Salt Sensitivity of Tubuloglomerular Feedback in Subtotal Nephrectomy

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Background

❖ The kidney brings about salt balance by matching excretion to intake.

❖ Excretion is adjusted by combined effects of nerves, hormones, and physical factors on GFR, proximal reabsorption (Jprox), and distal reabsorption (Jdist).

❖ Primary effects of nerves and hormones on GFR or Jprox are normally mitigated by tubuloglomerular feedback (TGF). This stabilizes distal delivery, but makes salt homeostasis less efficient.

❖ After subtotal nephrectomy (STN), solute clearance and salt homeostasis are inherently compromised due to fewer functioning nephrons, albeit the remaining nephrons engage in some degree of compensatory hyperfunction.

❖ Hyperfunctioning remnant nephrons may forego the stability normally conferred by TGF in favor of higher nephron GFR (SNGFR) and distal delivery (AJP 2009).

Study Aims

❖ Presently, we tested the hypothesis that remnant nephrons are more apt to modulate their TGF response in response to chronic salt loading, since this is one way to make salt balance less inefficient.

Methods

❖ Adult, male, Wistar rats underwent sham surgery or STN (right unilateral nephrectomy + ligation of 2/3 branches of left renal artery).

❖ Salt loading: Low or high salt diet was begun on the day of surgery and continued for 7 days until renal micropuncture. In addition, balance studies were done in transition from normal to high- salt using metabolic cages. High salt diet consisted of 1% NaCl added to drinking water.

❖ Micropuncture experiments:

SNGFR and tubular stop flow pressure (PSF) were measured during orthograde perfusion of Henle's loop (LOH) at zero or 50 nl/min to characterize the TGF response.

❖ Salt balance experiments:

Rats were placed in metabolic cages 2 days prior to switching from normal to high salt diet.

Body weight, food and water intake, stool and urine output, and Na intake and excretion were measured daily.
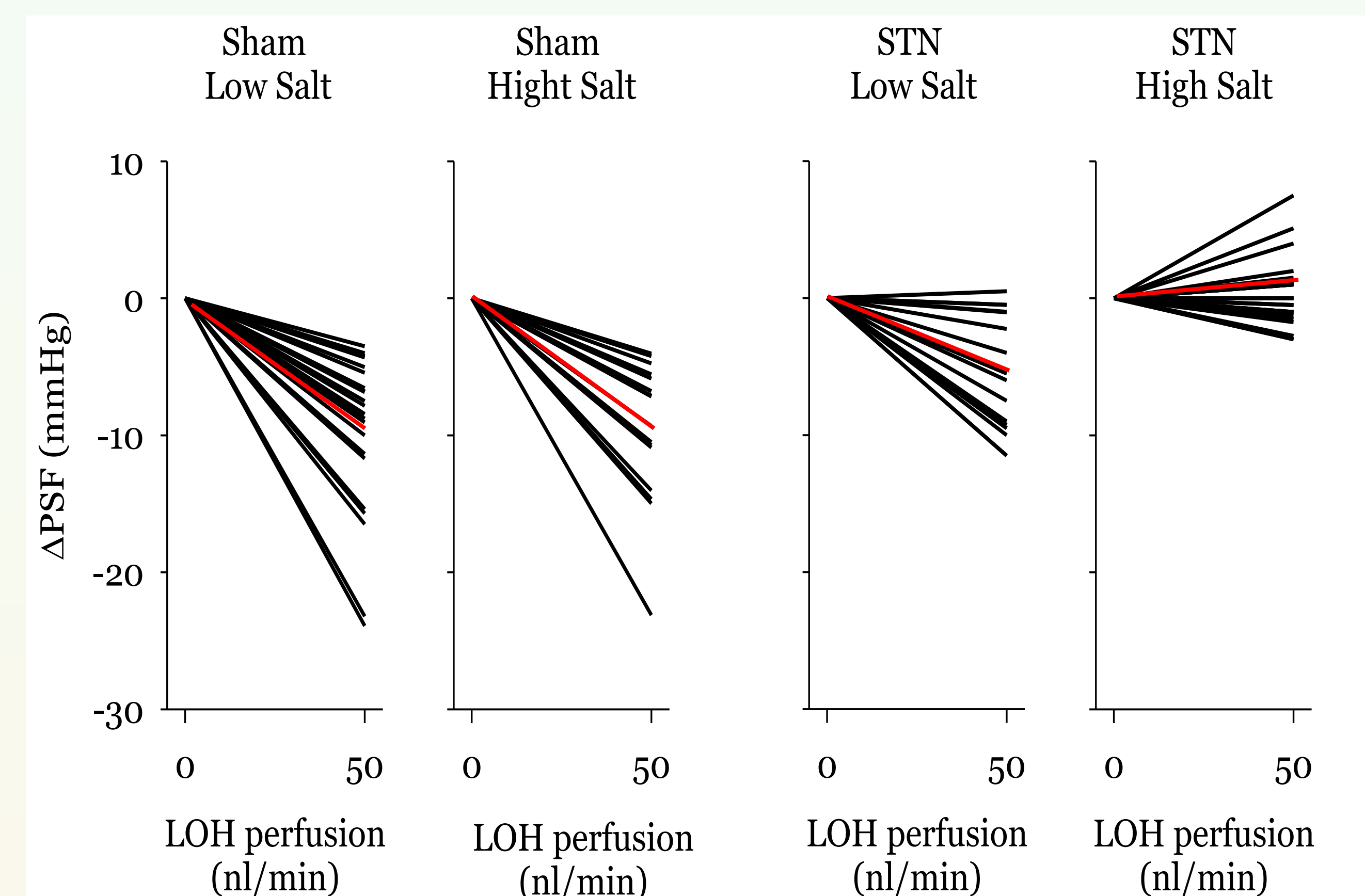
Results

