



# ***Assessment of Autonomic Function in the Collapsing Child***



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# Content

- Autonomic Influences on CVS
- Assessment of ANS
- Diagnostic insights
- ? Treat abnormalities in the ANS



# Autonomic Cardiovascular Control

Hypothalamic autonomic centre

Brainstem  
Solitary Tract Nucleus

Sympathetic  
outflow

Vagus  
nerve

Preganglionic  
neuron

$\alpha_2$

Sympathetic  
postganglionic  
neuron

Carotid sinus

Arterial  
baroreceptors

Aorta

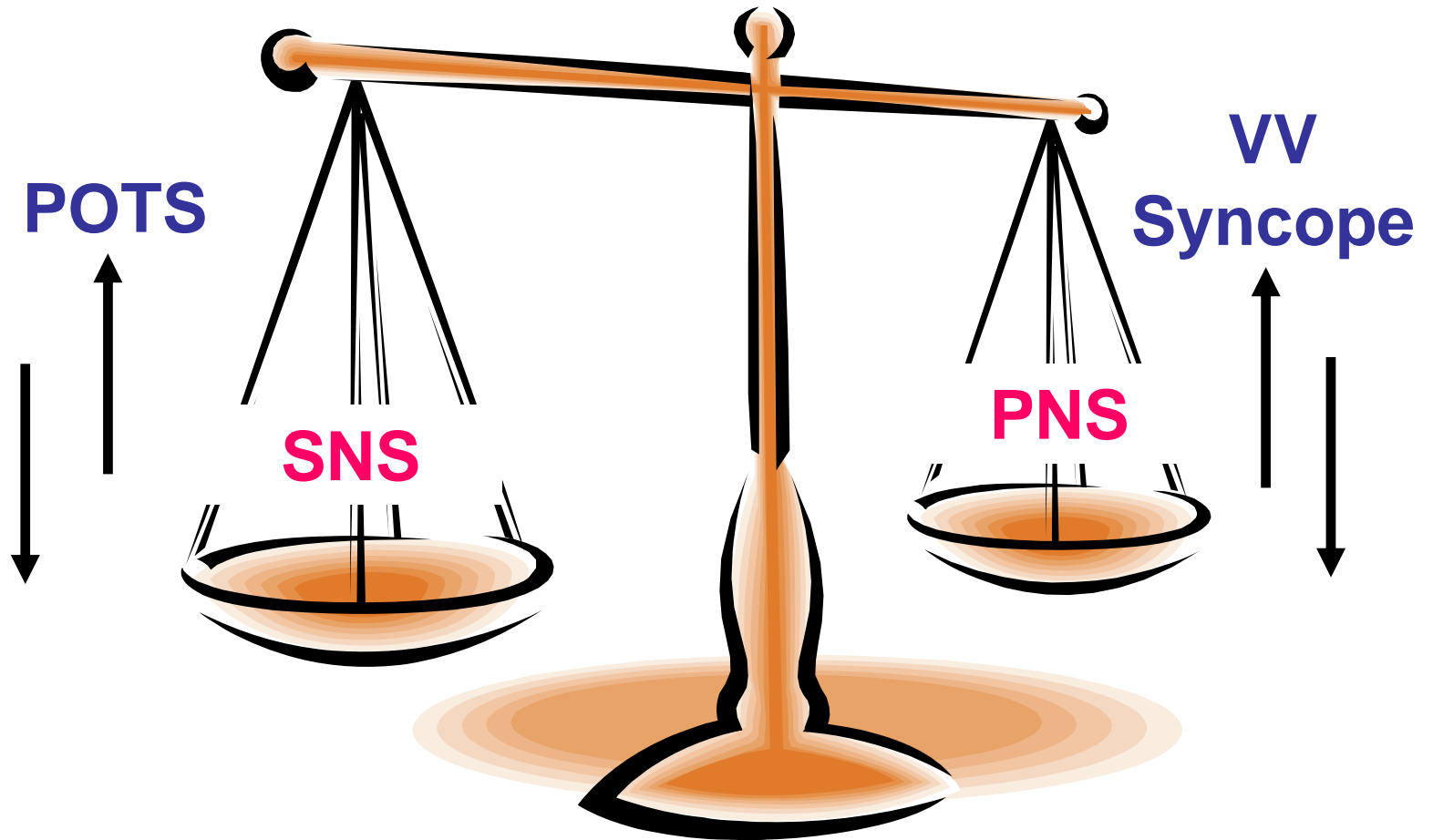
Cardiac baro-  
receptors

Sinus  
node  
 $\beta_1$ -receptors

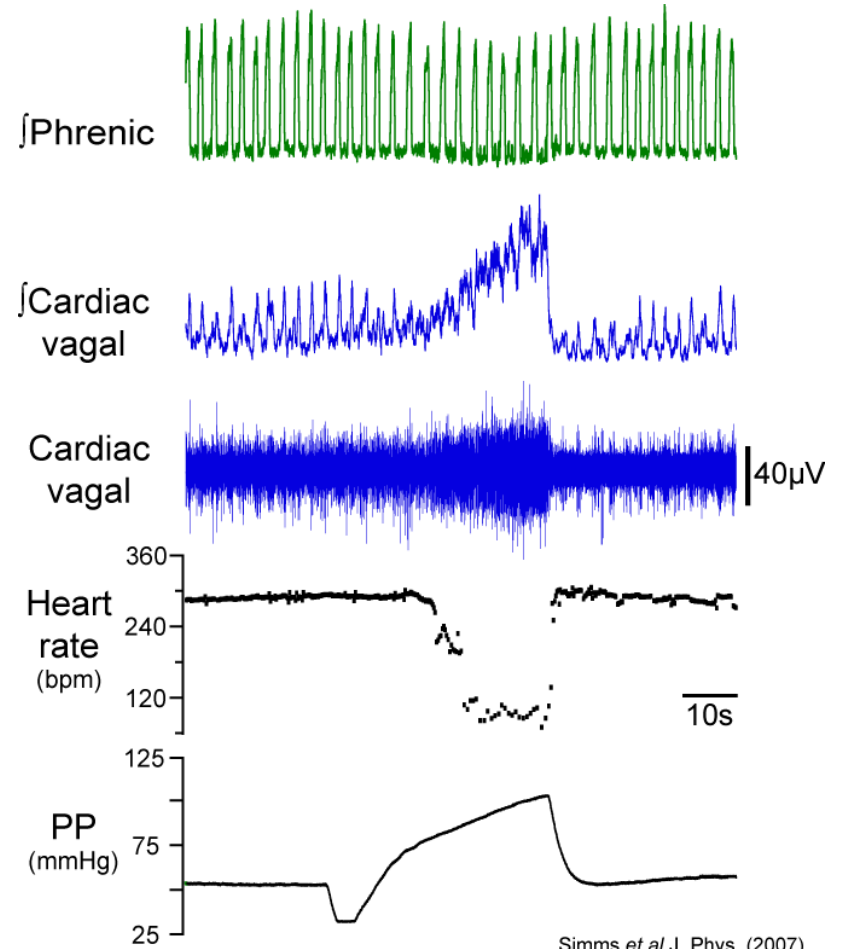
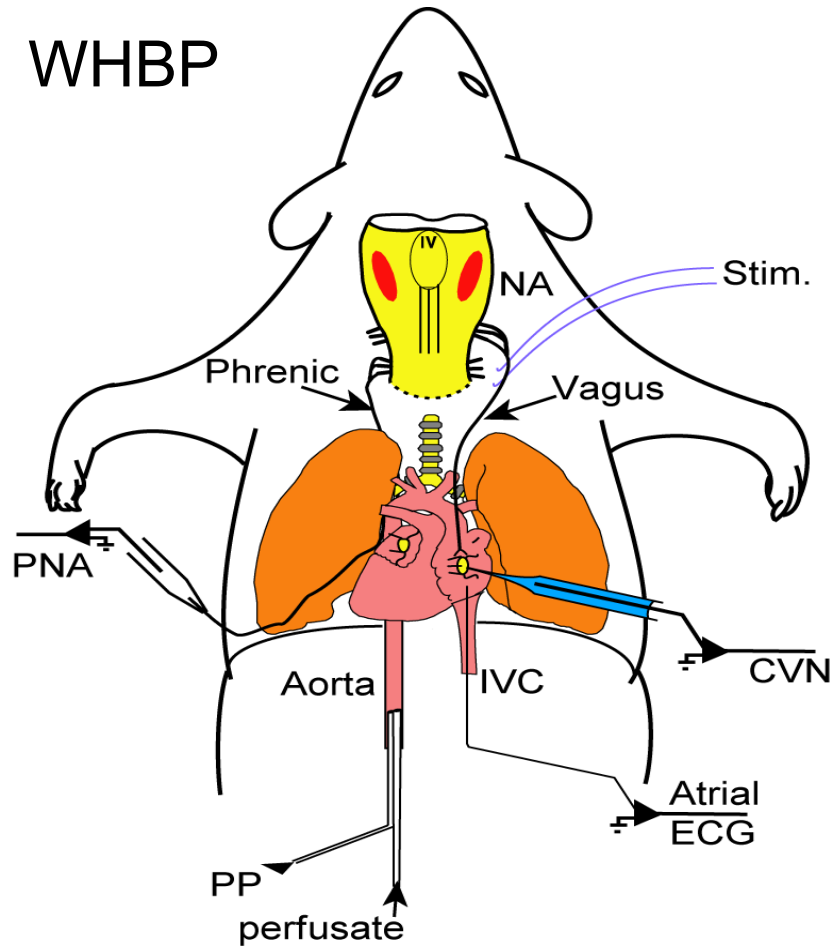
Arteriolar constriction  
 $\alpha_1$ -receptors



# Balance



# Assessment of ANS



Simms et al J. Phys. (2007)



