[c-fos expression] Spinal c-fos expression in urethane-anesthetized (1.2 g/kg, i.p.) female Wistar rats was examined with an immunohistochemical technique[4], following 2-hr infusion of saline(n=2) or 1% acetic acid(n=2) or 1% acetic acid with HGN transection in advance(n=2). The number of cells exhibiting c-fos immunoreactivity was counted at L1 and L6 spinal cord where HGN and PLN afferent terminals project, respectively. Specially, the number of c-fos positive cells was compared at 3 different regions; dorsal commisure, intermediolateral gray matter and dorsal horn.
Statistical analysis was performed by paired Student's t test and Mann-Whitney's U test.

RESULTS:

[continuous cystometry] (1)In control rats, acetic acid infusion elicited an irritative bladder responses characterized by a marked decrease in ICI (from 10.8±1.6 min during saline infusion to 6.1±1.9 min after acetic acid infusion, P<0.0002) and a marked increase in MVP (from 19.3±4.1 mmHg during saline infusion to 29.1±4.5mmHg after acetic acid infusion, P<0.002). (2)In capsaicin desensitization rats, there was no irritative bladder response; ICI:10.6±1.2 min in saline and 10.7±2.2 min in acetic acid, not significant(n.s.) or MVP:17.8±1.4 mmHg in saline and 18.3±1.7 mmHg in acetic acid (n.s.). (3)In HGP-transected rats, volume-evoked micturition reflex was preserved and there was no significant difference in ICI and MVP during saline infusion compared with control rats. After acetic acid infusion, although a marked increase in MVP was elicited (from 18.4±1.8 mmHg in saline to 29.3±3.1 mmHg in acetic acid, P<0.001), ICI did not decrease in HGP-transected rats(12.2±1.6 min in saline and 11.8±3.1 min in acetic acid, n.s.).

[c-fos expression] (1)L6 level: Acetic acid infusion with or without HGN transection significantly increased the number of c-fos positive cells at all 3 regions of L6 spinal cord compared with saline infusion, and there was no difference between rats with HGN intact or transected. (2)L1 level: HGN transection caused a significant decrease in the number of c-fos positive cells only at dorsal horn of L1 spinal cord following acetic acid infusion. The decrease was primarily noted in lamina I.

CONCLUSIONS:

(1)Acetic acid infusion in conscious rats provokes bladder irritative responses characterized by a decrease in ICI and an increase in MVP, both of which are mediated via capsaicin-sensitive nerves. (2)Since HGP transection prevented a decrease in ICI but not an increase in MVP following acetic acid infusion, nociceptive bladder afferents in HGN have a facilitating role in the urinary frequency caused by chemical bladder irritation. (3)Since HGN transection affects c-fos expression only at dorsal horn of L1 spinal cord, it is suggested that HGN bladder afferents convey nociception induced by chemical bladder irritation to the higher center for micturition, resulting in the facilitative modulation of micturition interval.

REFERENCES:

[1] Anesthesiology(1990), 73; 236-239
[2] Am J Physiol(1997), 272; R695-703
[3] J Urol(1996), 155; 355-360
[4] Am J Physiol(1996), 270; R990-996

130

Author(s):
S Lindström and C-H Jiang
Institution, city, country:
Department of Biomedicine and Surgery, Faculty of Health Sciences, University of Linköping, 581 85 Linköping, Sweden

Title (type in CAPITAL LETTERS, leave one blank line before the text):

REPEAT PERIODS OF ELECTRICAL STIMULATION PROLONG THE MODULATION OF THE MICTURITION REFLEX

Aims of study

Recent experimental studies in anaesthetised animals have shown that the micturition reflex can be modulated by brief periods of electrical stimulation of bladder and anogenital afferents (1). Stimulation of bladder afferents induces a decrease in the micturition threshold volume while the opposite effect is obtained by stimulation of ano-genital afferents. In both cases, the threshold change outlasts the period of stimulation by about one hour. These effects are due to enhancement or suppression of excitatory synaptic transmission in the central micturition reflex pathway (2), the mechanisms being similar to long term potentiation (LTP) or depression (LTD) as established for many cortical synapses (3). The present study was designed to determine if the duration of the micturition reflex modulation can be prolonged by repeated periods of afferent stimulation.

Methods

Thirteen adult female Sprague Dawley rats (250-350 g) were used for the study. Under methohexital anaesthesia (50 mg/kg i.p.), the animals were fully decorticated by gentle suction, sparing most of the diencephalon. This procedure rendered the animals unconscious so no further anaesthesia was required. For recordings the animals were paralysed by a continuos i.v. infusion of pancurone bromide (0.3 mg/kg.h) and artificially ventilated. Their body temperature was maintained at about 38 °C by a feed-back controlled heating lamp. Intravesical electrical stimulation was used to activate bladder afferents. The stimulation was delivered by a specially designed catheter inserted into the bladder via a surgical slit in the proximal urethra. The same catheter was used for cystometry. Ano-genital pudendal afferents were stimulated by ring electrodes placed in the vagina and anus. Repeated constant flow cystometries were performed with body-warm saline (0.06 - 0.1 ml/min) at about 10 minutes interval. The threshold volume of the micturition reflex was used as the dependent variable. When a bladder contraction occurred the infusion was immediately stopped and the catheter opened. Care was taken to empty the bladder completely after each cystometry. After four to six stable control recordings, the selected afferents were stimulated continuously for 5 minutes at maximal intensity. Stimulation frequency was 20 Hz for intravesical and 10 Hz for anogenital stimulation. The same stimulation was repeated 6 times with a pause of 5 minutes between the stimulations. To evaluate the effect of stimulation the mean threshold volume of cystometries performed during one hour before and each hour after the stimulation were compared.

Results

Decorticated rats survived in good condition for 1 - 3 days. In all animals, the micturition threshold volume was significantly decreased by intravesical electrical stimulation ($p < 0.01$). After six short periods of stimulation, the threshold volume remained well below the control level for more than 5 hours, the longest period systematically explored. Pooling the data of all animals ($n = 8$), the threshold volume decreased to its lowest value (62 % of control) during the first hour after stimulation and it remained at 80 % four hours later. Ano-genital afferent stimulation produced a corresponding increase in the micturition threshold volume. After 6 periods of stimulation, a lasting change was again observed for more than 5 hours ($n = 5$). During the first hour the mean threshold volume increased to 211 % of controls ($p < 0.01$) and it remained at about this level for the entire observation period. The opposite effect of ano-genital and bladder afferent stimulation could be shown in the same animal by successive stimulation of these afferent systems.

Conclusions

Micturition threshold changes in opposite directions were obtained by stimulation of bladder or ano-genital afferents. Repeated short periods of stimulation prolonged the modulatory effect well beyond the duration seen with a single period of stimulation. These effects were observed in animals lacking cortical control of the micturition reflex. Thus, the re-education seen in some patients with voiding disorders following repeated sessions of electrical afferent stimulation may at least in part result from LTP and LTD like modulations of synaptic transmission in the subcortical micturition reflex pathway.

References

(1) J Urol 155:1477-1481, 1996

(2) Neurourol Urodyn 17:543-553, 1998

(3) Curr Opin Neurobiol 4:389-399, 1994