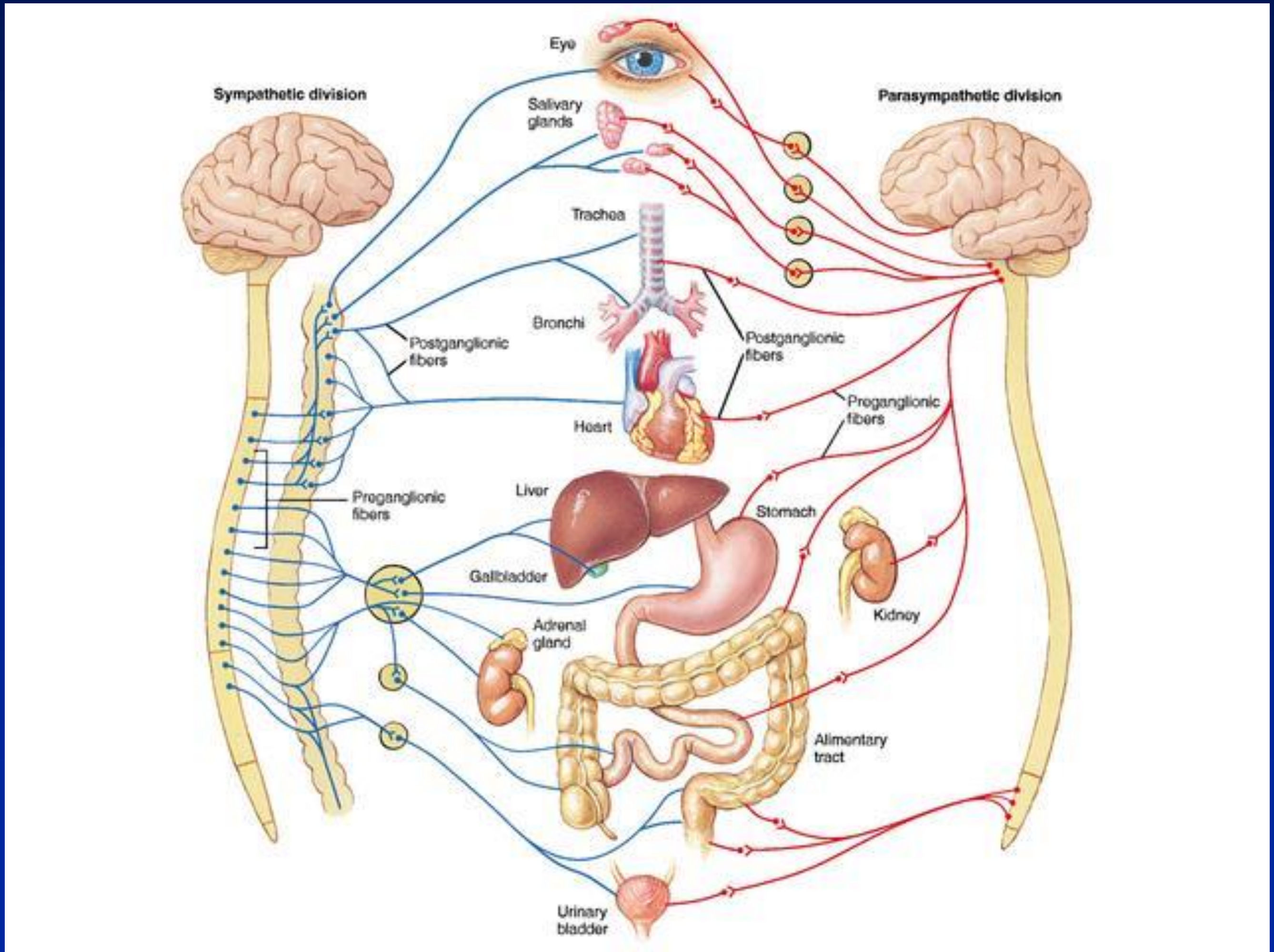
Why Should We Care About the Vagus? Implications for Emotion, Cognition, and Health

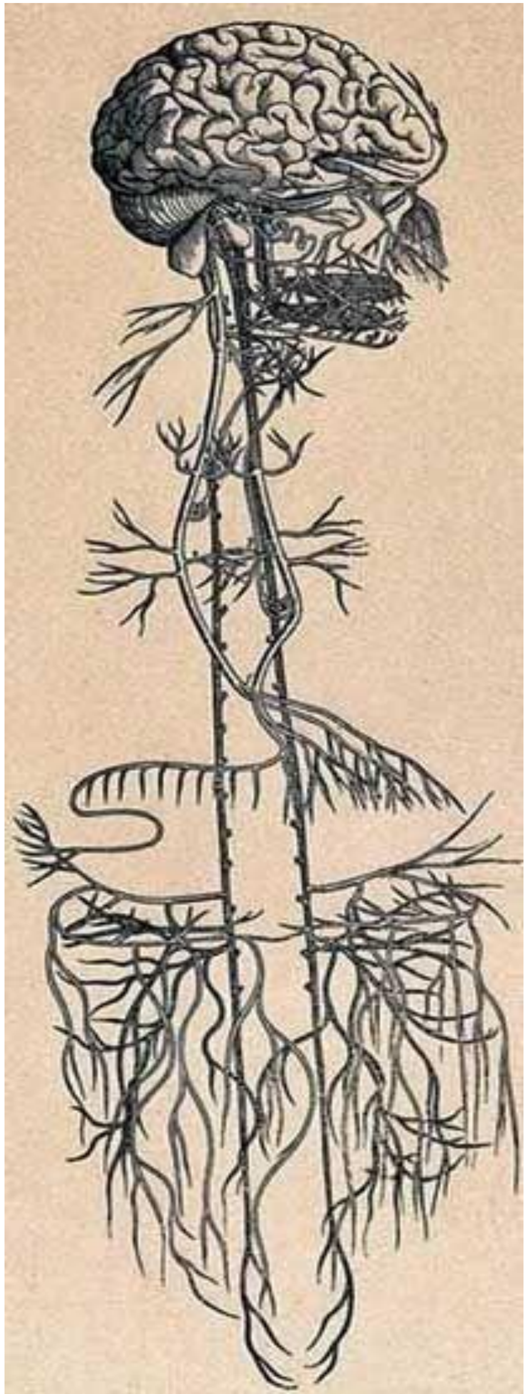
Julian F. Thayer, PhD
The University of California, Irvine

