

Hyperglycemia is the main determinant of cardiac autonomic dysfunction in youth with obesity across the spectrum of glycemic regulation

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BACKGROUND

- Heart Rate Variability (HRV) results from the autonomic nervous system activity at the heart
- Loss of parasympathetic function (PNS) and sympathetic (SNS) override, reflected in decreased HRV, is one of the earliest subclinical manifestations of cardiac autonomic dysfunction
- Lower HRV is associated with increased risk of cardiac events in adults

AIMS

- Characterize HRV in normal weight and overweight children with and without dysglycemia
- Investigate the determinants of HRV in these youth, including body composition, glycemia measures, beta-cell function and inflammatory markers.

STUDY POPULATION

- 94 adolescents (50 males and 44 females)
 - 22% were with normal weight and normal glucose tolerance (NW-NGT)
 - 24% with overweight and normal glucose tolerance (OW-NGT)
 - 54% with obesity and impaired glucose regulation (OB-IGR) including prediabetes and early T2D (mean duration 18.2 ± 18 months)
- Mean age (SD) 15 ± 2.1 years

METHODS

- Anthropometrics, Blood Pressure
- Body composition by dual-energy X-ray absorptiometry (DXA)
- Fasting and 2-hour oral glucose tolerance test (OGTT) glucose and insulin concentration
- Fasting blood for lipids and Inflammatory markers (hs-CRP and TNF-α)
- EndoPAT for HRV measurement in fasting resting state
- Calculation of HOMA-IR

STATISTICS

- ANOVA for 3 group comparison among NW-NGT, OW-NGT and OW-IGR
- Partial correlations and linear regression: examine the relationship of HRV to body composition, glycemia and inflammatory markers adjusting for age, sex, race-ethnicity and Tanner stage

OUTCOME MEASURES

- HRV measured using EndoPat
 - Frequency-domain indices: **High-frequency (HF)**, **Low-frequency (LF)** in Hz, **LF:HF ratio** reflecting the balance between SNS and PNS. Higher LF/HF is worse.
 - Time-domain indices: **NN** (Inter-beat interval of normal sinus beats in ms), **SDNN** (Standard deviation of NN), **RMSSD** (Square root of the mean squared difference of successive NN), **NN50** (NN intervals differing by more than 50 milliseconds). Lower values are worse.

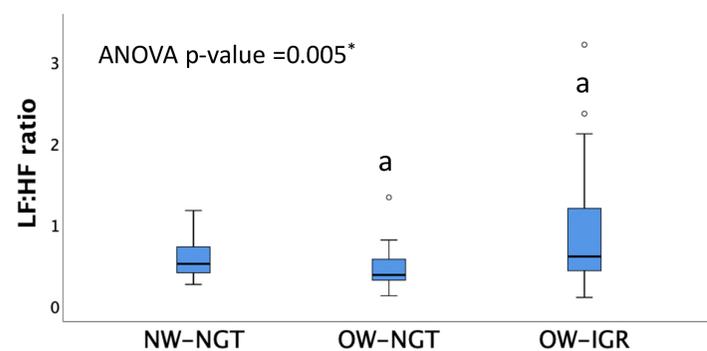
Table 1. Subject Characteristics and body composition

	NW-NGT	OW-NGT	OW-IGR	P-value
Age (yr)	15.1 ± 2.3	14.3 ± 2.4	15.3 ± 1.8	0.206
BMI Z-score	0.21 ± 0.69	1.84 ± 0.53	2.29 ± 0.38	<0.001
Percent body fat (%)	17.9 ± 6.2	37.2 ± 5.1	38.8 ± 6	<0.001
Truncal Fat Mass (kg)	3.6 ± 1.4	13.4 ± 4.7	18.2 ± 6.2	<0.001
SBP (mmHg)	113.2 ± 11.4	114.6 ± 10.8	120.4 ± 9.2	0.012
DBP (mmHg)	69.1 ± 6.2	71.8 ± 7.1	74.5 ± 6.2	0.006
MAP (mmHg)	83.8 ± 7.3	84.8 ± 9.1	89.8 ± 6.2	0.002
Heart Rate (beats/min)	65.9 ± 11.2	70.5 ± 8	71.6 ± 9.06	0.067

Table 2. Metabolic Data

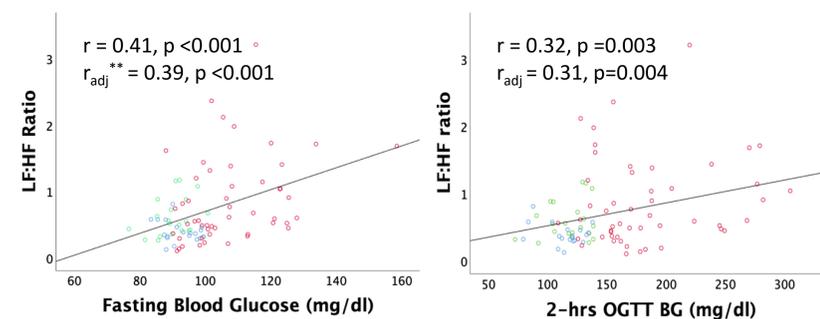
	NW-NGT	OW-NGT	OW-IGR	P-value
HbA1c (%)	5.55 ± 0.25	5.44 ± 0.24	5.99 ± 0.55	<0.001
Fasting BG (mg/dl)	90.6 ± 5.9	92.3 ± 5	107.6 ± 14	<0.001
2hrs OGTT BG (mg/dl)	118.1 ± 18.3	114.9 ± 16.2	183.6 ± 48.6	<0.001
Fasting Insulin (μu/ml)	11.4 ± 12.8	31.1 ± 25.7	38.7 ± 25.1	<0.001
HOMA-IR	2.6 ± 2.8	7.1 ± 6.1	10.5 ± 7.6	<0.001
Hs-CRP (mg/dl)	0.55 ± 0.69	1.53 ± 1.53	3.5 ± 3.24	<0.001
TNF-α (pg/ml)	2.21 ± 0.85	1.97 ± 1.05	3.75 ± 2.66	0.017

HRV among the 3 groups



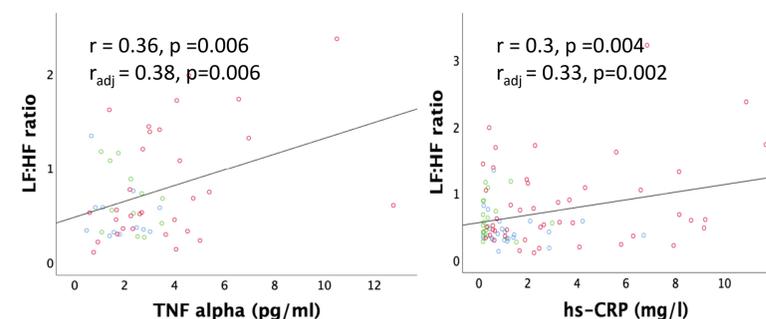
*Bonferroni post hoc test for significant (P < 0.05) differences between any two groups is indicated with the same letter

HRV and Glycemia



**Models adjusted for sex, Race-Ethnicity and Tanner stage

HRV and Inflammatory markers



○ NW-NGT
 ● OW-NGT
 ● OW-IGR

CONCLUSION

- Youth with impaired glucose metabolism have evidence of early cardiac autonomic dysfunction as reflected by decreased HRV
- Glycemia and systemic inflammation appear to be the main determinants of HRV in youth with obesity and dysglycemia