Cognitive functions of hippocampus lesioned mice assessed in the IntelliCage

Colacicco G (1), Voikar V (1), Vannoni E (1,4), Lipp HP (1), Wolfer DP (1,2,3)

(1) Institute of Anatomy, University of Zurich, Switzerland
(2) Institute for Human Movement Sciences, ETH Zurich, Switzerland
(3) Zurich Center for Integrative Human Physiology, University of Zurich, Switzerland
(4) NewBehavior AG, Zurich, Switzerland

The increasing number of genetically modified mice requires the refinement of existing behavioral tests, hence the IntelliCage has been introduced for monitoring different aspects of mouse behavior living in social groups with minimal human interference. C57BL/6J mice with bilateral excitotoxic lesion of the hippocampus (HIPP) or sham-operation (CON) were used for validating several learning tasks using this automated home cage featuring fully programmable learning corners. In these corners the access to water can be made dependent of the learning performance.
Following experimental designs were applied: adaptation to drinking sessions (two 1-hour sessions during dark phase), place preference learning and reversal, serial reversal (new correct corner assigned for each session), patrolling (correct corner moved to the next position by one step after correct visit), and chaining (correct corner moved to the next position after each visit). The HIPP mice showed impaired adaptation to the fixed schedule of drinking sessions that persisted throughout the testing period. It may be interpreted as an equivalent for behavioral disinhibition. Place preference learning was faster in the HIPP mice, probably due to the fact that they showed less alternation already during early adaptation. Impaired flexibility was evident in the early phase of reversal. More pronounced impairment was found in the serial reversal experiment. However, with prolonged training the difference between HIPP and CON mice disappeared. Patrolling and chaining revealed significant impairment in HIPP mice. A common finding in all modules was the transient hyperactivity in HIPP mice in response to changed rules. Duration and magnitude of hyperactive reaction depended on the complexity of the task. In summary, the set of learning tasks presented here may be taken as a battery for fast and reliable screening of mouse models for hippocampal deficit.