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PHYSIOLOGICAL AGING AND BLADDER FUNCTION: IN VIVO AND IN VITRO STUDIES IN MALE RATS

Hypothesis / aims of study

The prevalence of bladder dysfunctions increases with age.[1] In humans it is difficult to separate changes related to exogenous factors from alterations directly related to the aging process *per se*. Some of these confounding variables can be avoided by studying age-related changes in an animal model. This report focused on evaluating the impact of age on bladder function both *in-vivo* and *in-vitro*, as well as on characterization of the corresponding morphological changes.

Study design, materials and methods

Two groups of male Fisher/Brown Norway rats were used in the study: young (4-6 months) and old (>28-30 months). Cystometric studies were conducted on conscious, freely moving animals. After cystometry, tissue strips derived from the bladder body were used for *in vitro* studies of muscarinic receptor activation and electrical field stimulation (EFS), and for histological examination.

Results

Old rats had higher bladder weights than young – however, the ratio bladder weight/body weight did not change (Table 1). Bladder capacity, residual volume and spontaneous activity (non-voiding contractions) were higher in old than in young animals (Table 2). The responses of bladder strips to both carbachol and EFS were significantly lower in old rats when compared to young rats (Figure 1). Histological examination showed a thinning of the urothelium, lower muscle mass and higher collagen content in the bladders of old compared to young rats (Figure 2).

Table 1. Significant differences between bladder weight and rat body weight in old and young rats.

	Bladder weight (mg)	Rat body weight (g)	Bladder weight/ Rat body weight
Old (n=16)	330.13±13.07*	617.63±15.58*	5.33×10^{-4}
Young (n=15)	161.53±6.14	314.82±7.7	5.18×10^{-4}

The n means the number of rats.
*: Significantly different from young rats (student t test).

Table 2. The cystometric measurements in old and young rats.

	BC	RV	SA	MF	MV	BP	TP	MP	IMP	BCom
Old (n=16)	1.864* ±0.172	0.308* ±0.065	9.468* ±1.242	9.606* ±1.008	1.556* ±0.130	11.955* ±1.541	24.749 ±2.344	56.404 ±6.755	21.378* ±1.915	0.175 ±0.024
Young (n=15)	1.169 ±0.114	0.121 ±0.034	3.683 ±0.892	6.163 ±0.434	1.049 ±0.119	8.100 ±1.130	22.147 ±2.117	69.593 ±3.155	11.051 ±1.250	0.113 ±0.025

The n means the number of rats.
*: Significantly different from young rats (student t test).
BC: Bladder Capacity, RV: Residual volume, SA: Spontaneous activity, MF: Micturition frequency, MV: Micturition Volume, BP: Basal pressure, TP: Threshold pressure, MP: Micturition pressure, IMP: Intermicturition pressure, Bcom: Bladder compliance

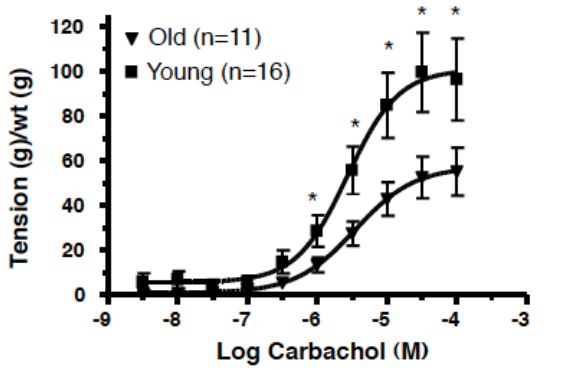

Fig 1: Concentration response curves to Carbachol on urinary bladder strips taken from old and young rats

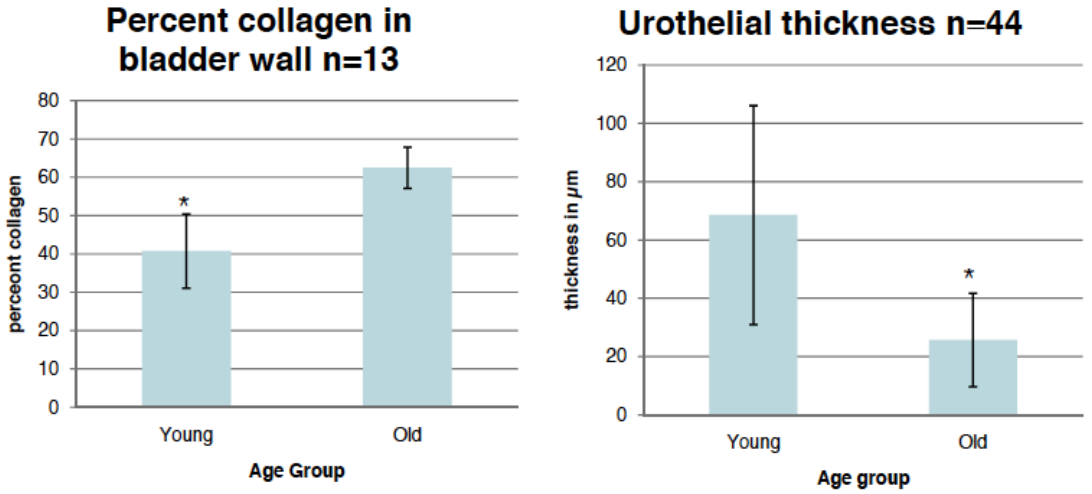

Fig 2: Quantification of histological data showed a significant difference in the amount of collagen deposition as well as urothelial thickness between young and old animals.

Interpretation of results

Physiological aging alters bladder function in male rats, even when external factors are kept constant.[2] Thus in old rats, bladder capacity, residual urine and spontaneous activity are higher and responses to muscarinic receptor stimulation and EFS lower than in young rats. Moreover, older animals have a higher collagen content and a thinner urothelial lining. Such changes correspond to findings in aging human bladders [3], supporting the view that the Fisher/Brown Norway rat is a useful model for study of age-related changes in bladder function.

Concluding message

The results of our study clearly demonstrate marked age-related differences in bladder function. These observations are in line with the corresponding clinical condition in humans. More extensive studies are needed to clarify the precise mechanistic basis for these findings at the molecular, cellular and pharmacological levels. Future investigations may shed light on improved therapeutic strategies to reverse the age-related decline in bladder function.

References

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Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**Wake Forest University ACUC**