

This rat model is the most widely used animal model of hypertension and develops many features of human hypertensive end-organ damage such as cardiac hypertrophy, cardiac failure and renal dysfunction.

## Pathophysiological features

### Cardiovascular features

- Spontaneous severe hypertension with blood pressure stabilization around 12 weeks of age (>160 mmHg) (figure 1). Blood pressure in conscious rats can be monitored using a non-invasive method i.e. tail-cuff measurement or invasive methods such as chronic arterial catheterization or telemetry. Prostatic enlargement (prostate wet weight) (table 1).

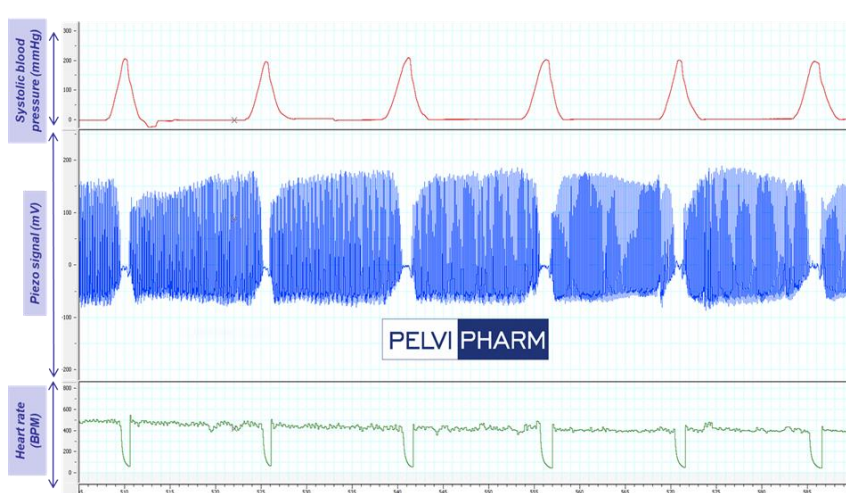


Figure 1: Illustration of blood pressure and heart rate recordings of SHR rat by the tail cuff system, a non-invasive measurement. (Pelvipharm internal data).

- Differential sensitivity to various hypertensive agents (figure 1)

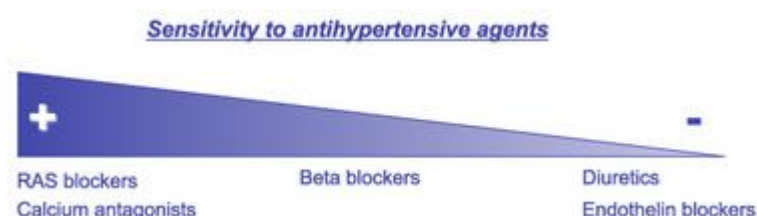


Figure 2: Blood pressure-lowering efficacy of common antihypertensive agents in SHR

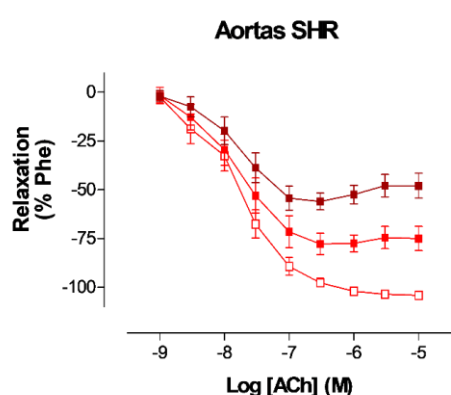


Figure 3: Relaxations induced by increasing concentrations of ACh in aortic rings from SHR at 6 (empty red), 12 (full red), and 24 wk of age (full brown) (n = 12 per age) (from Behr-Roussel et al., 2005)

- Endothelial dysfunction (figure 3)
- Vascular remodeling
- Cardiac hypertrophy
- Some features of metabolic syndrome: insulin resistance, hyperinsulinemia, hypertriglyceridemia, and hypertension
- Sympathetic hyperactivity

### Erectile function features

- Erectile dysfunction preceding the rise in blood pressure (figure 4).