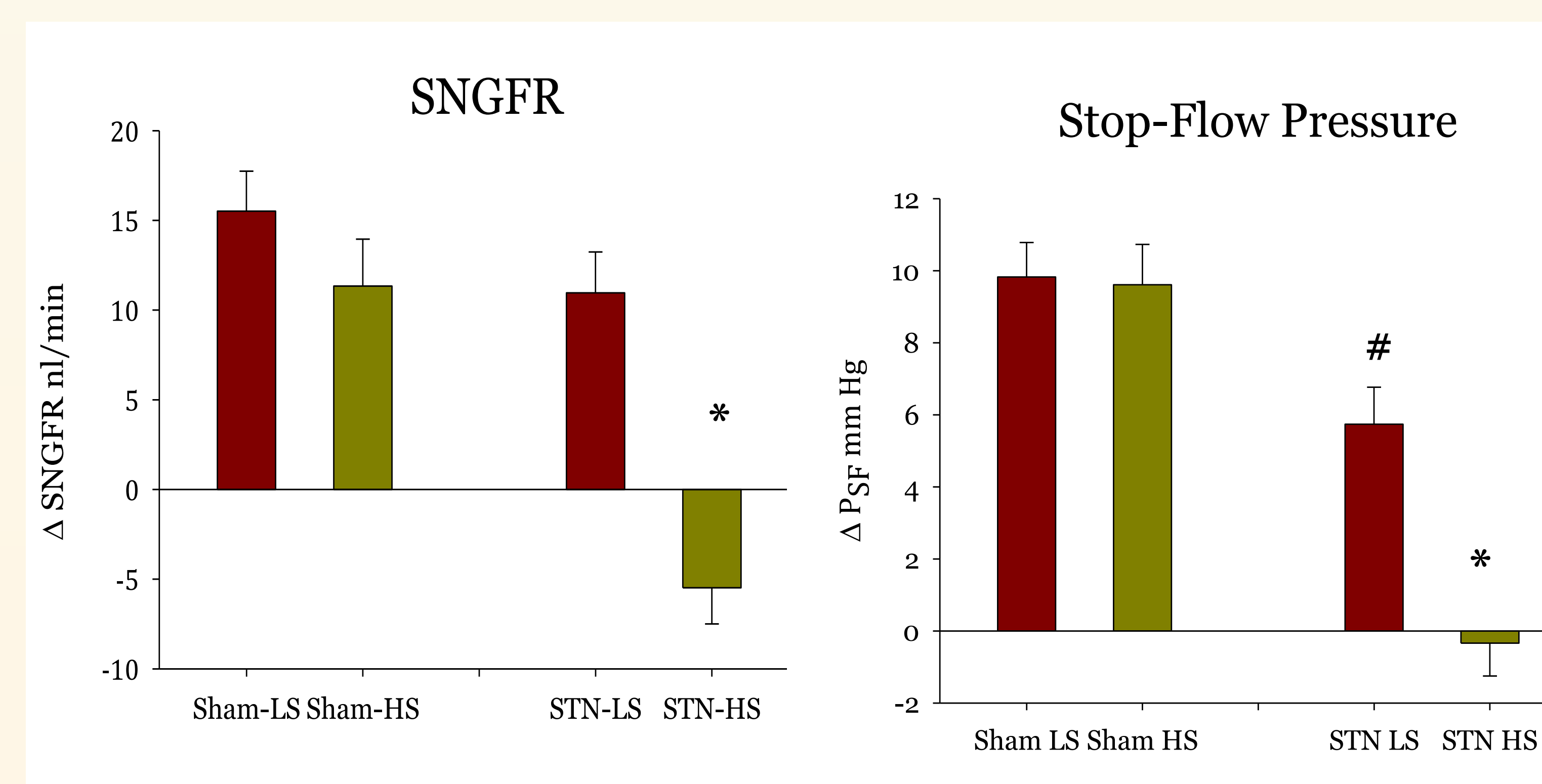### Figure 1. TGF: SNGFR Response to LOH Perfusion
