Development of automated conditioned taste aversion procedure in the IntelliCage

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Conditioned taste aversion (CTA) is a well established and widely applied model for testing learning and memory in rodents. It is based on classical conditioning by association of novel flavor (conditioned stimulus, CS) with sickness. Sickness (nausea) is most commonly induced by injection of LiCl (unconditioned stimulus, US). However, it has been shown that taste aversion can also be induced by oral self-administration of LiCl. In addition, mice can develop CTA from LiCl to NaCl due to perceiving taste of these compounds as qualitatively similar. Considering this knowledge, we have taken an advantage of the fully automated home-cage testing system, IntelliCage, where behaviour of group-housed mice can be individually monitored and conditioned with minimal human interference. IntelliCage comprises four conditioning corners; in each corner the mice can have access to two bottles. In total, 36 C57BL/6 and 36 DBA/2 mice were used for the validation. 12 mice (6 of each strain) were accommodated in each IntelliCage. The mice were randomly divided into control (CON) and conditioned (CTA) groups. Each group had access to water in two opposite corners during drinking sessions (2 x 30 min during dark phase), when both bottles were accessible for 7 seconds from the start of corner visit. For further drinking, mice had to initiate a new visit in one of the assigned corners. After mice learned to drink in the assigned corners during the sessions, the training was performed. Three different conditions were applied: i) CON and CTA groups mixed in one cage, 1 training session; ii) CON and CTA groups in 2 separate cages, 1 training session; iii) CON and CTA mixed in one cage, 2 training sessions (with interval of 24h). During training, water was replaced by 75 mM NaCl for CON mice, whereas 75 mM LiCl was available for CTA group. Both drinking solutions were made in 0.5% saccharin. The CTA group differed from the CON mice during training in several parameters: i) reduced activity (number of corner visits); ii) increased error rate (visits to incorrect corners); iii) reduced drinking (lick number). Twenty-four hours after training a choice test was performed, where one bottle in each corner contained water, whereas another bottle was filled with 75 mM NaCl (CS). The CON group showed indifferent preference for water and CS, whereas aversion to the CS was evident in the CTA group in all three conditions. The DBA/2 mice showed significantly stronger aversion to the CS than the C57BL/6 mice. In summary, we suggest the presented automation of the CTA procedure as a promising new approach for high-throughput testing of learning and memory in genetically modified mice.