Sympathetic Discharge Patterns in Human Type 2 Diabetes

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INTRODUCTION

- Sympathetic nervous system activity is predictive of cardiovascular morbidity and mortality – and has been shown to be elevated in individuals with Type 2 Diabetes.
- Muscle sympathetic nerve activity (MSNA) can be directly measured in humans using the technique of microneurography.
- Sympathetic neural recordings are often rectified and integrated to give multi-unit MSNA "bursts" that represent activity of several axons recorded simultaneously.
- A limitation of multi-unit MSNA is that it does not account for information regarding the coding patterns of single action potentials which can provide important information about central neural processing and have implications for end organ responses (e.g., blood pressure).

We sought to evaluate differences in the magnitude and patterning of sympathetic neural discharge in healthy adults and adults with Type 2 Diabetes

HYPOTHESES

- **Individuals with Type 2 Diabetes will display augmented action potential firing patterns compared to healthy controls.**
- **Action potential firing patterns will be associated with end organ responses (i.e., blood pressure).**

METHODS

- **Participants:** 5 healthy control participants (1M/4F, 59±4 yrs, HbA1c 5.6±0.1%) and 6 adults with Type 2 Diabetes (4M/2F, 51±2 yrs, HbA1c 7.6±0.7%)
- **Medications:** Type 2 Diabetes group: diuretic (n=1), ACE (angiotensin-converting enzyme) inhibitor (n=1), angiotensin II receptor blocker (n=1), GLP-1 receptor agonist (n=1), metformin (n=1), thiazolidinedione (n=1), statin (n=3). All control participants were free of medication.
- **Instrumentation:** Heart rate (HR, beats/min, electrocardiography), mean arterial blood pressure (MBP, mmHg, finger photoplethysmography), and multi-unit muscle sympathetic nerve activity (MSNA, bursts/min microneurography of the peroneal nerve)

Figure 1: Muscle sympathetic nervous system activity (MSNA) is measured using the technique of microneurography at the level of the peroneal nerve.

METHODS

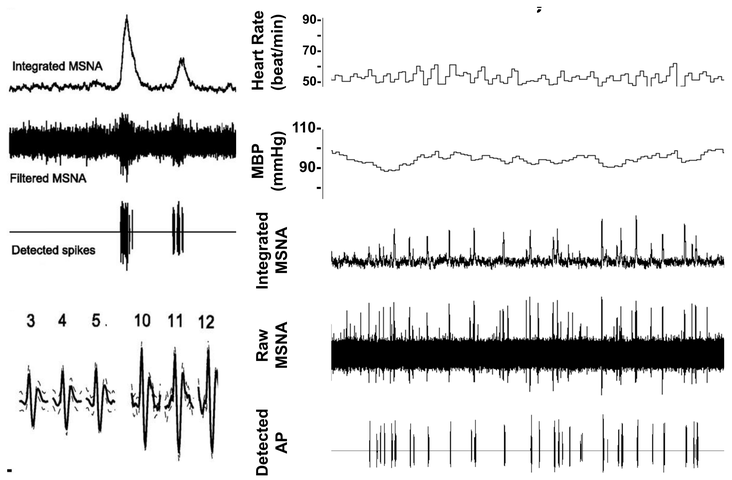

Figure 2: Sympathetic neural discharge analysis. In addition to the standard multi-unit method (integrated MSNA), sympathetic action potential (AP) patterns (detected spikes) were studied from the filtered raw MSNA signal. These AP were grouped by amplitude using matched wavelet methodology. This approach enables the quantification of firing characteristics of populations of sympathetic neurons (clusters) to comprehensively assess strategies used by the central nervous system in health and disease.

