



# Why Monitor the ANS?

**Chronic Disease →**

**Autonomic Dysfunction (PAN & DAN) →**

**Cardiovascular Autonomic Neuropathy (CAN) →  
Death**

- [Boulton, *et al.*, 2005]

***CAN = Denervated Heart***

**(No Parasympathetic Protection) =  
*Risk Of Sudden Death***

- Singer



# UNDERSTANDING ANS

*Requires monitoring both ANS branches  
(**Sympathetics** and **Parasympathetics**)  
simultaneously,  
independently,  
and  
quantitatively*



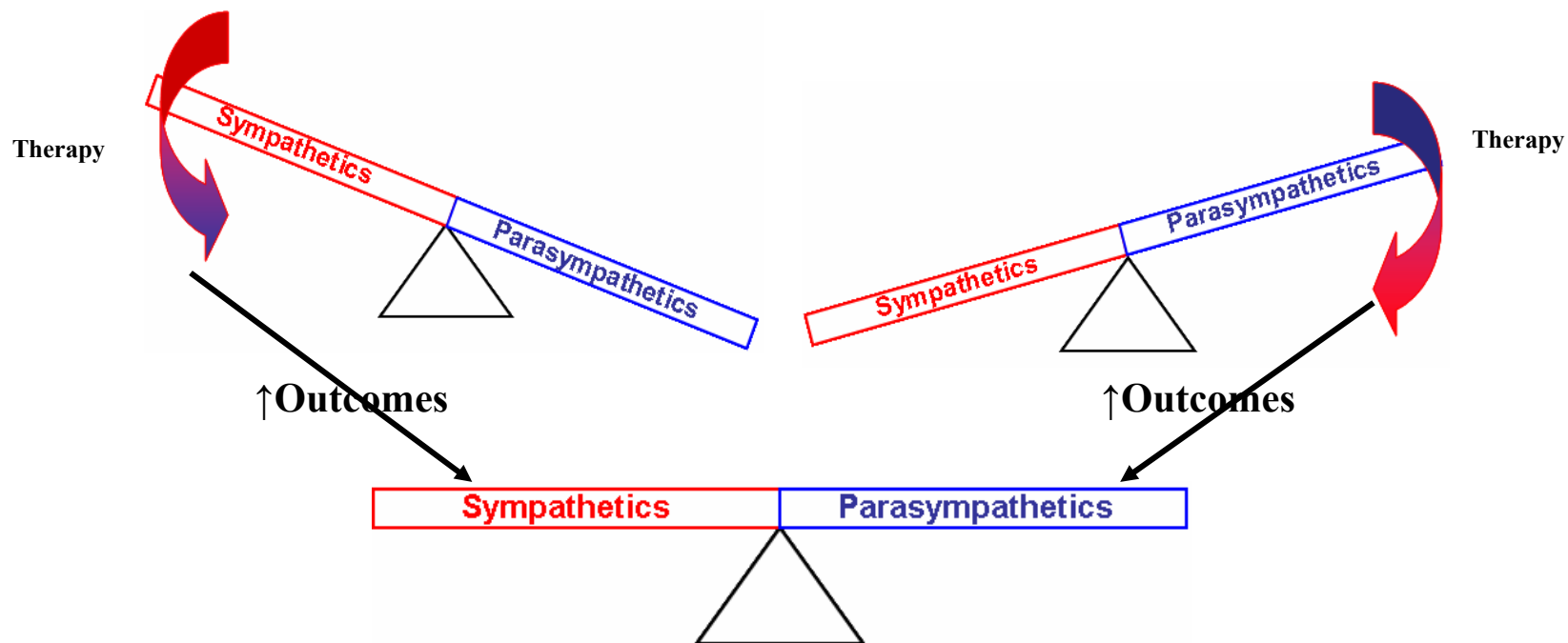
# Treatment

*“You are already treating your patient’s ANS.  
Now you can scientifically optimize therapy  
for the individual patient.”*

*- Bulgarelli*



# Serial Autonomic Function Assessment



**Restoring autonomic balance improves outcomes, preserves quality of life\*, and promotes longevity.**

\*(eating, sleeping, going to the bathroom, having sex)



# History

- 1984 Acquired MIT Technology
- 1987 Technology Patented
- 1989 – 1992 Funded 18 Beta-Sites Nationwide
- 1992: Documented Beta-Site activity in Symposia co-sponsored by
  - Cleveland Clinic
  - Harvard Medical School
  - Johns Hopkins Medical School



# History

- 1995 Received FDA Clearance
- 1997 Lobbied & had released CPT codes
  - 95921 & 95922
- 1999 Sole-source provider to US Government
- 2001 Released ANX-3.0 v. D
- 2002 – Present Additional Patents Awarded
- Doubled sales each year since 2001

*Over 450 Systems Placed Nationwide*



# RESPIRATION IS THE KEY

- Respiratory analysis together with HRV analysis [Katona et. al., Alcalay et. al.]
  - Two measures for a two component system
    - Characterized systemically
    - Quantified mathematically
  - Respiratory analysis determines Vagal outflow
    - “Measures” Respiratory Sinus Arrhythmia to determine systemic Parasympathetic activity



# Heart Rate Variability & Respirations

Akselrod  
at  
MIT

1981  
1985  
1987  
1988

} HRV WITH RESPIRATIONS

Classical HRV  
[Malek, Circulation]

1996

} RESPIRATIONS OMITTED

Malek, 1996

Low, 1997

Uijtdehaage and Thayer, 2002

Williams and Lopes, 2002

Cammann and Michel, 2002

Vinik and Freeman, 2003

} FOR ANS MONITORING  
HRV MUST INCLUDE  
RESPIRATIONS





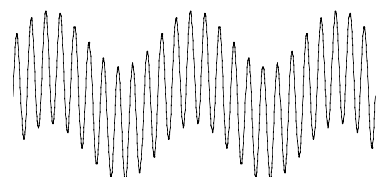
# Heart Rate Variability & Respirations +

- Heart Rate Variability (HRV) with Respiratory Activity (RA) = ANS testing
  - Consider healthy resting cardiogram:
    - Faster respiratory sinus arrhythmia (RSA) = Vagus (PSNS)
    - Slower mean heart rate (mHR) changes = SNS
  - Analyze separately (“peel apart”) = independent measures of both ANS branches
- Spectral analysis is the only method



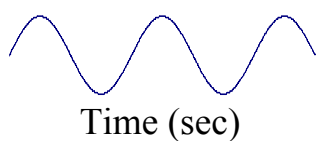
# HRV & RA = ANS

Normal, Healthy,  
Resting Cardiogram



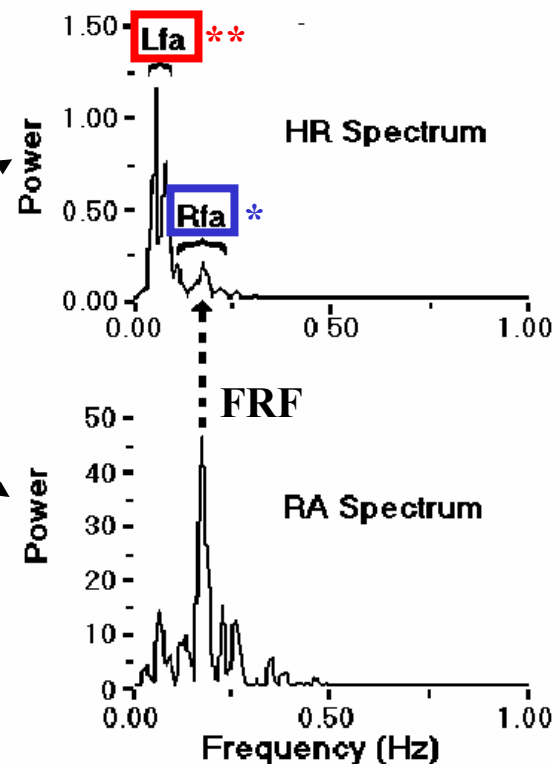
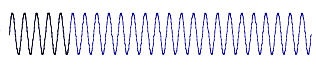
Time (sec)

Slower  
mHR



Time (sec)

Faster  
RSA



**\*Rfa = Parasympathetic Measure**

**\*\*LFa = Sympathetic Measure**

**LFa/Rfa = Sympathovagal Balance**

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# Spectral Analysis

- Common technique: Fourier Transform
  - Requires signal stationarity, *clinically requiring longer data collection times*
  - Forces compromise between time and frequency fidelity, *clinically reducing independence and accuracy*
- Current technique: Wavelet Transform
  - Relieves the signal stationarity requirement
  - Manages time and frequency together
    - Wavelets = shorter data collection times and enhanced sensitivity and specificity



