

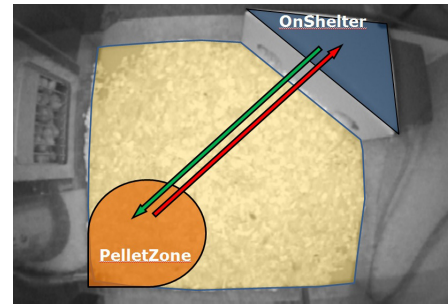
The PhenoTyper® is mainly used to study spontaneous behavior, but it can also be used to study learning or cognition. Therefore, Delta Phenomics has developed and validated two tasks in mice:

1. Free-operant conditioning of a specific place
2. Discriminative avoidance of a specific location

Both tasks are fully automated and can be easily activated and/or repeatedly used within a multi-day home cage study. No special treatments, such as food deprivation, are necessary to motivate the animals. Nonetheless, mice acquire the response in only a few days with limited repeated sessions. The protocols can be adjusted for specific research questions and are, thus, very versatile.

## Free-operant conditioning

In the free-operant conditioning task, mice learn that jumping on their shelter is followed by a reward from a sugar pellet dispenser in the opposite corner (figure 1). Jumping on the shelter will only be reinforced if the pellet zone where the sugar pellet drops from the dispenser is visited by the mouse. The performance of mice is represented by so-called "short movements bouts" (SMB) from OnShelter to PelletZone and vice versa. Especially, the change in movement bouts from the pellet zone back to the top of the shelter are indicative of the performance of mice in this task. Delta Phenomics

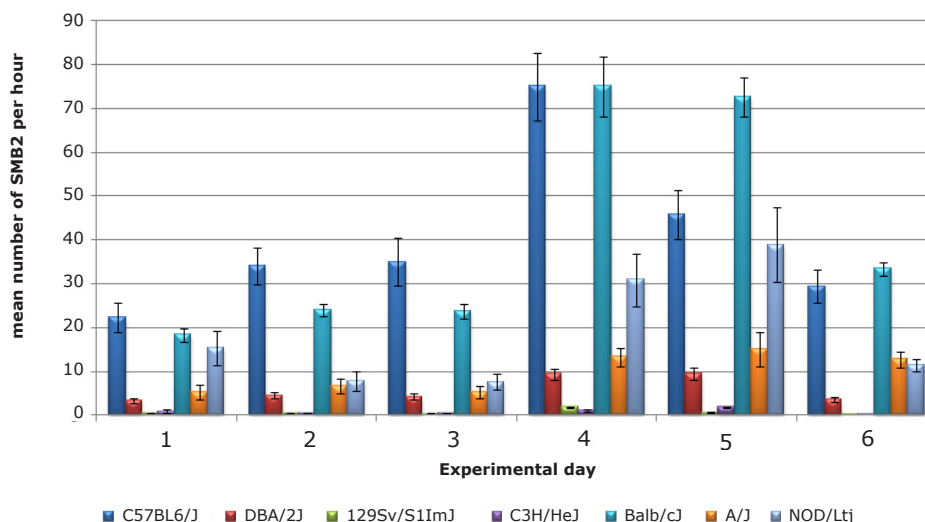


**Figure 1** Important zones in the free-operant conditioning task. The red arrow indicates short movement bouts from the shelter to the pellet zone (SMB-1) and the green arrow represents short movement bouts from the pellet zone to the shelter (SMB-2).

has developed and validated this automated free-operant conditioning task in C57BL/6J mice and in several other commonly used inbred strains (figure 2). C57BL/6J and Balb/cJ mice are the best performers, whereas 129Sv/S1Imj and C3H/HeJ mice are non-performers<sup>1</sup>.

