Amphetamine induced hyperlocomotion

What is it?

Locomotor activity (LMA) test consists of measuring a variety of physical movements displayed by the animal. In a simple box setting, this test can be used to assess:

1) The general physical baseline activity and how it is affected by different compounds.
2) The efficacy of novel compounds in reversing amphetamine-induced hyperlocomotion, which is a common way to study the aspects of positive symptomatology in schizophrenia.
3) More specific aspects of physical movement such as rearing, jump counts or stereotypic movements.

It is also possible to set time segments for LMA recording, for instance, if the activity of an animal is recorded for a total of 60 minutes, the experimenter can choose to get separate readings of LMA data every 5 minutes.

How does it work?

The LMA box is a plexiglass box with infrared beams (Figure 1). The beams consist of 3 axes; the X-axis set of beams are placed outside of the box on two opposing sides at the same height level. The Y-axis beams are placed at the same height as the X-axis ones but on the other two walls of the box facing one another. The Z-axis beams are placed above the X-axis beams on opposite sides of the box. The heights of the beams can be modified and are chosen such that the X- and the Y-axis beams detect the activity of the animal at all times, whereas the Z-axis beams only detect rearing activity or a jump. The activity is detected when the infrared photo beams are disrupted due to the presence and movement of the animal at a particular location within the box.

Figure 1: Locomotor activity test boxes and a schematic diagram how the beams record different physical movements of the animal.

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The effect of acute amphetamine challenge on locomotor activity

The b-neuro laboratory has demonstrated that an acute injection of amphetamine results in increased general physical activity in female Lister-hooded rats, termed amphetamine-induced hyperlocomotion (Figure 2) in both scVehicle and scPCP treated animals.

The rats are habituated to the LMA boxes for 3 days, 1 hour per day and the test is carried out the following day. During testing, the LMA is recorded for 30 minutes (for baseline activity) prior to amphetamine injection, and for a further 60-90 minutes post-amphetamine injection.

Recordings are taken every 5 minutes, with ambulatory counts used for analysis, as these represent the general physical activity of the animal regardless of the type of movements.

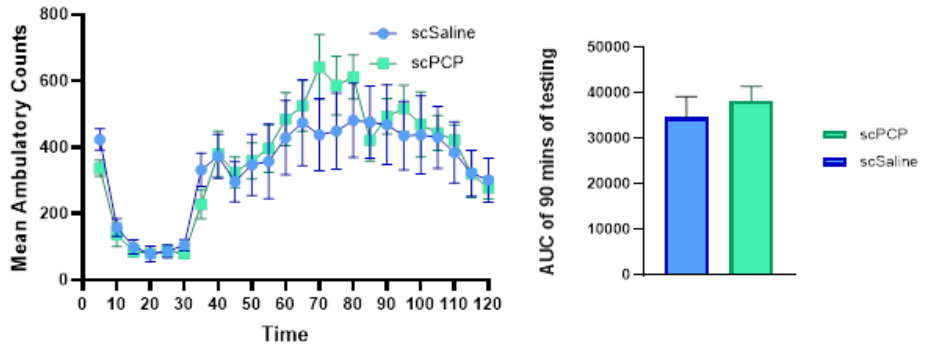

Figure 2: The effects of acute amphetamine (administered at 30 minutes) on the LMA of scVehicle and scPCP treated female Lister-hooded rats (*n*=10). Compared to the first 30-min baseline activity, amphetamine induces a hyperlocomotion in the 90 minutes post-injection.

Reversal of the amphetamine-induced hyperlocomotion by antipsychotics

Positive symptoms are usually modelled by acute amphetamine injection followed by measuring locomotor activity (LMA) in otherwise healthy rodents. At b-neuro we have demonstrated the ability of haloperidol and clozapine in reversing the amphetamine-induced hyperlocomotion in the LMA test. Reproducibility and validation data can be shared upon request. We work with clients to pick the most relevant reference compound. The data below is in scVehicle treated animals.

