

## 論文の内容の要旨

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論文題目 Functional Roles of Transient Receptor Potential Melastatin 8 (TRPM8) Channels in the Cold Stress-Induced Detrusor Overactivity Pathways in Conscious Rats (ラット冷えストレス誘発排尿筋過活動の機序における温度感受性受容体(TRPM8) の機能的役割の考察)	
(論文の内容の要旨)  <b>Aims:</b> To investigate functional roles of transient receptor potential melastatin 8 (TRPM8) channels, we determined if TRPM8 channel antagonist could inhibit the detrusor overactivity induced by menthol spray and low temperature.  <b>Methods:</b> Two days prior to cystometric investigation, the bladder of 10-week-old Spague-Dawley rats were cannulated. After 20 min of baseline cystometry period at room temperature (RT: 27±2°C), the TRPM8 channel antagonist, N-(4-tert-butylphenyl)-4-(3-chloropyridin-2-yl)pi-perazine-1-carboxamide (BCTC), or vehicle, was administered through a jugular vein catheter (n=6). A 90% menthol solution, which was TRPM8 channel agonist, was sprayed onto rump to leg skin once every 5 min for 20 min, and then cystometric measurements were repeated. After a 30-min recovery period, the rats were intravenously administered 0.1 µmol/kg BCTC. Five minutes later, they were again sprayed, and then cystometric measurements were recorded. In separate experiments, cannulated rats were intravenously administered 0.001, 0.01, or 0.1µmol/kg BCTC (n=6 each dose) at RT. Five minutes later, they were transferred to expose low temperature (LT: 4±2°C). During LT exposure, the cystometric measurements were recorded for 20 min.  <b>Results:</b> The rats sprayed with menthol exhibited the decrease of the voiding interval, micturition volume, and bladder capacity. After treatment of BCTC, the rats did not show these decreases. Exposure to LT elicited detrusor overactivity characterized with decreased voiding interval, micturition volume, and bladder capacity. However, at 0.01 and 0.1µmol/kg, BCTC inhibited the cold stress-induced detrusor overactivity.  <b>Conclusions:</b> TRPM8 channels antagonist, BCTC, inhibited detrusor overactivity in rats sprayed with menthol. Furthermore, the BCTC inhibited the cold stress-induced detrusor overactivity. Therefore, TRPM8 channels expressing within the skin mediate detrusor overactivity elicited by menthol spray and exposure to low temperature.	