RESULTS

	Control	T2D	*P*-value
Count (M/F)	1/4	4/2	---
Age (yrs)	59±4	51±2	0.11
Weight (kg)	73±3	87±7	0.06
Body Mass Index (kg/m^2)	26±2	32±3	0.20
Waist Circumference (cm)	87±9	108±7	0.07
Body Fat (%)	36±5	35±3	0.83
Glucose (mg/dL)	82±2	142±25	0.10
Insulin (uIU/L)	4.4±1.2	17.6±6.7	0.13
HbA1c (%)	5.6±0.1	7.6±0.7	0.07
HOMA-IR	0.9±0.3	6.7±3.5	0.19
QUICKI	0.40±0.02	0.33±0.03	0.05
Diastolic BP (mmHg)	67±3	71±2	0.14
Mean BP (mmHg)	95±5	94±3	0.90

Table 1: Participant characteristics. Type 2 Diabetic (T2D), Blood Pressure (BP). Statistical analysis: Student's t-test or Welch's t-test (Normality: Shapiro-Wilk, Equal Variance: Brown-Forsynthe).

RESULTS

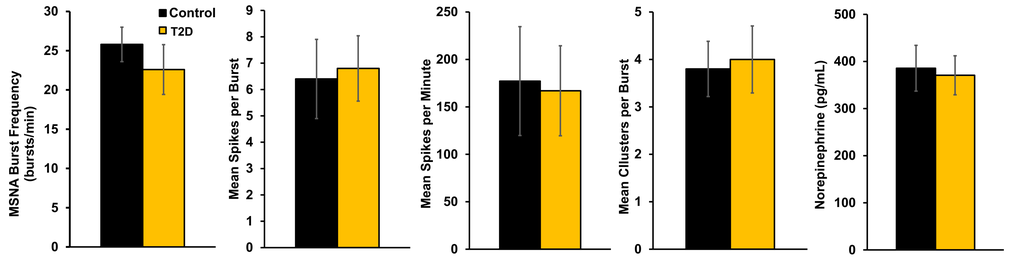

Figure 3: Muscle sympathetic nervous system activity (MSNA). Type 2 Diabetic (T2D). Statistical analysis: Student's t-test or Welch's t-test (Normality: Shapiro-Wilk, Equal Variance: Brown-Forsynthe). NS = no statistical significance detected.

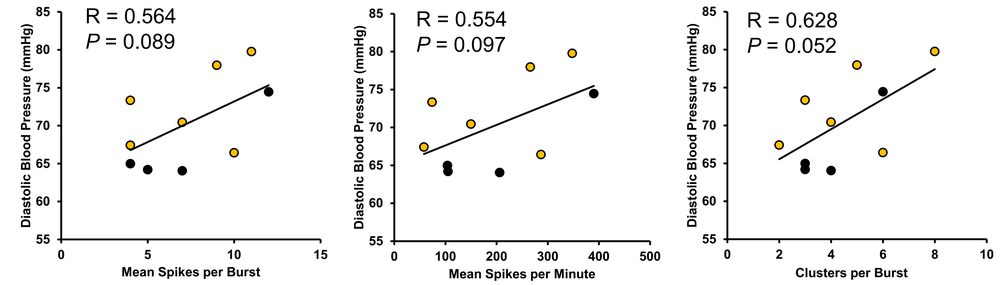

Figure 4: Relationship between muscle sympathetic nervous system activity (MSNA) and diastolic blood pressure. Control (black circles), Type 2 Diabetic (T2D, yellow circles). Statistical analysis: Pearson Correlation.

CONCLUSIONS

- Neither multi-unit muscle sympathetic nerve activity (MSNA) nor the firing and/or patterning of populations of sympathetic neurons comprising the integrated MSNA envelope differed between healthy controls and adults with Type 2 Diabetes. (**Figure 3**).
- A correlation between sympathetic firing patterns (spikes/min, clusters/burst) and diastolic blood pressure was observed, such that those individuals with greater sympathetic neural discharge exhibited higher resting diastolic blood pressure (**Figure 4**).

These data support a role for augmented sympathetic neural firing in exaggerated diastolic blood pressure that does not differ between healthy controls and adults with Type 2 Diabetes.

ACKNOWLEDGEMENTS

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