

A relevant and validated mice model to study erection: Potentiation of erectile responses by vardenafil

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OBJECTIVES

Due to advances in molecular biology, genetically engineered mice have now become available. Since these mice contribute to the understanding of physiological mechanisms implicated in erectile function as well as the various pathophysiological processes occurring during ED, it is of importance to validate their use i.e. verify that they respond adequately to currently-approved treatments of ED.

We aimed to examine the erectile responses elicited by electrical stimulation in mice following an acute treatment with vardenafil, a currently-approved treatment for ED in order to validate the use of this model for the characterization of other pharmacological agents with potential use in the treatment of ED.

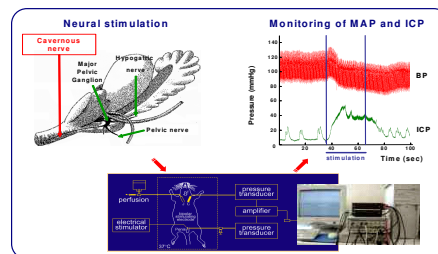
MATERIALS & METHODS

Experimental animals

Ten-weeks old C57BL6/J mice were used (Charles River, France).

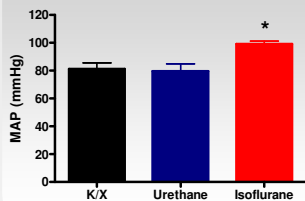
In vivo evaluation of erectile function

Simultaneous computerized measures of mean arterial blood pressure (MAP) and intracavernous pressure (ICP) following electrical stimulation of the cavernous nerve in vivo were performed. We have compared the effects of a ketamine (125 mg/kg)/xylazine (1 mg/kg) (K/X) anaesthesia with those of urethane (1.2 mg/kg) or isoflurane (1.5-2 %) on the erectile responses under various electrical parameters of stimulation of the cavernous nerve (0-15 Hz, 0.3-3 ms, 6V for 30 s). The best parameters were then selected to evaluate the effect of an acute injection of vardenafil (0.1 mg/kg *iv*) on the erectile responses. Erectile responses are expressed as the area under the curve (AUC) during the erectile response, normalized by the mean arterial pressure (MAP).



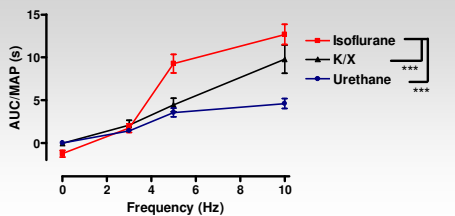
RESULTS

Mean arterial pressure under anaesthesia



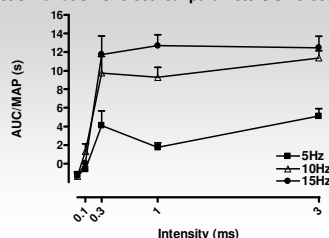
Mean arterial pressure is better preserved in mice anaesthetized with isoflurane compared to urethane or K/X.

Effect of anaesthetics on erectile responses

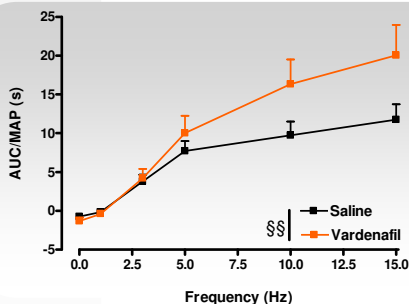


The AUC is also best when mice are anaesthetized with isoflurane although spontaneous erectile events occur more frequently.

Effect of variation of electrical parameters on erectile responses



Different trains of stimulation (0.1-3 ms) elicit variable erectile response curves in isoflurane-anaesthetized mice, thus indicating that an intensity of 0.3 ms is sufficient to elicit maximal responses at a given frequency.



Vardenafil treatment at 0.1 mg/kg *i.v.* significantly enhances erectile responses elicited by electrical stimulation (0.3 ms – 6 V – 30 s) in mice

CONCLUSIONS

- Anesthetic agents and electrical parameters of stimulation of the cavernous nerve are important determinants to conduct experimental studies on erectile function in vivo.
- This study has enabled the identification of the best experimental conditions to work with mice, validated by the potentiating effect of acute vardenafil on erectile function. It will allow future use of transgenic or knock-out mice to advance in the characterization of pharmacological agents with potential use in the treatment of ED.