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DOES SALT RESTRICTION RECOVER URINE STORAGE DYSFUNCTION INSALT-SENSITIVE RATS?

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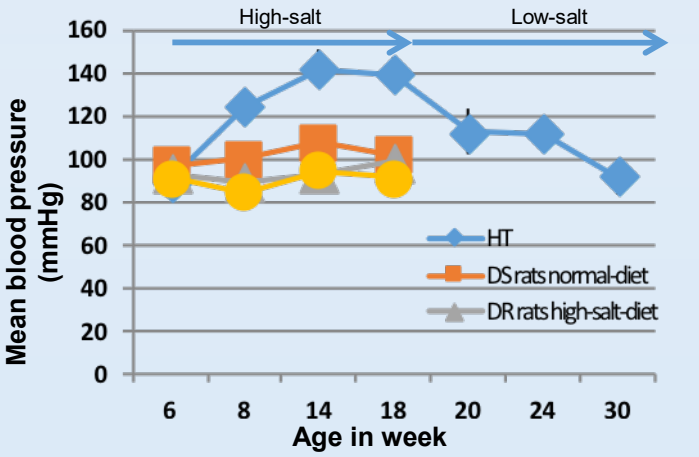
Hypothesis / aims of study

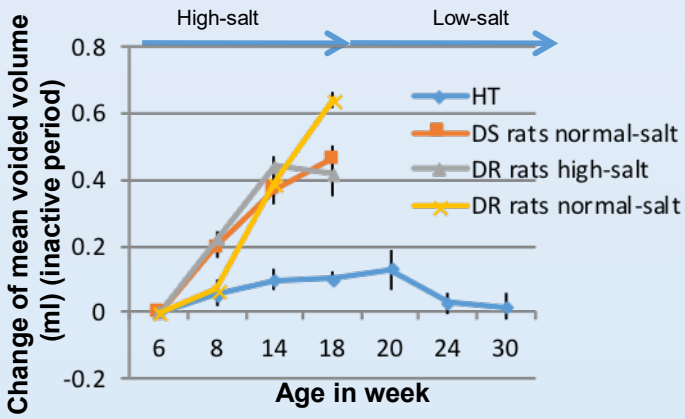
Clinical observations indicate that many non-urological diseases such as hypertension (HT), dyslipidemia and diabetes are associated with lower urinary tract symptoms (LUTS). Lifestyle factors, especially those that result in HT, can influence LUTS. HT is one of the risk factors for worsening lower-urinary-tract symptoms and degrading the improvement of storage symptoms by α1-blocker . The spontaneous hypertensive rats (SHRs) provides researchers a genetic model of HT, and is considered a valuable tool for exploring the pathogenesis of urine storage dysfunction related to HT. SHRs exhibit increased urinary frequency and non-voiding detrusor contractions compared with normotensive Wister Kyoto rats. The bladder storage dysfunction in SHRs reportedly depends on multiple factors including overproduction of nerve growth factor in the smooth muscle, autonomic hyperinnervation, altered caveolae-mediated purinergic signaling, enhanced sensitivity of afferent stimulation, and decreased blood supply to the bladder. In humans, however, hypertension develops by both genetic and environmental factors including lifestyle factors such as a high-calorie diet, excessive salt intake and stress. Therefore, it is necessary to examine which other factors essentially contribute to the development of storage dysfunction associated with HT. Therefore, the use of other types of HT models is of great importance to clarify the mechanisms leading to urine storage dysfunction.The spontaneous hypertensive rat is considered as a valuable tool for exploring the pathogenesis of detrusor overactivity, but pathological changes in the bladder are thought to be irreversible. We previously reported that salt loading induced HT and storage dysfunction in inactive period of Dahl salt-sensitive rats (DS rats). In the present study, we investigated the underlying mechanisms of salt loading-induced storage dysfunction and whether these changes could be reversible by the restriction of high salt diet.

