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## LONG-TERM CALORIC RESTRICTION MAY PREVENT *IN VIVO* LOWER URINARY TRACT DYSFUNCTION ASSOCIATED WITH AGEING IN MALE RATS

### Hypothesis / aims of study

A recent study using *in vitro* investigations revealed that ageing causes an impaired detrusor contractility, decreased expression of M3 muscarinic receptors and bladder wall fibrosis in male rats (1). Furthermore, interestingly, long-term caloric restriction (CR) prevented these age-related changes (1). Several groups have evaluated age-related changes in rodent bladder function but only a few used *in vivo* cystometry (CMG) to characterize the changes (2, 3). In addition, to date, the impact of long-term CR on *in vivo* bladder function has not been investigated. In this study, we aimed to clarify the age-related changes in *in vivo* lower urinary tract function, and impact of CR on the age-related changes by using conscious CMG measurements.

### Study design, materials and methods

Fischer 344 male rats were divided into three groups: young (6 months-old, Y: N = 7), old (26-28 months-old) fed fully *ad libitum* with normal food (O+AL: N = 7) or calorie restriction (O+CR: N = 8). The O+CR group has been fed the same normal food only three days (Monday, Wednesday and Friday) a week since 6 weeks-old.

Three days after a catheter-implantation through the bladder dome, single CMG measurements were performed with saline-instillation at a rate of 6 mL/hour under a conscious and restraint condition. At the end of each micturition, the residual volume was precisely measured by collecting naturally dripping of post-void residual through the bladder catheter for 10 minutes. After stable and reproducible recordings were obtained, 4 micturition cycles were averaged and the following parameters were analysed: basal pressure, threshold pressure, maximum pressure, non-voiding contractions (NVCs), voided volume, residual volume, bladder capacity, mean flow rate, voiding efficacy, and bladder compliance. Non-voiding contractions (NVCs) were defined as bladder contractions of which amplitude was more than 3 cmH<sub>2</sub>O observed during the filling phase.

### Results

The O+AL group had higher body weight than the other two groups, and the O+CR group had lower body weight than the other groups. In contrast, there were no significant differences in the mean bladder weight among the three groups (Table1).

The O+AL group showed higher threshold pressure, lower bladder compliance and the increased numbers of NVCs compared with Y group. The O+AL group also showed increased residual volume and decreased voiding efficiency compared with the O+CR as well as Y group. The remaining other parameters investigated were not significantly different among the three groups (Figures 1 and 2).

### Interpretation of results

Although maximum pressure did not change with ageing, increased residual volume and decreased voiding efficiency were observed in the O+AL group and these changes were not observed in the O+CR group. These results suggest that ageing impairs the voiding function and long-term CR has a preventive effect on the age-related voiding dysfunction. These present *in vivo* findings support the previous *in vitro* findings that ageing caused an impaired detrusor contractility (1).

Higher threshold pressure and lower bladder compliance observed in the O+AL group may be linked to the previous report (1) that ageing causes fibrotic changes in the bladder wall. In addition, the O+AL group showed frequent NVCs. These parameters did not differ from the O+CR group, suggesting that ageing also causes the storage dysfunction, but a preventative effect of CR on these age-related storage dysfunctions may be limited.

### Concluding message

The present *in vivo* CMG investigations demonstrated the age-related voiding and storage dysfunctions in the rat and also that long-term CR may have preventive effects on the age-related voiding dysfunction rather than the storage dysfunction.

Table1. The body weights and bladder weights in each group

	Y (N=7)	O+AL (N=7)	O+CR (N=8)
Body weight (g)	366.86 ± 4.89 <sup>##</sup>	402.85 ± 13.46 <sup>*.##</sup>	252.63 ± 5.96 <sup>**</sup>
Bladder weight (mg)	155.86 ± 9.71	162.71 ± 10.29	148.38 ± 17.92

The numerical values are expressed as mean ± SEM.

