

# **Symptoms of Orthostasis may be due to Sympathetic/Parasympathetic Autonomic Imbalance and can be Evaluated by HRV-Respiratory Analysis with Appropriate Pathogenesis Oriented Therapeutic Choices.**

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# Head-Up Posture

- Abnormal autonomic response to head-up postural change (PC) can cause Orthostatic symptoms and are an incapacitating feature of autonomic dysfunction
- Abnormal Sympathetic (SNS) and Parasympathetic (PSNS) changes occurring during and immediately following PC include:
  - SNS withdrawal (SW)
  - SNS excess (SE)
  - PSNS excess (PE)

# Enhanced Frequency Domain Analysis Method

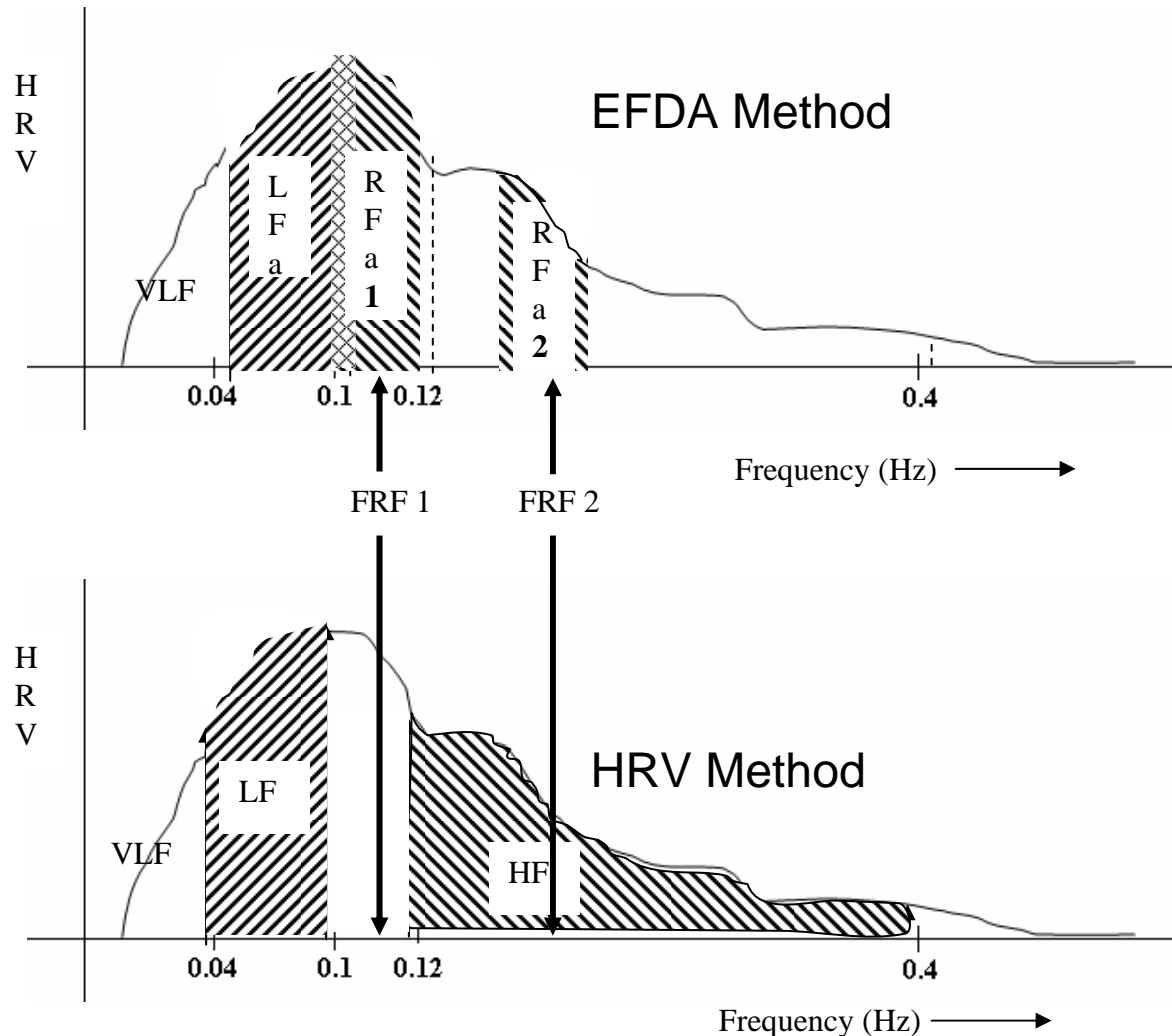
EFDA:

