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BLADDER FUNCTION IN MICE LACKING TRPV4

Hypothesis / aims of study

Transient receptor potential vanilloid 4 (TRPV4) is activated by heat or hypoosmolarity. Recent study reported that TRPV4 might be responsible for cutaneous mechanosensation (1). A role of TRPV1, a member of transient receptor potential family, in bladder function of mice was described previously (2). However, the contribution of TRPV4 to bladder function remains unclear. Therefore, we evaluated the bladder function in mice lacking the TRPV4 (TRPV4 KO mice).

Study design, materials and methods

1. Metabolic cage analysis.

Thirteen-week-old male TRPV4 KO mice (n = 35; weight, 26.04 ± 0.29 g) and matching wild-type mice (WT mice; n = 27; weight, 25.44 ± 0.29 g) were used. Each mouse was placed in a metabolic cage connected to a digital scale and personal computer. After mice were acclimatized for 2 days in the cage, voiding frequency and volume per void were recorded for 47hours. Each mouse was provided with free access to food and water. The mouse was subject to a 12/12-hour dark/light photocycle with lights on at 7:00 a.m. Voiding time and urine volume were recorded continuously at 1-minute intervals. We evaluated three parameters (voiding frequency, volume per void and total urine volume) at three kinds of periods (during the light photocycle, during the dark photocycle and during total 47hours).

2. Cystometry in conscious restrained mice.

Ten-week-old male TRPV4 KO mice (n = 4; weight, 24.25 ± 0.56 g) and matching WT mice (n = 5; weight, 25.45 ± 0.41 g) were anesthetized with sevoflurane for surgical insertion of an intravesical catheter (PE-50). After the surgery, cystometry was performed in conscious restrained mice by infusing saline into the bladder at a constant rate (0.5 ml/hr).

Data are expressed as mean ± S.E.M. The Mann-Whitney test was used when appropriate for statistical data analysis with $p<0.05$ considered statistically significant.

Results

1. Metabolic cage analysis.

Mean volume per void was significantly larger in TRPV4 KO mice (12 hours' light, 0.30 ± 0.03 ml; 12 hours' dark, 0.26 ± 0.02 ml; 47 hours, 0.25 ± 0.02 ml) than in WT mice (12 hours' light, 0.13 ± 0.02 ml; 12 hours' dark, 0.13 ± 0.02 ml; 47 hours, 0.12 ± 0.02 ml; $p<0.001$) at each period. Total urine volume was significantly larger in TRPV4 KO mice (12 hours' light, 0.68 ± 0.07 ml; 12 hours' dark, 1.65 ± 0.09 ml; 47 hours, 4.65 ± 0.22 ml) than in WT mice (12 hours' light, 0.34 ± 0.05 ml; 12 hours' dark, 0.79 ± 0.09 ml; 47 hours, 2.30 ± 0.18 ml; $p<0.001$) at each period. There was no significant difference in voiding frequency between TRPV4 KO mice and WT mice at each period.

2. Cystometry in conscious restrained mice.

Intercontraction interval was significantly larger in TRPV4 KO mice (708.5 ± 76.2 s) than in WT mice (324.3 ± 54.9 s, $p<0.05$). There was no significant difference in maximal voiding pressure between TRPV4 KO mice and WT mice.

Interpretation of results

Increase in total urine volume in TRPV4 KO mice indicated that TRPV4 KO mice might impair osmotic sensation and control of urine production. TRPV4 might be involved in micturition reflex of mice, because both mean volume per void and Intercontraction interval were increased in TRPV4 KO mice.

Concluding message

These findings indicated that TRPV4 might have an important role in regulating bladder function.

References

(1) Neuroscience letters 353: 189-192, 2003.
(2) Nature Neuroscience 5: 856-860, 2002.

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