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# Pancreatic β cell Hypersecretion of Insulin in Intermediate versus Morning Chronotype

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Insulin resistance promotes hypersecretion of insulin from pancreatic β cells to maintain normoglycemia. However, declines in pancreatic β cells cause Type 2 Diabetes (T2D). While evidence suggests disruption of circadian rhythms may lead to impaired β cell function and evening chronotypes are at greater risk of developing T2D, no data is available testing the association of chronotype with β cell function. **PURPOSE:** To assess pancreatic function in relation to incretin hormones in morning (MC) and intermediate (IC) chronotypes with obesity. **METHODS:** Adults with obesity were grouped into MC (n=25(4M), MEQ=63.6±0.9, 52.4±1.2y, 36.5±1.0kg/m$^2$) or IC (n=21(5M), MEQ=51.5±1.1, 56.4±1.9y, 36.2±1.2kg/m$^2$) per Morningness-Eveningness Questionnaire (MEQ). Glucose, insulin, C-peptide, GIP, and GLP-1 were collected in 30min intervals during a 120min 75g OGTT. Total area under the curve (tAUC) during the OGTT was calculated using the trapezoidal method. Early (0-30min) and total-phase (0-120min) incremental glucose-stimulated insulin secretion (GSIS: C-peptide/Glucose) and β cell function (disposition index (DI): GSIS scaled to insulin sensitivity) were determined. Peripheral insulin sensitivity (glucose infusion rate (GIR)) and hepatic insulin resistance (HOMA-IR) were assessed during a 120min euglycemic hyperinsulinemic clamp (40mU/m$^2$/min, 90 mg/dl). Body composition (DXA) and aerobic fitness ($VO_2$max) were also assessed. **RESULT:** No difference in body composition, peripheral insulin sensitivity or incretins were observed, though IC had higher hepatic insulin resistance ($P$=0.03) and lower $VO_2$max ($P$<0.01) compared with MC. However, IC had higher early phase C-peptide $tAUC_{0\text{-}30min}$ ($P$=0.04) and early phase $DI_{0\text{-}30min}$ when corrected to peripheral insulin sensitivity ($P$=0.059). Early phase C-peptide $tAUC_{0\text{-}30min}$ associated with lower peripheral insulin sensitivity (r=-0.38, $P$<0.01) and $VO_2$max (r=-0.40, $P$<0.01), but higher lean body mass (r=0.47, $P$<0.01). Hepatic insulin resistance correlated with early phase C-peptide $tAUC_{0\text{-}30min}$ (r=0.35, $P$<0.02) and lower GLP $tAUC_{0\text{-}120min}$ (r=-0.40, $P$=0.04). **CONCLUSION:** IC demonstrate early phase hypersecretion of insulin to potentially compensate for peripheral and hepatic insulin resistance for post-prandial glucose regulation compared to MC. Additional β cell function investigation across chronotypes is warranted to optimize treatments that reduce T2D risk. **SIGNIFICANCE/NOVELTY:** This study compared pancreatic function in response to a 75g glucose load between morning and intermediate chronotype in adults with obesity. We provide evidence that adults that identified as IC compared with MC have higher pancreatic insulin secretion in relation to insulin resistance and low GLP-1. Given chronotype reflects unique circadian rhythms, these data suggest chronotype plays a role in T2D development.

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