- 1) Spectral Analysis of Respirations to compute Fundamental Respiratory Frequency (FRF)
- 2) Spectral Analysis of HRV
- 3) Locate FRF in HRV spectrum
- 4) Compute Parasympathetic (RFa) activity
- 5) Compute Sympathetic (LFa) activity

HRV:

LF: Sympathetic activity as modulated by Parasympathetic activity

HF: Broad, fix frequency that can include parasympathetic activity



# EFDA Sample

(FRF = .08 Hz (~5 breaths/min))

A slice of Time-Frequency representation of Respirations at time n (Fig.1) A slice of Time-Frequency representation of IHR at time n (Fig.2). Isolation of high and low frequency power (RFa and LFa regions). Region corresponding to parasympathetic modulation (RFa) is missed in HRV analysis (LF & HF). tHRV indicates the HF area as a measure of parasympathetic.

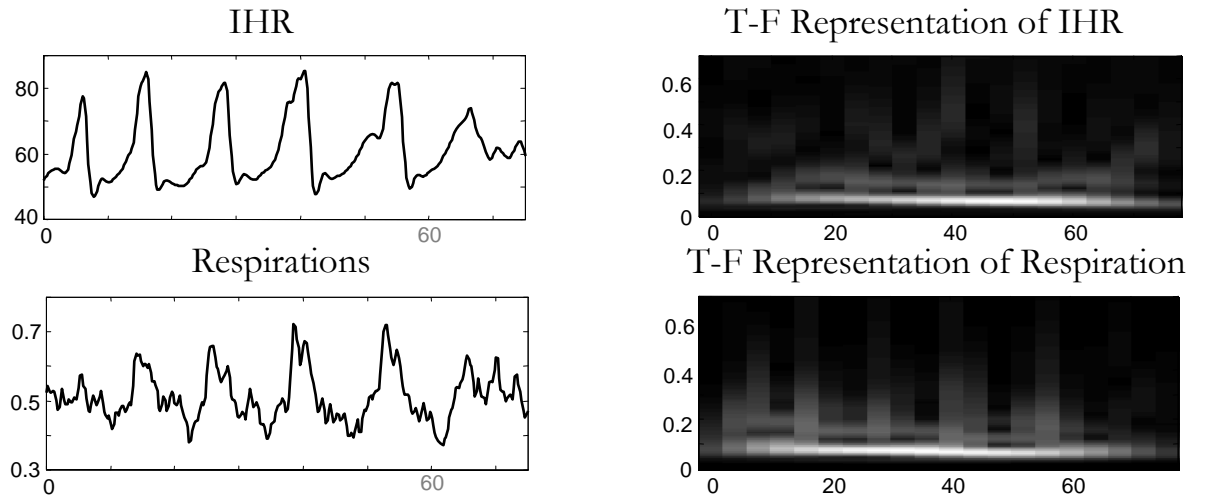


Fig.1

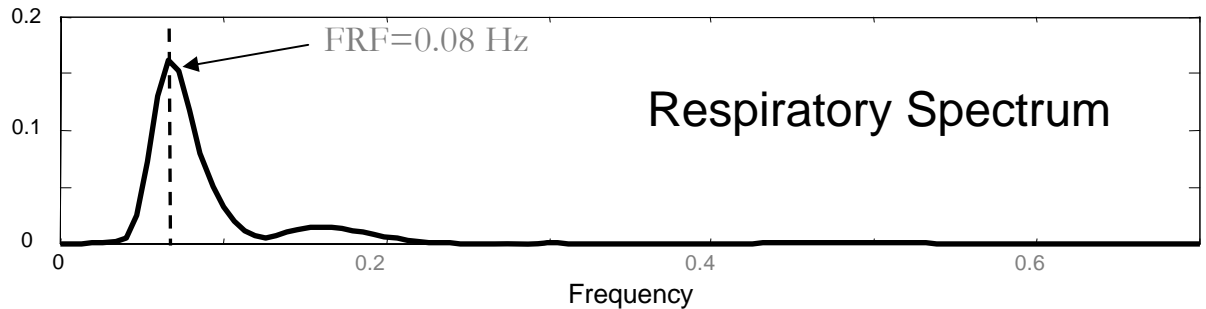
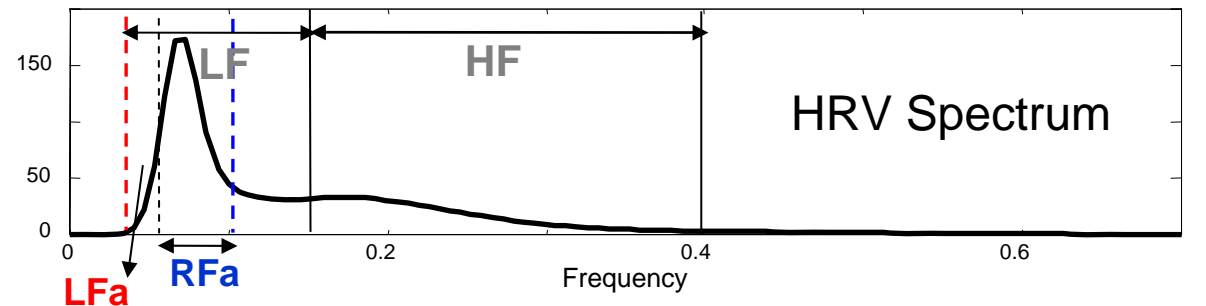


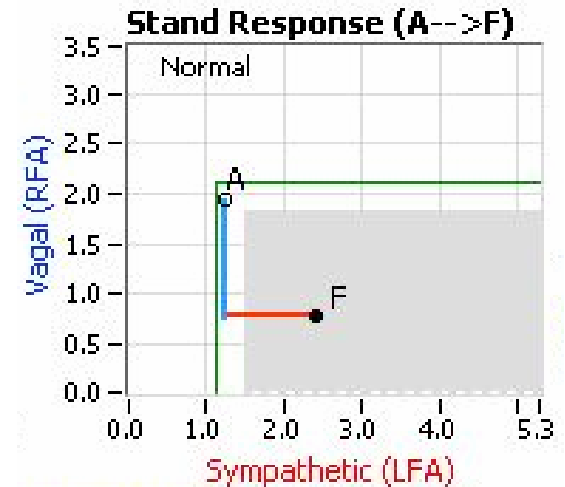
Fig.2



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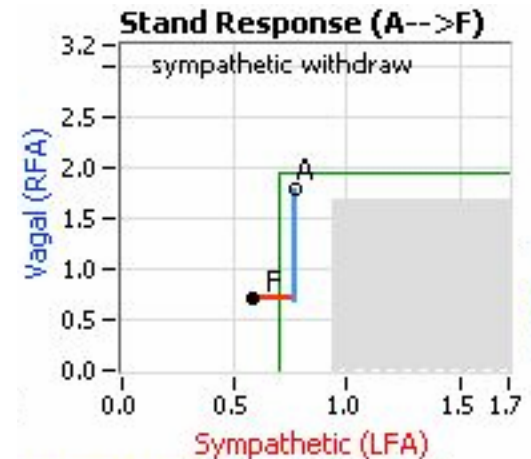
# Normal Head-Up Posture

- Normal upright posture:  
(A: sitting to F: standing)
  - Parasympathetics withdrawal
  - HR increases
  - Exercise Reflex helps to maintain blood pressure and flow to brain
  - Exercise Reflex ends
  - Sympathetic surge to maintain vascular tone, blood pressure and flow to brain



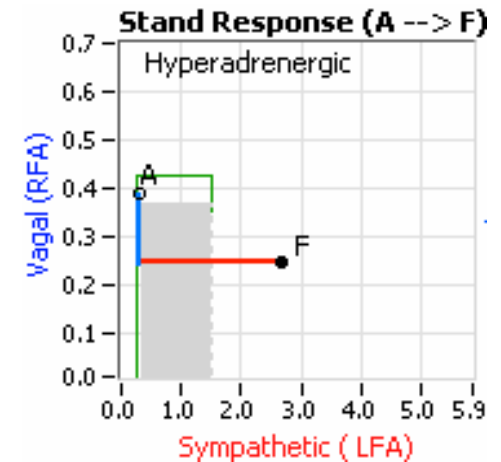
# Autonomic Dysfunction During Head-Up Postural Change (Sympathetic Withdrawal)