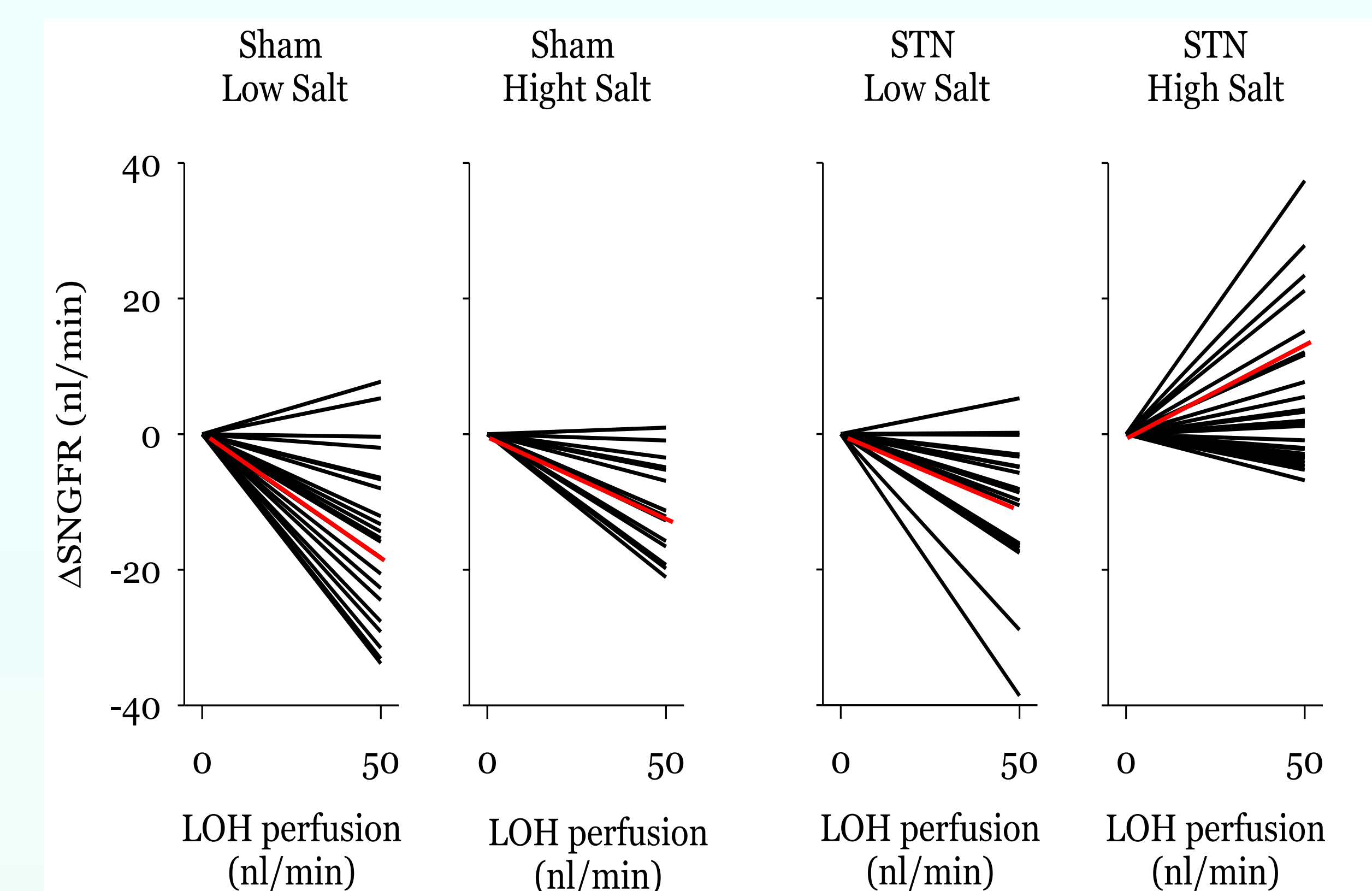
Black lines show individual nephron responses, red line represents the means.

