GPCR STIMULATED HYPOTHALAMIC PVN GαI2 PROTEIN-GATED PATHWAYS – THE KEY TO RENAL SYMPATHETIC NERVE MEDIATED SODIUM HOMEOSTASIS AND THE LONG-TERM CONTROL OF BLOOD PRESSURE

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Aim: We have demonstrated CNS Gαi2 proteins, which are highly expressed in the hypothalamic PVN, mediate the renal sympathoinhibition and natriuresis evoked by α2-adrenoceptor activation and volume expansion in-vivo. Therefore, we examined the role(s) of PVN Gαi2 proteins in fluid & electrolyte homeostasis and MAP regulation following elevated dietary salt-intake.

Methods: Intact or bilateral renal denervated (RDNX) Sprague-Dawley rats received a bilateral PVN or posterior hypothalamic (PH) infusion of a scrambled (SCR) or Gαi2 oligodeoxynucleotide (ODN-300ng/side/day) and a normal 0.4% (NS) or high 8% NaCl (HS) diet for 7-days. On day-7 MAP, 24h metabolic balance, plasma norepinephrine, (NE) and PVN Gαi2 protein levels were determined (N=5/group).

Results: HS-intake evoked a significant 3-fold site-specific increase in PVN Gαi2 proteins. ODN-mediated PVN Gαi2 down-regulation, but not PH miss-injection or PVN SCR ODN pre-treatment, caused renal nerve-dependent sodium retention (24h Na⁺ balance [meq] PH Gαi2 + HS 0.5±0.2, PVN Gαi2 + HS 2.3±0.4*, PVN Gαi2 RDNX + HS 0.8±0.3τ), global sympathoexcitation (plasma norepinephrine [nmol/L] PH Gαi2 + HS 17±4, PVN Gαi2 + HS 75±9*, PVN Gαi2 RDNX + HS 24±6τ) and hypertension (MAP [mmHg] PH Gαi2 + HS 128±3, PVN Gαi2 + HS 140±2*, PVN Gαi2 RDNX + HS 131±3τ) *p<0.05 vs. PH Gαi2 + HS, τp<0.05 vs. PVN Gαi2 + HS.

Conclusion: Renal nerve dependent dysregulation of sympathetically driven sodium retaining mechanisms occurred following PVN Gαi2-protein down-regulation evoking salt-sensitive hypertension. We conclude PVN Gαi2 protein-gated pathways regulate renal nerve-dependent sodium excretion to facilitate sodium homeostasis and maintenance of a salt-resistant phenotype – R01HL107330.