Changes in respiratory-sympathetic coupling during hyperinsulinemia in healthy young adults

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BACKGROUND

- Cardiovascular and autonomic nervous systems are modulated by breathing patterns.
- Under baseline conditions, sympathetic nervous system activity has a rhythmic component associated with respiratory activity, and the normal discharge pattern includes an increase in activity at end of expiration.
- Systemic insulin increases ventilation and sympathetic nervous system activity in young healthy humans.
- Chronic hyperinsulinemia (e.g., insulin resistance, type 2 diabetes) may expose patients to increased respiration rate, contributing to impaired autonomic modulation of the cardiovascular system.

A major gap in knowledge is whether respiratory changes which occur during hyperinsulinemia elicit altered sympathetic discharge patterns.

HYPOTHESIS

We hypothesized during high systemic insulin we would observe an increase sympathetic nervous system activity during late expiratory phase of the respiratory cycle (i.e., increased respiratory-sympathetic coupling) when compared to measures during baseline.

METHODS

- **Participants:** 20 young, healthy adults (13M/7F, 28±1 yrs, BMI: 25±1 kg/m^2) completed a single study visit.
- **Instrumentation:** Heart rate (ECG), blood pressure (brachial arterial catheter), MSNA (microneurography, of the peroneal nerve).
- **Infusion:** Intravenous insulin was infused at a constant rate of 1.0 mU/kg FFM/min during which time exogenous glucose was infused to maintain euglycemia.

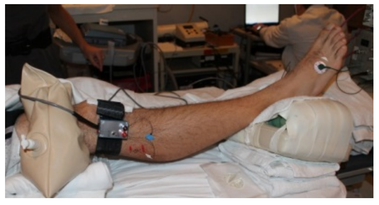

Fig 1: Microneurography for the measure of MSNA.

- **Protocol:** Data are reported from baseline (Pre-Insulin) and after a 60-min hyperinsulinemic, euglycemic infusion (Hyperinsulinemia).

METHODS

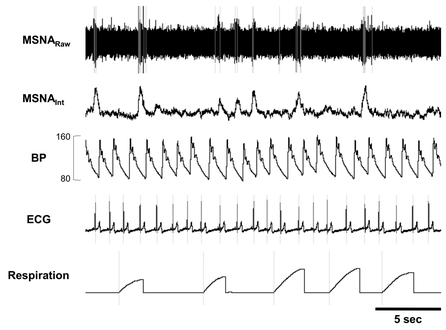

Figure 2: Multiunit recording of muscle sympathetic nerve activity from a female research participant. Discriminated spikes were extracted from the nerve recording (dashed lines). The times of occurrence of each heart beat (R waves) and end of each inhale (inspiratory peaks) are also shown (dashed lines). These timing events were used to generate the cross-correlation and autocorrelation histograms.

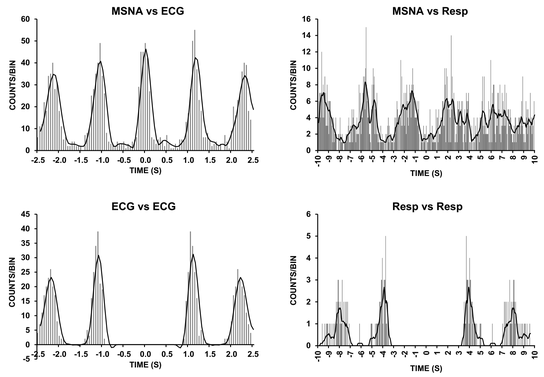

Figure 3: Correlations between MSNA and ECG and respiration. Cross-correlation histograms (upper traces) and autocorrelation histograms (lower traces) between sympathetic spikes and ECG and respiration. Data were obtained from the same female participant illustrated in Figure 1. Smoothed polynomials (black lines) have been fitted to the histograms. The numbers on the y-axes refer to the numbers of spikes per 50 ms bin. Time zero corresponds to the triggering event in the cross- or autocorrelograms.

RESULTS

	Pre-Insulin	Hyperinsulinemia	*P*-value
Heart Rate (beats/min)	65±2	68±2	0.06
Mean Blood Pressure (mmHg)	100±2	99±1	0.68
Respiratory Rate (breaths/min)	14±1	14±1	0.80
Tidal Volume (mL/breath)	500±41	542±32	0.14
Minute Ventilation (L/min)	6.8±0.4	7.3±0.3	0.08
Norepinephrine (pg/mL)	164±15	208±16*	<0.01
Epinephrine (pg/mL)	47±5	61±6*	0.02
MSNA Burst Frequency (bursts/min)	19±1	24±2*	<0.01
MSNA Burst Incidence (bursts/100 heart beats)	30±2	37±3*	0.01
Glucose (mg/dL)	96±1	96±1	0.49
Insulin (μIU/L)	7±1	52±2*	<0.01

Table 1: Hemodynamic and neurohumoral responses to acute hyperinsulinemia. Mean±SEM from n=20, unless noted (Epinephrine/Norepinephrine, n=18). Students paired t-test. *p≤0.05 vs Pre-Insulin.

RESULTS

Although analysis is ongoing, we expect to observe an increase in respiratory modulation during hyperinsulinemia compared to baseline.

We propose changes in the respiratory patterning of MSNA during hyperinsulinemia will include more activity during late expiration and less activity during post-inspiration.

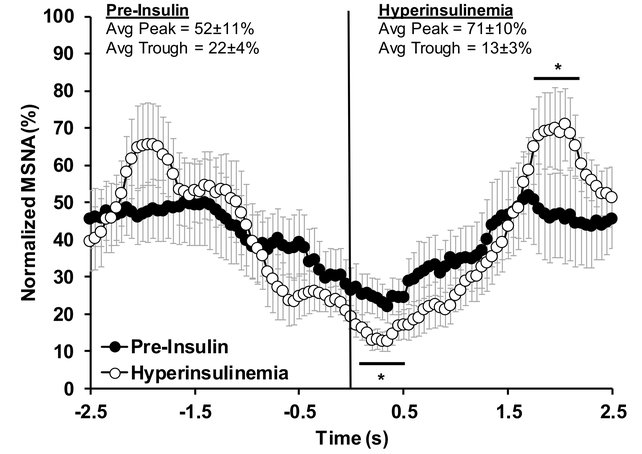

Figure 4: Anticipated Results. Cross-correlation histograms between sympathetic spikes and respiration. Normalized data (Means ±SEM) prior to and during hyperinsulinemia. Data were calculated by counting the percentage of spikes in each bin over specific time periods. Time zero corresponds to the peak of inspiration and is indicated by the vertical line. *p<0.05 vs Pre-Insulin.

CONCLUSIONS

Although analysis is ongoing, these data may have important implications for mechanistic understanding of sympathetic activation and cardiovascular regulation in conditions of hyperinsulinemia (e.g., insulin resistance, type 2 diabetes).

ACKNOWLEDGEMENTS

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