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Angaben zur Veröffentlichung / Publication details:

Goktas, Sevilay Sahoglu, Lotte Vanherle, Zeinab Rafiee, Joao Duarte, and Anja Meissner. 2023. "Sex-specific cardiovascular responses to long-term high-salt diet [Abstract]." *Journal of Vascular Research* 60 (Supplement 1): 30–31. https://doi.org/10.1159/000533846.

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Sex-specific cardiovascular responses to long-term High-Salt Diet

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Excess dietary sodium has been linked to elevations in blood pressure (BP). Recent pre-clinical and clinical data support that even in the absence of an increase in BP, excess dietary salt can adversely affect target organs, including blood vessels, heart, kidneys, and brain. Although women have a higher prevalence to develop salt-sensitive hypertension most pre-clinical studies are performed in male rodents. Thus, sex-specific responses to chronic high salt intake are largely elusive.

To investigate potential sex-specific responses to long-term high salt loading, we exposed 6-months old male and female mice to a high-salt diet (HSD; 8%) for a total of 14 months. A second study cohort was reversed to normal diet after 7 months of HSD exposure. BP and cardiac function were longitudinally assessed using tail cuff plethysmography and magnetic resonance imaging, respectively. Endpoint vascular function and morphological vessel alterations were determined via wire myography and histology.

In response to 12-months HSD, BP increased only in female mice (132.6 ± 7.1 vs. 122.1 ± 2.1 mmHg BP sys). Cardiac parameters were only altered in male mice exposed to HSD. Specifically, male HSD mice presented with higher stroke volume (34.6 ± 4.3 vs. 25.4 ± 5.2 µl), left ventricular end-diastolic volume (52.8 ± 8.7 vs. 41.4 ± 7.9 µl) and left ventricle mass (132.1 ± 15.7 vs. 102.4 ± 13.6 mg). Male but not female HSD mice had increased aorta wall thickness and stiffness. Moreover, mesentery artery showed significantly lower tension in response to adrenergic stimuli. Normalizing dietary salt after 7 months of high HSD normalized BP in female mice (118.4 ± 6.2 vs. 131.2 ± 5.8 mmHg BP sys) and reversed the cardiovascular phenotype in males. Specifically, stroke volume (28.2 ± 6.3 vs. 33.6 ± 8.3 µl) and left ventricular mass (93.1 ± 22.5 vs. 103.2 ± 18.9 mg) were lower compared to the 7-months HSD timepoint.

Together, the data support pronounced sex-specific responses to chronic high salt loading, calling for sex-specific health monitoring and treatment approaches. Diet reversal improves cardiovascular health in both sexes, further highlighting the importance of moderating salt intake.

Keywords: Cardiovascular, High-salt diet, Sex-specificity, hypertension