- Orthostatic Intolerance (OI)
  - SW plus normal BP change upon standing
- Orthostatic Hypotension (OH)
  - Clinical: SW plus 20 mmHg systolic and 10 mmHg diastolic BP decrease upon standing
  - Pre-clinical: SW plus any BP decrease upon standing
- SW can be corrected with Alpha-adrenergic Agonists



# Autonomic Dysfunction During Head-Up Postural Change (Sympathetic Excess)

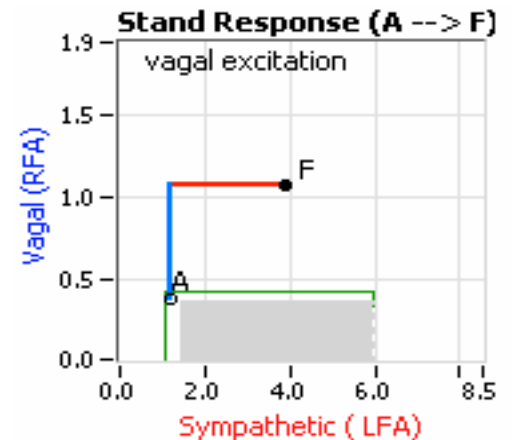
- Postural Tachycardia Syndrome (POTS)
  - Clinical: SE plus 30 bpm increase in HR or HR > 120 bpm upon standing
  - Pre-clinical: SE plus excessive HR increase (>15%) upon standing



- SE can be corrected with Beta1-adrenergic Antagonists

# Autonomic Dysfunction During Head-Up Postural Change (Parasympathetic Excess)

- PE (or SW) can present with bradycardia
  - Can be corrected with Cholinergic Antagonists or Alpha-adrenergic Agonists
- SE can present with a large increase in BP
  - Can be corrected with adrenergic antagonists
- PE can mask SW



# Patient Population

- Adult diabetic patients
  - Age (avg) 63.2 yrs; range 25-96 yrs
  - 354 Type 2 Diabetics (avg 63.5 yrs, 161 females)
  - 35 Type 1 Diabetics (avg 61.1 yrs, 17 females)
- Resting Baseline (Bx) and PC Autonomic measures taken and averaged over 5 minutes each

# Expected Normal Changes From Bx to PC

- Parasympathetics: a decrease of 5%
- Sympathetics: an increase of between 120% and 500%
- HR: an increase of 10% or more, but no more than 30 bpm
- BP: (systolic) an increase of between 10 and 30 mmHg

# Results

- *EFDA revealed 50.8% positive for SW or PE*
- *Clinically, 58.7% were positive for symptoms of Orthostasis*
- *ANS indications were not found in 13.3% of the population with symptoms. Symptoms were found to be due to non-autonomic effects.*
- *ANS indications were found in 12.0% of the population without symptoms. These indications tended to be early signs of clinical disorders.*

% Pts with	POTS	OH	POBS	POHS
Clinical Symptoms	7.5	44.9	1.6	4.7
ANS Indications w/in Clinical Group	95.8	66.7	80.0	73.3

POTS = Postural Orthostatic Tachycardia Syndrome, *SE w/ Tachycardia*

OH = Orthostatic Hypotension, *SW w/ Hypotension*

POBS = Postural Orthostatic Bradycardia Syndrome, *SW or PE w/ Bradycardia*

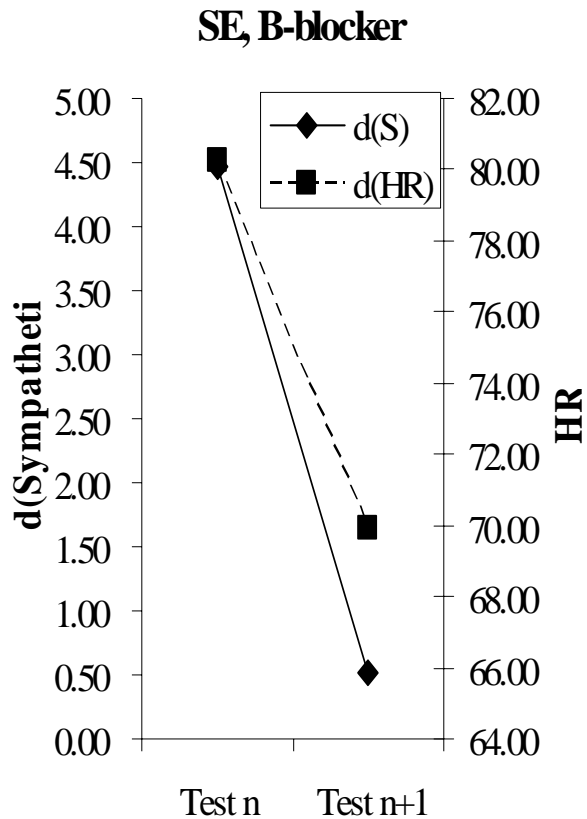
POHS = Postural Orthostatic Hypertensive Syndrome, *SE w/ Hypertension*

