

Over the years, Delta Phenomics has gained considerable experience in research with animal models of depression based on social stress. Important advantage of our approach is that we make use of continuous behavioral monitoring (i.e. longitudinal testing) after an experimental treatment that induces a specific psychopathology. Automated longitudinal testing offers a cost-effective, high-throughput tool to monitor various slowly developing behavioral changes in rats or mice, such as aging and depression.

Protocols

The details of the analysis protocol depend on the specific research question, but in studies of depression the emphasis is on general activity including sleeping patterns, appetitive and consummatory aspects of behavior. We have experience with different social stress protocols for mice and rats regarding the consequences of chronic or repeated social stress using defeat paradigms combined with individual housing.

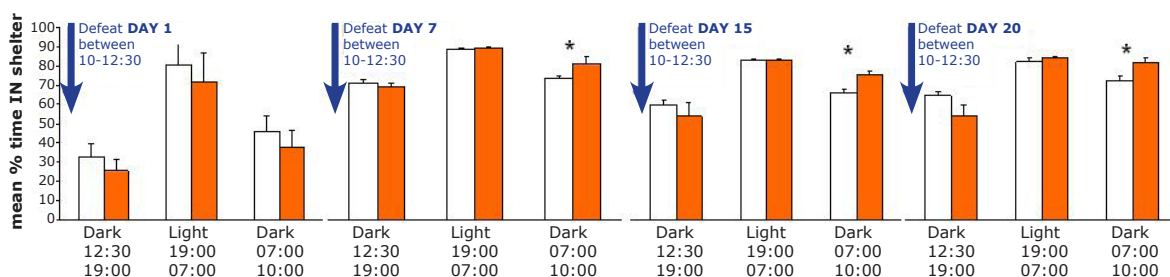
In rats, the experimental rat is the intruder that is defeated on multiple consecutive days by an aggressive resident that is housed with a sterilized female to elicit territorial aggression. As a part of the social stress paradigm, the experimental rat is housed individually for a long period (2-3 months). During this period, the animals are continuously monitored in the PhenoTyper® home cage.

For mice, we use a resident-intruder paradigm in which the experimental animal is the resident that is defeated in its home cage by an aggressive intruder for 21 consecutive days (paradigm modified after several social stress models¹).

Behavioral end points

During and after the monitoring period in the PhenoTyper, the following parameters are computed:

- Changes in activity in time and space (circadian rhythm). For each spatial zone in the cage and for each time bin: time spent in zone, distance moved, velocity, angularity of movement, number of stops, etc.
- Changes in pattern of sleeping: time spent in the shelter, number of visits to the shelter
- Appetitive aspects: changes in activity when a conditioned stimulus announces the arrival of sucrose
- Consummatory aspects: amount of sucrose solution consumed
- Optional: parameters related to anxiety and a cognitive task



This graph shows that the defeated mice spent significantly more time in the shelter during the second half of the dark (active) period from day 7 onwards.

Control
Defeat

Conclusion and validation

In defeated mice we see a diminished number of visits to the shelter, and an increasing amount of time spent in the shelter, developing over 3 weeks of repeated stress. In rats we have observed the development of anhedonia²: lack of anticipatory activity for a sucrose reward. Our rat model has been validated on behavioral and physiological level with known anti-depressants such as imipramine³ and fluoxetine⁴. Furthermore, it is shown that behavioral therapy (repeated enriched housing for short periods) has a high and long-lasting counter-acting effect on stress-induced alterations of hippocampal synaptic plasticity⁵.

Contact us!

Are you interested in using these social stress models to test your antidepressants or other compounds, investigate the effects of this paradigm on your transgenic animals, or for other purposes, please contact us for further information. We can conduct the social stress paradigm, apply drug-treatment, execute stand-alone behavioral tests, all possible with or without long-term continuous behavioral monitoring.

¹ Kudryavtseva et al. (1991) *Pharmacology Biochemistry and Behavior*, **38**; and Merlot et al. (2003) *Physiology & Behavior*, **80**.

² Von Frijtag, J.C.; Reijmers, L.G.J.E.; van der Harst, J.E.; Leus, I.E.; van den Bos, R.; Spruijt, B.M. (2000). Defeat followed by individual housing results in long-term impaired reward- and cognition-related behaviours in rats. *Behavioural Brain Research*, **117**, 137-146.

³ Von Frijtag, J.C.; van den Bos, R.; Spruijt, B.M. (2002). Imipramine restores the long-term impairment of appetitive behavior in socially stressed rats. *Psychopharmacology*, **162**, 232-238.

⁴ Cornelisse, L.N.; Van der Harst, J.E.; Lodder, J.C.; Baarendse, P.J.J.; Timmerman, A.J.; Mansvelde, H.D.; Spruijt, B.M.; Brussaard, A.B. (2008). Reduced 5-HT_{1A}- and GABA_B receptor function in dorsal raphe upon chronic fluoxetine treatment correlates with relief from symptoms of depression in rats. *Journal of Neurophysiology*, **98**, 196-204.

⁵ Kamal, A.; van der Harst, J.E.; Kapteijn, C.M.; Baars, A.J.M.; Spruijt, B.M.; (2010). Announced reward counteracts the effects of chronic social stress on anticipatory behavior and hippocampal synaptic plasticity in rats. *Experimental brain research*, **201**, 641-651.