Southeast Biofeedback and Clinical Neuroscience Association

SBCNA

2017 SBCNA Annual Conference *co-sponsored by AAPB*

"Biofeedback and Neurofeedback: Cognitive and Physiological Processes for Behavioral and Physical Regulation

Integrative Management of Sensitized Chronic Pain using Autonomic Self-Regulation

Saturday, November 4, 2017

JP (Jack) Ginsberg, PhD

1. Define and describe the meaning of integrative medical management, centrally sensitized chronic pain, and Autonomic Self-Regulation (ASR)
2. Describe the basic science of heart rate variability (HRV) and its relationship to ASR technique
3. Summarize the nervous system pathways shared by sensitized chronic pain and ASR
4. Identify HRV parameters that are biomarkers of emotional and physical health
5. Discuss how ASR can be used for health assessment and behavioral change

JP (Jack) Ginsberg, PhD

Licensed Clinical Psychologist/Neuropsychologist
and Principal Investigator,
Dorn VA Medical Center
Basic Science Research Assistant Professor
University of South Carolina, School of Medicine,
Dept of Pharmacology, Physiology & Neuroscience
Columbia, SC
jay.ginsberg@va.gov
803.776.4000 x6644

Disclaimer and Disclosure

- Not expert in cardiology, pain, or medication
  - Neuropsychologist with some specialization in cognitive psychophysiology
- No conflict of interest, affiliations, or product endorsement
- Slides are original or freely available from internet with acknowledgment

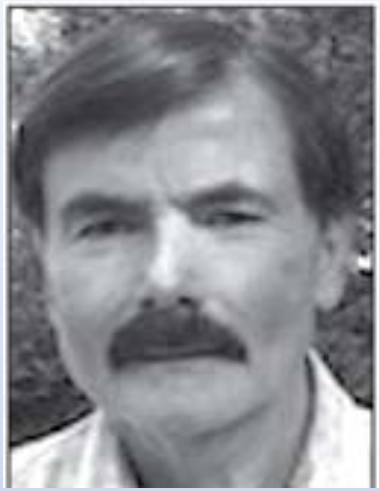
"Materials that are included in this course may include interventions and modalities that are beyond the authorized practice of mental health professionals. As a licensed professional, you are responsible for reviewing the scope of practice, including activities that are defined in law as beyond the boundaries of practice in accordance with and in compliance with your professions standards."

ACKNOWLEDGEMENTS

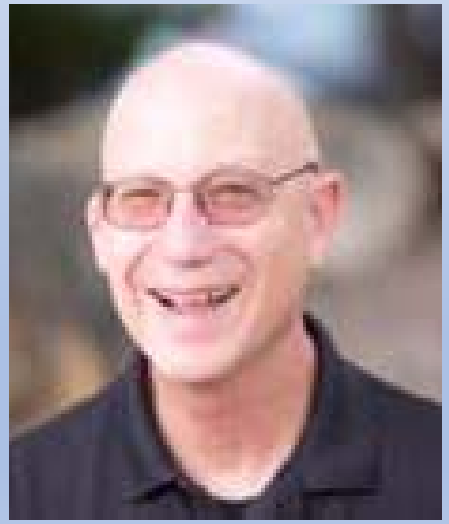
D.A. Powell, PhD

Rollin McCraty, PhD

Paul Lehrer, PhD



Wasyl Malyj, PhD



Fred Shaffer, PhD

Carmen Russeniello, PhD

Jan B. Newman, MD

Prelude

The Opioid Epidemic in the U.S.

In 2015...

12.5 million
People misused prescription opioids[1]

2.1 million
People misused prescription opioids for the first time[1]

33,091
People died from overdosing on opioids[2]

2 million
People had prescription opioid use disorder[1]

15,281
Deaths attributed to overdosing on commonly prescribed opioids[2,3]

828,000
People used heroin[1]

9,580
Deaths attributed to overdosing on synthetic opioids[2,5]

135,000
People used heroin for the first time[1]

12,989
Deaths attributed to overdosing on heroin[2,4]

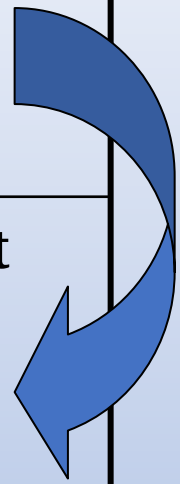
$78.5 billion
In economic costs (2013 data)[6]

Sources: [1]2015 National Survey on Drug Use and Health (SAMHSA), [2]MMWR, 2016; 65(50-51);1445–1452 (CDC), [3]Prescription Overdose Data (CDC), [4]Heroin Overdose Data (CDC), [5]Synthetic Opioid Data (CDC), [6]The Economic Burden of Prescription Opioid Overdose, Abuse, and Dependence in the United States, 2013. Florence CS, Zhou C, Luo F, Xu L. Med Care. 2016 Oct;54(10):901-6

Updated May 2017. For more information, visit: http://www.hhs.gov/opioids/

PSYCHOLOGIST'S MODEL OF PAIN MEDICATION (OPIOID) ADDICTION

Negative Punishment *Suspension* *'Time-out'*	Negative Reinforcement *Medication* *Self-Medication*
Positive Punishment *Fines* *Shocks (experimental)*	**Positive Reinforcement** ***Honors*** ***Addiction***



PAIN MEDICATION ADDICTION INCLUDES SUFFERING DUE TO STRESS AND DEPRESSION IN ADDITION TO UNRELIEVED PAIN AND THE BEHAVORAL DYSFUNCTION OF ADDICTION – NEED TO REPLACE POSITIVELY REINFORCING CHARACTERISTICS OF MEDICATION WITH SOMETHING ELSE

The Backfire Effect

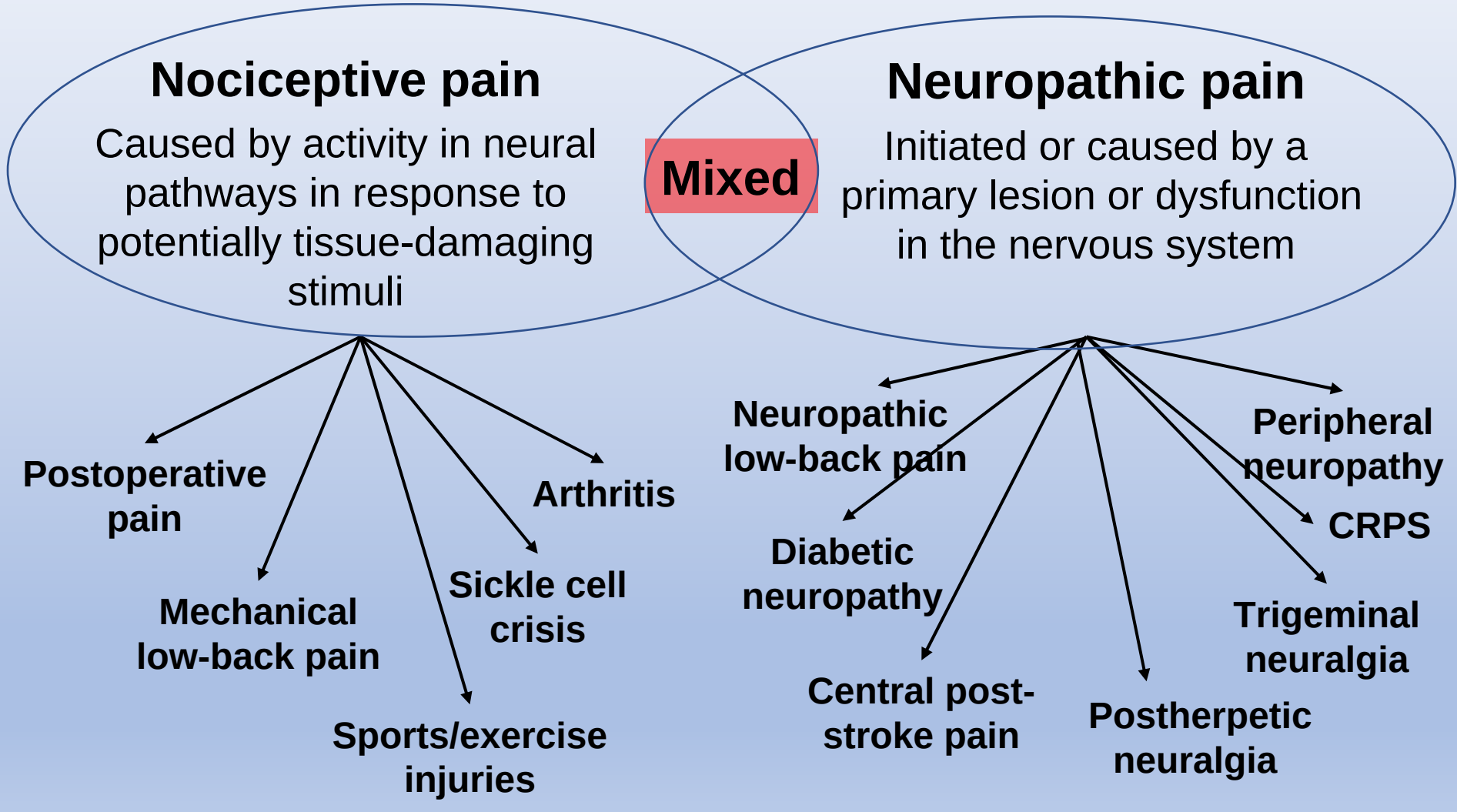
I. Sensitized Chronic Pain (SCP) and Autonomic Self-Regulation (ASR)

- Define SCP and ASR
- Shared physiological basis of SCP and ASR
- How ASR reduces SCP

II. Research on using ASR for SCP

Sensitized Chronic Pain: Stress and Depression

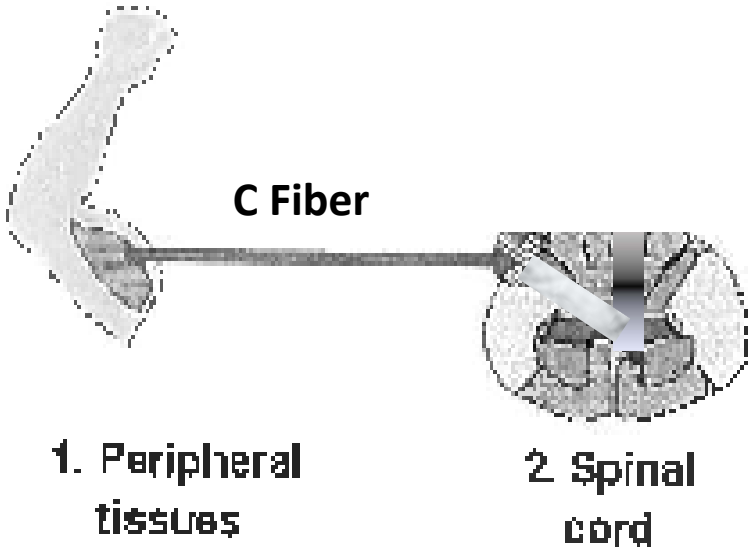
Not all pain is the same: The pathophysiology of painful diseases



Rollin Gallagher, MD, MPH

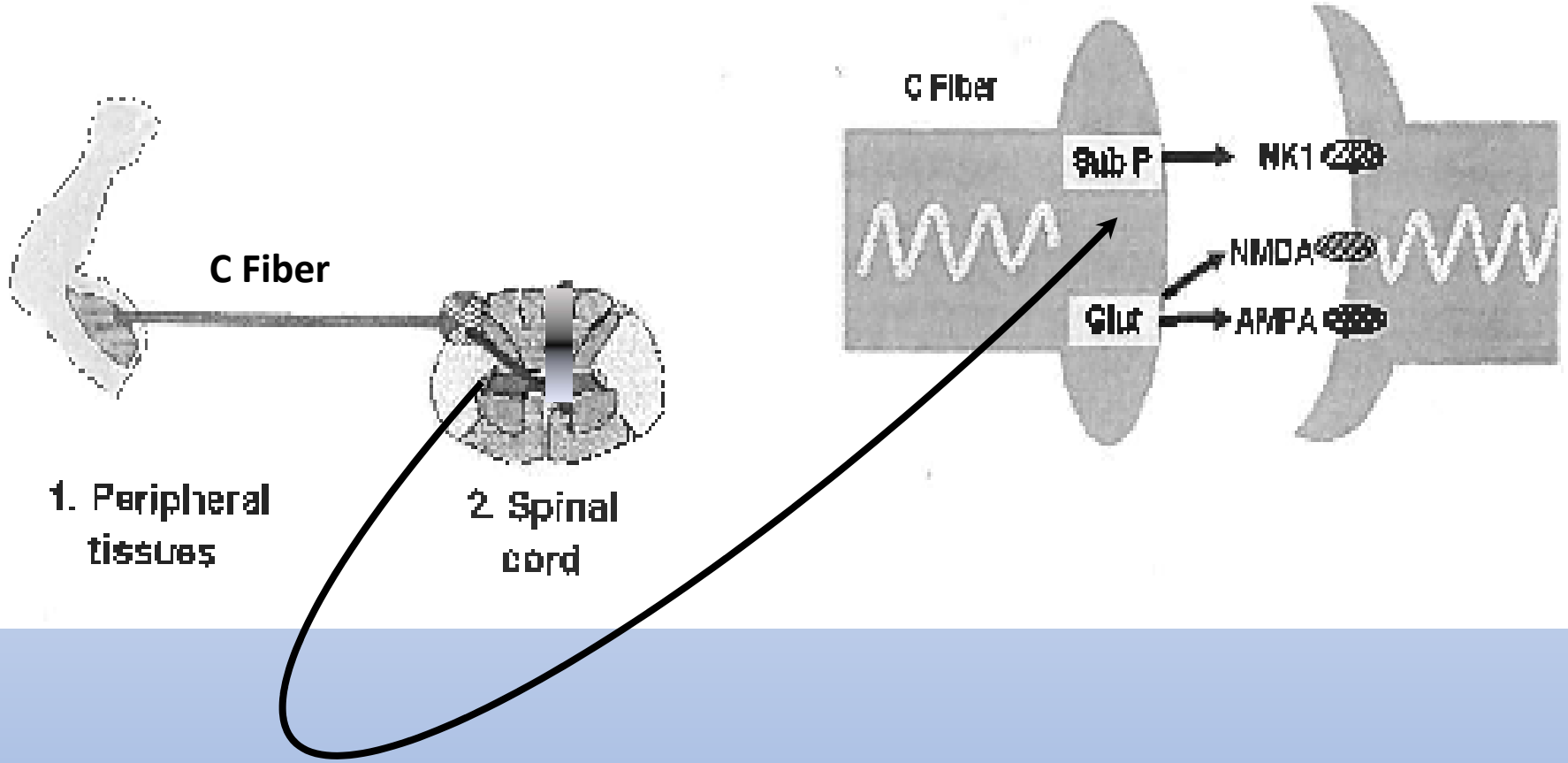
*dhss.delaware.gov/dsamh/files/2007**gallagher**ii.pps*

Nociceptive Pain

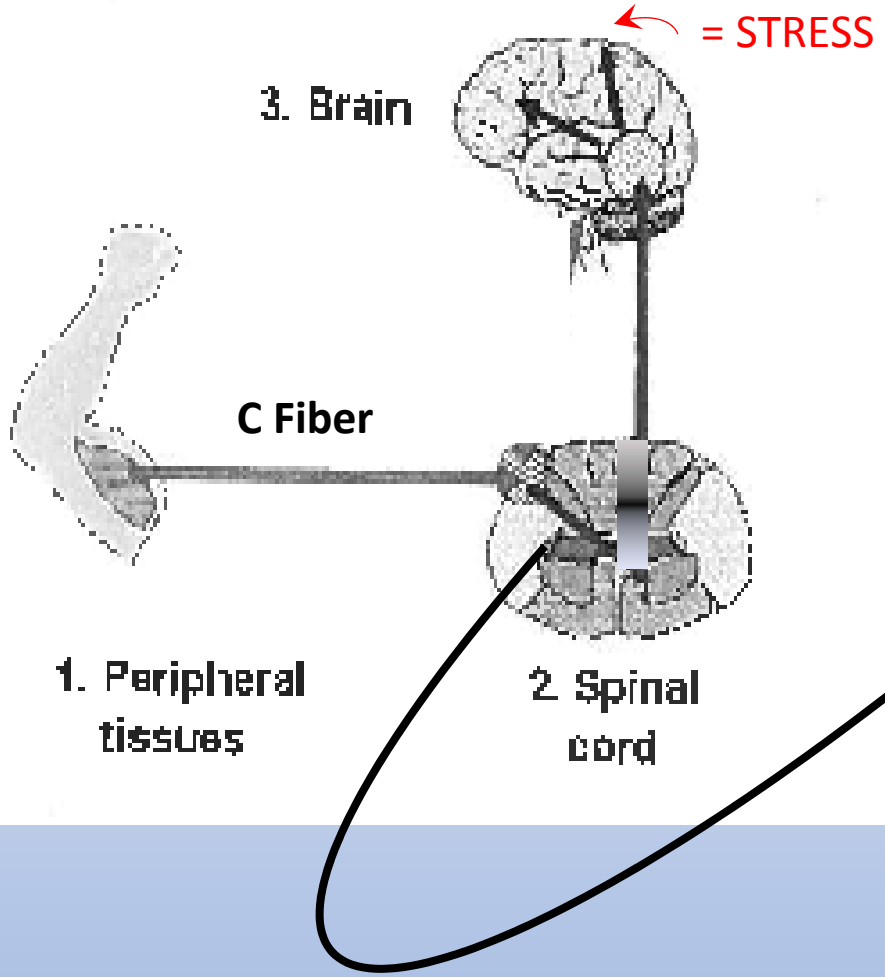


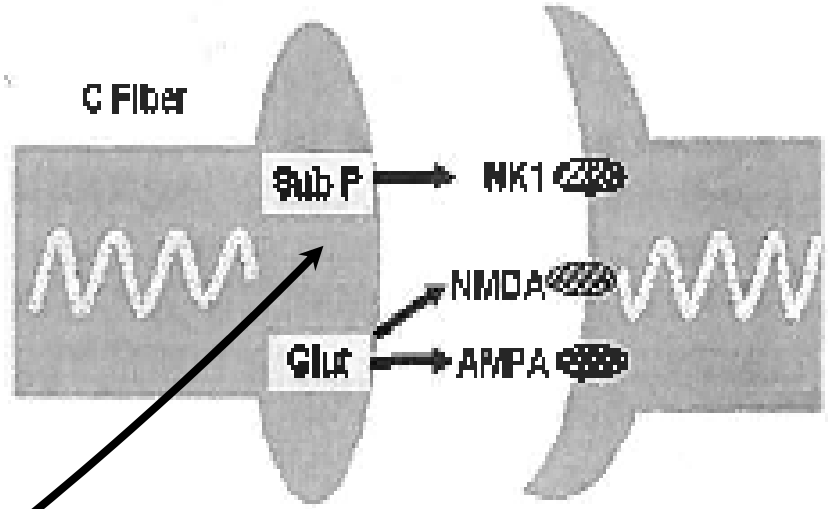
Understanding Pain and Pain Amplification. Robert Benett, MD.
http://www.myalgia.com/Pain_amplification/Overview.htm

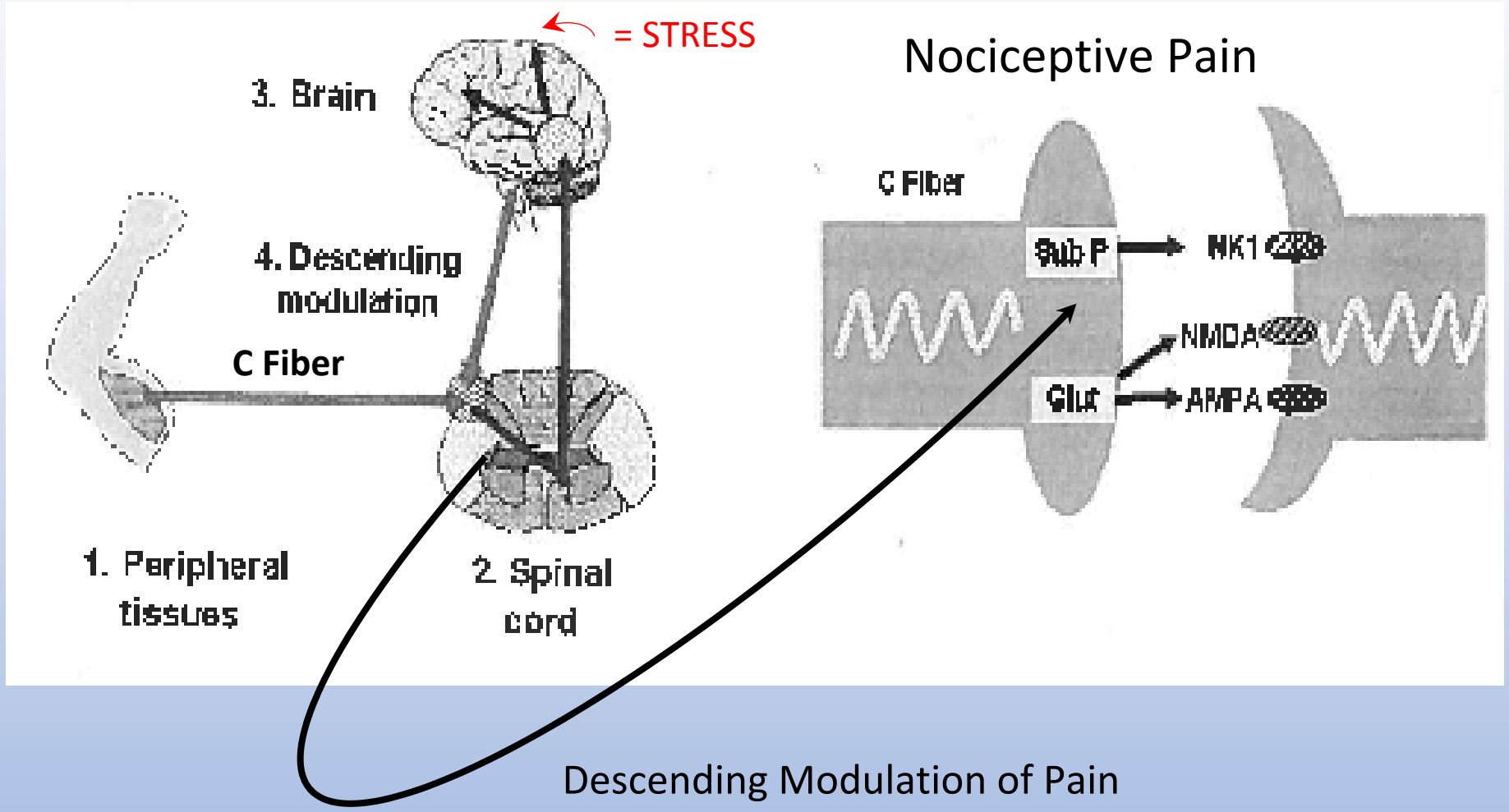
Nociceptive Pain



Nociceptive Pain



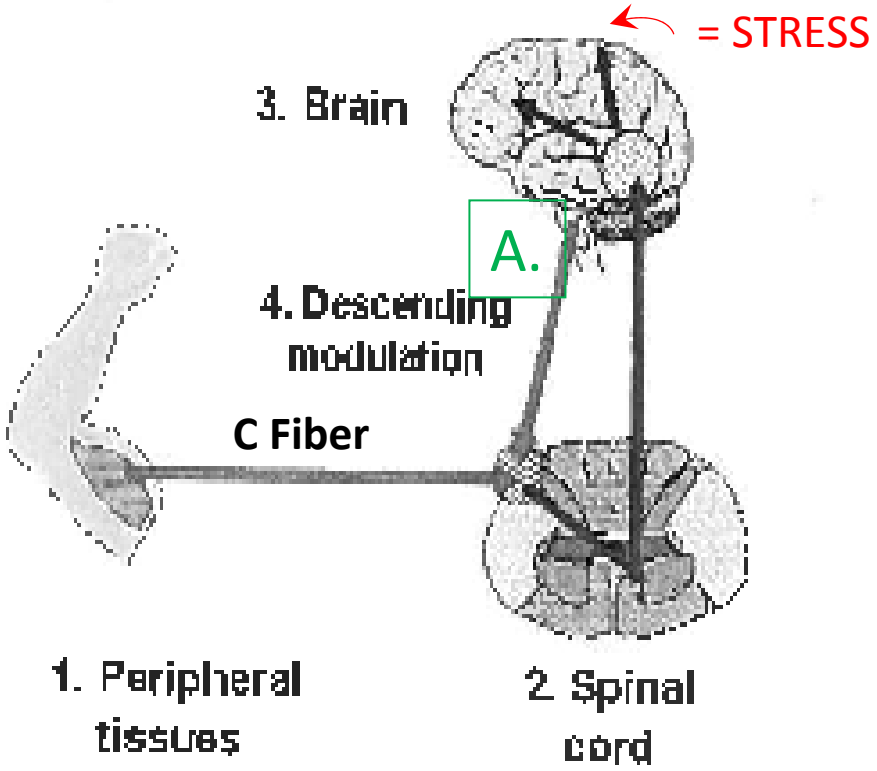


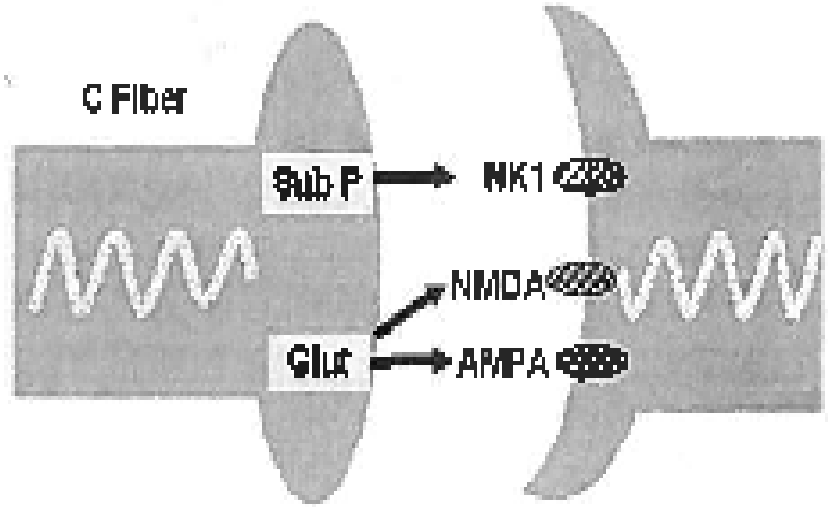


Descending Modulation of Pain

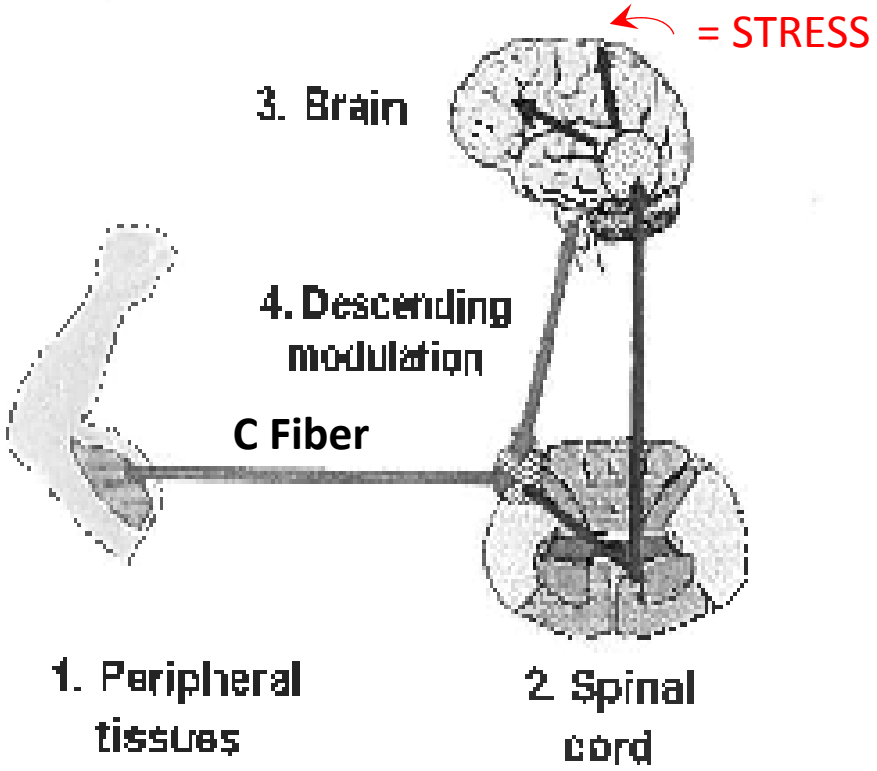
Influences from brainstem nuclei and forebrain on spinal transmission of incoming peripheral pain signals :

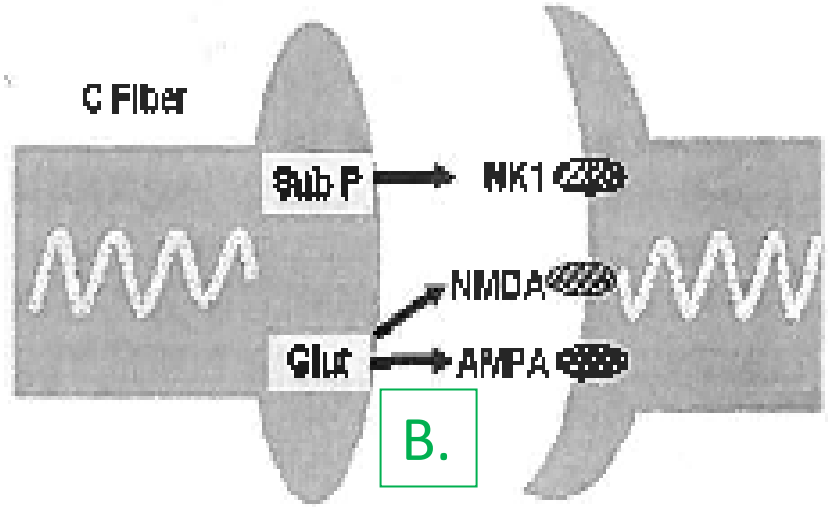
- periaqueductal gray in upper brain stem
- serotonergic from nucleus raphe magnus
- adrenergic from locus coeruleus
- dopaminergic from ventral tegmental area and hypothalamus



