HIGH SALT EXACERBATES PROGRAMMED HYPERTENSION IN MATERNAL FRUCTOSE-FED MALE OFFSPRING

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OBJECTIVES

1. Widespread consumption of food and drink that contain high fructose is rising steeply, which is related to hypertension. Additionally, increased salt intake is significantly raising the risk of hypertension.
2. We thus examined whether maternal high fructose (HF) and postnatal high salt (HS) intake have synergistic effect on blood pressure elevation and underlying mechanisms in adult offspring.

METHODS

1. Pregnant Sprague-Dawley rats received regular chow or chow supplemented with 60% fructose (HF) during the whole period of pregnancy and lactation. One half of male offspring rats received 1% NaCl (HS) in their drinking water from weaning to 3 months of age. Male offspring were assigned to four groups: control, HF, HS, and HF+HS. All rats were sacrificed at 12 weeks old.
2. Blood pressure was measured in conscious rats by an indirect tail-cuff method.
3. Plasma L-arginine, L-citrulline, asymmetric symmetric dimethylarginine (ADMA, SDMA) levels were measured using HPLC with OPA/3MPA derivatization reagent.
4. Components of the RAS and sodium transporters were analyzed by qPCR.
5. Protein levels of type-3 sodium hydrogen exchanger (NHE3), Na+ /Cl- cotransporter (NCC), Na-K-2Cl cotransporter (NKCC2), and Na+/K+ATPase α 1 subunit (NaKATPase) were determined by Western blot.

Table 1. Weights and functional parameters

Groups	Control N=8	HF N=8	HS N=10	HF+HS N=10
Mortality	0%	0%	0%	0%
Body weight (g)	483 ± 11	470 ± 11	492 ± 8	479 ± 13
Left kidney weight (g)	2.21 ± 0.09	2.22 ± 0.08	2.10 ± 0.05	2.2 ± 0.08
Left kidney weight/100 g body weight	0.46 ± 0.01	0.47 ± 0.02	0.4 ± 0.01	0.5 ± 0.01
Systolic blood pressure (mm Hg)	152 ± 2	166 ± 5[a]	163 ± 2[a]	172 ± 2[a,b,c]
Mean arterial pressure (mm Hg)	116 ± 3	127 ± 4[a]	111 ± 2[b]	122 ± 4[a,c]
Creatinine (μM)	30.8 ± 2.5	28.5 ± 1.6	27.2 ± 1.3	27.4 ± 1.1

[a]P < 0.05 vs. control; [b]P < 0.05 vs. HF; [c]P < 0.05 vs. HS

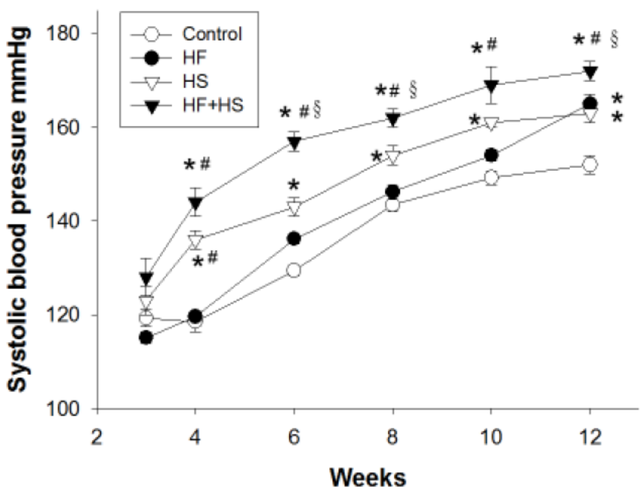

Fig. 1. Effect of maternal high-fructose (HF) and postnatal high-salt (HS) on systolic blood pressure in 12-wk-old male offspring, *P<0.05 vs. control; #P<0.05 vs. HF; §P<0.05 vs. HS.

