

Fear Conditioning in an Automated Home Cage (DualCage) Environment

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Fear conditioning is an important test in behavioral neuroscience to investigate the neural systems and molecular basis of various aspects of emotional learning across a wide range of species [1]. Dysfunction of the fear circuits is assumed to underlie mechanisms of affective disorders and is frequently investigated in rodent models. Traditional fear conditioning methods require frequent handling of the animals which compromises the accuracy with which fear-related parameters such as the behavioral response and autonomic responses such as heart rate of the animal can be measured. We therefore developed a novel fully automated DualCage environment to explore the dynamics of fear conditioning during spontaneous/voluntary behavior of male C57BL/6J mice.

The DualCage environment consists of a home cage attached to one or more additional cages separated from another by automated sliding doors. The sliding doors can be operated automatically, e.g. by the position of an animal, that is monitored by a camera tracking system (Viewer© software, Biobserve, Bonn, Germany). Each cage has an area of 24 x 30 cm thereby doubling the area offered in a type II cage. In the case of fear conditioning the attached

cage contains a shock grid and a loudspeaker. The animal is allowed to voluntarily enter the shock cage after the sliding door has been opened. As soon as the animal has fully entered the shock cage, the door is closed. Initially the mouse is allowed to explore the shock cage before a series of tone/shock stimuli are used to condition the mouse to the tone and the shock cage (context). After this training episode, the door is opened and the mouse can return to its home cage.

Retention tests are performed at different time points after the training session to explore the dynamics of memory formation and its expression. Tone retention tests can be performed in the home cage or in the shock cage. The latter obviously works only if and when the conditioned mouse voluntarily returns to the shock cage. Note that during the entire period of habituation, training and testing the mouse is not handled and allowed to show spontaneous exploratory behavior. The spontaneous behavior is characterized by risk assessment when access to the conditioning cage is granted by peeking through the door in stretch-attend posture before eventually revisiting the shock cage. Revisits of the shock cage eventually occur despite the lack of e.g. rewarding reinforcement indicating the naturalistic drive of mice to explore their environment if given a chance despite previous negative experiences. This behavior parallels the one observed in rats in a visible burrow system [2]. A separation between home cage and shock cage is necessary to exploit the novelty-seeking behavior of mice at distinct times after training, i.e. to investigate short- and long-term memory.

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This novel approach mimics naturalistic-like behavior that is characterized by trade-offs between avoidance and curiosity that can now be quantified on long time scales based on a voluntary choice of mice. Extracellular electrical activity in the brain as well as the heart rate of the animal are measured by wireless telemetry systems with signal receivers that are an integral part of the DualCage system. The DualCage system is designed to integrate any commercially available hardware into the system for multi-purpose use depending on the scientific aims. This approach with a separation of home cage and versatile add-on components will allow to perform a spectrum of diverse tests with full choice (voluntary decision) of the experimental animal and minimal unspecific interference by the experimenter. The importance of voluntary choice for the temporal organization of behavior has recently been demonstrated in open field behavior in mice [3]. Behavioral measures can now be complemented to autonomic [4] and neural measures of conditioned contextual fear without the adverse consequences of handling [5]. For the integration of electrophysiological measures see our presentation entitled "Extracellular Multi Unit Recording in Fear Conditioning in Mice Using a Telemetry Approach in an Automated Home Cage (DualCage) Environment" at this Measuring Behavior Meeting 2010.

Author Keywords

Behavior tracking, fear, anxiety, novelty, exploration, motivation.

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