Facilitator proerectile activity of Melanotan II (MT-II) in anesthetized rats

ABSTRACT

ABSTRACT

Facilitator proerectile activity of Melanotan II (MT-II) in anesthetized rats

Julien Allard1, Laurent Alexandre1, Jacques Bernabe2, Gérard Benoit1, Stéphane Droupy3, François Giuliano1,2

1PELVIPHARM Laboratories, Gif-sur-Yvette, France
2Medical University of Paris South Research Group in Urology, Le Kremlin-Bicêtre, France
3Contact email: giulianof@lycomang.org

Intracavernous (ICP) and blood pressure (BP) were monitored in urethane-anesthetized Sprague Dawley rats.

Methods: Intracavernous (ICP) and blood pressure (BP) were monitored in urethane-anesthetized Sprague Dawley rats.

Results: Single-trial/bilateral cavernous nerve stimulation elicited electro-mechanical responses in urethane-anesthetized rats. The facilitator effect of MT-II (1 mg/kg) was abolished after LSCx transection and inferior mesenteric ganglion removal.

Conclusion: MT-II displays a significant proerectile activity in urethane-anesthetized rats. Persistence of the proerectile activity of MT-II in DNPx and PNx rats rules out an action on sensory afferences from the penis and on the proerectile input issued from the spinal parasympathetic nucleus respectively. The decrease of the facilitator proerectile activity of MT-II after removal of the LSC points to an involvement of the sympathetic pathway to the point in this effect.

Introduction and Objective: MT-II, a cyclic peptide analog of α-MSH, elicits anagost activity at 4 of the 5 known melanocortin receptors (MC1R, MC3R, MC4R, MC5R). The ability of MT-II to induce penile erections without any sexual stimulation has been demonstrated in conscious and anesthetized rats. Because a selective MC4R agonist was shown to facilitate penile erection in anesthetized rat (Pauwels, 2002, 2013), we assessed whether MT-II could induce proerectile facilitatory activity and sought for the site of action for such effect.

Methods: Intracavernous (ICP) and blood pressure (BP) were monitored in urethane-anesthetized Sprague Dawley rats.

Results: Single-trial/bilateral cavernous nerve stimulation elicited electro-mechanical responses in urethane-anesthetized rats. The facilitator effect of MT-II (1 mg/kg) was abolished after LSCx transection and inferior mesenteric ganglion removal.

Conclusion: MT-II displays a significant proerectile activity in urethane-anesthetized rats. Persistence of the proerectile activity of MT-II in DNPx and PNx rats rules out an action on sensory afferences from the penis and on the proerectile input issued from the spinal parasympathetic nucleus respectively. The decrease of the facilitator proerectile activity of MT-II after removal of the LSC points to an involvement of the sympathetic pathway to the point in this effect.

METHODS

Potential sites of action for MT-II

Melanot II (MT-II) is a cyclic synthetic peptide analog of α-MSH with an anagost activity at 4 of the 5 known melanocortin receptors: MC1R, MC3R, MC4R, MC5R.

Melanot II is a potent initiator of erections in men with psychogenic and organic erectile dysfunctions (Wessells et al., 2000).

MT-II induces penile erection in conscious and anesthetized rats (Wessells et al., 2003a; 2003b).

OBJECTIVES

To determine the site of action for the facilitator/conditioner effect of MT-II.

RESULTS

MT-II (1 mg/kg) induced a significant proerectile facilitator activity in urethane-anesthetized control rats (CT).

CONCLUSION

The involvement of sensory afferences from the penis in the proerectile facilitator effect of MT-II (1 mg/kg) was ruled out by the lack of effect of dorsal penile nerve transections.

The proerectile facilitator activity was abolished after LSCx transection.

The facilitator effect of a treatment on an erectile response elicited by cavernous nerve stimulation can be evidenced using electrical parameters eliciting submaximal or maximal erectile responses.

MT-II displayed a significant proerectile facilitator activity in control, PNx and DNPx rats. The proerectile facilitatory effect was not anymore significant in LSCx rats.

Conditions: MT-II displays significant facilitator proerectile activity in urethane-anesthetized rats. Persistence of the proerectile activity of MT-II in DNPx and PNx rats rules out an action on sensory afferences from the penis and on the proerectile input issued from the spinal parasympathetic nucleus respectively. The decrease of the facilitator proerectile activity of MT-II after removal of the LSC points to an involvement of the sympathetic pathway to the point in this effect.

References

2. melanocortin-stimulating hormone analog on penile erection and sexual desire in men with
7. c[Asp-His-DPhe-Arg-Trp-Lys]-NH2 induces penile erection via brain and spinal melanocortin