Rat or Mouse Exhibiting Behaviors Associated with Human Schizophrenia

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Technology description

Summary

A newly developed animal model for schizophrenia is valuable for assaying pharmaceutical compounds for treating this disorder. Schizophrenia is a neuropsychiatric disorder characterized by cognitive deficits, bizarre behavior and/or hallucinations. Presently, there has been no satisfactory animal model for testing promising therapies for this disorder.

This invention provides a unique and surprisingly accurate animal model for human schizophrenia. The animals are brain damaged while prepubescent. The brain damage consists of a ventral hippocampus lesion induced by exposure of the hippocampus region to a neurotoxin. When the animal reaches puberty, abnormal behavior and a number of biological phenomena associated with schizophrenic symptoms emerge.

The present invention also provides methods of assaying the anti-schizophrenic potential of pharmaceutical compositions. The methods involve (a) inducing or creating a lesion in the ventral hippocampus of a prepubescent mammal, (b) nurturing or raising the mammal until postpuberty, (c) administering to the mammal a pharmaceutical composition thought to have anti-schizophrenic properties; and (d) determining the mammal's response to the pharmaceutical composition. The anti-schizophrenic potential of the pharmaceutical composition is assessed by objectively measuring the mammal's behavior following administration of the pharmaceutical composition. The behaviors which are measured typically include the following: locomotor activity in a cage, in unfamiliar or novel environments, after injection or administration of drugs (e.g., amphetamines), after mild electric shock, after exposure to sensory stimuli (e.g., noise), in water (swim test), after immobilization, in social interactions, and in various learning and reward paradigms.

The neurotoxin used can be selected from a number of known agents which lethally affect neurons usually, but not exclusively, by over-exciting their glummate receptors. Examples of such neurotoxins include ibotenic acid, N-methyl-D-aspartic acid, kainic acid, dihydrokainate, DL-homocysteate, L-cysteate, L-aspartate, L-glutamate, colchicine, ferric chloride, omega-conotoxin GVIA, 6-hydroxy-dopamine.

Application area

Animal model for human schizophrenia
Screening methods for Anti-schizophrenics

Advantages

This is the first model showing postpubertal emergence of abnormalities similar to those reported in schizophrenia.

Institution

NIH - National Institutes of Health

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