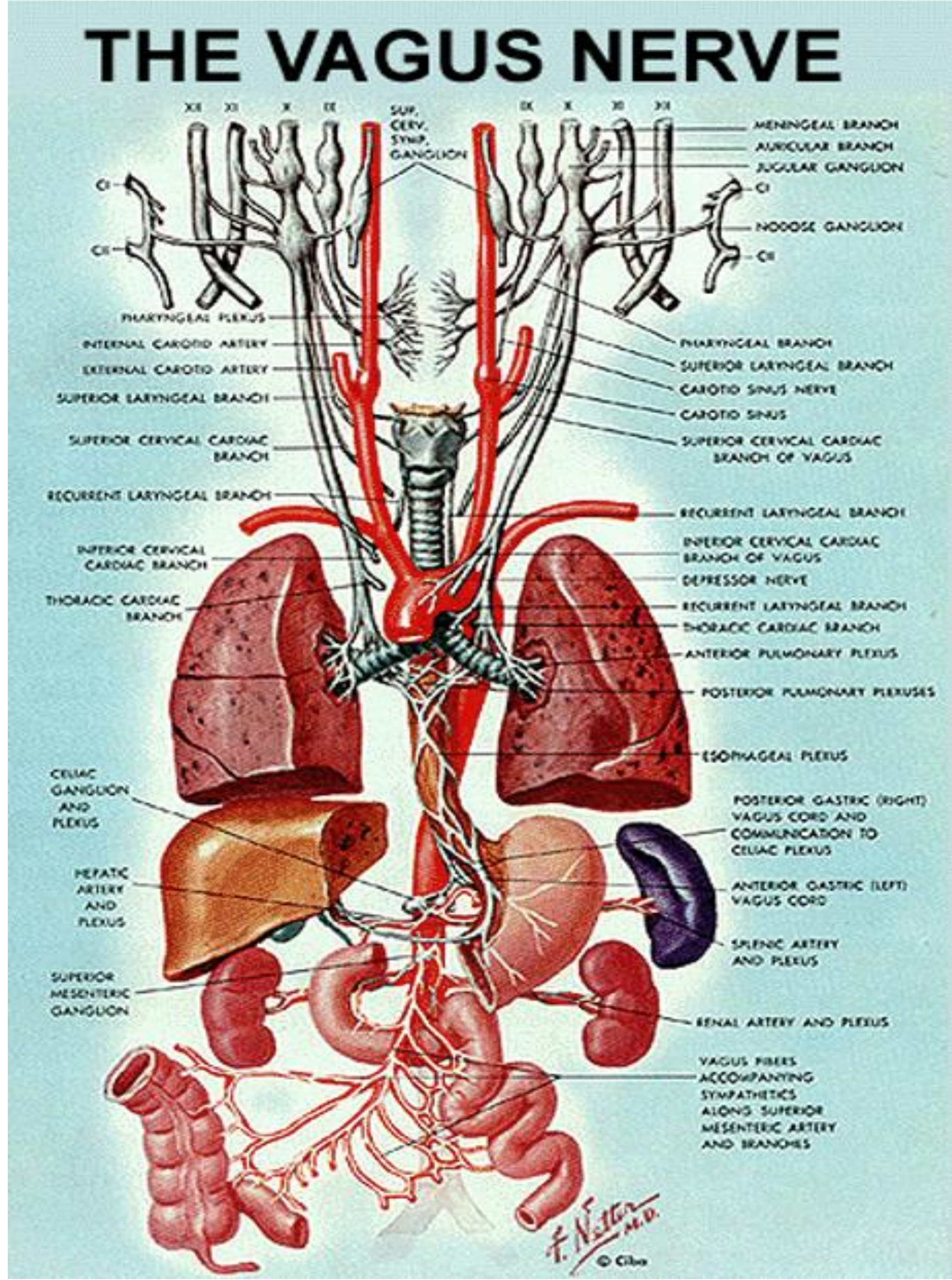
“Claude Bernard also repeatedly insists, and this deserves especial notice, that when the heart is affected it reacts on the brain; and the state of the brain again reacts through the pneumo-gastric (vagus) nerve on the heart; so that under any excitement there will be much mutual action and reaction between these, the two most important organs of the body”

