Lab: Effects of Preconception Drug use on the Development of Adult Psychiatric Disorders.

Purpose:

Behavioral Pharmacology is a field in which the majority of the bachelor’s level positions require previous experience administering drugs and behaviorally testing animals. The goal of this lab is to provide you with career relevant skills in addition to expanding your knowledge of Behavioral Pharmacology.

Background:

The relationship between drug use during pregnancy and subsequent fetal abnormalities is well established. But there is now evidence that preconception drug use can carry over and impair brain development (e.g., Floyd, Decoufle and Hungerford, 1999). While the exact mechanisms vary from drug to drug, one common link is that drug use often disrupts the function of the thyroid gland for weeks after use. For example, cocaine use blunts the responsiveness of the hypothalamus-pituitary axis to thyroid releasing hormone (TRH) producing a state of hyperthyroidism (Vescovi and Pezzarossa, 1999). Vescovi and Pezzarossa (1999) reported that this abnormal TRH response was also connected to impaired production of growth hormone that persists for at least 30 days after abstinence. Abnormal function of the thyroid gland during pregnancy produces abnormal brain development that results in behavioral disorders (e.g., depression and anxiety) in both childhood and adulthood (e.g., Lazarus, 2005). Since triadimefon shares many of the characteristics of cocaine a similar teratogenic profile is expected.

Preparation:

Before the next class period read the articles posted on neurosciencecourses.com. In addition, find one additional source not referenced in this handout or on posted on neurosciencecourses.com.

Research Design:

Subjects:

Fifty C57BL/6J male mice age 8-10 weeks old will be housed in groups of 4-5 during all phases of the study. Twenty-five subjects will be derived from C57BL/6J females that had been given 50 mg/kg/0.01 cc g/body weight three weeks before breeding. Twenty-five controls will be obtained from the same colony but from breeders who were untreated. All subjects will be maintained on a standard laboratory diet and housed in a colony room that will be kept on a reverse light/dark cycle (12 h off/ 12 h on) at 22 degrees C.
Student Choices for Behavioral Tests

The behavioral tests for this lab are limited to the choices described below. One or more of these tests may be used.

Tail Suspension Test for Depression

Apparatus:

The tail suspension model will consist of a chamber with a metal rod suspended by two supporting rods. An infrared photodiode connected to a laptop microcomputer will be placed in front of subject to monitor and record movement for six consecutive minutes.

Procedure:

Subjects in each group will be individually placed in the test chamber and taped to the tail suspension rod. The infrared sensor will then be placed in front of each subject and the computer program will be started. The program will record and time each movement for a total of six minutes.

Light/Dark Test for Anxiety

Apparatus:

The apparatus will consist of two chambers separated by a black plastic door. The start box will be a black plastic holding chamber measuring 19.5 x 14.5 x 20 cm and maintained at 0 lux. The second chamber measured 50 x 40 x 20 cm and will be brightly illuminated (1000 lux). Room lights will be kept off during testing. Behaviors will be recorded using a video camera that will be suspended above the chamber.

Procedure:

Mice will be weighed and then individually placed in the start box. After 30 seconds, a door will be opened providing access to the brightly illuminated chamber for five minutes. The amount of time required for the animal to place all four paws into to the illuminated chamber (emergence latency), the amount of time spent in the light, spontaneous activity and measures of emotion will be recorded.

Open-field Test for Emotion, Motor Systems and Learning

Apparatus:
The apparatus will consist of a 43.5 x 43.5 cm Plexiglas chamber. The chamber will be kept in a sound resistant test room. A video camera will be suspended above the chamber to record behavior.

Procedure:

Mice will be individually placed in the chamber for a total of five minutes. The amount of spontaneous activity, and measures of emotionality will be recorded digitally and then recoded on DVD prior to scoring by the students in the class. This method will allow the students to gain experience handling and testing the animals and then also give them the chance to still score the behaviors and control for experimenter bias.

Drug Reversibility Tests

After initial behavioral tests are completed. The students will be given the option to retest all or a subset of animals to attempt to ameliorate any detected deficits. Students will be required to justify the choice of psychotropic based on their literature review and the results of the first round of behavioral testing. Dosages and route will be based on peer-reviewed papers in which the method was approved by a university IACUC. If a drug trial is designed it would be restricted to a choice between a single behavioral test and a single injection per subject or oral administration of the drug to the food ration for several weeks followed by retesting on one or more behavioral tests.

Assays

Immediately following the final behavioral tests the animals will be overdosed using CO₂ followed by decapitation by guillotine. The brains will removed and plasma samples will be taken for analyses to be determined by the students.

References

