SB-277011, A SELECTIVE Dopamine D3 RECEPTOR ANTAGONIST, DELAYS EJACULATION IN ANESTHETIZED AND CONSCIOUS RATS

Pierre Clément1, Chiara Pozzato, Christian Heidbreder2, Pierre Denys3, François Giuliano1,3, Sergio Melotto2

1 PELVIPHARM Laboratories, Orsay, France 2GlasSmithInk @ P.a. Dept. of Biology, Verona, Italy 3Raymond Poincaré Hospital, Neuro-Uro-Andrology Unit, Garches, France 4e-mail address: giuliano@cyber-orange.org

ABSTRACT

OBJECTIVE

We aimed at clarifying the role of D3 receptors in the male sexual activity in anesthetized and conscious rats by using standardized experimental paradigms.

RESULTS

For this purpose, we used (i) the 7-OH-DPAT-induced sexual responses in anesthetized rats to explore the effects of SB-277011 on emission and expulsions phases of ejaculation as well as on erection; and (ii) the sexual incentive motivation and mating tests for the exploration of SB-277011 effects on, respectively, motivational and copulatory aspects of male rat sexual behavior.

METHODS

All animal experiments were carried out in accordance with the European Community Council Directive (86/609/EEC) on the use of laboratory animals.

Anesthetized rat study

Adult sexually naive male Wistar rats were anesthetized with isoflurane (1:2:1) and the carotid artery catheterised for measurement. Seminal vesicle pressure (SVP) was measured with a catheter, filled with mineral oil, inserted in one seminal vesicle through the apex. Intracavernous pressure (ICP) was measured with a catheter inserted into one corpus cavernosum. Electrical activity of the bulbospongious muscle (BS) was recorded by passing a Teflon insulated stainless-steel wire laterally throughout the muscle with two 1-2 mm pieces (separated by 1-2 mm) of insulation stripped off. SB-277011 was delivered i.p. and 30 min after sexual responses were induced by i.v. 7-OH-DPAT.

Behavioral study

Sexual incentive motivation test: Sexually experienced male Wistar rats placed, for 10 min, in testing arena with sexually naive females. Latency to copulate was measured. Mating test: Sexually experienced male Wistar rats placed, for 30 min, in mating chamber with receptive females. Mating test was performed immediately after sexual incentive motivation test.

CONCLUSIONS

In the 7-OH-DPAT model, selective antagonism of D3 receptors impairs ejaculation by specifically altering the expulsion phase of ejaculation with no effect on other aspects of sexual functions.

In sexual incentive motivation test, selective antagonism of D3 receptors exerts no effect on male rat sexual motivation.

In mating test, selective antagonism of D3 receptors increases ejaculation latency and post-ejaculatory interval with no effect on other aspects of male rat copulatory behavior.

These results open new avenues for the development of pharmacological management of premature ejaculation.