Courtesy of Professor Julian Paton, University of Bristol

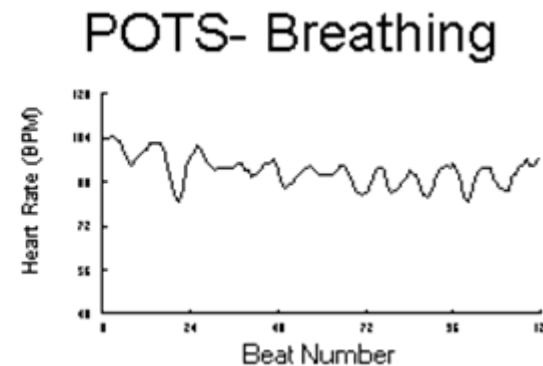
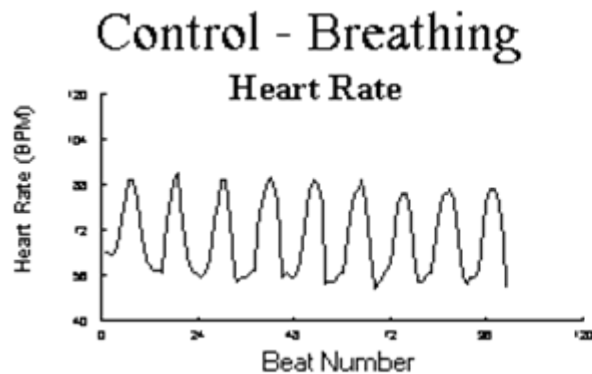
# Assessment Modalities

- Clinical
  - Cardiovagagal Function
    - HRV (deep respiration)
    - HR response to Valsalva
    - HR response to postural change
  - Sympathetic Function
    - BP response to Valsalva
    - BP response to postural change
    - Isometric Exercise
    - Cold Pressor and Mental Stress
  - Others
    - Tilt test
    - Carotid Sinus Massage
- Research
  - Power Spectral Analysis
  - Baroreflex Function
  - Microneurography
  - Pharmacological Testing
  - Catecholamine Measures
  - Imaging



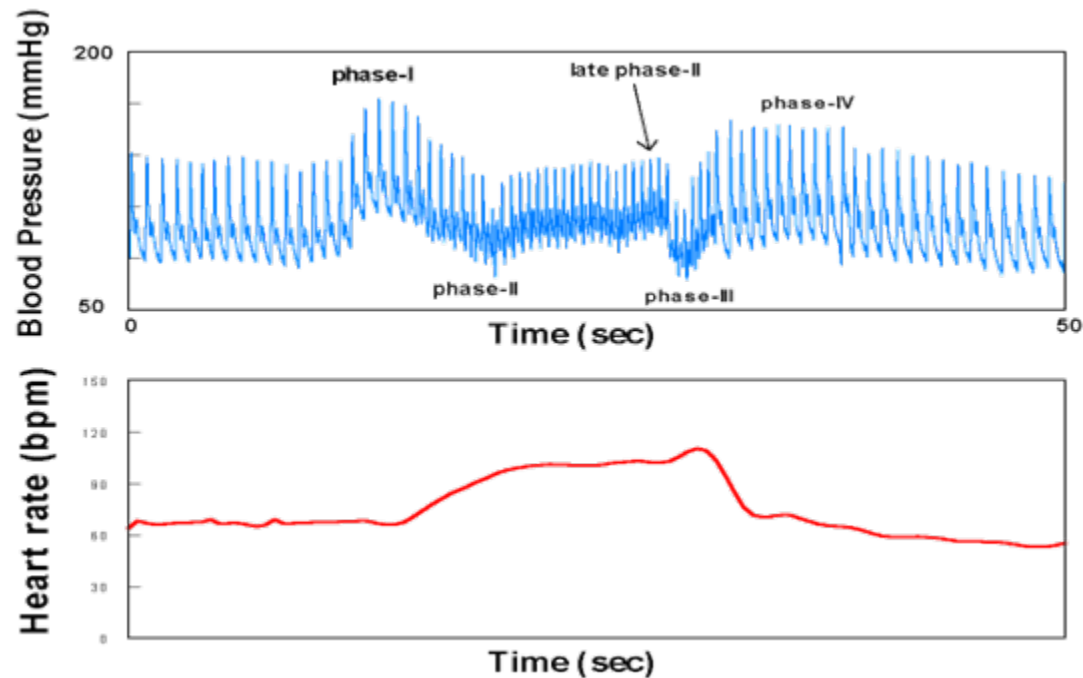
# Clinical Assessment

- Cardiovagagal Function
  - HRV (deep respiration)
  - Metronome
  - 6-15 cycles