## Discriminative avoidance

The shelter is used by mice to build their sleeping nest and consequently mice spend about 80% of their day inside the shelter. The standard shelter in the PhenoTyper has two entrances, left and right respectively. The results of various studies<sup>2,3</sup> clearly indicate that each mouse prefers either the left or the right entrance. In the discriminative avoidance task, mice need to learn to avoid their initially



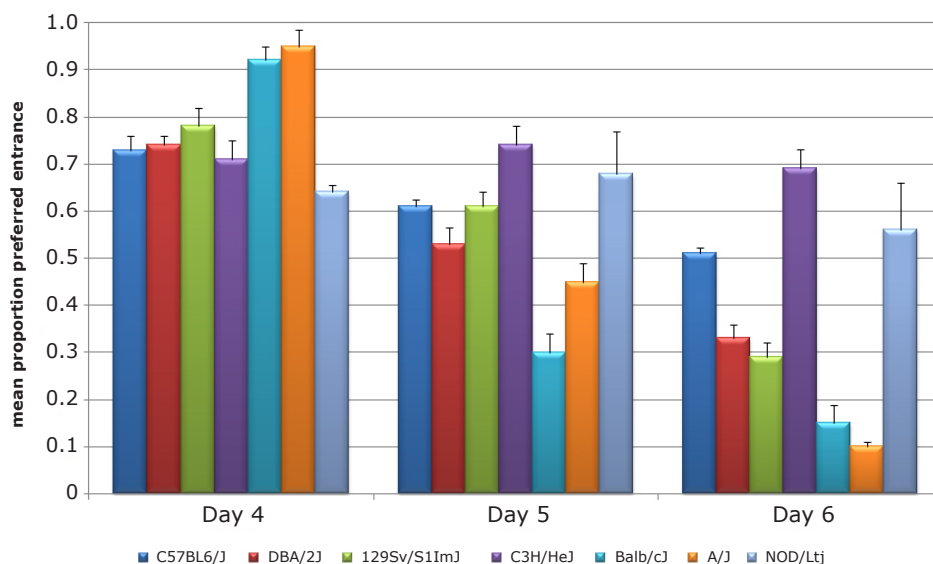
**Figure 2** Performance in the free operant conditioning tasks of commonly used mice inbred strains. Depicted is the mean number of short movement bouts ( $\pm$ SEM) between pellet zone and on shelter (SMB-2) over a period of 6 days.

preferred entrance because using it is followed by the onset of a bright (aversive) light inside the shelter. In this task the pre-



ferred entrance is first automatically assessed over some days. Thereafter, a bright light is switched on inside the shelter when the mouse uses its preferred entrance. A normal healthy animal will learn to avoid its first preferred entrance and switches to use the alternative entrance. The performance in this task can be assessed by calculating the proportions of entrances used by the mice. In general mice learn to avoid the initially preferred shelter entrance in a few sessions over two days.

The discriminative avoidance task has been validated by testing several commonly used inbred strains, as is shown in figure 3. The C57BL/6J mice is considered to be an intermediate learner, whereas DBA/2J, Balb/cJ, 129Sv/S1Imj and A/J are the best performers in this task. Nod/LtJ and C3H/HeJ do not show any difference in the use of the preferred entrance during the test<sup>4</sup>.



**Figure 3** Performance in the discriminative avoidance tasks of seven commonly used inbred strains. For each strain the mean  $\pm$  SEM is shown.

## Conclusion

Both automated learning tasks reveal significant differences between mouse strains; strains that perform well in the free-operant conditioning task do not necessarily perform well in the discriminative avoidance task. Both tasks do not require any special conditions (e.g. food deprivation). The protocol of both tests can be adapted and it is possible to study extinction as well. As an example, the discriminative avoidance task can be easily turned into an automated reversal learning task and is available as such at Delta Phenomics.

## Contact us!

We can conduct these learning tasks in your transgenic mouse model or administer your compound that is expected to affect cognitive capacities. Moreover, integrating these tasks in the home cage of mice allows quick and efficient screening of both acute or chronic drug treatment. Please contact us for further information or to discuss your research question.

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