I. Vagus Anatomy
II. Show how vagal activity is measured. lnHF
III. Vagal withdrawal
IV. Variety of effects
    I. Gene Expression
    II. Biome
V. Disorders
    I. GI
    II. Muscle Pain
    III. Anxiety
    IV. Trauma
    V. Cardiac Rehab
VI. Treatments
    I. VNS
    II. HRVB

    III. Scientific literature, particularly regarding Vagus Nerve Stimulation (VNS) and its role in the inflammatory reflex, has seen a sharp increase in citations, with tens of thousands of publications mentioning the nerve

The Nerve of those Disorders: Vagal Withdrawal and a Unifying Theme in Health and Illness

Richard Gevirtz, PhD, BCB

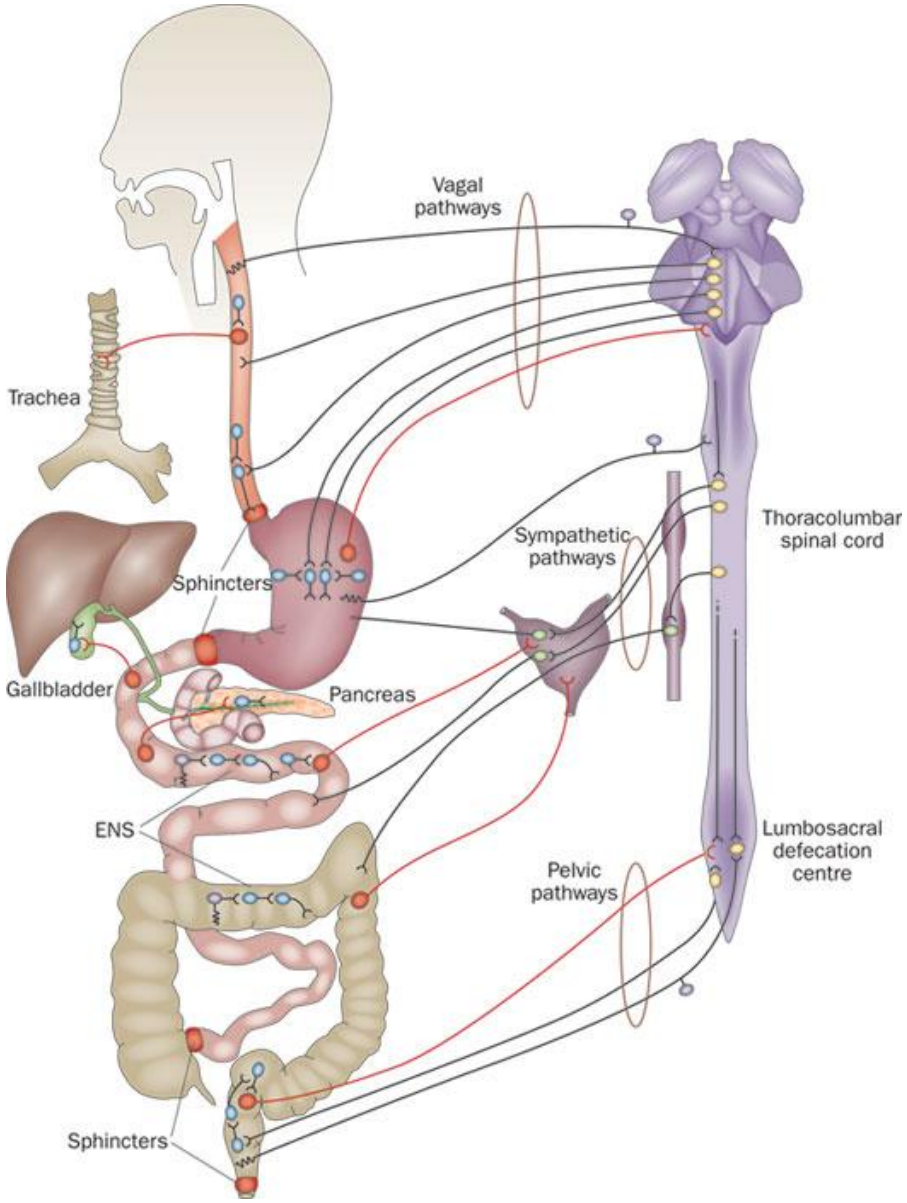
CSPP@Alliant International University

San Diego, CA

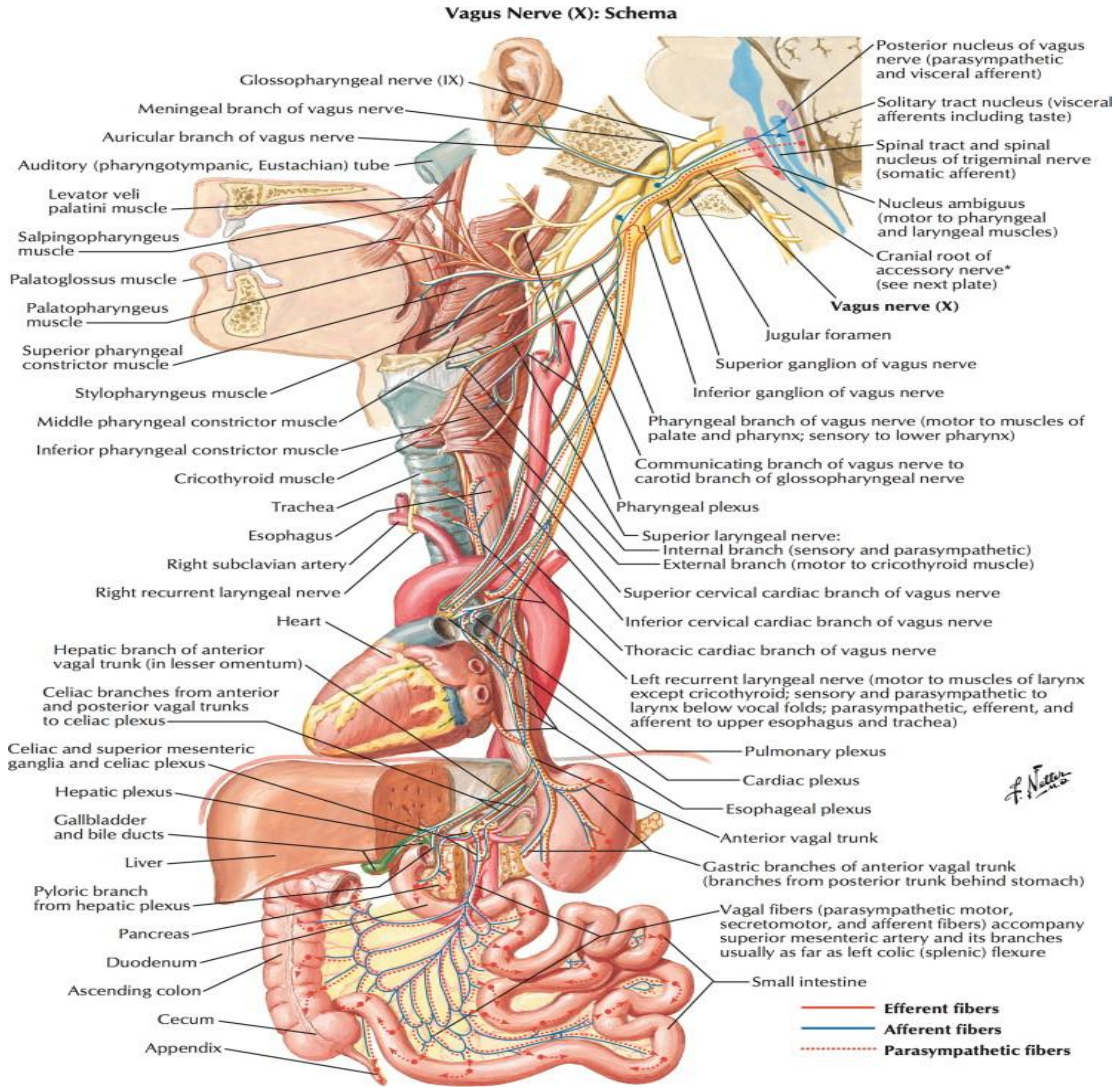
Charles Darwin, The Expression of the Emotions in Man and Animals (1872), Chapter 3

"The great physiologist, Claude Bernard, has shown how the least excitement of a sensitive nerve reacts on the heart; even when a nerve is touched so slightly that no pain can possibly (69) be felt by the animal under experiment. Hence when the mind is strongly excited, we might expect that it would instantly affect in a direct manner the heart; and this is universally acknowledged and felt to be the case. Claude Bernard also repeatedly insists, and this deserves especial notice, that when the heart is affected it reacts on the brain; and the state of the brain again reacts through the pneumo-gastric nerve *(vagus nerve)*on the heart; so that under any excitement there will be much mutual action and reaction between these, the two most important organs of the body."

"Stimulation of the vagus nerve, specifically its cardioinhibitory fibers, triggered the release of a substance—which I termed Vagusstoff—that slows cardiac rhythm." **This seminal observation by Otto Loewi established the foundation for understanding chemical neurotransmission and facilitated the subsequent identification of acetylcholine (ACh), a discovery honored with the Nobel Prize in Physiology or Medicine in 1936 (Loewi, 1921).**



Vagus Nerve in all of its complexities

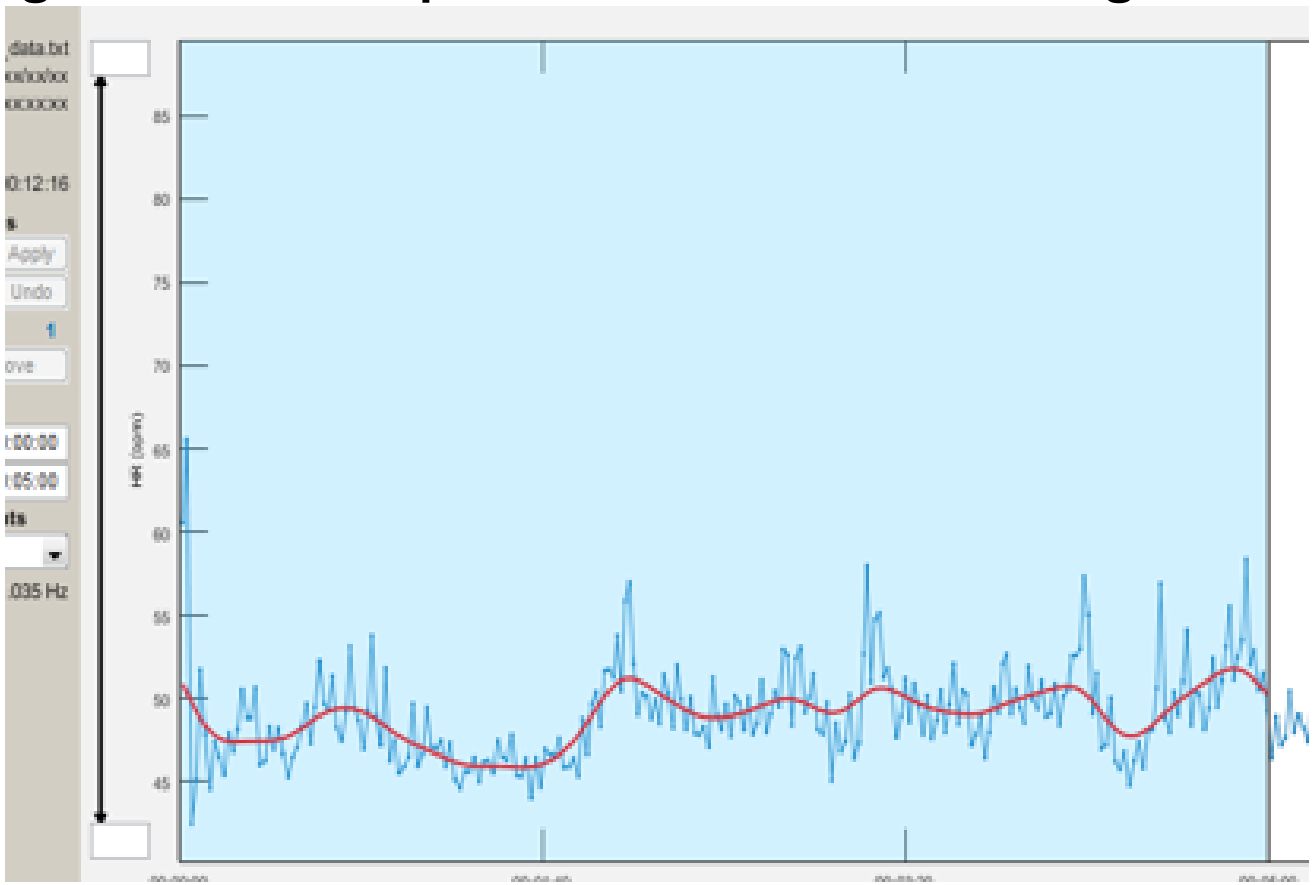


"Owing to its exceptional length—the longest of the cranial nerves—it extends from rootlets on the lateral surface of the medulla oblongata, passes through the jugular foramen, and innervates thoracic and abdominal viscera including the lungs, heart, and gastrointestinal tract (Dolphin et al., 2022; Kenny & Bordoni, 2022; Tewfik, 2025). Approximately 80–90 % of its fibres are afferent, relaying visceral information to the brainstem; the remaining 10–20 % are efferent, conveying parasympathetic output back to the body (Berthoud & Neuhuber, 2000; Bonaz et al., 2018)."

How vagal activity is measured.

We can measure vagal activity indirectly by observing beat to beat heart rate patterns.

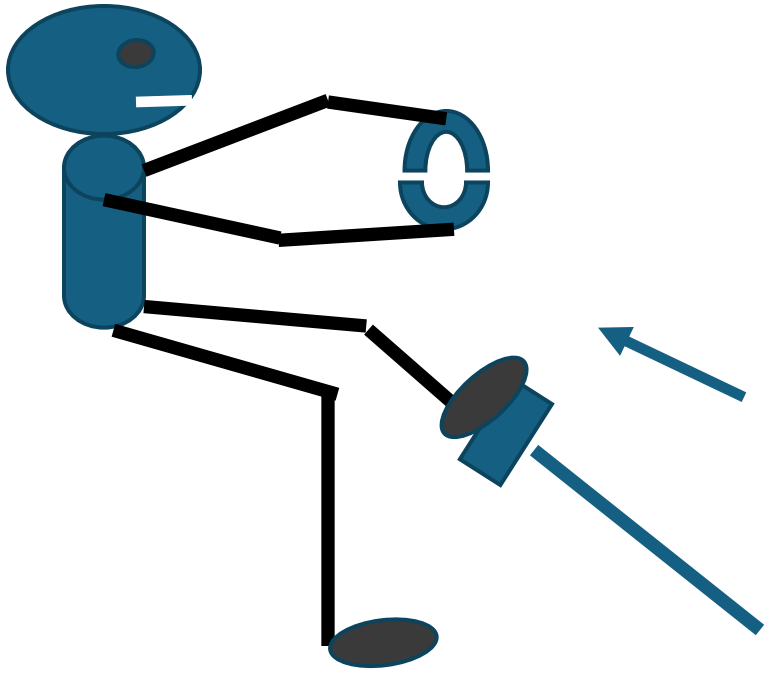
In a healthy person a reflex in the brain stem inhibits the vagal brake, speeding heart rate during inhalation and puts the brake back on during exhalation.

