Mice with hippocampal lesions are hypersensitive to environmental change but can learn simple spatial tasks in their familiar home cage

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Cognitive functions of mice are traditionally assessed in test batteries in which animals are tested individually. Fully automated systems such as IntelliCage promise to eliminate many disadvantages of these test batteries, such as inefficiency, lack of standardization and poor reliability. We used C57BL/6 mice with bilateral NMDA lesions of the hippocampus (HIPP) or prefrontal cortex (PFC) to validate IntelliCage as a tool to monitor cognitive performance. Confirming earlier data, HIPP mice were strongly hyperactive during their first days in IntelliCage. After 3 weeks, however, levels and circadian distribution of activity had become similar to controls. PFC mice were slightly hypoactive during the first few days. After familiarization with IntelliCage, the mice learned to obtain water from only one of four learning corners. All groups showed similar performance, but HIPP mice responded to the protocol change with transient hyperactivity. When air puffs were introduced to punish incorrect corner visits, HIPP mice were even more hyperreactive and their performance fell slightly below that of controls. When availability of water was restricted to one 2-hour session per day, HIPP learned the new location, but showed many more attempts than controls to drink outside the drinking sessions. PFC mice performed normally in all 3 tasks. Our results show that mice with hippocampal damage are hypersensitive to environmental change and aversive stimuli, but can learn simple spatial tasks in a familiar environment. Thus, reliable testing of cognitive function in mice requires thorough familiarization with testing environment and stimuli.