# Who To Test?

## (A Partial List of ICD-9 Codes)

### Neurology

307.4 Sleep Disorders  
Manifestations of thiamine deficiency  
332.0 Paralysis agitans  
333 Parkinsonism & Huntington's chorea  
Other degenerative diseases of the basal ganglia,&  
Olivopontocerebellar degeneration  
333.9 Extrapyramidal disease & abn. movement  
disorders (incl., Stiff-man syndrome)  
Cerebellar degeneration, Spinocerebellar & Amyotrophic  
diseases, Syringomyelia & Syringobulbia  
336 Diseases of the spinal cord  
**337.0 Idiopathic peripheral autonomic neuropathy**  
337.9 Unspecified disorder of ANS  
340 Multiple sclerosis  
352.3 Disorders of Pneumogastric (10<sup>th</sup>) N.  
Mononeuritis, Peripheral & Poly-Neuropathies, incl., DM  
358.1 Myasthenic syndromes (Eaton-Lambert, LEMS)  
372 Conjunctivitis  
Chronic Pain

458 Orthostatic & Chronic Hypotension  
596.54 Neurogenic bladder  
Urogenital Dysfunctions  
705.0 Anhidrosis  
710.2 Sicca syndrome (Sjögren's disease)  
780.2 Syncope and collapse  
780.71 Chronic fatigue syndrome  
785.0 Tachycardia (postural)  
796.1 Abnormal reflex  
Migraines and other headaches

### Internal Medicine

All of the rest, plus:  
278.01 Morbid Obesity  
279.3 AIDS  
296 Depression or Bipolar Disease  
300 Anxiety  
309.81 Post-traumatic Stress Syndrome  
314.0 Attention Deficit Disorder  
729.1 Fibromyalgia

*Low, Assessment: Clinical autonomic testing. Neurology. 1996; 46: 873-80.*



# Who To Test?

## (A Partial List of ICD-9 Codes)

### **Cardiology**

401.0 - 405.99 Hypertension  
412 Post-MI  
413 Angina  
414 Atherosclerosis  
424 Mitral Valve Prolapse  
Syndrome  
425.4 Cardiomyopathy  
427 Cardiac Dysrhythmias  
428 Congestive Heart Failure

### **Pulmonology**

780.51, 780.53, 780.57 Sleep Apnea  
493.90 - 493.93 Asthma  
493.2 COPD

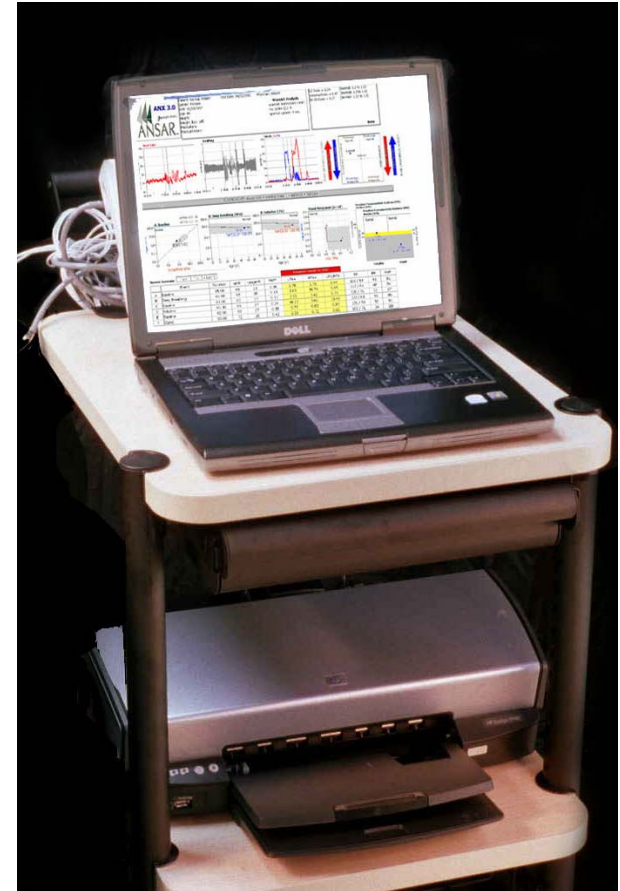
### **Endocrinology**

244 Acquired Hypothyroidism  
246 Thyroid Disorders  
250.0 - 250.8 Diabetes  
256.3 Premature Menopausal  
Symptoms  
627 Menopausal Syndromes



# ANS Testing

- Fully automated, any Technician can be trained and certified by Ansar in an hour
- The test itself is 15.5 minutes in duration
- Requires a plain straight-back chair, the test equipment, and a quiet room
- Technicians and nurses love it, one-on-one time with the patient and no interruptions
- Automated Interpretation Reports





# Interpretation

- There are very few reasons why a test is not valid.
- In almost all cases, test anomalies still provide clinical information about both branches of the ANS, and that is the purpose of the test.



# Interpretation

- Resting Baseline
  - Sympathovagal Balance enables direct, objective indications of therapy titration
  - Assess cardiac stability
- Breathing Challenges
  - Assess degree of autonomic dysfunction
- Upright Posture (Stand) Challenge
  - Detect and differentiate causes of vertigo





# Treatment

1. If  $RFa < 0.1$  clinically protect heart and deal with rest later
2.
  - a) Correct Orthostasis (stand response)
  - b) Return (baseline) balance
    - Considering PPS
3. Normalize baseline
4. Twweek treatment to normalize remainder of ANS responses
  - Deep Breathing and Valsalva



# Therapy Summary

- Standard Practices titrated to the individual's own needs at the time, considering
  - ANS imbalance
    - Standard therapies, perhaps **lower doses**, considering individual responses (balance)
    - Possible **earlier detection** of asymptomatic pts (DM, HTN)
    - Without end-organ effects ANS therapy may be **short term**



# Follow-up Testing

- 10% to 15% changes are significant, less than 10% are significant if with symptoms
- Autonomic changes tend to take 4 to 6 weeks to complete
- Medicare pays for 2 or more tests/yr
- Goal: slow or stay the progression of ANS decline and protect the heart



# ANS Testing

- Six challenges include:
  - A) resting (initial) baseline,
  - B) the **parasympathetic** challenge of deep breathing,
  - C) return to baseline,
  - D) the **sympathetic** challenge of a series of short Valsalva maneuvers,
  - E) return to baseline, and
  - F) Quick postural change (seated to standing) followed by quiet standing



# THE CLINICAL EXAM

- Phase 1: Initial Baseline
  - A 5 minute period where the patient is breathing normally and is relaxed.
    - Provides measures of resting **LFa**, **RFa**, and Ratio

- Normal baseline (resting) ranges are:

For adults (> 21 y/o)

$$1.0 < \text{LFa} < 10.0$$

$$1.0 < \text{RFa} < 10.0$$

$$0.4 < \text{Ratio} < 3.0$$

For children (< 21 y/o)