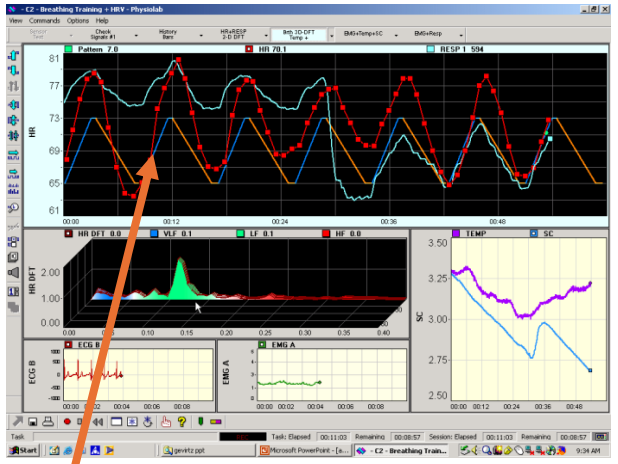


A graphic representation of beat-to-beat heart rate

Dominant source of Variability:
Respiratory Sinus Arrhythmia RSA

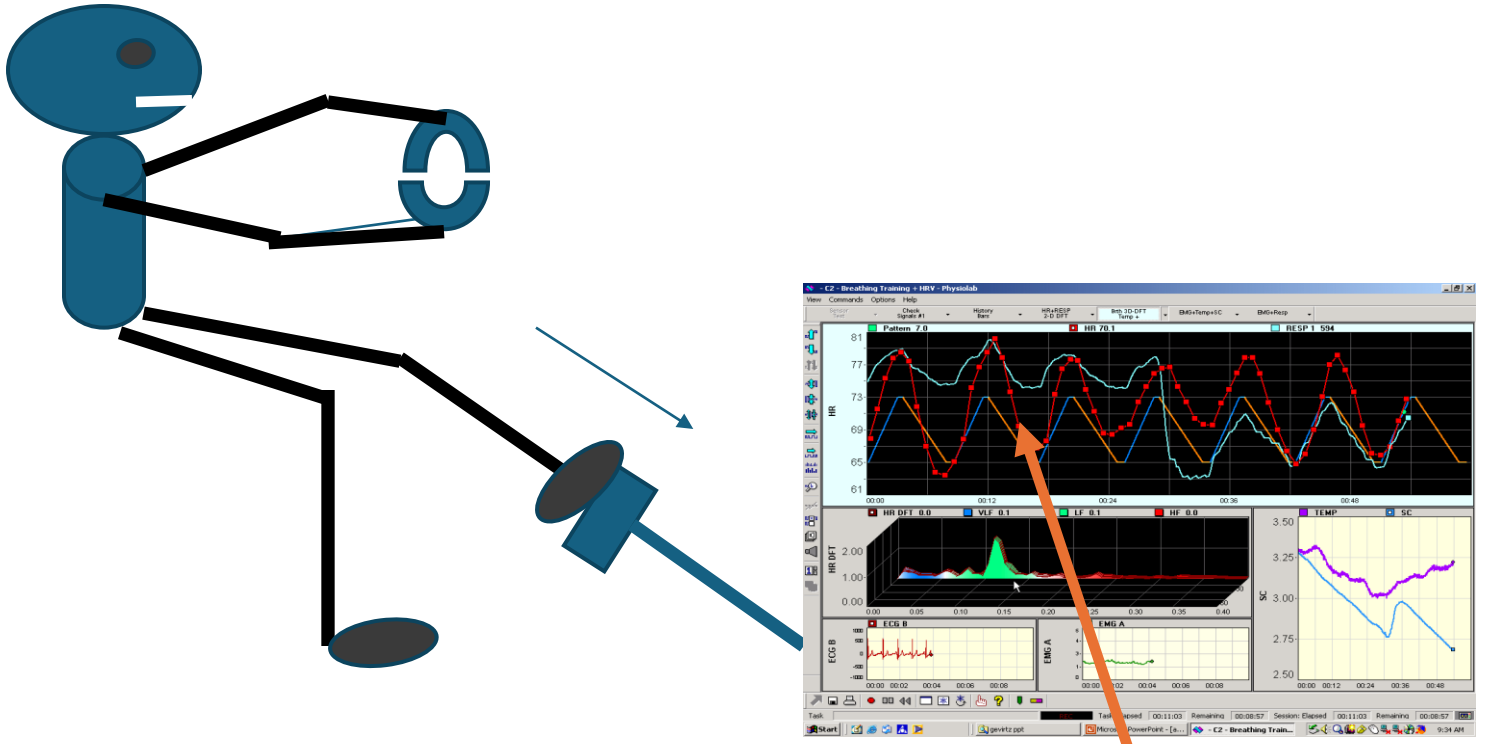
Inhale, Vagal Brake Off, HR increases





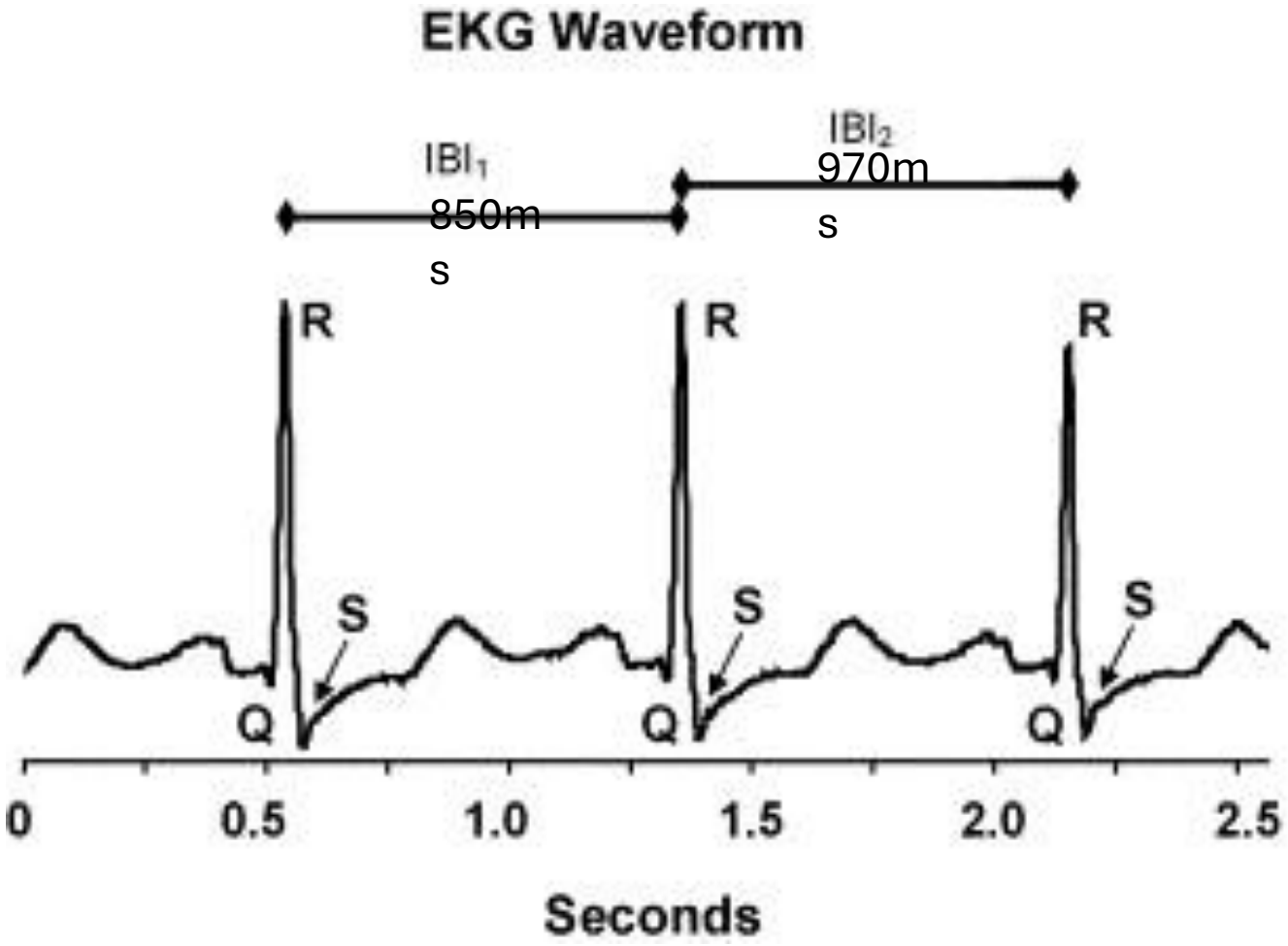
HR increase

Exhale, **Vagal Brake On**, HR Decreases

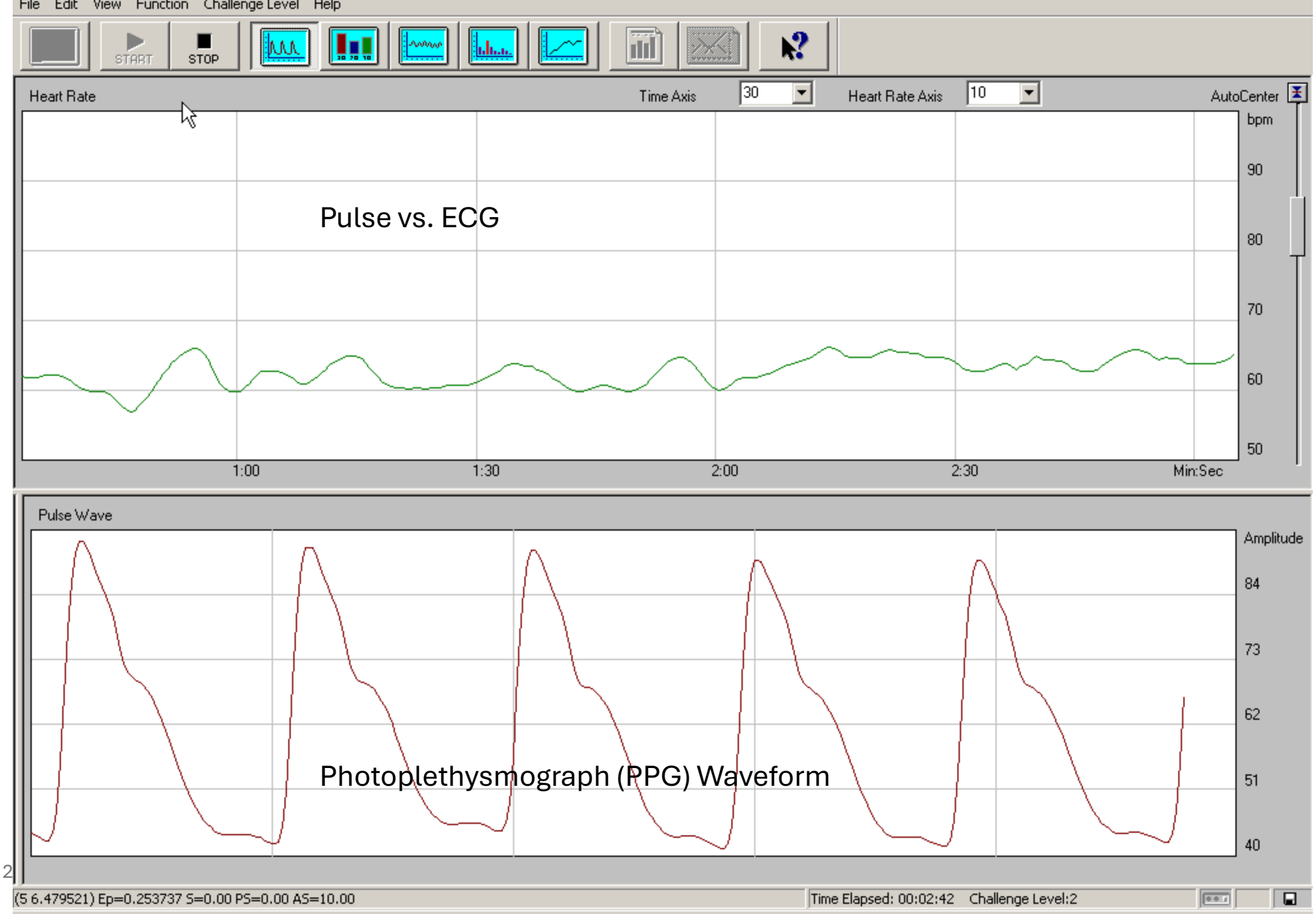


HR decrease

Quick review of measurement of vagal activity

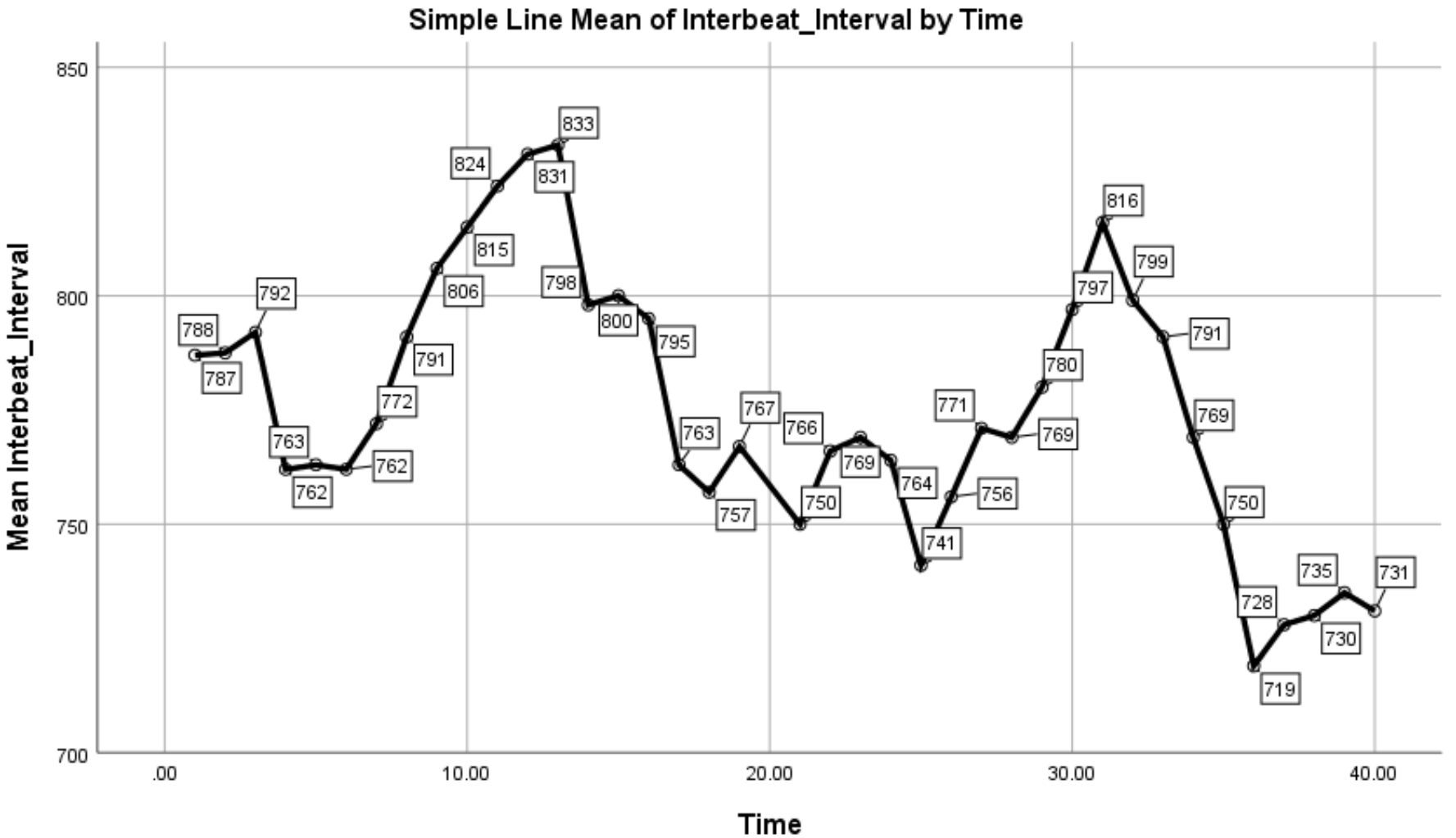


HRV metrics are derived from sequential R waves measured during normal breathing periods

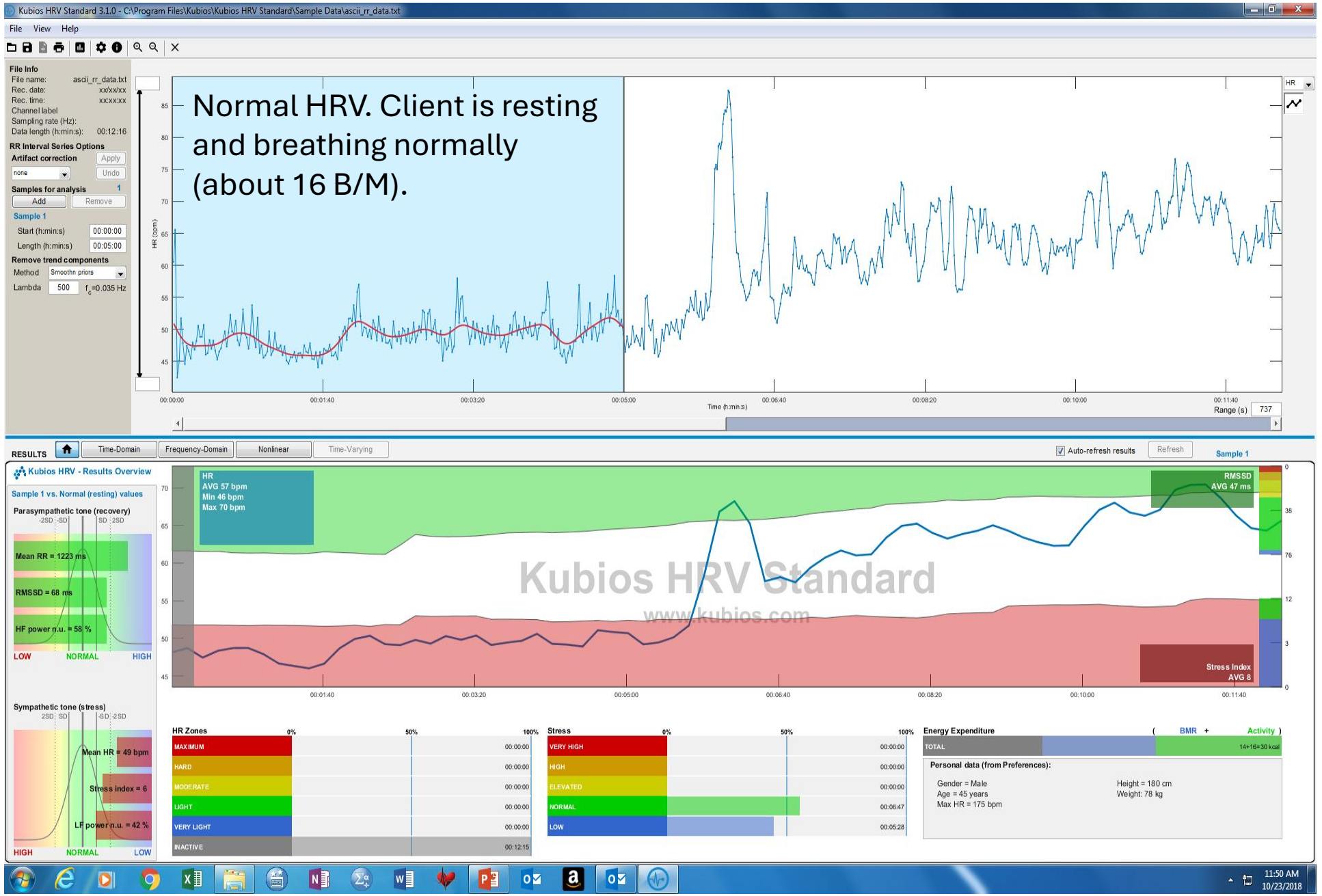

File Edit View Function Challenge Level Help
START
STOP
Heart Rate
Time Axis
30
Heart Rate Axis
10
AutoCenter
bpm
90
80
70
60
50
1:00
1:30
2:00
2:30
Min:Sec
Pulse vs. ECG
Pulse Wave
Amplitude
84
73
62
51
40
Photoplethysmograph (PPG) Waveform
(5 6.479521) Ep=0.253737 S=0.00 PS=0.00 AS=10.00
Time Elapsed: 00:02:42
Challenge Level:2

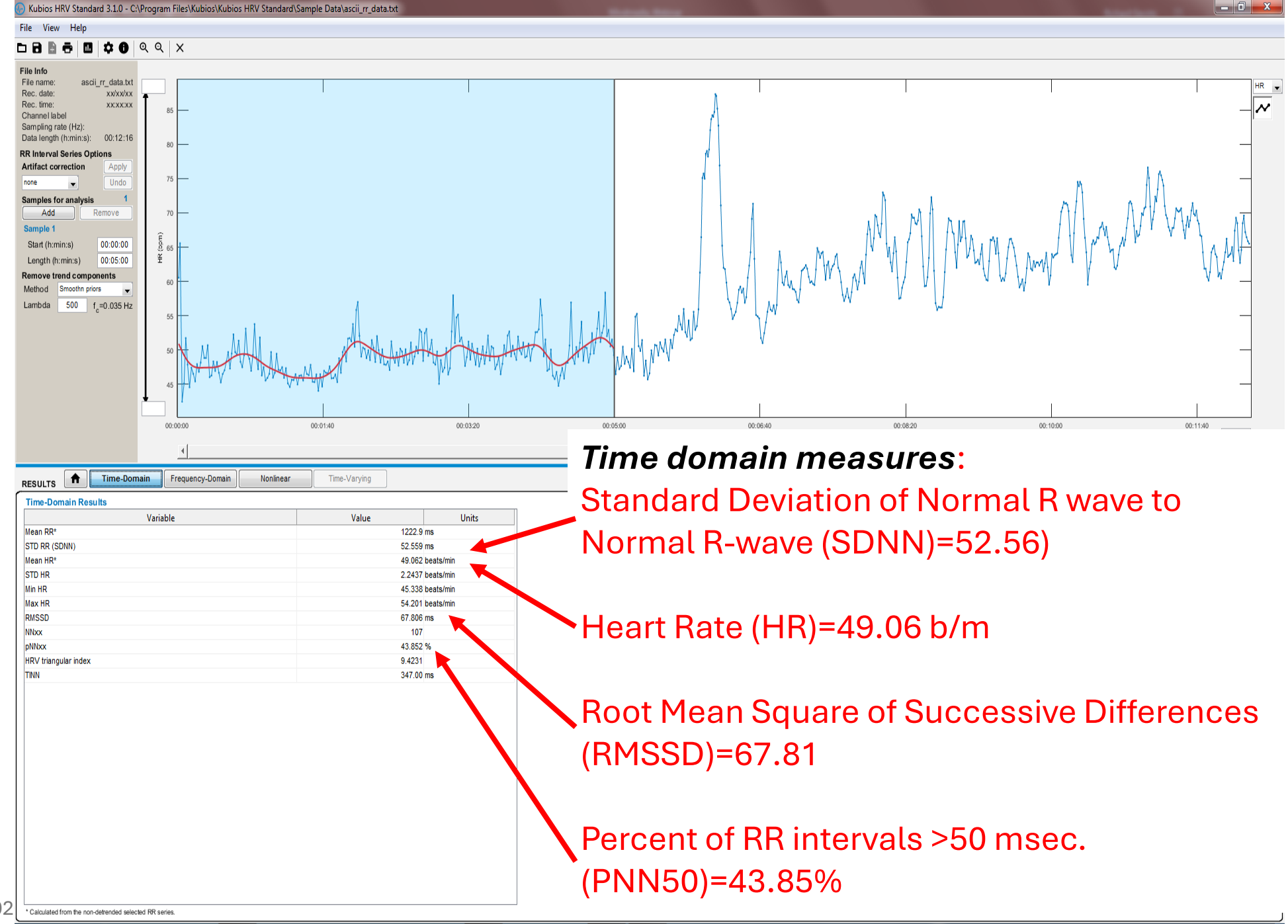
Software programs such as Kubios _HRV use these simple text files of Inter-Beat Intervals (IBIs) (RR intervals) in msec.

- 850
- 970
- 991
- 915
- 1414
- 1331
- 1160
- 1254
- 1347
- 1266
- 1290
- 1322
- 1252
- 1282
- 1246
- 1187
- 1229
- 1229
- 1184



Notice that the longitudinal record of IBIs results in wave forms


Kubios HRV Standard 3.1.0 - C:\Program Files\Kubios\Kubios HRV Standard\Sample Data\ascii_rr_data.txt
File View Help
Normal HRV. Client is resting and breathing normally (about 16 B/M).
RESULTS
Time-Domain
Frequency-Domain
Nonlinear
Time-Varying
Auto-refresh results
Refresh
Sample 1
Kubios HRV - Results Overview
Sample 1 vs. Normal (resting) values
Parasympathetic tone (recovery)
Mean RR = 1223 ms
RMSSD = 68 ms
HF power n.u. = 58 %
LOW NORMAL HIGH
Sympathetic tone (stress)
Mean HR = 49 bpm
Stress index = 6
LF power n.u. = 42 %
HIGH NORMAL LOW
HR
AVG 57 bpm
Min 46 bpm
Max 70 bpm
RMSSD
AVG 47 ms
Stress Index
AVG 8
Kubios HRV Standard
www.kubios.com
HR Zones
MAXIMUM
HARD
MODERATE
LIGHT
VERY LIGHT
INACTIVE
Stress
VERY HIGH
HIGH
ELEVATED
NORMAL
LOW
Energy Expenditure
BMR + Activity
TOTAL
14+16=30 kcal
Personal data (from Preferences):
Gender = Male
Age = 45 years
Max HR = 175 bpm
Height = 180 cm
Weight: 78 kg
11:50 AM
10/23/2018



Time domain measures:

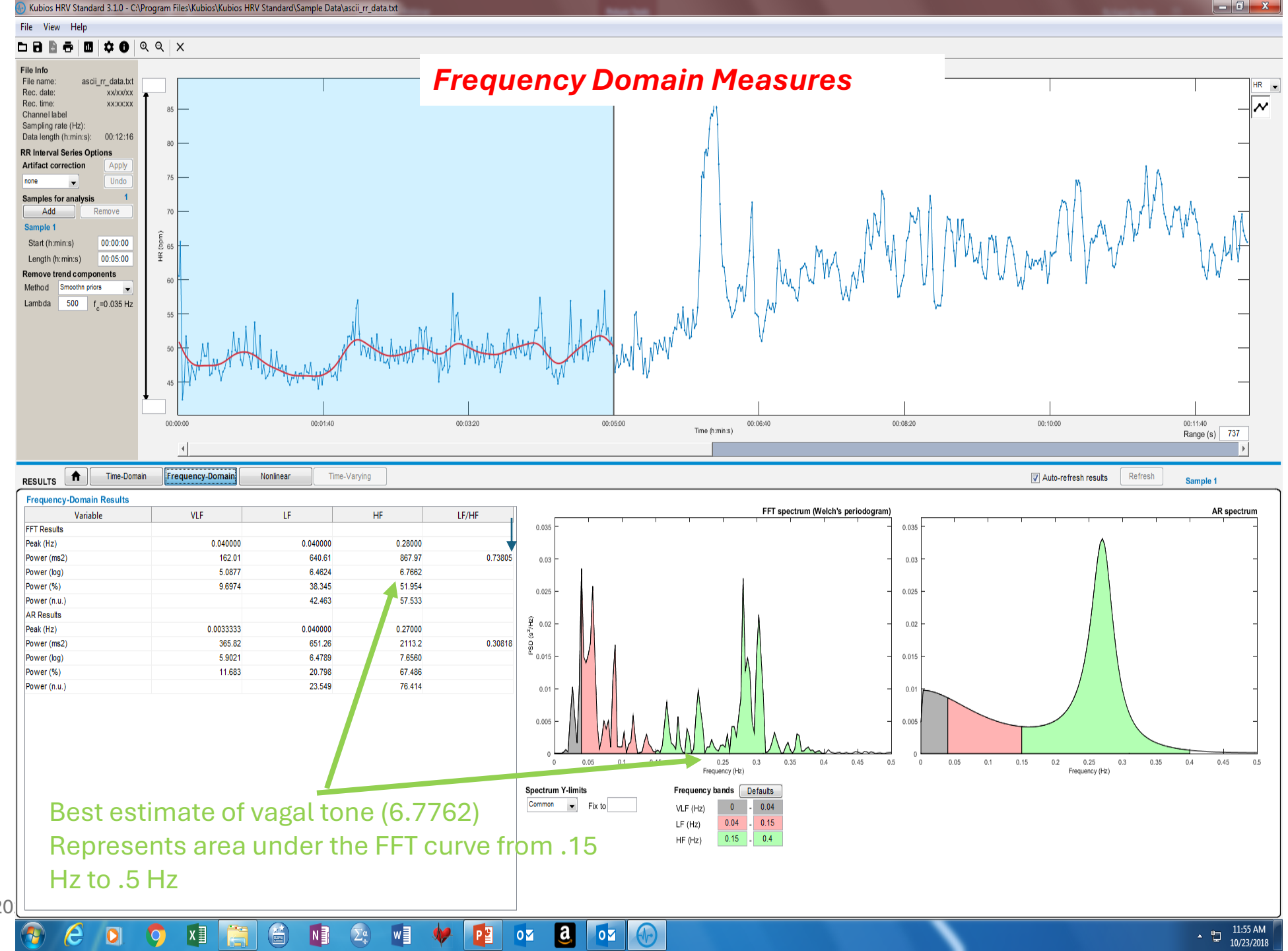
Standard Deviation of Normal R wave to Normal R-wave (SDNN)=52.56)

Heart Rate (HR)=49.06 b/m

Root Mean Square of Successive Differences (RMSSD)=67.81

Percent of RR intervals >50 msec. (PNN50)=43.85%

Frequency Domain Measures



Best estimate of vagal tone (6.7762)
Represents area under the FFT curve from .15 Hz to .5 Hz

Our best estimate of Vagal Tone using non-invasive technology is the area in the spectral analysis for the frequencies related to normal respiration, the HF band.

