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Reliability assessment of an automated forced swim test device using two mouse strains

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Abstract

The Porsolt forced swim test (FST) is one of the most widely used behavioral tests in the evaluation of the antidepressant effects of drugs. It is based on the fact that these drugs reduce the depression-related behaviors of learned helplessness. The model has been modified for use in mice. In contrast to rats, mice are exposed to forced swimming only once and their immobility behavior is measured and considered a "depression-like" phenotype. Like many other behavioral tests, FST can be affected by observer-related artifacts. In recent years, automated testing systems have been developed to decrease artifacts that may greatly influence the interpretation of results. In this work, we used two strains of mice, i.e., C3H/HeJ and C57BL/6J, which differ in their FST immobility times. We employed a new commercially available automated FST device and a blinded observer-based FST, and we examined their ability to measure behavioral differences between these two mouse strains. Our results suggest that the tested automated FST system generates reliable data comparable to results obtained by trained observers.

Keywords: Hamilton–Kinder; Automated forced swim test; C57BL/6J; C3H/HeJ; Mice; Strain differences; Depression; Behavior test

1. Introduction

Since its introduction almost three decades ago, Porsolt's forced swim test (FST) (Porsolt et al., 1977a,b) has been used extensively as an animal model to evaluate the antidepressant activity of drugs. It is one of the most widely accepted models to assess helplessness in rats and mice and to test the putative antidepressant and anxiolytic effects of drugs. FST has proven its usefulness and efficacy in experiments with a number of known medications used to treat human depression. Furthermore, the test has been used to evaluate "depression-like" behaviors of genetically modified animals (Lucki, 2001; Uz and Manev, 2001; Lira et al., 2003; Manev and Uz, 2003; Cryan and Mombereau, 2004).

The original Porsolt FST is conducted by placing a rat into a tank filled with water (Porsolt et al., 1977a) and is divided into two sessions with a 24-h pause in between. The first day session consists of a 15 min swimming period during which a rat experiences "*helplessness*" in the tank. The second day session has a swimming time of only 5 min. Following an initial period of futile struggling, an animal shows three movement patterns, i.e., keeping its head above water without any effort (floating), trying to get out of the tank (climbing), or other movements (unclassifiable movements) in between. The climbing and floating times are recorded. The climbing and floating behaviors are believed to represent non-depressive behavior and depressive "*learned helplessness*", respectively.

The test was originally developed in rats and has been modified for use in mice by omitting the first day session and by extending the experiment to 6 min (Porsolt et al., 1977b). In this modified use, the first 2 min are accepted as a habituation period and the duration of floating is recorded during the last 4 min of the 6 min testing period. Although the testing procedure seems to be very straightforward and observers can easily be trained to monitor and record FST behaviors, the interpretation of a wide range of movement patterns cannot always be easily characterized or evaluated. This limits

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the reproducibility and the reliability of the tests conducted by observers. To overcome this problem and to ease labor intensive experimental conditions, several automated FST testing systems have been developed and validated (Hédou et al., 2001; Crowley et al., 2004). These behavioral testing instruments not only reduce the required testing time but also produce less subjective data by providing a wide variety of results that are practically impossible to detail by observation alone.

The currently used automated system for FST in mice is based on a procedure consisting of digital videorecording associated with computer-assisted image analysis (Crowley et al., 2004). A new system has recently been developed that consists of two 4×4 photobeam arrays that allow monitoring of swimming and climbing behaviors. In this work, we compared and tested this new automated system against a manual scoring technique. To assess the generated data, we used C3H/HeJ mice with a normal gene arylalkylamine *N*-acetyltransferase (AANAT) and melatonin-deficient C57BL/6J mice with a mutant AANAT-gene (Roseboom et al., 1998). Previously, it was shown that these mice differ in their FST behavior; AANAT-mutant mice express prolonged swim-test immobility (Uz and Manev, 2001).

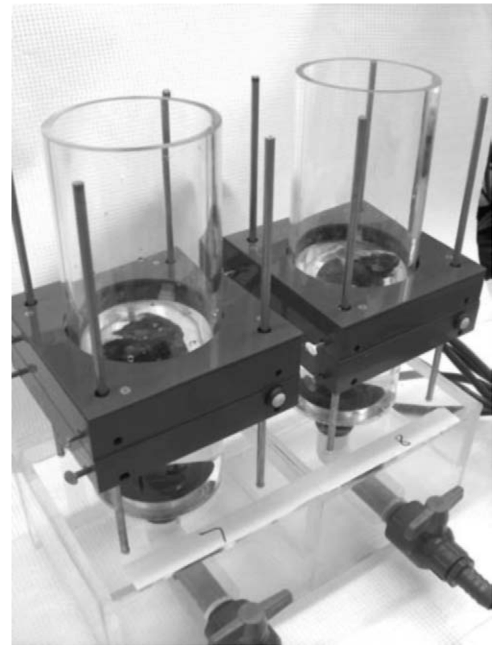

Fig. 1. The computer controlled Hamilton–Kinder forced swim test (FST) device.

2. Materials and methods

2.1. Animals

Experiments were performed with eight-week-old male C57BL/6J (AANAT-mutant) and C3H/HeJ (AANAT-normal) mice (Jackson Laboratory, ME, USA) (16 mice per group). The animals were housed under conditions of controlled temperature (23 ± 2 °C) and illumination (14 h light/10 h dark; darkness commenced at 18:00). Experiments were performed between 12:00 and 16:00 h. The experimental protocol was approved by the institutional animal care committee.

2.2. FST procedure

Automated FST experiments were conducted using the computer controlled Hamilton–Kinder forced swim test device (Hamilton–Kinder; Poway, CA, USA), which consists of two clear water-filled tanks, each equipped with two 4×4 photobeam arrays that allow monitoring of swimming and climbing behaviors (Figs. 1 and 2). The chassis of the FST device is connected to a portable computer, which is operated

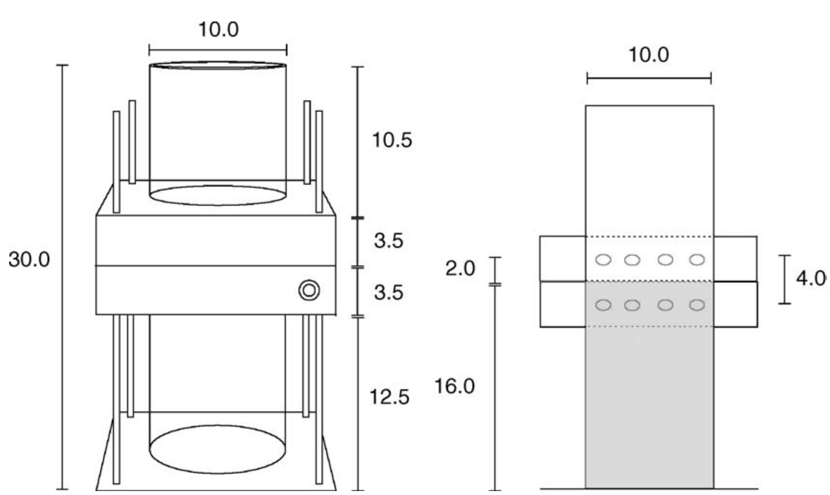

Fig. 2. Detailed description of the experimental setting and dimensions of the Hamilton–Kinder forced swim test (FST) device (units in cm). The water content is shown as a shaded area in the tank.