Hyperactive Rats

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Technology description

Technical Summary

We have developed different lines of rats by behavioral testing and then selective breeding of those showing desired characteristics in attempting to rat models for study of affective disorders. The lines were directed at possibly improving both drug screens (i.e., improved sensitivity and selectivity of detection of antidepressant drugs) and "homologous" models of depression (i.e., rats that show characteristics seen in human depression).

While simply measuring baseline home-cage ambulatory activity of a large group of normal Sprague-Dawley rats, the male and female rats from a single litter were observed to be moderately hyperactive. Brother-sister breeding was done, and the offspring of these animals have continued to show higher-than-normal spontaneous ambulation in the home cage in all succeeding generations. These animals have been designated as the "Hyperactive" (HYPER) line. An important characteristic of these animals is their response to a stressor. Following exposure to a stressor, animals of the HYPER line show a period of extreme hyperactivity (i.e., nocturnal ambulatory activity counts often exceeding 1000 counts per hour) that begins 2-5 days after the stressor has been applied and lasts for 3-6 days before their activity returns to its pre-stress baseline. Another characteristic of HYPER rats is that they can also show profound behavioral depression as well. The "depressive" phase tends to become more pronounced as the HYPER rat becomes older. Thus, when male HYPER rats are 10-14 months old, exposure to a single 3-hour stress session (uncontrollable shock) causes ambulatory activity in the home cage to be reduced for 3-5 weeks thereafter and also causes reduced food and water intake that lasts for 2-3 weeks. In female HYPER rats that are 10-14 months of age, these animals respond to this single 3-hour stress session by thereafter varying between periods of depressed motor activity and outbursts of hyperactivity, thus mimicking both aspects (i.e., depression and mania) seen in bipolar disorder. There are presently no animal models of bipolar disorder; insofar as the HYPER rat appears to show attributes of bipolar disorder, it would be the first animal model of this disorder to have been created.

Application area

Antidepressant drug screening for depression studies.

Institution

Emory University

Inventors

Jay Weiss
Professor
SOM: Psychiatry & Behavioral Sciences
Katherine Boss-Williams
Post Doc Fellow
SOM: Psychiatry
David Weinshenker
Professor, Department of Human Genetics
SOM: Hum Gen: Admin