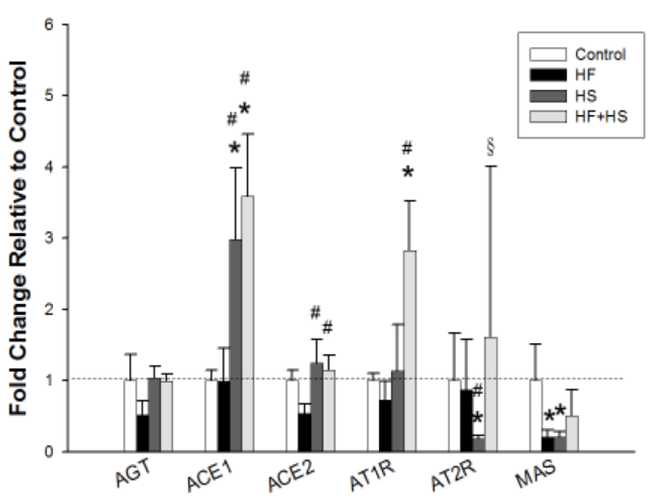

Fig. 2. Effect of maternal high-fructose (HF) and postnatal high-salt (HS) on gene expression of RAS components in the kidney. *P<0.05 vs. control; #P<0.05 vs. HF; §P<0.05 vs. HS.

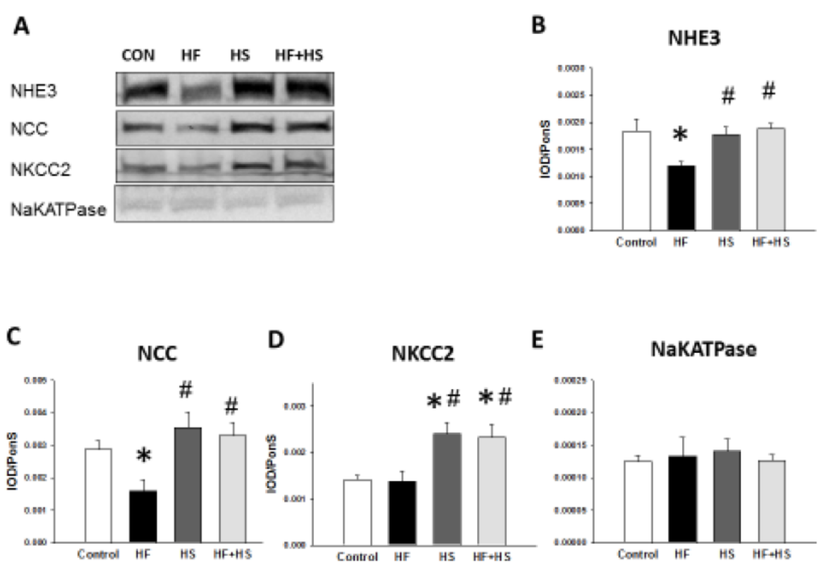

Fig. 3. Representative western blots (A) show NHE3 (~90kDa), NCC (~130kDa), NKCC2 (~160kDa), and NaKTAPase (~112kDa) at 12 weeks of age in controls and in off spring from rats with maternal high-fructose (HF) and postnatal high-salt (HS) exposure. Relative abundance of renal cortical (B) NHE3, (C) NCC, (D) NKCC2, and (E) NaKATPase were quantified. N=8/group, *P<0.05 vs. control; #P<0.05 vs. HF.

RESULTS

1. HF and HS group both developed hypertension (Table 1); both have a synergistic effect on the increase of BP (Figure 1).
2. Postnatal HS increased *Ace*, whereas decreased *Agtr1b* and Mas1 in the kidney (Figure 2). Next, renal mRNA of *Ace*, and *Agtr1a* were significantly higher in the HF+HS group vs. control.
3. Renal protein level of NKCC2, NHE3, and NCC were higher in HS and HF+HS group vs. control (Figure 3).

CONCLUSIONS

1. Maternal HF and postnatal HS both induced hypertension in adult male offspring.
2. Postnatal HS intake exacerbates maternal HF-induced programmed hypertension.
3. HF and HS induced programmed hypertension by mediating the RAS and sodium transporters in the kidney differentially.
4. With better understanding the inter-relationships between HF and HS on the development of hypertension will aid in the prevention of programmed hypertension in mother and children exposed to high fructose and salt.

ACKNOWLEDGMENTS

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