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SUPRASPINAL AMPA AND NMDA GLUTAMATERGIC TRANSMISSION IN THE MICTURITION REFLEX IN THE RAT

Aims of Study

Previous studies revealed that glutamatergic transmission mediated by AMPA and NMDA receptors in the lumbosacral spinal cord plays an essential role in the micturition reflex pathway. The present study was conducted to determine if glutamatergic mechanisms in the brain as well as the spinal cord are important for the control of micturition, by evaluating the effect of intracerebroventricular (i.c.v.) as well as intrathecal (i.t.) administration of an AMPA receptor antagonist and an NMDA receptor antagonist on the micturition reflex in the urethane-anesthetized rat.

Methods

Female Sprague-Dawley rats (240-300 g) were anaesthetized with urethane (1.2 g/kg s.c.). The trachea was cannulated with a polyethylene tube (PE-240) to facilitate respiration. To administer drugs by the i.c.v. route, the rat was placed in a stereotaxic apparatus and a small craniotomy was performed in order to insert a 30-gauge needle into the right lateral ventricle. The needle connected with PE-10 polyethylene tube for i.c.v. injection was introduced stereotaxically: the tip of the needle located in the right lateral ventricle was at 0.8 mm posterior to bregma, 1.4 mm lateral to midline, and 3.8 mm below the surface of the skull. For i.t. catheterization, the occipital crest of the skull was exposed and the atlanto-occipital membrane was incised on its midline. A catheter (PE-10) was inserted through the slit and passed caudally to the L_6-level of the spinal cord. A transurethral bladder catheter (PE-50) connected to a pressure transducer was used to record the bladder pressure during cystometrograms when the bladder was filled with a constant infusion (0.04 ml/min) of physiological saline and allowed to empty around the catheter. Drugs used were LY215490, a competitive AMPA receptor antagonist and MK-801, a non-competitive NMDA receptor antagonist. All values are expressed as mean ± S.E.M. Repeated measures analysis of variance (ANOVA) and Dunnett multiple comparisons test were used when appropriate for statistical data analysis. For all statistical tests, $P<0.05$ was considered significant. Parameters measured included: bladder contraction amplitude (BCA), pressure threshold for inducing micturition (PT), volume threshold for inducing micturition (VT), residual volume (RV) and voiding efficiency (VE).

Results

Table 1: Effects of LY215490 on the voiding parameters in the urethane-anesthetized rats

i.c.v. (µg) (n=6)	BCA (cm H2O)	PT (cm H2O)	VT (ml)	RV (ml)	VE (%)
0	37 +/- 3	2.6 +/- 0.4	0.67 +/- 0.17	0.39 +/- 0.13	40 +/- 9
0.01	33 +/- 5	6.5 +/- 1.8	1.06 +/- 0.31	0.99 +/- 0.31*	14 +/- 5**
0.1	8 +/- 5**	22.5 +/- 3.5**	1.84 +/- 0.15**	1.82 +/- 0.15**	1 +/- 1**
1	4 +/- 4**	22.9 +/- 3.5**	1.93 +/- 0.15**	1.92 +/- 0.15**	1 +/- 1**
i.t. (µg) (n=5)					
0	29 +/- 3	2.4 +/- 0.4	1.11 +/- 0.17	0.74 +/- 0.21	38 +/- 9
0.01	28 +/- 3	2.3 +/- 0.4	1.10 +/- 0.14	0.76 +/- 0.24	38 +/- 15
0.1	12 +/- 5**	7.5 +/- 2.8	1.77 +/- 0.20*	1.65 +/- 0.22*	8 +/- 4*
1	8 +/- 5**	9.3 +/- 2.4*	1.93 +/- 0.25**	1.87 +/- 0.27**	5 +/- 3*

Table 2: Effects of MK-801 on the voiding parameters in the urethane-anesthetized rats

i.c.v. (µg) (n=5)	BCA (cm H2O)	PT (cm H2O)	VT (ml)	RV (ml)	VE (%)
0	32 +/- 2	4.1 +/- 0.7	0.83 +/- 0.18	0.54 +/- 0.17	39 +/- 9
0.6	31 +/- 2	6.4 +/- 2.1	0.99 +/- 0.15	0.83 +/- 0.15	17 +/- 7
6	6 +/- 3**	25.4 +/- 5.4**	1.56 +/- 0.11**	1.55 +/- 0.12**	0.8 +/- 0.5**
60	4 +/- 2**	21.6 +/- 5.4**	1.66 +/- 0.16**	1.66 +/- 0.17**	0.4 +/- 0.4**
i.t. (µg) (n=6)					
0	26 +/- 1	4.2 +/- 0.5	1.08 +/- 0.17	0.41 +/- 0.14	61 +/- 11
0.6	27 +/- 2	3.4 +/- 0.3	1.04 +/- 0.16	0.42 +/- 0.14	57 +/- 12
6	26 +/- 2	6.4 +/- 1.6	1.26 +/- 0.23	0.72 +/- 0.22	42 +/- 15
60	12 +/- 4**	13.1 +/- 5.5	1.44 +/-0.24*	1.31 +/- 0.30*	14 +/- 11*

Conclusions

I.c.v. as well as i.t. administration of AMPA or NMDA glutamatergic receptor antagonists suppressed BCA, increased PT, RV and VT, and decreased VE, in the urethane-anesthetized rat. These data indicate that AMPA and NMDA glutamatergic mechanisms in the brain as well as the spinal cord are essential for controlling micturition.