# Clinical Assessment

- Cardiovagagal Function
  - HR response to Valsalva
  - HR in phase II and IV

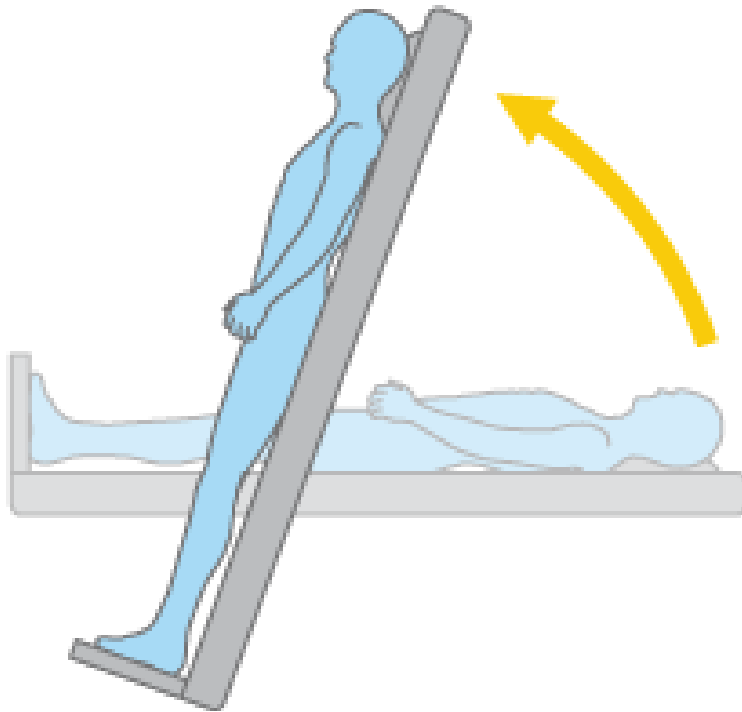


# Assessment

- Sympathetic Function
  - BP response to Valsalva -  $\uparrow$  phase IV
  - BP response to postural change
  - Isometric Exercise
  - Cold Pressor and Mental Stress



# Tilt Test

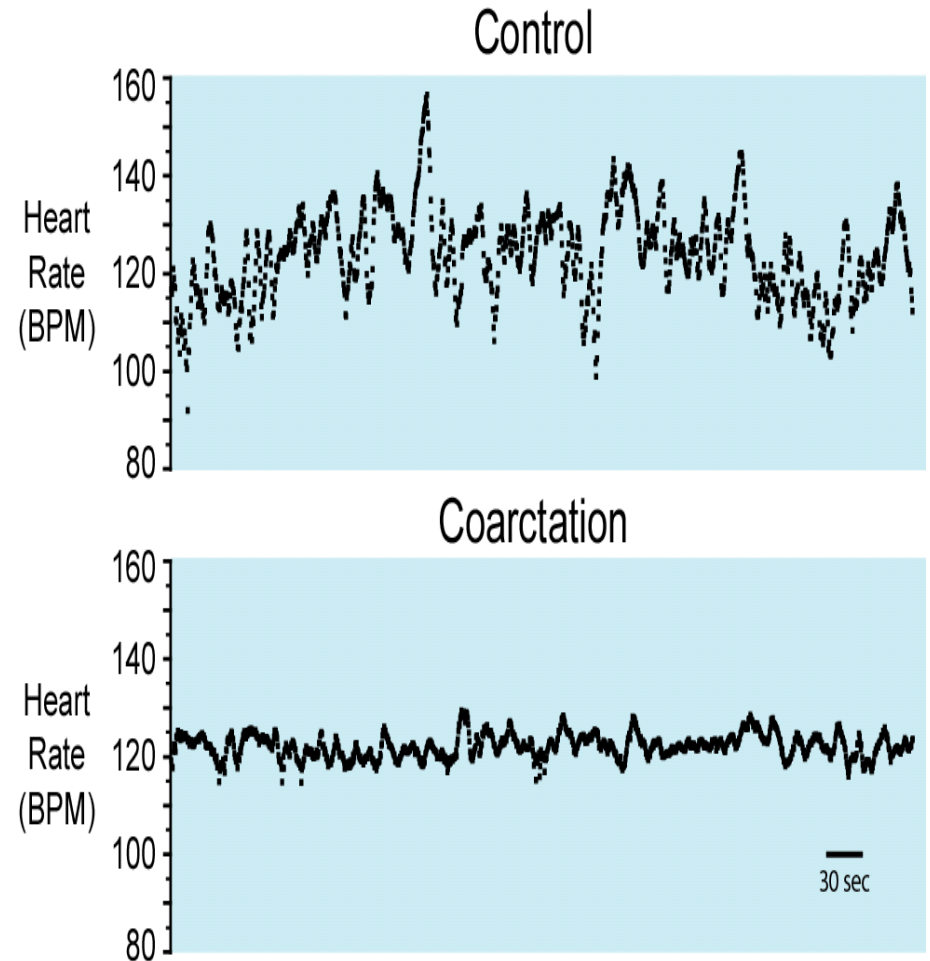


- Reflex  $\uparrow$  SNS activity
- $\downarrow$  PNS activity
- Vasoconstriction
- $\uparrow$  Heart Rate
- Assessment



