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Title: EXPRESSION OF CYCLOOXYGENASE ISOFORM IN THE PONTINE TEGMENTAL AREA OF RATS WITH OVERACTIVE BLADDER FOLLOWING CEREBRAL INFARCTION

Aims of Study

To investigate the expression of cyclooxygenase (COX) isoform in the pontine tegmental area (PTA) of rats with overactive bladder induced by cerebral infarction (CI). The influence of COX-2 inhibitor on bladder overactivity was examined.

Methods

CI was induced by left middle cerebral artery occlusion (MCAO) in female Sprague-Dawley rats. Bladder activity was monitored with continuous infusion cystometrography of conscious rats. Specimens were obtained from the PTA 1, 3, 5, 12 and 24 hours after CI or a sham operation (SO). The effects of MK-801 (0.1 mg/kg, i.v.), an NMDA (*N*-methyl-D-aspartate) glutamatergic receptor antagonist, on bladder activity and COX-1 and -2 expression following MCAO were studied. Real-time RT-PCR with the LightCycler system was performed to evaluate CI influences on gene expression in the PTA. The effects of NS-398 (0.01 - 10 mg/kg, i.v.), a COX-2 inhibitor, on bladder activity was examined.

Results

Bladder capacity of CI rats was significantly reduced 1 - 24 hours after MCAO as compared to that of SO rats ($p<0.05$ or 0.01). One hour after MCAO, COX-2 mRNA expression had significantly increased, to 25.3±4.1 in terms of its density relative to the outer control (sample obtained immediately after MCAO), as compared to that in SO rats ($p<0.05$). It returned to the control level within 12 hours after MCAO. The expression of COX-1 was not influenced by MCAO. Pretreatment with MK-801 inhibited the development of bladder overactivity and significantly reduced the expression of COX-2 mRNA in the PTA ($p<0.05$).

Treatment with NS-398 before MCAO prevented the development of bladder overactivity dose-dependently□$p<0.01$), and did not influence infarction volume.

Conclusions

These results indicate that the development of bladder overactivity following MCAO is mediated by the activity of an NMDA receptor and accompanied by an increase in COX−2 mRNA expression in the PTA. Further research on the COX−2 molecular mechanism in the brain related to bladder overactivity may lead to pharmacological therapy which targets the micturition center.