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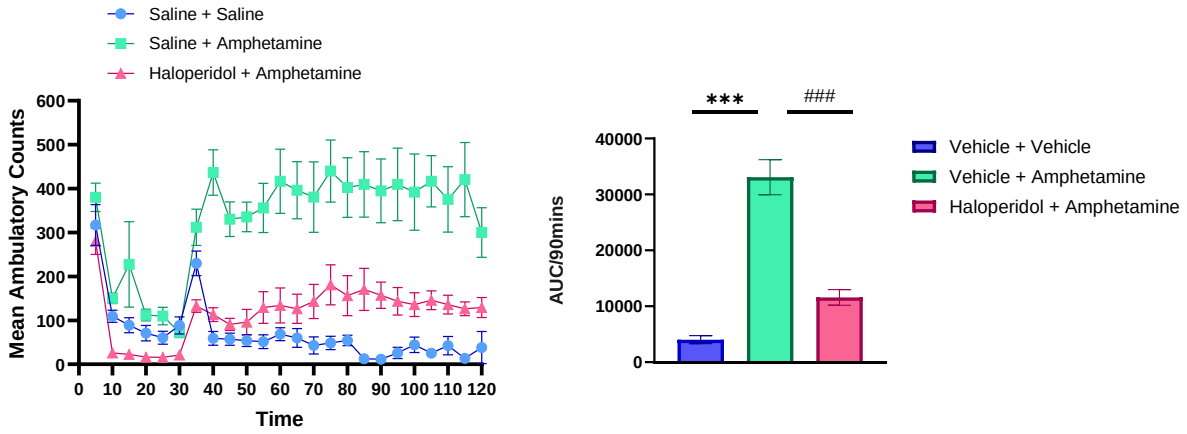

Figure 3: The effects of haloperidol on amphetamine-induced hyperlocomotion in scVehicle treated animals.

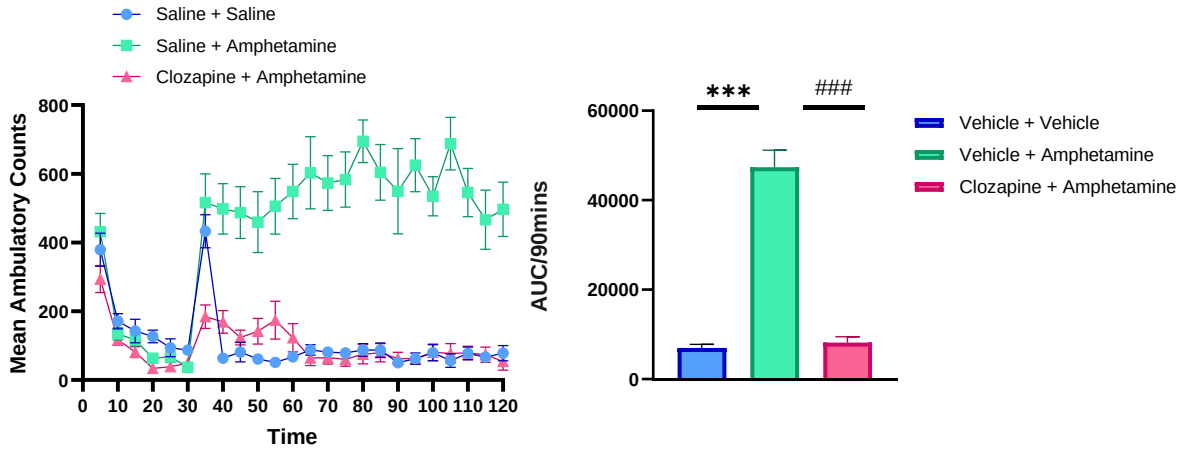

Figure 4: The effects of clozapine on amphetamine-induced hyperlocomotion in scVehicle treated animals.

Utilisation of the scPCP model for positive symptomatology is not common thus the dopaminergic system is not well-studied in this model. Studies in the b-neuro lab demonstrate that amphetamine increases LMA in both scVehicle and scPCP groups.

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Haloperidol and clozapine, at clinically relevant doses, both reversed the amphetamine-induced hyperlocomotion in scVehicle (Figures 3&4), but only clozapine fully reversed the effect in scPCP-treated rats (Data available on request). The efficiency of clozapine may involve other neurotransmitter signalling pathways such as serotonergic or muscarinic.

Our recent studies highlight the importance of assessing symptomatology in relevant preclinical models and suggest the scPCP model may display striatal pathophysiology of relevance to schizophrenia.