ABSTRACT

A SELECTIVE NEUROKININ-1 RECEPTOR ANTAGONIST MODULATES PHARMACOLOGICALLY-INDUCED EJACULATION IN ANAESTHETISED MALE RATS

Pierre Clément¹, Magali Peeters¹, Jacques Bernabé¹, Miguel Laurin¹, Pierre Denys¹, François Giuliano²∗

¹ PELVIPHARM Laboratories, Orsay, France ² Magna Medical, University of Ganges, France  ∗ e-mail address: juliano@cyber-sante.org

OBJECTIVE

Introduction and Objective

Evidence indicate a role for substance P in the control of ejaculation although its mode of action still needs to be clarified. The aim of this study was to investigate the role of brain, spinal, and peripheral neurokinin-1 receptors (NK1) in the control of ejaculation using an already described pharmacological model in anaesthetised rats (Clément et al., 2007).

For this purpose, ejaculation was elicited by delivering the dopamine D3 receptor preferring agonist [R(+)-7-hydroxy-2-(di-N-propylamino)tetralin; 7-OH-DPAT] into the cerebral ventricle (i.c.v.). The effects of a non peptide NK1 antagonist (RP67580) administered by different routes [i.e.c., intrathecal (i.t.), i.v.] were tested on 7-OH-DPAT-induced ejaculation.

METHODS

Surgical preparation

Adult male Wistar rats weighing 250-300 g were anaesthetised with urethane (1.2 g/kg), tracheotomised, and the carotid artery catheterised for i.t. catheter insertion. Drugs

The catheter was inserted in the cerebral ventricle with a 17G needle under aseptic conditions. After a recovery period of 5 min, rats were placed in a stereotaxic apparatus. The needle was lowered into the cerebral ventricle until it reached the isocentre of the ventricle. The needle was withdrawn and the position of the needle was checked before delivering the pharmacological agents.

Intrathecal catheter implantation

For i.t. catheter insertion, the rat’s head was placed in a stereotactic frame, and was rotated nose downwards. The catheter was a polyethylene tubing (PE10) stretched to 150% of its original length in hot water, and cut to the required length so that its distal opening reached the targeted levels of the spinal cord; i.e. 3rd lumbar (L3) segment of the spinal cord. The atlanto-occipital membrane was opened and the catheter was carefully advanced in the caudal direction. The rostral free end of the catheter was secured with ligatures that closed the neck muscles and skin layers. The exact location of the caudal tip of the catheter was checked at the end of each experiment after sacrifice of the animal and exposure of the spinal cord.

Recordings

Seminal vesicle pressure (SVP) was measured with a catheter, filled with mineral oil, inserted in the right seminal vesicle through the apex. Electrical activity of the bulbospongiosus muscle (BS) was recorded by passing a Teflon insulated wire through the rectum of each animal. The wire was collected outside the skin, and BS activity was amplified (gain, 10000; Low pass, 1 KHz; High pass, 10 Hz).

RESULTS

Intrathecal catheter implantation

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CONCLUSIONS

Multi-level NK1 receptor modulatory role on ejaculation in the 7-OH-DPAT model.

Targeting of NK1 receptors as a potential therapeutic strategy for the treatment of premature ejaculation.

References


3 Clément P, Peeters M, Laurin M, Bernabé J, Deny P, Giulianno F. A selective neurokinin-1 receptor antagonist modulates pharmacologically-induced ejaculation in anaesthetised male rats. PELVIPHARM Laboratories, Orsay, France

4 Parc d’Orsay, Orsay, France. Web site: www.pelvipharm.com

Statistical analysis

Results are expressed as mean ± SEM. Statistical analysis was performed using a two-way ANOVA with Bonferroni’s post hoc test. The Student’s t-test or one-way ANOVA were used to detect differences between means. The Fisher’s exact test was used for the statistics of the number of ejaculations. All i.c.v. and i.t. drug treatments were delivered in a volume of 10 µl at a flow rate of 2 µl/min. i.t. and i.p. deliveries were performed in volumes of 10 µl and 5 ml/kg b.w., respectively. RP67580 was administered 15 min (i.p.) or 5 min (i.c.v. and i.t.) prior i.c.v. 7-OH-DPAT (10 µg). RP67580 delivered via different routes on 7-OH-DPAT-induced ejaculation. The number of ejaculations (expulsion of a seminal plug), seminal vesicle pressure (SVP), and bulbospongious muscle (BS) responses were determined following i.c.v. 7-OH-DPAT (10 µg) delivery in separate groups of 12 rats.