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A NEW EXPERIMENTAL RAT MODEL COMBINING BOTH DYNAMIC AND STATIC COMPONENTS OF VOIDING LUTS/BPH: CONSEQUENCE ON BLADDER FUNCTION

Hypothesis / aims of study
Lower urinary tract symptoms resulting from benign prostatic hyperplasia (BPH) comprise storage symptoms, currently largely encompassed by the term overactive bladder (OAB) and which are more specifically related to bladder dysfunction. They also comprise voiding symptoms due to prostate enlargement (static component) and/or an increased □-adrenergic tone of prostatic, urethral and/or bladder neck smooth muscles (dynamic component).
In order to explore new effective therapies for the treatment of LUTS, an understanding of the physiopathological mechanisms involved in the development of this pathology is required. In this regard, animal models that most closely resemble the human pathological condition are very useful. Therefore, the aim of this study was to evaluate if spontaneously hypertensive rats (SHR), which present an increase in the □-adrenergic tone of the bladder outlet, supplemented with testosterone could represent a new and complete model of LUTS/BPH, particularly in terms of bladder dysfunction.
Study design, materials and methods
Four groups of animals (12 weeks; n=7 per group) were considered: 2 groups treated with testosterone (T, daily sub-cutaneous treatment 3 mg/kg during 3 weeks): wistar kyoto rats-testosterone (WKY-T), SHR-T and 2 groups without T treatment: WKY and SHR.
Cystometry experiments were performed in conscious rats (bladder filing rate: 50 µl/min). The following urodynamic parameters were analysed: maximal amplitude of micturition pressure (MP); baseline intravesical pressure (BP); pressure threshold for inducing micturition (PT); intercontraction interval, (ICI); voided volume; amplitude and frequency of non-voiding contractions (NVC). At the end of the experiment, rats were euthanized. Prostate and bladders were harvested for evaluation of prostate enlargement and bladder hypertrophy. Statistical analysis was performed using Student's t-test.
Results
T treatment in WKY and SHR rats induced an increase in prostate and bladder weights compared to WKY and SHR without T treatment ($p<0.001$ for the prostate weights and $p<0.05$ for the bladder weights).
WKY-T displayed a significant increase in MP ($p<0.05$) and an increase in NVC ($p<0.05$ for the frequency). SHR displayed a significant decrease in the ICI ($p<0.05$) and in the voided volume ($p<0.05$). The filling phase of SHR was also associated with an increased in NVC compared to WKY ($p<0.05$ and $p<0.01$ for the amplitude and the frequency respectively).
SHR-T rats exhibited decreases in voided volume ($p<0.05$) and in ICI which were more pronounced than SHR ($p<0.05$). The frequency of NVC in SHR-T was increased compared to SHR. Moreover, PT tended to decrease in SHR-T compared to SHR.
Interpretation of results
WKY-T displayed an increase in micturition pressure in accordance with the bladder obstruction caused by the prostate enlargement induced by T. SHR exhibited the abnormal bladder function which has previously been described. Interestingly, SHR-T exhibited an exacerbated bladder dysfunction compared to SHR. Such an increase in bladder dysfunction is probably due to the combination of testosterone-induced prostate enlargement and the increase in □-adrenergic bladder outlet smooth muscle tone.
Concluding message
The model of SHR supplemented with testosterone is the first animal model of BPH which combines both the static and the dynamic component of voiding symptoms associated with bladder dysfunction. It would therefore be of great interest to assess the efficacy of new therapy for the treatment of LUTS/BPH.

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What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**All procedures were performed in accordance with the legislation on the use of laboratory animals (NIH publication N°85-23, revised 1996) and Animal Care Regulations in force in France as of 1988 (authorization from competent French Ministry of Agriculture – Agreement No. A91-471-109, May 2009).**