BRAIN OXYTOCIN RECEPTOR BLOCKADE INHIBITS PHARMACOLOGICALLY-INDUCED SEXUAL RESPONSES IN ANAESTHETISED MALE RATS

Objective: The present study was undertaken to clarify the role of brain, spinal, and peripheral oxytocin receptors (OTR) in the control of ejaculation and erectile responses. For this purpose, we aimed at clarifying the role of brain, spinal, and peripheral oxytocin (OT) receptors in the control of ejaculation and erectile responses occurring in form of coordinated increases in seminal vesicle and bulbospongiosus EMG activity, and intraventricular (i.c.v.) 7-hydroxy-2-(di-N-propylamino)tetralin (7-OH-DPAT) into the cerebral ventricle (i.c.v.). The effects of a peptide OT antagonist administered via different routes [i.c.v., intrathecal (i.t.), i.v.] were tested on 7-OH-DPAT-induced sexual responses.

Methods: Adult male Wistar rats weighing 250-300 g were anaesthetised with urethane (1.25 g/kg), tracheotomized, and the carotid artery catheterized for blood pressure measurement. All animal experiments were carried out in accordance with the European Community Council Directive (86/609/EEC) on the use of laboratory animals. Intracerebroventricular cannula implantation A guide cannula (22G) was stereotaxically placed above the cerebral ventricle (coordinates according to Paxinos and Watson rat brain atlas: 0.5 mm posterior to bregma, 1 mm lateral to midline, and 4 mm below the skull). The internal cannula (with 0.5 mm projection below the guide cannula) was connected to a Hamilton syringe placed in a micropump allowing delivery of microvolumes. At the end of the experimental session, methylene blue dye was injected through the cannula and the brain, removed and grossly dissected, was inspected for the presence of blue dye in the ventricles.

Drugs 7-OH-DPAT and the peptide OT antagonist (de(3,6)-Tyr(Me)5-Oxytocin) were dissolved in NaCl 0.9%. All i.c.v. treatments were delivered in a volume of 5 µl at a flow rate of 1 µl/min. I.t. and i.v. deliveries were performed in volumes of 10 µl and 1 ml/kg b.w. OT antagonist was administered (whatever the route) 15 min before i.c.v. 7-OH-DPAT (10 µg) and recording was continued over 30 min after 7-OH-DPAT delivery. Each route was tested in separate groups of 10 rats.

Conclusions: From these results, we concluded that in the 7-OH-DPAT model, (i) brain OT receptors modulate ejaculation and erection, and (ii) L6 spinal OT receptors have a modulating role on ejaculation but not on erection whereas peripheral OT receptors are not involved in either ejaculation or erection, thus highlighting the existence of functional relationships between dopaminergic and oxytocinergic pathways in the central control of sexual responses. reference 1, Clement P, Bernabe J, Denys P, Alexandre L, Parc d’Orsay, Orsay, France. Web site: www.pelvipharm.com

Statistics: Student’s t-test; * different from 0 µg OT antagonist dose (control); § different from 0.001 µg OT antagonist dose.

In the 7-OH-DPAT model, erections (reflected by ICP responses) are less reflexive. Delivered i.v. the OT antagonist has no effect on 7-OH-DPAT-induced sexual responses. Delivered i.c.v. the OT antagonist dose-dependently inhibits 7-OH-DPAT-induced sexual responses. Delivered i.t. at L6 but not T13 level the OT antagonist has a modulatory role on 7-OH-DPAT-induced ejaculation.The results indicate the key role that brain OT receptors may play in ejaculation.

Objectives: The present study was undertaken to clarify the role of brain, spinal, and peripheral oxytocin receptors (OTR) in the control of ejaculatory and erectile responses using an already described pharmacological model in anaesthetised rats (Clement et al., 2007).

For this purpose, ejaculatory and erectile responses were 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 peptide OT antagonist administered via different routes [i.c.v., intrathecal (i.t.), i.v.] were tested on 7-OH-DPAT-induced sexual responses.

Methods: Surgical preparation Adult male Wistar rats weighing 250-300 g were anaesthetised with urethane (1.25 g/kg), tracheotomized, and the carotid artery catheterized for blood pressure measurement. All animal experiments were carried out in accordance with the European Community Council Directive (86/609/EEC) on the use of laboratory animals. Intracerebroventricular cannula implantation A guide cannula (22G) was stereotaxically placed above the cerebral ventricle (coordinates according to Paxinos and Watson rat brain atlas: 0.5 mm posterior to bregma, 1 mm lateral to midline, and 4 mm below the skull). The internal cannula (with 0.5 mm projection below the guide cannula) was connected to a Hamilton syringe placed in a micropump allowing delivery of microvolumes. At the end of the experimental session, methylene blue dye was injected through the cannula and the brain, removed and grossly dissected, was inspected for the presence of blue dye in the ventricles.

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Effects of the OT antagonist delivered via different routes on 7-OH-DPAT-induced sexual responses. The number of ejaculations (expulsion of a seminal plug), seminal vesicle pressure (SVP), bulbospongiosus muscle EMG (BS EMG) obtained in anaesthetised rats after i.c.v. delivery of 7-OH-DPAT.

Effects of L6 OT antagonist delivery on duration of bulbospongiosus muscle (BS) responses elicited by L6 OT antagonist delivery on duration of bulbospongiosus muscle (BS) responses elicited by 7-OH-DPAT.