Vagal Withdrawal: An alternative to Sympathetic Activation

- .: Neurosci Biobehav Rev. 1995 Summer;19(2):225-33.
  -

    Cardiac vagal tone: a physiological index of stress.

    Porges SW.

    Institute for Child Study, University of Maryland, College Park 20742, USA.

    “Cardiac vagal tone is proposed as a novel index of stress and stress vulnerability in mammals. A model is described that emphasizes the role of the parasympathetic nervous system and particularly the vagus nerve in defining stress. The model details the importance of a branch of the vagus originating in the nucleus ambiguus. In mammals the nucleus ambiguus not only coordinates sucking, swallowing, and breathing, but it also regulates heart rate and vocalizations in response to stressors. In mammals it is possible, by quantifying the amplitude of respiratory sinus arrhythmia, to assess the tonic and phasic regulation of the vagal pathways originating in the nucleus ambiguus. Measurement of this component of vagal tone is proposed as a method to assess, on an individual basis, both stress and the vulnerability to stress.”

Pergamon

Neuroscience and Biobehavioral Reviews, Vol. 19, No. 2, pp. 225–233, 1995

0149-7634/95 $9.50 + .00

0149-7634(94)00066-2

Cardiac Vagal Tone: A Physiological Index of Stress

STEPHEN W. PORGES

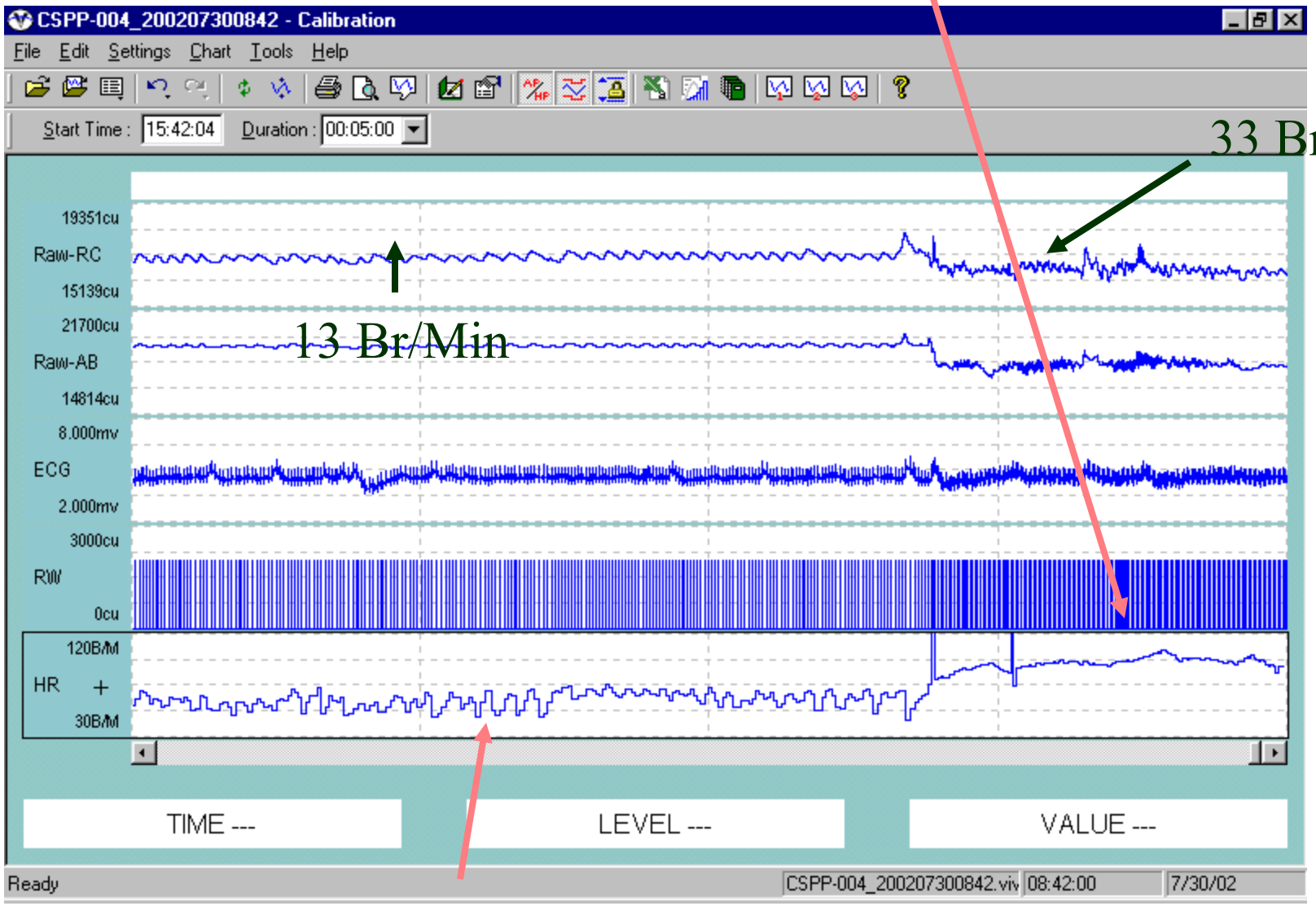
Institute for Child Study, University of Maryland, College Park, MD 20742

PORGES, S. W. *Cardiac vagal tone: A physiological index of stress.* NEUROSCI BIOBEHAV REV **19**(2) 225–233, 1995.—Cardiac vagal tone is proposed as a novel index of stress and stress vulnerability in mammals. A model is described that emphasizes the role of the parasympathetic nervous system and particularly the vagus nerve in defining stress. The model details the importance of a branch of the vagus originating in the nucleus ambiguus. In mammals the nucleus ambiguus not only coordinates sucking, swallowing, and breathing, but it also regulates heart rate and vocalizations in response to stressors. In mammals it is possible, by quantifying the amplitude of respiratory sinus arrhythmia, to assess the tonic and phasic regulation of the vagal pathways originating in the nucleus ambiguus. Measurement of this component of vagal tone is proposed as a method to assess, on an individual basis, both stress and the vulnerability to stress.

Vagal tone Stress Autonomic nervous system Heart rate Respiratory sinus arrhythmia

Vagal Withdrawal

Worrying about being late for an appointment.
Notice the elevated, flattened HR.



Here you can see an example of VAGAL Withdrawal

Beat by beat HR during driving to appointment.

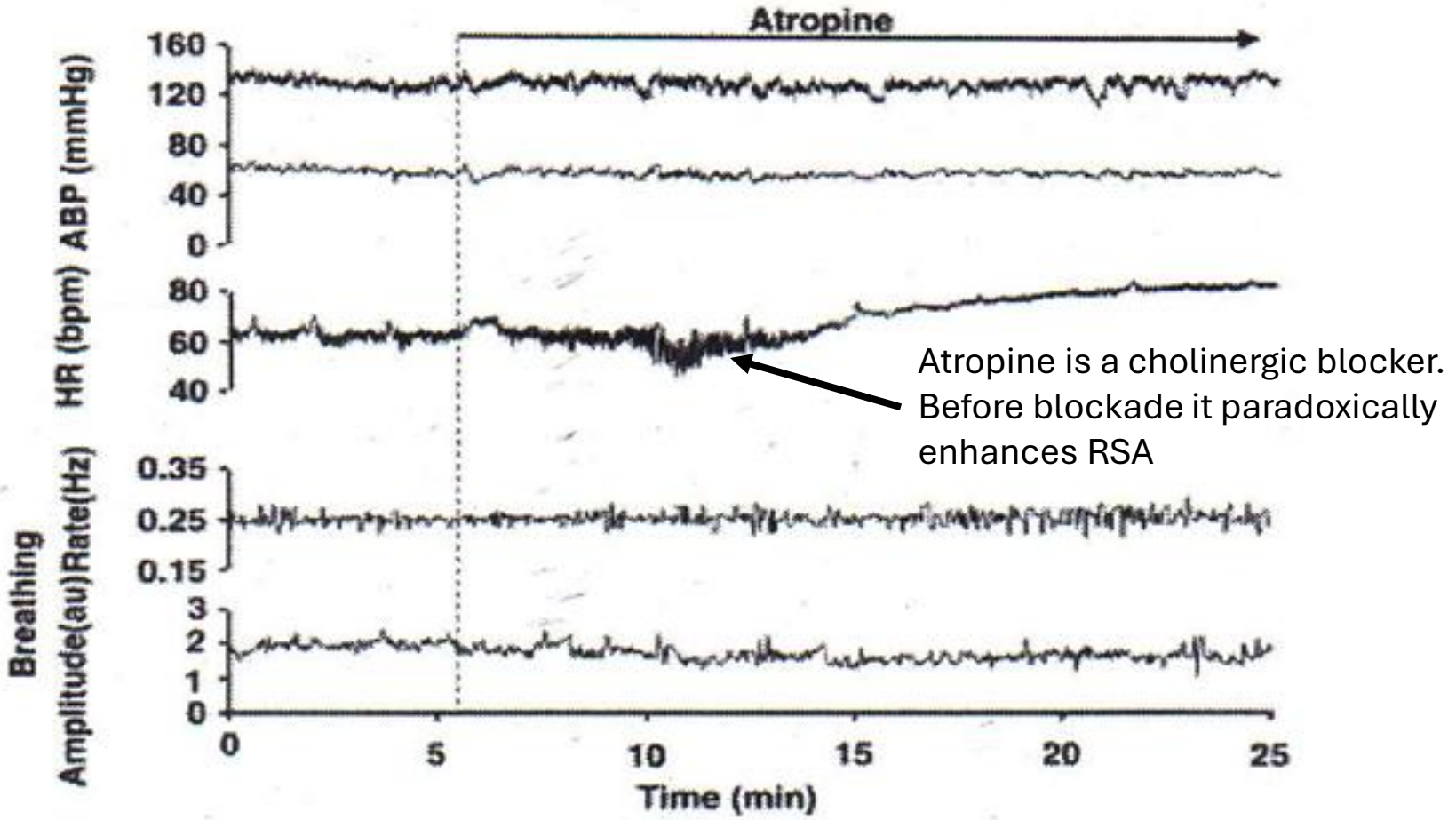
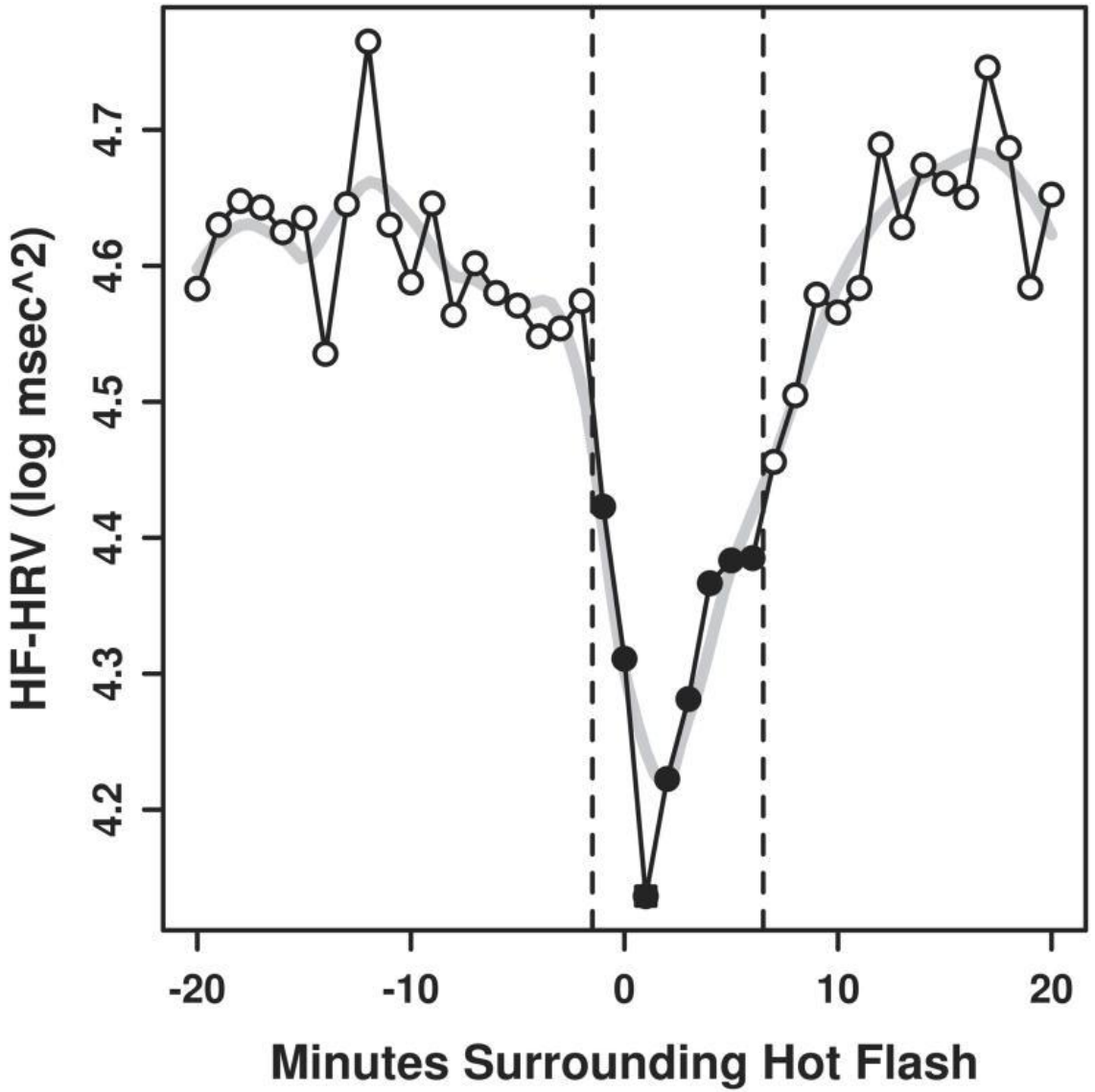


Fig. 1 Typical example of the effect of a slow infusion of atropine on systolic and diastolic arterial blood pressure (*ABP*, mmHg), heart rate (*HR*, beats/min) and amplitude (arbitrary units) and rate of respiration (Hz) in a healthy volunteer pre-treated with bisoprolol. Respiration was timed at 0.25 Hz

HF-HRV= “vagal tone” derived from RSA



Dramatic example of vagal withdrawal in perimenopausal hot flashes

Minute by minute changes in HF-HRV during hot flash

Note: Closed circles represent minutes significantly different from open circles at $p<0.05$, N=21

(Hot flashes and cardiac vagal control during women's daily lives
Menopause. ;19(4):406-412.)

Parasympathetic:

"Accentuated Antagonism"

PNS acts as a "governor" for the SNS

"Sympathetic heart rate effects were substantially smaller with high levels of vagal tone than with low vagal background activity. Furthermore, vagal effects became progressively stronger with increasing sympathetic background activity, demonstrating the predominance of parasympathetic control of human heart rate. This finding implies that changes in cardiac activity resulting from changes in sympathetic control cannot be interpreted accurately unless concurrent vagal activity is taken into account, as well."

(Uijtdehaage & Thayer, 2000, p. 107)

"Vagal 'tone' predominates over sympathetic tone at rest. Under normal physiological conditions, abrupt parasympathetic stimulation will inhibit tonic sympathetic activation and its effects at rest and during exercise. This response is known as 'accentuated antagonism"

(Olshansky et al., 2008, p.863)

(Yang and Levy, 1984; Schwegler and Jacob, 1975; Levy, and Zieske, 1969; Stramba-Badiale MA, Vanoli E, De Ferrari GM, Cerati DO, Foreman RD, Schwartz PJ; Miyazoe, H., Harada, Y., Yamasaki, S., & Tsuji, Y. (1998); Tulppo, M. P., Makikallio, T. H., Seppanen, T., Airaksinen, J. K., & Huikuri, H. V. (1998))

The opposite of vagal withdrawal
Direct Activation

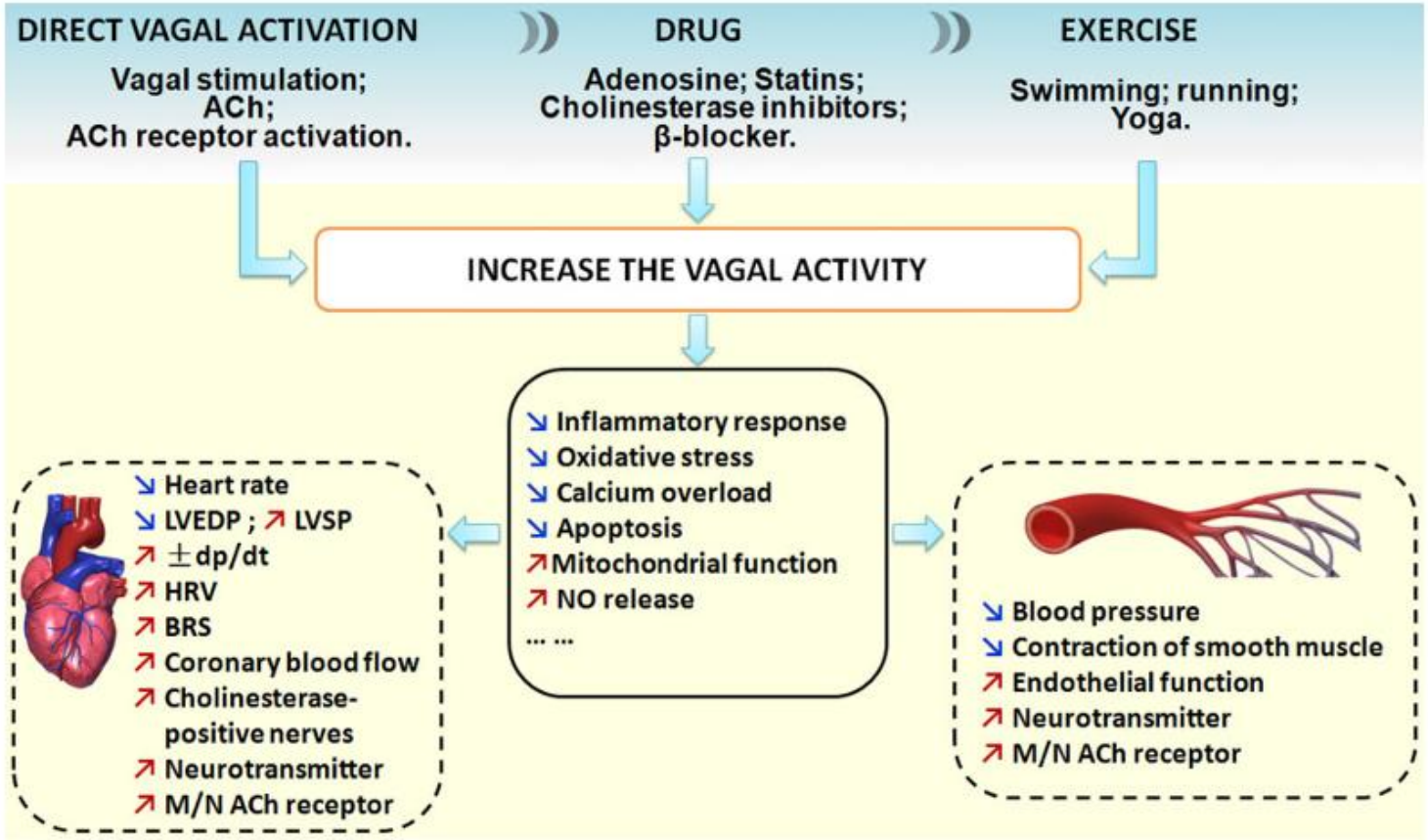


Figure 2

Beneficial effects on cardiac and vascular function are provided by the modulation of vagal activity, including direct vagal activation (vagal stimulation, ACh administration and ACh receptor activation), pharmacological modulation (adenosine, cholinesterase inhibitors, statins) and exercise training.