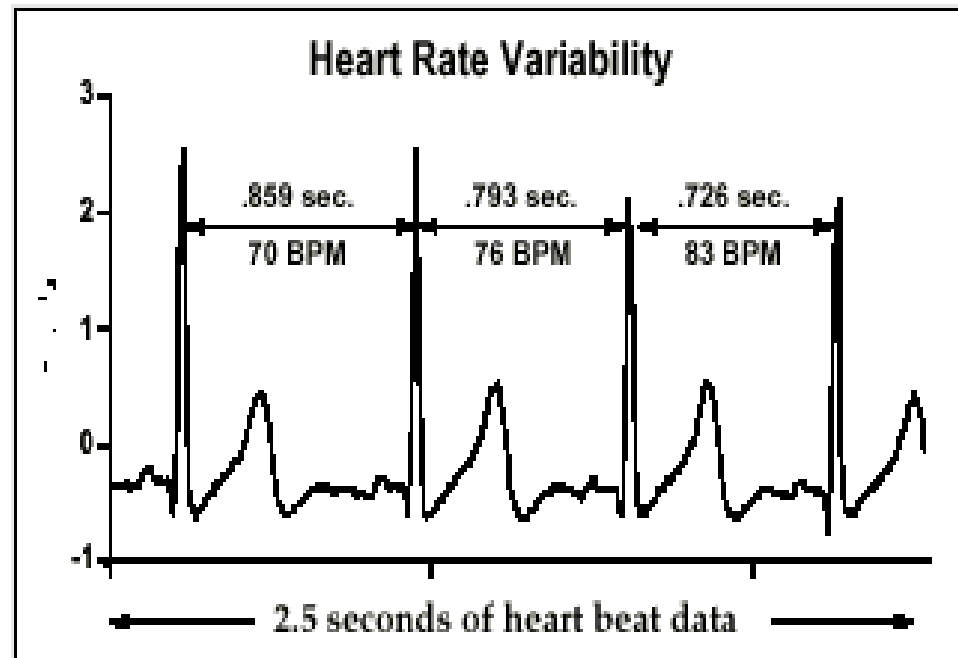
# Research Assessment

- Heart Rate Variability – beat to beat control
- PNS and SNS – fluctuations at different frequencies
- Time Domain  
Frequency Domain



# Heart Rate Variability

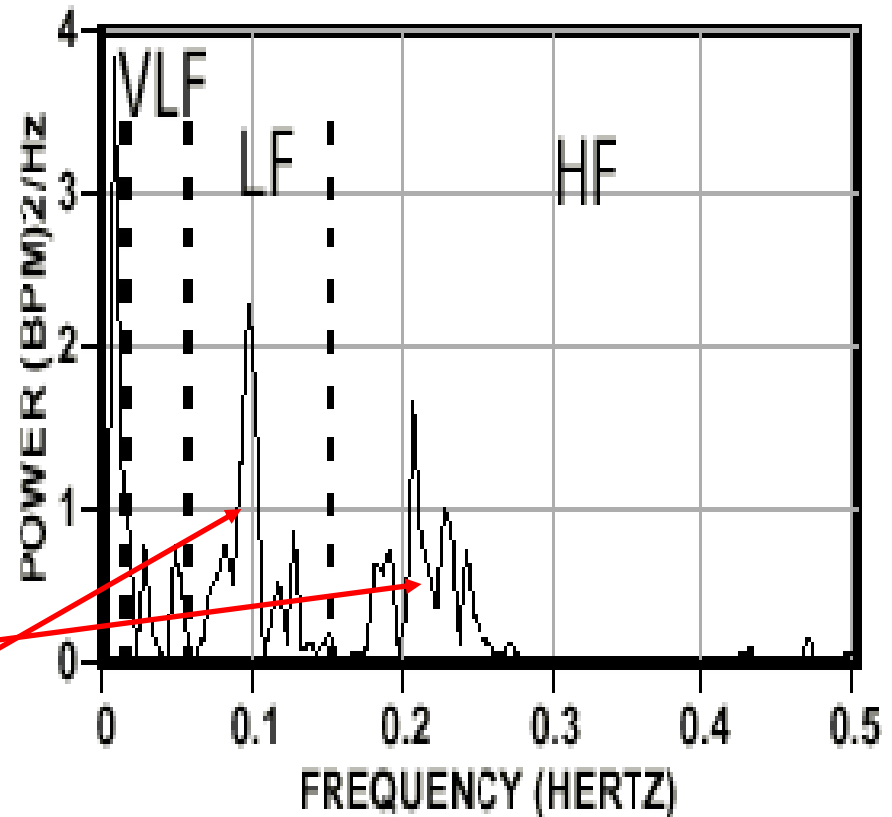
- Time Domain
  - SDNN: Total Power
  - RMSSD: HF
  - NN50: HF
  - pNN50: HF



