IN OBESE ZSF1 RATS, FEMALES SHOW INCREASED SALT-SENSITIVITY COMPARED TO MALES

Isabel Nguyen1, Anne-Maj Samuelsson2, Jaap Joles1, Marianne Verhaar1
1Nephrology and Hypertension, University Medical Center Utrecht, Utrecht, Netherlands and 2Biomedicine, University of Bergen, Bergen, Norway

INTRODUCTION AND AIMS: The obese Zucker fatty/spontaneously hypertensive heart failure F1 hybrid (ZSF1) rat has been proposed as a viable animal model to study the metabolic cardioenal syndrome as these rats spontaneously develop diastolic heart failure and chronic kidney disease in the presence of obesity, hyperglycemia and hypertension. Risk factors associated with the metabolic syndrome correlate strongly with salt-sensitivity of blood pressure. In Dahl-salt sensitive rats, a non-obese rat strain commonly used in salt-induced hypertension, males were more susceptible to develop high blood pressures during high salt intake than females. Therefore this study aimed to investigate the effects of obesity and sex on salt-sensitivity in the obese ZSF1 rat model and their lean counterparts. We hypothesized that obesity and male sex would both promote salt-sensitive hypertension.

METHODS: Male and female ZSF1 rats, lean as well obese (n=4-8/subgroup), were either implanted with a deoxycorticosterone acetate (DOCA) pellet and fed a high salt diet (6% NaCl) or with a placebo pellet and fed a normal salt diet from 19 weeks of age.

RESULTS: Obese ZSF1 developed signs of metabolic syndrome, with high cholesterol and triglyceride levels. However, only male obese ZSF1 became hyperglycemic. SBP was higher in both obese compared to lean DOCA + 6% salt groups (p<0.0001). Natriuresis was higher in male obese vs. lean DOCA + 6% salt groups (p<0.0001). The SBP response to high salt intake occurred in a stepwise manner in all four DOCA + 6% salt groups (with constant SBP from 22 to 24 weeks). Comparison of slopes of the natriuresis-pressure relations using 18 and 26 weeks data (figure) showed differences between male obese and lean (p<0.01) and female obese and lean ZSF1 rats (p<0.01), suggesting that obesity promotes salt-sensitivity. Additionally, slopes between obese males and females differed (p<0.01) suggesting that salt-sensitivity was most marked in female obese ZSF1 rats.

CONCLUSIONS: Our results in ZSF1 rats indicate i) a phased blood pressure response to high salt intake, ii) an adverse effect of obesity on salt-sensitivity, and iii) a further increased salt-sensitivity in obese females vs. obese males.

Figure. Natriuresis-pressure relations in ZSF1 rats corrected for mm tibia length (TL).