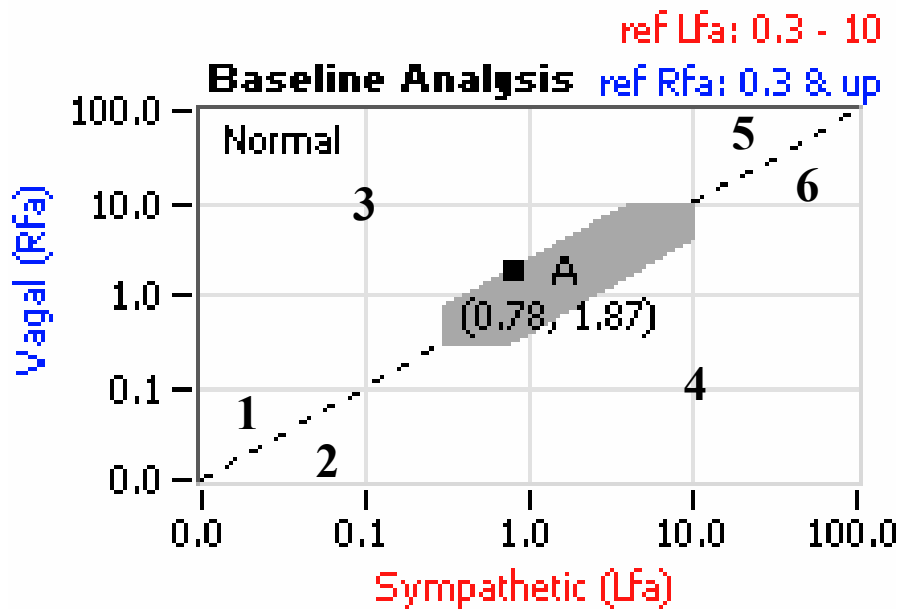
$$2.0 < \text{LFa} < 15.0$$

$$2.0 < \text{RFa} < 15.0$$

$$0.4 < \text{Ratio} < 3.0$$

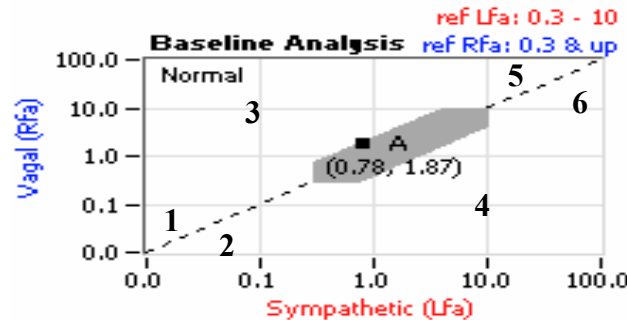


# BASELINE ANALYSIS





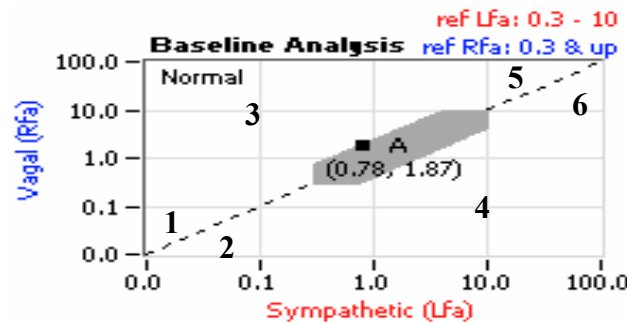
# BASELINE ANALYSIS



- A. Normal Region, based on published results (HRV without respiratory analysis).
- Vagal (RFa) < 0.1 indicates high risk of sudden death, if the patient has had a coronary event in the past year or is in late stage diabetes.
1. Insufficient resting autonomic activity with slightly more Parasympathetic protection (high risk less severe).
  2. Insufficient resting autonomic activity with slightly more More Sympathetic activity (high risk more severe).



# BASELINE ANALYSIS



3. Excess resting **Parasympathetic** activity.
4. Excess resting **Sympathetic** activity.
5. Excess resting autonomic tone; if arrhythmia exists, suggests a **parasympathetic** component to arrhythmia.
6. Excess resting autonomic tone; if arrhythmia exists, suggests a **sympathetic** component to arrhythmia.





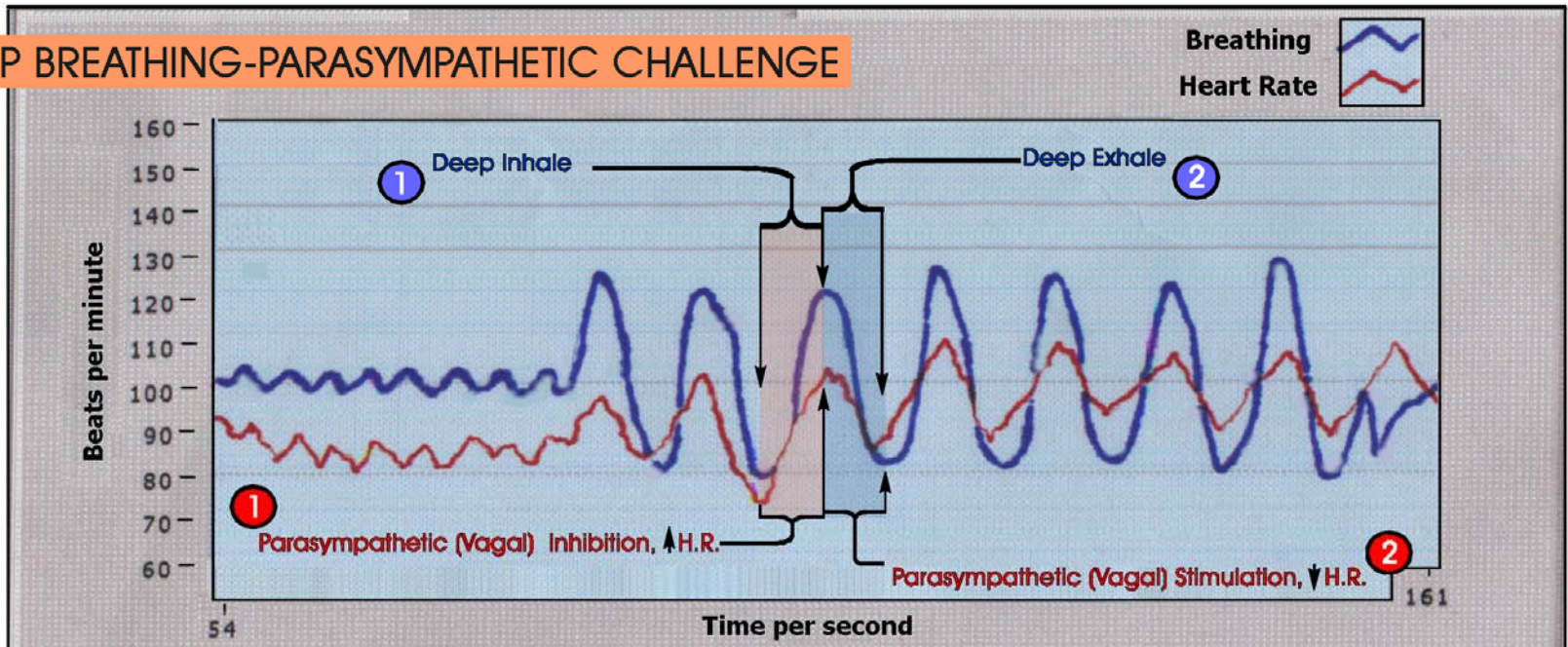
# THE CLINICAL EXAM

- Phase 2: Deep Breathing
  - A 1 minute period where the patient is breathing slowly and smoothly at a target rate of 6 breaths per minute in a very relaxed mood.
  - A **Parasympathetic** challenge
  - Expected results: a roughly 50-fold increase in **RFa** from initial baseline to deep breathing
    - Actual normal results are based on an age-adjusted and baseline-adjusted varying scale that is approximated by the average 50-fold increase. This scale is programmed into the ANX-3.0 monitor.



# THE DEEP BREATHING RESPONSE

## DEEP BREATHING-PARASYMPATHETIC CHALLENGE



a graphical example

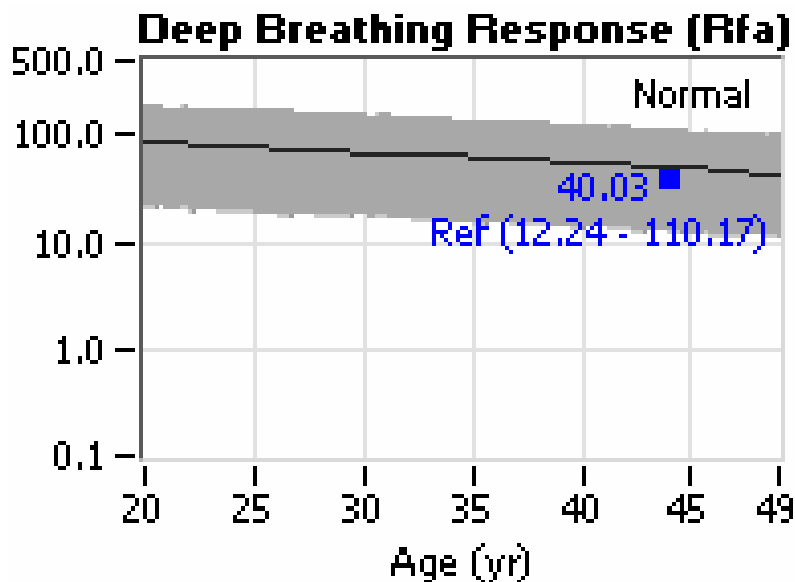


# THE DEEP BREATHING RESPONSE

- *Physiology:* Breathing deeply at a constant rate accentuates the normal sinus rhythm that occurs in most individuals. With every inhalation **1** there is an accentuated heart rate increase **1**, and with every exhalation **2** there is an accentuated heart rate decrease **2**. The human respiratory system is solely innervated by the parasympathetic nervous system through the Vagus nerve. Increased pulmonary activity caused by relaxed deep breathing (i.e., without any stress or other cortical activity) is directly related to increased Vagal activity. Thus, during the deep breathing challenge, the actions that predominate are parasympathetic, mediated by stimulation and inhibition of the Vagus nerve through stretch receptors located throughout the thorax (i.e., within the lungs, the aorta, and all chambers of the heart).



# DEEP BREATHING ANALYSIS



- Age-adjusted normal region is in gray, assumes a normal baseline.
- Excess **parasympathetic** response to challenge is indicated if the result is above the gray region.
- Insufficient **parasympathetic** response to challenge is indicated if the result is below the gray region.

Recent findings suggest that insufficient **parasympathetic** response to deep breathing while all else is normal may be the early indications of peripheral autonomic neuropathy due to chronic disease (*e.g.*, diabetes). This seems more sensitive than the Nerve Velocity Conduction study.



# THE CLINICAL EXAM

- Phase 3: Baseline
  - A 1 minute rest period where the patient is breathing normally and is relaxed.
    - This allow the system to recover from the previous challenge.