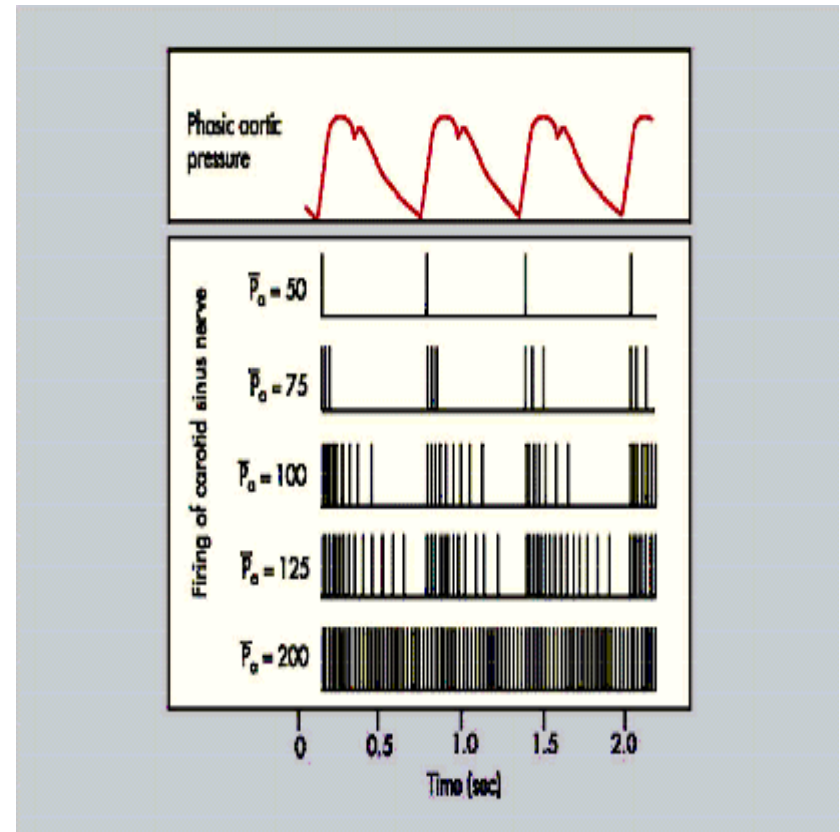
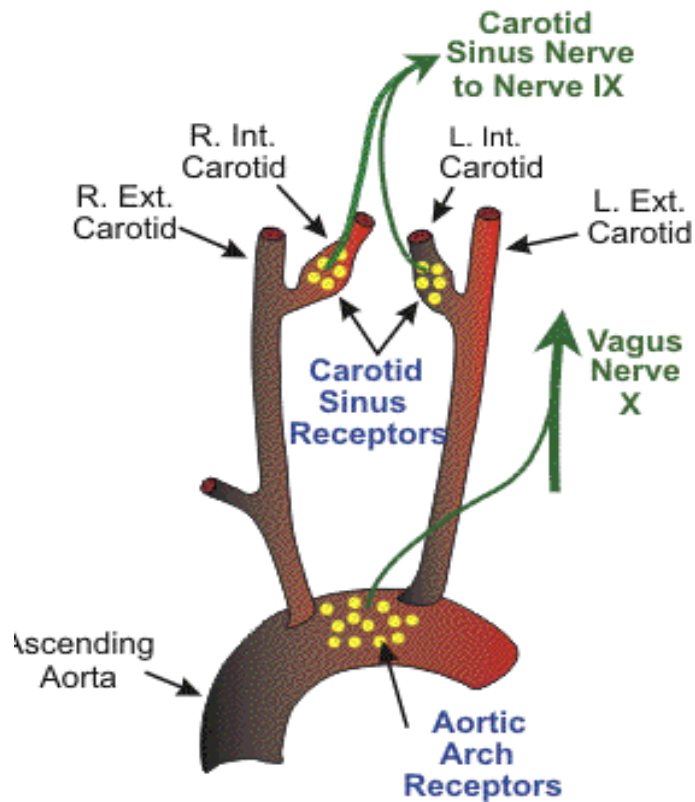
# Heart Rate Variability

