Test to the use of translational biomarkers. Regul Toxicol Pharmacol. 2021;125:105002. doi:10.1016/J.YRTPH.2021.105002
31. Silverman E. Activists get new ammunition in their battle over a controversial animal test. statnews.com. https://www.statnews.com/pharmalot/2021/07/27/peta-animal-rodent-swim-test-uk/. Published July 27, 2021. Accessed June 9, 2022.
32. European Medicines Agency Committee for Medicinal Products for Human Use. Assessment Report: Spravato. Amsterdam; 2019. https://www.ema.europa.eu/en/documents/assessment-report/spravato-epar-public-assessment-report_en.pdf. Accessed June 9, 2022.
33. Economic Development S and IC. Petition of Tara Jackson on Behalf of the NZ Anti-Vivisection Society, SAFE, and 7,861 Others: End the Use of the Forced Swim Test in New Zealand.; 2020. https://www.parliament.nz/resource/en-NZ/SCR_95117/50c60dcb87e9ee8360c19c45739ff919854c66c8. Accessed June 9, 2022.
34. Garner JP. The significance of meaning: Why do over 90% of behavioral neuroscience results fail to translate to humans, and what can we do to fix it? ILAR J. 2014;55(3):438-456. doi:10.1093/ilar/ilu047