

## Low Heart Rate Variability is Related to Decreased Microvascular Insulin Sensitivity in People with Obesity

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Heart rate variability (HRV) is an index of autonomic nervous system tone that is reportedly low in individuals with obesity. While low HRV is associated with hyperinsulinemia and large conduit artery dysfunction, it is less clear how HRV relates to insulin-stimulated capillary perfusion rates. PURPOSE: To determine if HRV relates to microvascular insulin sensitivity. METHODS: Individuals with obesity (n= 32, 25F; 55.3 $\pm$ 1.2y; 36.4 $\pm$ 0.9kg/m<sup>2</sup>) with HIGH (n=16, 13F) insulinstimulated microvascular flow velocity ( $\Delta$ MFV) were compared to those with LOW (n=16, 12F)  $\Delta$ MFV in this cross-sectional study. A 120min euglycemic clamp (40mU/m<sup>2</sup>/min, 90 mg/dl) determined metabolic insulin sensitivity (glucose infusion rate (GIR)), and indirect calorimetry was used to depict non-oxidative glucose disposal (NOGD). MFV was measured with ultrasound at 0 and 120min of the clamp via intravenous infusion of microbubbles. Resting supine ECG was monitored for 5min to calculate HRV indices: mean RR, standard deviation of HR (STDHR), RR (STDRR), and NN (SDNN) intervals, the root mean square of NN interval differences (RMSSD), and the proportion of consecutive NN intervals >50 ms (pNN50). Body composition (DXA), aerobic fitness (VO<sub>2</sub>max), and glucose tolerance (180min 75g OGTT; total area under the curve (tAUC)) were also assessed. **RESULTS:** There were no differences in age (P=0.34), body fat % (P=0.46), VO<sub>2</sub>max (P=0.90), or GIR (P=0.22) between groups. However, HIGH had a longer mean RR (P=0.02) and lower mean HR (P=0.02) than LOW, independent of differences in STDHR (P=0.82), RMSSD (P=0.72), STDRR/SDNN (P=0.69), or pNN50 (P=0.33). RMSSD associated with GIR (r=0.36, P=0.04) and glucose tAUC<sub>180min</sub> (r=-0.36, P=0.04). Further, STDRR/SDNN related to GIR (r=0.46, P<0.01) and NOGD (r=0.40, P=0.03) as well as glucose tAUC<sub>180min</sub> (r=-0.46, P<0.01). CONCLUSIONS: Insulin-stimulated capillary perfusion rates related to favorable HRV, independent of GIR. Yet, greater HRV associated with metabolic insulin sensitivity and glucose tolerance. Thus, the autonomic nervous system may regulate microvascular capillary perfusion during insulin-stimulation to promote skeletal muscle nutrient delivery for glucose homeostasis. SIGNIFICANCE/NOVELTY: While insulin resistance and endothelial dysfunction have been linked to impaired HRV in those with obesity, the relationship between insulin-stimulated capillary perfusion rates and HRV has not yet been investigated. These findings highlight that the autonomic nervous system may regulate insulin-stimulated capillary perfusion rates in people with obesity to coordinate nutrient delivery to skeletal muscle for glucose uptake and storage.

Supported by NIH RO1-HL130296 (SKM) and NSF Award 2125872 (PS)