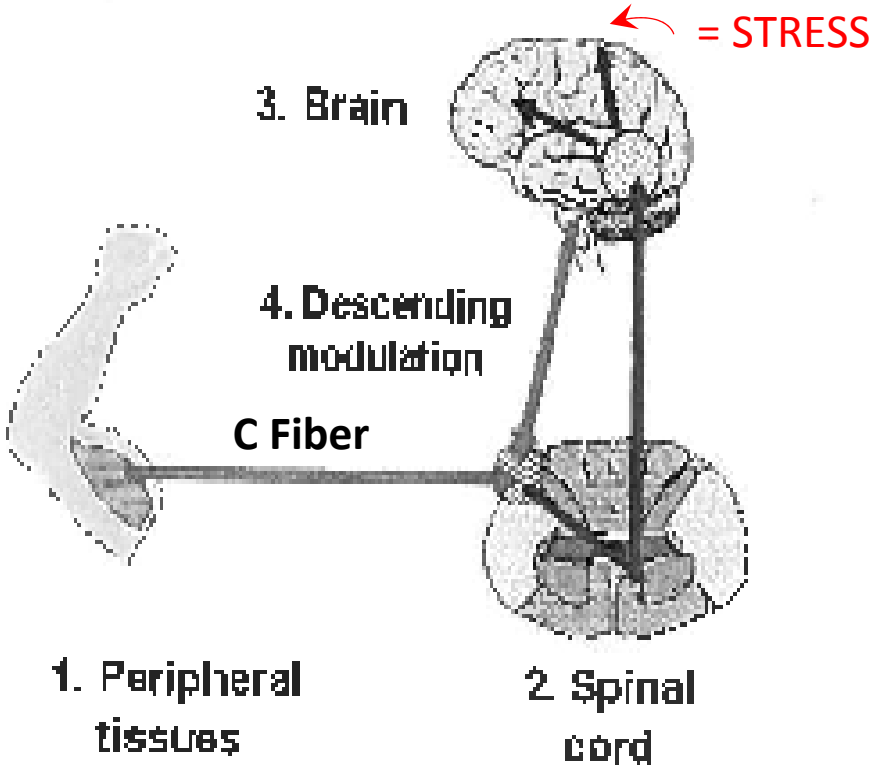


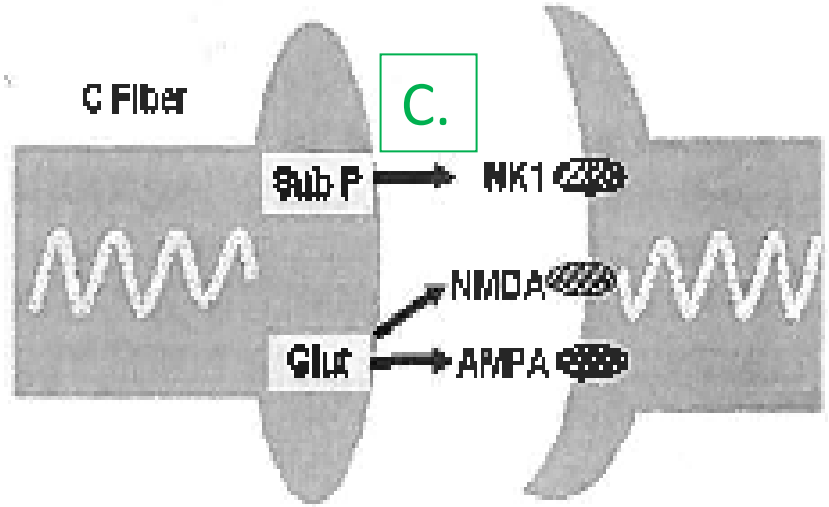
A. Antidepressants (e.g. amitriptyline, duloxetine) reduce pain by ***increasing descending pain inhibition from catecholamines***





B. *Anti-epileptics* (e.g. gabapentin, pregabalin) reduce pain by ***limiting release of glutamate from afferent peripheral C fiber***



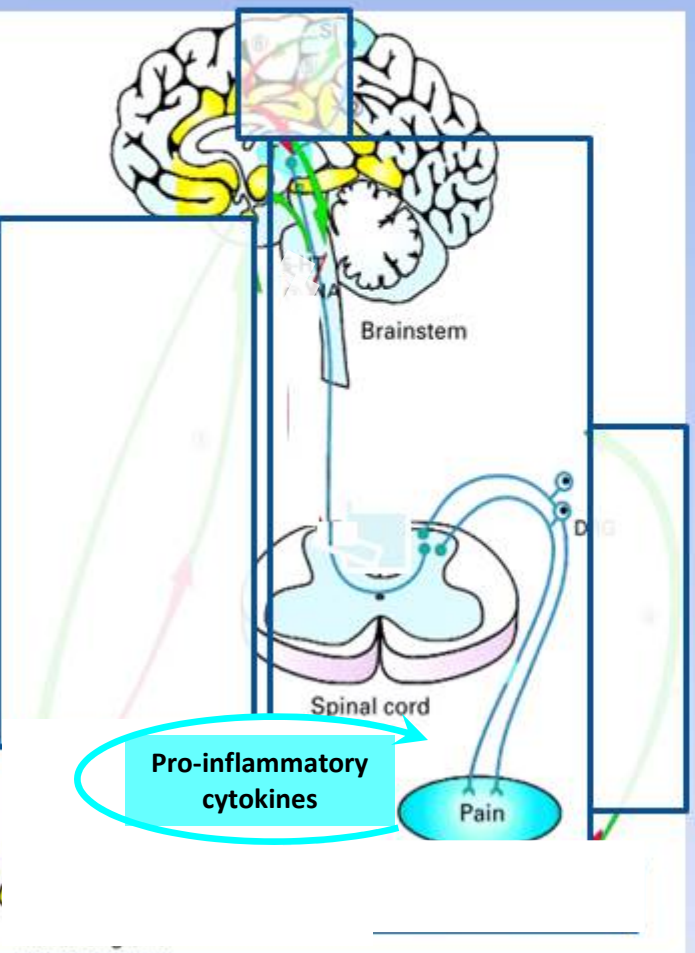


C. *Opioids (*e.g. morphine) block pain by ***activating opioid receptors and inhibiting substance P***

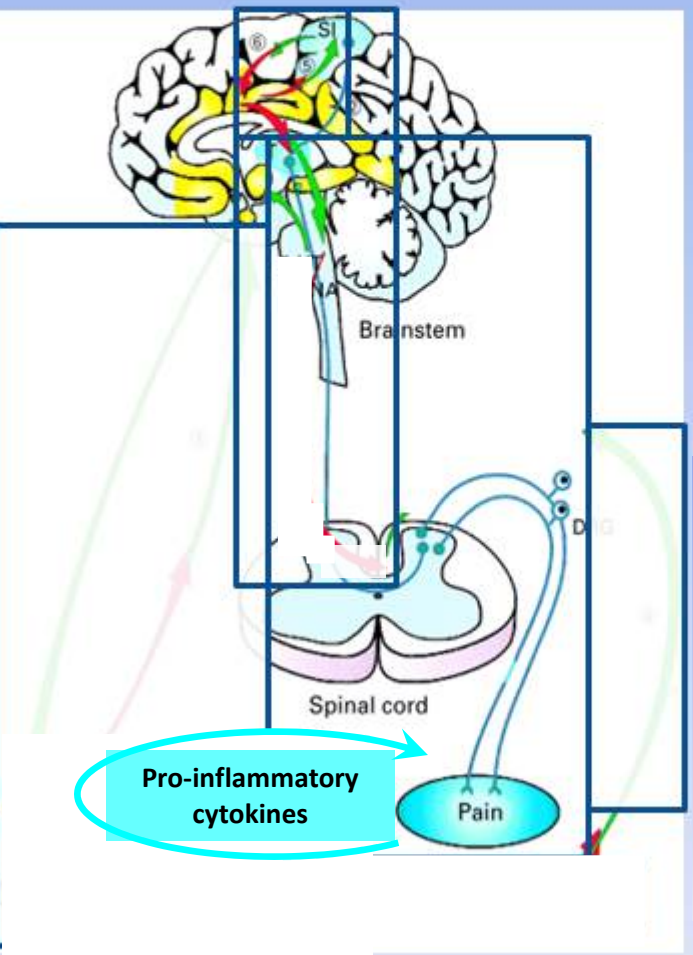
ACUTE NOCICEPTIVE PAIN – I

Blackburn-Munro, G. & Blackburn-Munro, R.E. (2001). Chronic Pain, Chronic Stress and Depression: Coincidence or Consequence? *Journal of Neuroendocrinology*. Volume 13 (12), 1009-1023. Springer

- Inflammation / nerve injury stimulate nociceptive information to dorsal horn
- Ascends to brainstem, gated in thalamus

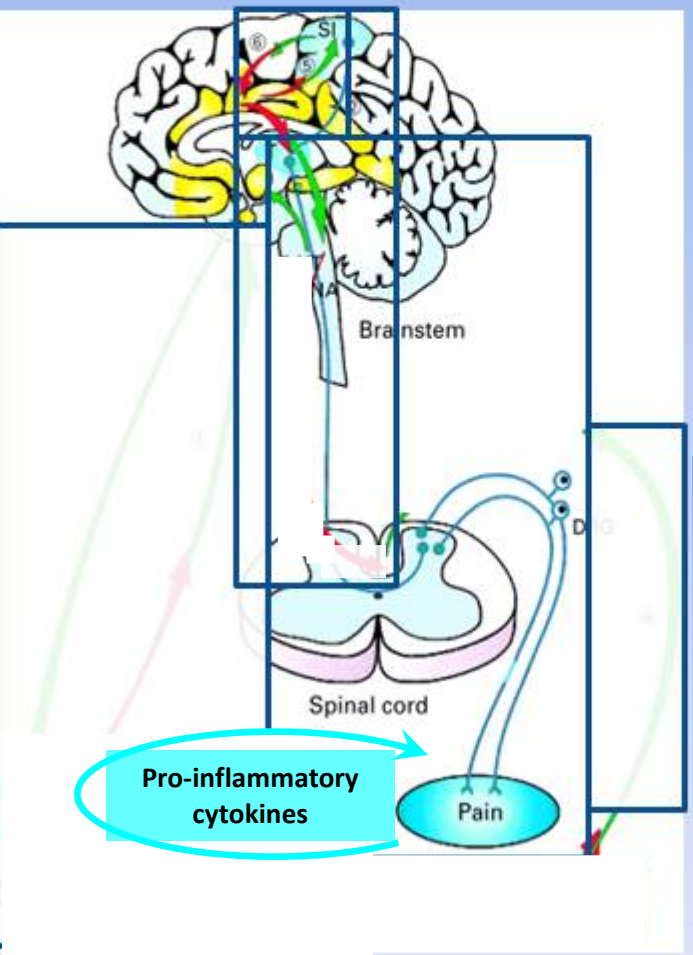


ACUTE NOCICEPTIVE PAIN – II



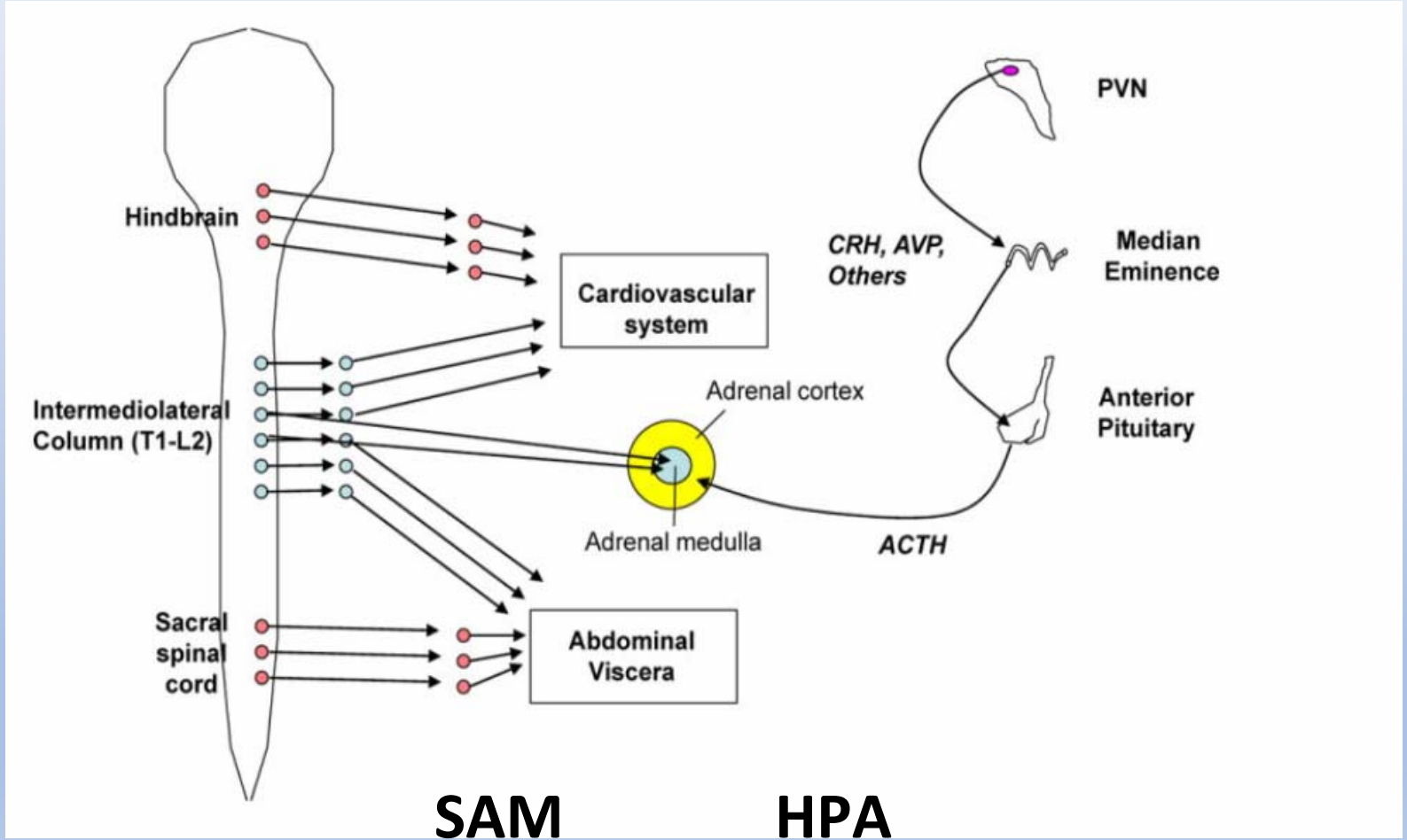
- Inflammation / nerve injury stimulate nociceptive information to dorsal horn
- Ascends to brainstem, gated in thalamus
- Cognitive appraisal in SI cortex
- Acute pain increases arousal via sympathetic and GC routes (excitatory reciprocal link between somatosensory and limbic cortices)

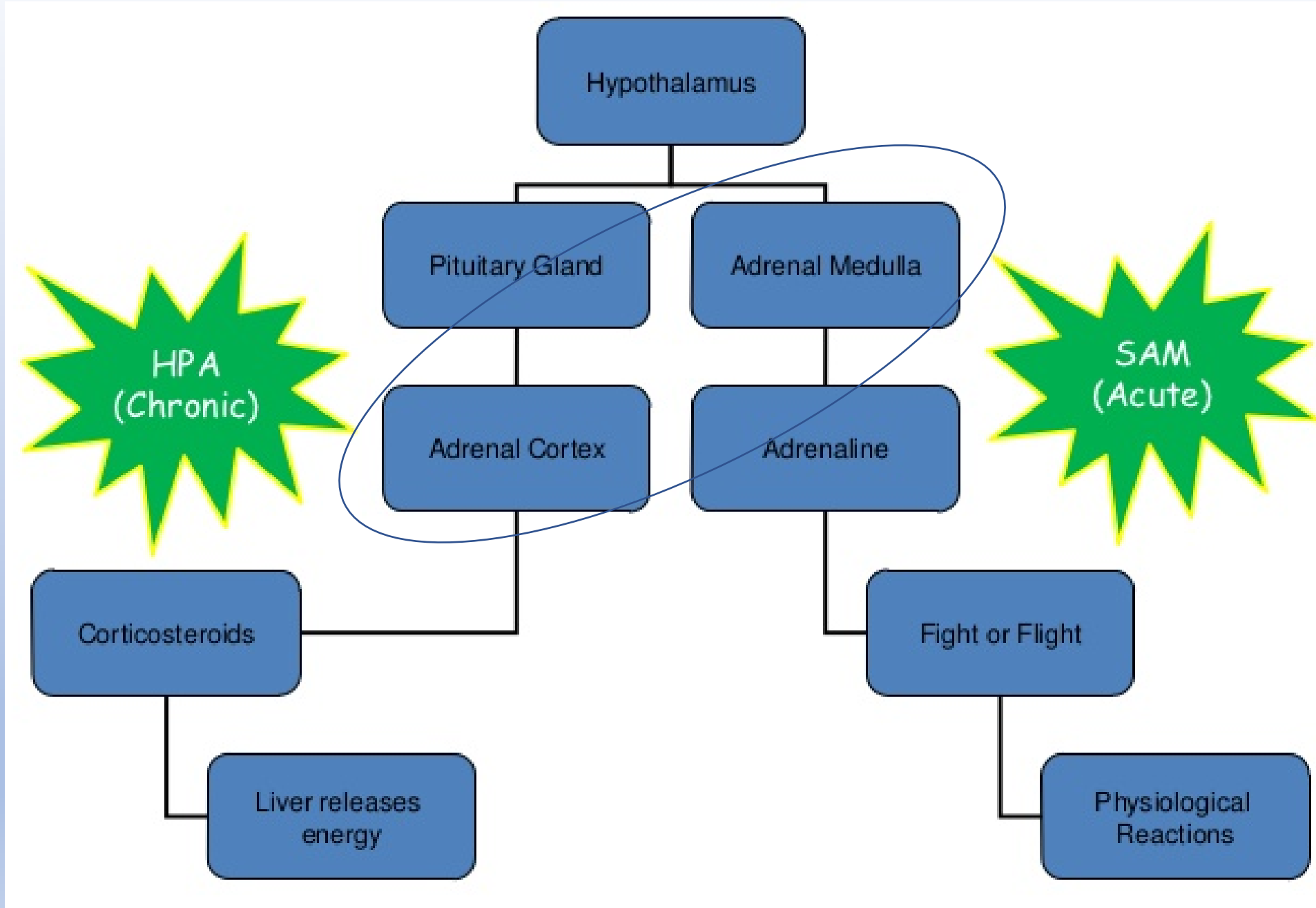
ACUTE NOCICEPTIVE PAIN – II

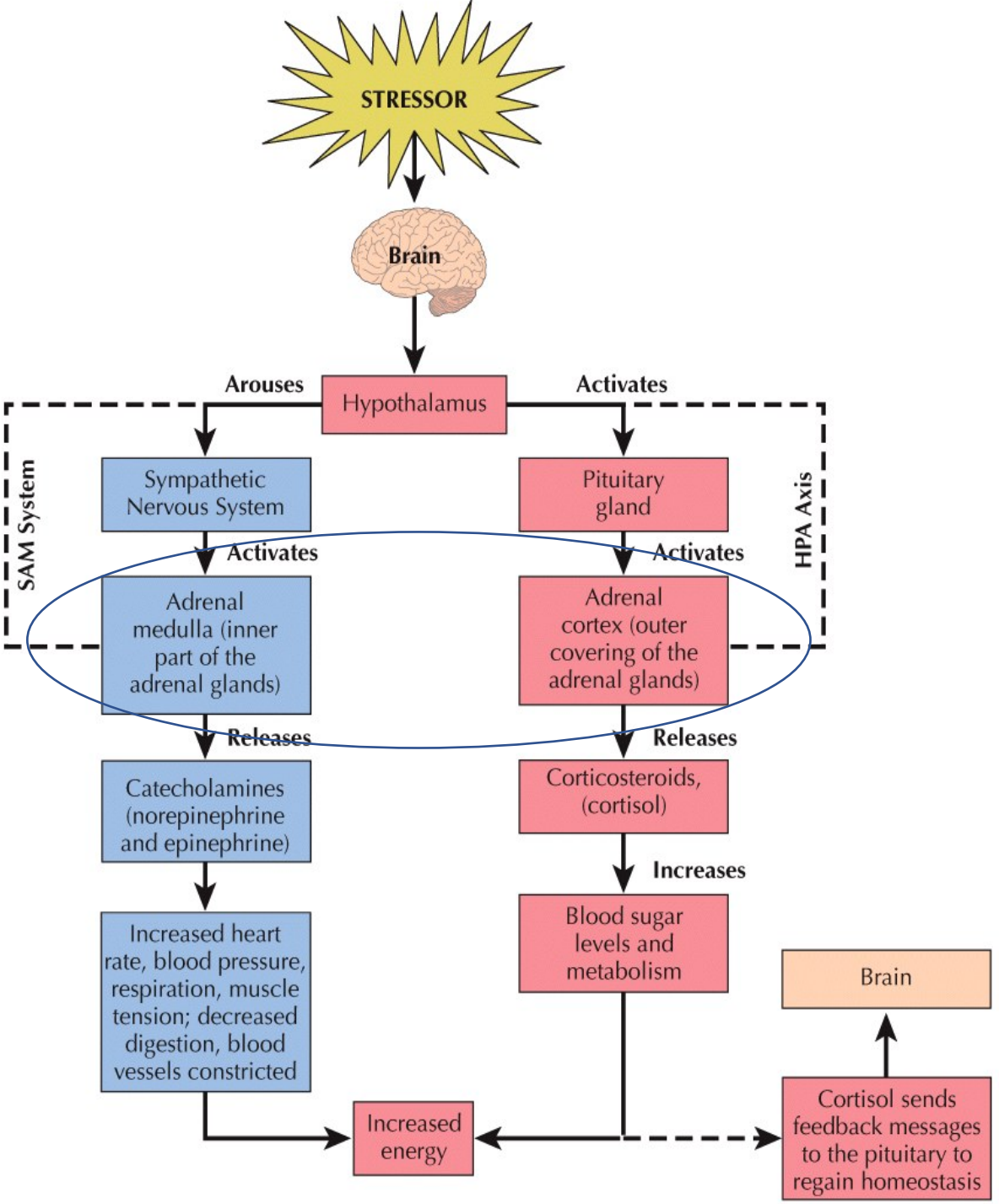


- Inflammation / nerve injury stimulate nociceptive information to dorsal horn
- Ascends to brainstem, gated in thalamus
- Cognitive appraisal in SI cortex
- Acute pain increases arousal via sympathetic and GC routes (excitatory reciprocal link between somatosensory and limbic cortices)
- → **Stress response**

The Stress Response:
Sympathomedullary Pathway (SAM)
The Hypothalamic Pituitary-Adrenal (HPA) System

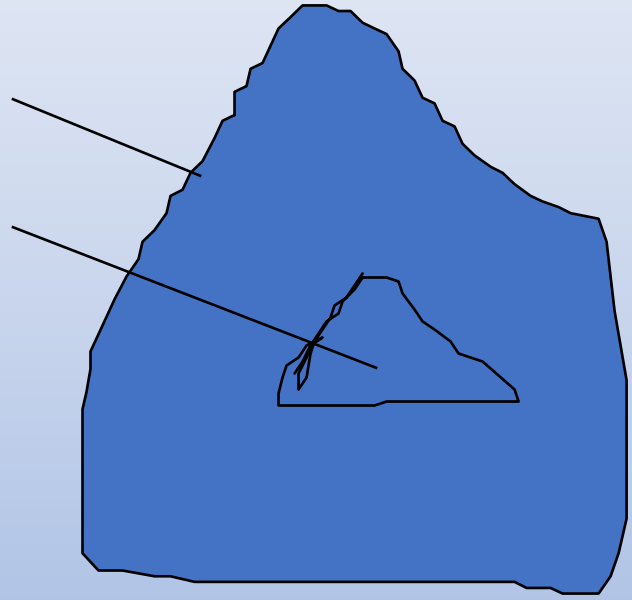



Hypothalamus
Pituitary Gland
Adrenal Medulla
HPA (Chronic)
SAM (Acute)
Adrenal Cortex
Adrenaline
Corticosteroids
Fight or Flight
Liver releases energy
Physiological Reactions

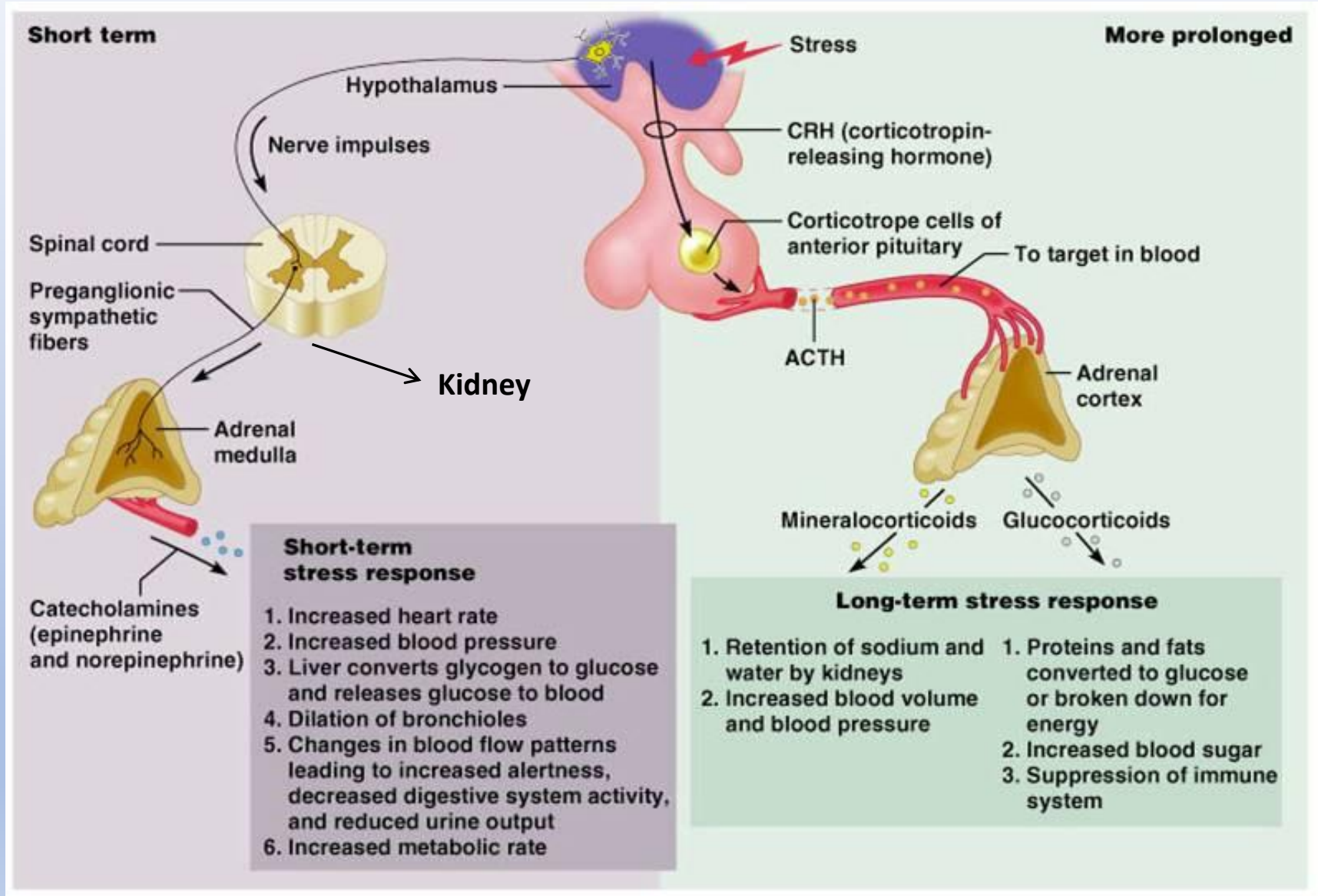

STRESSOR
Brain
Arouses
Hypothalamus
Activates
SAM System
Sympathetic Nervous System
Pituitary gland
HPA Axis
Activates
Activates
Adrenal medulla (inner part of the adrenal glands)
Adrenal cortex (outer covering of the adrenal glands)
Releases
Releases
Catecholamines (norepinephrine and epinephrine)
Corticosteroids, (cortisol)
Increases
Increased heart rate, blood pressure, respiration, muscle tension; decreased digestion, blood vessels constricted
Blood sugar levels and metabolism
Brain
Increased energy
Cortisol sends feedback messages to the pituitary to regain homeostasis