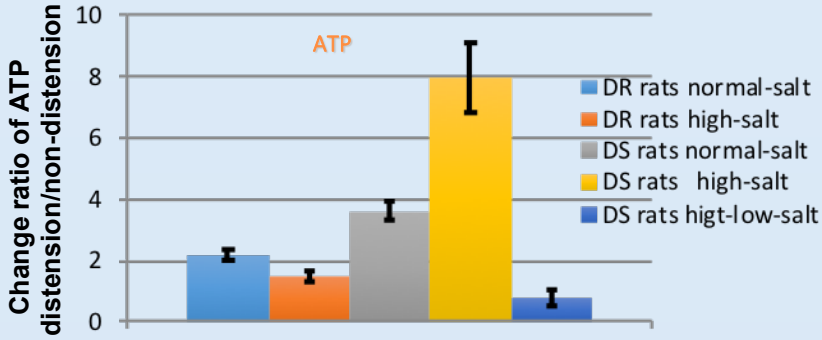
Study design, materials and methods

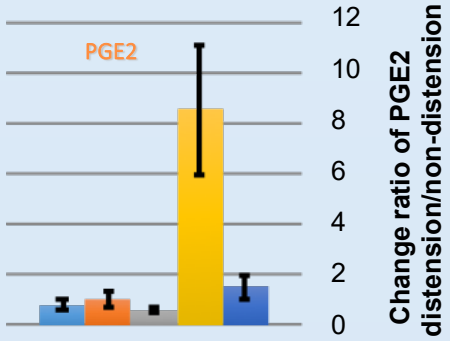
Six-week-old male DS rats were fed with high-salt(8%) diet and 35ml water/day for 12 weeks. Blood pressure was measured through the tail artery in a non-anesthetized state. Urine volume and frequency were recorded all day long in a metabolic cage. We calculated the inactive period (sleeping) urine volume, which was defined as urine volume during inactive period divided by 24-h urine output. We changed the bait to low salt (0.08%) diet after 12 week-high salt. We measured blood pressure and calculated the inactive period urine volume 12 weeks after the diet changed. Furthermore, changes in bladder blood flow were determined with a laser speckle blood flow imaging system (Omegazone OZ-1; Omegawave, Tokyo). And the amount of ATP and PGE2 from the collected solution released fromthe stretched bladder epithelium at the age of 30 weeks was measured according to the method described by Tanaka et al.

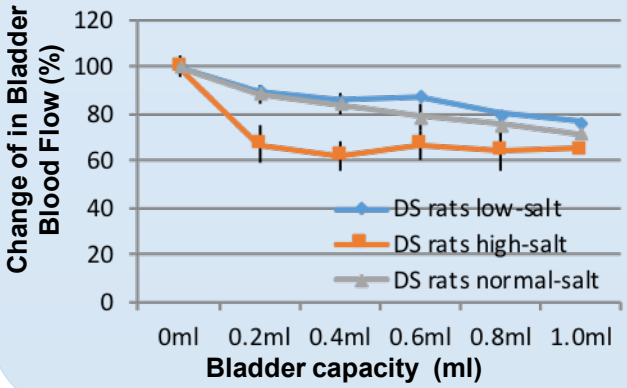
Results & Discussion











A 20-to 30- mmHg increase in systolic and diastolic blood pressure was noted in DS rats after 2- week- salt loading. In the inactive period, the mean voided volume gradually increased in Dahl salt-resistant rats (DR rats) fed with a normal or high-salt diet, while it did not change in DS rats fed with a high-salt diet. There were significant differences in mean voided volume after 10- week- salt loading between DR and DS rats fed with a high-salt diet.

After having changed a diet, the blood pressure decreased. The weight increased, and the quantity of urination decreased, but the voided volume was not improved. Because blood pressure was improved by a meal, the bladder blood flow was improved.

ATP and PGE2 release from the urothelium in DS rats fed the low-salt diet decreased. These became same as approximately normal quantity.

Concluding message

Although salt restriction recovered the bladder blood flow, 12 weeks might be too short to recover from salt loading changes in the bladder. Or neurodegeneration may be hard to return to the origin of beginning.