Abstract

Introduction

Methods

Subjects. Breeding pairs consisting of one B6SJLF1/J and one B6SJLTg(APPSwFlLon,PSEN1*M146L*L286V)6799Vas/Mmjax mouse each were obtained from the Mutant Mouse Regional Resource Center through Jackson Labs (Bar Harbor, ME). Fourteen adult male subjects (140 days old) derived from these original breeding pairs served as subjects. Subjects were housed in groups of 3-5 on a standard laboratory diet during all phases of the study. Prior to each test the body weight of each animal was recorded.

Apparatus. The training apparatus was a 28.2 x 21.7 x 21.0 cm chamber consisting of two Plexiglas sides and two stainless steel sides. An insulated plastic platform that measured 3.0 cm high, 8.2 cm wide and 9.6 cm long was placed on the left end of a series of steel bars that constituted the floor of the apparatus. A video camera was fixed in front of the the testing area to record responses. The entire apparatus was placed in a sound-resistant chamber that included a 55 dB fan to mask background noise.

Procedure. The procedure followed those described previously by Izquierdo, Fiorenza, Rosa and Myskiw, (2012). All tests were completed at 0 lux at 22°C during the 7-8th h of the dark phase of the light/dark cycle. During the training session, the camera was started and each subject was gently placed on the platform facing the left
rear corner of the training chamber. When they stepped down and placed their four paws on the steel bars, they received a 2-second, 0.4 mA scrambled electrical pulse to the foot. The animals were put on the training box platform until they eventually stepped down from it or five minutes elapsed. The animal was immediately removed from the chamber and returned to its home cage.

Twenty-four hours after initial training, the animal was returned in the same manner to the testing chamber and the time to move completely off of the insulated box was recorded again. Seven days after initial training, the step down latency was again recorded for each animal. No electrical pulses were administered during retesting.

Trained observers scored the behavioral videos for the amount of time required to step down from the elevated platform (step-down latency) at 24 h and 7 days post-training as an index of memory. Rearing was also scored to evaluate the ability of the subjects to learn to habituate to the chamber. The number of boli and grooming were used to assess the emotional response of the subjects. Spontaneous activity (movement) on the platform was also scored to evaluate motor skills. Software developed in our lab was used by the scorers to time and record all behaviors.

**Histology.** Immediately after the last test session, brains were removed and fixed in 3% buffered formalin for at least 14 days prior to sectioning. The brains were blocked in the coronal plane and section serially at 8 µ or 40 µ at –29 C using a microtome placed within a cryostat (Vibratome model Ultra 5050, St. Louis, MO). Sections were thaw mounted on subbed slides and then warmed to room temperature.
Slides were then stained for beta-amyloid plaques with Bielschowsky’s stain or cresyl violet. Trained observers that were unaware of the treatment conditions during scoring then evaluated the slides for the presence of β-amyloid plaques.

Genotyping. In order to minimize experimenter bias the genotyping was not completed until all of the behavioral tests and histological tests were completed. We followed the protocols for genotyping the strain provided by the Jackson Laboratory (Jax Mice Database. http://jaxmice.jax.org/strain/005252.htm). Genotyping was completed for the APP allele using protocol "Generic Tg(APP) version 5.1 and the presenilin-1 allele using protocol "Generic Tg(PSEN1) version 3.1 by standard PCR.

Results

Discussion

References

Don’t forget to add the citations for the papers used in your introduction.