- Frequency Domain
- Fast Fourier Transformation
- Frequency Modulations

- HF: Parasympathetic
- LF: Sympathetic +/- Parasympathetic



# The Baroreceptor

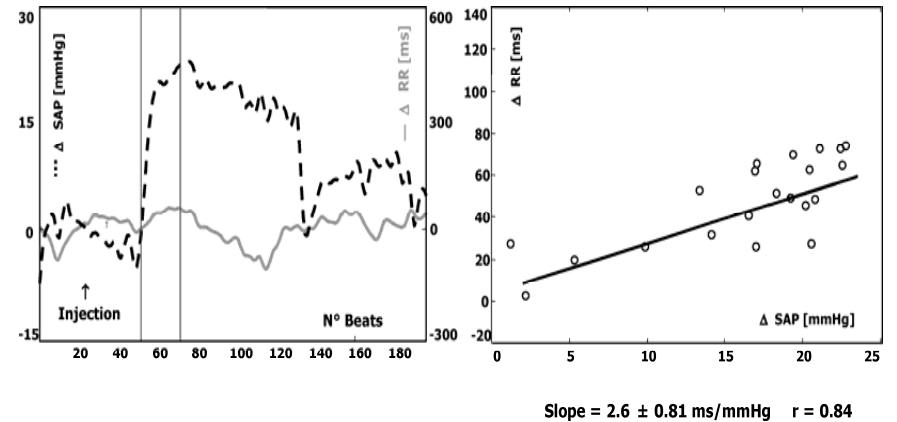
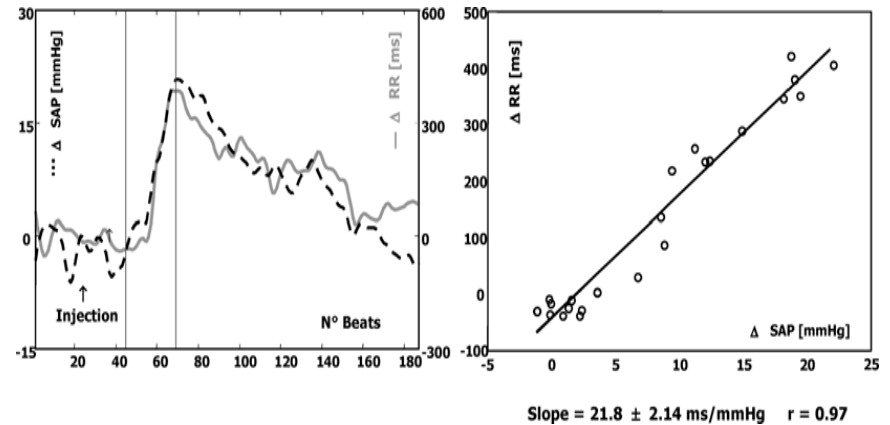


*La Rovere et al for the ATRAMI investigators. Baroreflex sensitivity and heart rate variability in prediction of total cardiac mortality after myocardial infarction. Lancet 1998; 351:478-484.*



# BRS Assessment

- “Oxford” technique – Phenylephrine
- Vasopressors – assess vagal component
- Vasodilators – assess sympathetic mechanisms

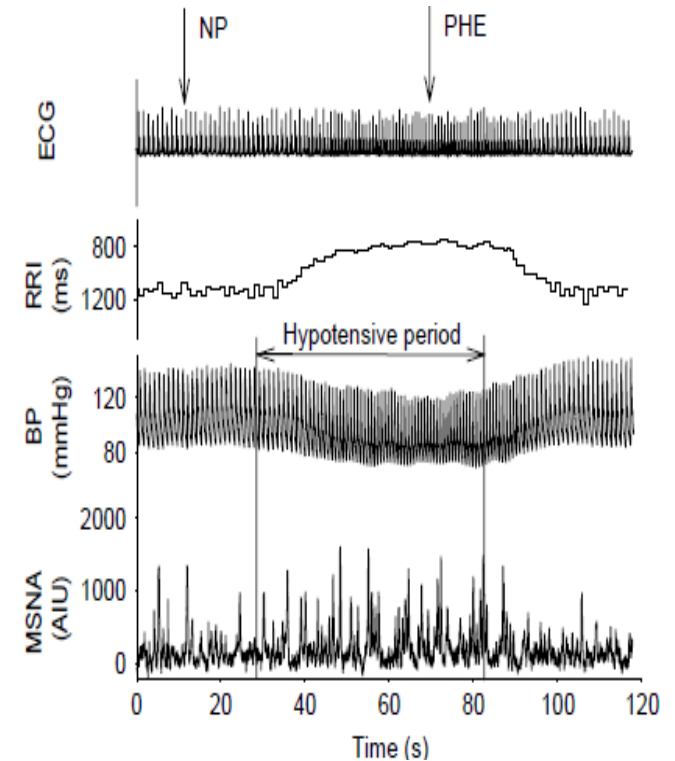
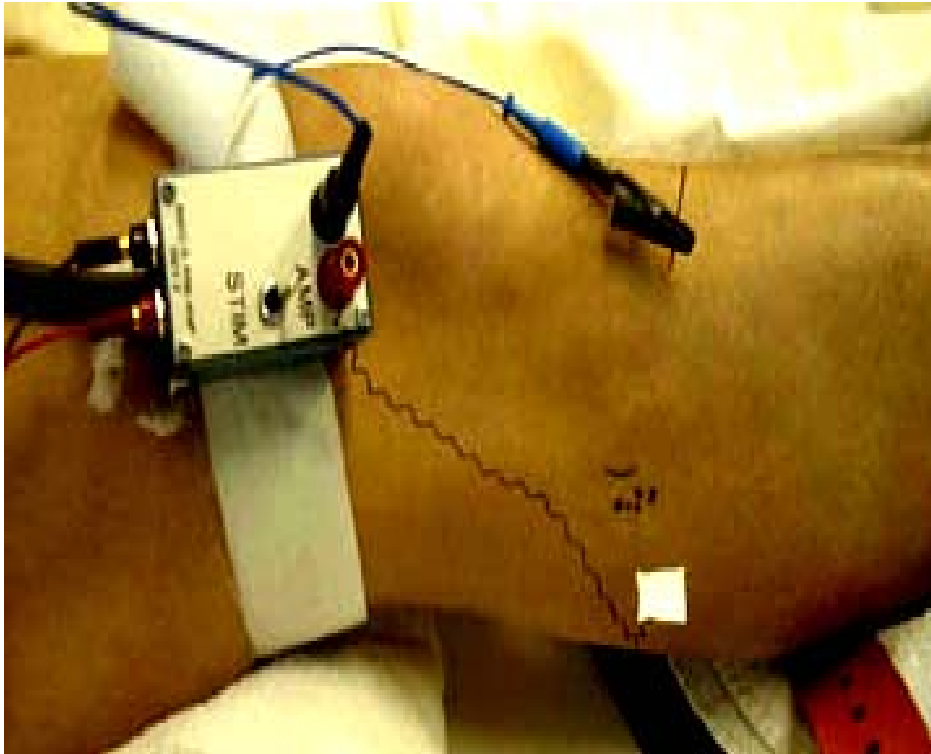


