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EFFECTS OF A SELECTIVE METABOTROPIC GLUTAMATE RECEPTOR AGONIST ON THE MICTURITION REFLEX PATHWAY IN URETHANE-ANESTHETIZED RATS.

Aims of study:

Glutamate receptors (GluR) can be broadly classified as ionotropic GluR that are ligand-gated ion channels and metabotropic GluR that are coupled to GTP binding protein. Previous studies revealed that glutamate is an important transmitter in the central neural pathways in controlling lower urinary tract function. Ionotropic GluR (e.g. NMDA receptors and AMPA / kinate receptors) were proved to be involved in the descending and ascending limb of micturition reflex pathway between lumbosacral spinal cord and pontine micturition center [1 2]. The aim of this study was to determine the role of metabotropic GluR in spinobulbospinal micturition reflex, using a selective metabotropic GluR agonist, trans-(+/-)-1-Amino-1,3-cyclopentanedicarboxylic acid (trans-ACPD).

Methods:

Experiments were performed on 28 Wistar rats anesthetized with subcutaneous injection of urethane (1.2 gm./kg.). A cystostomy catheter was inserted from the bladder dome to monitor the bladder pressure and an intrathecal (i.t.) catheter was implanted for administration of the drugs. The amplitude of rhythmic bladder contractions (RBC) evoked by bladder distention under isovolumetric condition as well as the amplitude of bladder contraction elicited by electrical stimulation of pontine micturition center (PMC) were investigated before and after i.t. injection of trans-ACPD, respectively. The effect of trans-ACPD on the urethral activity during isovolumetric bladder contraction was also examined by using urethral perfusion pressure and electromyography of the external urethral sphincter (EUS).

Results:

I.t injection of trans-ACPD (3 -10 µg) completely inhibited RBC evoked by bladder distension and the duration of inhibition was dose-dependent (3 µg: 11.4±/5.5min, 5 µg: 13.2±/2.5min, 10 µg: 34.8±/5.1min). The amplitude of bladder contraction evoked by electrical stimulation of PMC was decreased to 12.4±/8.7% of control by trans-ACPD (10 µg i.t.). In addition, bursting activity of EUS and corresponding high frequency oscillation of urethral pressure during isovolumetric bladder contraction were completely abolished by trans-ACPD (10 µg i.t.).

Conclusions:

The present experiments indicated that i.t. administration of a selective metabotropic glutamate receptor agonist to lumbosacral spinal cord has an inhibitory effect on spinobulbospinal micturition reflex in urethane-anesthetized rats. This pharmacological action is attributed at least to the inhibitory effect on the descending pathway from the PMC to the lumbosacral spinal cord.

References:

1. Neurosci. Lettt., (1995), 183, 58-61.
- J. Pharm. Exp. Ther., (1998), 285, 22-27.