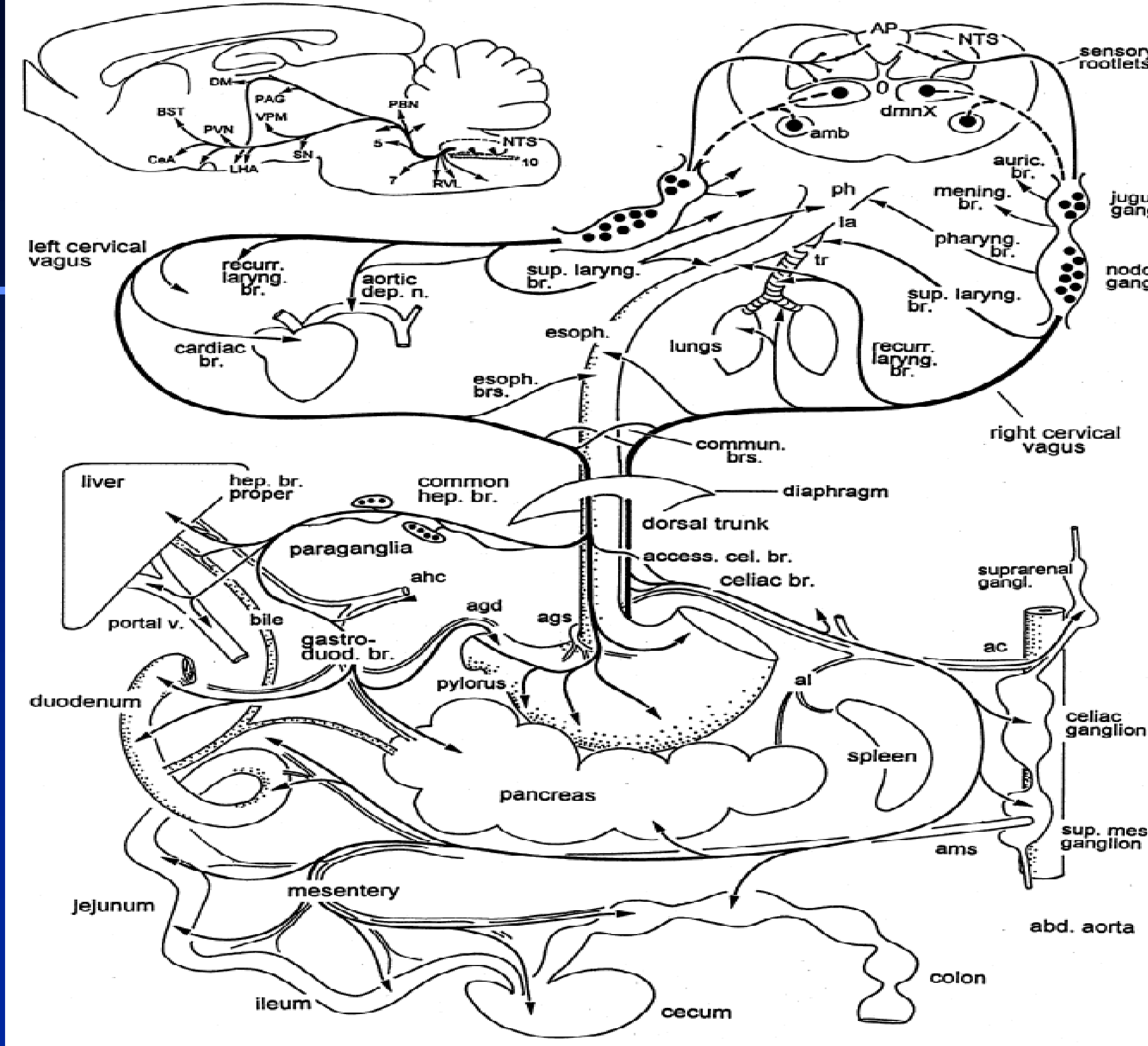
(Darwin, 1872)

Overview of the autonomic nervous system






THE VAGUS NERVE
XII XI X IX
SUP. CERV. SYMP. GANGLION
IX X XI XII
MENINGEAL BRANCH
AURICULAR BRANCH
JUGULAR GANGLION
CI
CI
NODOSE GANGLION
CII
CII
PHARYNGEAL PLEXUS
INTERNAL CAROTID ARTERY
EXTERNAL CAROTID ARTERY
SUPERIOR LARYNGEAL BRANCH
SUPERIOR CERVICAL CARDIAC BRANCH
RECURRENT LARYNGEAL BRANCH
INFERIOR CERVICAL CARDIAC BRANCH
THORACIC CARDIAC BRANCH
PHARYNGEAL BRANCH
SUPERIOR LARYNGEAL BRANCH
CAROTID SINUS NERVE
CAROTID SINUS
SUPERIOR CERVICAL CARDIAC BRANCH OF VAGUS
RECURRENT LARYNGEAL BRANCH
INFERIOR CERVICAL CARDIAC BRANCH OF VAGUS
DEPRESSOR NERVE
RECURRENT LARYNGEAL BRANCH
THORACIC CARDIAC BRANCH
ANTERIOR PULMONARY PLEXUS
POSTERIOR PULMONARY PLEXUSES
ESOPHAGEAL PLEXUS
CELIAC GANGLION AND PLEXUS
HEPATIC ARTERY AND PLEXUS
SUPERIOR MESENTERIC GANGLION
POSTERIOR GASTRIC (RIGHT) VAGUS CORD AND COMMUNICATION TO CELIAC PLEXUS
ANTERIOR GASTRIC (LEFT) VAGUS CORD
SPLENIC ARTERY AND PLEXUS
RENAL ARTERY AND PLEXUS
VAGUS FIBERS ACCOMPANYING SYMPATHETICS ALONG SUPERIOR MESENTERIC ARTERY AND BRANCHES
F. Netter M.D.
© Ciba