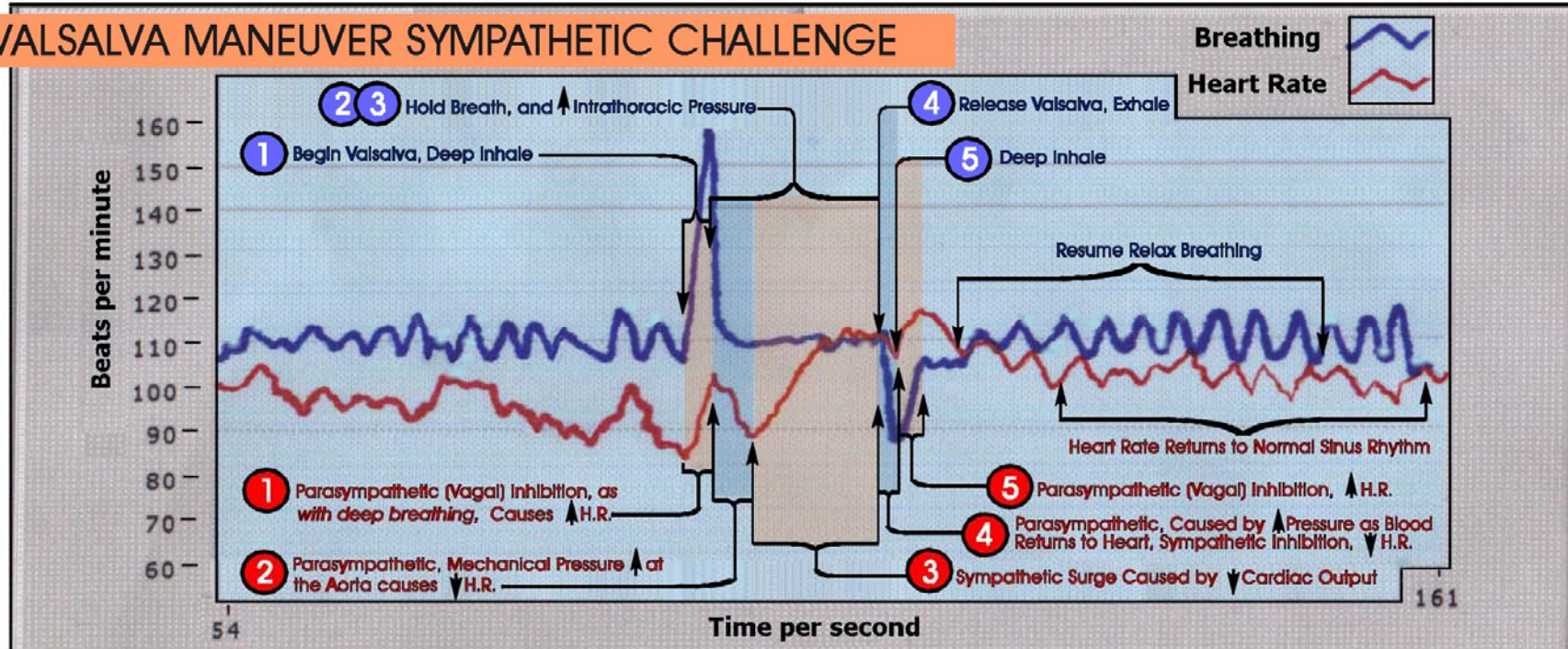
# THE CLINICAL EXAM

- Phase 4: Valsalva
  - A 1:35 minute period where the patient is asked to perform 5 short Valsalva maneuvers of no more than 15 seconds, with an equal amount of time to rest in between each maneuver.
    - A **Sympathetic** challenge
    - Expected results: a roughly 50-fold increase in **LFa** from initial baseline to Valsalva, with an increase in **RFa** of 60% or less or a decrease
      - Actual normal results are based on an age-adjusted and baseline-adjusted varying scale that is approximated by the average 50-fold increase. This scale is programmed into the ANX-3.0 monitor.



# THE SHORT VALSALVA RESPONSE

## VALSALVA MANEUVER SYMPATHETIC CHALLENGE



a graphical example



# THE SHORT VALSALVA RESPONSE

- *Physiology:* The VALSALVA Maneuver is initiated by a deep inhalation **1** causing Vagal inhibition. As with deep breathing, this causes an immediate increase in heart rate **1** as stretch receptors in the lungs are unloaded. During the next phase, the patient creates a sudden increase in intra-thoracic pressure **2/3**, which mechanically stimulates the thoracic baroreceptors, causing a momentary parasympathetic response, and heart rate drops **2**. As blood is shunted out of the thorax, two reflexes, the baroreceptor reflex and the venoarteriolar axon reflex, stimulate the sympathetics. Due to decreased venous return to the heart, there is a pressure drop at the aorta caused by a decrease in cardiac output (and the baroreceptors are unloaded).





# THE SHORT VALSALVA RESPONSE

In addition, since there is no opposing peripheral vasoconstriction (no pre-existing sympathetic activity upon initiation of the first Valsalva), as blood is shunted freely into the peripheral vessels the venoarteriolar axon reflex is initiated as the transmural pressure within the blood vessels begins to exceed 25 mm Hg. Sympathetic activity is stimulated and there is a gradual increase in heart rate **3**. Upon release of the Valsalva **4**, there is an overshoot of BP resulting from the sudden rush of blood back to the heart. This overshoot is compounded by the fact that the residual sympathetic activity (causing peripheral vasoconstriction) exaggerates the blood rush into the thorax and opposes blood return into the extremities.

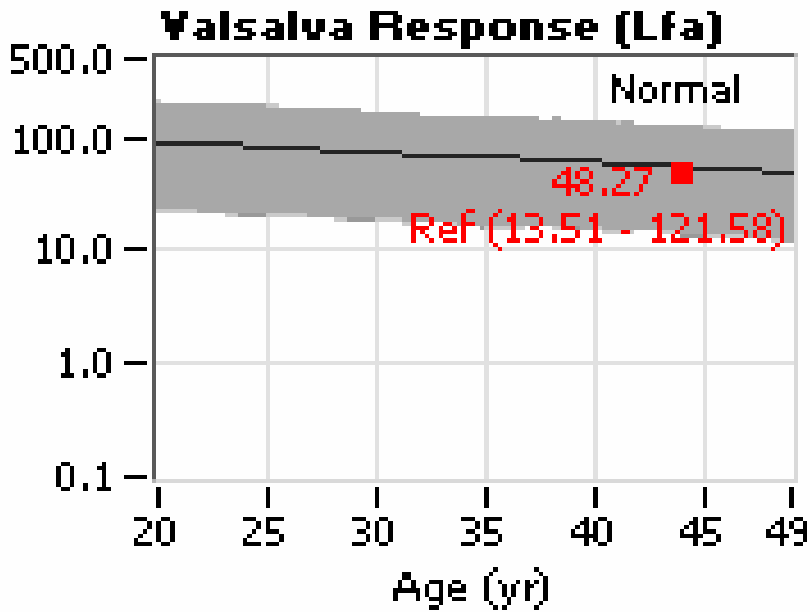


# THE SHORT VALSALVA RESPONSE

- The baroreceptors in the thorax sense this sudden stretch causing a parasympathetic surge to inhibit sympathetic activity and return the heart rate to normal **4**. Immediately following the release of the Valsalva, the heart rate continues to increase for a short period of time for two reasons. Just as the sympathetics are slower to rise, they are slower to shut off, so there is a short period of residual sympathetic activity. Also, it is the natural response upon release of the Valsalva to inhale deeply **5** causing Vagal inhibition (as with deep breathing) and the heart rate will rise **5**.



# VALSALVA ANALYSIS



- Age-adjusted normal region is in gray, assumes a normal baseline.
- Excess **sympathetic** response to challenge is indicated if the result is above the gray region.
- Insufficient **sympathetic** response to challenge is indicated if the result is below the gray region.

Recent findings suggest that excess **sympathetic** response to Valsalva may be a pre-clinical indication of hypertension.



# THE CLINICAL EXAM

- Phase 5: Baseline
  - A 2 minute rest period where the patient is breathing normally and is relaxed.
    - This allow the system to recover from the previous challenge.