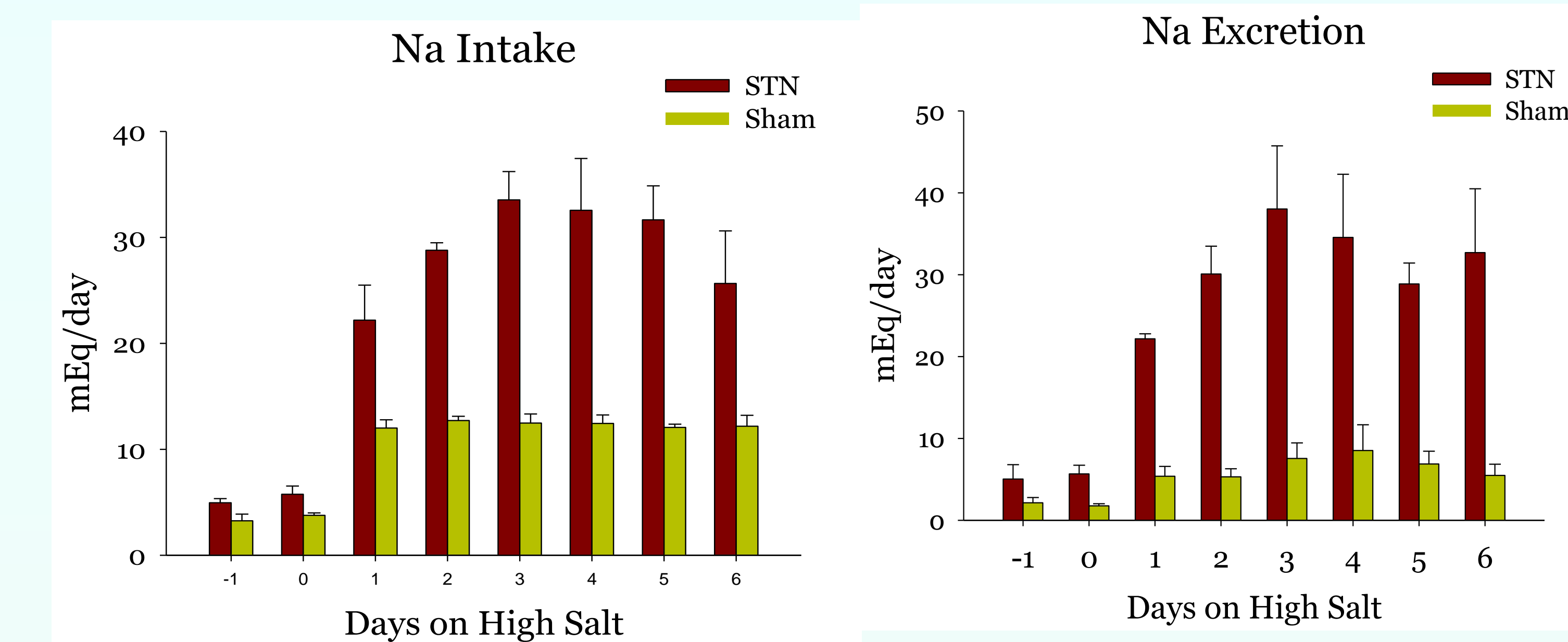### Figure 2. TGF: Stop-Flow Pressure Response to LOH Perfusion

