CHAPTER 8
Behavioral Neuroscience

INTRODUCTION

Behavioral neuroscience is the study of the neural mechanisms mediating normal and abnormal behaviors. Behavior is the final output of the nervous system at the level of the whole organism. Discrete animal behaviors are used to test hypotheses about anatomical, neurochemical, neurophysiological, and genetic substrates of behavior. Appropriate animal behavior paradigms provide the critical functional tools for translational research, moving discoveries at the molecular level toward clinical applications. The study of user-friendly behavioral tasks that model specific symptoms of neuropsychiatric disorders is a critical phase in the testing of new psychotherapeutic treatments in vivo.

The protocols presented in Chapter 8 are designed to serve both as a solid introduction for the novice and as a guide to specific methods for the established behavioral neuroscientist. To facilitate their use in the functional analysis of new compounds for the treatment of neuropsychiatric disorders, an attempt has been made to present only protocols that are well-validated, quantitative, easily replicated, rapid, and simple. Nonetheless, hands-on training and/or collaboration with a good behavioral neuroscience laboratory with expertise in the chosen behavioral tasks is highly recommended.

The chapter highlights many of the best major protocols developed in the long and illustrious history of behavioral neuroscience, and presents protocols in common use for both rats and mice. Classic methods for measuring spontaneous motor activity are described in UNIT 8.1. Exploratory locomotion underlies almost all behavioral output, and is considered a specific measure of mesolimbic dopaminergic pathway activation. Methods for quantitating male and female sexual receptivity and activity in rats are described in UNIT 8.2. Well-characterized animal models of anxiety-related behaviors, including the traditional Geller-Seifter conflict test, social interaction, light/dark exploration, and the elevated plus maze, are presented in UNIT 8.3. Stress paradigms, including restraint, footshock, social isolation, maternal separation, and sleep deprivation, are described in UNIT 8.4. Defensive behaviors in rats and mice are explored in UNIT 8.19.

Established protocols for evaluating cognitive processes in mice and rats are presented in UNITS 8.5A-8.5E. Spatial learning tasks, including the Morris water maze, T-maze, and radial maze tasks are described in UNITS 8.5A & 8.5B. An emotional memory task, cued and contextual fear conditioning, is explained in UNIT 8.5C. A social memory task, social transmission of food preference, is presented in UNIT 8.5D for rats and UNIT 8.5G for mice. Attention, an essential component of cognitive processes, is evaluated using protocols described in UNIT 8.5E for rats and UNIT 8.5H for mice. A procedure for rapid autoshaping of operant responding is described in UNIT 8.5F.

Numerous considerations for measuring various aspects of feeding behavior are discussed as an overview in UNIT 8.6A. In UNIT 8.6B, a protocol for measuring food intake over a set period of time is detailed; in-depth methodologies for analyzing feeding behaviors and the behavioral satiety sequence in rodents are presented in UNIT 8.6C. Sham feeding in the rat with a reversible, chronic gastric fistula, including details on surgical implantation of the fistula, is described in UNIT 8.6D. A simple but very versatile procedure for measuring...
conditioned flavor aversions, in which administration of a drug following ingestion of a novel food or solution can suppress subsequent intake of the food or solution (conditioned taste aversion), is presented in UNIT 8.6E. The associative learning is extremely robust, and provides a sensitive and widely used behavioral index of drug side effects. Another approach, in which conditioned flavor preferences are induced by pairing a novel flavor with another, preferred flavor, is presented in UNIT 8.6F. This method has been used to study the underlying mechanisms functioning in the development and expression of conditioned flavor preferences. Macronutrient choice tests are described in UNIT 8.6G. Consumption of fat, carbohydrate, and protein from pure macronutrient sources is independently quantitated.

Behavioral tasks relevant to neuropsychiatric disorders are explicated in UNITS 8.6F to 8.13. Sensorimotor reflexes and gating processes abnormal in schizophrenia, including measures of prepulse inhibition and habituation of the startle response, are described for rats in UNIT 8.7 and for mice in UNIT 8.17. Observation of stereotyped behavior in rats is described in UNIT 8.8. Analysis of stereotyped behavior (motor responses that are repetitive, invariant, and seemingly without purpose or goal) is useful to the investigation of behavioral responses to dopaminergic drugs, and the procedure described in this unit can be adapted to sampling many forms of spontaneous behaviors including locomotion, rearing, grooming, eating, and drinking. Methods for evaluating nociception, including hot-plate, tail-flick, and formalin tests, are presented in UNIT 8.9. Behavioral despair tasks sensitive to antidepressant drugs are described in UNITS 8.10A, B, and C. The Porsolt swim test, learned helplessness, and the tail suspension test are applied to both rats and mice. Fear-potentiated startle measures emotional memory and models components of posttraumatic stress disorder. UNIT 8.11A describes procedures for measuring fear-potentiated startle in rats; UNIT 8.11B describes procedures for fear-potentiated startle in mice. Motor coordination and balance tests, described in UNIT 8.12, can be used in rodent models of neurodegenerative diseases such as Parkinson’s disease and amyotrophic lateral sclerosis. Latent inhibition, described in UNIT 8.13, is a task that measures the ability to ignore irrelevant stimuli, and which models aspects of attentional deficits in schizophrenia.

Social behaviors in rats and mice are well documented in the ethological literature. Continuing the series begun with UNIT 8.2 on the topic of sexual behaviors, protocols for measuring parent-infant interactions are presented in UNITS 8.14 & 8.15. Infant rodent pups emit vocalizations that elicit parental responses. As explained in UNIT 8.14, these ultrasonic vocalizations, in the range of 30 to 80 kHz, communicate distress and prompt the mother to retrieve the pup back to the nest. Active parental behaviors, described in UNIT 8.15, include carrying, licking, and nursing the pups, nest building, and quiescent contact in the nest. Methods for evaluating social interactions, social preference, and social habituation/dishabituation are elegantly presented in UNIT 8.16.

Quantitative measures of developmental milestones in mice and rats, relevant to modeling many neurodevelopmental diseases, are described in UNIT 8.18.

Applications of these behavioral protocols to forefront research areas are highlighted throughout the chapter. In particular, most of these protocols can be applied to the behavioral phenotyping of transgenic and knockout mice. The protocols collected in Chapter 8 are designed to provide a comprehensive overview of the behavioral neuroscience armamentarium.

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