

The LOU rat, a new model of healthy aging to study bladder diseases

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Background: Aging is associated with the development of several benign urological conditions such as voiding dysfunction and benign prostatic hyperplasia. Using a rodent model of healthy aging (the LOU rats), we examined the effect of partial urethral obstruction on proteins involved in bladder contraction and protein markers of OAB (NGF and proNGF).

Methods: LOU rats aged 6 or 36 months were subjected to partial bladder urethral obstruction (PUO) for 2 weeks. Conscious cystometry was then carried out to assess voiding parameters, followed by in vitro assessment of detrusor contractile properties. Tissue proteins were examined by immunoblotting and microscopy (Masson trichrome and hematoxylin-eosin).

Results: Body weight and glycaemia were not affected by age or surgery. PUO increases significantly the ratio bladder mass/body weight with increased thickness and fibrosis of the bladder wall as revealed by histology. Cystometry parameters were unchanged by PUO in old LOU rats while the inter-micturition intervals, micturition volume and bladder capacity were increased in young LOU rats. Contraction of bladder strip in vitro was not affected by age or PUO, which could be related to an increase of smoothelin content with PUO in both age groups, a protein of the cytoskeleton essential to detrusor contraction. On the other hand, levels of smooth muscle myosin heavy chain 1 (SMMHC1), alpha- and beta- actin and connexin were not different across all groups. CK17 expression, an index of urothelial integrity, was also similar between groups. PUO in old rats only led to an increase in E-cadherin, a junction protein essential in cell

proliferation, as well in phospho-JNK, an index of detrusor contractility. Finally, the ratio NGF/proNGF, a marker of OAB was decreased with PUO in both groups of animals, with decreased expression of p75^{NTR} and unchanged expression of its cofactor sortilin.

Conclusions: Young LOU rat bladders respond to PUO by increasing their bladder capacity and micturition volume, while old ones maintain the same voiding parameters. The old LOU rats, a model of healthy aging, showed several changes in protein expression in response to PUO, all the while maintaining their voiding efficiency after PUO. Together, our findings introduce a new interesting model to study the effect of age and the evolution of diseases affecting the bladder.