Black lines show individual nephron responses, red line represents the means.

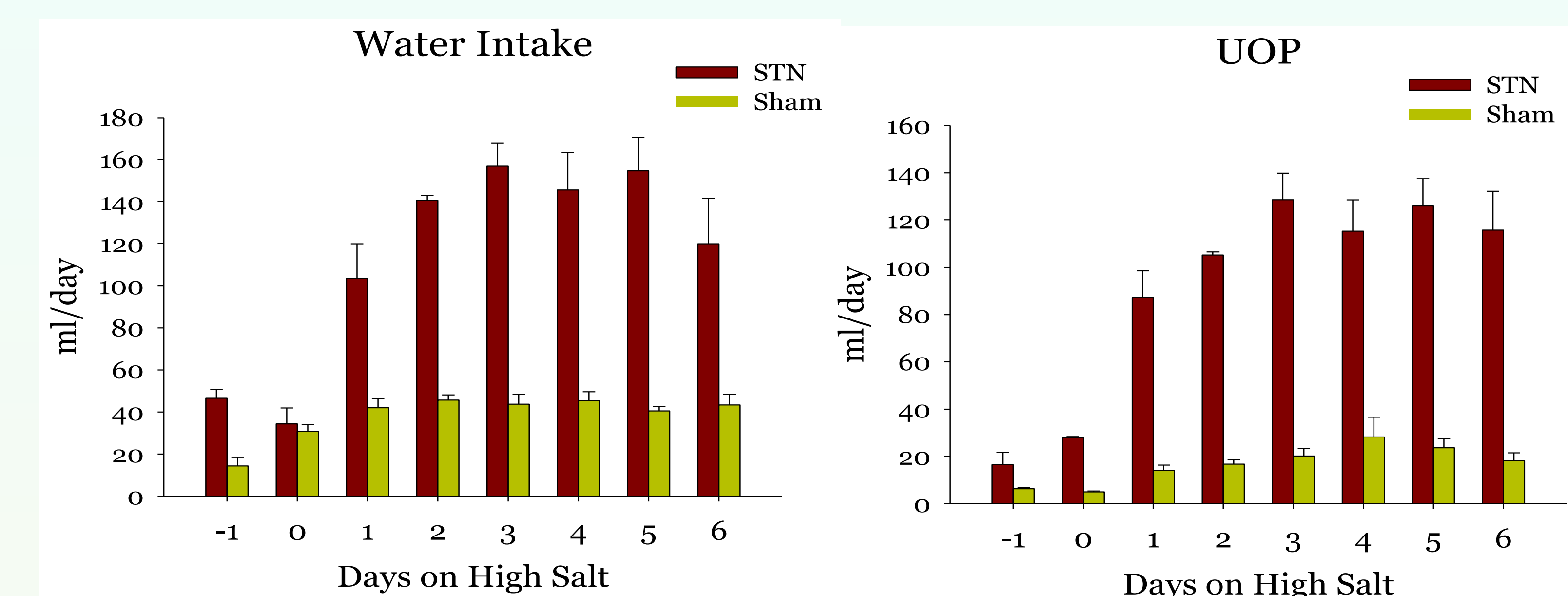### Figure 3. Mean TGF Responses: SNGFR and Stop-Flow Pressure

