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NEUROGENIC DETRUSOR OVERACTIVITY INDUCES CHANGES IN ATP LEVEL AND MRNA EXPRESSION OF SEVERAL RECEPTORS IN THE BLADDER

Hypothesis / aims of study

Although some studies have provided many new insights into the bladder sensory pathways, the neural mechanisms that regulate bladder function are still too complex to be elucidated. Recently, a rat model of impaired suprapontine regulatory system induced by cerebral infarction, is considered to be a useful tool for understanding the brain mechanisms on detrusor overactivity. In order to observe the change in the bladder following impairment of the brain, we used this animal model. We examined the mRNA expression of different receptors and the amounts of chemical mediators in the bladder.

Study design, materials and methods

Eighteen of 9 week-old female Sprague-Dawley rats were divided into 2 groups of 9 rats each as CI (Cerebral Infarction), and SO (Sham Operated). Left middle cerebral artery was occluded using 4-0 monofilament nylon thread to create CI model. Bladder cystometric examination and forebrain slices TCC (2% 2,3,5-triphenyl chloride) staining were performed to check the detrusor overactivity and cerebral ischemic status.
Bladder tissues were harvested 6 hours after left middle cerebral artery occlusion (MCAO). Total RNAs were extracted, and 1 μg of RNA of each sample was used to synthesize cDNA. Quantitative PCR reactions of COX1, COX2, M1, M2, M3, ASIC1, ASIC2, ASIC3, P2X3 and TRPV1 were performed with SYBR green PCR Master Mix Kit.
ATP and PGE2 amounts in bladder tissue were measured with lufiferin-luciferase assay and ELISA assay, respectively.

Results

Compared with that of SO rats, the mRNA expression of P2X3, ASIC2, TRPV1, M2 and M3, respectively, increased 3.15±0.21, 4.04±0.52, 1.77±0.31, 3.74±0.71, 1.97±0.26 times in urinary bladder 6 hours after MACO, while the mRNA expression of COX1, COX2, M1, ASIC1, ASIC3 showed no obvious change.
The ATP amount in bladder of CI rats was 2.24±0.37 times than that of SO rats 6 hours after MCAO, however, difference in PGE2 between the CI and SO rats was not significant.

Interpretation of results

These results suggest that the receptors of P2X3, ASIC2, TRPV1, M2 and M3 are dynamically activated in the bladder 6 hours after the brain ischemia. This kind of receptors-triggered feedback system in the bladder is beneficial to explain the detrusor overactivity and reduced bladder capacity induced by CI.
ATP production and overexpression of P2X3 receptor in the bladder may play a role in the development of detrusor overactivity following cerebral infarction.

Concluding message

The receptors mRNA expression of P2X3, ASIC2, TRPV1, M2 and M3 and amount of ATP significantly increased in the overactive bladder induced by cerebral infarction within 6 hours.

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Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
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