ADRENAL GLANDS

- Adrenal Cortex
- Adrenal Medulla

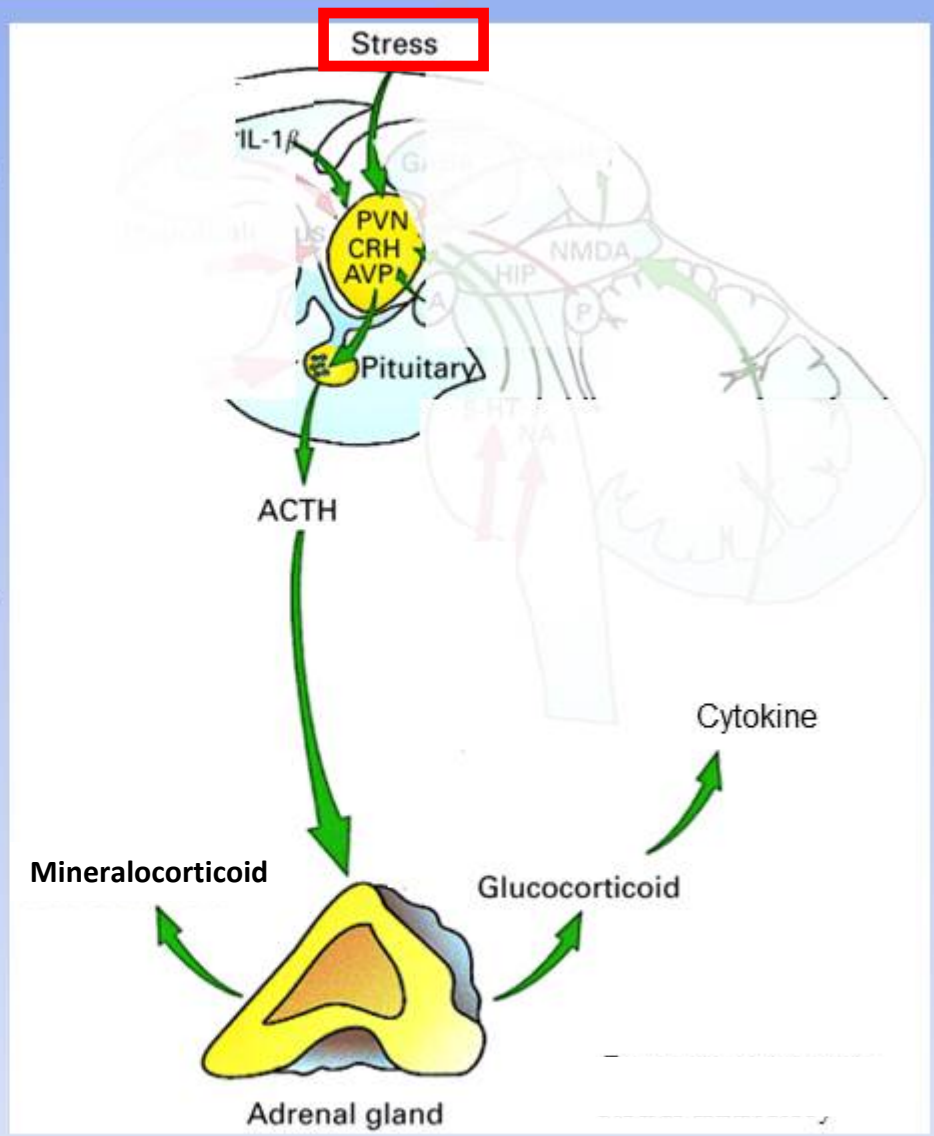


SAM **HPA**


Short term
More prolonged
Stress
Hypothalamus
Nerve impulses
CRH (corticotropin-releasing hormone)
Corticotrope cells of anterior pituitary
To target in blood
Spinal cord
Preganglionic sympathetic fibers
Kidney
ACTH
Adrenal cortex
Adrenal medulla
Mineralocorticoids
Glucocorticoids
Catecholamines (epinephrine and norepinephrine)
Short-term stress response
1. Increased heart rate
2. Increased blood pressure
3. Liver converts glycogen to glucose and releases glucose to blood
4. Dilation of bronchioles
5. Changes in blood flow patterns leading to increased alertness, decreased digestive system activity, and reduced urine output
6. Increased metabolic rate
Long-term stress response
1. Retention of sodium and water by kidneys
2. Increased blood volume and blood pressure
1. Proteins and fats converted to glucose or broken down for energy
2. Increased blood sugar
3. Suppression of immune system

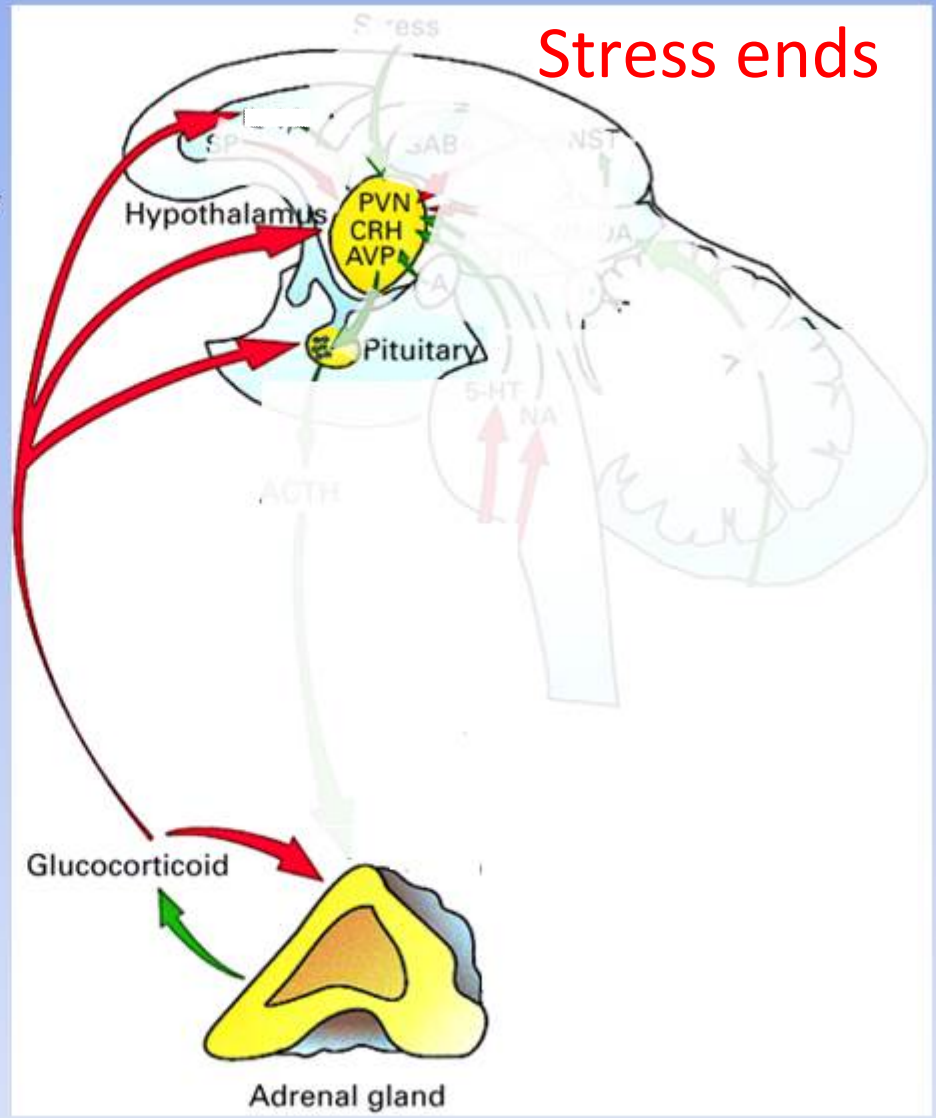
HPA STRESS RESPONSE

- CRH and/or AVP released
  - → anterior pituitary gland
- Stimulates ACTH release
  - → adrenal cortex
  - → triggers release of glucocorticoid and pro-inflammatory cytokines (e.g. IL-1β) release



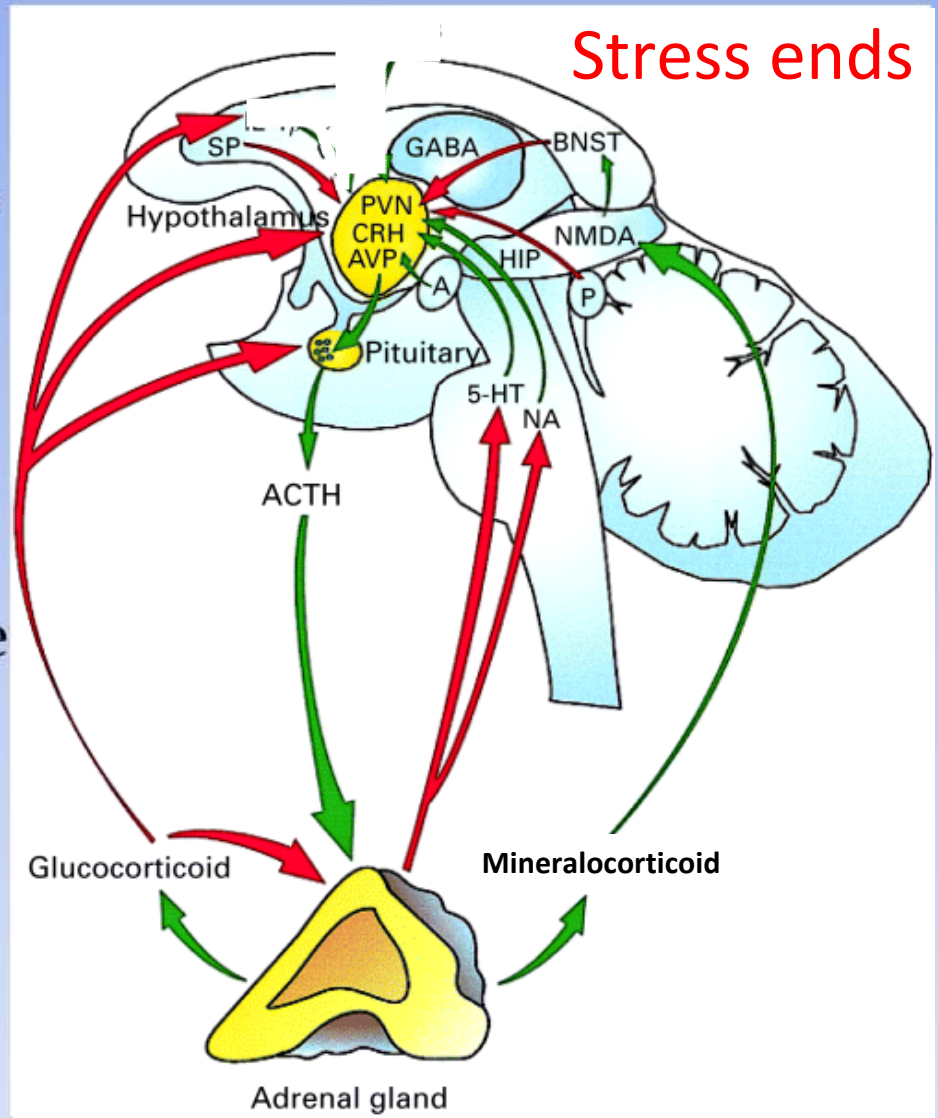
STRESS RESPONSE NEGATIVE FEEDBACK: I

- Glucocorticoid → negative feedback via GR of HC, PVN, P, and AC
  - ↓ CRH, AVP release
  - ↓ ACTH release
  - ↓ GC
  - ↓ IL-1β

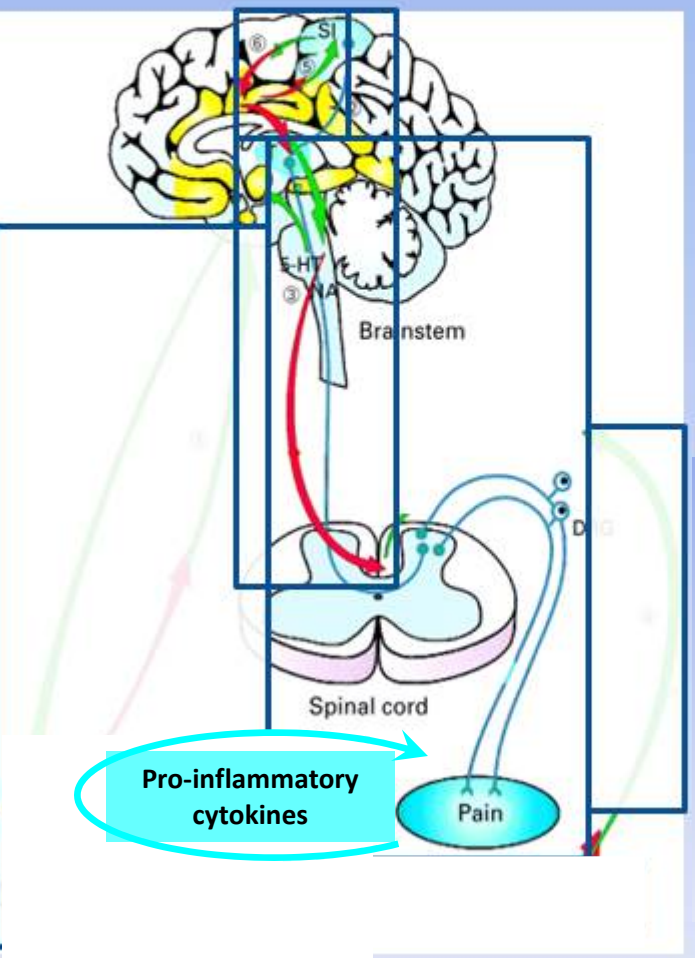


STRESS RESPONSE NEGATIVE FEEDBACK: II

- Glucocorticoid → negative feedback via GR of HC, PVN, P, and AC
  - ↓ CRH, AVP release
  - ↓ ACTH release
  - ↓ GC
  - ↓ IL-1β
- Mineralocorticoid → negative feedback via GR in HC
  - ↑ Glu → GABA ↑
- Brainstem 5-HT/NE release
- Amy
- P
- neurokinin SP



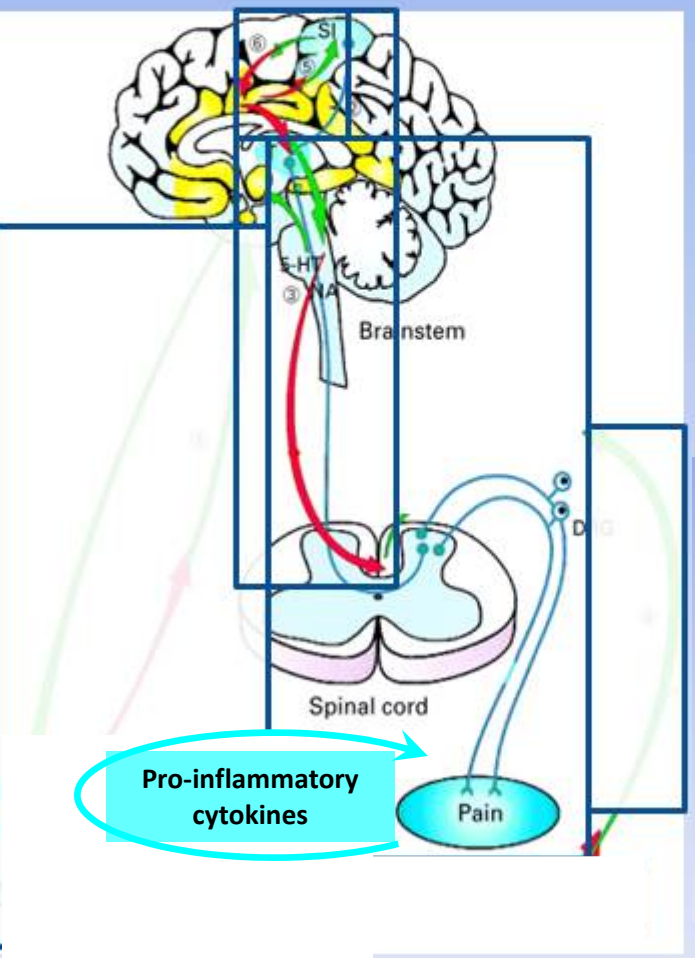
ACUTE NOCICEPTIVE PAIN – III



- Inflammation / nerve injury stimulate nociceptive information to dorsal horn
- Ascends to brainstem, gated in thalamus
- Cognitive appraisal in SI cortex
- Acute pain increases arousal via sympathetic and GC routes (excitatory reciprocal link between somatosensory and limbic cortices)
- →**Stress response**
- →Descending pain modulation

PAIN ENDS

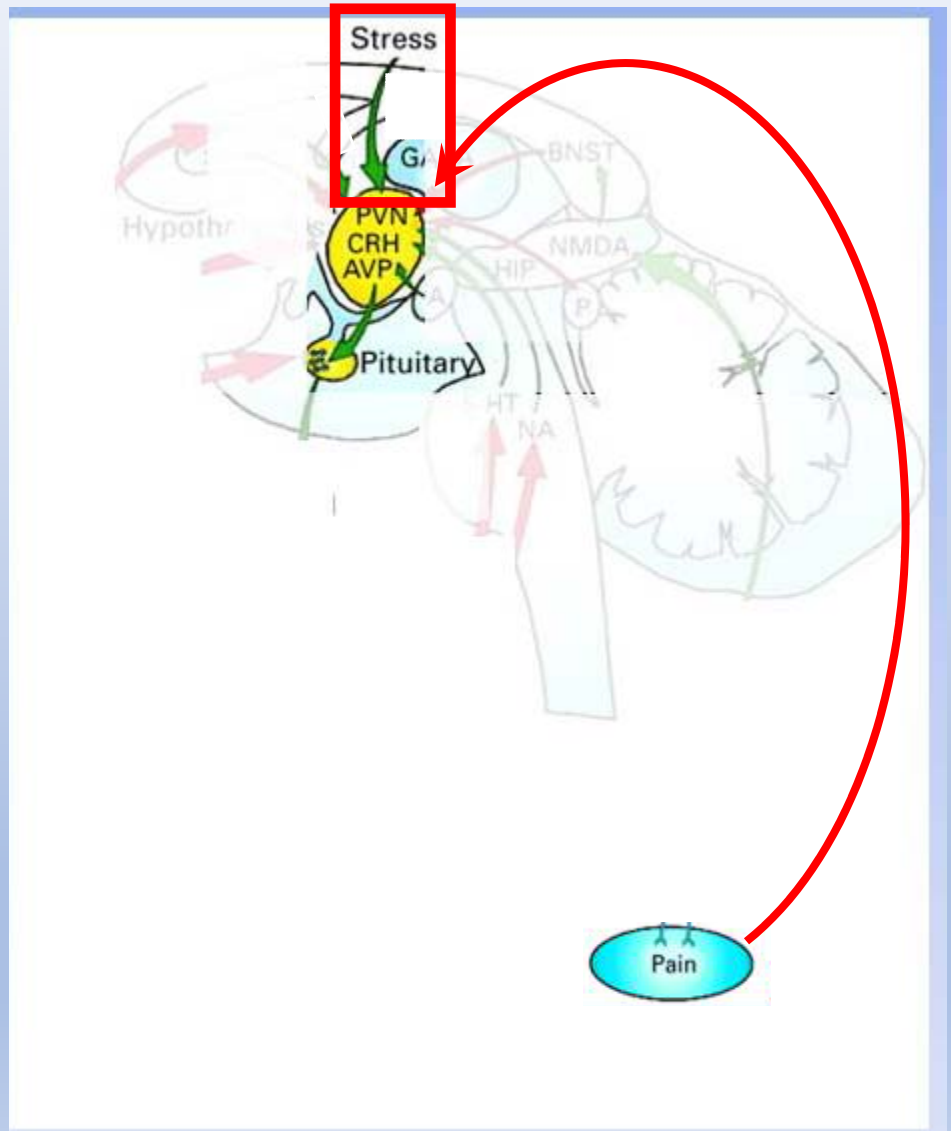
ACUTE NOCICEPTIVE PAIN – III



- Inflammation / nerve injury stimulate nociceptive information to dorsal horn
- Ascends to brainstem, gated in thalamus
- Cognitive appraisal in SI cortex
- Acute pain increases arousal via sympathetic and GC routes (excitatory reciprocal link between somatosensory and limbic cortices)
- →**Stress response**
- →Descending pain modulation

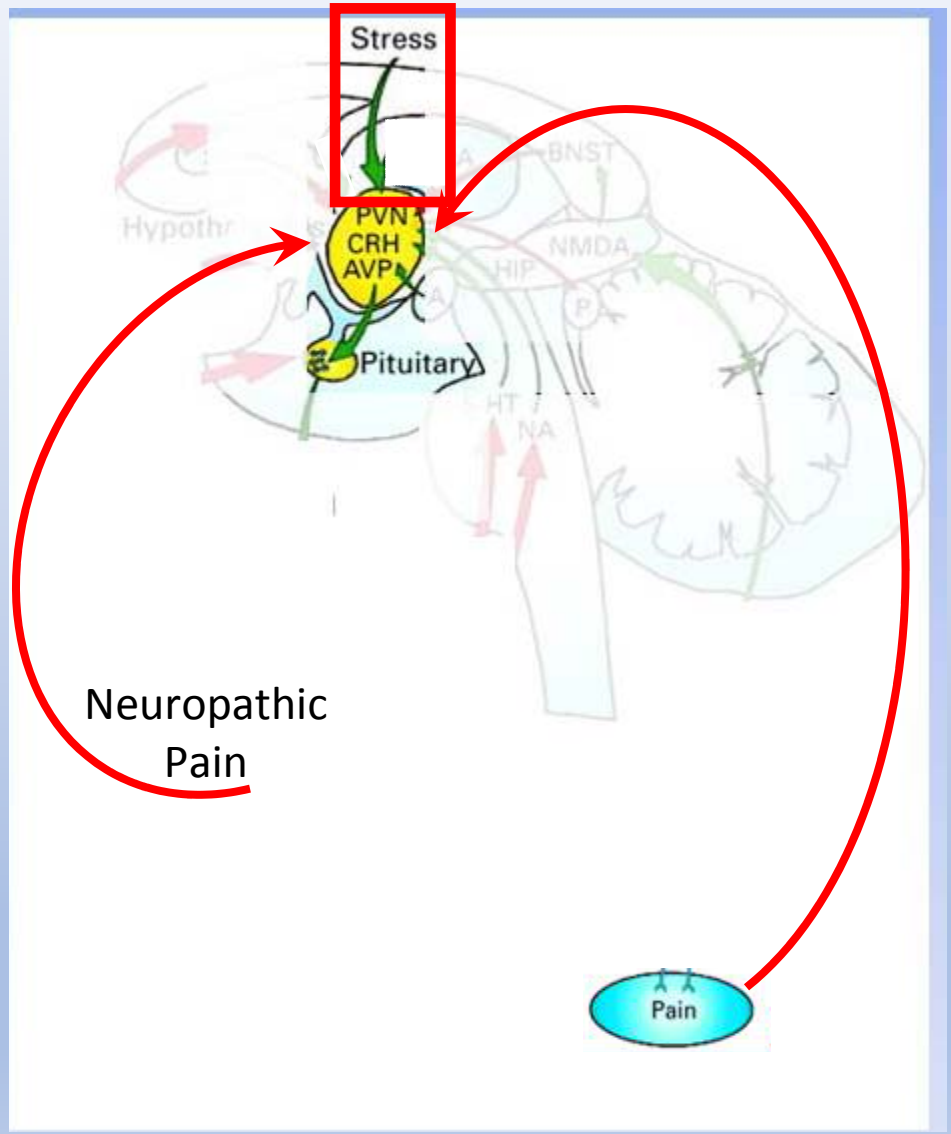
PAIN DOES NOT END

CHRONIC STRESS AND PAIN
HPA AXIS

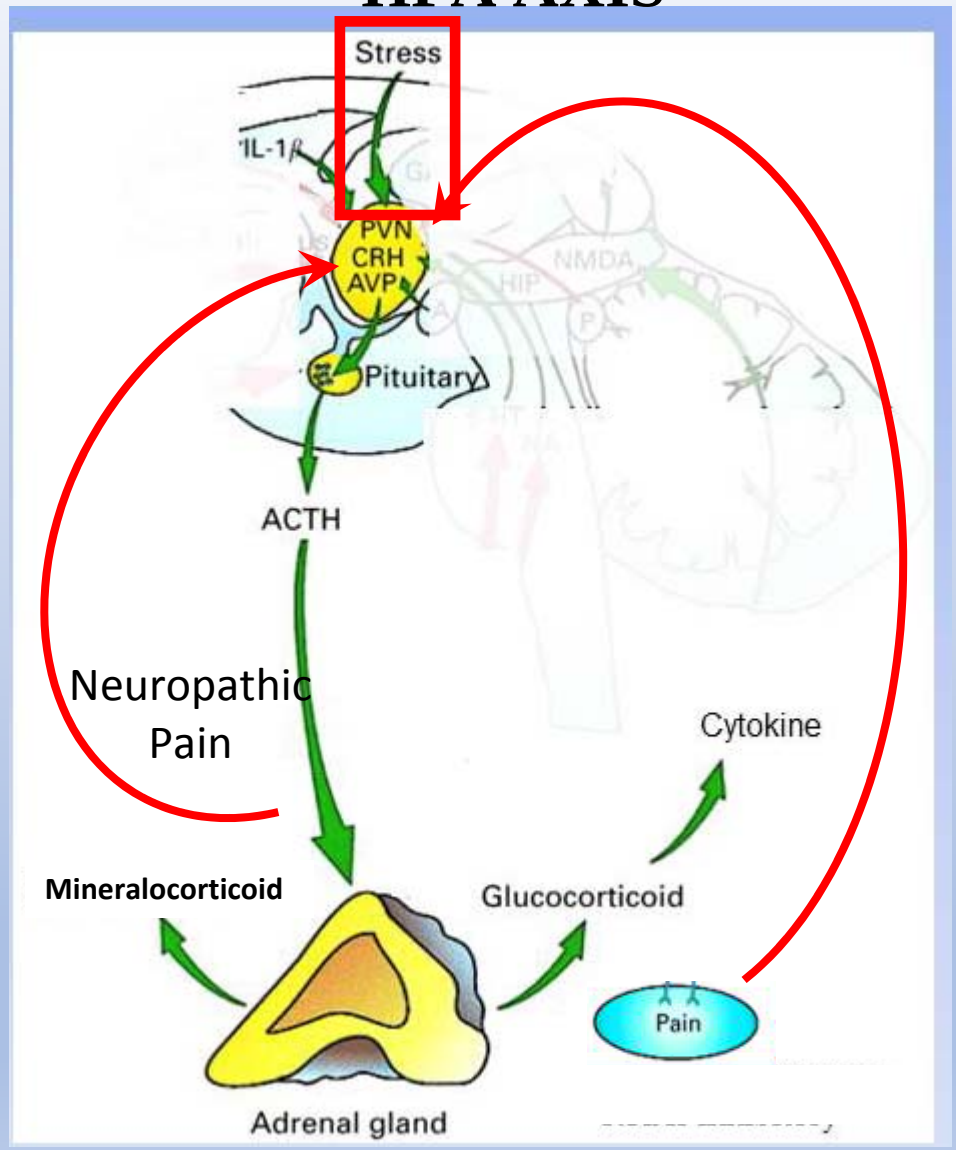


Neuropathic pain also becomes centrally sensitized

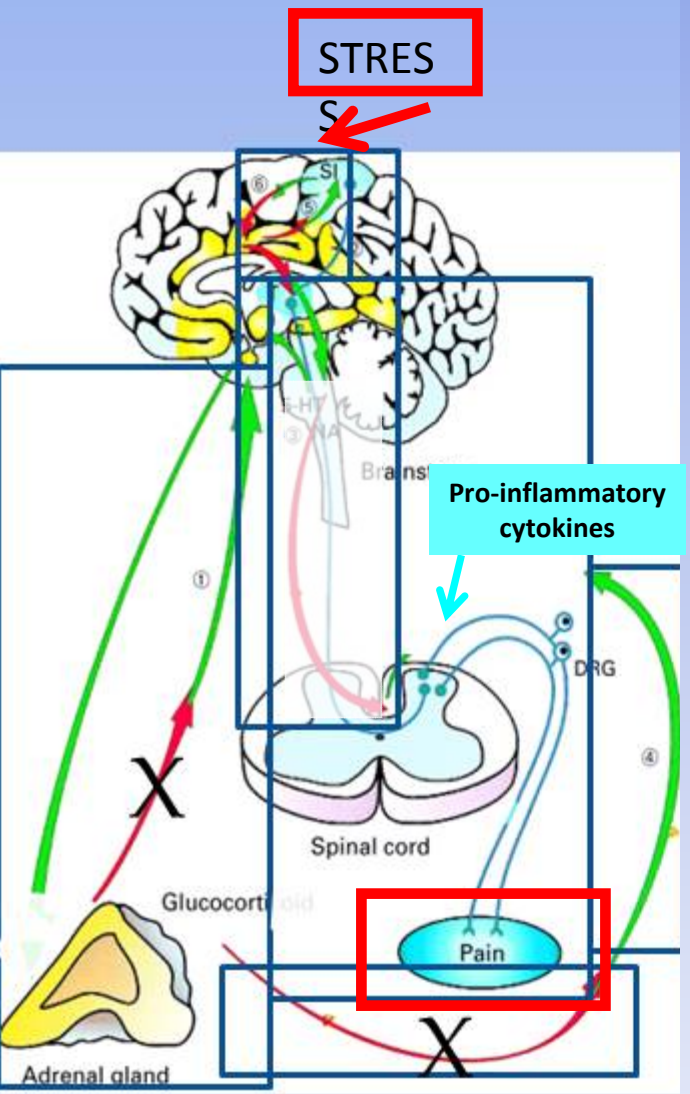
CHRONIC STRESS AND PAIN
HPA AXIS



CHRONIC STRESS AND PAIN
HPA AXIS



CHRONIC STRESS AND PAIN CAUSES CENTRAL SENSITIZATION AND DEPRESSION

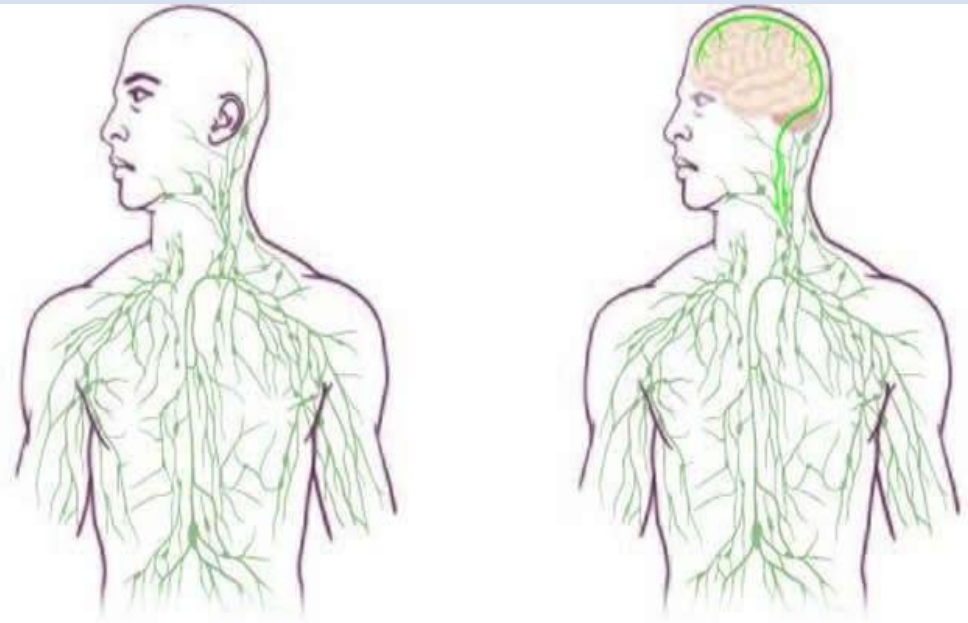


- Pain does not end →
- Stress does not end →
- 'HPA overdrive' →
- Loss of GC inhibition of pro-inflammatory cytokines
- Proliferation of peripheral inflammation
- Heightened pain
- Disinhibition of descending cortical pain modulation ('nociceptive braking')
- Depletion of catecholaimes – (nor)adrenaline from locus coeruleus and dopamine from hypothalamus
- Depressed behavior and mood
- "THE IMMUNE RUNAWAY TRAIN"

Absinta M, Ha SK, Nair G, Sati P, Luciano NJ, Palisoc M, Louveau A, Zaghloul KA, Pittaluga S, Kipnis J, Reich DS. (2017). Human and nonhuman primate meninges harbor lymphatic vessels that can be visualized noninvasively by MRI. Elife. 2017 Oct 3;6.