# Non-invasive Assessment

- Valsalva
- Neck Cuff
- Lower Body Negative Pressure
- Assessment of Spontaneous Variations



# Microneurography



*Kamiya A et al. Low-frequency oscillation of sympathetic nerve activity decreases during development of tilt-induced syncope preceding sympathetic withdrawal and bradycardia. Am J Physiol Heart Circ Physiol 289:1758-1769, 2005.*

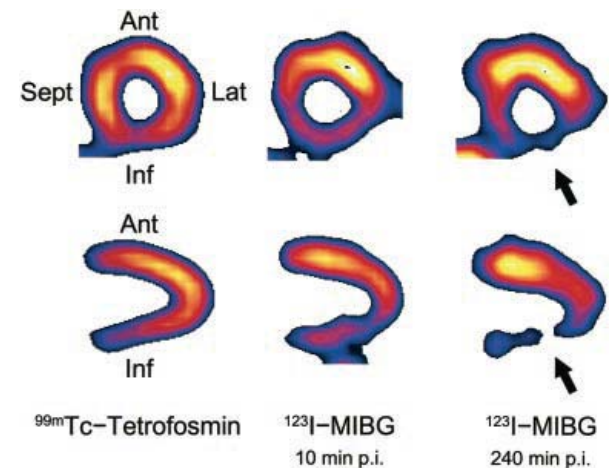
# Pharmacological Testing

- Noradrenaline
  - Limitations
- Precursors
  - DHPG – 3,4-dihydroxyphenylglycol
  - DOPAC – 3,4-dihydroxyphenylacetic acid



# Imaging

- $^{123}\text{I}$ -MIBG – sympathomimetic amine
- Imaged with SPECT
- Abnormalities in Brugada<sup>1</sup>
- Suggests presynaptic dysfunction



1. *Wichter T et al. Cardiac Autonomic Dysfunction in Brugada Syndrome. Circulation. 2002 ;105:702-6.*

# Diagnostics - Syncope

- **Conflicting Data**

- **Kochiadakis GE et al.** *Assessment of autonomic function at rest and during tilt testing in patients with vasovagal syncope. Am Heart J. 1997;134:459-66.*
- **Picirillo G et al.** *Heart rate and blood pressure variability in subjects with vasovagal syncope. Clin Sci (Lond). 2004;107:55-61.*
- **Virag N et al.** *Prediction of vasovagal syncope from heart rate and blood pressure trend and variability: experience in 1,155 patients. Heart Rhythm. 2007 ;4:1375-82.*
- **Alehan D et al.** *Heart rate variability and autonomic nervous system changes in children with vasovagal syncope. Pacing Clin Electrophysiol. 2002 ;25:1331-8.*



# Sudden Cardiac Death

- Adrenergic stimuli and Arrhythmia
  - LQTS - High sensitivity to sympathetic stimulation
  - CPVT -  $\uparrow$  RyR2 open probability
- ? Represent normal ANS responses with abnormal genes
- ? Abnormal ANS responses with abnormal genes

*Malfatto et al. Sympathetic neural modulation of cardiac impulse initiation and repolarization on the newborn rat. Circ Res. 1990 ;66:427-37.*



# Sudden Cardiac Death

- If autonomic heterogeneity - ? Stratify
- Monitor responses to treatment
  - Beta Blockade
- Place for Neurohormonal remodelling
  - Can we alter the ANS to reduce the impact of adrenergic effects of the myocardium
  - ? Exercise<sup>1</sup>

1. *Perhonen MA et al. Effect of physical training on ventricular repolarization in type 1 long QT syndrome: a pilot study in asymptomatic carriers of the G589D KCNQ1 mutation. Europace. 2006 Oct;8(10):894-8.*



# Summary

- ANS – complex balance between S/PNS
- Numerous methods to assess
- ? Predictive responses in VV syncope
- ? Abnormal in channelopathies
  - ? Risk Stratification +/- modulation

