

Corridor shuttling spatial learning task: Automated analysis of behavioral flexibility and reversal learning-set in mice using IntelliCage system

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To achieve a highly reproducible behavioral assay for analyzing higher order cognitive function in mice, we established here a novel test protocol using a computerized IntelliCage system. This system allows a fully-automated behavioral analysis for up to 16 RFID-tagged mice living in a home cage equipped with four operant conditioning units. The task comprises spatial discrimination task, named “reward-driven corridor shuttling task”, and the subsequent serial reversal learning task which requires behavioral flexibility. In this study, we verified the availability of this protocol by using three strains of adult male mice (C57BL/6, DBA/2 and ICR) in three laboratories (the University of Tokyo, Jichi Medical University, and University of Zurich). As a result, all cohorts of mice effectively acquired the initial spatial discrimination within a few days, and showed clear process of behavioral adaptation to the reversal learning, i.e., behavioral flexibility. More intriguingly, the adaptive performance in the subsequent serial reversals was continually improved by the end of the reversals. To our knowledge, this is the first evidence for mice showing a “reversal learning-set”. Essentially the same results were obtained in inter-laboratory comparisons, which assure the advantage of IntelliCage and this newly-developed protocol with high reproducibility. In conclusion, our newly-developed protocol for IntelliCage provides an automated quantitative assessment of learning of spatial patterns, behavioral flexibility and reversal learning-set in mice as representative indices for higher order cognitive functions. This protocol also made it possible to reveal emotional abnormalities, which is presented in our another presentation “Corridor shuttling spatial learning task[2]: Chemically-induced emotional dysfunctions in group-housed mice as an animal model of perseveration and social anxiety”.