Louveau, A., Smirnov, I., Keyes, T.J., Eccles, J.D., Rouhani, S.J., Peske, J.D., Derecki, N.C., Castle, D., Mandell, J.W., Kevin, S.L. and Harris, T.H.,(2015). Structural and functional features of central nervous system lymphatics. *Nature*, *523*(7560), 337

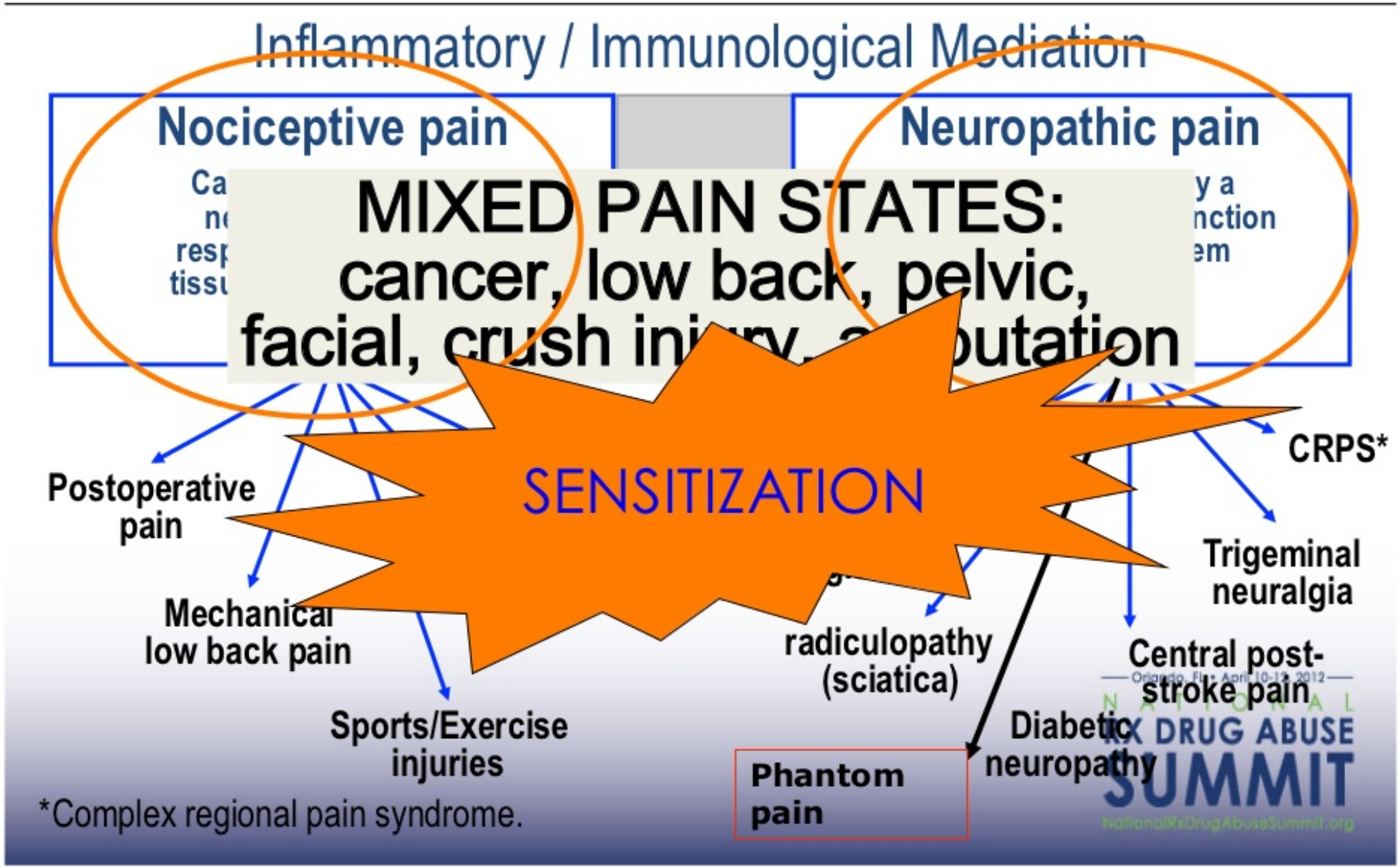
- CNS previously thought to lack a lymphatic system
- yet CNS undergoes immune surveillance within meningeal compartments
- mechanisms governing entrance/exit of immune cells from CNS recently discovered
- T-cell gateways into and out of the meninges
- lymphatic vessels line dural sinuses.



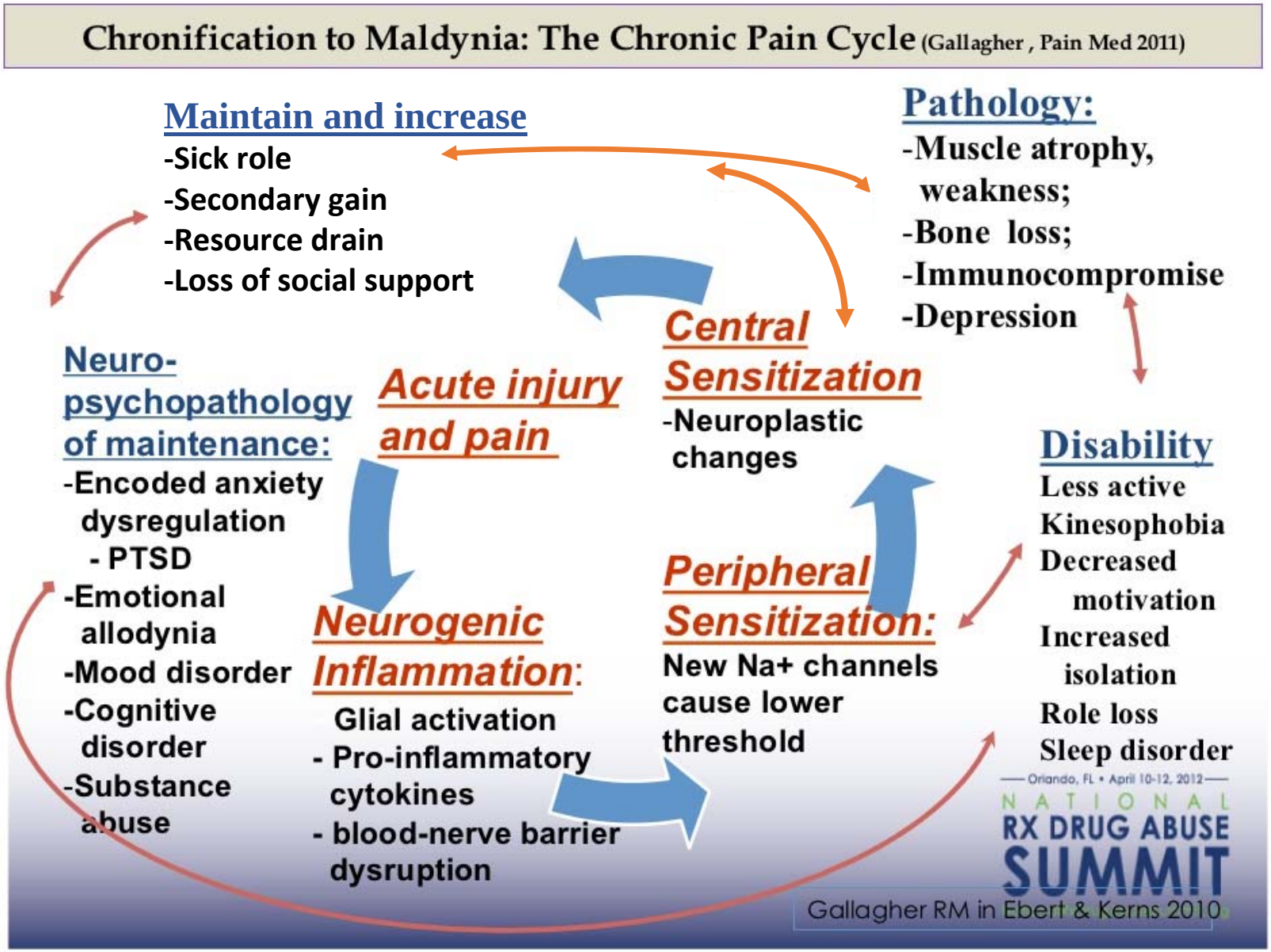
Old and updated maps of the lymphatic system

In sensitized chronic nociceptive pain, descending top-down modulation of pain is lost.

There Are Many Painful Diseases and Pain Diseases



Rollin Gallagher, MD, MPH, dhss.delaware.gov/dsamh/files/2007gallagherii.pps


Chronification to Maldynia: The Chronic Pain Cycle (Gallagher , Pain Med 2011)
Maintain and increase
-Sick role
-Secondary gain
-Resource drain
-Loss of social support
Pathology:
-Muscle atrophy, weakness;
-Bone loss;
-Immunocompromise
-Depression
Central Sensitization
-Neuroplastic changes
Neuro-psychopathology of maintenance:
-Encoded anxiety dysregulation - PTSD
-Emotional allodynia
-Mood disorder
-Cognitive disorder
-Substance abuse
Acute injury and pain
Neurogenic Inflammation:
Glial activation
- Pro-inflammatory cytokines
- blood-nerve barrier dysruption
Peripheral Sensitization:
New Na+ channels cause lower threshold
Disability
Less active
Kinesophobia
Decreased motivation
Increased isolation
Role loss
Sleep disorder
Orlando, FL • April 10-12, 2012
NATIONAL RX DRUG ABUSE SUMMIT
Gallagher RM in Ebert & Kerns 2010

Depression is an expression of chronic stress in humans

Rodents show stress in their behavior; humans show stress in their behavior and mood

- Chronically stressed rodents have a neuromodulator profile strikingly similar to depressed people
    - Animals cannot report mood!

- Depressed people are stressed and report depressed mood

- However, not all stressed people are depressed (.e. not all stressed people report depressed mood)

- The difference between stress and depression in people appears to be cortisol: when high, depression is expressed; when low, stress is the phenotype

Chronic stress (rodents)	Clinical depression (humans)
↑CRH/CRH mRNA	↑CRH/CRH mRNA
↓CRH receptor affinity/number	↓CRH receptor affinity/number
↑AVP/AVP mRNA	↑AVP/AVP mRNA
↑CSF levels of CRH/AVP	↑CSF levels of CRH/AVP
↑Co-expression of CRH/AVP	↑Co-expression of CRH/AVP
↓GR/MR number/function	↓GR/MR number/function
Altered plasma ACTH concentration	Altered plasma ACTH concentration
Altered circadian rhythmicity	Altered circadian rhythmicity
Adrenal supersensitivity to ACTH	Adrenal supersensitivity to ACTH
↑Corticosterone	↑Cortisol **(*cortisol is ↓ in PTSD)**
↓Negative feedback	↓Negative feedback
Adrenal hypertrophy	Adrenal hypertrophy
Pituitary hypertrophy	Pituitary hypertrophy
Exaggerated corticosterone response	Exaggerated cortisol response
Cognitive deficit	Cognitive deficit
Behavioral disturbance	Behavioral and mood disturbance

Blackburn-Monro & Blackburn-Monro (2011).

Selection of Diagnoses and Symptoms that Suggest Central Sensitization

- Chronic abdominal pain
- Chronic fatigue
- Chronic joint pain
- Chronic low-back pain
- Chronic non-specific pain
- Chronic tension headaches
- Fibromyalgia
- Irritable bowel syndrome
- Multiple drug or food allergies or intolerances (self-diagnosed)
- Chronic pelvic pain
- Postural orthostatic tachycardia syndrome (POTS)
- Temporomandibular, myofascial pain disorders
- Whiplash-associated pain disorders
- Widespread non-specific pain

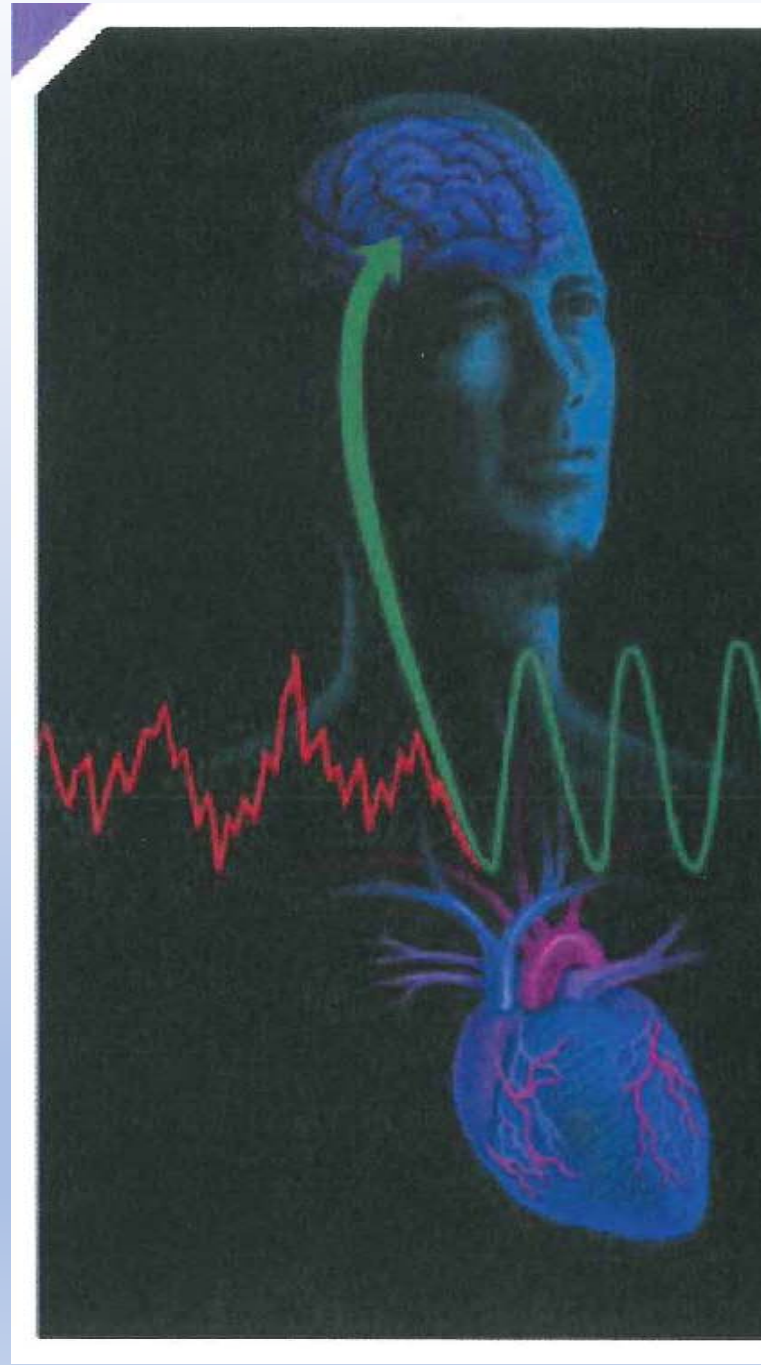
Autonomic Self-Regulation (ASR)

Heart Rate Variability, Chronic Pain, and Rehabilitating the Autonomic Nervous System

BY RAOUF GHARBO, DO, AND J.P. GINSBERG, PHD

Integrative Management of Sensitized Chronic Pain with Ambulatory Autonomic Self-Regulation

By JP Ginsberg, PhD



The three components of Autonomic Self-Regulation are:

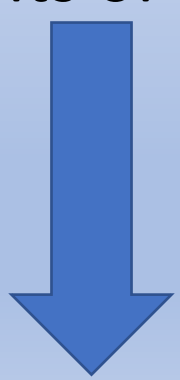
1. HRV Biofeedback = resonant frequency breathing
2. Mindful attention
3. Positive emotional state

ASR coaching essential elements

- Paced breathing at resonant frequency and the production of HRV Coherence through HRV Biofeedback

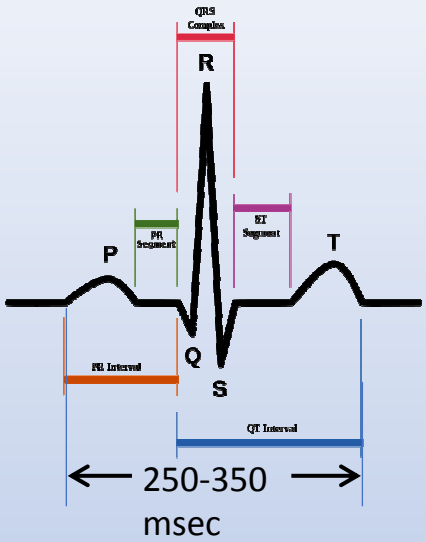
- Mindfulness or imagery focused on breathing and the heart. Focused attention on air entering and exiting the chest and passing thorough the heart

- Positive emotional state (PES). Occupy the mind during the HRVB session with thoughts of **compassion**, gratitude, apreciation, etc.

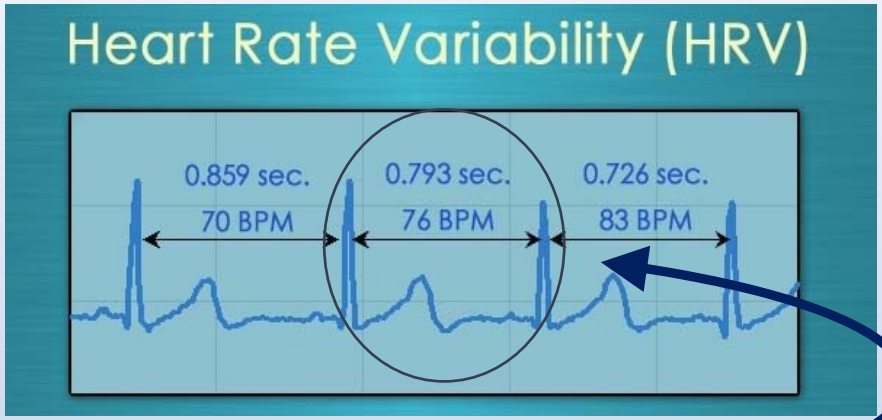


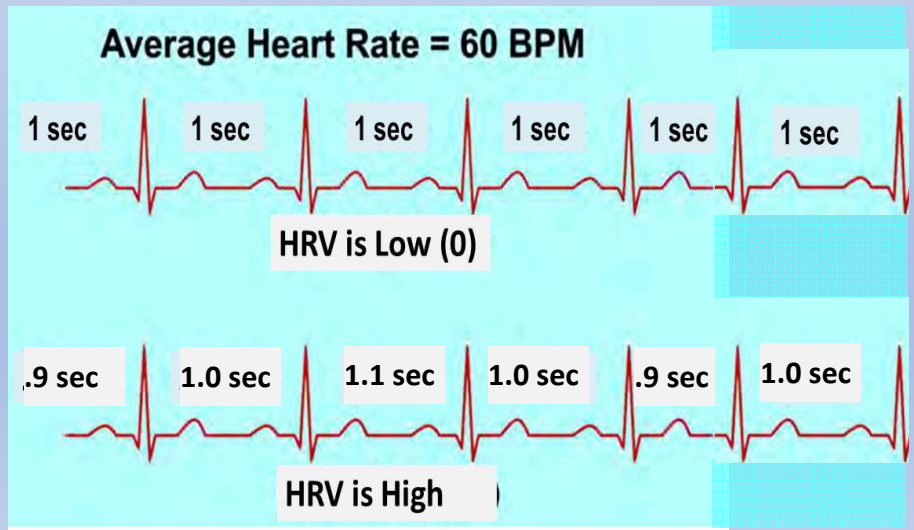
'COHERENCE'

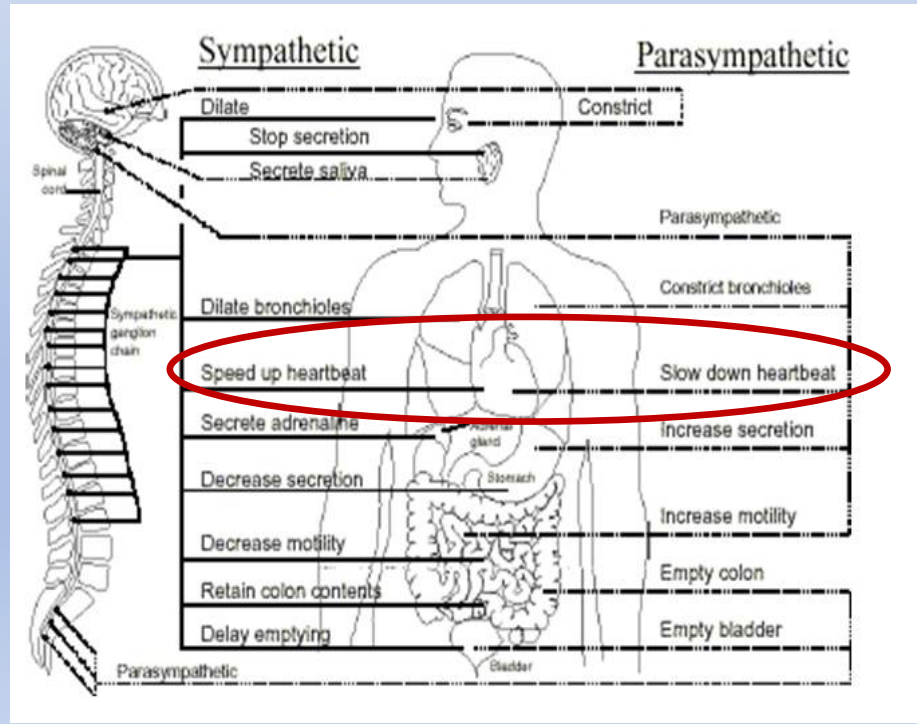
HRV, HRV Coherence, and HRV Biofeedback (HRVB)



- Interbeat Interval – 'ibi'
- instantaneous heart rate (HR)
- R-R or N-N





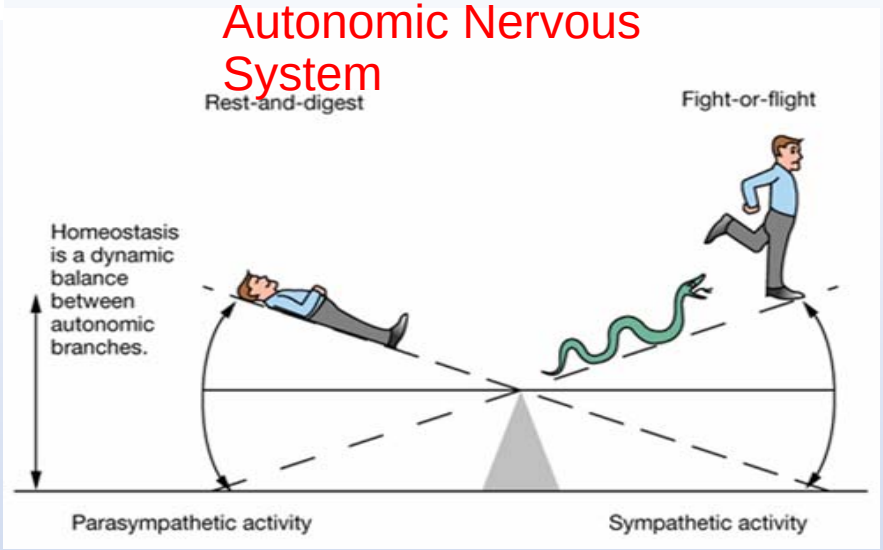


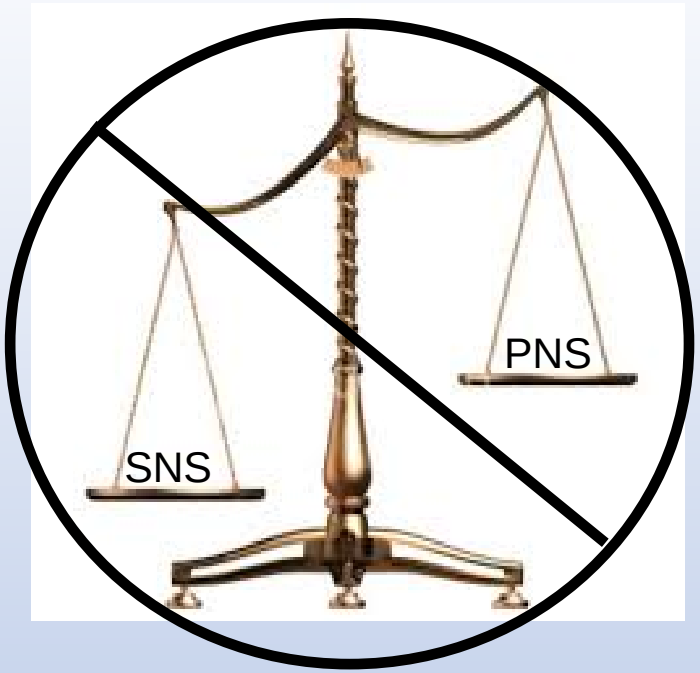
Cardiac acceleration is mediated through the sympathetic nervous system with [nor]adrenaline (=[nor]epinephrine) onto the heart, other organs, and throughout the circulatory system.

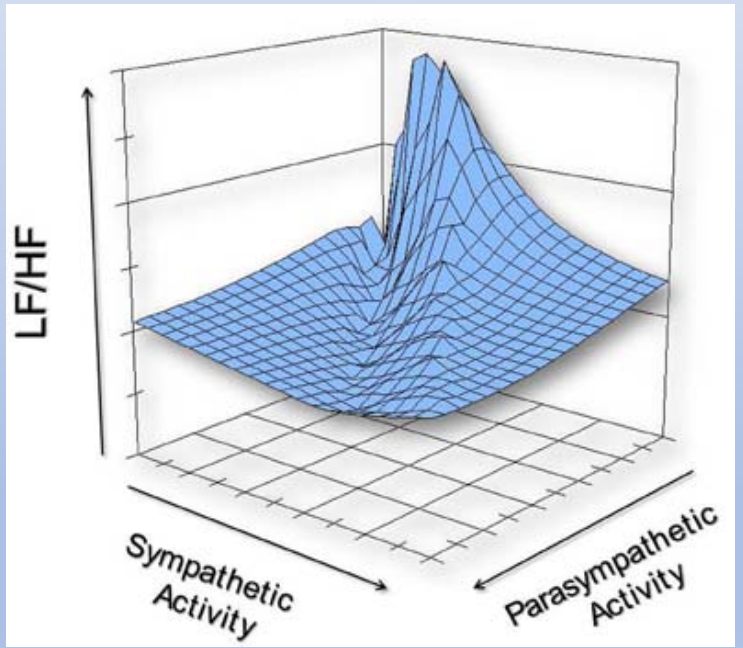
Cardiac deceleration is mediated through the parasympathetic nervous system by the vagus nerve ('vagal tone') which outputs acetylcholine onto the heart and other organ systems, notably the gut.

The pacemaker control of heart is adrenertic (i.e. sympathetic); cholinergic (i.e. vagal) output is added and withdrawn very raplidly (msecs). When vagal tone is engaged – which is normal function - additional sympathetic adrenergic control is exerted on a slower time scale (seconds) but the pacemaker rate of HR is not reached unless parasympathetic influence is abolished by blockade.

