

GALANIN-MEDIATED REGULATION OF MICTURITION REFLEX IN URETHANE-ANESTHETIZED RATS

Hypothesis / aims of study

Galanin, a 29 amino acid peptide, distributes widely in the peripheral and central nervous systems, including the primary afferents, spinal dorsal horn interneurons and the descending bulbospinal tracts (1). Recent studies have demonstrated that galanin is involved in nociceptive responses, especially in the transmission of nociceptive information in the spinal cord (2). Moreover, in intact rats, the spinal antinociception induced by morphine is attenuated by galanin receptor antagonists (3). It is suggested that there may be an interaction of galanin and opioids at the spinal level in modulating the transmission of nociceptive information. However, it is not known whether galanin has a role in the control of the micturition reflex. The aim of this study is to elucidate the effects of galanin on the micturition reflex in rats. Furthermore, the involvement of opioid systems in the galanin-mediated regulation of micturition reflex was also studied.

Study design, materials and methods

Adult female Sprague-Dawley rats weighing 225 to 248 g were used. Rats were anesthetized with isoflurane followed by urethane (1.2 g/kg subcutaneously). Thereafter the abdomen was opened through a midline incision and a PE-60 polyethylene catheter connected to a pressure transducer and amplifier was implanted into the bladder through the bladder dome. This catheter was used to fill the bladder by continuous infusion of saline and record intravesical pressure during cystometry. After intravesical catheter insertion, saline was continuously infused into the bladder for 2 hours at a rate of 0.04 ml per minute to record cystometrograms during a control period. Galanin (1, 3 and 10 µg/kg, n=6 per dose) was then administered intrathecally and changes in bladder activity were monitored. Intrathecal administrations were made through a catheter (PE-10) implanted via a small incision of the dura at the Th11 vertebra under isoflurane anesthesia 3 days before the experiments. The intrathecal catheter was directed caudal in the spinal subarachnoid space and positioned at the level of the L6-S1 spinal cord. The volume of fluid in the catheter was kept constant at 6 µl. Single doses of drugs were then administered in a volume of 2 µl, followed by a 7 µl flush with saline. In another group of animals, galanin (10 µg) was administered intrathecally when the first bladder contraction was observed after intrathecal administration of naloxone, an opioid receptor antagonist (10 µg, n=6) to determine whether the effect of galanin was mediated by the opioid systems. Cystometric parameters were recorded and compared before and after drug administration. All data values are expressed as the mean ± SE. Statistical significance was determined with one-way ANOVA with p<0.05 considered significant.

Results

Intrathecal administration of galanin at 1, 3 and 10 µg increased intercontraction intervals in dose dependent fashion to 117.7 ± 2.4%, 141.1 ± 7.8% and 159.8 ± 12.5% of the control value, respectively (p<0.01) (Figure 1). These inhibitory effects were seen immediately after administration and returned to the pre-control level within 70 minutes. Intrathecal administration of galanin at 1, 3 and 10 µg also increased threshold pressure in dose dependent fashion to 9.52 ± 0.98 cmH₂O, 11.2 ± 1.12 cmH₂O and 12.9 ± 1.67 cmH₂O, respectively, from the control value of 5.46 ± 0.88 cmH₂O (p<0.01). There were no significant changes in basal pressure, maximum pressure or post void residual at any doses tested. When naloxone was administered one voiding cycle before galanin administration, the increases in intercontraction intervals and threshold pressure induced by galanin administration alone were not seen (Figure 2).

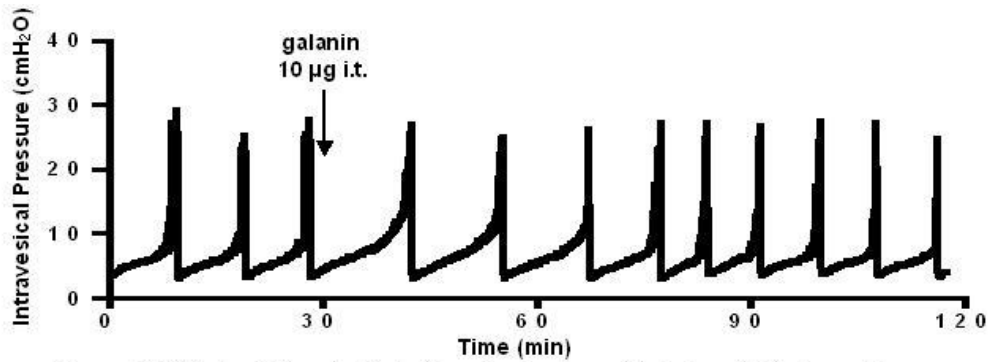


Figure 1. Effects of i.t. administration of galanin on bladder activity in urethane anesthetized rats. Arrow indicates drug administration.

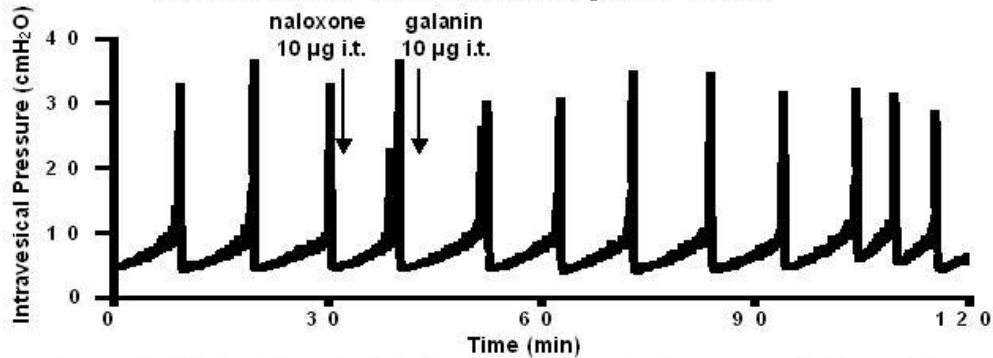


Figure 2. Effects of i.t. administration of galanin and naloxone on bladder activity in urethane anesthetized rats. Arrows indicate drug administration.

Interpretation of results

In the present study, galanin administered intrathecally increased intercontraction intervals and threshold pressure in urethane-anesthetized rats. These findings indicate that galanin has an inhibitory action on the micturition reflex at the spinal cord level in urethane-anesthetized rats. The main function of galanin seems to be mediated by modulation of afferent activity because galanin induced increases in intercontraction intervals and threshold pressure without affecting maximum pressure or basal pressure. In addition, because the galanin-induced increases in intercontraction intervals and threshold pressure were prevented when naloxone was administered prior to galanin application, indicating that the effects of galanin were mediated by activation of the opioid system.

Concluding message

These results in this study suggest that galanin plays an important role in the control of the micturition reflex and that galanin can inhibit the micturition reflex through activation the opioid system at the spinal level in rats. Thus, galanin could be effective for the treatment of bladder dysfunction such as overactive bladder.

References

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Is this a clinical trial?	No
What were the subjects in the study?	ANIMAL
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	Yes
Name of ethics committee	Institutional Animal Care and Use Committees of University of Pittsburgh and Tottori University