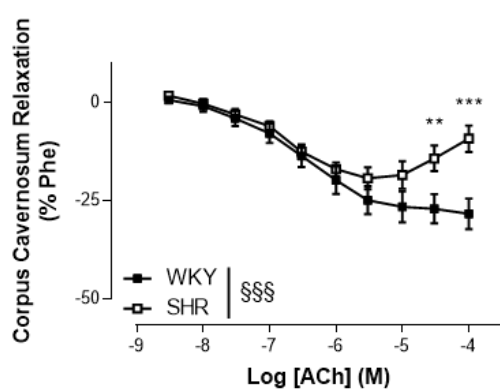
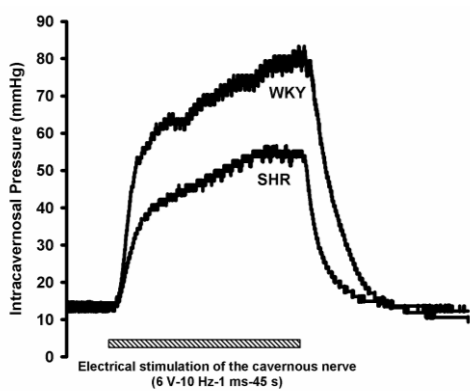


Figure 4: In vivo (left panel) and in vitro (right panel) evidence of erectile dysfunction in 12-week-old SHR.  $p < 0.01$ ,  $***p < 0.001$ , two-way ANOVA compared to age-matched normotensive Wistar-Kyoto (WKY) rats. (From Behr-Roussel et al., 2005).

- Corpora cavernosa remodeling
- Cavernosal endothelial dysfunction

### Bladder function features

- Changes in neuronal morphology (increase in bladder afferents) and function similar to those that occur with obstruction of the bladder outlet as it is the case in patients with lower urinary tract symptoms associated with benign prostatic hyperplasia.
- Exhibits abnormal bladder function: decreased bladder capacity and voided volume, increased urinary frequency, and occurrence of non-voiding contractions associated with changes in the noradrenergic control of the micturition reflex.

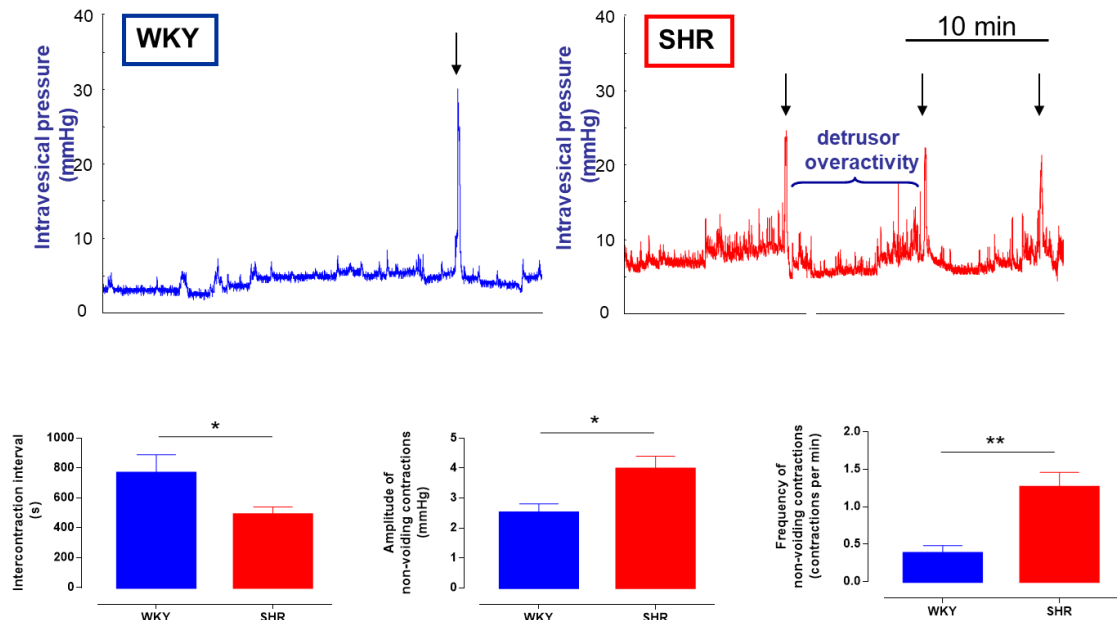


Figure 5: Representative cystometrograms in conscious SHR and WKY rats. Arrows indicate the voiding contractions. Detrusor overactivity occurs in SHR rats but not in WKY rats  $p < 0.05$ ,  $**p < 0.01$  Student's t-test. (Pelvipharm, internal data).

- Increase in  $\alpha$ -adrenoceptor agonist responsiveness of detrusor strips in vitro in organ baths
- Increase in urethral  $\alpha$ -adrenoceptor agonist responsiveness in vitro in organ baths

#### Related Pelvipharm bibliography:

Giuliano F et al. **J sex med** (2022):19:899-906  
 Assaly R et al. **BMC Urol** (2020):20:132  
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 Oudot A et al. **BJU Int** (2012):110:1352-1358  
 Behr-Roussel D et al. **Am J Physiol – Regul** (2005):288:R276-R283  
 Behr-Roussel D et al. **Am J Physiol – Regul** (2003):284:R682-R688