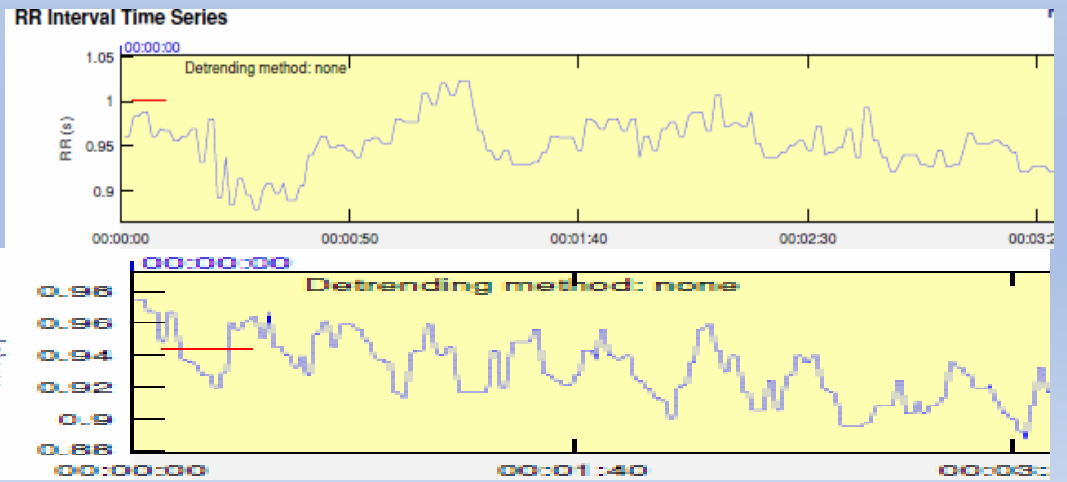
Autonomic Nervous System







The sympathetic and parasympathetic branches of the ANS are related by a complex non-liner function. A change in one branch may cause and increase, decrease, or no change in the other branch.

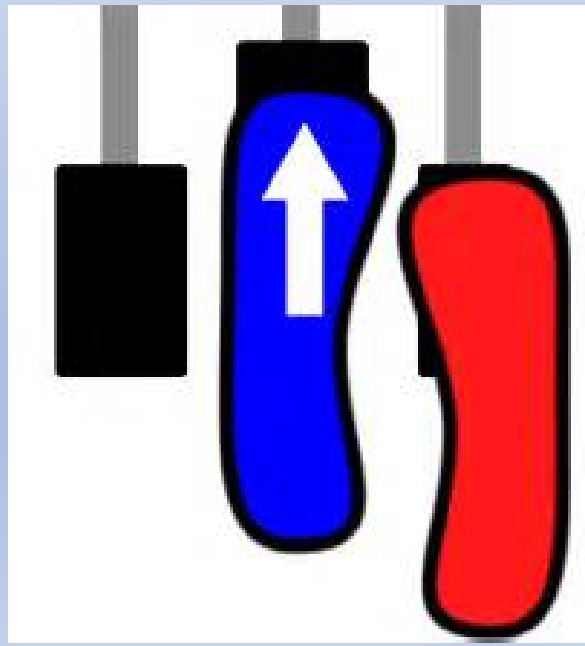


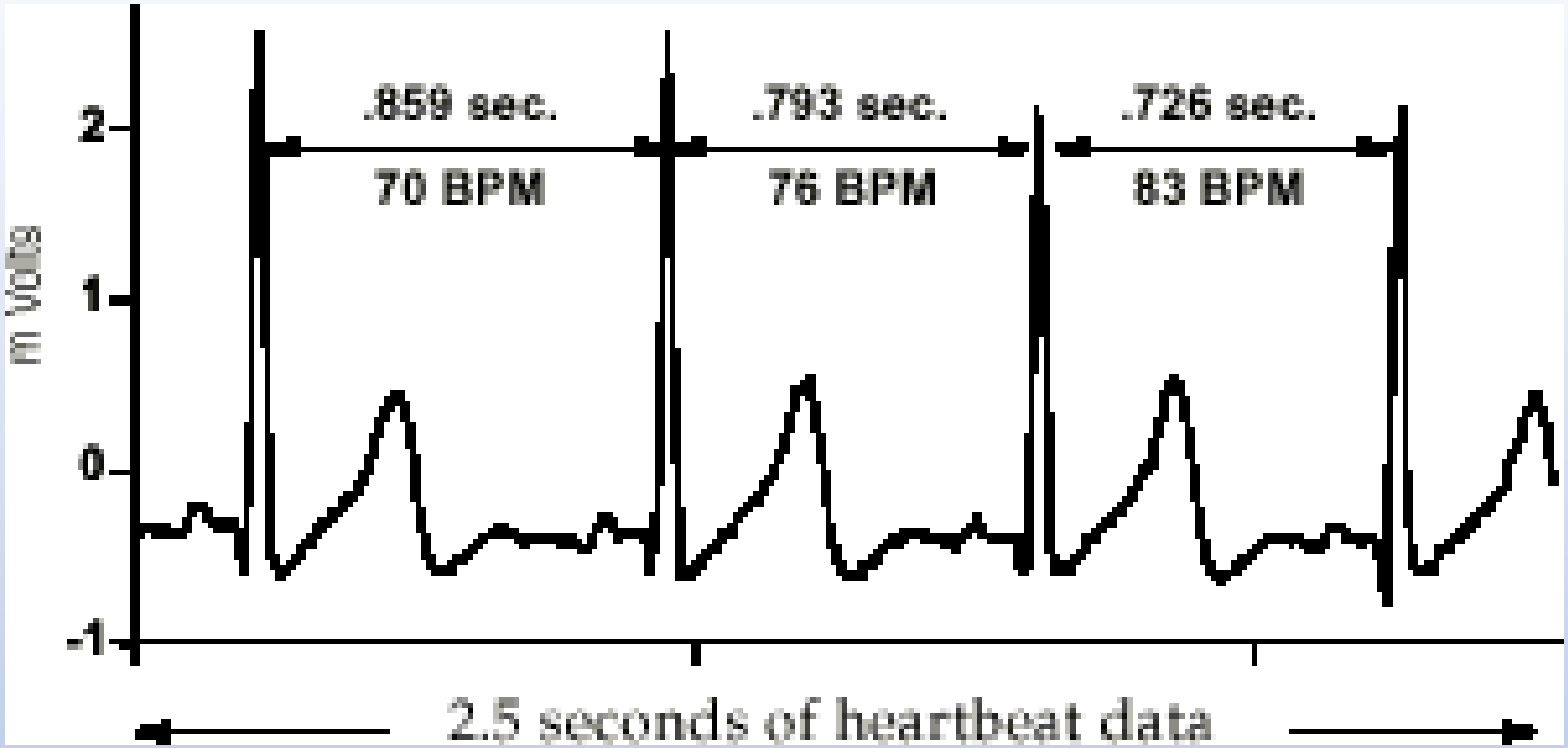
Billman, G. (2013). The LF/HF ratio does not accurately measure cardiac sympatho-vagal balance. Frontiers in Physiology, doi: 10.3389/fphys.2013.00026

The sympathetic and parasympathetic brances of the ANS are related by a complex non-liner function.

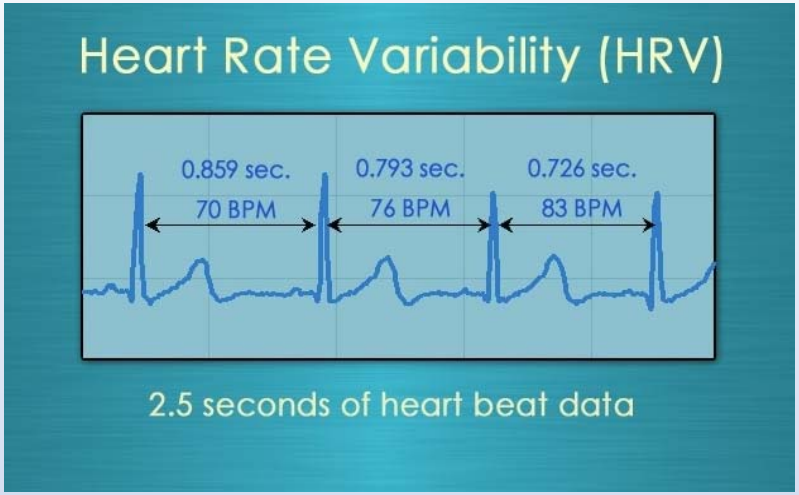
A change in one branch may cause and increase, decrease, or no change in the other branch.

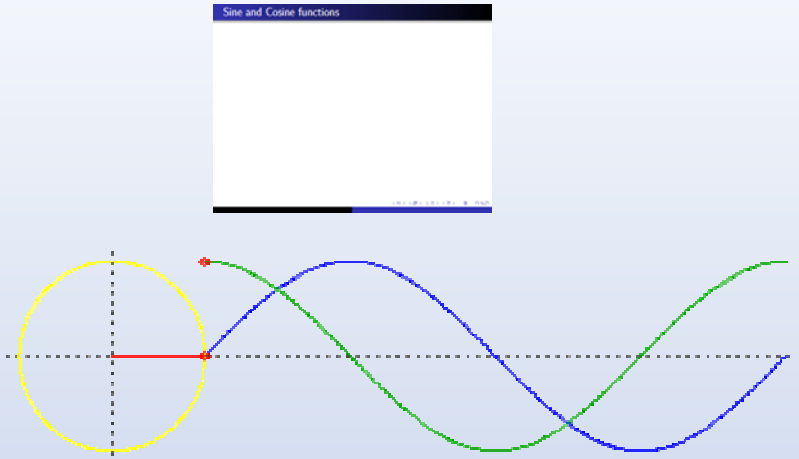
“Left foot braking”





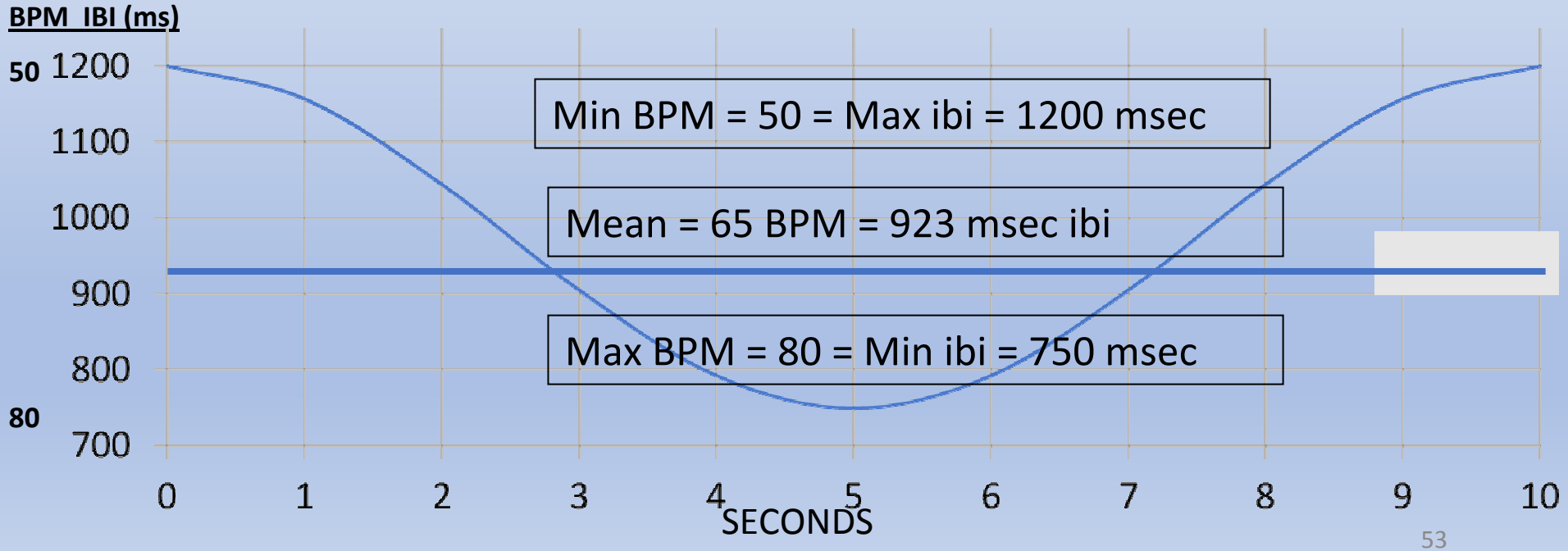
HRV is an indicator of autonomic function. Variability is equal to variance, which is maximized when beat-to-beat intervals increase and decrease in a smooth rhythm, one that approximates a sine wave. A smooth sinusoidal rhythm of ibi's is characteristic of a healthy heart under resting conditions; the amount of variability is directly related to respiration rate, and many inter-individual factors such as age, gender, height, and fitness level



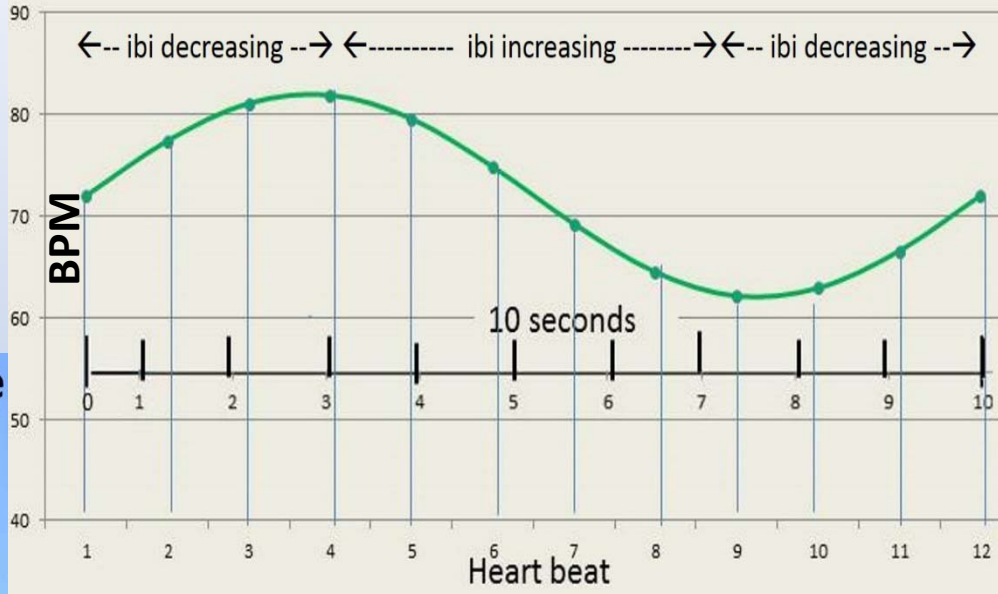


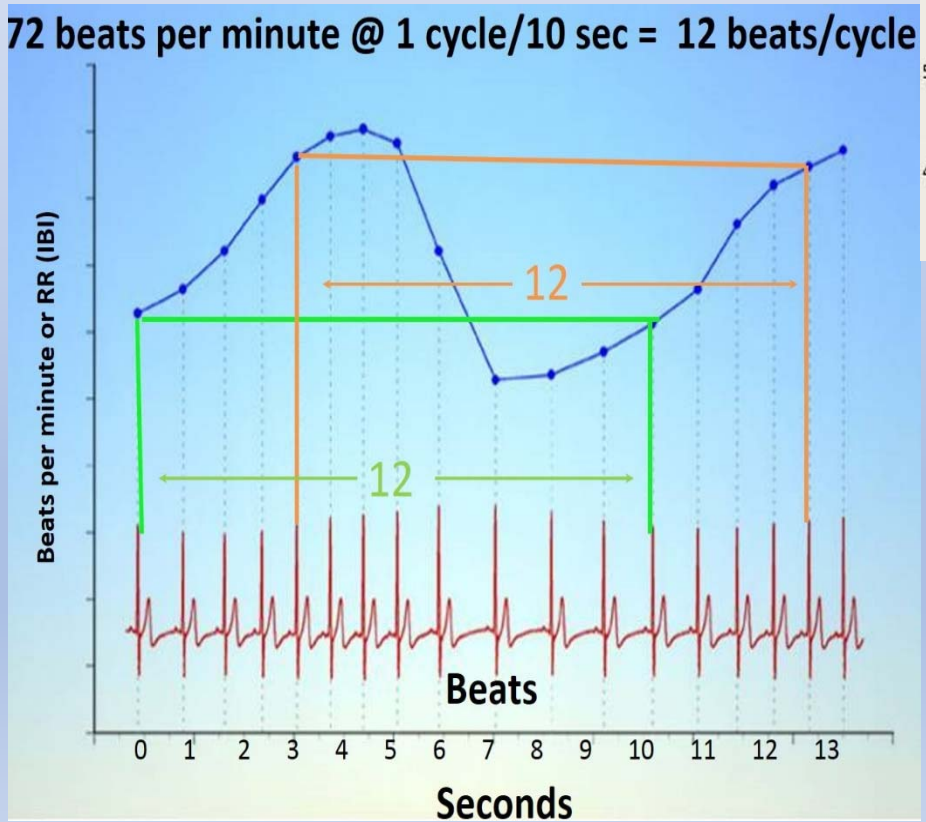
IBI = 975+225*COS(t*PI)

IBI-	1200	1157	1045	905	793	750	793	905	1045	1157	1200
BPM-	50	52	57	63	76	80	76	63	57	52	50

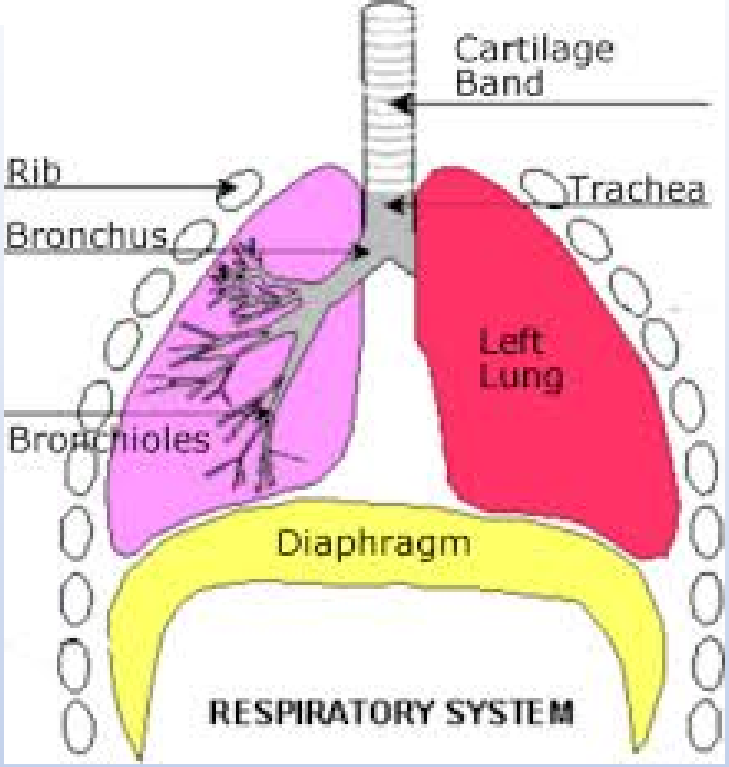


72 BPM, Max-Min 20
1 cycle/10 secs, 12 beats/cycle
1 cycle (10 secs)



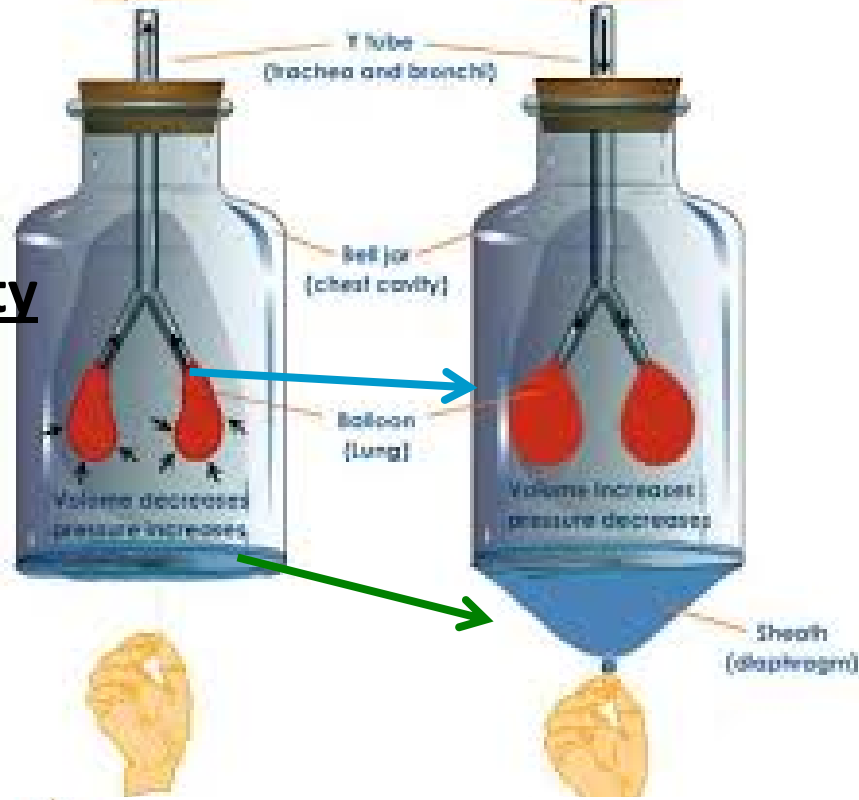


HRV is directly related to respiratory cycle

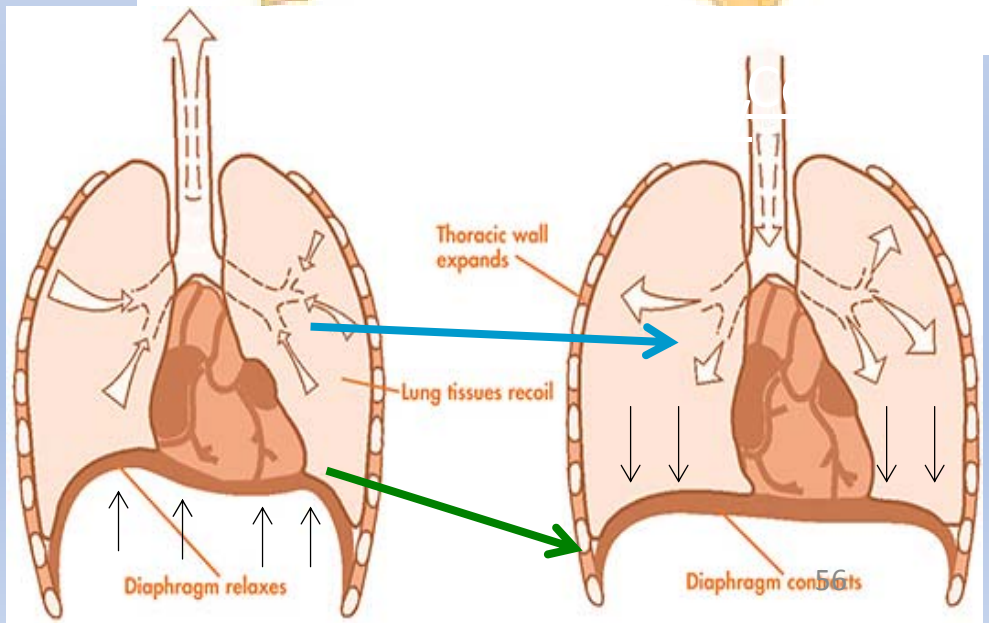


1. Exhale, relax diaphragm, reduce cavity

2. Inhale, contract diaphragm, increase cavity

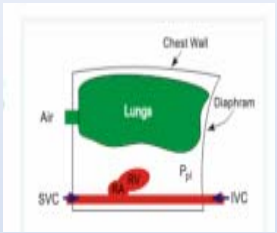


In Diaphragmatic Breathing inhalation increases thoracic cavity volume (draws air in) due to active contraction of diaphragm; exhalation decreases cavity volume (expels air) and is passive.



Bainbridge Reflex: RSA, cardio-respiratory coupling, lung-heart pump

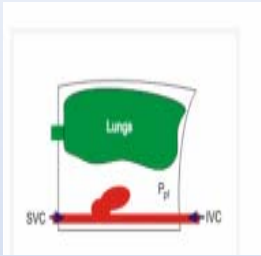
Respiration produces cardiac acceleration and deceleration



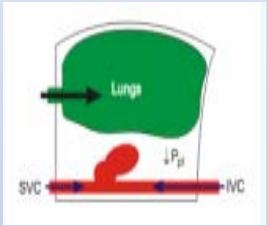
←Lung

←Stretch receptor

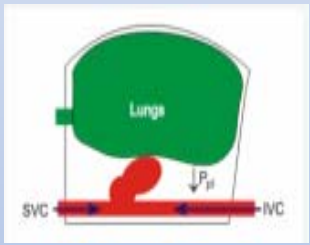
Inhale, start cycle again

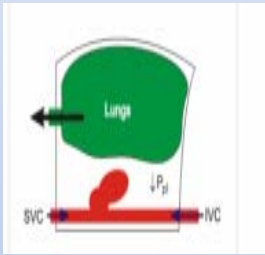


Inhale, intra-thoracic pressure decreases



Venous blood Flow, HR increase





Exhale, intra-thoracic pressure increases

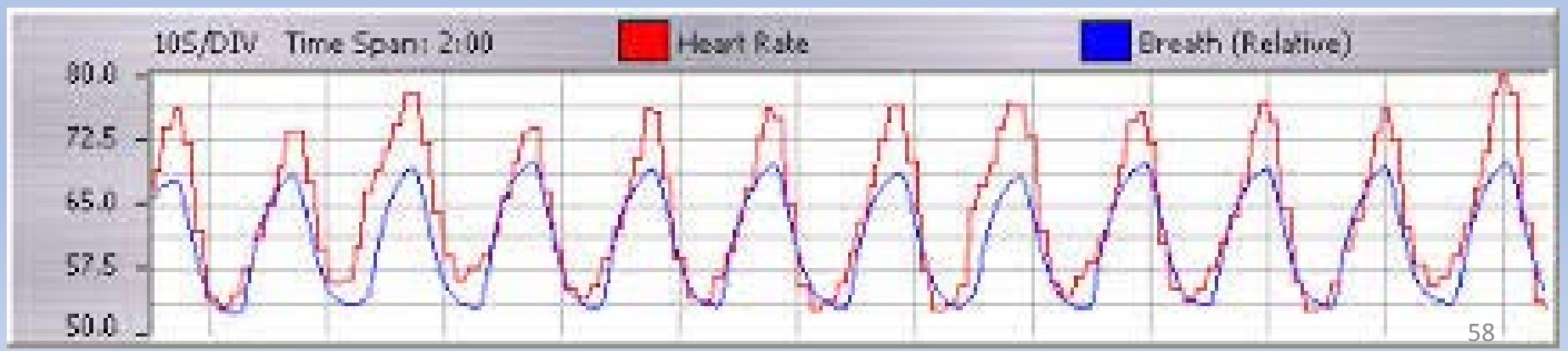
HR, blood flow decrease

Increasing the depth of respiration promotes venous return through changes in right atrial (chest cavity) pressure. During inspiration, the chest wall expands and the diaphragm descends, causing right atrial pressure to fall which facilitates venous return. When pressure falls and venous return rises, cardiac rate accelerates. During expiration, the opposite occurs. Increasing right atrial pressure impedes venous return and slows HR. Increasing the depth of ventilation increases the range of HR during respiration.