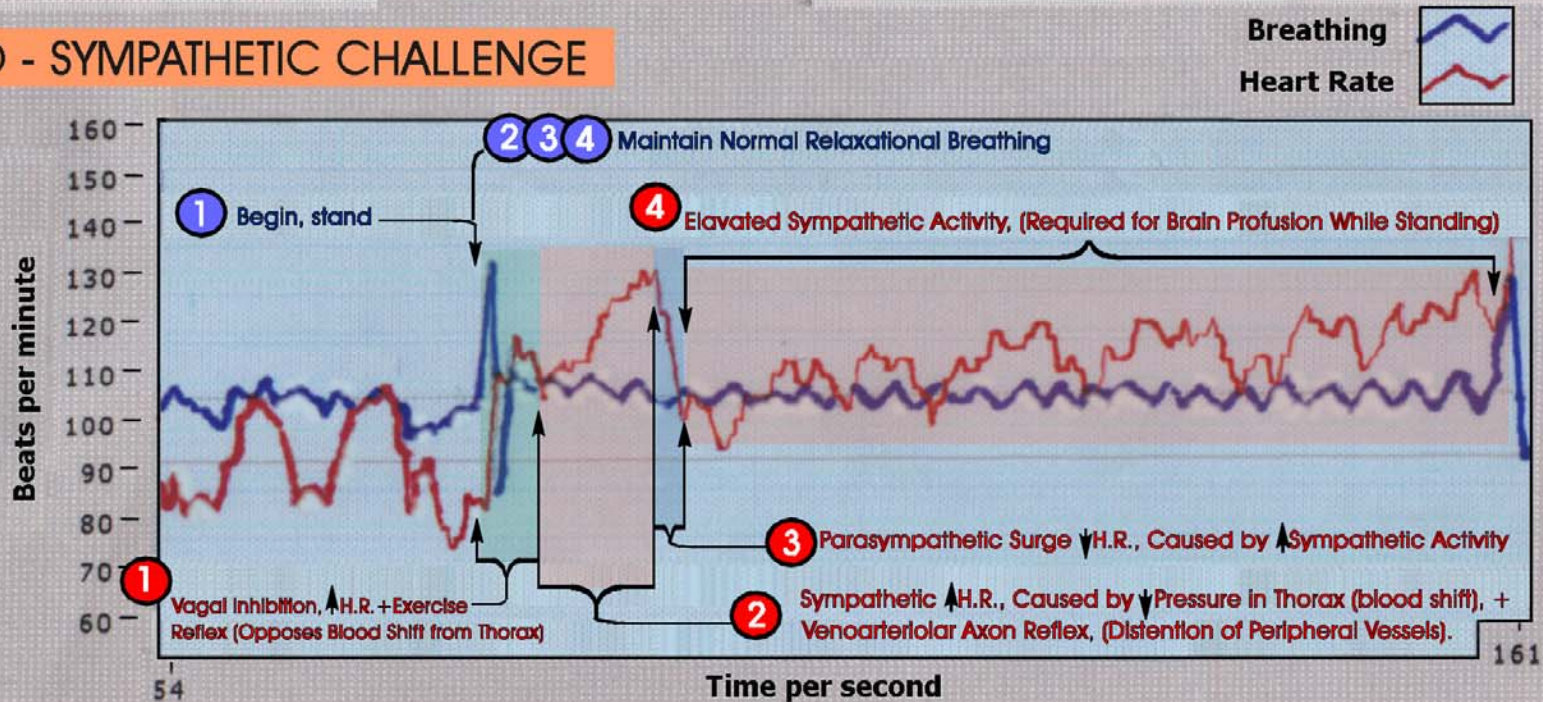


# THE CLINICAL EXAM

- Phase 6: Stand
  - A 5 minute period where the patient is asked to stand quickly and remain standing for the duration of the 5 minutes.
    - A **Sympathetic** challenge and a System Challenge
    - Expected results: a decrease in **RFa** and a concurrent increase in **LFa** as compared to initial Baseline.

# THE STAND RESPONSE

## STAND - SYMPATHETIC CHALLENGE



a graphical example



# THE STAND RESPONSE

- *Physiology:* When standing **1**, there is a large shift in blood from the thorax to the abdomen and lower extremities with a corresponding decrease in cardiac output—a strong sympathetic stimulus. The fluid shift upon standing is immediate, and there is initially an abrupt increase in heart rate (in the first 3 seconds) **1** followed by a more gradual increase (occurring in the next 3-12 seconds) **2**. Since the sympathetics take 3-5 seconds to respond, this means that the first three (3) seconds of tachycardia during stand is not due to sympathetic activity, but rather to a combination of Vagal inhibition and the exercise reflex. As the patient stands and the leg muscles are engaged they manually clamp down on the peripheral blood vessels (exercise reflex).



# THE STAND RESPONSE

This is the body's attempt to oppose the gravitational flow of blood while standing until the sympathetics can initiate peripheral vasoconstriction. An additional sympathetic stimulus is the venoarteriolar axon reflex. The venoarteriolar reflex is thought to account for 40% of the peripheral vascular resistance during stand. Activation of sympathetic activity can be seen in as a gradual increase in heart rate **2**. This increase in sympathetic activity maintains cardiac filling pressure by constriction of splanchnic (visceral) capacitance vessels. As peripheral vascular resistance increases, diastolic blood pressure increases with little change in the systolic pressure at the level of the heart.



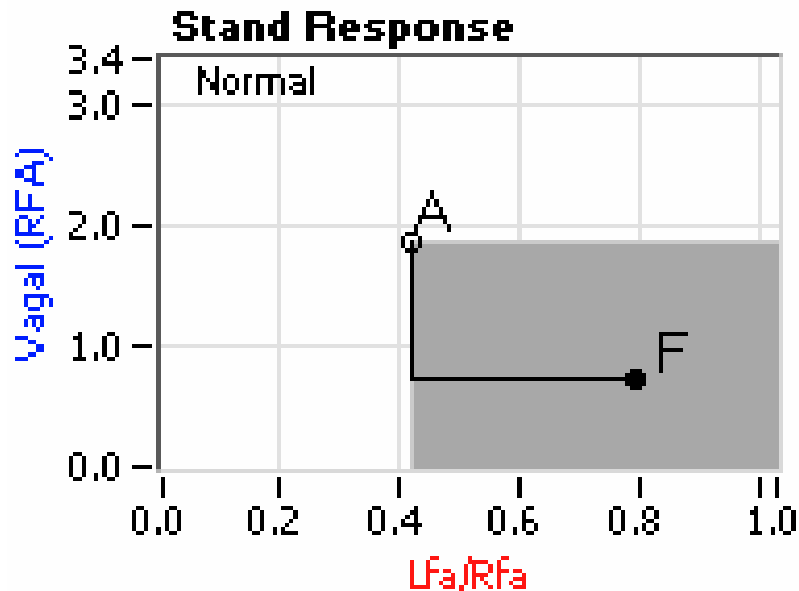


# THE STAND RESPONSE

Finally a saturation point is reached within the baroreceptors, and the parasympathetics are stimulated in an attempt to normalize heart rate to a new standing baseline level **3**. In general, during STAND there is a 15%-30% increase in heart rate, an increase in mean arterial pressure of 0-10%, a 10% increase in diastolic pressure, and the systolic pressure is usually unchanged. This is due to the fact that the baroreceptors located in the carotid artery (transporting blood to the brain) now sense a lower capillary pressure than during sitting. This pressure differential provides the stimulus, which maintains increased sympathetic activity during stand **4**.



# STAND ANALYSIS

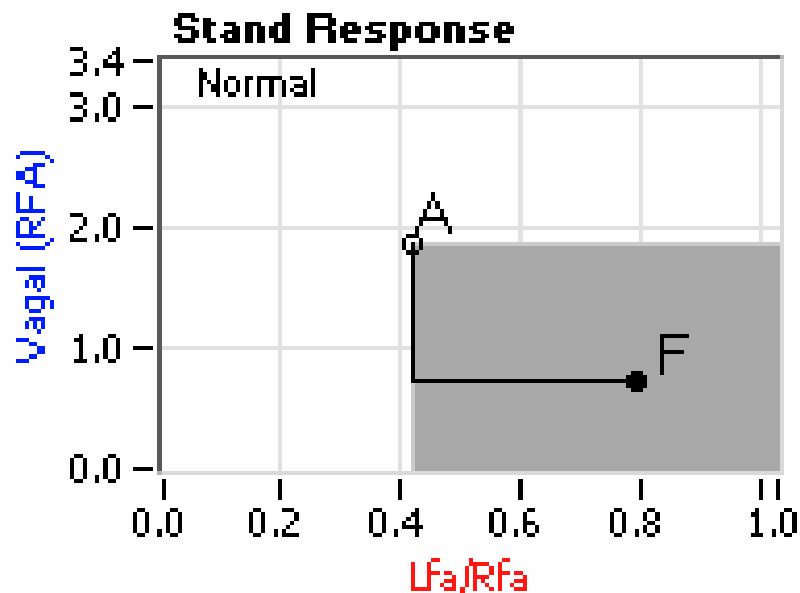


- Normal region is in gray (A represents sitting, initial baseline, and F represents stand period). Thus, a decrease in **RFa** with an increase in **LFa** from initial baseline to stand is normal.

- Anything to the left of the gray region indicates a **sympathetic** withdrawal suggesting Orthostasis.
- Anything above the gray region indicates an abnormal **parasympathetic** increase
- **Sympathetic** Withdrawal can be treated with a range of options: increased fluids or salt, Fludrocortisone, Pyridostigmine, or Vasopressors.