\* p<0.05, \*\* p<0.01: significant differences from Y (Tukey's test)

<sup>##</sup> p<0.01: significant difference from O+CR (Tukey's test)

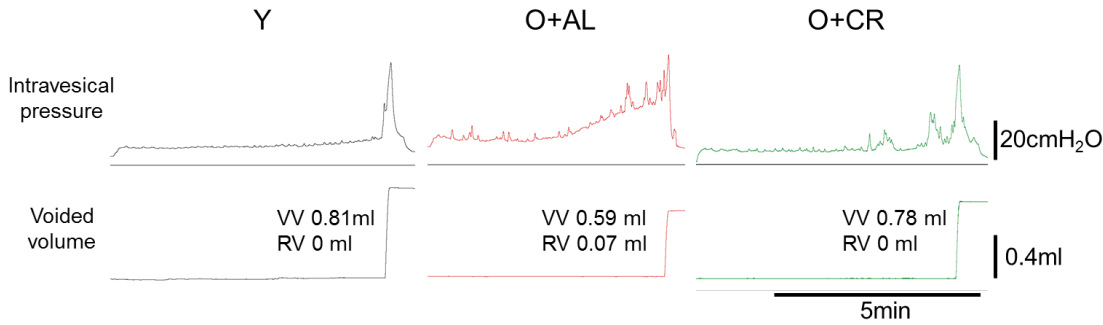


Figure1. Representative tracings of intravesical pressure and voided volume during CMG with constant saline-instillation (6.0 ml/hour) taken from a young rat (Y), an old rat fed with normal food (O+AL) and an old rat with caloric restriction (O+CR) VV: Voided Volume, RV: Residual Volume

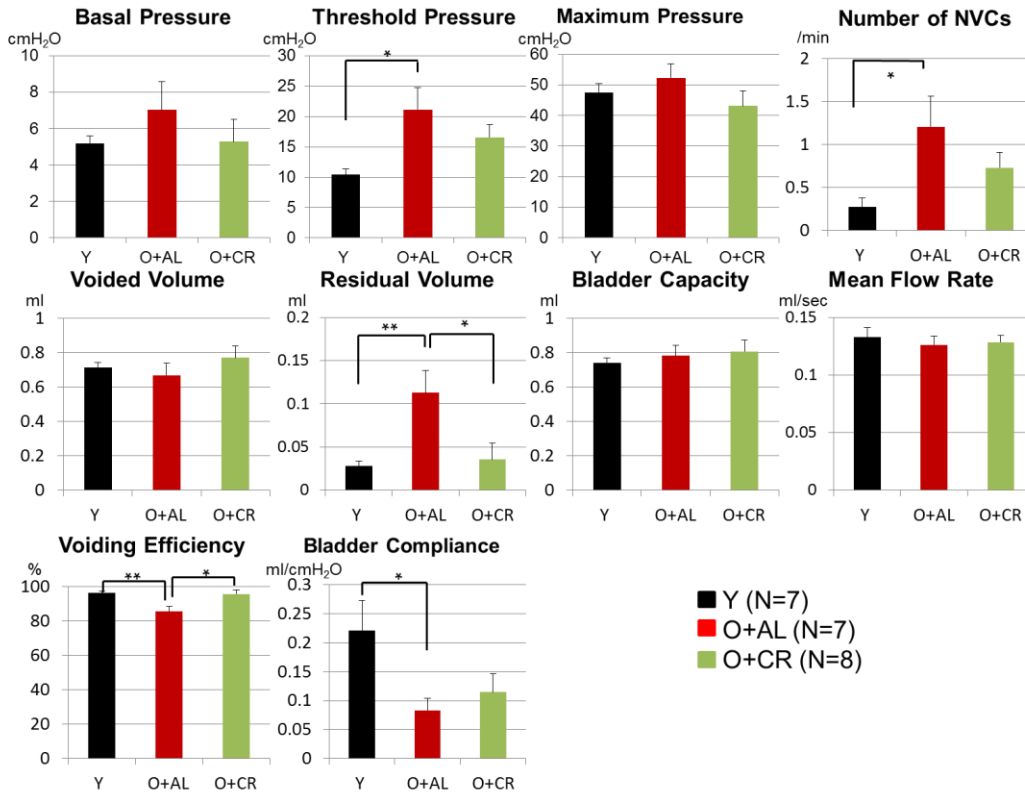


Figure2. Comparative results of CMG parameters among the three groups

The values are expressed as mean  $\pm$  SEM.

Y: young rats, O+AL: old fed with normal food, O+CR: old with caloric restriction

NVCs: Non-voiding contractions

\*p<0.05, \*\*p<0.01: significant differences between two groups (Tukey's test)

#### References

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#### Disclosures

**Funding:** None **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Rat **Ethics Committee:** Animal Ethics Committee, The University of Tokyo Graduate School of Medicine