Attaining Coherence: Resonance Frequency Breathing (RFB)

- HRV is related to respiratory cycle
- At ~ 6 breaths/minute
  - HRV and respiratory cycle synchronize
  - HRV is maximized
  - Resonant Frequency Breathing
- 'Coherence'

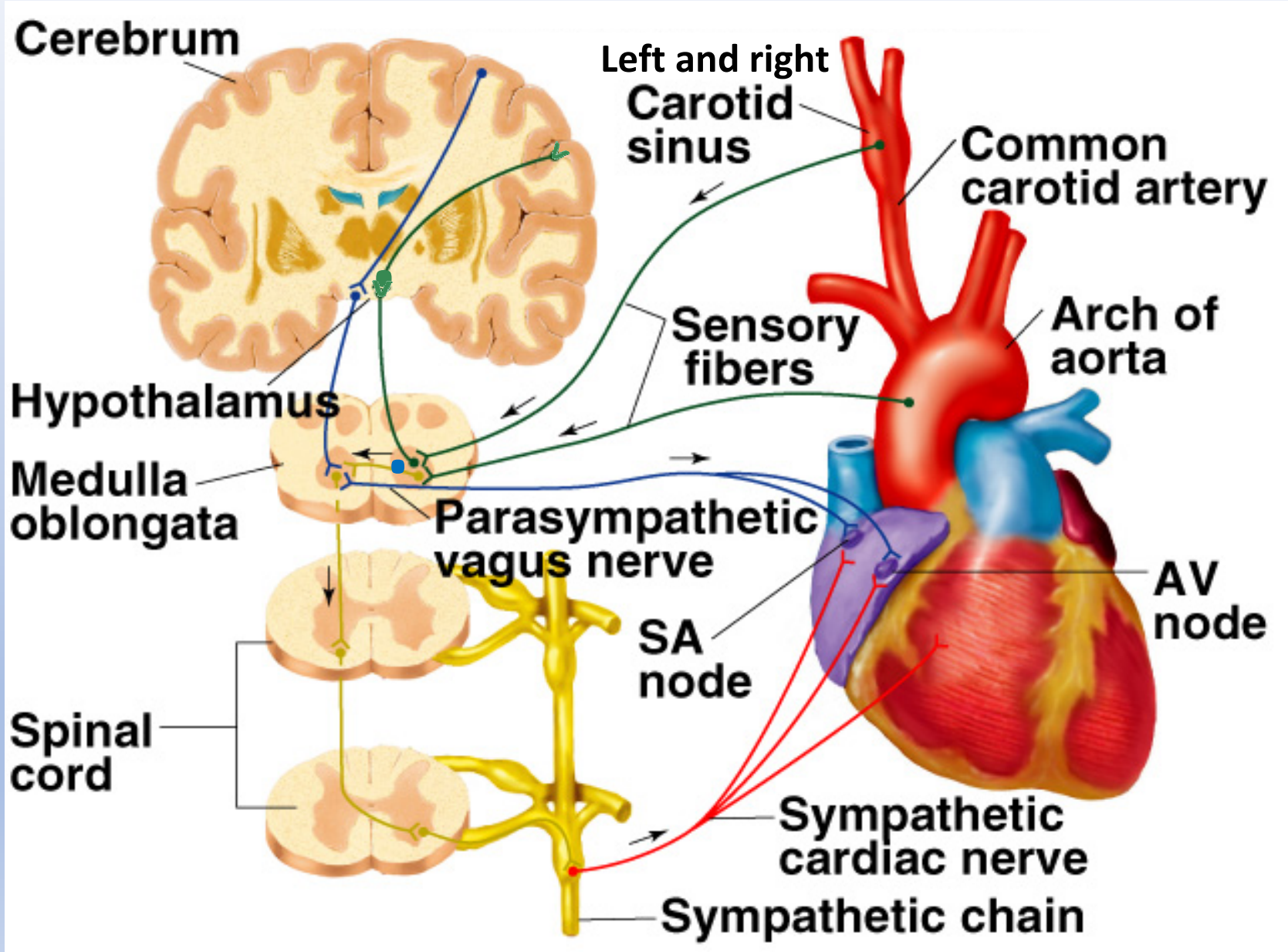
Note: 6 breaths/min=10 seconds per breath=0.1 Hz)



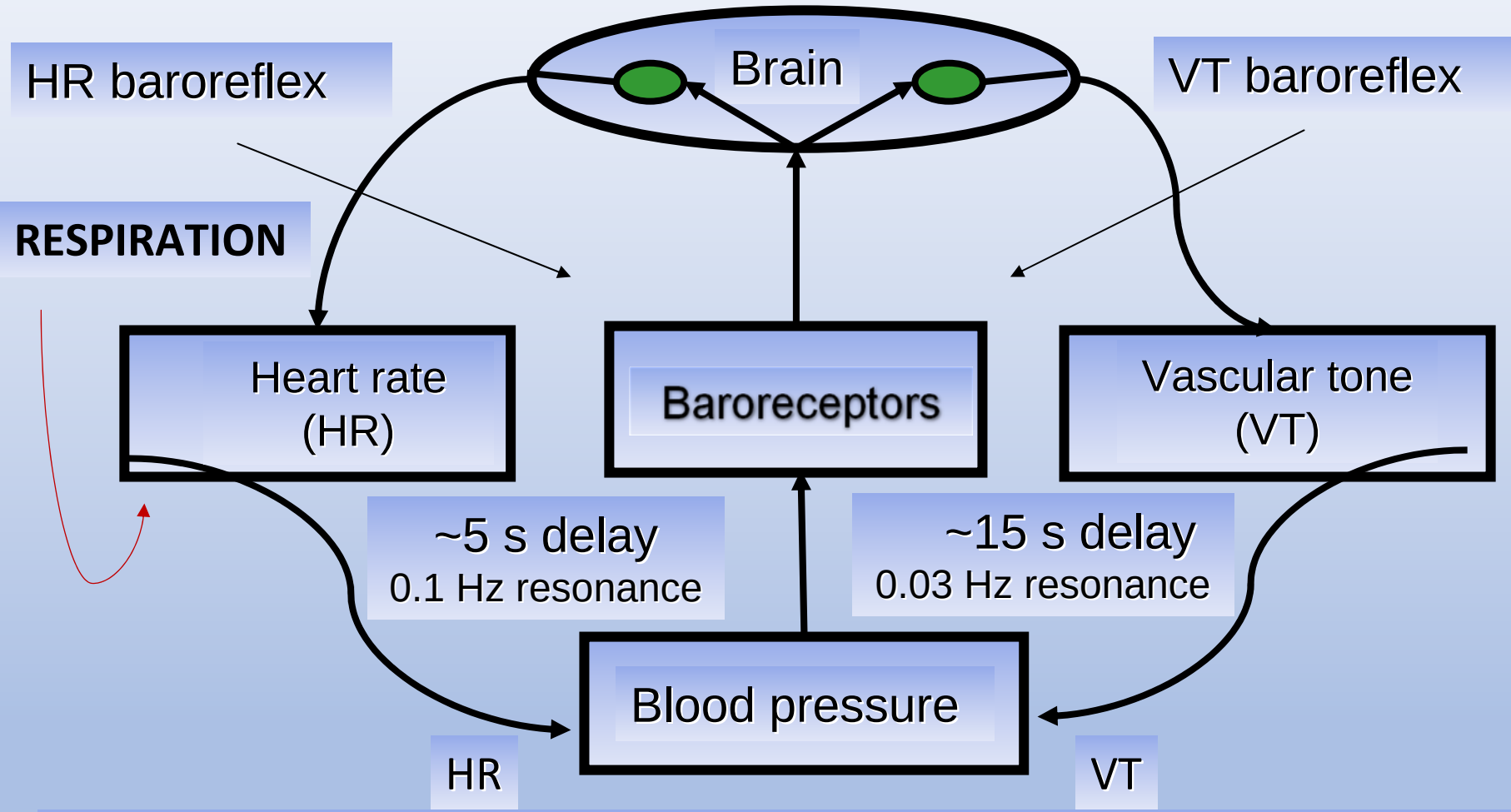
Resonance is the tendency of a system to oscillate with greater amplitude at some frequencies than at others. Relative maximum frequency of oscillation is the system's **resonance frequency**. At these resonance frequency, even small periodic driving forces can produce large amplitude oscillations

Pushing a person in a swing is an example of resonance. Pushing a swing in time with its resonant frequency will make the swing go higher and higher (maximum amplitude), while attempts to push it at a faster or slower tempo results in smaller arcs.

Baroreceptor Reflex Connections



Two Closed-Loops Model of Baroreflex System



Initiated by respiration, the baroreflex links HR and VT via CNS using feedback from blood pressure. Oscillations in each system reach maximum amplitude at resonance frequency.

Nervous system pathways shared by sensitized chronic pain and ASR:

-Somatosensory cortex

-Hypothalamus (periventricular nucleus) → dorsal spinal column

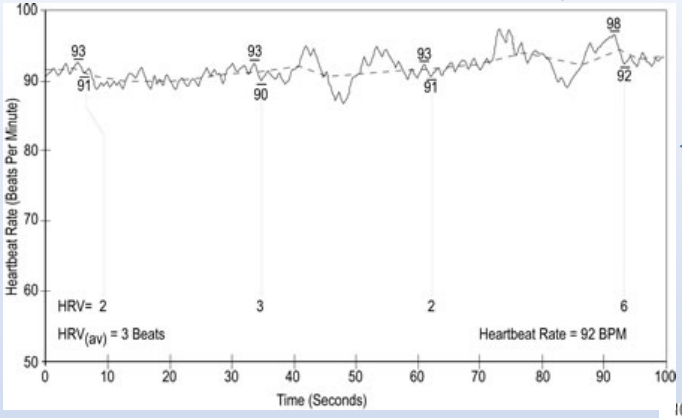
-HPA → adrenal cortex

-Adrenal cortex → glucocorticoids

-Peripheral pro-inflammatory cytokines

Coherence of Cardiac Rhythm

coherence.com (Richard Brown, MD and Stephen Elliot, Ph.D.)

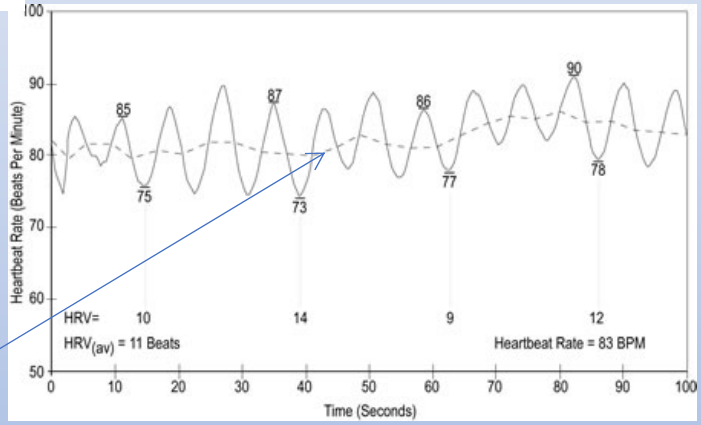


30 BrPM (0.5 Hz) , HRV(avg) = 2

7.5 BrPM (0.125 Hz), HRV(avg) = 11

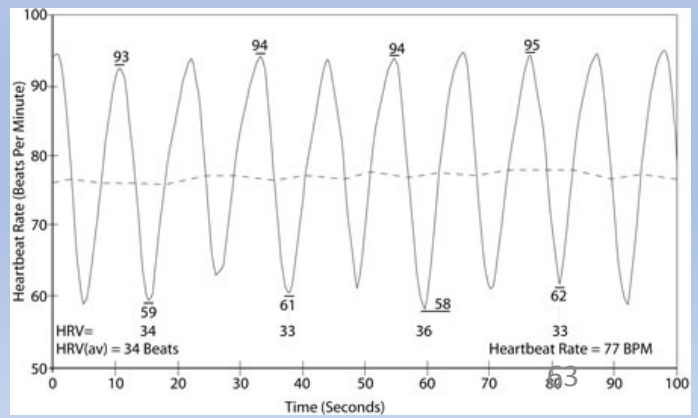
5.5 BrPM (0.092 Hz), HRV(avg) = 34

The difference between the highest and lowest BPM is shown along the center; averaging across consecutive maxima yields HRV(avg), one of the many measures of HRV



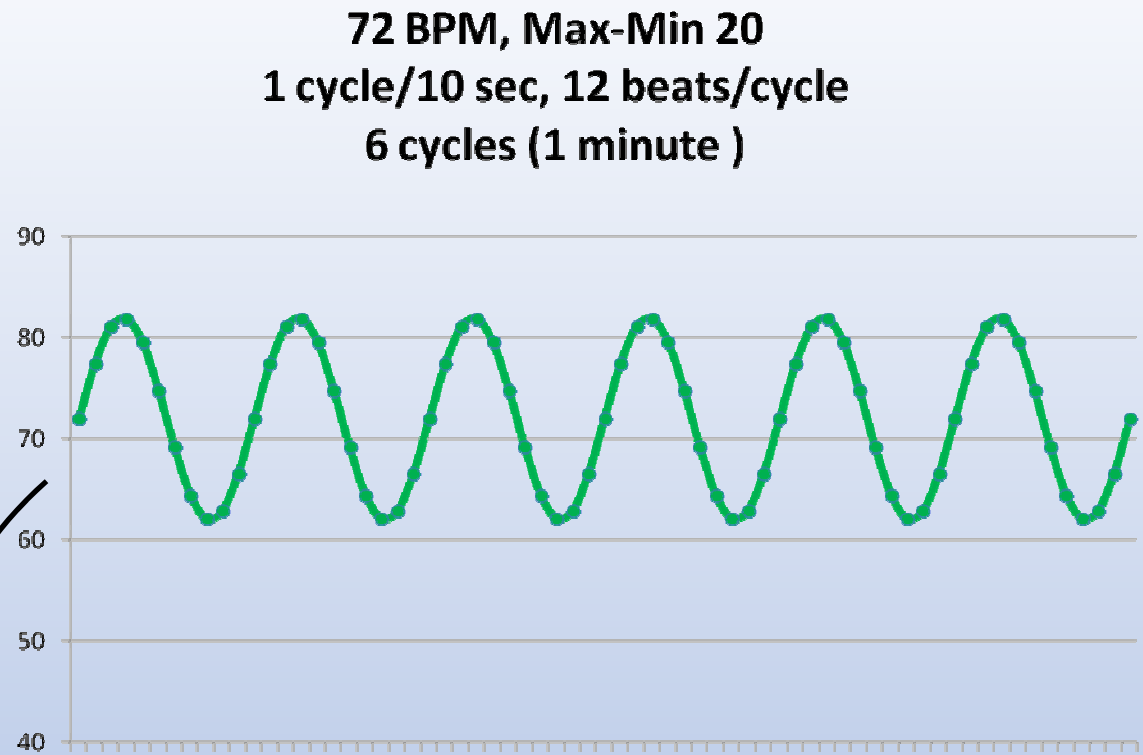
Baroreflex activates resonance ('Coherence')

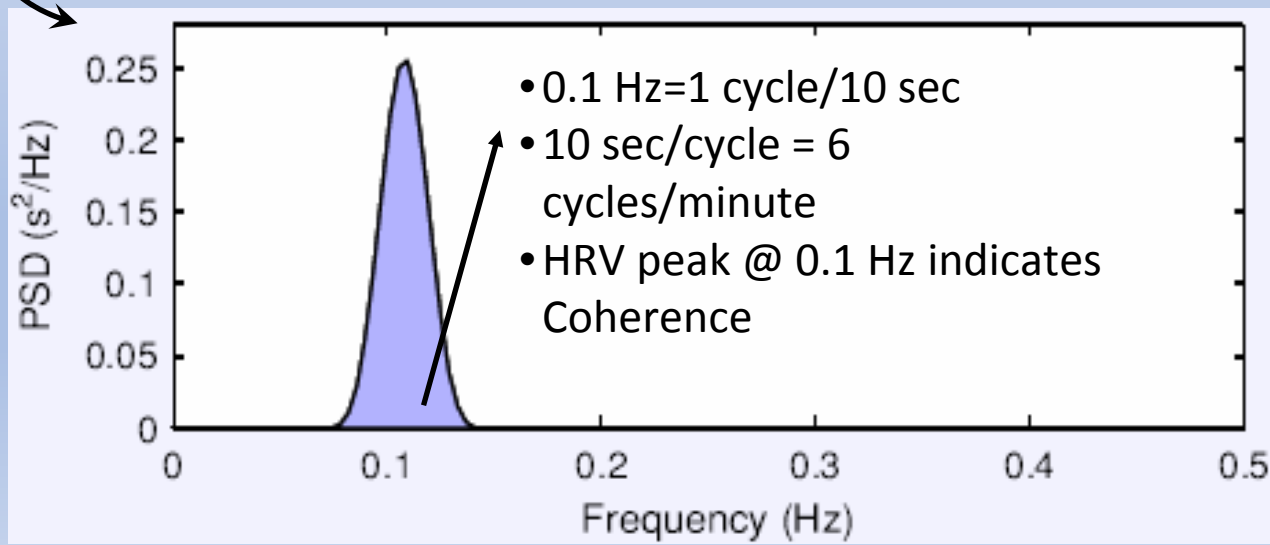
RFB →



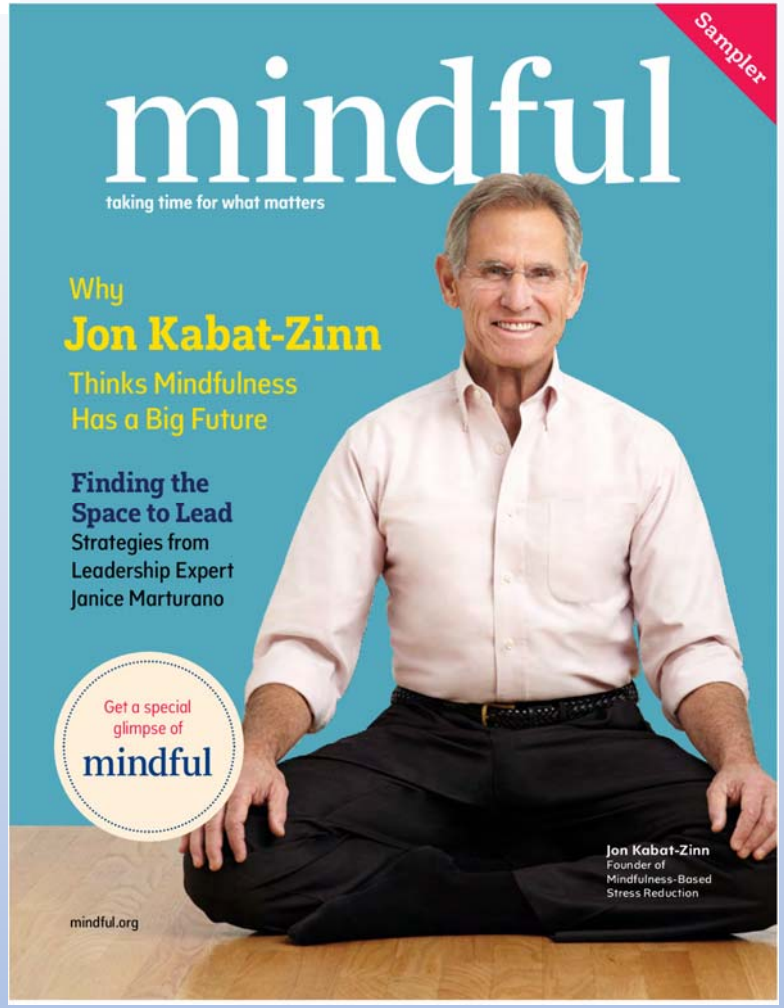
When HRV Coherence is attained, the spectral peak occurs at a frequency around 0.1 Hz

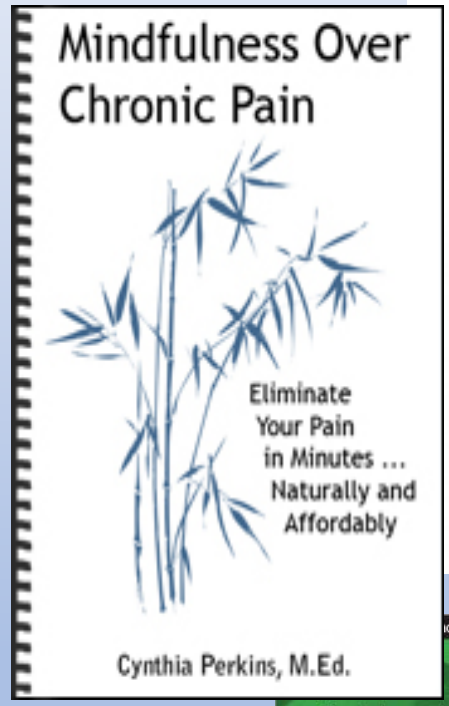
Transformation of a time series to a frequency spectrum is done with the Fourier transform. The transformed frequency spectrum is analyzed in terms of 'power' or area under the curve, across a range of frequencies. Power is directly related to variance of the untransformed time series.

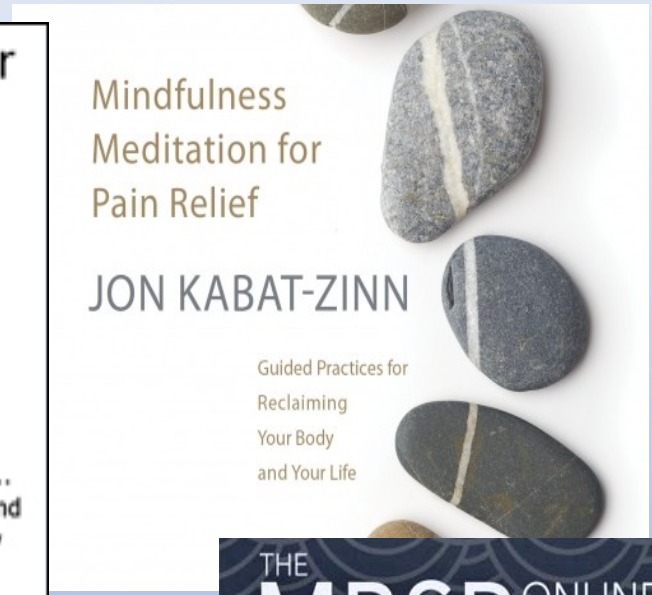


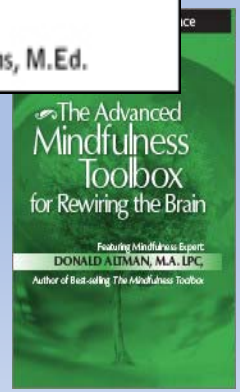


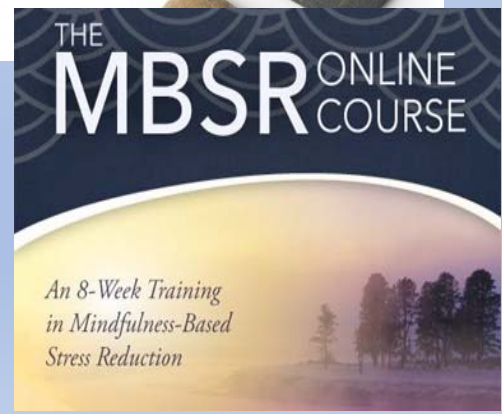
Mindfulness books, cd's, online courses, ceu's











Mindfulness Defined

"Moment-to-moment non-judgmental awareness"

Mindfulness in Practice

- Body Scanning
  - Lying on back
  - Quiet
  - Focus attention on organs
- Mindfulness (meditation)
  - Secular
- Yoga postures

Effects of Mindfulness

- Improves quality of life
- No evidence that Mindfulness prevents or cures disease
  - Not recommended to lower blood pressure

Exploring the Promise of Mindfulness as Medicine

Laura Ruchinski

A new frontier in treatment for mental illnesses and other chronic conditions may not come from pharmaceutical companies, but from within, as mindfulness practices gain traction.

Mindfulness practices as we know them today are rooted in 2500-year-old Buddhist meditation practices and are often described as "...paying attention to the present moment's experiences with openness, curiosity, and a willingness to be with what is" (http://marc.ucla.edu/). Herbert Benson, MD, founder of the Benson-Henry Institute for Mind Body Medicine at Massachusetts General Hospital, is often credited with bringing mindfulness into the realm of Western medicine. His 1975 book The Relaxation Response outlined techniques to combat the harmful effects of stress with relaxation methods similar to meditation.

These practices did not stay lodged in the 1970s like a macramé plant holder, however. Several structured mindfulness programs have since been developed and are being implemented in clinical practice. One of these is mindfulness-based stress reduction (MBSR), pioneered by Jon Kabat-Zinn, PhD, MPH, founding executive director of the Center for Mindfulness in Medicine, Health Care, and Society at the University of Massachusetts Medical School (http://tinyurl.com/KabatZinnMBSR).

Another is mindfulness-based cognitive therapy (MBCT), a blend of MBSR and cognitive-behavioral therapy established by Zindel Segal, PhD, a cognitive psychologist at the University of Toronto, along with colleagues Mark Williams, PhD, and John Teasdale, PhD (http://1.usa.gov/1eOquCo).

According to Gregory Lewis Fricchione, MD, director of the Benson-Henry Institute, "...mindfulness and other meditative techniques can provide adjunctive benefits for health and that includes mental health."

Fricchione does acknowledge pockets of resistance. "Many physicians who consider themselves grounded in Western science will see mindfulness-based programs for mental health disorders as being somewhat foolish and relatively impotent in treating mental disorders, especially severe ones," he said.

That attitude may be slowly changing as researchers have begun to systematically investigate the effects of mindfulness interventions for various physical and mental health conditions, including cancer, stress, multiple sclerosis (MS), pain, anxiety, and depression (http://1.usa.gov/15JXT3R). The results of these studies may help inform physicians of the effectiveness and possible uses of mindfulness interventions in clinical practice.

Why the Growing Trend?

According to a recent work, 79% of medical schools offer some element of mindfulness training. Noted eminent psychologist David Black, PhD, MPH, director of the Ameri-

Journal of the American Medical Association, 314(13), 1327-1329 (October 6, 2015)

AUTONOMIC SELF-REGULATION

Mindful attention

RFB

PES
Compassion, gratitude, etc

HRV

HRV COHERENCE

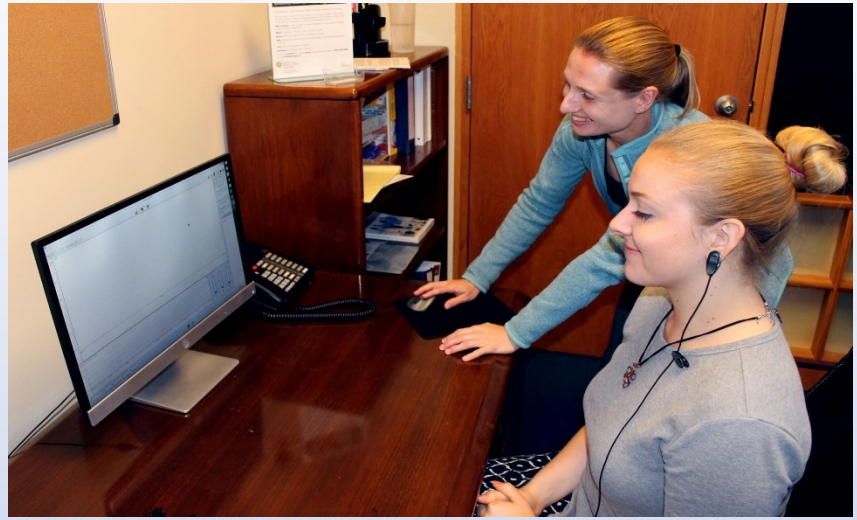
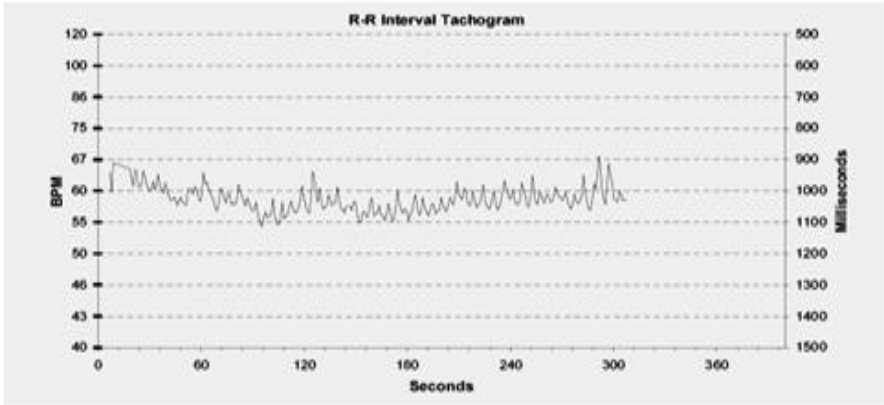


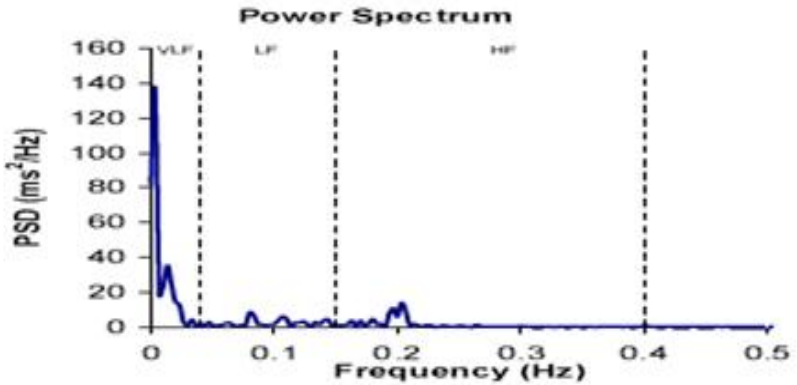
Figure 1 (a – d) depicts the Pre-Post HRVB Training the R-R Interval Tachogram and Power Spectra Density of one PTSD+ subject.

