Use of Automated Tracking System Across Anxiety and Depression Models in Rodents

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INTRODUCTION

A variety of animal models for anxiety and depression are available in rats and mice. The anxiety models are typically based on avoidance of an unpleasant stimulus like a large open space in the open-field test (OF), bright light in light-dark (LD), and elevation in elevated-plus maze (EPM). Here, the position of the animal within the arena is determined continuously resulting in measures for motor activity and anxiety separately. In depression models like the forced-swim (FS) and tail-suspension (TS) test, the resistance to an unpleasant situation (inescapable swimming or hanging by a tail) is observed where the key measure is development of immobility. It is important to work towards reliable and experimentator-independent observation in animal experiments in order to enhance reproducibility of results in an already difficult research area.

Ethical Statement

All experiments described in this abstract have been approved by the local Ethical Committee at Johnson and Johnson, Turnhoutseweg 30, Beerse, Belgium**.**

RESULTS

The Noldus Ethovision system allows tracking of both position of animal (focus on center of gravity) and movement (focus on change of animal surface). In our hands, we evaluated the usability of this tracking software across various assays and rodent species using infra-red (IR) background lighting where possible. The advantage of IR light is that detection becomes insensitive to the fur color of the rodent and also to the room light intensity and/or reflection resulting in highly accurate detection.

As an example, in the LD set up two problems have been solved in different ways. First, the IR-non transparent wall separating dark from light actually cut the animals in two parts when they moved through the opening. This resulted in inaccurate detection of the subject based on relative size of the two body parts. Second, anxious mice like the BALB/c strain tend to spend a large amount of time right at this separation resulting in very high levels of zone transitions, while the actual distance travelled indicates that these mice are not very explorative. This clearly hampers the usability of automated tracking systems above human observation. Software-matic extrapolation of object detection prevented the first problem, where the undetectable missing section between the two body parts was filled in automatically generating the actual shape of the subject. The second problem was solved by adding a small expansion of the dark zone into the light zone. Here, BALB/c mice sitting in the opening with very little movement were now recorded as still being in the dark. This is similar to the definition of zone-transition as frequently is being used for manual observations: in order to count a transition all four paws have to cross an arbitrary border. This however, cannot be replicated in the automated tracking system based on center point of gravity. However, the dark-zone expansion is the closest and most pragmatic solution to such a human observation. For the OF test, we show the importance of mouse strain as well as shape of arena (square versus circular). Mice were tested in a square open field where they spend an important proportion of their time in the corners. In a circular open field arena, in contrast, rats showed circular movements without spending time in a clearly preferred part of the arena. Still, in both cases, there was active avoidance of the center zone. In the EPM set up we demonstrate the importance of room illumination on exploration levels on the open arms. The level of exploration of the open arms seen with the room lights turned off was significantly higher compared to when

the room lights were turned on. For the depression assays based on movement, we successfully calibrated automated detection towards results by two independent human observations. Here, across a dose-response curve for the positive control imipramine (doses 0-5-10-20 mg/kg s.c.) individual results generated by two independent observers as well as the automated tracking system showed highly significant correlations. Finally, we were able to pick up relevant pharmacological effects of drugs that are known to influence anxiety- and depression-like behaviors in the models used.

CONCLUSION

In conclusion, a variety of experimental variables should be properly controlled for reliable baseline levels and pharmacologically induced responses in order to allow proper automated tracking. The Noldus Ethovision system can be used efficiently for tracking of position in the anxiety models as well as for movement in the depression models employed.