324

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PROSTAGLANDIN E SYNTHESIS ARE RELATED TO BLADDER OVERACTIVITY FOLLOWING CEREBRAL INFARCTION IN THE RAT

Aims of Study
Development of bladder overactivity (BO) caused by cerebral infarction is believed to require transcription in the pontine micturition center (PMC). We previously reported that the expression of cyclooxygenase-2 (COX-2) mRNA was mediated by the activity of an NMDA (N-methyl-D-aspartate) receptor in the PMC and necessary for the development of BO. This study was undertaken to examine whether the expression of prostaglandin (PG) E or D synthase, downstream gene of COX-2, was related to BO induced by left middle cerebral artery (MCA) occlusion and the concentration of several kinds of prostaglandins in the brain.

Methods
Cerebral infarction (CI) was induced by left MCA occlusion in female SD rats. Awake rats were cystometrically examined. Specimens were obtained from the dorsal pontine tegmentum (DPT) 0.25, 1, 3, 5, 12, and 24 hours after MCA occlusion or a sham operation (SO). The effects of MK-801 (0.1 mg/kg, iv), an NMDA receptor antagonist, on PGES or PGDS expression following MCA occlusion were studied. Expressions of PGES and PGDS in the DPT were monitored with real-time PCR. The concentration of several kinds of prostaglandins (PGE2, PGD2, 6-keto PGF1 alfa, PGF2 alfa, Thromboxane(TX) B2) were measured by EIA kit respectively in the area of the left infarcted cerebrum, the right non-infarcted cerebrum and the DPT at the 0, 1, 3, 5, 12 and 24 hours after left MCA occlusion.

Results
Bladder capacity of CI rats was significantly reduced 1-24 hours after MCA occlusion. One hour after MCA occlusion, PGES and PGDS mRNA expression had significantly increased, as compared to that in SO rats. PGES and PGDS expressions remained consistently higher than those in SO rats at least 12 hours after MCA occlusion. Pretreatment with MK-801 inhibited the development of bladder overactivity and significantly reduced the expression of PGES mRNA in the DPT. The expression of PGDS mRNA was not influenced by pretreatment with MK-801. The concentration of all kinds of prostaglandins increased in the area of the left infarcted cerebrum at 1 hour after left MCA occlusion and increased again at 12-24 hours after left MCA occlusion except that of TXB2. All prostaglandin levels increased slightly in the area of the right non-infarcted cerebrum. In the DPT, the concentration of PGE2 and 6-keto PGE1 alfa inceased at 3 and 24 hours after left MCA occlusion diphasicly.

Conclusions
These results indicate that the development of BO following MCA occlusion is mediated by the activity of an NMDA receptor and accompanied by increases in PGES mRNA expression and the concentration of PGE2 in the DPT.