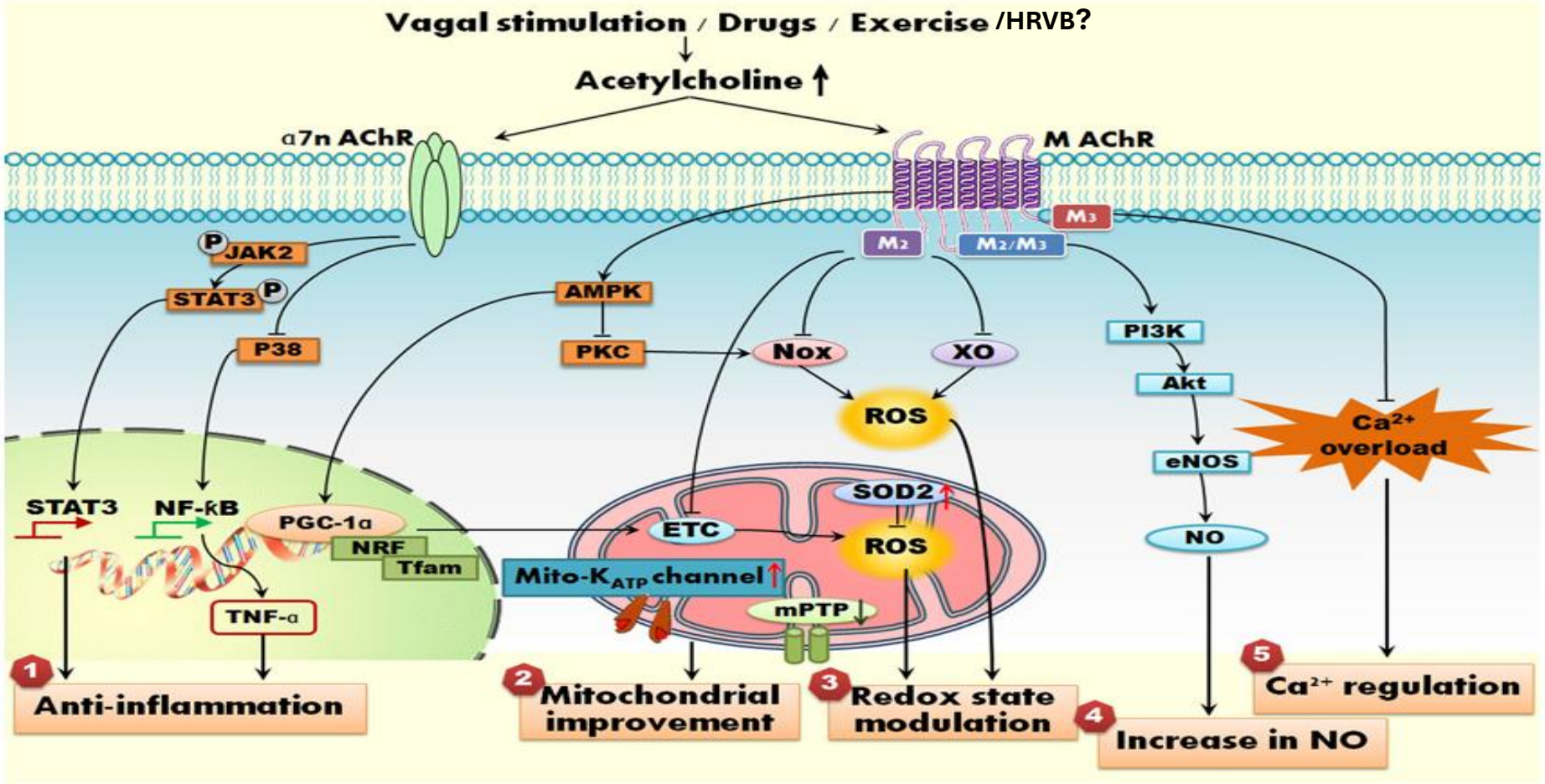
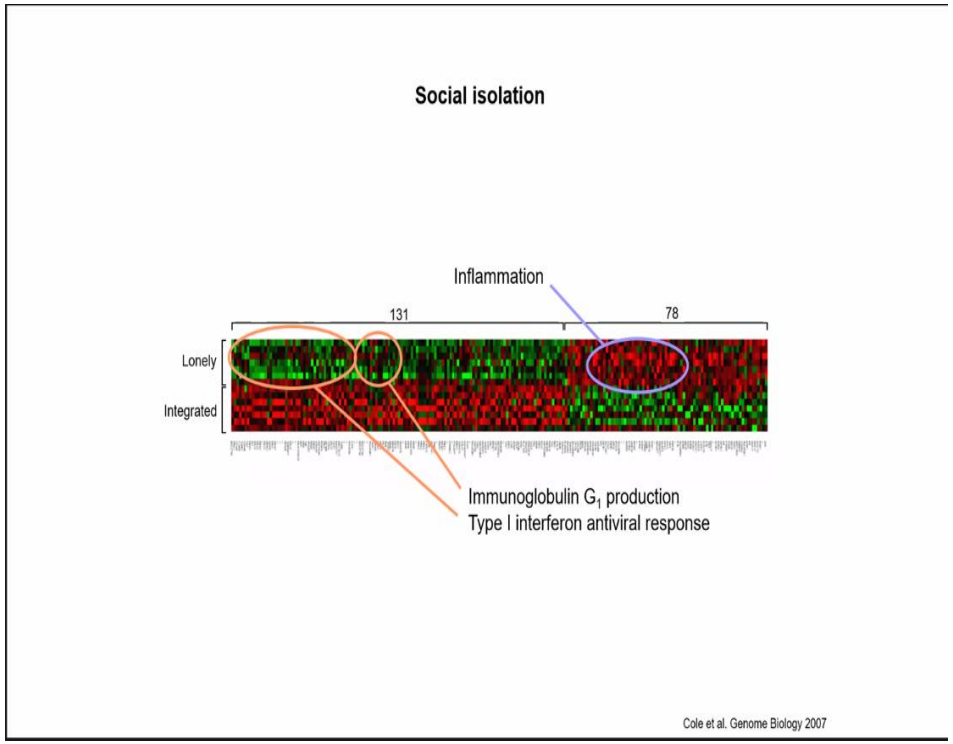


Figure 1

Schematic representation of signalling pathways and mechanisms regulated by vagal activation. The mechanisms contributing to the beneficial effect of improved vagal activity are multifactorial, including (1) its anti-inflammatory effects by activating JAK2/STAT pathway and inhibiting NF-κB activation which is dependent upon α7nACh receptor; (2) mitochondrial improvement (increasing mitochondrial biogenesis and function, mitochondrial K_{ATP} activation and inhibiting mitochondrial permeability transition pore (mPTP) opening); (3) redox state regulation (suppressing ROS generation and promoting ROS elimination); (4) increase in NO through PI3K/Akt/eNOS pathway; (5) down-regulation of calcium overload. SOD2, Mn superoxide dismutase.

A wide variety of physiological systems are activated by vagal stimulation

Redox modulation involves the balance between reduction and oxidation reactions within cells, which is crucial for maintaining cellular homeostasis.



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Current Opinion in Behavioral Sciences

The Conserved Transcriptional Response to Adversity

Steven W Cole

Gene expression profiling studies of people exposed to chronic threat have identified a Conserved Transcriptional Response to Adversity (CTRA) in circulating immune cells. This physiological pattern is characterized by upregulated expression of genes involved in inflammation and downregulated expression of genes involved in Type I interferon responses. The CTRA is mediated by beta-adrenergic signaling pathways that transduce sympathetic nervous system activity into changes in transcription factor activity and hematopoietic output of myeloid lineage immune cells (monocytes, neutrophils, and dendritic cells). Recent research has begun to identify the CNS processes that regulate peripheral CTRA activity, define its implications for disease, and explore the role of positive psychosocial factors in buffering such effects. The CTRA provides a genomic framework for understanding PNI relationships and connecting macro-level psychosocial processes to the micro-level biology of health and disease.

Address
Department of Medicine, Division of Hematology-Oncology, and Department of Psychiatry & Biobehavioral Sciences, UCLA School of Medicine, 11-934 Factor Building, Los Angeles, CA 90095-1678, United States

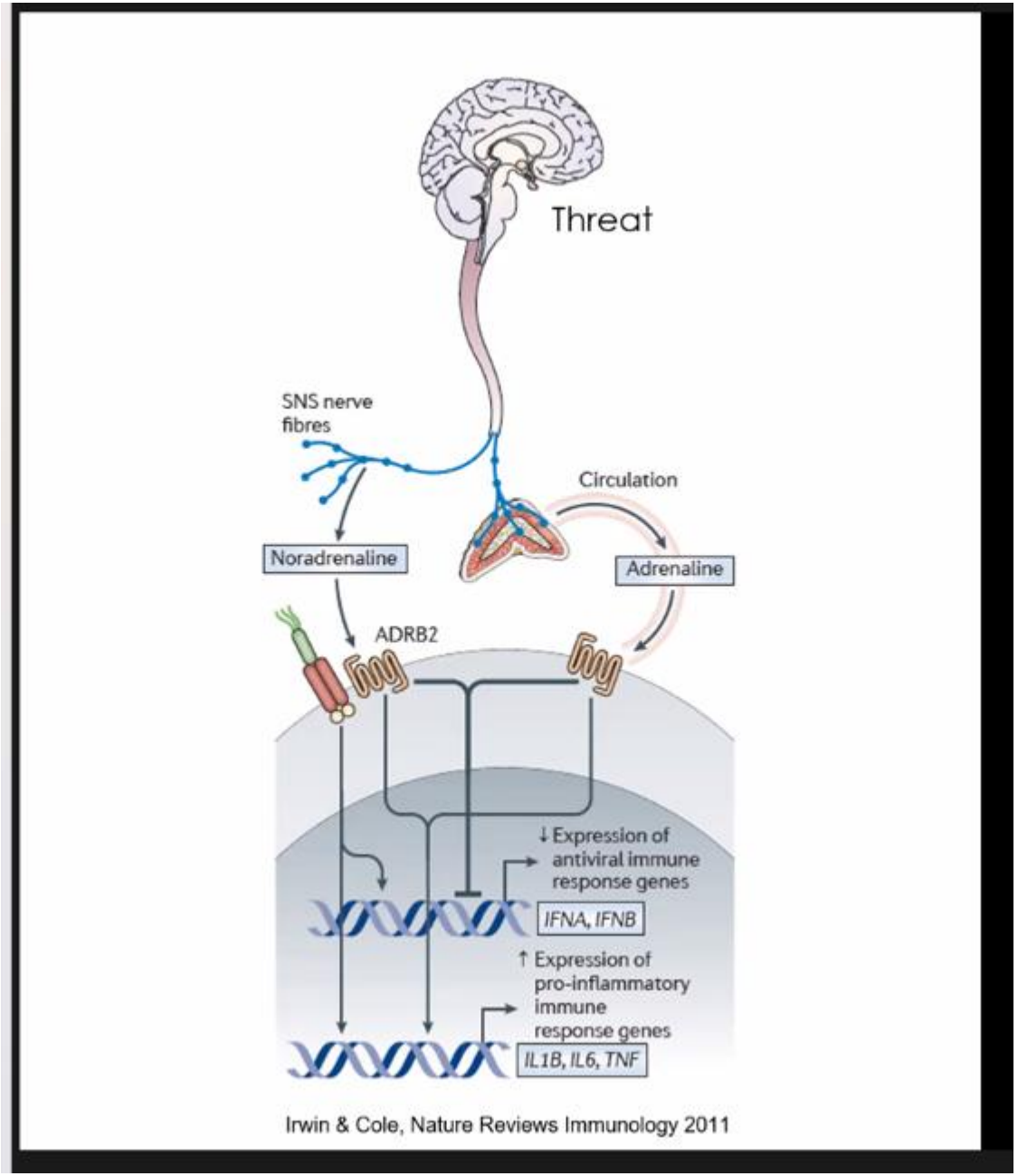
Corresponding author: Cole, Steven W (steve.cole@ucla.edu)

poverty, bereavement, chronic stress) and in subsequent experimental animal models [3–9]. The broad consistency of these effects across species and across different forms of adversity led to its description as a Conserved Transcriptional Response to Adversity (CTRA). This article reviews the CTRA's discovery and theoretical conceptualization, early laboratory analyses mapping its biological mechanisms, and more recent studies assessing its implications for disease and the development of interventions to block its detrimental impact on health. It also surveys some key issues in CTRA measurement and research questions currently under analysis.

A Conserved Transcriptional Response to Adversity

Epidemiologic studies have long documented social gradients in disease, but the molecular mechanisms of these effects have only recently become a topic of significant scientific attention. In the late 1990s and early 2000s, the MacArthur Foundation convened a network of behavioral and biological scientists to analyze the pathways by which social environmental risk factors influenced host resistance to disease. Research on human genome function was surging in parallel with the completion of the human

Gene expression that controls anti-viral immune responses and pro-inflammatory immune responses are partially mediated by the vagus



Well-Being linked to Type I Interferon immune biology

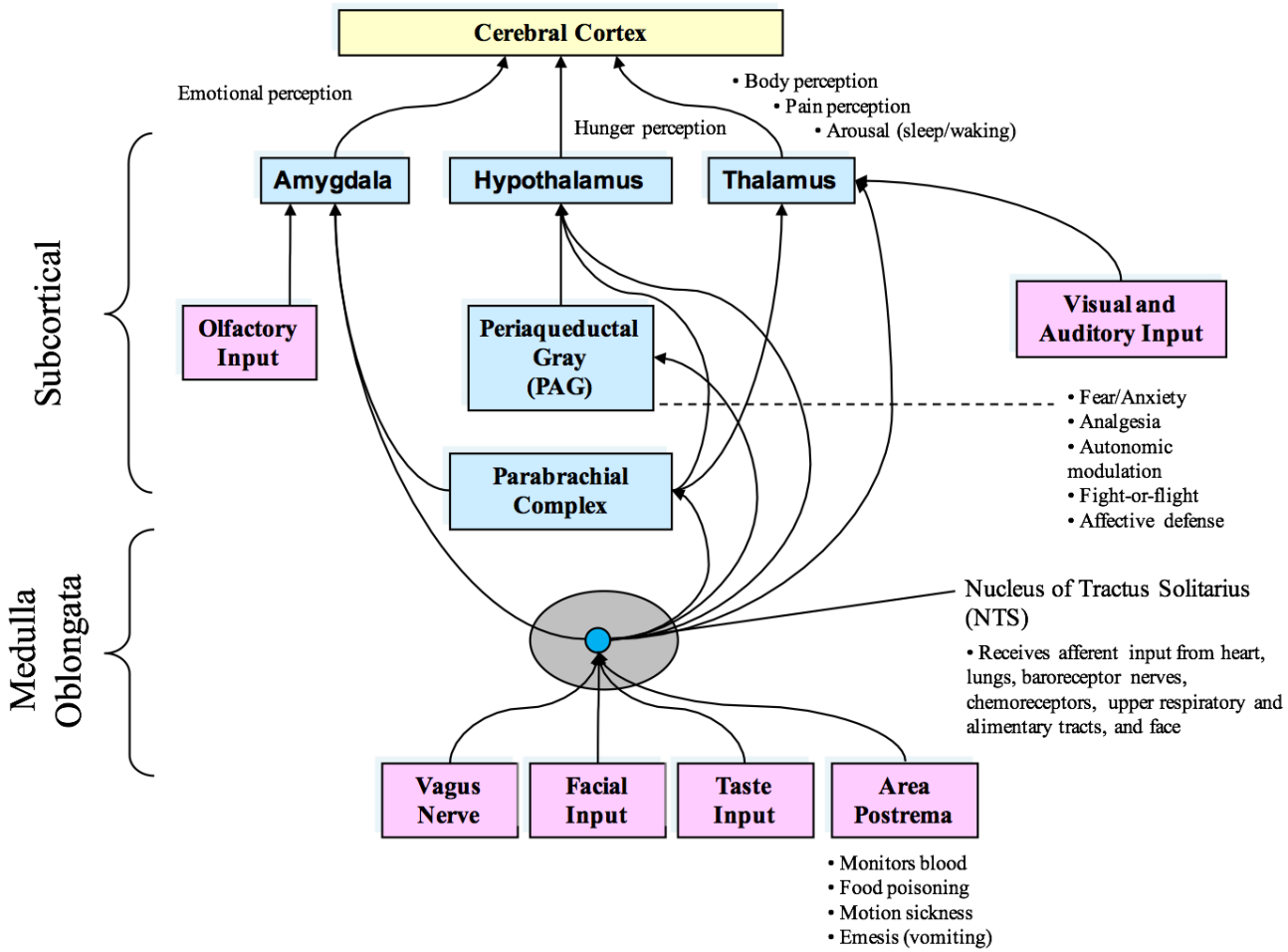
- Particularly the "social: aspects of individual well-being
- This possibly an allostatic adaptation to "social pathogens" i.e. viruses

Mammalian"social" parasympathetic activity (the vagus) appears to mediate:

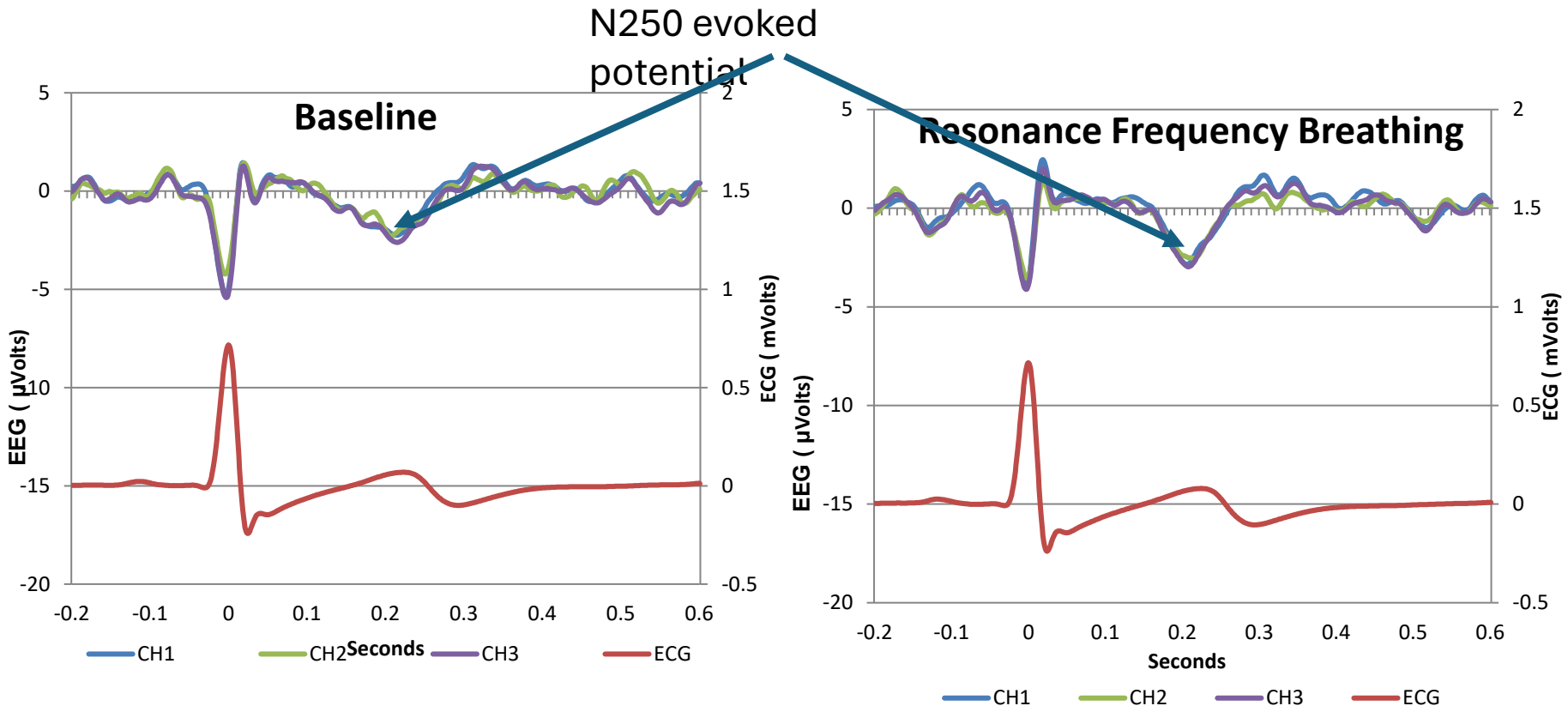
- Type I Interferon
- Social well-being can enhance Type I Interferon

The Afferent pathways

"The brain listening to the heart by way of the Vagal Afferents"