DM
PAG
PBN
BST
VPM
PVN
5
NTS
CeA
LHA
SN
10
7
RVL
AP
NTS
sensory rootlets
0
dmnX
amb
auric. br.
mening. br.
pharyng. br.
ph
la
tr
left cervical vagus
recurr. laryng. br.
aortic dep. n.
sup. laryng. br.
sup. laryng. br.
cardiac br.
esoph.
lungs
recurr. laryng. br.
esoph. brs.
right cervical vagus
commun. brs.
liver
hep. br. proper
common hep. br.
diaphragm
dorsal trunk
paraganglia
access. cel. br.
celiac br.
ahc
suprarenal gangl.
agd
ags
portal v.
bile
gastro-duod. br.
ac
pylorus
al
duodenum
celiac ganglion
spleen
pancreas
sup. mes. ganglion
ams
mesentery
jejunum
abd. aorta
colon
ileum
cecum

Autonomic Balance

- Predictor of Mortality and Morbidity
- Underlies a broad range of responses linked to allostatic load
- Associated with central nervous system
- may explain how psychosocial factors are instantiated in physiology and disease
- may explain known health disparities

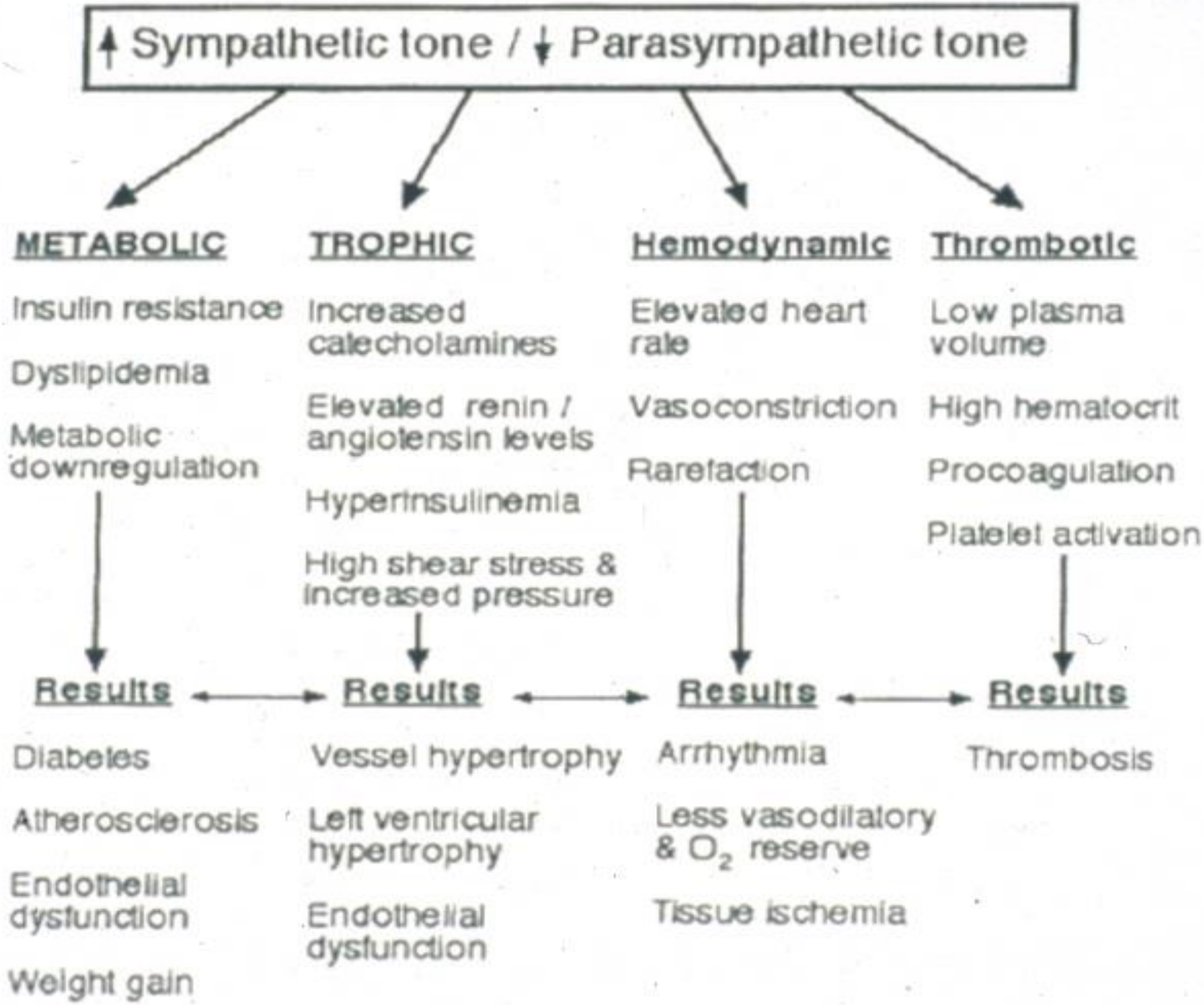
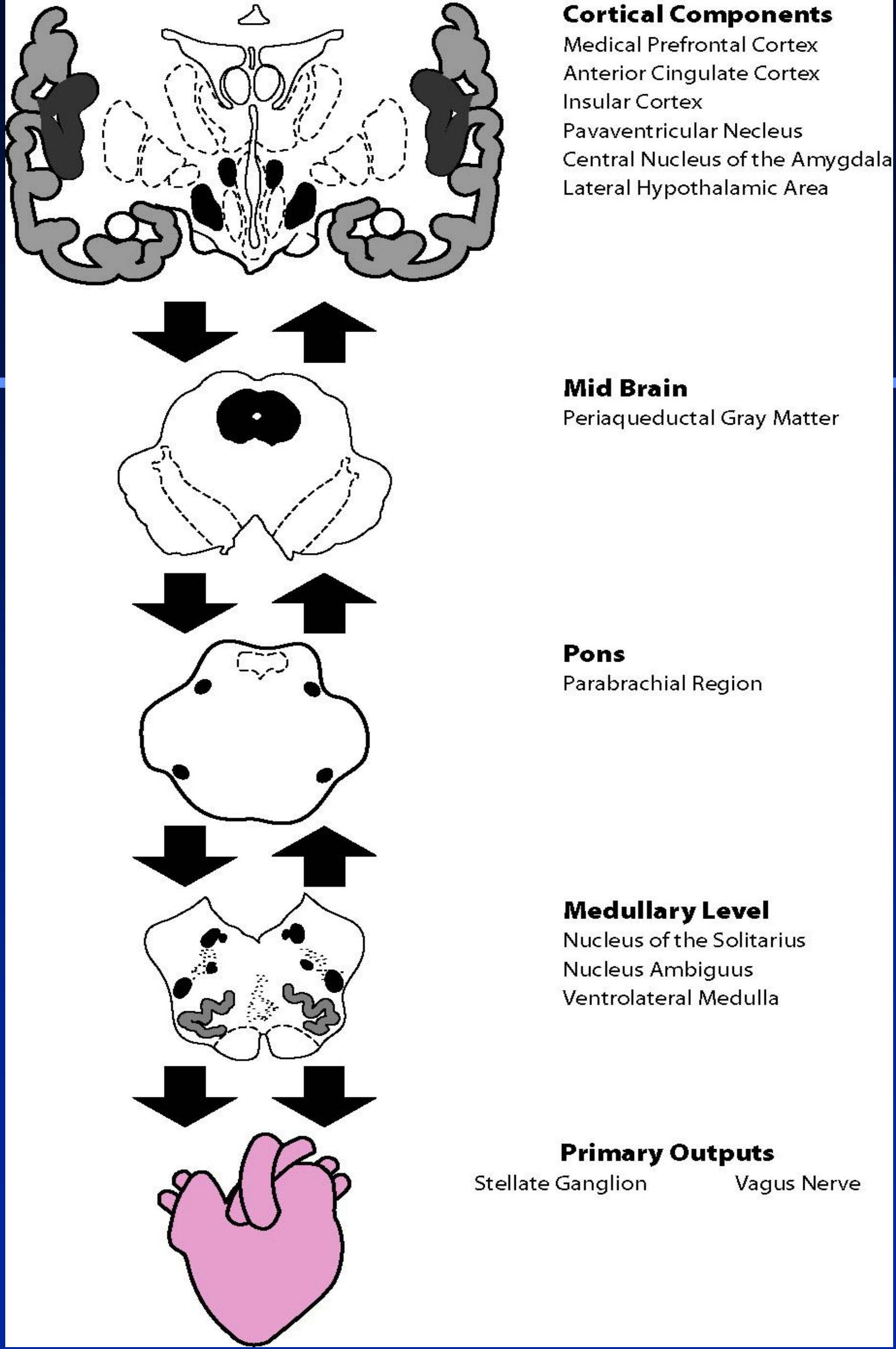
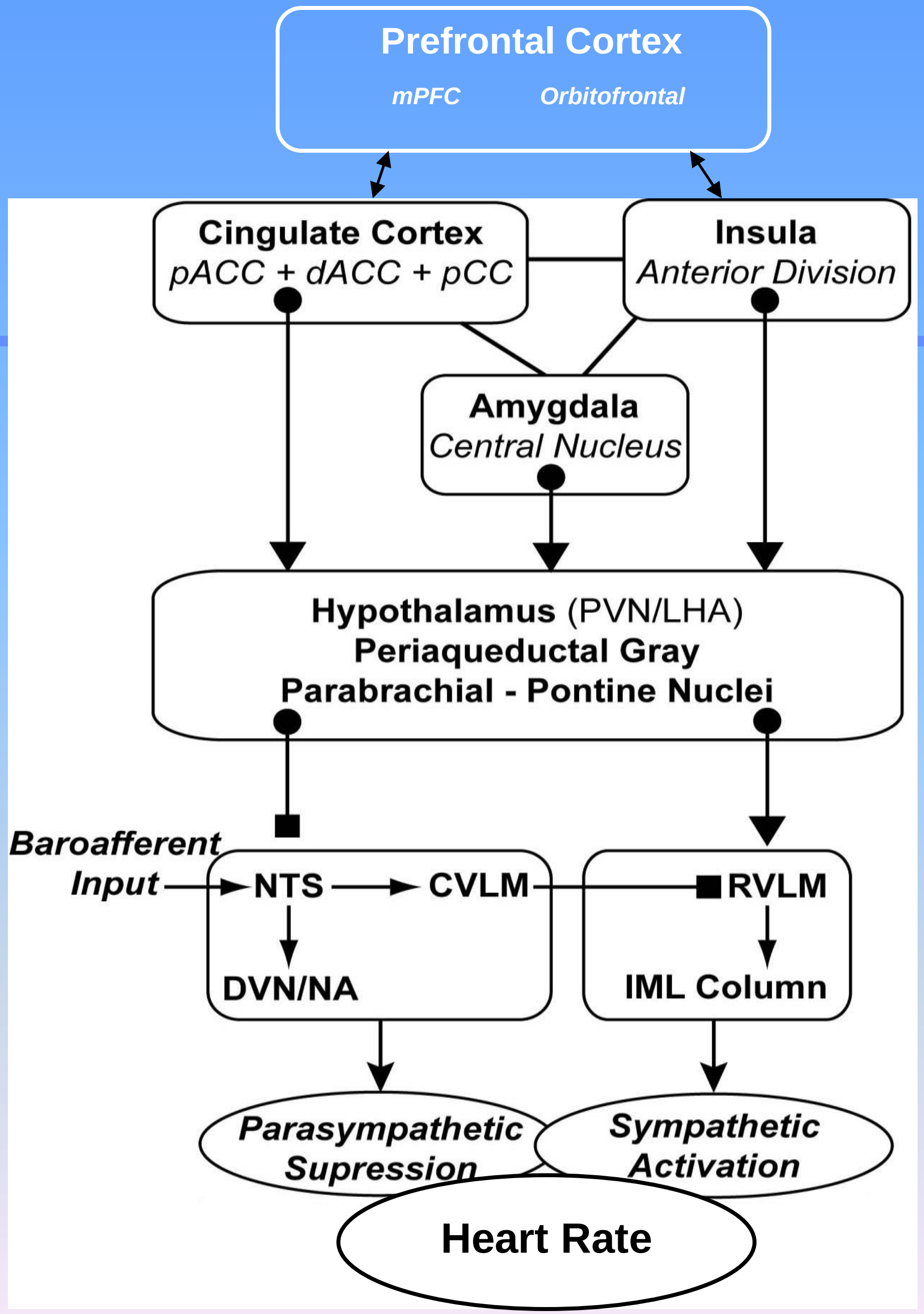