# STAND ANALYSIS

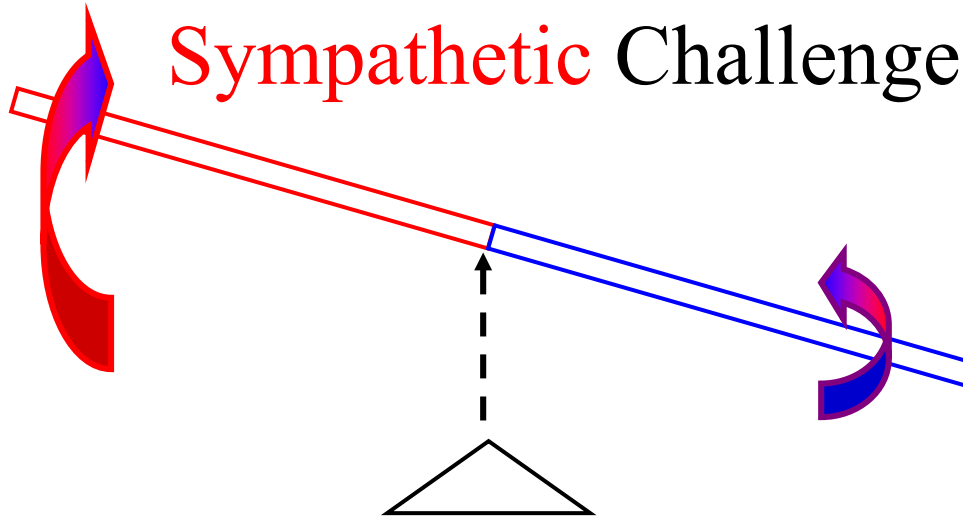


- Recent findings from using the ANX-3.0 suggest that the LFa rather than the **LFa/RFa** (Ratio) is a better measure of **Sympathetic** activity and produces fewer false positives and false negatives.



# Dynamic ANS Imbalance

Parasympathetic Excess During  
Sympathetic Challenge



- Sympathetics are reactionary
- Parasympathetics set metabolic threshold
- If P abnormally respond to S challenges, S forced into greater responses



# Dynamic ANS Imbalance

## Paradoxical Parasympathetic Syndrome

- PPS is the term created to label **Parasympathetic** Excess During **Sympathetic** Challenge
- PPS in general destabilizes the patient's response to disease and therapy (i.e., BP, HR, Diabetes, Thyroid)
- Common to our Database (> 50%)



# Dynamic ANS Imbalance

## Paradoxical Parasympathetic Syndrome

- A finding unique to measuring both ANS branches simultaneously
- PPS is defined by several diffuse symptoms including: Sleep difficulties, GI upset, Frequent migraines or morning headaches, evening edema or restless leg syndrome



# Dynamic ANS Imbalance

## Paradoxical Parasympathetic Syndrome

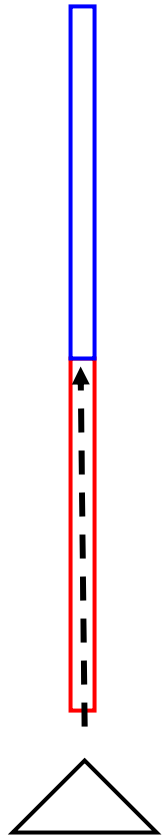
- PPS can help to differentiate CRPS (plexus damage) from other forms of pain
- PPS associated with migraine, CFS, ADD/ADHD, Fibromyalgia, Sleep difficulties, Unexplained seizures, Depression/Anxiety/Bipolar Disorders



# Dynamic ANS Imbalance

## Paradoxical Parasympathetic Syndrome

- Requires centrally acting agents to correct
  - Peripherally acting agents further destabilizes the patient
    - Not all adrenergic channels are block, so pt's systems finds a way to defeat the therapy to ensure proper brain perfusion
  - Central agents help to settle the whole ANS by stabilizing both branches at the central communication point
    - Effects the feedback point in the upper Medullary brain stem nuclei where the Limbic and systemic sympathetics input on to the nuclei that give rise to the Vagus N.

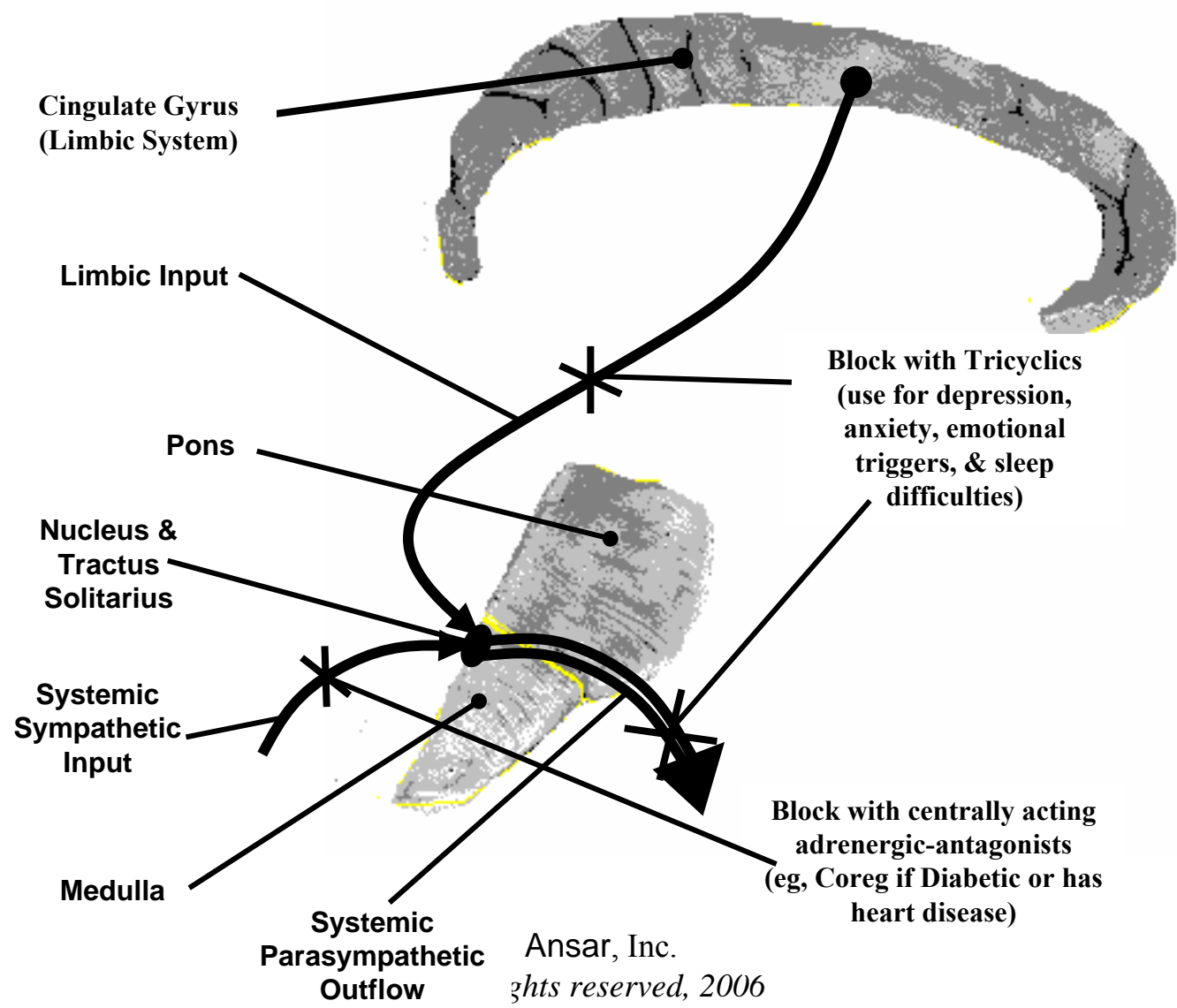






# Dynamic ANS Imbalance

## Paradoxical Parasympathetic Syndrome





# Dynamic ANS Imbalance

## Paradoxical Parasympathetic Syndrome

- Therapy typically corrects PPS in 12-15 months, and can be weaned over 3 months (assuming no end-organ effects)
  - Reset and hold ANS “set point” (nervous system plasticity)
  - Patient (ANS) drug free until some other clinical event



# PPS Therapy Example

- PPS and ANS monitoring differentiates 5 sub-populations for hypertension (HTN)
  1. **White Coat HTN:** normal Valsalva sympathetic response (possible PPS) with BPs that start high and fall throughout the test (no expected BP variations)
    - Little or no therapy depending on history
  2. **Pre-clinical HTN:** high Valsalva sympathetic response (no PPS) with normal resting BP
    - Light anti-HTN therapy, d/c after correction of hypersympathetic Valsalva response