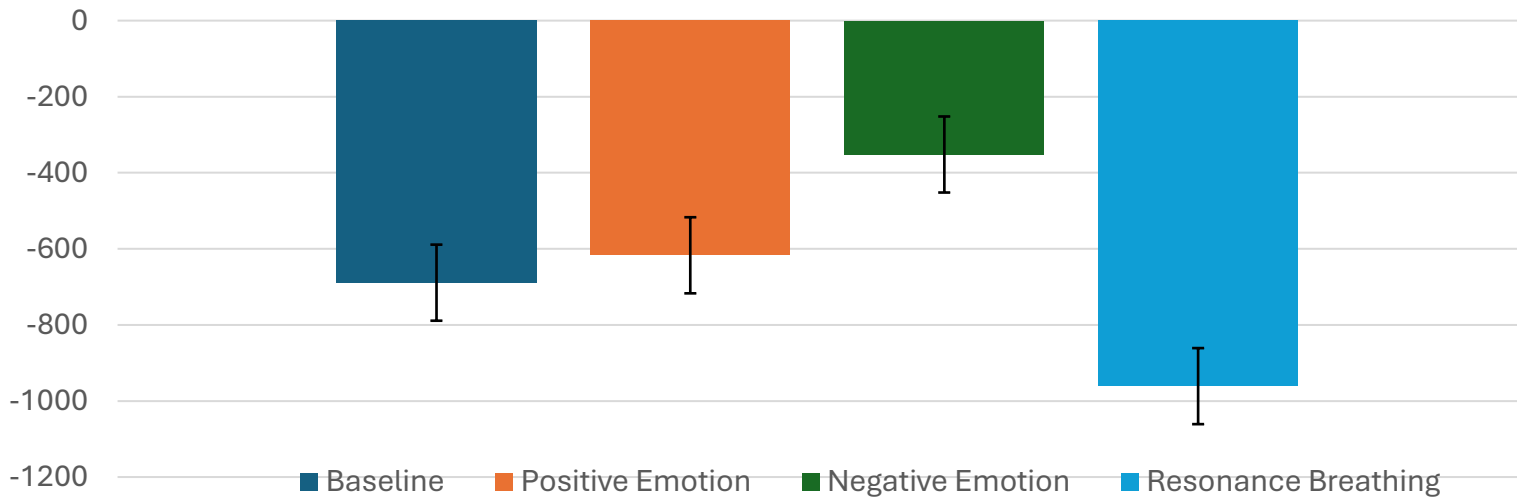

Cerebral Cortex
Emotional perception
• Body perception
• Pain perception
• Arousal (sleep/waking)
Hunger perception
Amygdala
Hypothalamus
Thalamus
Subcortical
Olfactory Input
Periaqueductal Gray (PAG)
Visual and Auditory Input
• Fear/Anxiety
• Analgesia
• Autonomic modulation
• Fight-or-flight
• Affective defense
Parabrachial Complex
Medulla Oblongata
Nucleus of Tractus Solitarius (NTS)
• Receives afferent input from heart, lungs, baroreceptor nerves, chemoreceptors, upper respiratory and alimentary tracts, and face
Vagus Nerve
Facial Input
Taste Input
Area Postrema
• Monitors blood
• Food poisoning
• Motion sickness
• Emesis (vomiting)

Heartbeat-evoked Potentials (HEPs)

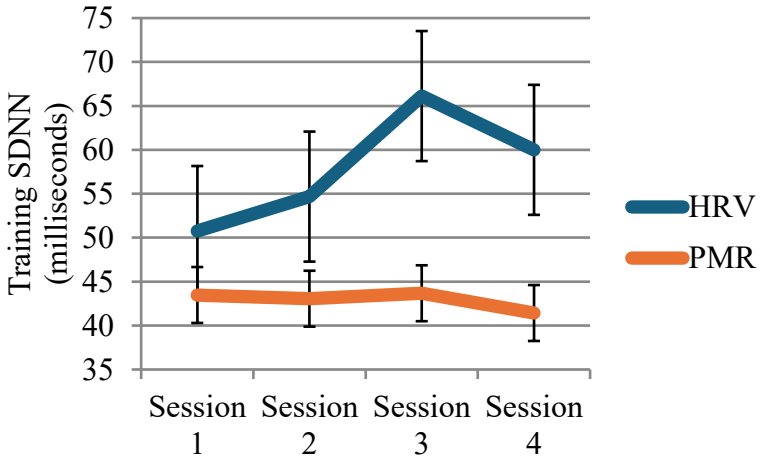


MacKinnon, S., Gevirtz, R.N. & Mc Craty, R. (2013). "Utilizing heartbeat evoked potentials to identify cardiac regulation of vagal afferents during emotion and resonant breathing." *Applied Psychophysiology and Biofeedback* ***38****(4): 241-255*.

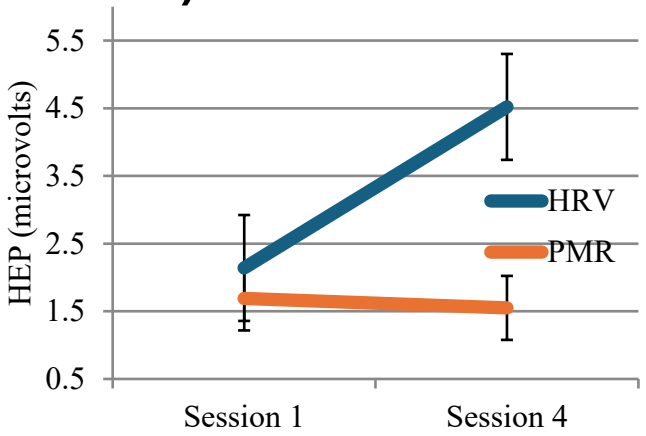
Heart Period Evoked Potential Across Conditions



SDNN between groups over time (p<.01)



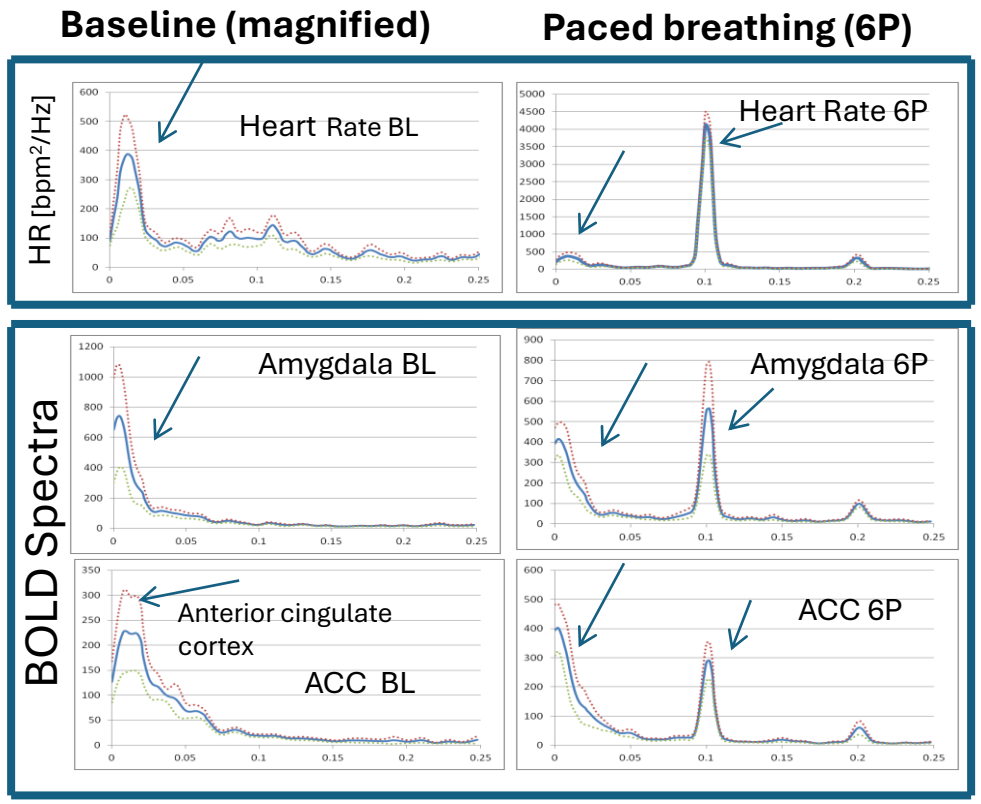
HEP at 250 microseconds for both groups pre vs. post training (sign reversed)



With improvement (29%) in resting baseline HRV over 4 weeks, comes increased cortical signaling ,presumably from vagal afferents.

Vaschillo et al, 2018

Averaged Across 15 Subjects HRV and BOLD Spectra (M ± s.e.)



The power of the BOLD spectra were dominant in the same range of 0.003– 0.025 Hz as the power in HRV spectra at baseline.

Both BOLD and HRV showed a high peak at 0.1 Hz in response to paced breathing

The major part of baseline power in all BOLD spectra was located in the range of 0.003-0.05 Hz.

Can we improve brain mechanisms of emotion regulation with five weeks of HRV-biofeedback?

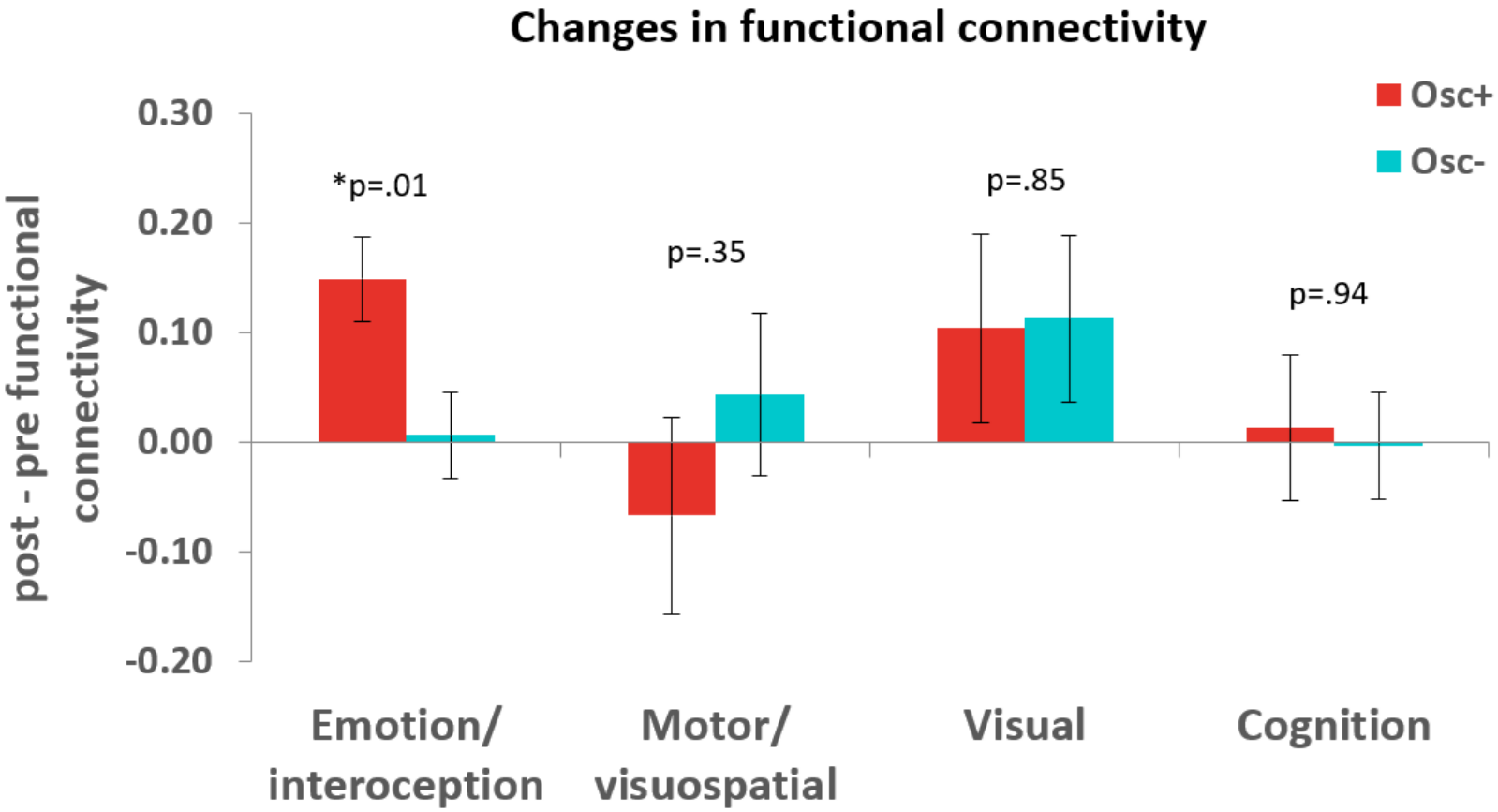
Yoo, H. J., Nashiro, K., Min, J., Cho, C., Bachman, S. L., Nasseri, P., ... & Mather, M. (2022). Heart rate variability (HRV) changes and cortical volume changes in a randomized trial of five weeks of daily HRV biofeedback in younger and older adults. International Journal of Psychophysiology.

Mara Mather

University of Southern California

Project funded by NIH R01AG057184
“Why Does Heart Rate Variability Matter for Emotion Regulation?”

The Osc+ group showed increased functional connectivity within networks involved in emotion/interoception



So, we know that Vagal stimulation from whatever source, has profound effects on almost every biological system in the body and that vagal withdrawal, especially when prolonged, leaves the most vulnerable systems at risk.

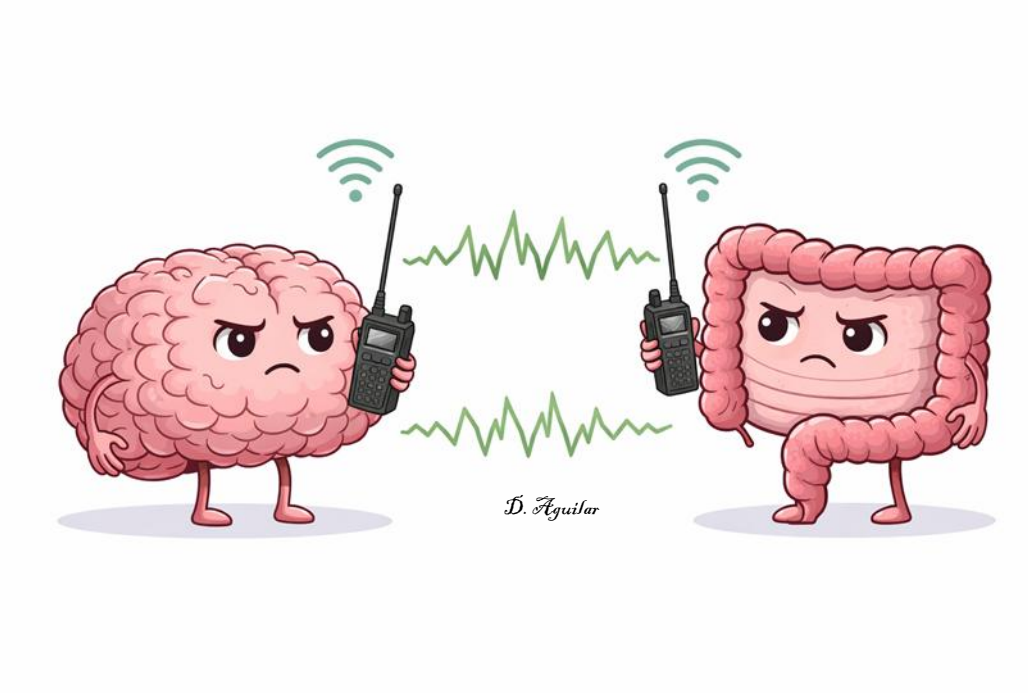
We now have well designed studies that show that HRV Biofeedback produces profound changes in the brain, presumably by way of the vagal afferents.

Disorders that appear to be mediated by vagal withdrawal

-Disorders of Gut Brain Interaction (DGBI)
-Chronic Muscle Pain
-Anxiety
-Trauma
-Cardiovascular Disease

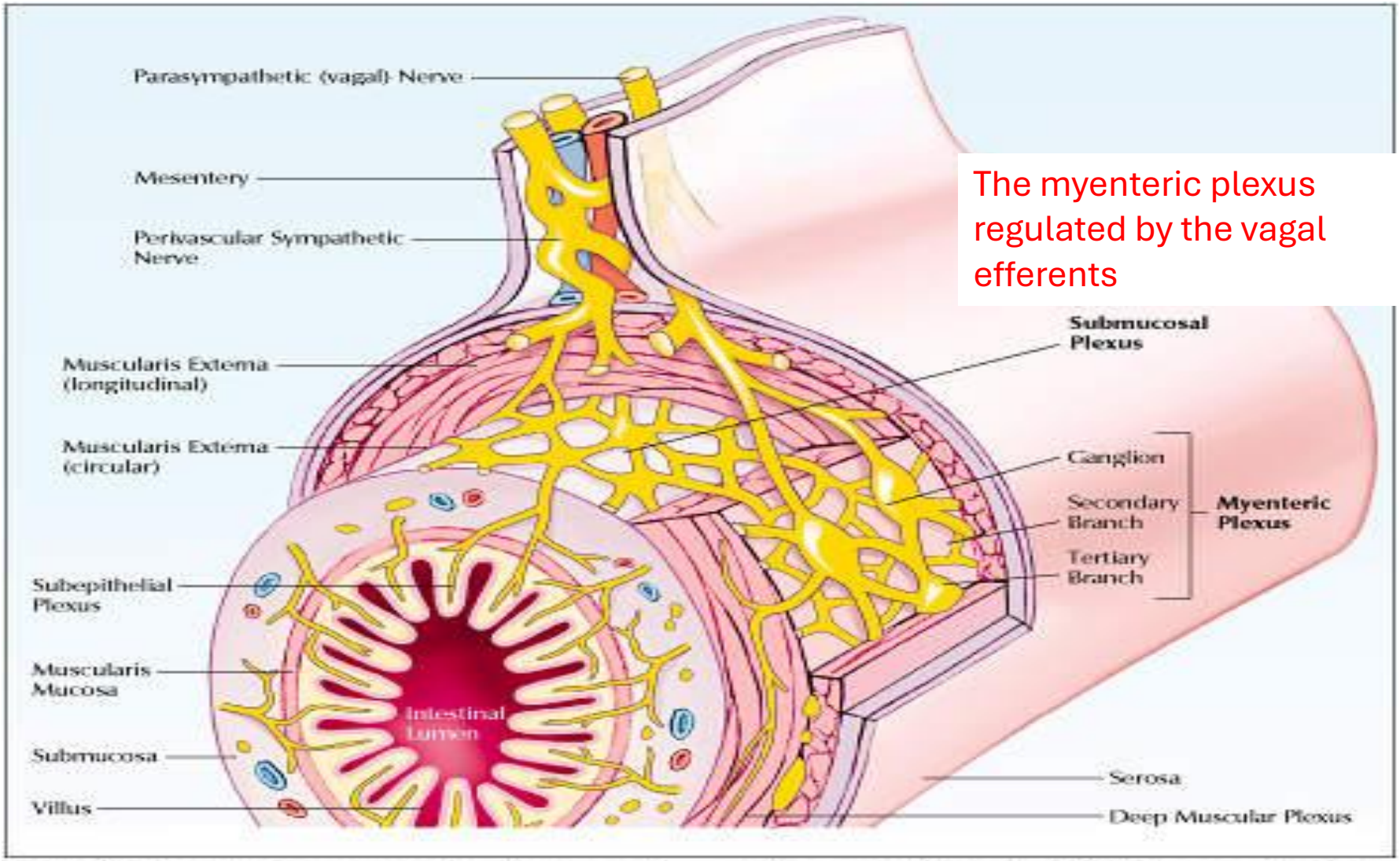
Disorders of Brain Gut Interaction DGBIs

IBS
Constipation
Diarrhea
Bloating
Nausea
GERD



"Functional gastrointestinal (GI*)[now called DGBI]* disorders are highly prevalent, occurring in 10%–20% of population worldwide (Saito, Schoenfeld, & Locke III, 2002; Chang, Lu, & Chen, 2010; Lewis, Palsson, Whitehead, & van Tilburg, 2016). These disorders constitute the primary reason for GI referral in pediatric tertiary care centers (Rouster, Karpinski, Silver, Monagas, & Hyman, 2016) and do not respond well to gut-targeted drug therapies (Drossman et al., 2018; Sobin, Heinrich, & Drossman, 2017). They encompass a range of problems with digestion, defecation, abdominal pain, vomiting, nausea, and swallowing without an identifiable structural pathology. Some specific pain-associated functional GI diagnoses include irritable bowel syndrome (IBS), functional dyspepsia, abdominal migraine, and functional abdominal pain."

Kolacz, J., Kovacic, K. K., & Porges, S. W. (2019). Traumatic stress and the autonomic brain-gut connection in development: Polyvagal theory as an integrative framework for psychosocial and gastrointestinal pathology. *Developmental psychobiology*, *61*(5), 796-809.