Pre-Training

(a)

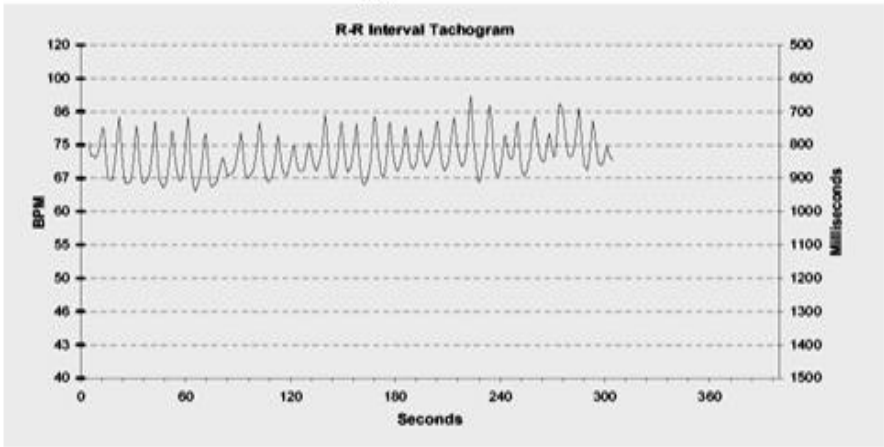


(b)

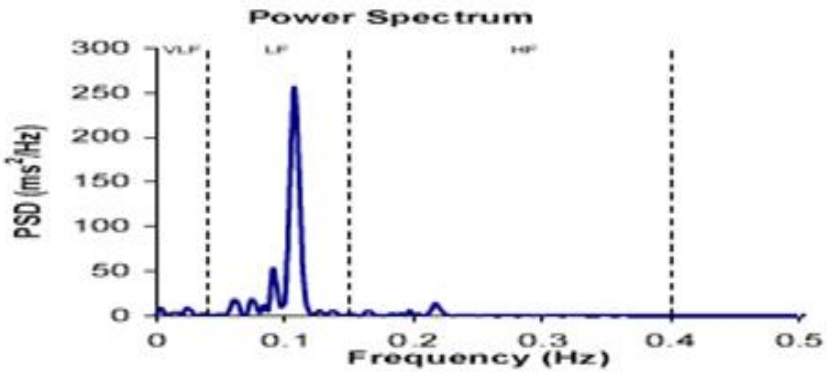


Post-Training

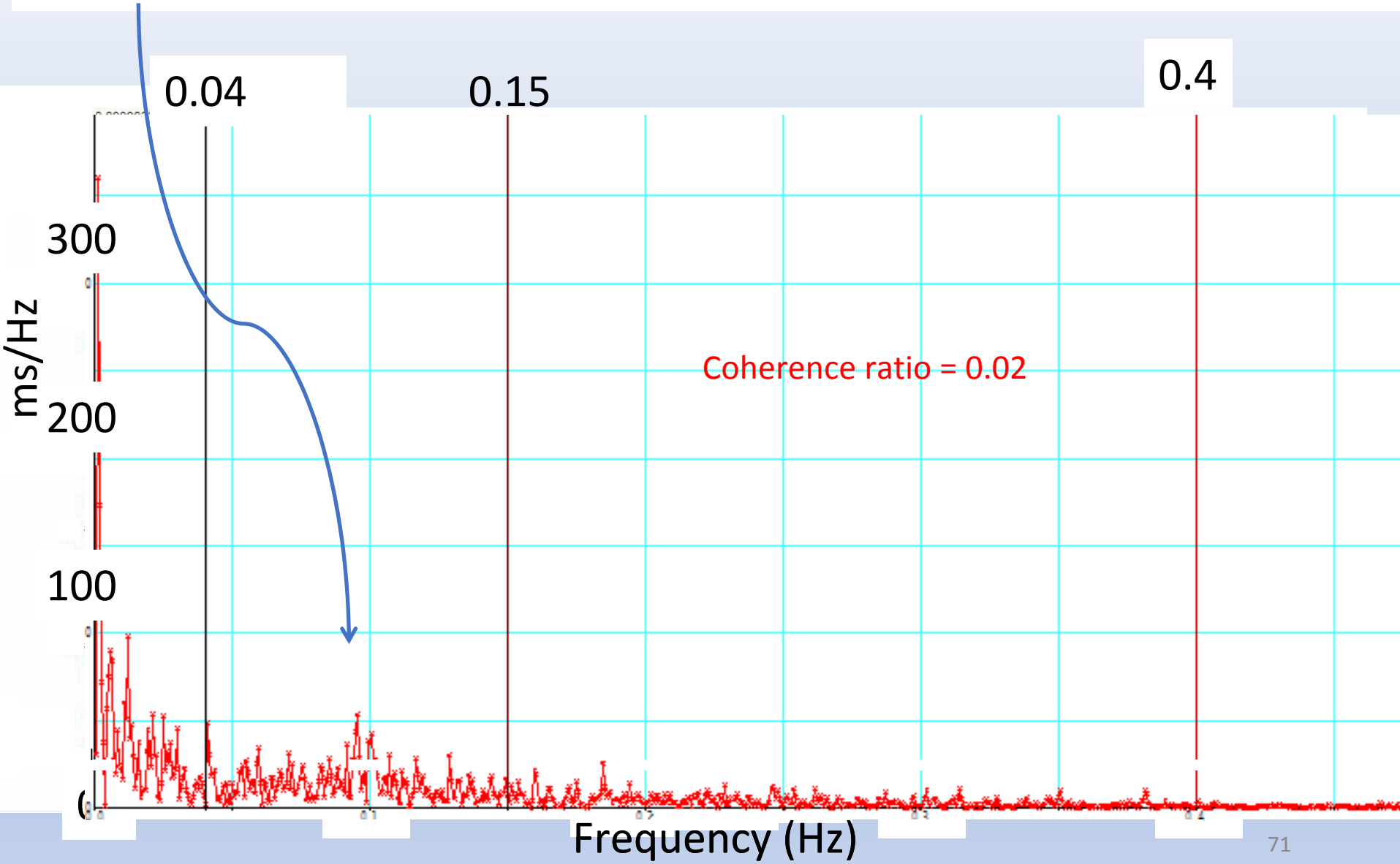
(c)



(d)

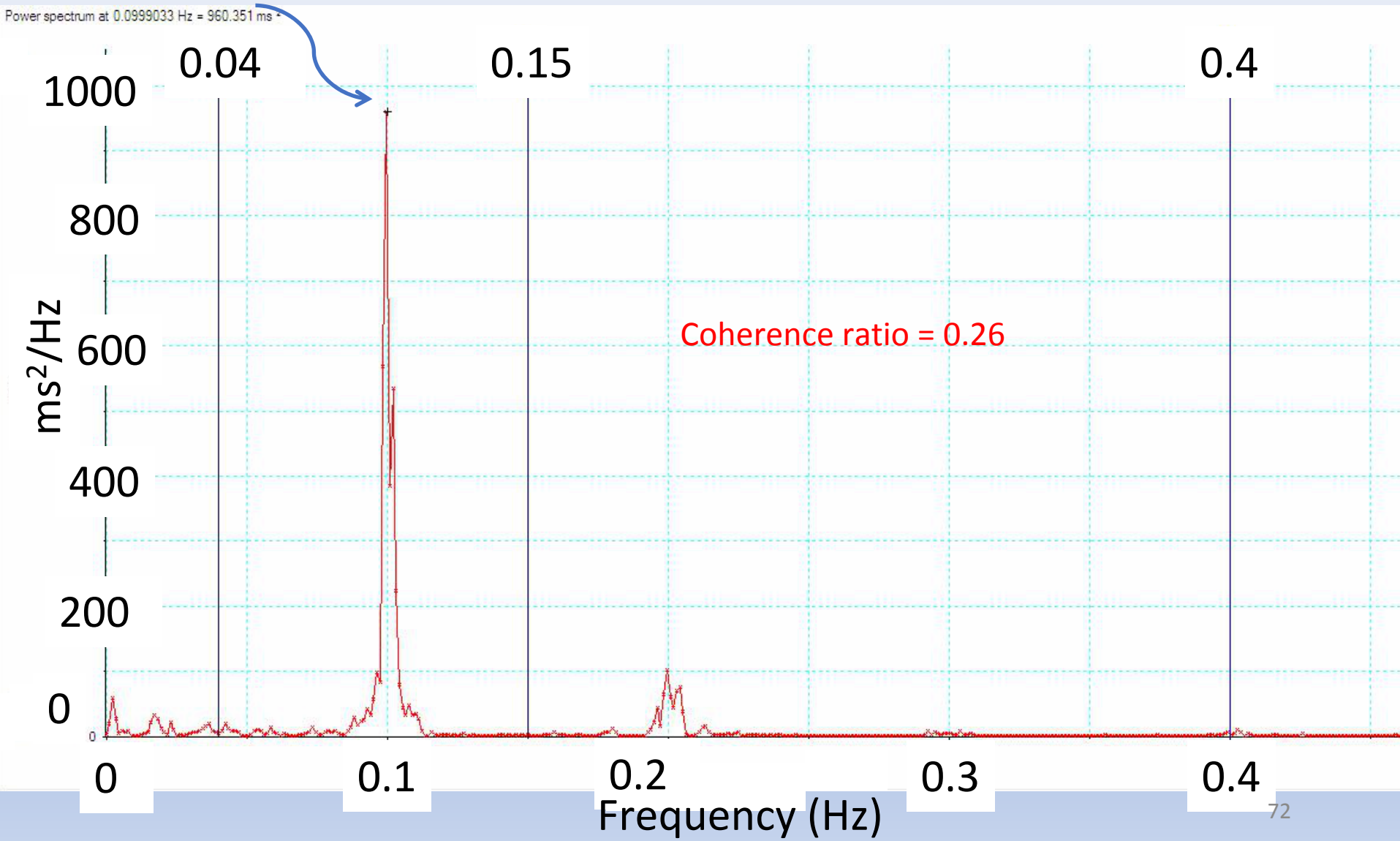


Peak Power at 0.095 Hz = 53.5 ms/Hz ; Total LF power = 3695.9 ms²/Hz



HRV Power Spectrum

Peak Power at 0.099 Hz = 960.4 ms^2 ; Total LF Power = 2344.4 ms^2/Hz



II. Research in Application of ASR for SCP

Lorimer Moseley, a globally known Australian pain researcher, tells this story about himself:

He was hiking in the Australian Outback with friends when he felt something scratch his left ankle. It was painful enough to make him pull his leg away, but he just kept walking, figuring he'd scraped his ankle on a stick. He woke up two days later in a hospital where doctors told him he'd been bitten by the deadly poisonous eastern brown snake, and was lucky to be alive.

Being resilient, he was out hiking again six months later when he was stopped dead in his tracks by a searing pain in his left ankle. He fell to the ground and screamed for help. His friends called an ambulance but and when they examined him they found a twig stuck in his sock. Yet, his ankle continued to hurt, he had groin pain for a week (just as he had after the snake bite), and he could not talk himself out of it.

ASR
Coherence
Autonomic Balance

Chronic Stress, Pain
Sensitization
Symptom Cluster

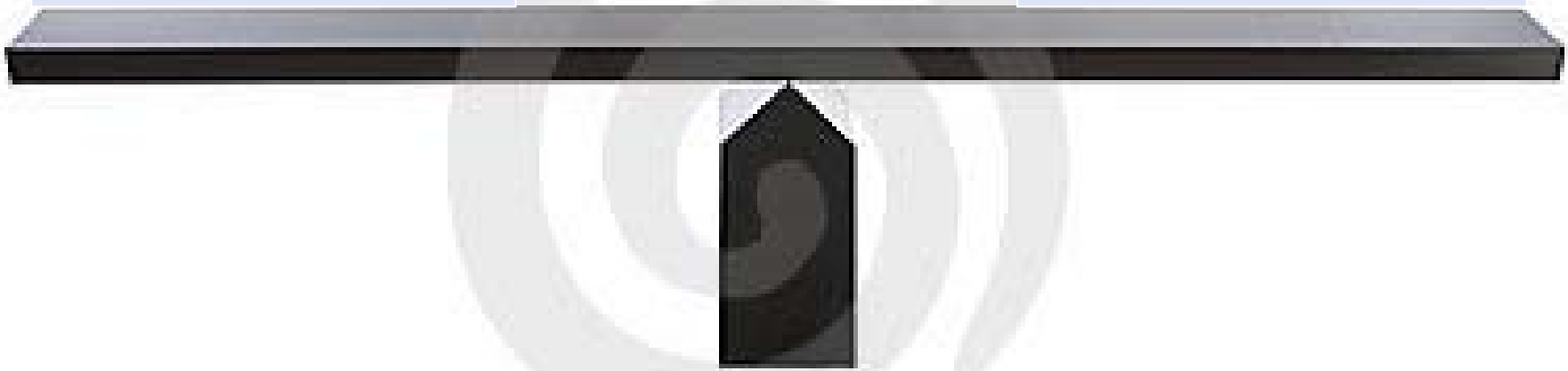
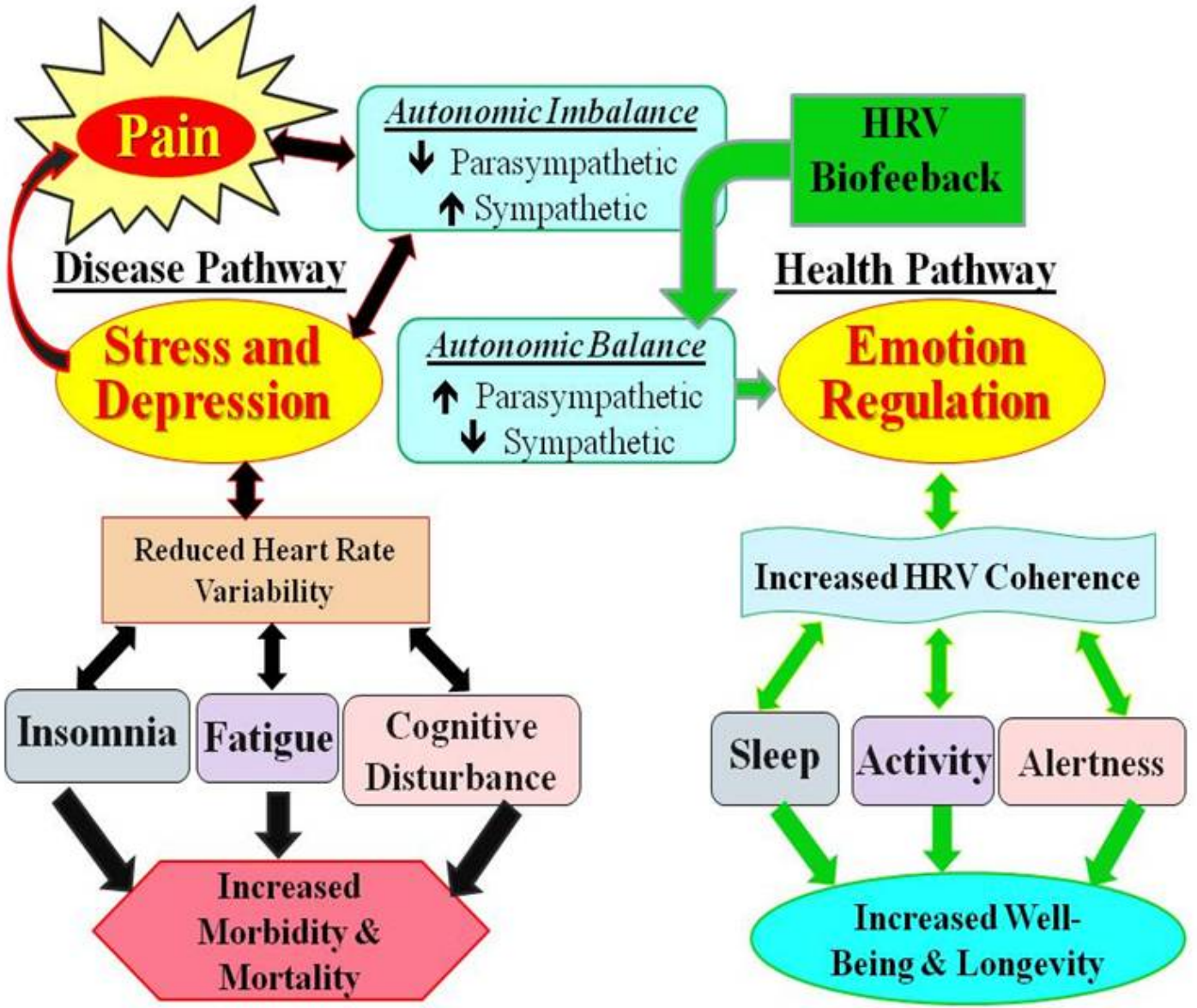
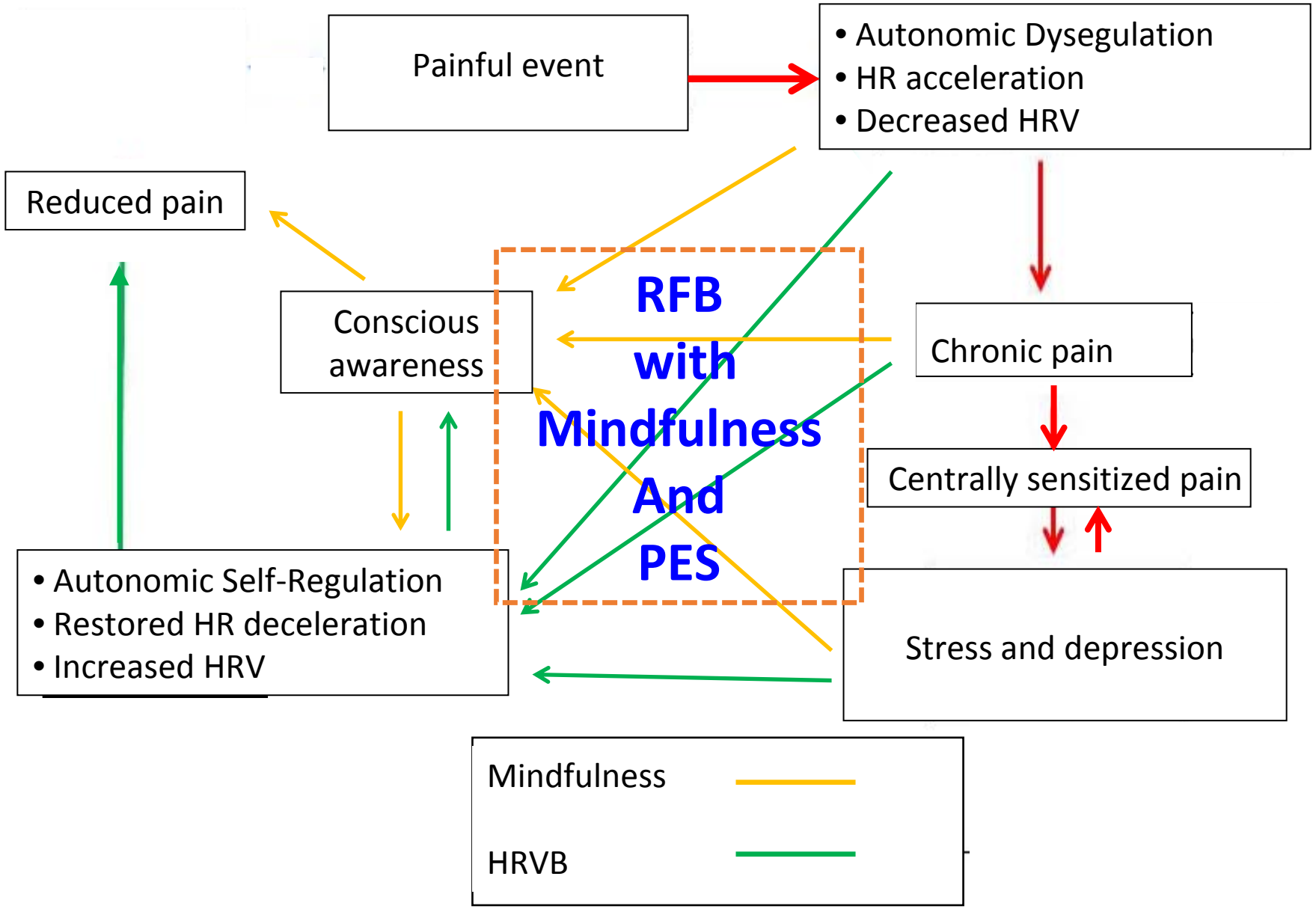


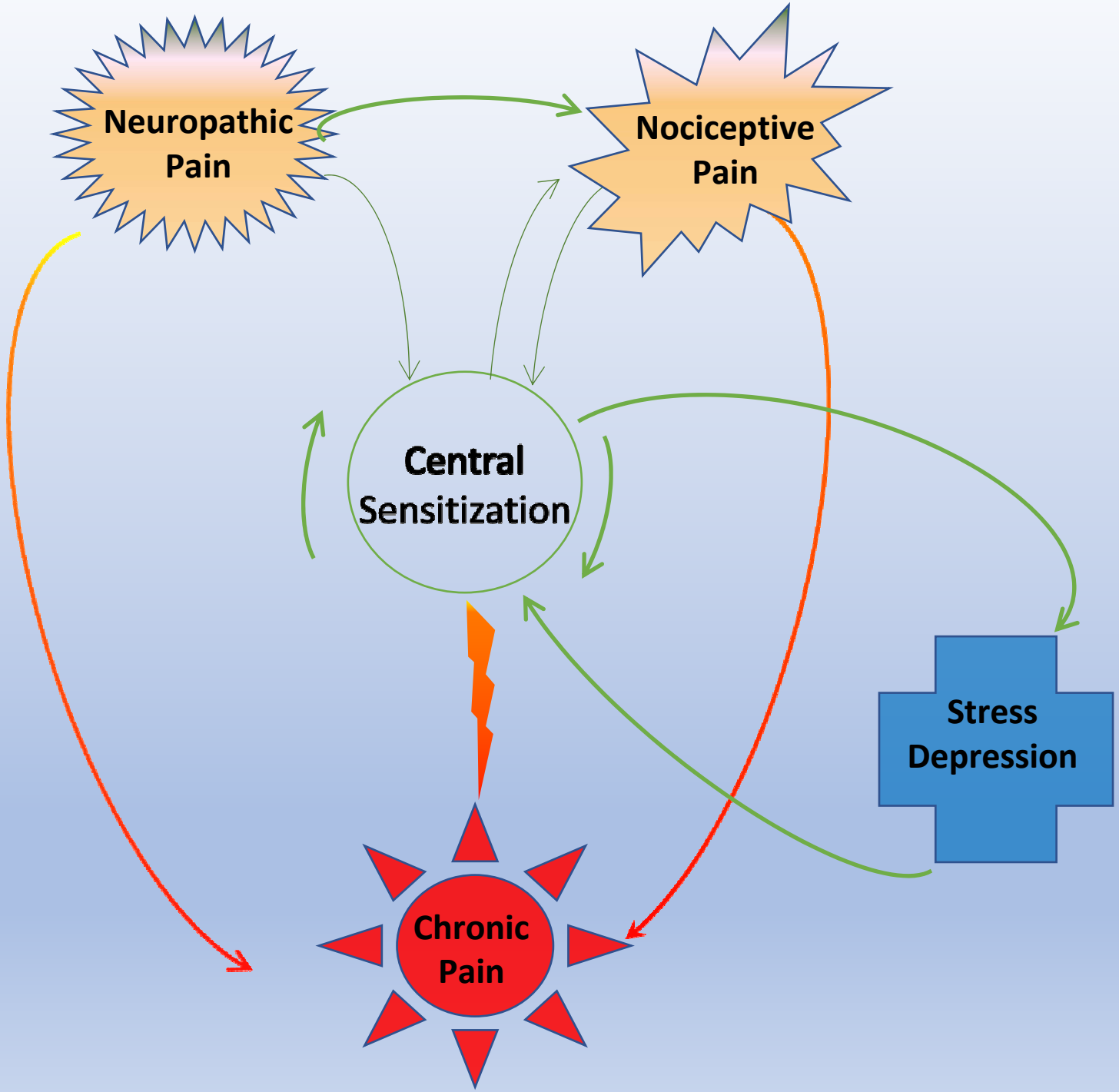
Fig. 1. HRV Biofeedback reduces effects of chronic pain

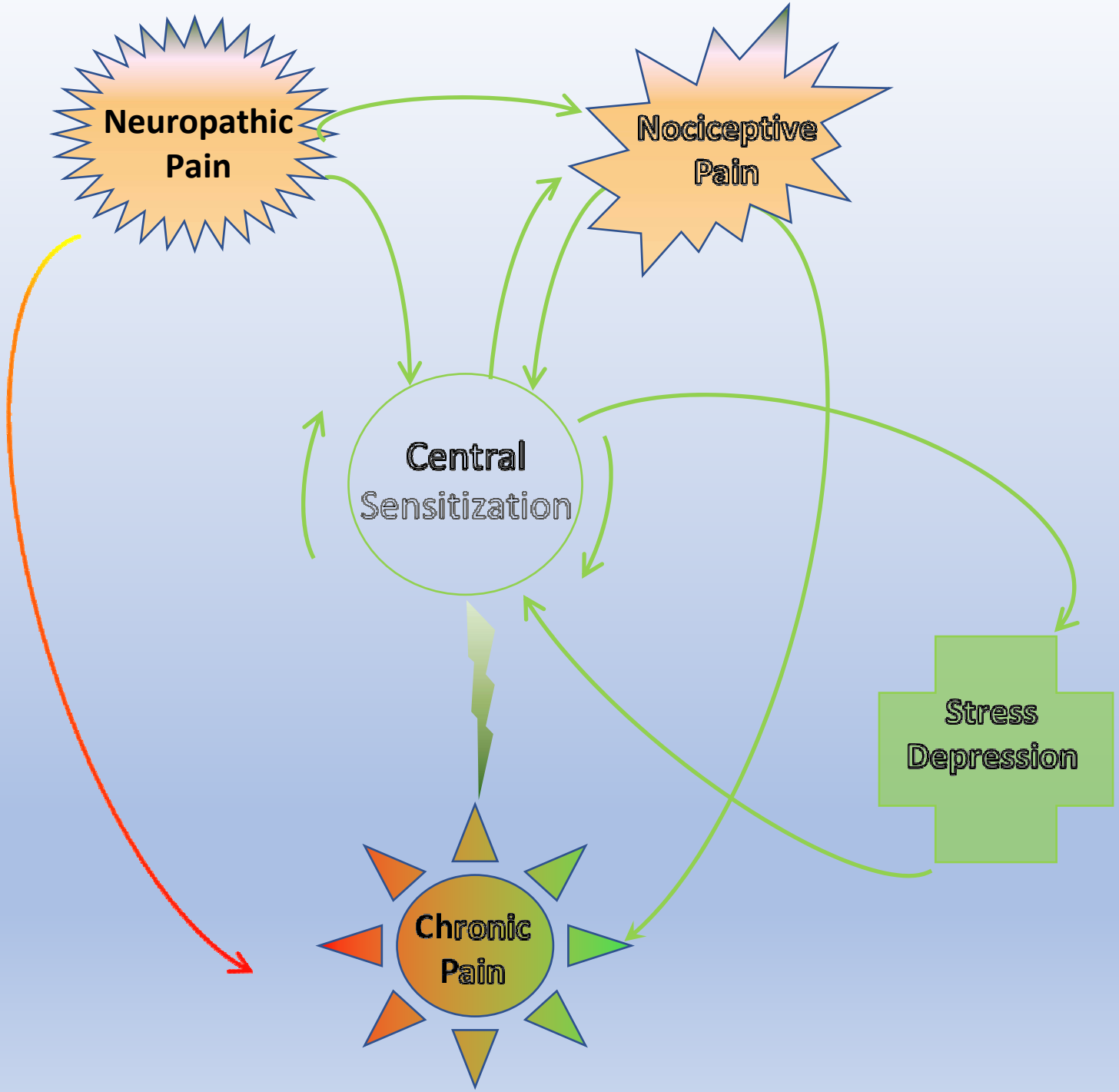


Chronic pain causes central sensitization and loss of negative feedback regulation of the stress response, leading to autonomic imbalance, allostatic stress, and depressed mood (Disease Pathway). When autonomic balance is restored, stress is reduced and emotional regulation is recovered (Health Pathway).



Management of Centrally Amplified Pain using Autonomic Self-Regulation


Neuropathic Pain
Nociceptive Pain
Central Sensitization
Stress Depression
Chronic Pain


Neuropathic Pain
Nociceptive Pain
Central Sensitization
Stress Depression
Chronic Pain

Study 1 – “Non-pharmacological intervention for chronic pain in Veterans: A pilot study of Heart Rate Variability”

Study 2 – “Use of Heart Rate Variability (HRV) Biofeedback for Symptom Management among Cancer Survivors”

Study 3 – “HRV Biofeedback in pain patients: Pilot intervention for pain, fatigue, & sleep”

Study 1 – “Non-pharmacological intervention for chronic pain in Veterans: A pilot study of Heart Rate Variability”

PILOT STUDY

Non-pharmacological Intervention for Chronic Pain in Veterans: A Pilot Study of Heart Rate Variability Biofeedback

Melanie E. Berry, MS, *United States*; Iva T. Chapple, MD, *United States*; Jay P. Ginsberg, PhD, *United States*; Kurt J. Gleichauf, PhD, *United States*; Jeff A. Meyer, PhD, *United States*; Madan L. Nagpal, PhD, *United States*

Author Affiliations
Wm. Jennings Bryan Dorn VA Medical Center, Columbia, South Carolina.

Correspondence
Jay P. Ginsberg, PhD
Jay.Ginsberg@va.gov

Citation
Global Adv Health Med. 2014;3(2):28-33. DOI: 10.7453/gahmj.2013.075

Key Words
Coherence, heart rate variability (HRV), HRV coherence biofeedback (HRVCB); chronic pain, non-pharmacological intervention

Disclosure
The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and had no conflicts to disclose.

ABSTRACT

Objective: Chronic pain is an emotionally and physically debilitating form of pain that activates the body's stress response and over time can result in lowered heart rate variability (HRV) power, which is associated with reduced resiliency and lower self-regulatory capacity. This pilot project was intended to determine the effectiveness of HRV coherence biofeedback (HRVCB) as a pain and stress management intervention for veterans with chronic pain and to estimate the effect sizes. It was hypothesized that HRVCB will increase parasympathetic activity resulting in higher HRV coherence measured as power and decrease self-reported pain symptoms in chronic pain patients.

Study Design: Fourteen veterans receiving treatment for chronic pain were enrolled in the pre-post intervention study. They were randomly assigned, with 8 subjects enrolled in the treatment group and 6 in the control group. The treatment group received biofeedback intervention plus standard care, and the other group received standard care only. The treatment group received four HRVCB training sessions as the intervention.

Measures: Pre-post measurements of HRV amplitude, HRV power spectrum variables, cardiac coherence, and self-ratings of perceived pain, stress, negative emotions, and physical activity limitation were made for both treatment and control groups.

Results: The mean pain severity for all subjects at baseline, using the self-scored Brief Pain Inventory (BPI), was 26.71 (SD=4.46; range=21-35) indicating a moderate to severe perceived pain level across the study subjects. There was no significant difference between the treatment and control groups at baseline on any of the measures. Post-HRVCB, the treatment group was significantly higher on coherence (P=.01) and lower (P=.02) on pain ratings than the control group. The treatment group showed marked and statistically significant (1-tailed) increases over the baseline in coherence ratio (191%, P=.04) and marked, significant (1-tailed) reduction in pain ratings (36%, P<.001), stress perception (16%, P=.02), negative emotions (49%, P<.001), and physical activity limitation (42%, P<.001). Significant between-group effects on all measures were found when pre-training values were used as covariates.

Conclusions: HRVCB intervention was effective in increasing HRV coherence measured as power in the upper range of the LF band and reduced perceived pain, stress, negative emotions, and physical activity limitation in veterans suffering from chronic pain. HRVCB shows promise as an effective non-pharmacological intervention to support standard treatments for chronic pain.

The pre- treatment values for control and treatment groups were not statistically different for self-ratings of pain, negative emotion, physical activity limitation, or stress.

