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## Reduced Aortic Waveform Responses to Insulin in Late Chronotype with Metabolic Syndrome

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PURPOSE: Late chronotype (i.e. evening people) is linked to metabolic insulin resistance and cardiovascular disease. However, it is unknown if insulin reduces aortic waveforms and inflammation in late chronotype (LC) compared with early chronotype (EC; i.e. morning people). METHODS: Thirty-nine sedentary adults (54.9±1.1 y; VO<sub>2MAX</sub> 22.2±0.7 ml/kg/min) with metabolic syndrome (MetS) (3.5±0.1 ATP-III score) & obesity (DXA body fat: 45.2±0.9%) were classified as either LC (n=19 (16F)) or EC (n=20 (16F)) using the Morning-Eveningness Questionnaire (MEQ). A 120 min euglycemic hyperinsulinemic clamp (40mU/m<sup>2</sup>/min, 90 mg/dl) was performed to determine metabolic insulin sensitivity (glucose infusion rate (GIR)). Measurements were taken before & after the clamp to assess substrate oxidation, pulse waveform, and inflammation. Carbohydrate (CHO<sub>OX</sub>) & fat oxidation (F<sub>OX</sub>), with non-oxidative glucose disposal (NOGD) were measured by indirect calorimetry while aortic waveform and blood pressure were characterized via applanation tonometry including: augmentation index (AIx75); augmentation pressure (AP); central (CPP) and brachial (BPP) pulse pressure; mean arterial pressure (MAP); forward (Pf) & backward (Pb) pulse wave. **RESULTS**: Age, fat mass, and ATP III score were similar between LC (MEQ=45.5±1.3) & EC (MEQ=63.5±1.2). However, LC had higher FFM (P=0.04) and lower VO<sub>2MAX</sub> (P=0.05), GIR (P<0.01), and NOGD (P<0.01), as well as blunted suppression of  $F_{OX}$  during insulin infusion (P=0.03). Although fasted aortic waveforms were comparable, LC had higher insulin-stimulated BPP (P<0.001) & AP (P<0.01). Additionally, LC had greater reductions in AP (P<0.01) & AIx75 (P=0.09), but attenuated responses in Pf (P<0.01) & MAP (P=0.08) with the clamp. Further, LC had elevated insulin-stimulated TNF-\alpha (P=0.04) & blunted insulin-mediated reductions in VCAM (P<0.01) versus EC. VO<sub>2MAX</sub> correlated with insulin-mediated reductions in AIx75 (r=-0.56, P<0.01) & AP (r=-0.49, P<0.01) while NOGD correlated with insulin-mediated reductions in AP (r=-0.44, P= 0.03) & Pf (r=-0.43, P=0.04). Insulin-mediated changes in VCAM also correlated with reductions in MAP during the clamp (r=0.41, P=0.03). CONCLUSIONS: Late chronotype was characterized by blunted aortic waveform and inflammatory responses to insulin in people with MetS.

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