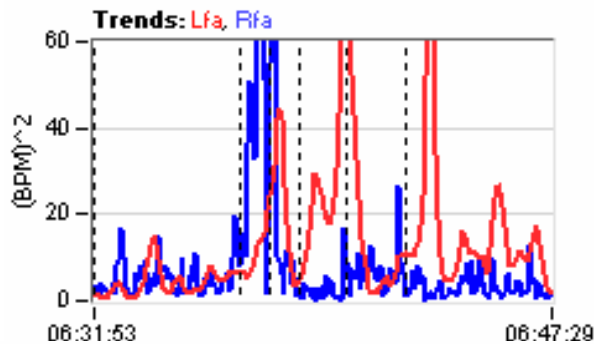


# PPS Therapy Example (con't)

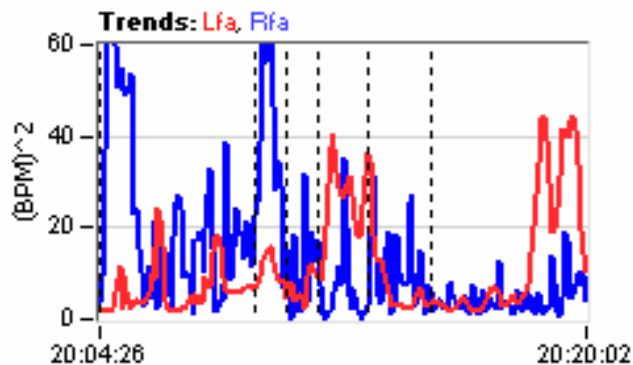
3. **ANS HTN:** PPS with secondary hypersympathetic response, elevated or high BP that may also be labile or difficult to control, but no end-organ effects
  - PPS therapy, Sympathetics will follow, BP should follow after a couple months, d/c after correction of PPS
4. **Labile HTN:** PPS with secondary hypersympathetic response, elevated or high BP that may also be labile or difficult to control, with end-organ effects
  - PPS therapy, Sympathetics will follow, BP might follow after a couple months, end-organ effects may require life-long therapy
5. **Clinical HTN:** Primary hypersympathetic response, high BP
  - Standard anti-HTN therapy



# Normal Children



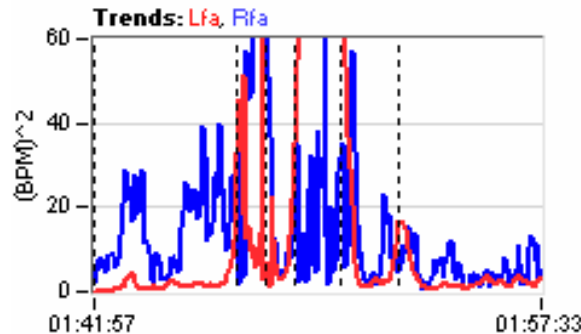
	Event	mHR'	rangeHR'	FRF''	LFA+	RFA+	LFA/RFA
A	Baseline	107	30	0.38	3.90	4.76	0.82
B	Deep Breathing	100	38	0.23	10.69	69.41	0.15
C	Baseline	105	38	0.32	25.73	7.57	3.40
D	Valsalva	115	38	0.31	36.43	2.67	13.62
E	Baseline	109	32	0.39	5.05	5.52	0.92
F	Stand	114	33	0.36	11.79	3.08	3.83



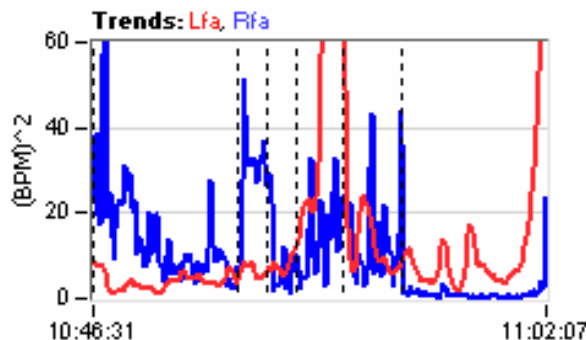
	Event	mHR'	rangeHR'	LFA+	RFA+	LFA/RFA	BP
A	Baseline	95	34	5.86	20.17	0.29	95 / 64
B	Deep Breathing	92	32	12.48	52.45	0.24	90 / 63
C	Baseline	91	24	6.48	11.45	0.57	91 / 64
D	Valsalva	97	33	26.23	6.31	4.16	85 / 64
E	Baseline	91	30	4.10	10.24	0.40	91 / 62
F	Stand	106	39	9.85	3.62	2.72	98 / 63



# Normals Teenagers

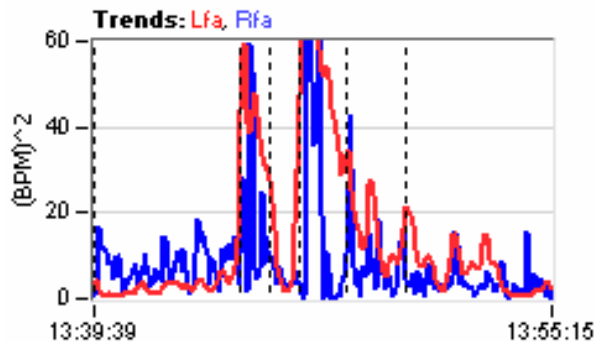


	Event	mHR <sup>1</sup>	rangeHR <sup>1</sup>	FRF <sup>2</sup>	LFA+	RFA+	LFA/RFA	BP
A	Baseline	86	25	0.32	1.49	14.66	0.10	112 / 66
B	Deep Breathing	87	38	0.15	15.30	69.34	0.22	113 / 67
C	Baseline	84	29	0.28	5.57	7.11	0.78	114 / 65
D	Valsalva	87	55	0.28	196.01	20.48	9.57	109 / 74
E	Baseline	83	40	0.32	2.34	9.22	0.25	105 / 64
F	Stand	99	33	0.35	1.60	4.10	0.39	108 / 71

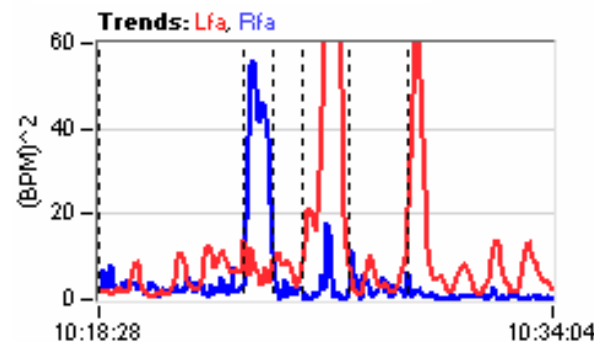


	Event	mHR <sup>1</sup>	rangeHR <sup>1</sup>	FRF <sup>2</sup>	LFA+	RFA+	LFA/RFA	BP
A	Baseline	82	43	0.32	3.84	12.96	0.30	112 / 65
B	Deep Breathing	87	37	0.13	6.59	32.95	0.20	113 / 66
C	Baseline	90	29	0.25	6.97	4.07	1.71	114 / 62
D	Valsalva	86	54	0.17	67.85	17.48	3.88	96 / 66
E	Baseline	86	37	0.24	14.49	11.71	1.24	102 / 62
F	Stand	114	86	0.33	6.68	0.54	12.39	115 / 57

# Normals: The Transition Years



	Event	mHR'	rangeHR'	FRF''	LFA+	RFA+	LFA/RFA	BP
A	Baseline	87	26	0.34	2.69	7.70	0.35	113 / 64
B	Deep Breathing	93	42	0.22	40.39	19.11	2.11	113 / 65
C	Baseline	93	19	0.32	4.16	4.35	0.96	118 / 67
D	Valsalva	84	56	0.27	42.65	3.72	11.45	129 / 68
E	Baseline	86	35	0.35	13.68	6.50	2.11	116 / 74
F	Stand	88	39	0.35	6.28	3.19	1.97	118 / 82

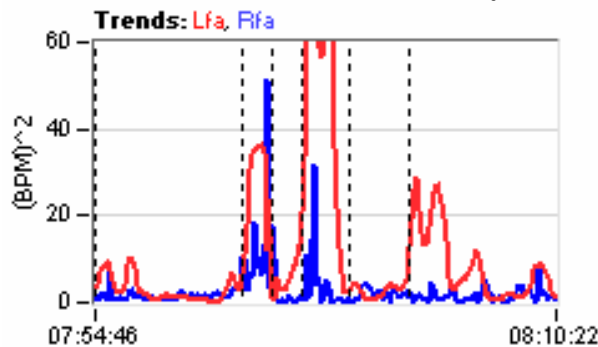


	Event	mHR'	rangeHR'	FRF''	LFA+	RFA+	LFA/RFA	BP
A	Baseline	79	29	0.42	4.70	2.85	1.64	114 / 73
B	Deep Breathing	82	25	0.11	6.60	46.19	0.14	109 / 69
C	Baseline	84	16	0.40	7.28	1.79	4.06	116 / 69
D	Valsalva	85	38	0.24	65.33	3.05	21.39	116 / 75
E	Baseline	81	20	0.42	4.35	2.65	1.64	122 / 67
F	Stand	98	38	0.42	4.78	0.45	10.74	112 / 68