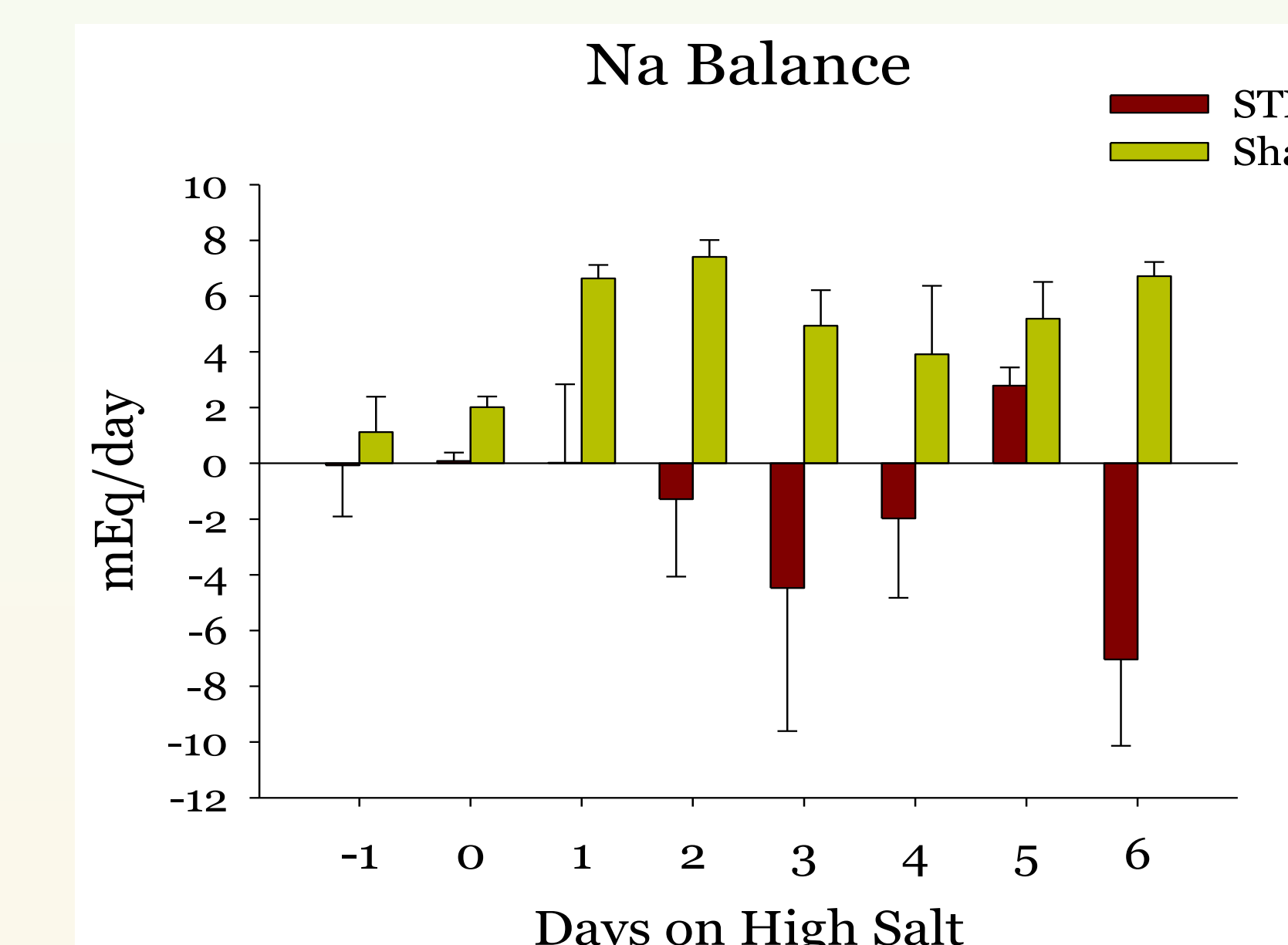*p<0.001 STN HS vs. other groups, #p <0.02 P_{SF} response diminished in STN LS

Figure 4. Daily Na Intake and Excretion in Metabolic Cages

Figure 5. Daily Water Intake and Excretion in Metabolic Cages

Figure 6. Daily Sodium Balance in Metabolic Cages

By two way ANOVA, effects of group (p<0.001) and group x salt (p=0.012) were significant.

Summary and Interpretation

STN makes TGF sensitive to dietary salt. To facilitate salt balance, the remnant kidney compromises stability of distal delivery by converting TGF from negative to positive feedback.

Positive feedback from the macula densa is inherently destabilizing to nephron function and may explain erratic salt balance from day-to-day in STN.