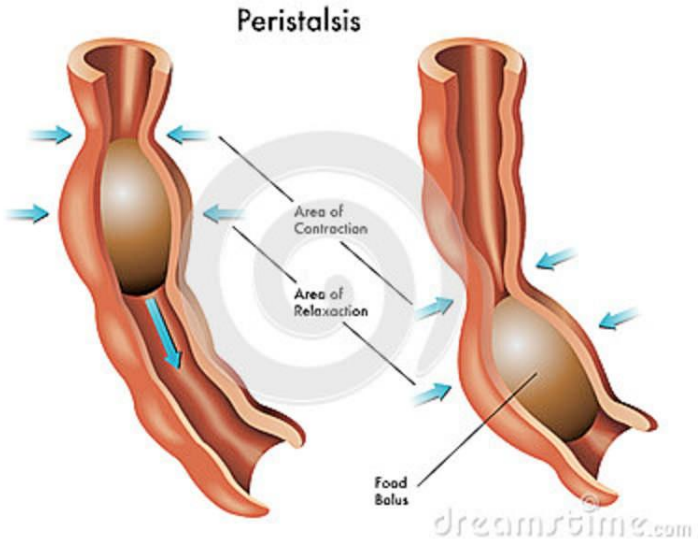


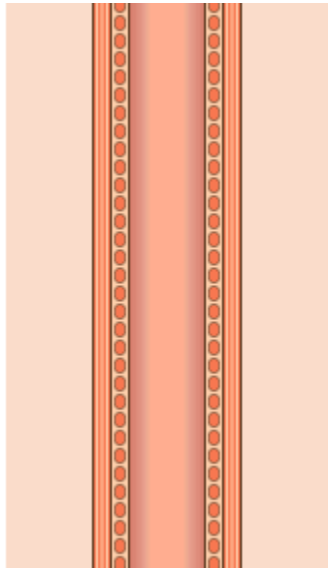
The myenteric plexus regulated by the vagal efferents

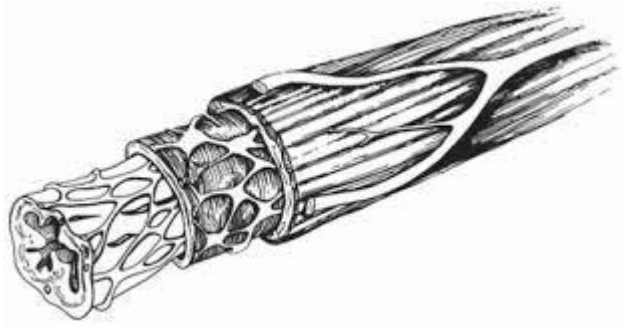
Figure 3. The enteric nervous system is composed of two ganglionated plexuses. The larger myenteric plexus, situated between the circular and longitudinal layers of the muscularis externa, contains the neurons responsible for motility and for mediating the enzyme output of adjacent organs. The smaller submucosal plexus contains sensory cells that "talk" to the motor neurons of the myenteric plexus, as well as motor fibers that stimulate secretion from epithelial crypt cells into the gut lumen. Other anatomical landmarks of note include parasympathetic (vagal) fibers entering the bowel in the mesentery, perivascular sympathetic input to the gut, and the subepithelial plexus of nerve fibers in the lamina propria of the mucosa. (Adapted from Gershon and Erde, 1981)

The Long Road:
Esophageal, Gastric and Colonic Motility

Stretch in the gut is the primary source of pain. Poor vagal regulation seems to greatly am plify the pain signals to the central nervous system.







Peristalsis – Wave like propulsions that push the bolus forward. At each structure when the smooth muscle contracts, its contents are propelled through the gut. The action of the smooth muscle surrounding the intestines is controlled by the specialized enteric nervous system. As a result, the enteric nervous system is connected to the CNS (brain) by the interconnecting autonomic nervous system (ANS). Natural flow of hyper and hypo polarization of the interstitial cells of Cajal (ICC) form a slow wave rhythmicity. Stimulated by either reflex or vagal efferents and modulated by the rhythm of the ICC. Large amounts of epinephrine or norepinephrine will inhibit the entire peristaltic process.

Appl Psychophysiol Biofeedback (2010) 35:199–206
DOI 10.1007/s10484-010-9128-8

Restoration of Vagal Tone: A Possible Mechanism for Functional Abdominal Pain

Erik Sowder · Richard Gevirtz · Warren Shapiro · Crystal Ebert

Published online: 14 March 2010

Abstract Functional abdominal pain (FAP) causes disruption of daily activities/missed school days, over utilization of healthcare, unnecessary surgeries, and anxiety in 10–15% of children. Its etiology is not clearly understood, however the success of several clinical protocols suggests that autonomic dysregulation is a factor. In this study autonomic activity, including heart rate variability (HRV), was compared between children with FAP and a comparison group. Twenty children with FAP and 10 children without FAP between the ages of 5 and 17 years old were compared on autonomic regulation using an ambulatory system at baseline and 8 weeks later. Children with FAP participated in 6 sessions of HRV biofeedback aimed at normalizing autonomic balance. At baseline, children with FAP appear to have more autonomic dysregulation than children without FAP. After completing HRV biofeedback, the FAP group was able to significantly reduce their symptoms in relation to significantly increasing their autonomic balance. In a sample of children with FAP, it appears that HRV biofeedback treatment improved their symptoms and that a change in vagal tone was a potential mediator for this improvement. The present study appears to point to excessive vagal withdrawal as an underlying mechanism of FAP.

Keywords Recurrent abdominal pain · FAP · Vagal tone · Biofeedback

Introduction

Of the Functional Gastroenterolgical Disorders (FGD) (including Functional Abdominal Pain [FAP], Irritable Bowel Syndrome [IBS], and Functional Dyspepsia [FD]), FAP has been identified as recurrent episodes of abdominal pain severe enough to interfere with a patient's usual activates but not caused by an identifiable organic disease and unrelated to bowel function (Sanders et al. 1994). Minimal criteria for patient inclusion in studies of FAP consist of at least 3 bouts of pain severe enough to affect activities during a period of not less than 3 months, with episodes occurring in the year preceding the examination (Clouse et al. 2006). FAP affects approximately 10–15% of the population (Apley and Naish 1958; Kristjansdottir 1996; Oster 1972; Parcel et al. 1977).

FAP is the cause of disruption of daily activities/missed school days, over-utilization of healthcare (Hyams et al. 1996), unnecessary surgeries, learning difficulties (DiPalma and DiPalma 1997), and anxiety (Jansdottir 1997). Even though FAP has generated these extensive negative outcomes, researchers have yet to clearly identify its etiology.

Investigators have found various combinations of treatments to be effective (Bremner and Sandhu 2009) at reducing symptoms in some patients with FAP. The effective combinations include cognitive-behavioral therapy (Huertas-Ceballos et al. 2008b; Sanders et al. 1989, 1990, 1994), consumption of fiber (Edwards and Bonner 1991; Feldman et al. 1985), hypnotherapy (Vlieger et al.

Procedures

- RAP group (n=20)
  - Reviewed patients' medical records at Kaiser/Children's Specialists
    - Routine 6 HRV biofeedback sessions conducted on-site
    - 2 sessions ambulatory HRV monitoring

- Healthy control group (n=10)
  - Recruited participants (verbal / flyers) during well-checks at Kaiser / Children's Specialists
    - 2 sessions ambulatory HRV monitoring

Pre/Post Assessment:
VivoMetrics, Inc. LifeShirt,tm

•The first non-invasive, ambulatory monitoring system that continuously collects, records and analyzes a broad range of cardiopulmonary parameters. Made it possible to monitor children in their natural environments over a full day.

Procedures

Healthy Control Group

- Attend Kaiser or Children's Specialists for 2 30-minute sessions (8 weeks apart) to connect LifeShirt
- Non-invasively monitored during 4 to 8 hours of daily activities both occasions.
- Total participating time, including explanation of the study and forms, ambulatory monitoring sessions, and answering any questions, was approximately 9-17 hours.

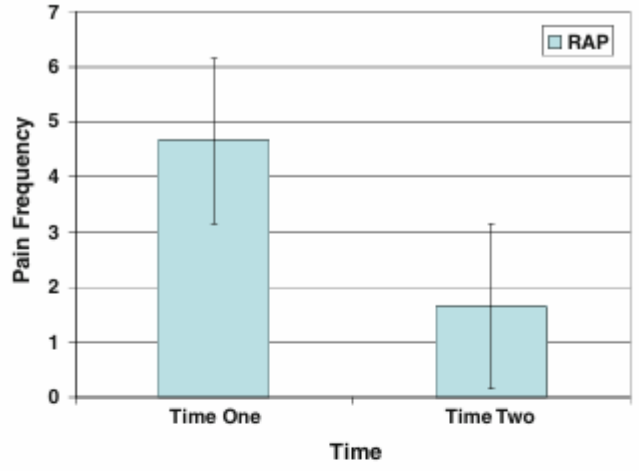


Fig. 1 Mean changes in pain frequency in the recurrent abdominal pain group from time one to time two (8 weeks later), after completion of heart rate variability biofeedback treatment. Pain frequency was measured by number of reported pain episodes per week

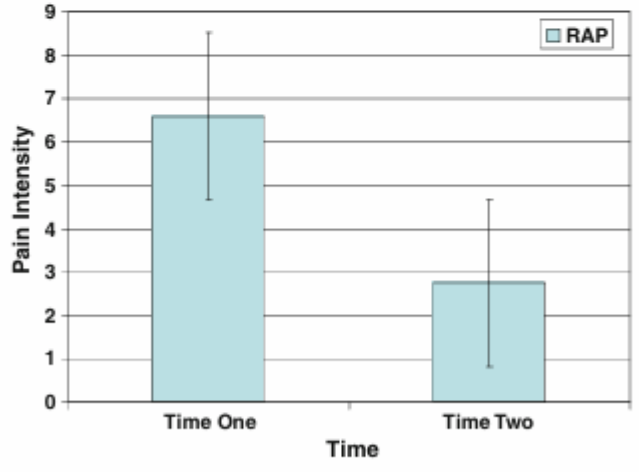


Fig. 2 Mean changes in pain intensity in the recurrent abdominal pain group from time one to time two (8 weeks later), after completion of heart rate variability biofeedback treatment. Pain intensity was measured using a visual analogue scale with a rating scale from one to ten, with one equaling least severe pain and ten equaling most severe pain

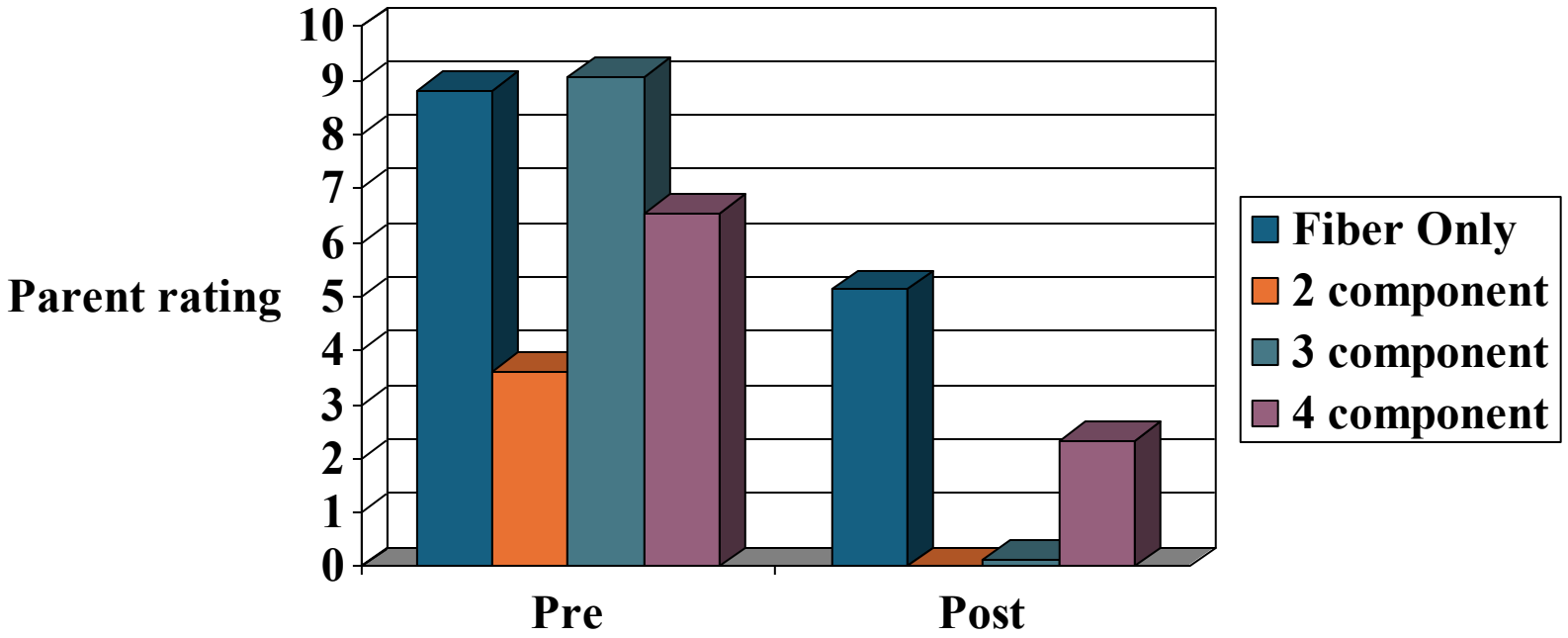
We examined 5-minute records of every breath and inter-beat interval for a day in school.
We looked for segments that were free of movement with normal breath rates and analyzed them in Kubios for Time and Frequency domain HRV measures.

The treatment was highly successful in that pain ratings and other measures were greatly improved.

There was also a positive correlation between an increase in measures of vagal tone and a decrease in pain intensity (**$r = 0.62$, $p = 0.004$, $r^2 = 38.4\%$**) from time one to time two. This analysis appears to indicate that the changes in vagal tone following treatment mediated the improvement in symptoms.

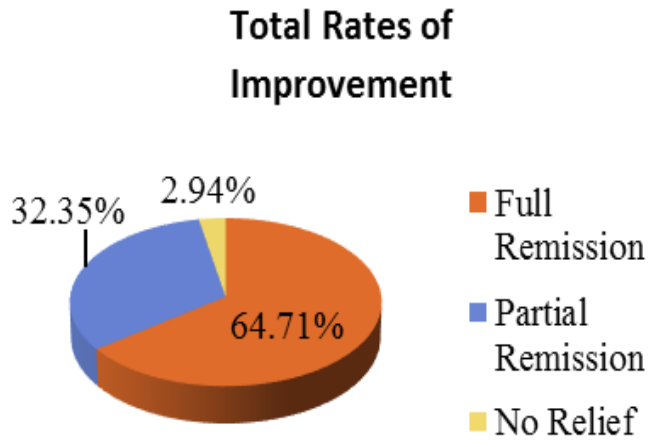
Figure 2. Parent observation rating of pain, pre & post treatment, by group
(Humphreys& Gevirtz, 2000)

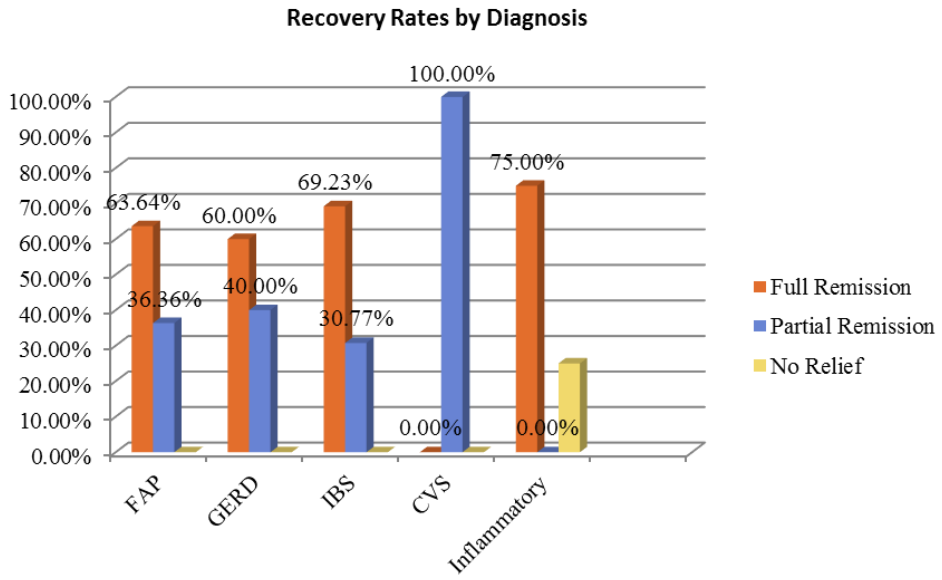
Pre = Pre-treatment
Post = Post-treatment
4 component = fiber + biofeedback + cognitive restructuring + parental support
3 component = fiber + biofeedback + cognitive restructuring
2 component = fiber + biofeedback



Results from our case series

- All patients clinically improved.
- 3/4 Patients with inflammatory GI disorders showed symptom remission.
- 64.71% were symptom free post Tx, 32.35% achieved partial remission, and only 2.94% (1 Pt) did not improve at all.
- FAP: 63.64% full remission, 36.36% partial remission. IBS: 69.23% full remission, 30.77% partial remission. GERD: 60% full remission, 40% partial remission. CVS: 0% full remission, 100% partial remission. Inflammatory: 75% full remission, 25% no relief.
- Chi^2 test revealed that there is no significant group difference in level of recovery by type of diagnosis.





Heart Rate Variability Biofeedback (HRV-B): A Novel Approach to Autonomic Nervous System Regulation and Gastric Motility Improvement

Sharmista Chintalapalli, B.A.; Naomi Maxwell, B.A; Richard Gevirtz, Ph.D

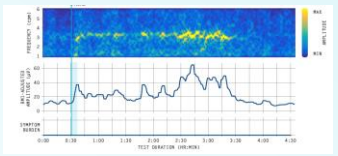
CSPP
CALIFORNIA SCHOOL OF PROFESSIONAL PSYCHOLOGY

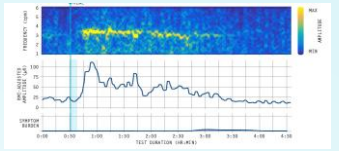
Introduction

- Decreased gastric motility and delayed gastric emptying have been linked to distressing gastrointestinal (GI) symptoms, including nausea, vomiting, bloating, and abdominal pain (Basnayake et al., 2020).
- The gut-brain axis is modulated by the Autonomic Nervous System (ANS), particularly through the vagus nerve, which plays a central role in regulating digestive function (Muth & Stern, 2000; Kolacz et al., 2018).
- Dysregulation of the ANS, often marked by sympathetic dominance, can exacerbate GI symptoms and contribute to functional disorders (Kolacz et al., 2018).
- Heart Rate Variability Biofeedback (HRV-B) offers a non-invasive method for individuals to enhance parasympathetic activity by training heart rate variability and improving autonomic regulation (Lehrer & Gevirtz, 2014).
- This is achieved by guiding participants to breathe at their resonance frequency, the optimal pace at which baroreceptors align with heart rate rhythms, leading to strengthened vagal tone and reduced vagal withdrawal (Lehrer et al., 2000; Lehrer & Gevirtz, 2014).
- Slow-paced diaphragmatic breathing, combined with psychoeducation and therapeutic support, further enhances vagal activation and parasympathetic engagement (Huang et al., 2017).
- The goal of HRV-B is to reduce symptom burden by rebalancing the ANS and reinforcing vagal function, ultimately hoping to improve overall gastric motility and (Freeman et al., 2023).

Current Results

- To date, 3 cases have been completed (one participant began taking the medication Sucraid (Sacrosidase) to aid with digestion of sugar halfway through treatment, therefore making their data more difficult to interpret).
- Based on self-report measures (COMPASS, NSS, API, Gastrointestinal Symptom Scale, ROME IV, and PedsQL), abdominal pain, bloating, nausea, and constipation improved after 8 session of HRV-B.
- As seen on the results of the EGG, gastric motility for this participant was greatly improved. In the initial baseline they had a delay in gastric motility and activity was elevated for longer. In the final measure gastric motility was immediate with a slow taper, as one would expect.
- The improvement of symptoms was contingent on consistent breathing practice and session attendance/participation.
- These preliminary findings suggest HRV-B may be a promising low-risk intervention for functional GI disorders in pediatric populations.





Category	Value Pre	Value Post	Change
PNS Index	-0.39	-0.43	-0.04
SNS Index	0.82	0.6	-0.22
Mean RR	827	759	-68
Mean HR	73	79	6
Min HR	69	68	-1
Max HR	81	96	15
SDNN	29.6	77	47.4
RMSSD	37.8	55.7	17.90
NN50	65	119	54
pNN50	18.16	37.54	19.38
RR Triangular Index	7.98	17.67	9.69
TINN	159	359	200
Stress Index (SI)	12.8	7.4	-5.4
LnHF	6.46	7.71	1.25
Sample Entropy	1.76	1.24	-0.52
Approximate Entropy	1.13	0.97	-0.16

Methods

Participants

- Ages 8 to 18, referred to the Center for Biobehavioral Services (CABS)
- Diagnosed with a functional gastrointestinal and/or motility disorder
- Actively undergoing Heart Rate Variability Biofeedback (HRV-B) treatment at CABS

Measures

- 5-minute resting HRV baseline
- Nijmegen Questionnaire and Capnometer $ETCO_2$ Reading
- Gastrointestinal Symptom Scale
- PROMIS Pediatric Anxiety and Depression Scales
- COMPASS-31 (Autonomic Symptom Profile)
- Nausea Severity Scale (NSS)
- Abdominal Pain Index (API)
- Rome IV Criteria (child and parent report)
- PedsQL - GI Symptoms Module (child and parent report)

Gut Motility Assessment

- A 4-hour gastric motility evaluation using a gastric mapping system (EGG) is conducted after a 6-hour fast.
- Participants lie on their back with EGG sensors placed on the stomach for an initial 30-minute baseline recording.
- They then consume a standardized meal (240 kcal Ensure drink + 250 kcal Clif Bar) within 10 minutes.
- Following the meal, participants remain lying down for 4 hours, minimizing movement, speech, and contact with the abdominal area.
- Every 15 minutes, participants rate their upper and lower gut pain, discomfort, and gas symptoms using standardized scales.

