

Background: Obesity is a risk factor for the development of cardiovascular complications. High-fat (HF) diet-induced obesity models are often used to analyze the translational impact of obesity but differences in sex and Western diet type complicate comparison between studies. In addition, the local modulation of vascular tone by perivascular adipose tissue (PVAT) is suggested to be impaired in obesity. Although obesity prevalence is higher in women versus men, sex-specific aspects of PVAT function in obesity remain unclear. We hypothesized that obesity induced by two types of obesogenic diets impact PVAT function in females versus males differently along time. **Methods:** Male and female C57Bl6/J mice (2-month-old) were fed with chow-diet (CD, 9% of cal. from fat), HF (60% of cal. from fat) or HF plus high sucrose (HF+HS; 45% of cal. from fat, 30% cal. from sucrose) for 3 or 5 months (CEUA 4914-1/2018, 5474-1/2020). Vascular function was studied in small mesenteric arteries (SMA) without (-) or with (+) attached PVAT by using a wire myograph. Statistics: * $P < 0.05$, Student's *t* test. **Results:** HF and HF+HS increased body weight, adiposity, fasting glucose and insulin without affecting blood pressure and adiponectin levels in both sexes. HF or HF+HS diet impaired PVAT anticontractile effect in SMA from females but not males at 3 and 5 months. PVAT mediated endothelial dysfunction in SMA from female mice with 3 months of HF+HS (Rmax: PVAT- = 98 ± 0.6 vs. PVAT+ = $85 \pm 5.3^*$), while in males this effect was observed only at 5 months of HF+HS diet feeding (Rmax: PVAT- = 94 ± 1.7 vs. PVAT+ = $61 \pm 8.0^*$). However, PVAT did not impact acetylcholine-induced relaxation in SMA from male and female mice fed HF alone. **Conclusion:** The findings suggest that the addition of sucrose to a HF-diet accelerates PVAT dysfunction in both sexes and a susceptibility of female sex to PVAT mediated vascular complications in the setting of obesity.

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