Table 1 Demographics

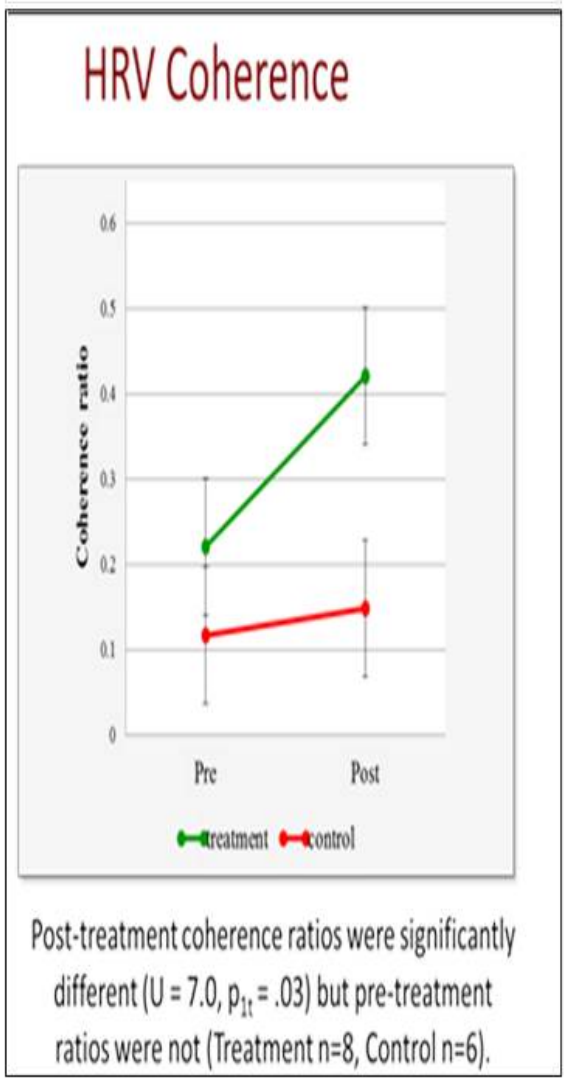
	Control	Treatment
	n (%)	n (%)
Total	6 (43)	8 (57)
Male	6 (100)	7 (88)
	Mean (SD)	Mean (SD)
Age (y)	44.8 (7.4)	44.5 (6.6)

Table 2 Pre- and Post-training Measures for Both Groups, Mean (SD)

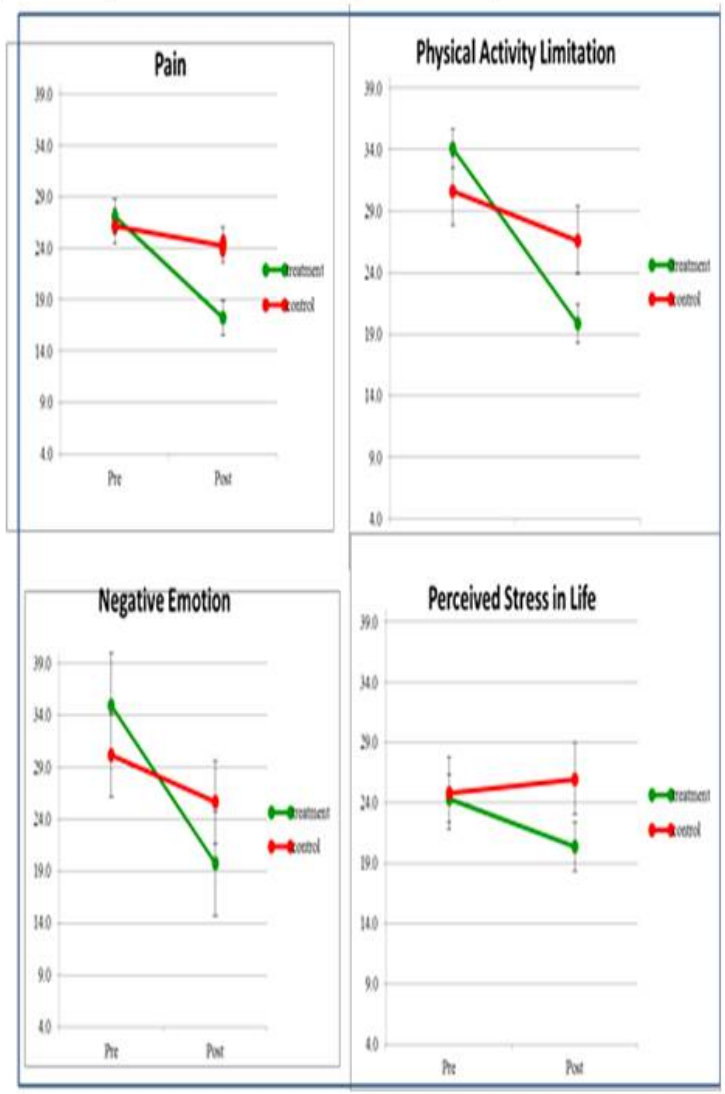
Variable	Control	Treatment	t-value[a]	P[b]	95% CI of difference
Coherence_Pre	0.12 (0.07)	0.22 (0.19)	−1.2	.24	(−0.3, 0.8)
Coherence_Post	0.15 (0.09)	0.42 (0.24)	−2.6	.02	(−0.5, −0.1)
Pain_Pre	26.2 (4.2)	27.1 (4.9)	−0.4	.70	(−6.4, 4.5)
Pain_Post	24.3 (6.9)	17.3 (4.6)	2.3	.04	(0.4, 13.8)
Stress_Pre	24.8 (6.8)	24.4 (5.8)	0.1	.90	(−6.8, 7.8)
Stress_Post	26.0 (6.9)	20.4 (6.1)	1.6	.14	(−1.9, 13.2)
Neg_Emotion_Pre	30.2 (9.7)	35.0 (3.5)	−1.2	.28	(−15.0, 5.3)
Neg_Emotion_Post	25.7 (12.7)	19.8 (10.4)	1.0	.36	(−7.5, 19.4)
Activ_Red_Pre	30.7 (7.1)	34.1 (4.6)	−1.1	.30	(−10.2, 3.3)
Activ_Red_Post	26.7 (11.6)	19.9 (10.4)	1.2	.26	(−6.1, 19.7)

[a] Independent t-test, 12 df, all variances equal except Neg_Emotion_Pre.
[b] 2-tail.
Abbreviations: Activ_Red, activity reduction; CI, confidence interval; Neg_Emotion, negative emotion.

Figure 4. Changes in HRV Coherence and their associated effect on measures of pain, physical activity, negative emotion, and perceived stress in Veterans with chronic pain who received HRV-B + standard care (green lines) vs only standard care (red lines).



Post-treatment coherence ratios were significantly different ($U = 7.0$, $p_{1t} = .03$) but pre-treatment ratios were not (Treatment n=8, Control n=6).



Treatment effects were analyzed with ANCOVA of post scores by group, using pre scores as the covariate.

Post-HRVB training, the treatment group was significantly lower than the control group on all outcome measures (all p's <0.05).

Table 3 Pre-Post Changes of Measures in the Active HRVCB Treatment Group, Mean (SD)

Variable	Pre	Post	% Change	Corr_Coeff (P[a])	t-value[b]	P[a]	95% CI of difference
Coherence	0.22 (0.19)	0.42 (0.24)	191	–0.05 (0.45)	–1.8	.05	(–0.5, 0.0)
Pain	27.1 (4.9)	17.3 (4.6)	–36	0.52 (0.09)	6.0	<.001	(6.0, 13.7)
Stress	24.4 (5.8)	20.4 (6.1)	–16	0.70 (0.03)	2.5	.02	(0.2, 7.84)
Neg_Emotion	35.0 (3.5)	19.8 (10.4)	–49	0.53 (0.08)	4.8	<.001	(7.7, 22.8)
Activ_Red	34.1 (4.6)	19.9 (10.4)	–42	0.22 (0.30)	3.9	<.001	(–16.0, –7.72)

[a] 1-tail.
[b] dependent t-test, df 7.
Abbreviations: Activ_Red, activity reduction; CI, confidence interval; Corr Coeff, correlation coefficient; Neg_Emotion, negative emotion.

Study 2 – “Use of Heart Rate Variability (HRV) Biofeedback for Symptom Management among Cancer Survivors”

GREENVILLE HEALTH SYSTEM

GREENVILLE HEALTH SYSTEM
Cancer Institute
Center for Integrative Oncology & Survivorship

UNIVERSITY OF SOUTH CAROLINA
Arnold School of Public Health

...ility Biofeedback for Symptom Management among Cancer Survivors

Mark A. O'Rourke, MD, Medical Director
Center for Integrative Oncology and Survivorship
Greenville Health System Cancer Institute
Greenville, South Carolina

Investigators and Staff

Greenville Health System

- Mark A. O'Rourke, MD, co-PI
- Regina Franco, MSN, ANP-C
- Kerri Susko, MSW, LISW-CP
- William M. Hendry, DOM, L.Ac.
- Elizabeth Crowley, Ph.D, RN, LMSW
- Sherry A. Stokes, M.S.
- W. Larry Gluck, M.D.
- Katie Daniels, BS

University of South Carolina

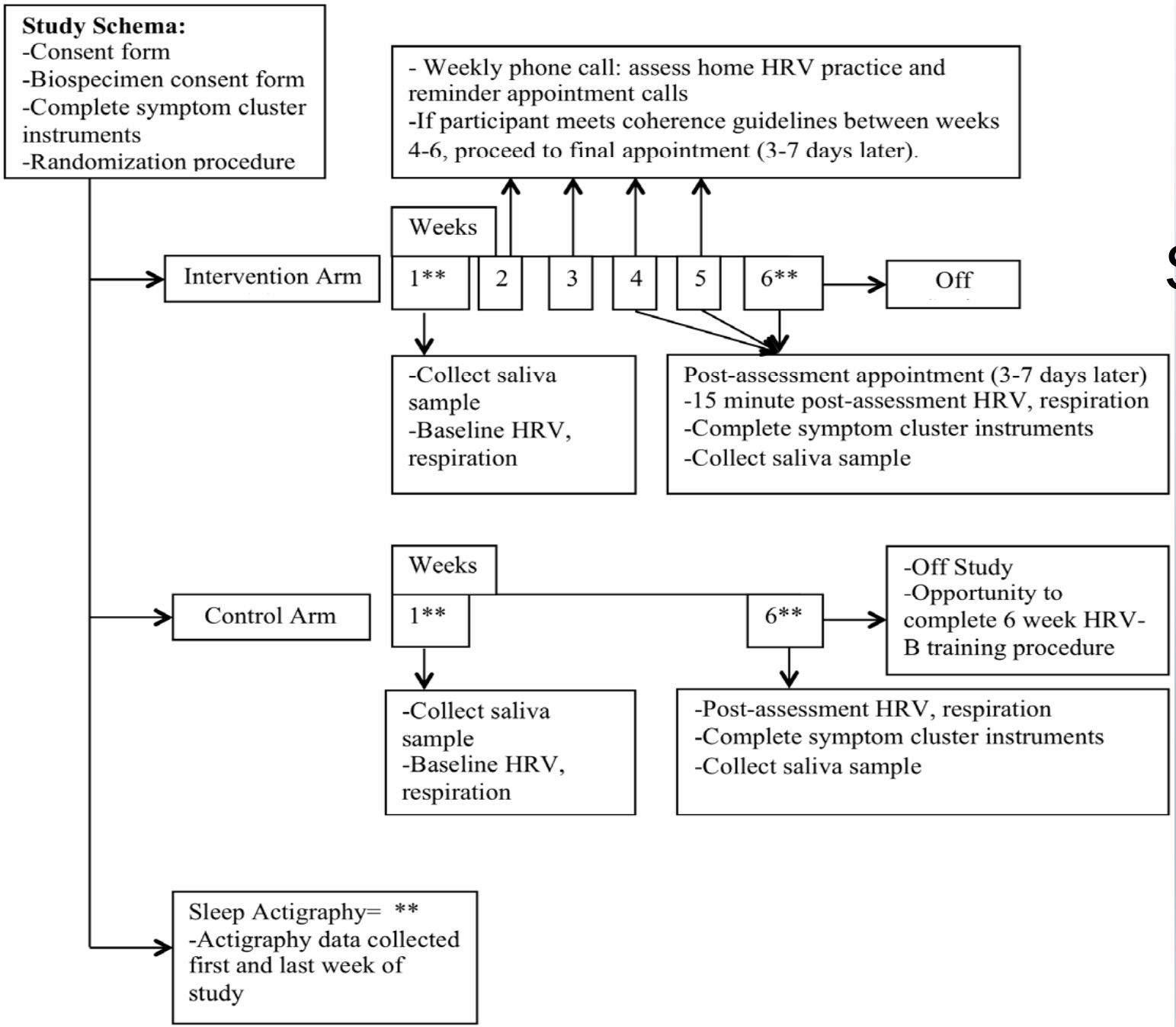
- James Burch, MS, Ph.D, co-PI
- J.P. Ginsberg, Ph.D.
- Jameson Sofge, MS
- James Hébert, MSPH, ScD

Background:
Cancer survivors have lower HRV coherence than normal controls and HRVB training improves HRV coherence, restores autonomic health

Research Question:
Will HRVB reduce late effects of cancer and its treatment, including stress, pain, depression, fatigue, and insomnia?

Method:
Randomized, waitlist controlled, clinical trial. Participants in the intervention arm receive weekly HRV-B training up to six weeks; a wait-list control group was matched to the intervention arm. Outcome measures were assessed at baseline (pre) and after week six (post)

Schema


Study Schema:
-Consent form
-Biospecimen consent form
-Complete symptom cluster instruments
-Randomization procedure
- Weekly phone call: assess home HRV practice and reminder appointment calls
-If participant meets coherence guidelines between weeks 4-6, proceed to final appointment (3-7 days later).
Weeks
Intervention Arm
1**
2
3
4
5
6**
Off
-Collect saliva sample
-Baseline HRV, respiration
Post-assessment appointment (3-7 days later)
-15 minute post-assessment HRV, respiration
-Complete symptom cluster instruments
-Collect saliva sample
Weeks
Control Arm
1**
6**
-Off Study
-Opportunity to complete 6 week HRV-B training procedure
-Collect saliva sample
-Baseline HRV, respiration
-Post-assessment HRV, respiration
-Complete symptom cluster instruments
-Collect saliva sample
Sleep Actigraphy= **
-Actigraphy data collected first and last week of study

Symptom Cluster Assessment

- ***STRESS***
  - ***Perceived Stress Scale (PSS)***
- ***DEPRESSION***
  - ***Beck Depression Inventory–II (BDI-II0***
- ***FATIGUE***
  - ***Multidimensional Fatigue Inventory (MFI)***
- ***PAIN***
  - ***Brief Pain Inventory (BPI)***
- ***SLEEP***
  - ***Insomnia Symptom Questionnaire***
- PTSD
  - Posttraumatic Stress Disorder Checklist
- Chronotype
  - Munich Chronotype Questionnaire

Status	Total
Screened	179
Ineligible	117
Enrolled	38
Dropped Out	4
Completed	34

	Group A (N=17) HRVB	Group B (N=17) Wait List Control	two-tailed p-value
Age (years), mean ± stderr	60.0 ± 2.5	58.9 ± 2.5	0.7621
Sex, count(%)			0.0445
Male	5 (29.4)	0 (0)	
Female	12 (70.6)	17 (100)	
Ethnic Group, count (%)			0.6012
Hispanic or Latino	1 (5.9)	0 (0)	
Not Hispanic or Latino	15 (88.2)	14 (82.3)	
Refuse/Don't Know/Missing	1 (5.9)	3 (17.7)	
Race, count (%)			0.349
White	14 (82.3)	13 (76.4)	
Black or African American	1 (5.9)	2 (11.8)	
Other	2 (11.8)	0 (0)	
Refused/Don't Know/Missing	0 (0)	2 (11.8)	
Education (years), mean ± stderr			0.9279
High School	4 (23.5)	4 (23.5)	
College	7 (41.1)	6 (35.3)	
Graduate School	3 (17.7)	5 (29.4)	
Missing	3 (17.7)	2 (11.8)	
Income, count (%)			0.7665
Under $50,000	6 (35.3)	5 (29.4)	
$50,000-$100,000	4 (23.5)	5 (29.4)	
$100,000 or more	6 (35.3)	4 (23.5)	
Refuse/Don't Know/Missing	1 (5.9)	3 (17.7)	

	Depression	Fatigue	Pain Interferes	Sleep
Stress	***	***	*	**
Depression	xxxxxxx	***	***	***
Fatigue	-----	xxxxxxx	*	***
Pain Interferes	-----	-----	xxxxxxx	*
*<0.05;**<0.01;*<0.005;				

Significance of Differences of Outcome Variables			
Group	**Pre- HRVB v Control**	**Post- HRVB v Control**	**Mixed Model HRVB x Control**
SDNN			
HRVB	ns	*	*
Control			
STRESS			
HRVB	ns	*	**
Control			
DEPRESSION			
HRVB	ns	**	***
Control			
FATIGUE			
HRVB	ns	***	**
Control			
PAIN INTERFERENCE			
HRVB	ns	*	#
Control			
SLEEP			
HRVB	ns	***	***
Control			

#<.1,*<.05, **≤.01,*≤.005**

Study 3 – “HRV Biofeedback in pain patients: Pilot intervention for pain, fatigue, & sleep”

PI: **Ginsberg, Jay**	Title: HRV Biofeedback in Pain Patients: Pilot Intervention for Pain, Fatigue & Sleep	
Received: 09/08/2014	FOA: CX14-006	Council: 01/2015
Competition ID:	FOA Title: CSR&D MERIT REVIEW AWARD FOR CLINICAL TRIALS	
1 I01 CX001182-01A1	Dual:	Accession Number: 3732973
IPF: 10018661	Organization: VETERANS HEALTH ADMINISTRATION	
Former Number:	Department: Mental Health	
IRG/SRG: CLNA	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: 198,078 Year 2: 149,913 Year 3: 149,932 Year 4: 149,935	Animals: N Humans: Y Clinical Trial: N Current HS Code: 20 HESC: N	New Investigator: N Early Stage Investigator: N

Senior/Key Personnel:	*Organization:*	*Role Category:*
Jay Ginsberg Ph.D	WJB Dorn VA Medical Center	PD/PI
James Burch Ph.D	University of South Carolina	MPI
Alexander McLain Ph.D	University of South Carolina	Co-Investigator
Raouf Gharbo Ph.D	Hampton Roads Riverside Regional Medical Center	Consultant
James Hebert ScD	University of South Carolina	Consultant
Francis Spinale M.D.	WJB Dorn VA Medical Center	Consultant
Tarek Sobeih Ph.D	Dorn Research Institute	Other Professional-Recruitment Coordinator

HYPOTHESIS FOR VA MERIT PROPOSAL

- COHERENCE REDUCES CENTRAL SENSITIZATION OF PAIN, STRESS, AND DEPRESSION

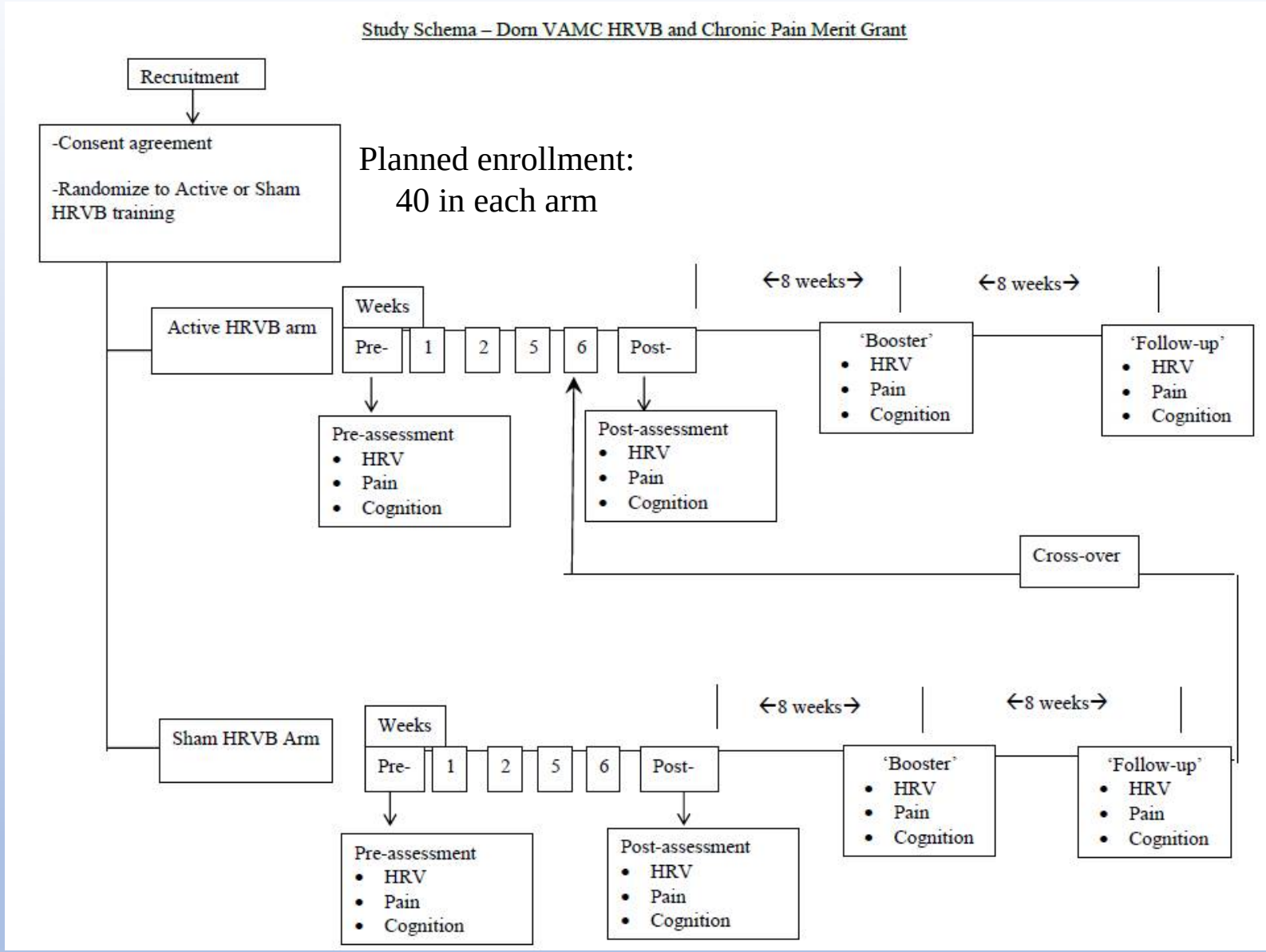
- HRV BIOFEEDBACK PRODUCES COHERENCE

- HRV BIOFEEDBACK WILL REDUCE CENTRALLY SENSITIZED PAIN, STRESS, AND DEPRESSION

- HRVB AND COHERENCE WILL REDUCE CENTRALLY SENSITIZED PAIN AND ASSOCIATED STRESS AND DEPRESSION BECAUSE THE SAME NEURAL STRUCTURES AND CIRCUITS ARE INVOLVED IN BOTH

HYPOTHESIS COROLLARY

- HRVB AND COHERENCE WILL NOT IMPROVE PAIN THAT IS SOLELY FROM A NEUROPATHIC SOURCE



Number of veterans screened or prescreened: 220
Number of veterans enrolled: 30
Number of veterans completed: 27

Symptom Cluster Assessment

- ***STRESS***
  - ***Perceived Stress Scale (PSS)***
- ***DEPRESSION***
  - ***Beck Depression Inventory–II (BDI-II0***
- ***FATIGUE***
  - ***Multidimensional Fatigue Inventory (MFI)***
- ***PAIN***
  - ***Brief Pain Inventory (BPI)***
- ***SLEEP***
  - ***Insomnia Symptom Questionnaire***
- ***CATASTROPHIZING***
  - ***Pain Catastrophizing Scale (PCS)***

The Pain Catastrophizing Scale

- 13-item self-report
- Thoughts/feelings about pain experience
- "When I'm in pain ..
  - " .. I worry all the time."
  - " .. I can't stand it anymore."
- 5-point scale
  - 0 (not at all) to 4 (all the time)
- Total score with three subscales
  - magnification, rumination and helplessness.

Sullivan MJL, Bishop SR, Pivik J (1995) The Pain Catastrophizing Scale: Development and validation. Psychol Assess 7: 524–532.

" .. general psychological acceptance is a strong predictor of pain-related catastrophizing, independent of gender, age and pain intensity. Mindfulness did not predict levels of pain-related catastrophizing. "

de Boer, M. J., Steinhagen, H. E., Versteegen, G. J., Struys, M. M., & Sanderman, R. (2014). Mindfulness, acceptance and catastrophizing in chronic pain. *PLoS One*, *9*(1), e87445.

Pain Catastrophizing Scale

Sullivan MJL, Bishop S, Pivik J. (1995)

Name:	Age:	Gender:	Date:
_____	_____	☐Male ☐Female	_____

Everyone experiences painful situations at some point in their lives. Such experiences may include headaches, tooth pain, joint or muscle pain. People are often exposed to situations that may cause pain such as illness, injury, dental procedures or surgery.

Instructions:
We are interested in the types of thoughts and feelings that you have when you are in pain. Listed below are thirteen statements describing different thoughts and feelings that may be associated with pain. Using the following scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

RATING	0	1	2	3	4
MEANING	Not at all	To a slight degree	To a moderate degree	To a great degree	All the time

When I'm in pain ...

Number	Statement	Rating
1	I worry all the time about whether the pain will end.	
2	I feel I can't go on.	
3	It's terrible and I think it's never going to get any better	
4	It's awful and I feel that it overwhelms me.	
5	I feel I can't stand it anymore	
6	I become afraid that the pain will get worse.	
7	I keep thinking of other painful events	
8	I anxiously want the pain to go away	
9	I can't seem to keep it our of my mind	
10	I keep thinking about how much it hurts.	
11	I keep thinking about how badly I want the pain to stop	
12	There's nothing I can do to reduce the intensity of the pain	
13	I wonder whether something serious may happen.	

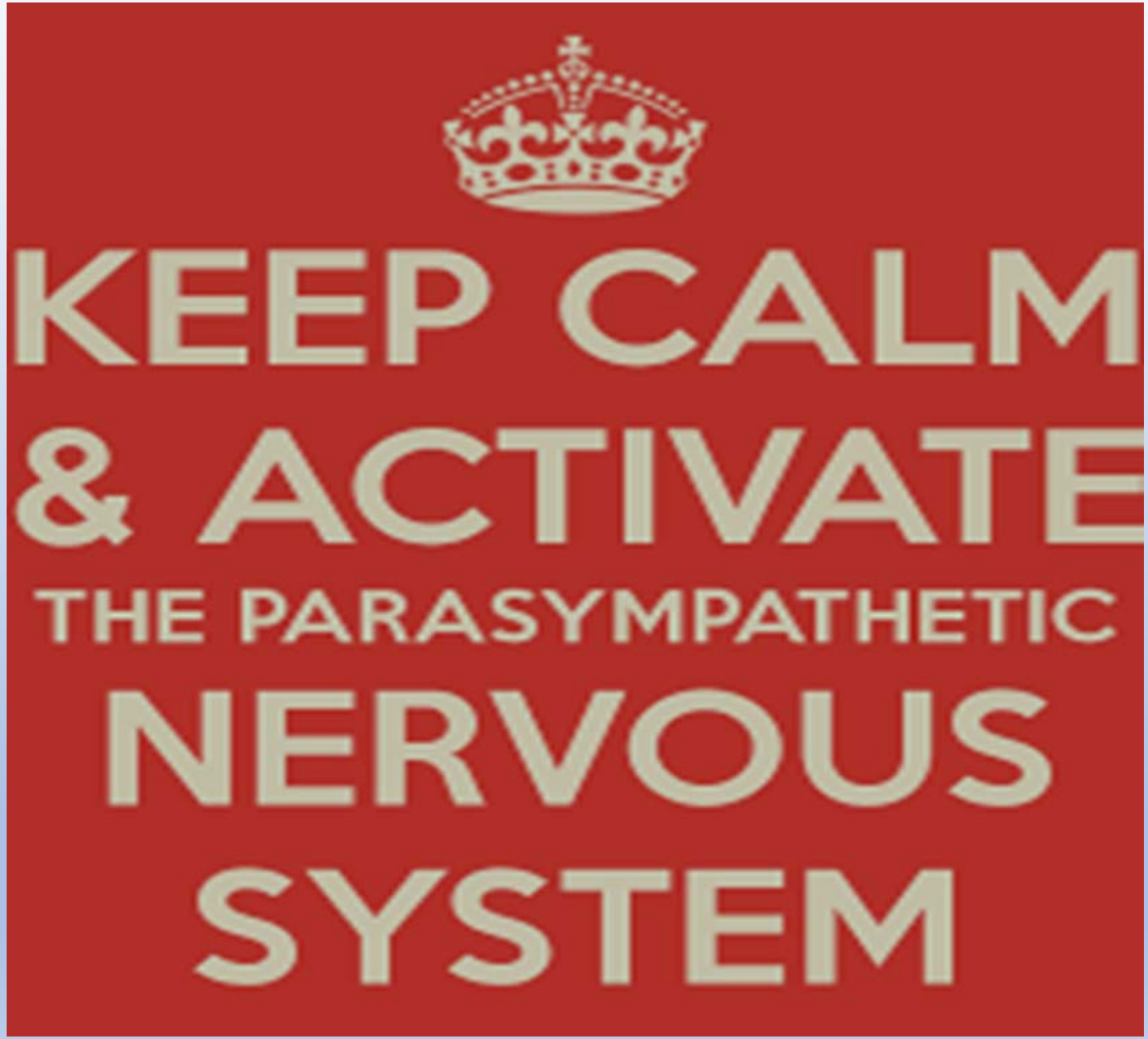
Source: **Sullivan MJL, Bishop S, Pivik J. The pain catastrophizing scale: development and validation.** *Psychol Assess*, **1995**, 7: 524-532

	Depression	Catastrophize	Fatigue	Pain Interferes	Sleep
Stress	***	***	***	*	**
Depression	xxxxxxx	***	***	***	***
Catastrophize		xxxxxxx	***	***	***
Fatigue			xxxxxxx	*	***
Pain Interferes				xxxxxxx	*
*<0.05;**<0.01;*<0.005;					

Planned research

(1) NIH RO1, Phase 2, single site, Veteran cancer survivors; psychoeducational self-management control; 4 timepoints; primary, secondary, exploratory endpoints

(2) NCI NCORP, Phase 2, multi-site, cancer survivors.; pre-post; primary, secondary, exploratory endpoints.


KEEP CALM
& ACTIVATE
THE PARASYMPATHETIC
NERVOUS
SYSTEM


time for questions