Treatment Protocol

- Conducted at the Center for Biobehavioral Services (CABS) under the supervision of Dr. Richard Gevirtz, Ph.D
- Participants complete 9 weekly sessions of Heart Rate Variability Biofeedback (HRV-B)

Session 1:

- A 5-minute resting HRV baseline is recorded
- Participants are formally enrolled in the study

Session 2:

- Diaphragmatic breathing is introduced
- Each participant's individual resonance frequency (RF) is identified (typically 5.5–7 breaths per minute)
- A personalized paced breathing tool is provided for home practice

Sessions 3–9:

- Participants practice breathing at their RF while receiving real-time biofeedback to ensure accuracy
- They are instructed to practice at home daily for 20–30 minutes (either in one or two sessions)
- Breathing techniques are also recommended for use during symptomatic episodes to enhance vagal regulation

Supplemental Materials

Future of the Study

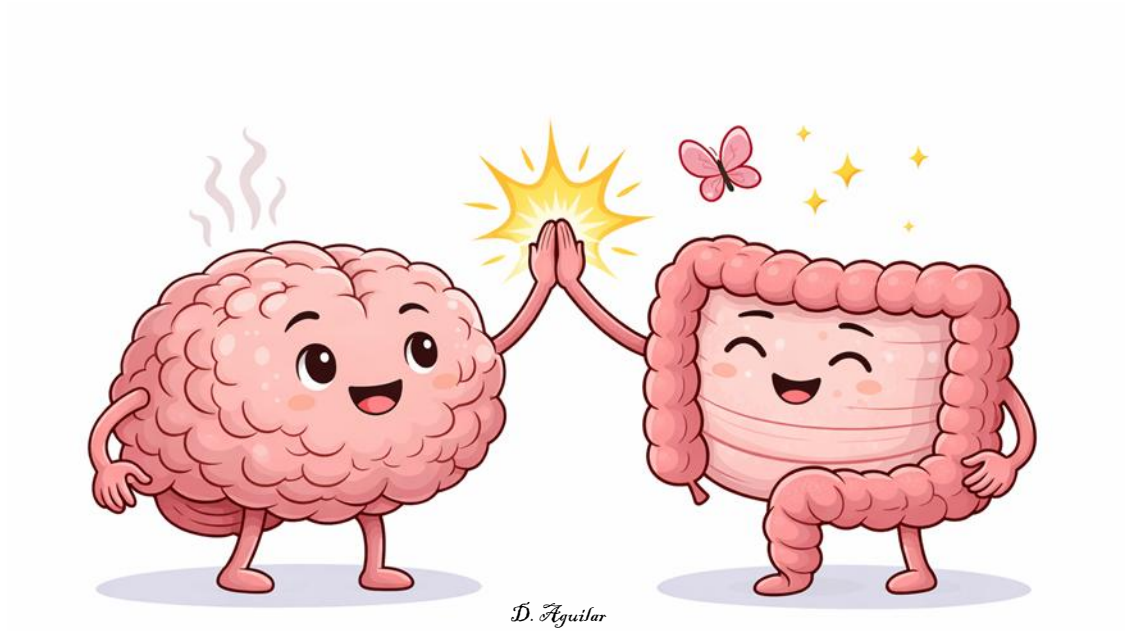
Data

While the current sample size is limited, preliminary findings are promising. Based on existing literature and early data, we anticipate that HRV-B may emerge as an effective intervention for improving gastric motility and reducing GI pain associated with autonomic dysregulation.

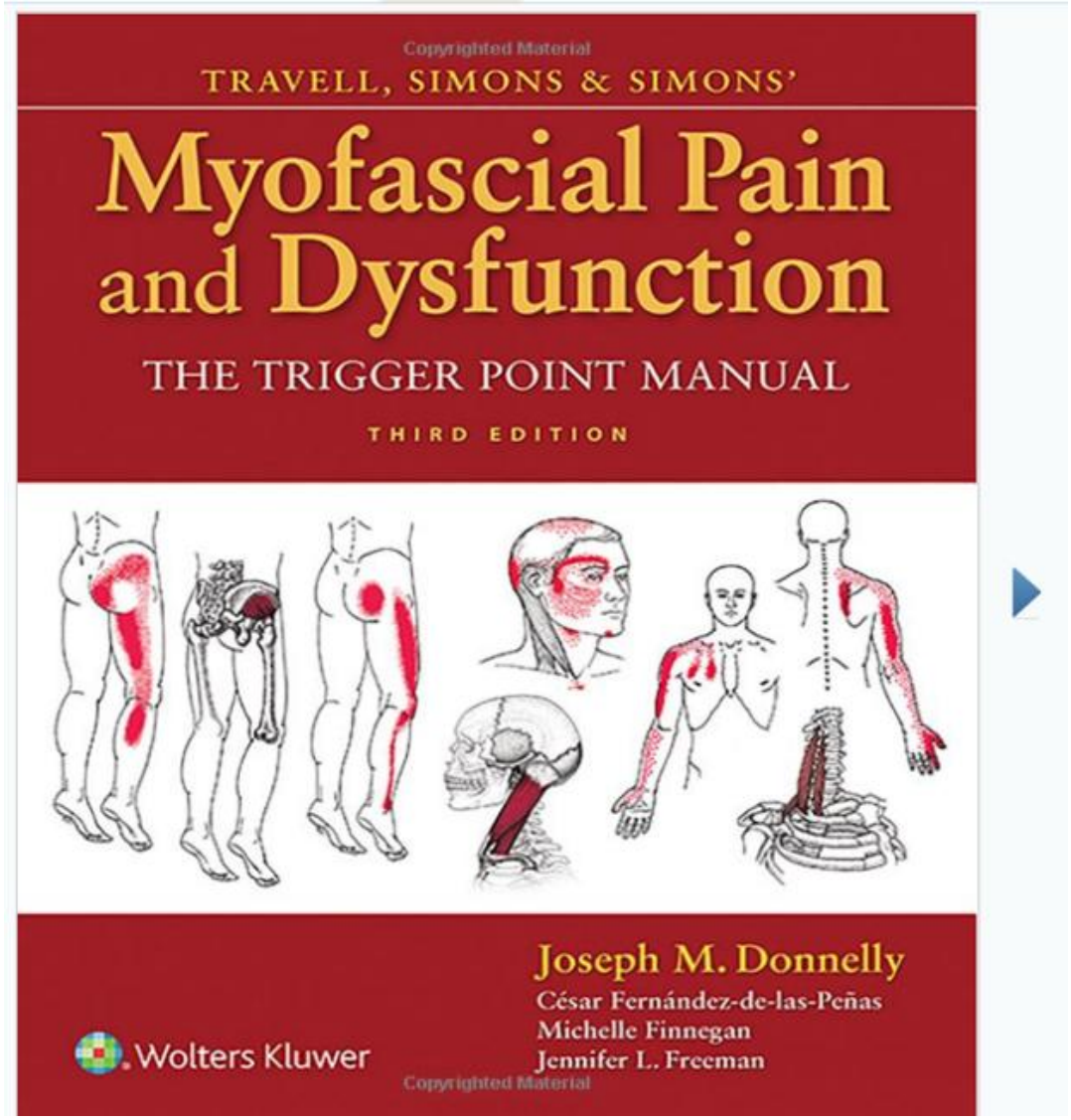
Recruitment

Recruitment is ongoing, with most participants referred to CABS by Rady Children's Hospital. New patient intakes are continuously evaluated for study eligibility to expand the sample and strengthen the generalizability of findings.

Presented at AAPB 55th Annual Scientific Meeting, San Diego (2025, May)

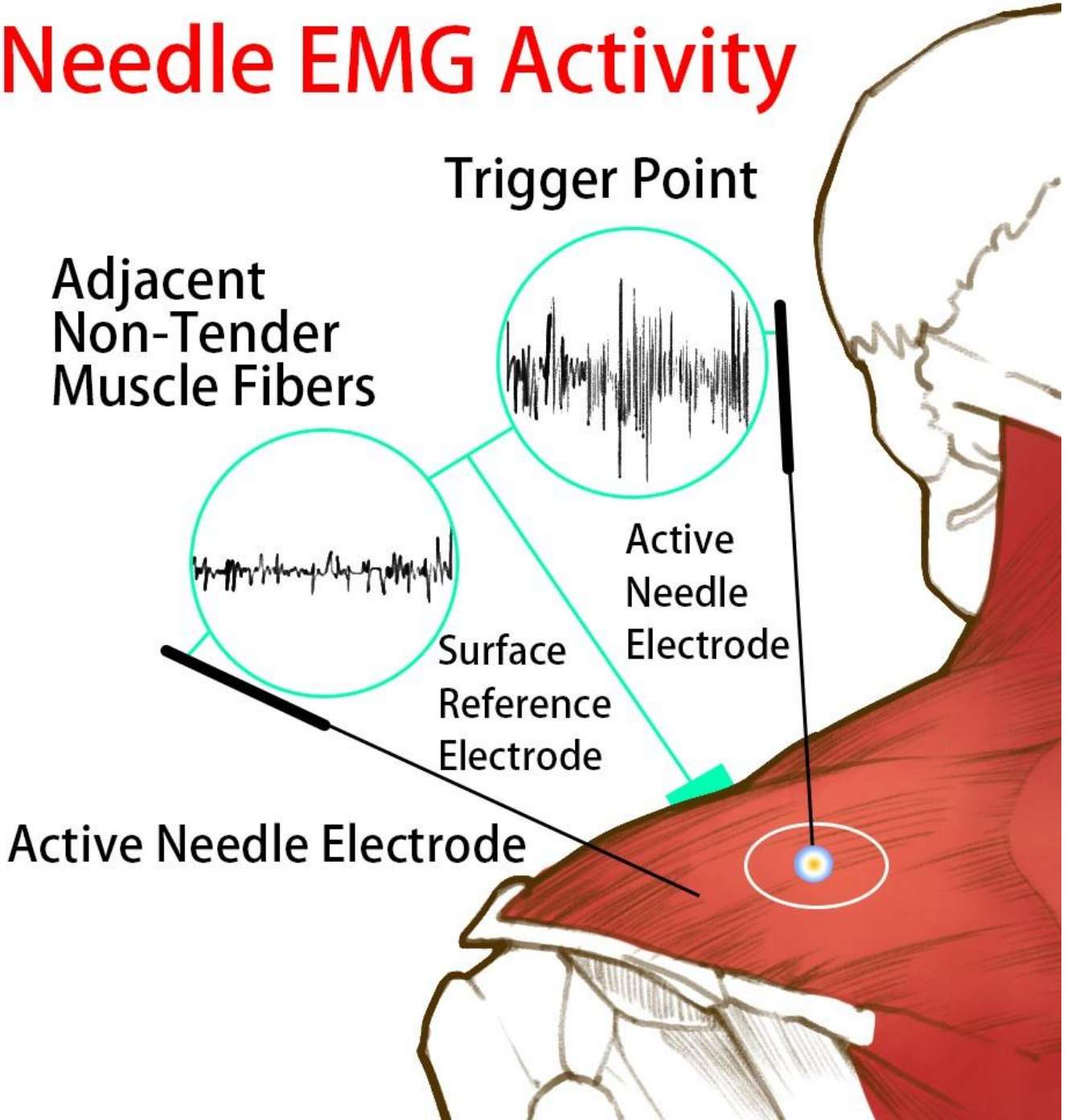

D. Aguilar

Chronic Muscle Pain- Myofascial Pain

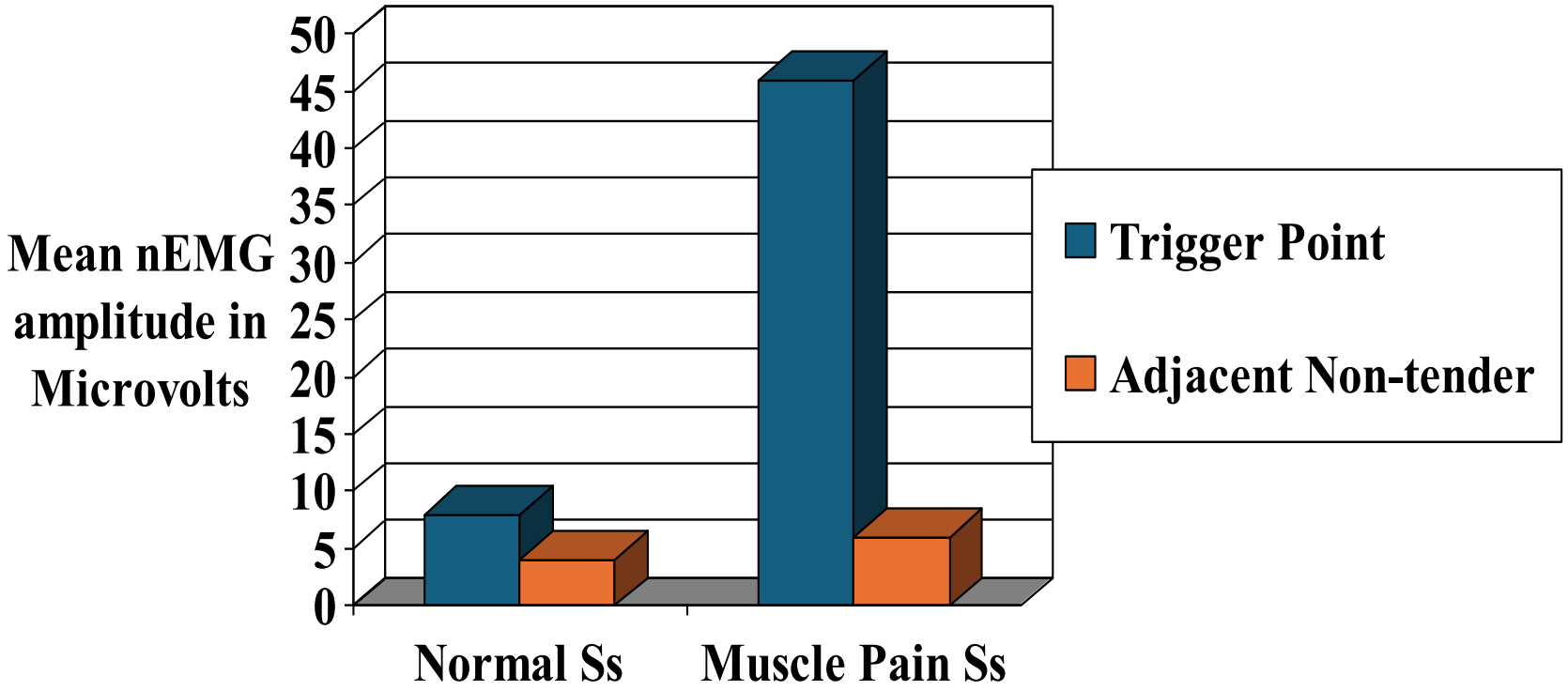


Needle EMG Activity

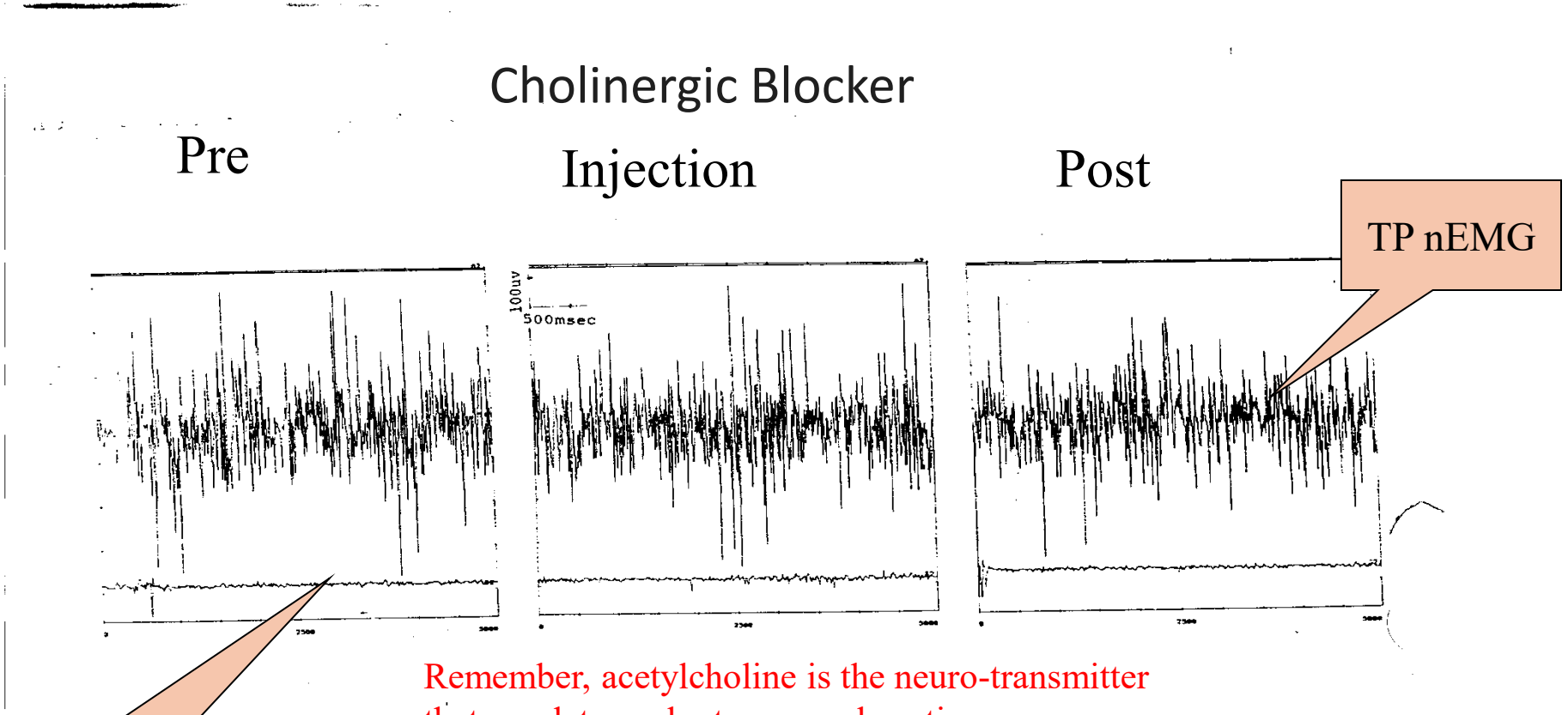
Tip of the needle is the active electrode



Myofascial Trigger Points Show Spontaneous Needle EMG Activity (Hubbard & Berkoff, 1993)



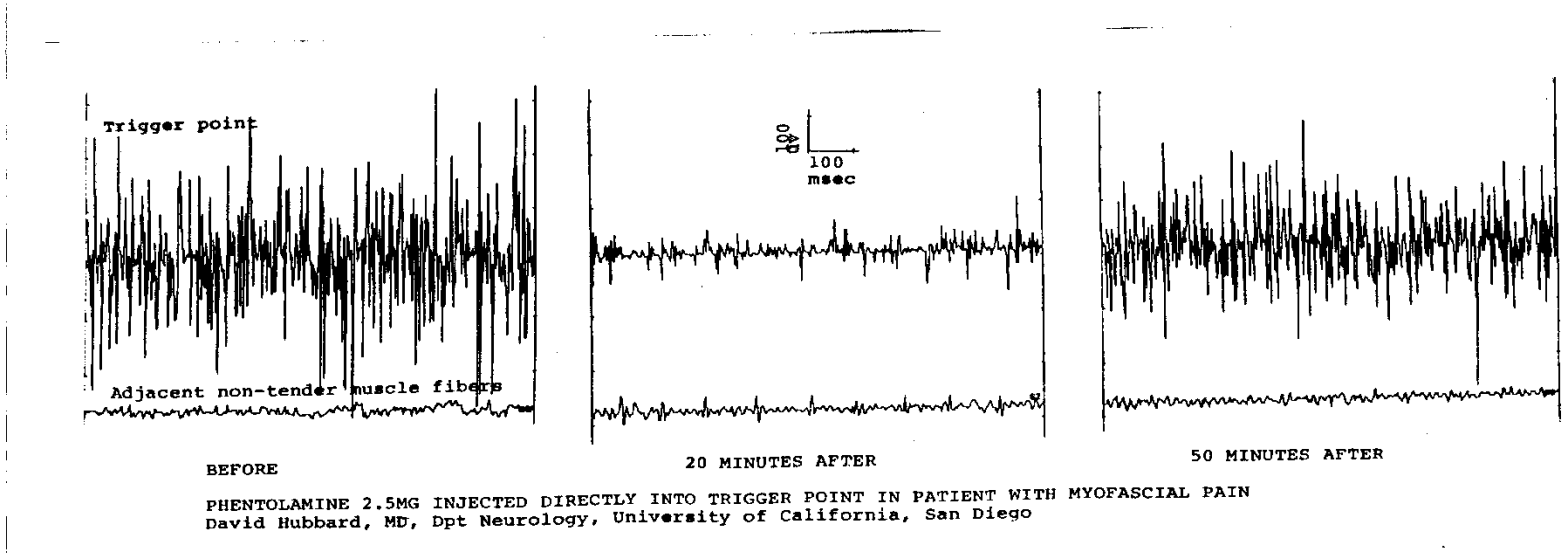
Effects of Curare on nEMG in TPs and Adjacent, (Non-tender) Sites



Remember, acetylcholine is the neuro-transmitter that regulates voluntary muscle action

Curare is a plant-derived substance that affects voluntary muscles by blocking the motor end plate, leading to muscle paralysis. It was historically used in surgery and as a treatment for conditions like tetanus and strychnine poisoning. AI generated definition based on: Encyclopedia of Toxicology (Third Edition), 2014. Cholinergic Blocker. We can see that it not effect TP activity,

The Effect of Phentolamine Injection on TP & Adjacent nEMG



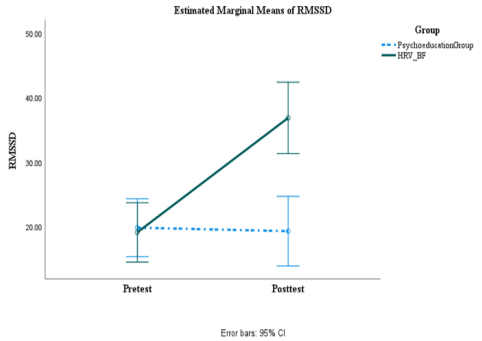
Phentolamine is a short-term alpha sympathetic blocker. (An alpha-adrenergic blocker). Here we see that it temporarily knocked out EMG activity in a TP.