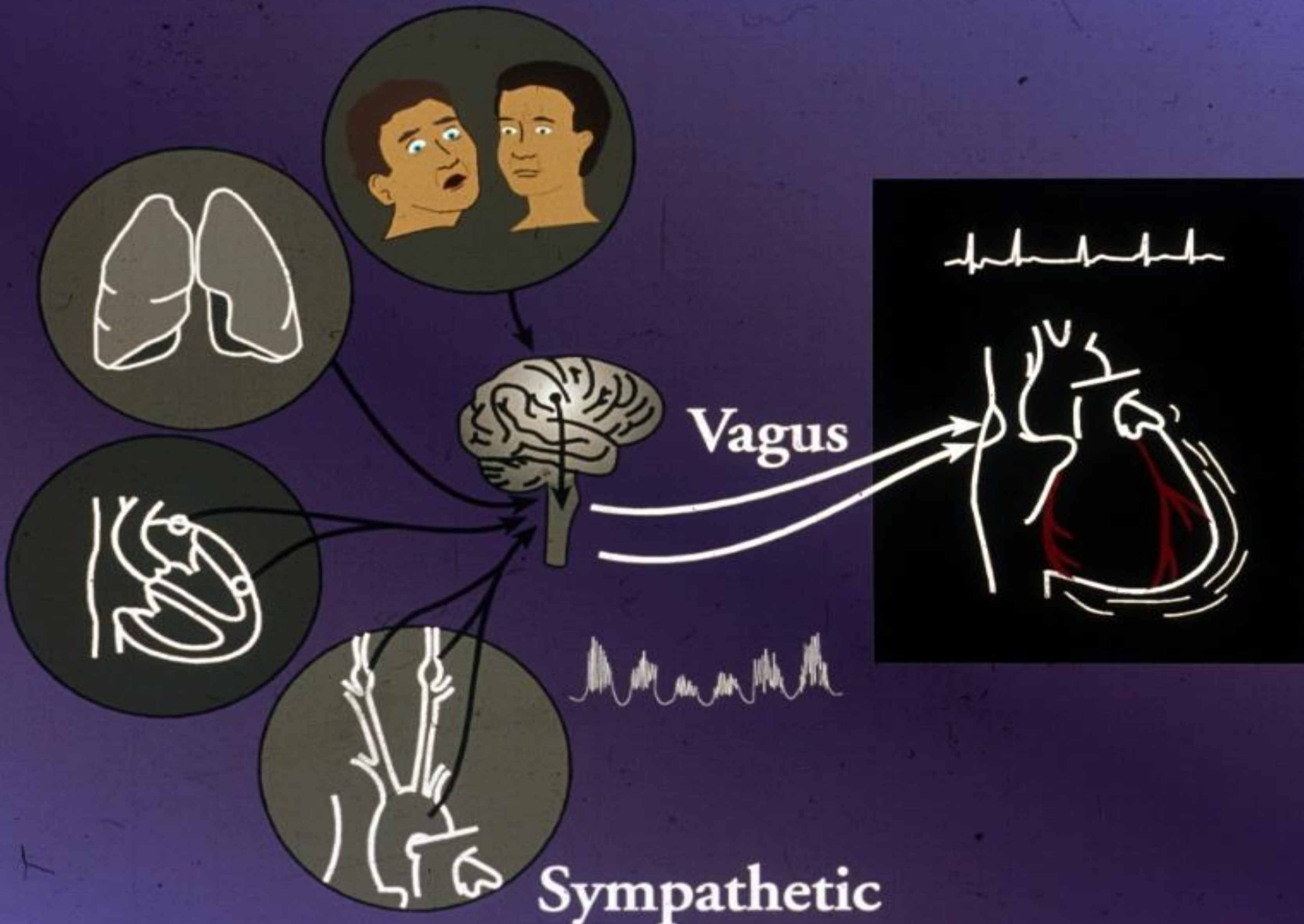
FIGURE 1. *Autonomic imbalance.*

Neurovisceral Integration Model

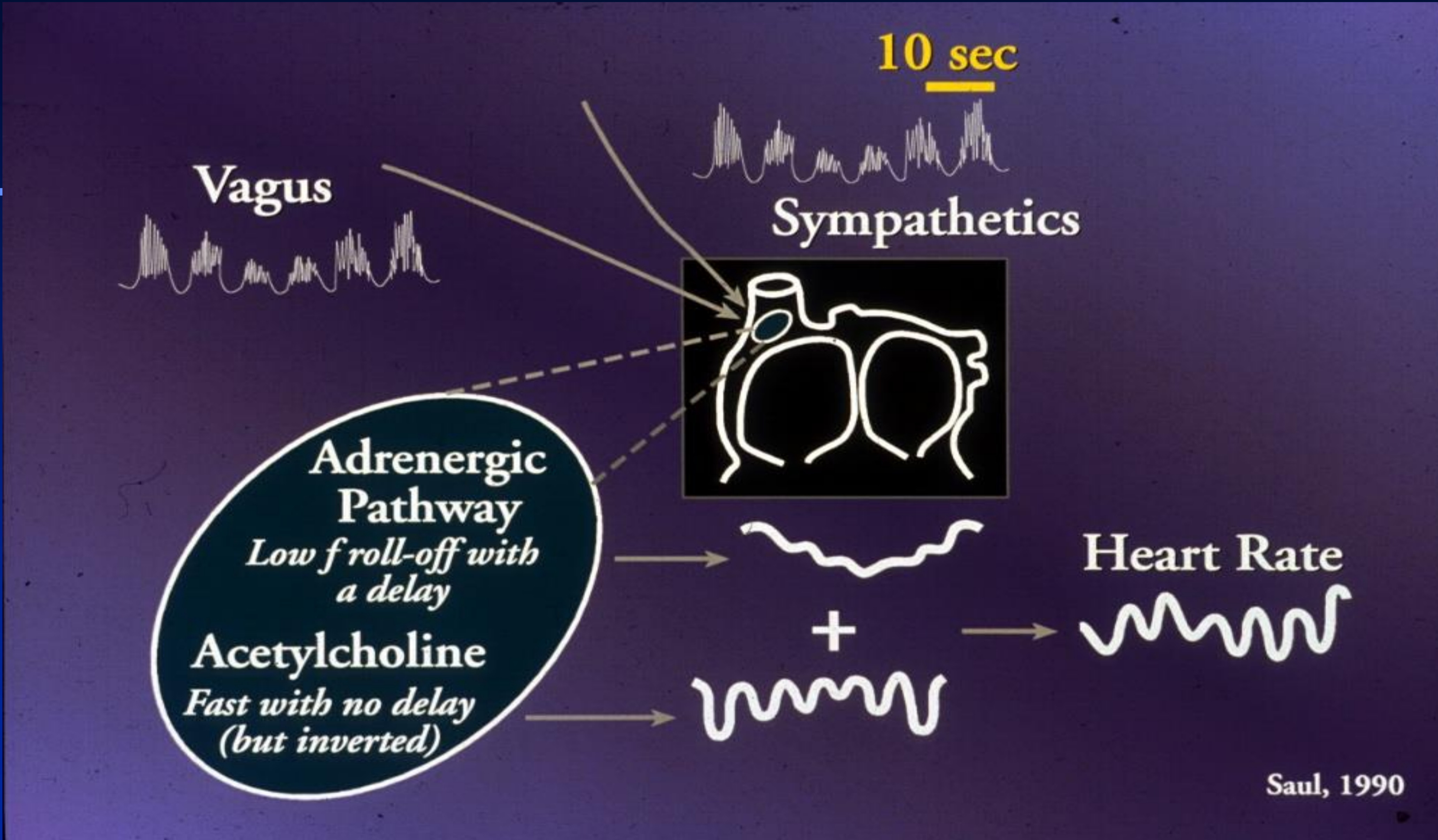
- This neural network can be indexed by heart rate variability
- Higher HRV associated with greater prefrontal inhibitory tone
- Lack of inhibition leads to undifferentiated threat response to environmental challenges (less flexibility)

