Certain Harms and Uncertain Benefits in Animal Models for the Study of Human Depression and Anxiety

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INTRODUCTION

Anxiety and depressive disorders, often comorbid conditions, are the most common mental disorders, affecting 4.4 and 3.6 percent of the global population, respectively. In efforts to use mice and rats as models to study these illnesses, experimenters employ a variety of behavioral tests, many of which have come under scrutiny due to their over-simplicity, unreliability, and lack of specificity. These tests are acutely stressful to animals, so the practices, and in some countries the law, require that they only be conducted after a cost-benefit analysis, i.e. when the expected benefits (understanding and treating human conditions) would outweigh the costs (harms to the animals). Here we contrast various aspects of validity and prevalence of commonly-used tests with the harms experience by the animals

METHODOLOGY

Literature searches were performed using PubMed, Google Scholar, and ClinicalTrials.gov. To determine publication frequency of each assay, we employed a search using PubMed to identify empirical studies that utilized these assays in nonhuman animals to assess depression and/or anxiety. To determine NIH-funding rates, a comparable search was conducted using NIH Reporter. A veterinarian was consulted on harms experienced by animals.

HARMS

Inherent harms of laboratory life

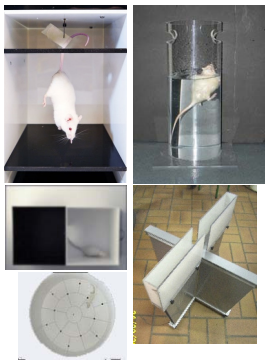
- Lack of autonomy
- Inability to engage in species-specific behaviors
- Premature weaning
- Unnatural rearing practices
- Absent or incompatible socialization, potential for experiencing fighting/aggression due to inappropriate social groupings and/or stress
- Cumulative experience of procedures
- Unnatural laboratory environment (lighting, temperature, sound, little to no access to the outdoors)
- Disrupted sleep patterns
- Inadequate living space
- Cold stress
- Ulcerative dermatitis (common)

Protocol-associated harms (under proper procedures)

- Unrelieved fear/distress
- Unrelieved pain (TST)

Protocol-associated harms (potential for deviation from protocol)

- Exhaustion (FST)
- Water inhalation (FST)
- Drowning (FST)
- Muscle/skeletal damage (TST)
- Degloving injuries (TST)
- Falling injuries (TST, EPM, ZM)



Images Credits: Wikimedia - Sora Mitamura (TST), TaoPan (FST, LDB, OFT), Bd008 (EPM)

VALIDITY

Test	Construct Validity	Face Validity	Predictive Validity	Internal Validity
Forced Swim Test (FST)	X	X	?	X
Tail Suspension Test (TST)	X	X	?	X
Elevated Plus Maze (EPM), Zero Maze (ZM)	X	X	?	X
Light/Dark Box Test (LDB)	X	X	?	X
Open Field Test (OFT)	X	X	X	X

FST SPOTLIGHT

A retrospective review assessed whether compounds tested in the FST by major pharmaceutical companies were shown to have antidepressant effects in humans. Of 31 compounds explored for antidepressant effects in humans, only seven had congruent results with the FST. Of these, none are currently approved to treat any type of depression.

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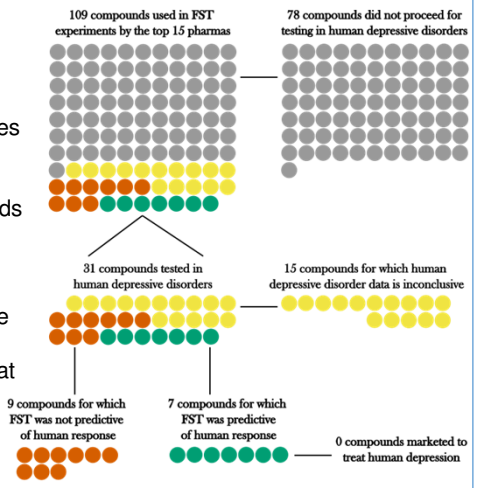
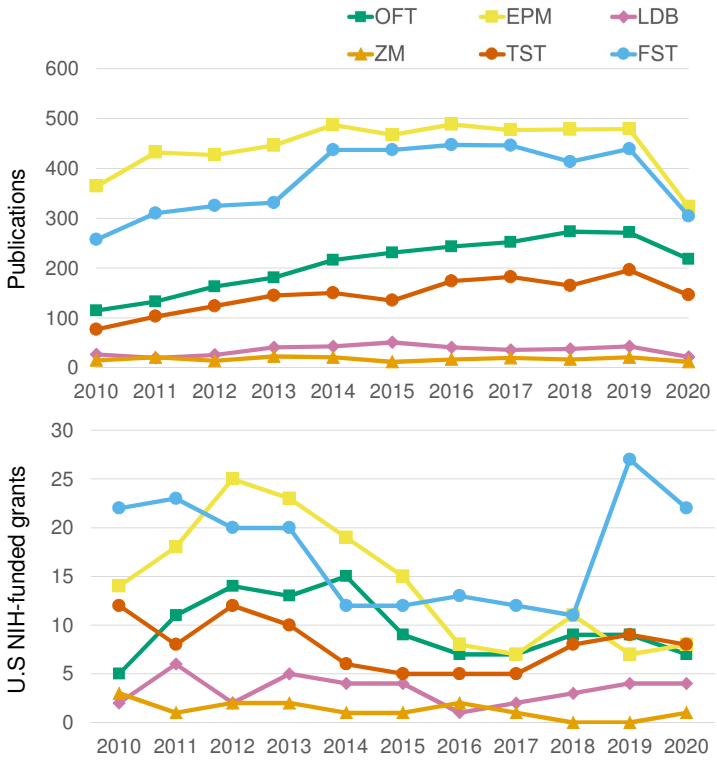


10-YEAR PREVALENCE



CONCLUSIONS

This report demonstrates that, despite lacking most, if not all, forms of validity, the FST, TST, EPM or ZM, LDB, and OFT continue to be performed. Interestingly, the FST, which rates higher in terms of harm and is the most scrutinized, continues to be among the most utilized and funded test. The data suggest that oversight bodies are not performing adequate cost-benefit analyses and that greater scrutiny of animal use protocols is urgently needed.

CONTACT INFO AND REFERENCES

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References: https://www.peta.org/wp-content/uploads/2021/07/WC11-poster-KR-ET-refs.pdf