Learning (in) the PhenoTyper: an integrative approach to conducting cognitive behavioural challenges in a home cage environment

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Mice are extensively used in neurobehavioural research as a model for many human (behaviour) disorders. In order to characterize the behaviour of certain mouse strains, many uni-dimensional tests have been developed, which allow characterizing the mouse on a few aspects of the behavioural domain of interest. In addition Stand alone tests have been combined into test batteries. Mice will then be sequentially exposed to different tests and are usually handled and "transported" to a different experimental set-up. But the validity of studies of animal behaviour ignoring the interaction of more motivational systems, either by a strong focus in the ethogram or a focus in the design on predominantly activity, is limited. An alternative approach is the modification of existing "traditional" tests into more complex tests by trying to incorporate more behavioural domains into it. The discriminative elevated plus-maze and the discriminative avoidance task using a Y-maze are examples of such modifications.

e developed a reliable tool for observing and analysing various behavioural systems in a home-cage-like environment, without any handling and/or transport of animals. This High Throughput Phenotyping-system (HTP-system) is an extension of the PhenoTyper-system (Noldus, Wageningen, The Netherlands).

In addition to the measurement of activity and anxiety we have designed and implemented two fully-automated cognitive challenges for mice in this set up. Both tests have in common that we do not employ techniques to enhance the motivation of a mouse, e.g. food deprivation or other strong aversive stimuli. In fact the cognitive performance relies on the willingness of the animal to collaborate The tests will commence automatically at a certain, predefined time (e.g. several days) in the PhenoTyper, which makes it possible to compare behaviour of mice during the test with that of base line behaviour before and behaviour after the test. Furthermore, the HTP-system allows the mouse to display more of its natural behavioural repertoire and thus enables the researcher to carry out more complex analyses and allows studying the potential interaction of different behavioural dimensions with data from the same experiment.

The first task is a discriminative avoidance task, in which a mild aversive stimulus is used. After 4 days of continuous monitoring, the number of shelter entries using both the left and right entrance was determined; the entrance that was used most frequently was considered to be the preferred entrance and was subsequently designated as incorrect on day 5 and day 6. If the mouse used this incorrect entrance on day 5 and day 6, a bright light inside the shelter was switched on. The light stayed on as long as the mouse remained inside the shelter after making the incorrect choice. Using the non-preferred entrance had no consequences. In front of the shelter we defined two areas and each area is linked to either the left or the right shelter entrance. Whenever the mouse enters the zone linked to the preferred and hence "incorrect" entrance, a cue (a short light flash) was given. This test allows us to analyse discrimination and avoidance learning, in interaction with anxiety and locomotion.

The second test we designed is a free-operant conditioning task, consisting of several sessions in which the mouse has to learn that jumping onto its shelter will result in dropping a sucrose pellet elsewhere in the cage (an area around a pellet dispenser adjacent to the feeder. The mouse first has to go to the area where the pellet is dropped, before the next trial could be initiated. Prior to testing the mice are not food deprived and during the test mice still had access to food ad libitum. This experiment demonstrates place preference in interaction with activity, locomotion and motivation for the food incentive.

We will present data of two inbred strains of mice (C57BL/6 and DBA/2), showing that it is not only possible to carry out fully automated behavioural challenges in a homecare-like environment in relatively short period of time, but that is possible to separate these strains from each other based on their performance in these tasks.