# Conclusion

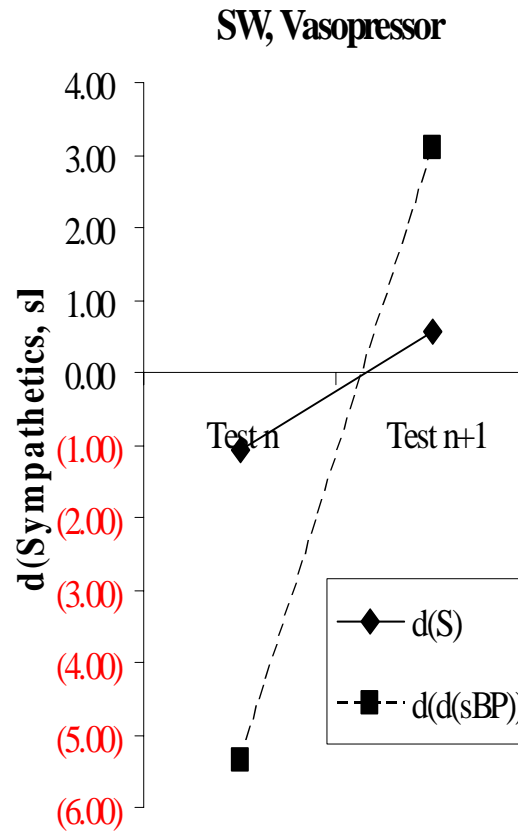
- EFDA appropriately depicts the autonomic responses associated with HR and BP responses to PC
- This non-invasive methodology
  - Correctly evaluates the physiologic changes attributable to orthostatic symptoms
  - Provides a rational- or functional-basis for therapies to improve autonomic dysfunction and relieve the symptoms of these disorders

# Therapeutic Results

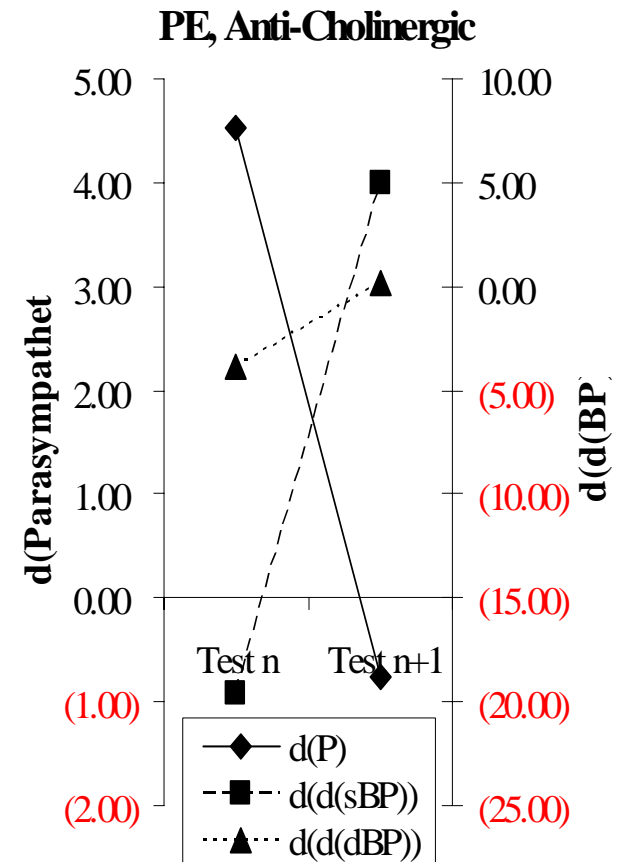
## (Single Agent Changes Only)



N = 57



N = 185



N = 50