

SELF-ADMINISTRATION

Key-words: Pharmacodependence, Drug Abuse, Opiates, Self-administration, Morphine, Addiction

Rationale – The development of novel drugs dedicated to the treatment of CNS pathologies needs a preclinical evaluation of their dependence potential. Due to their positive reinforcing effects, opiates lead to self-administration in rodents. Consequently, the experimental paradigm of self-administration in rodents allows to detect the positive reinforcing effects of a new drug and thus, to investigate its addictive potential.

Method – The procedure is adapted from the one described by Kuzmin et al.⁽¹⁾. Male Swiss mice are tested in pairs in identical test cages. Pairs of animals are selected on the basis of approximately equal levels of nose poking during preliminary testing without injections. Each cage has a frontal hole for nose poking. Both mice are partially immobilized by fixing their tails, which protruded through a vertical slot in the back wall, by Scotch tape to a horizontal surface. Each nose poke of the active mouse results in a contingent injection of 1µl of either saline or drug solution to the lateral tail vein of both the active mouse and the yoked passive mouse. Nose pokes of the yoked passive mice are counted but have no programmed consequences. After 10 min of habituation to the test cage, an injection is made contingent upon each nose poke of the active animal during a 30-min period.

The data recorded are:

- NPR_A = the number of nose poke responses made by the active mouse.
- NPR_P = the number of nose poke responses made by the passive mouse.
- $\% NPR_A = 100 \times NPR_A / (NPR_A + NPR_P)$

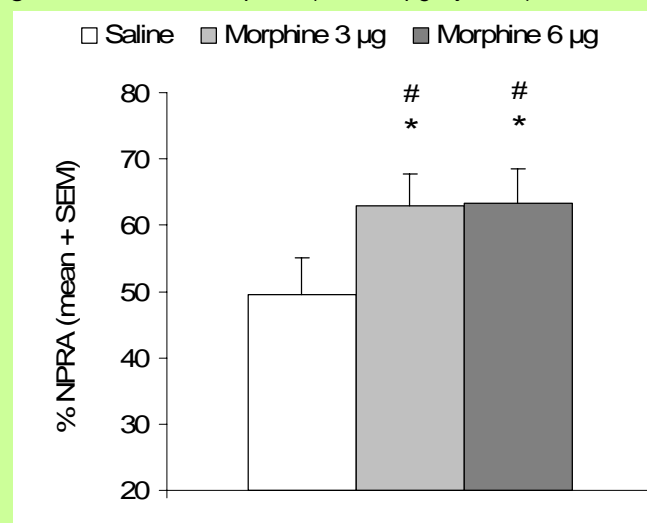
A higher number of responses in active mouse (i.e. $NPR_A > 50\%$) indicates a positive reinforcing effect of the drug t

References;

1. Kuzmin A et al., *Eur J Pharmacol* 295:19-25, 1996.

Example – Fig. 1 shows morphine self administration behaviour, i.e. the positive reinforcing effect of morphine.

Figure 1 – Effect of morphine (3 and 6 µg/injection) on the $\%NPR_A$



Difference vs. control group * $p < 0.05$ – Difference vs. 50%: # $p < 0.05$