Differential involvement of the central amygdala in appetitive versus aversive learning in mice trained in the IntelliCage system

E. Knapska[1], F. Neuhäusser-Wespy[3], H.-P. Lipp[3], L. Kaczmarek[2], and T.Werka[1]
[1]*Department of Neurophysiology and* [2]*Department of Molecular and Cellular Neurobiology, Nencki Institute, Warsaw, Poland;*
[3]*Division of Neuroanatomy and Behavior, Institute of Anatomy, University of Zurich,Zurich, Switzerland*

The IntelliCage is a large home cage containing four operant conditioning chambers placed in the corners. Access into each chamber is provided via a tubular antenna reading transponder codes. Before entering the cage every mouse is injected subcutaneously with a glass-covered microtransponder. This passive transponder emits a unique animal identification code when activated by a magnetic field. The design of the cage restricts access to the learning chamber for a single mouse only. Each chamber contains two openings that give access to the nipples of drinking bottles. These openings are crossed by photobeams recording nose-pokes of the mice. Access to the tubes can be barred by small motorized doors. Moreover, an aversive stimulation can be delivered in forms of air-puffs directed to the head of the mouse through tubing controlled by electric valves. The whole set-up of the IntelliCages is controlled by a microcomputer recognizing visits, nose-pokes, and tube-lickings of individual mice, and delivering reward (by opening the access to water after a nose-poke) or punishment (by applying air puffs after a mouse enters the test chamber) according to preprogrammed schedules depending on the assignment of the mice to different test groups within the same cage. Activity and learning of up to 16 transponder-tagged mice per cage can be continuously monitored and controlled by a computer without human interference. Thus, the system allows automated cognitive and behavioral screening of mice living in social groups.

I would like to present one of many possible applications of the IntelliCage system. The aim of this study was to compare the engagement of various nuclei of the amygdala in appetitive and aversive instrumental training procedures [1]. We used the IntelliCage system to balance the conditions of those trainings. The mice were exposed to a place preference and place avoidance training. In the place preference training, the animals were supposed to associate the sweetened water with a specific corner within the cage (appetitive motivation), whereas in the aversive training they were learning to avoid a corner where the air-puffs were applied (aversive motivation). Appetitive and aversive training was performed in three cages each. Two 8-day sessions were carried out: (i) the first one with the place preference group and their controls and (ii) the second one with the place avoidance group and their controls. Every cage contained four or five mice assigned to the different treatment groups. A session started with a 48-h adaptation period to the cage during which the mice learned to open the gates barring access to plain water from both openings by means of nose-pokes. For the next 3 days, the animals were temporarily deprived of water. They had access to water for 2 h per day, at the same time of the active phase every day. This procedure evoked intense consummatory activity during a limited time span. On the following day at the same time, the mice were assigned to different treatment groups within the cages. One group was designed as the "place preference group". They received sweetened water (10% sucrose) in the corner least preferred during the previous drinking sessions. In the "place avoidance group", the mice received an air puff when entering the corner that was the most preferred during the previous drinking session. Control groups consisted of mice that were in the same cages as the experimental mice, but obtained sweetened water in all four corners or received no air-puffs but only plain water, respectively. The whole experimental schedule in the second and third cage for each type of the training was shifted by 1 and 2 h, respectively, with respect to the schedule in the first cages in order to allow timely removal of animals for immunohistochemistry. All animals learned the required tasks very effectively.

Then, these behavioral paradigms were used to map the patterns of c-Fos expression in the amygdala. The brains for immunocytochemistry were taken on the first day of place conditioning, from three mice from each cage. We have found much more intense c-Fos expression in the medial part of the central amygdala after the appetitive training as compared to the aversive training. In contrast, the similar level of c-Fos expression was evoked by both types of training within the lateral nucleus of the amygdala. The data support the hypothesis that the central nucleus of the amygdala is particularly involved in appetitively motivated learning processes.

Supp. by FP6 037965 and NCCR "Neural Plasticity and Repair"

References

1. Knapska, E., Walasek, G., Nikolaev, E., Neuhäusser-Wespy, F., Lipp, H.P., Kaczmarek, L., Werka, T. (2006). Differential involvement of the central amygdala in appetitive versus aversive learning. *Learning & Memory* **13(2)**:192-200.