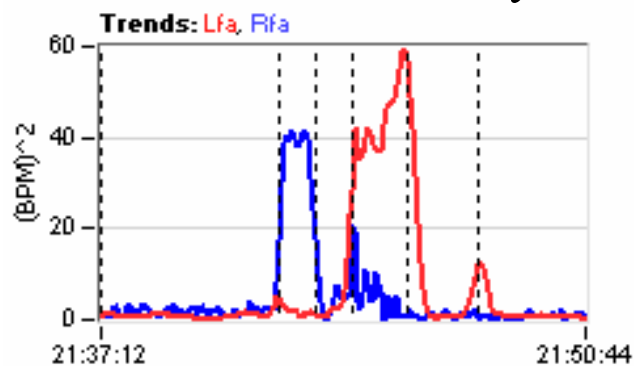
# Normal Adults

34 y/o



	Event	mHR'	rangeHR'	FRF''	LFA+	RFA+	LFA/RFA	BP
A	Baseline	58	19	0.26	2.73	1.35	2.03	116 / 82
B	Deep Breathing	61	29	0.24	32.35	14.56	2.22	120 / 80
C	Baseline	60	12	0.30	5.22	0.44	11.88	115 / 84
D	Valsalva	68	57	0.27	34.95	0.92	37.95	
E	Baseline	55	12	0.25	1.98	2.51	0.79	118 / 74
F	Stand	63	27	0.28	4.57	1.30	3.52	118 / 80

44 y/o



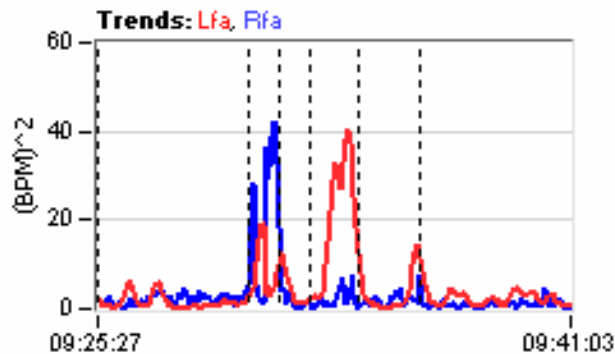
	Event	mHR'	rangeHR'	LFA+	RFA+	LFA/RFA	BP
A	Baseline	65	13	0.78	1.87	0.42	102 / 59
B	Deep Breathing	68	28	1.37	40.03	0.03	112 / 64
C	Baseline	62	17	2.55	3.46	0.74	128 / 76
D	Valsalva	69	27	48.27	2.36	20.46	122 / 63
E	Baseline	66	27	0.77	0.84	0.91	120 / 70
F	Stand	72	20	0.59	0.74	0.79	105 / 71





# Normal Adults

60 y/o

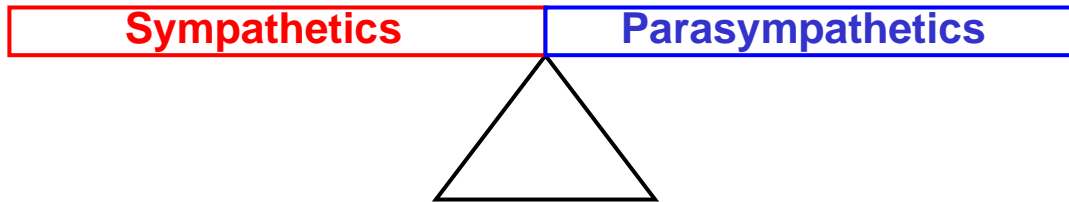


	Event	mHR <sup>1</sup>	rangeHR <sup>1</sup>	FRF <sup>2</sup>	LFA+	RFA+	LFA/RFA	BP
A	Baseline	68	17	0.35	1.26	2.11	0.60	108 / 62
B	Deep Breathing	71	21	0.19	9.37	21.07	0.44	92 / 61
C	Baseline	69	16	0.34	2.86	1.06	2.71	100 / 66
D	Valsalva	68	26	0.22	30.31	3.15	9.62	103 / 62
E	Baseline	69	18	0.37	0.54	1.95	0.28	104 / 61
F	Stand	79	30	0.36	2.40	0.79	3.04	113 / 56



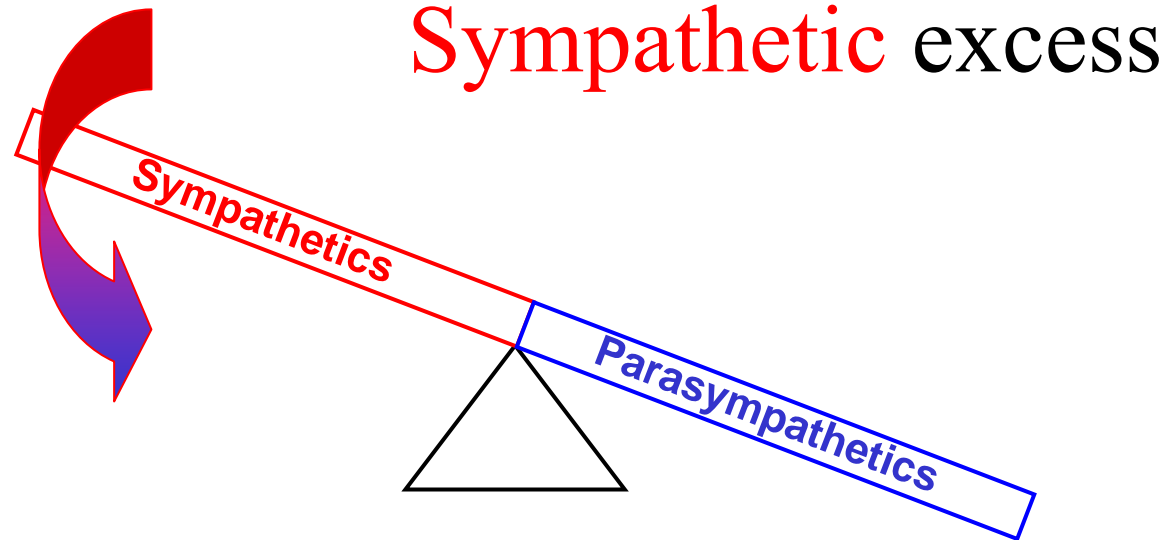
# Resting Balance

- GOAL: Establish and maintain normal autonomic balance





# Correcting Resting Imbalance

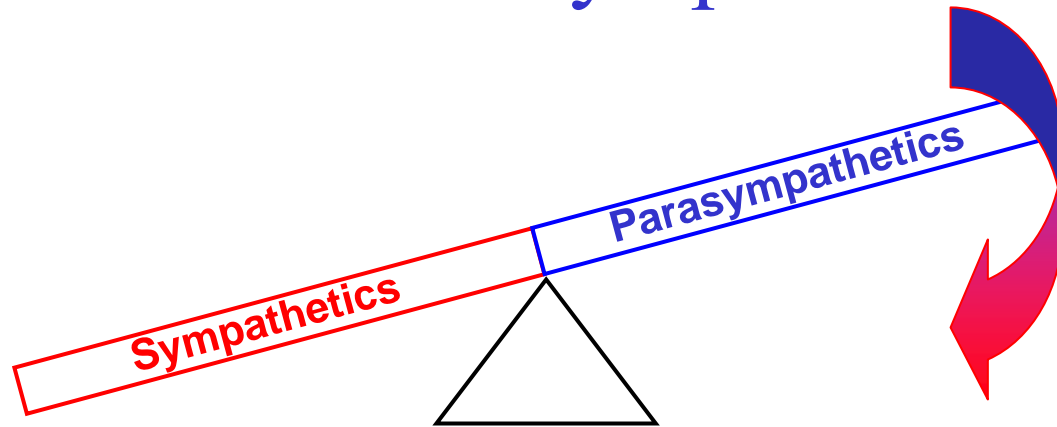


- Correct by reducing **sympathetic** levels
  - Adrenergic Blockade:
    - Beta-blockers,
    - Angiotensin blockers,
    - Calcium Channel Blockers



# Correcting Resting Imbalance

Parasympathetic excess



- Correct by reducing **parasympathetic** levels
  - Cholinergic Blockade, *e.g.*, tri-cyclics, SSRIs
  - Reduce Adrenergic Blockade



# General Therapy Options

<b>Agent</b>	<b>Associated Nervous System</b>	<b>Primary Site of Action</b>	<b>Primary Effect</b>
Beta-1 Adrenergic Antagonists	Sympathetics	Heart	↓ Heart Rate
Beta-2 Adrenergic Agonists	Sympathetics	Lungs	↑ Air Flow
Alpha Adrenergic Agonists	Sympathetics	Vasculature	Constrict Vasculature
Cholinergic Antagonists	Parasympathetics	Entire Body	↓ Parasympathetic activity
Angiotensin Blockers	Sympathetics	Kidneys	↓ Blood Pressure
Calcium-Channel Blockers	Sympathetics	Heart	↓ Blood Pressure