The Accentuated Antagonism Treatment Model

- "Vagal 'tone' predominates over sympathetic tone at rest. Under normal physiological conditions, abrupt parasympathetic stimulation will inhibit tonic sympathetic activation and its effects at rest and during exercise. This response is known as 'accentuated antagonism' (Olshansky et al., 2008, p.863; Yang and Levy, 1984; Schwegler and Jacob, 1975; Levy, and Zieske, 1969)

- Since we have evidence that TPs are stimulated by sympathetic input, our strategy is to reduce this input using HRVB, which we and others have shown increases the homeostatic ability of the Vagus to govern sympathetic activity.

- We typically get 20-40% increases in Vagal tone and RMSSD in 4-7 weeks when patients practice at least 10 minutes daily.



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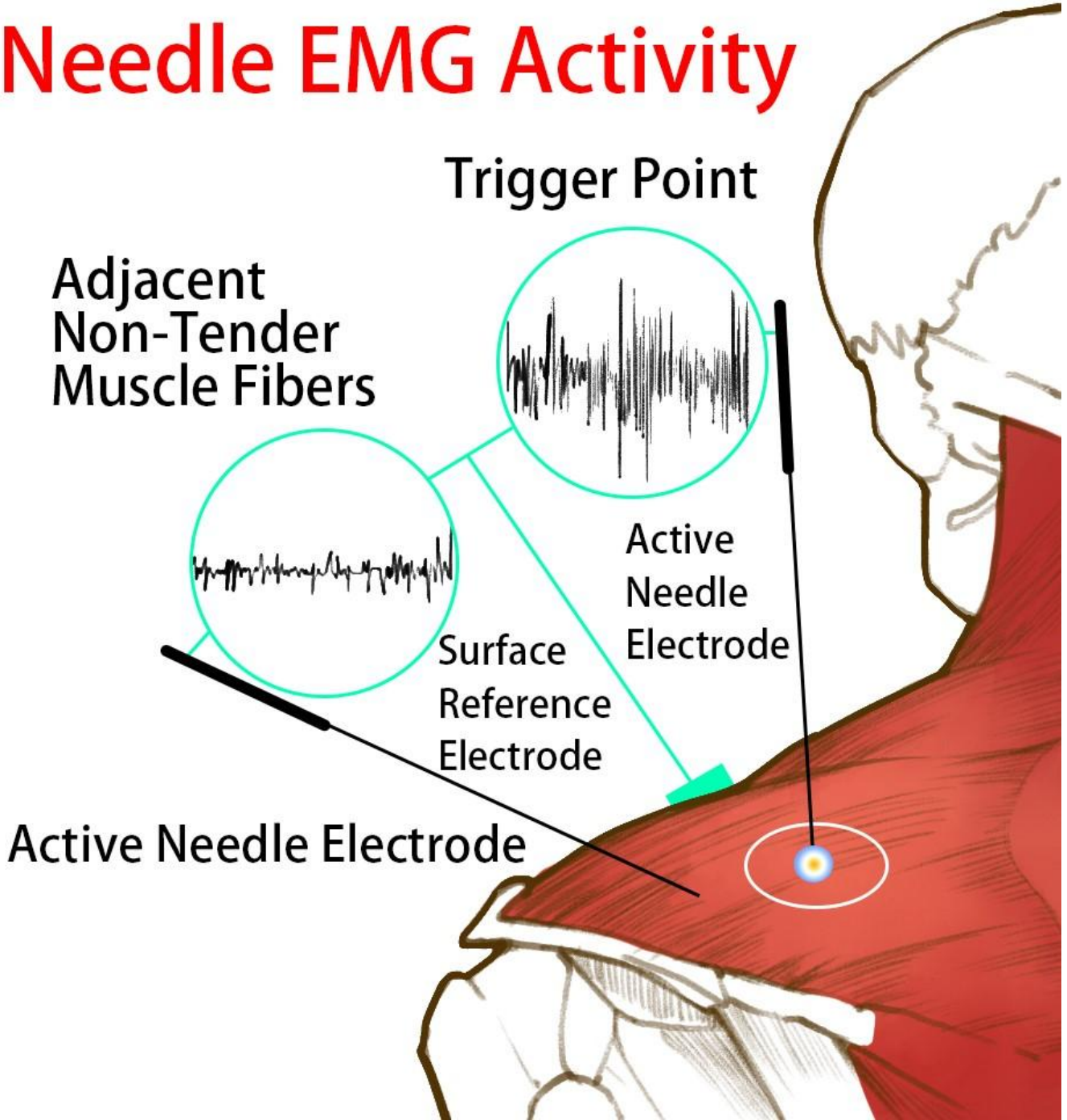

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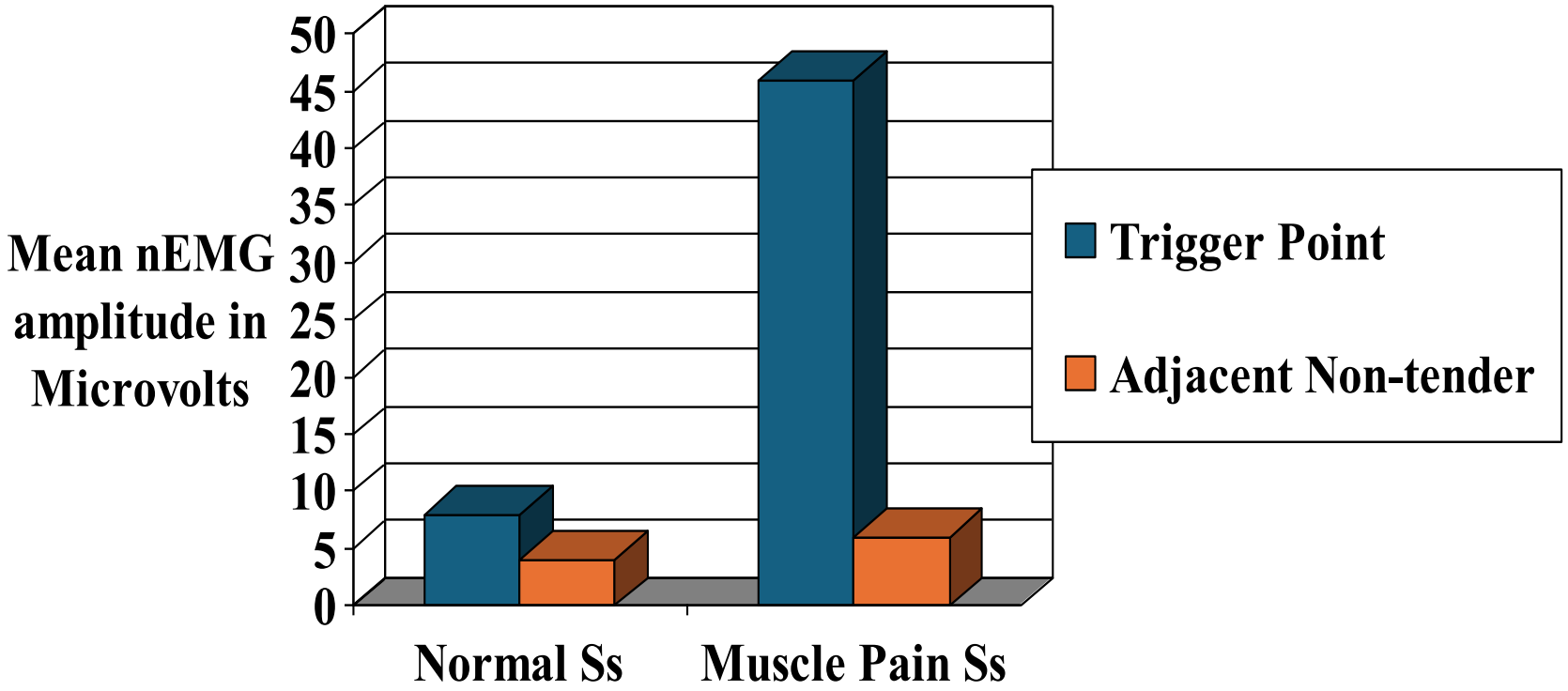

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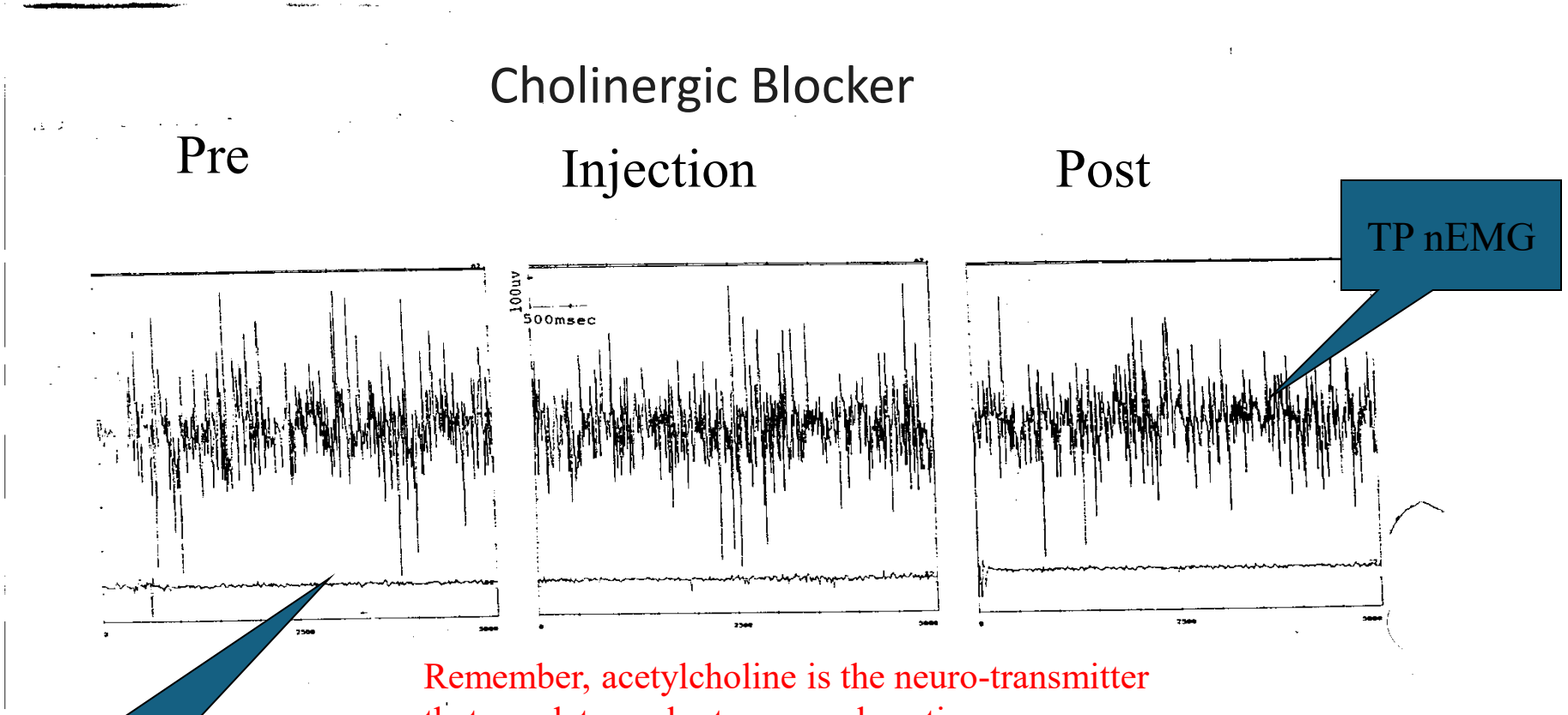

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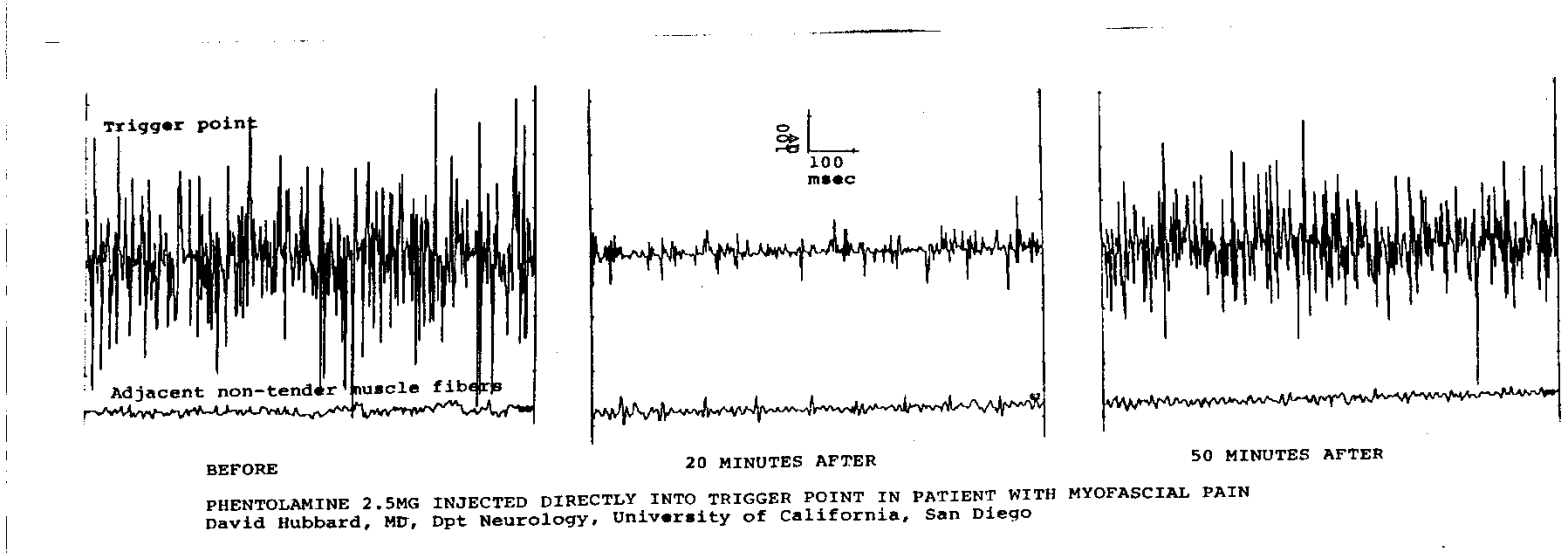

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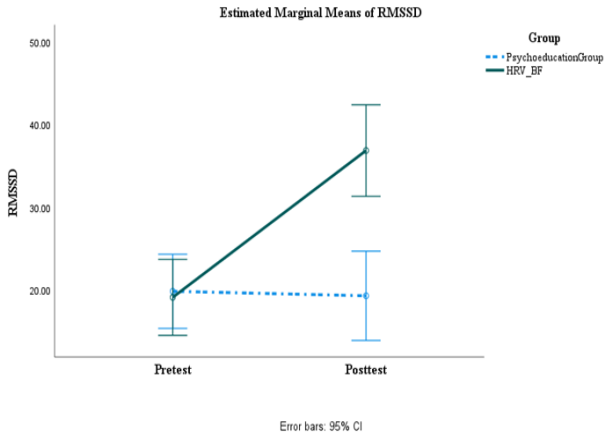

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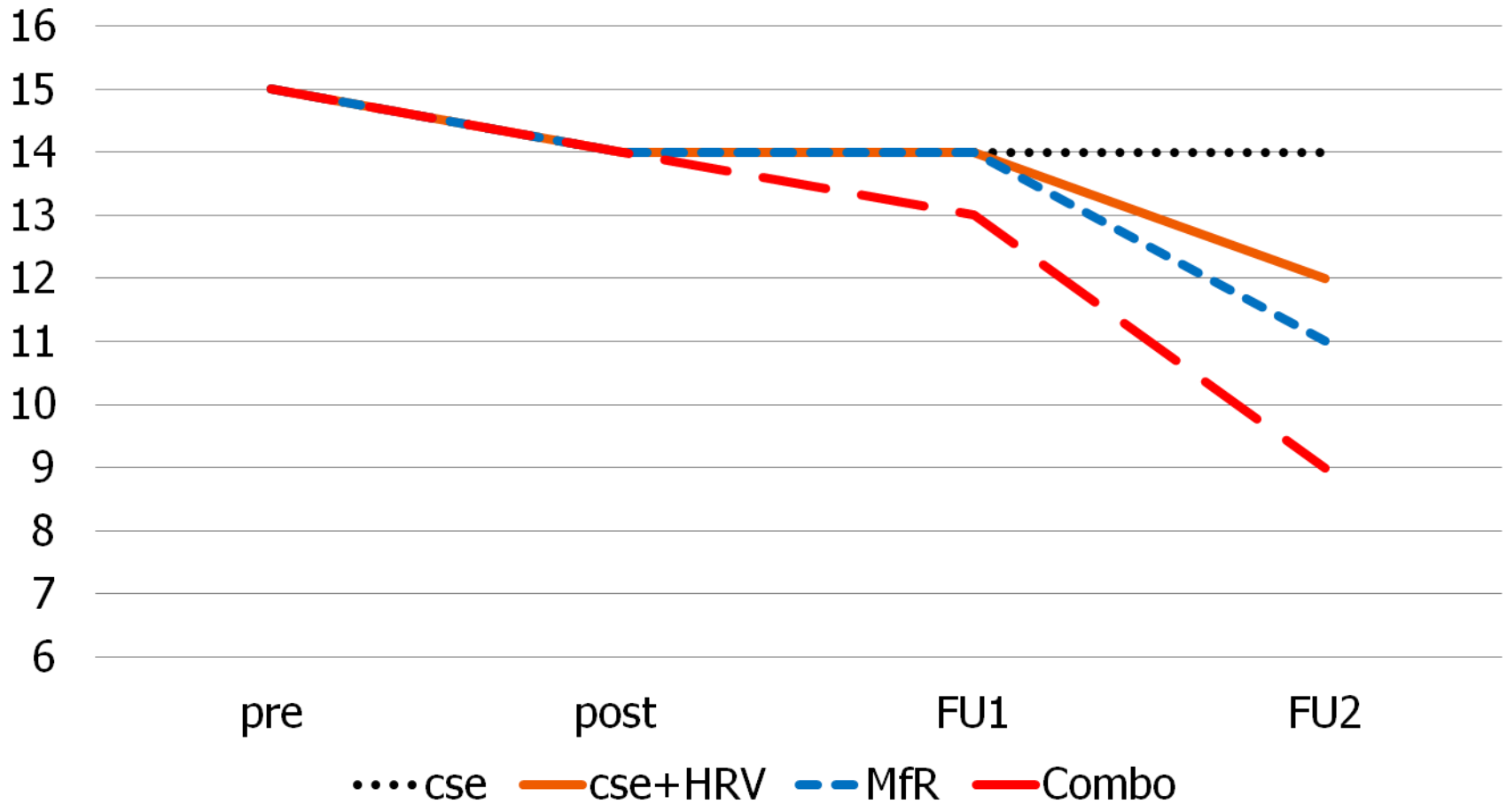
Pain ratings across time

(Vagades, Gordon, Gevirtz, Andrasik (2013) N=124



Vagally mediated HRV measures as Biomarkers

Massive literature for vagally mediated HRV as a biomarker for a wide variety of disorders.

“One of the best established and most widely used non-invasive methods for the quantitative assessment of ANS activity is the computerized analysis of heart rate variability (HRV). HRV, which is determined by different methods from those used to determine the fluctuation of instantaneous heart rate (HR), has been used in many studies as a powerful index of autonomic (re)activity and an indicator of cardiac risk and ageing. Psychiatric patients regularly show altered autonomic function with increased HR, reduced HRV and blunted diurnal/circadian changes compared to the healthy state. ”

D. Aguilar

Agorastos, A., Mansueto, A. C., Hager, T., Pappi, E., Gardikioti, A., & Stiedl, O. (2023). Heart rate variability as a translational dynamic biomarker of altered autonomic function in health and psychiatric disease. *Biomedicines*, *11*(6), 1591.

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FDA cleared throughout the USA in 2025.

5-minute, medical-grade, precision heart rate variability (HRV) analysis of both aspects of autonomic nervous system (ANS) neuroregulatory activity:

the sympathetic (fight-or-flight) and the parasympathetic (rest/restorative).

>1000 procedures completed and covered by most insurance since July

in Washington, Oregon, Michigan and Florida.

More sites to follow ASAP

"The ANS is the command-and-control center within our brain impacting nearly every clinical aspect of healthcare. It often plays a role in why patients respond differently to the same treatment. No longer can we or should we guess why or how this ever-present biology impacts disease onset, treatment efficacy and even prevention. As a clinician, being able to quantify ANS state with FDA-cleared, precision HRV appears to be an exciting opportunity to address unmet healthcare needs."

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Critical Review of Transcutaneous Vagus Nerve Stimulation: Challenges for Translation to Clinical Practice

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6. CONCLUSION

tVNS has proven to be an effective way to modulate the central nervous system in some cases. However, the mechanism of action is not clear, and the robustness of the results is yet to be proven. The technique is safe and convenient with only a few relatively minor side effects reported. More rigorous systematic studies are required to investigate the effects of stimulation parameters, sites of stimulation, and electrode types on brain activation and clinical outcomes. Current limitations in study protocols may lead to difficulties in obtaining regulatory approval and challenges in translating research studies into clinical practice.

HRVB offers an inexpensive, non-invasive, method to improve reflexes in the autonomic nervous system. When the system is working adequately, the vagal systems protect vulnerable biological systems from creating symptoms and pathology. Given the mixed results from the VNS literature, and the other positive aspects of biofeedback, HRVB should be considered a first line treatment for vagally mediated symptoms.