# DECEMBENT OF ANIMALS

## Welfare and Scientific Limitations of the Forced Swim Test

Kimberley Jayne<sup>1</sup>, Julia Baines<sup>1</sup>, Emily R. Trunnell<sup>2</sup> <sup>1</sup>People for the Ethical Treatment of Animals (PETA) UK, <sup>2</sup>PETA US KimberleyJ@peta.org.uk





## Introduction to the Forced Swim Test

The forced swim test (FST), also known as the Porsolt test, is a behavioural experiment initially popularised in the 1970s to test antidepressant drugs and then, 20 years later, adopted as an animal model of depression.

In the test, a small animal is put into an inescapable beaker filled with water, with no rest platform. Initially, the animal will swim in search of an escape, pawing at the sides of the beaker or diving under the water. Eventually, the animal stops swimming and floats on the surface, moving only to keep their head above water. The latency to become immobile, and float on the water, is recorded.

Historically this behaviour has been interpreted as "behavioural despair", under the assumption that those with depression-like behaviour "give up swimming earlier than those [who] are not depressed" and, that antidepressant drugs reverse this effect.



The FST is one of the most commonly used tests to assess depressive-like behaviour in animals worldwide.

### Scientific Concerns About the Forced Swim Test

Floating ≠ behavioural despair	No construct validity	No face validity	Not reproducible	Does not translate	
Immobility in the FST may not be a sign of despair but indicative of learning and a way to conserve energy and adapt to a new environment.	The development of depression is a slow process, and a test of 15 minutes or even one conducted over a 24- hour period cannot be used to determine depression.	No single symptom of depression is modelled apart from an anthropomorphic interpretation of floating behaviour, for which there is little similarity with the clinical condition.	Results of the FST vary depending on an animal's age, weight, sex, strain, handling, social environment, and diet, as well as temperature and depth of the water.	Substantial differences exist between rodent and human brain cells and the ways they produce proteins critical to neuropsychiatric function (e.g. serotonin, glutamate, and gamma aminobutyric acid).	
For the second seco					

#### Welfare Concerns About the Forced Swim Test

#### Severity

By its nature, the FST is stressful but it can be categorised as "mild", as well as "moderate" and "severe" in licences.

#### Discouraged on welfare grounds

The National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) has identified the test as "highly contentious" and "under considerable scrutiny" due to "its severity and effect on animal welfare".

In the UK some projects have stated that they will not use the FST due to its severity.

#### Use as a stressor

The FST is also used as an acute stressor, however, human stressors that contribute to poor mental health are typically chronic in nature and involve psychological symptoms.

The increased levels of baseline stress experienced by animals housed and used in laboratories further undermine the data from the test and its relevance to human stress research. For example, exposure to unnatural routines, being caught and handled,

being observed at close proximity by humans, and unfamiliar sounds, sights, and smells

that can disrupt communication, all contribute to poor research outcomes.

#### Other concerning uses

The FST has also been used to induce hyperalgesia, an increased sensitivity to pain, where it is used alongside pain sensitivity tests, such as the hot plate and formalin tests, for which the clinical relevance has been questioned.

Additionally, immobility in the test has been used as an assessment for sickness behaviour.

- A 2021 publication, initiated by the Animals in Science Regulation Unit (ASRU) at the UK Home Office, with authors from the Medicines and Healthcare products Regulatory Agency, the NC3Rs, and King's College London (KCL), concluded that researchers should **seek alternatives** to the FST for antidepressant drugs to "**reduce dependence on the use of animals**", that the test is **not a regulatory requirement**, that it **could rule out the discovery of effective new drugs for humans**, that there is an "absence of compelling data on the neurobiological basis of the [test] and its translatability to [humans]", and that the test is a **poor model of human depression**.
- A 2021 review of the use of the FST by the 15 most profitable pharmaceutical companies in the world found that the FST is poor at accurately identifying antidepressants for human use. Of 109 compounds identified, the test appeared to positively predict antidepressant efficacy for only three, but none were approved to treat any type of depression.
- A number of pharmaceutical companies and academic institutions have policies that prevent the FST from being used at their establishment or



declared that they do not intend to use it in the future, including AstraZeneca, GlaxoSmithKline, Pfizer, and KCL.

**Ending the Forced Swim Test** 

- In the Netherlands, Radboud University's Animal Welfare Body rejected requests to perform the FST, noting it as "burdensome".
- The director of the US National Institute of Mental Health has said that the institute "been discouraging the use of certain behavioral assays, including the forced swim and tail suspension test, as models of depression" for some time.
- The European Medicines Agency has stated that animal models of depression are "poorly predictive" for humans.

#### **Conclusions and Recommendations**

- Despite recommendations for, and examples of, ending the FST on scientific and welfare grounds, preliminary analysis of project licences, non-technical summaries, and
  publications indicates that the test is still used for modelling human depression and screening antidepressant drugs at UK and EU establishments, as well as for other uses.
- We recommend that those involved in the project licence application process including the project licence applicant, funders, the Animal Welfare and Ethical Review Body, and ASRU – remove the FST from project protocols to ensure that a proposed programme of work complies with UK and EU legislative requirements for the robust application of the 3Rs (replacement, reduction and refinement of animals used in scientific procedures) and in line with the Harm-Benefit Analysis.