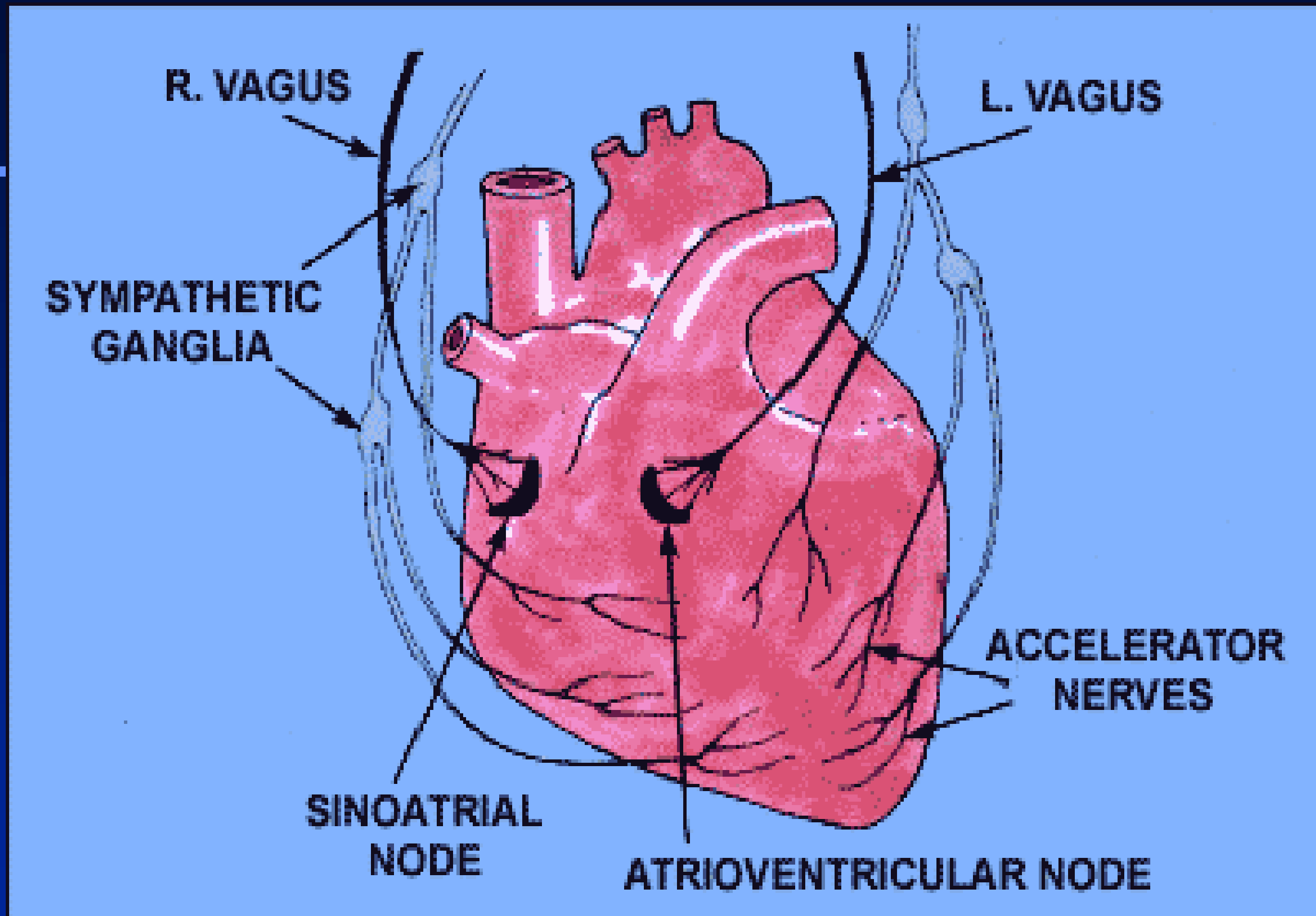

Cortical Components
Medical Prefrontal Cortex
Anterior Cingulate Cortex
Insular Cortex
Pavaventricular Necleus
Central Nucleus of the Amygdala
Lateral Hypothalamic Area
Mid Brain
Periaqueductal Gray Matter
Pons
Parabrachial Region
Medullary Level
Nucleus of the Solitarius
Nucleus Ambiguus
Ventrolateral Medulla
Primary Outputs
Stellate Ganglion
Vagus Nerve


Prefrontal Cortex
mPFC
Orbitofrontal
Cingulate Cortex
pACC + dACC + pCC
Insula
Anterior Division
Amygdala
Central Nucleus
Hypothalamus (PVN/LHA)
Periaqueductal Gray
Parabrachial - Pontine Nuclei
Baroafferent Input
NTS
CVLM
RVLM
DVN/NA
IML Column
Parasympathetic Supression
Sympathetic Activation
Heart Rate



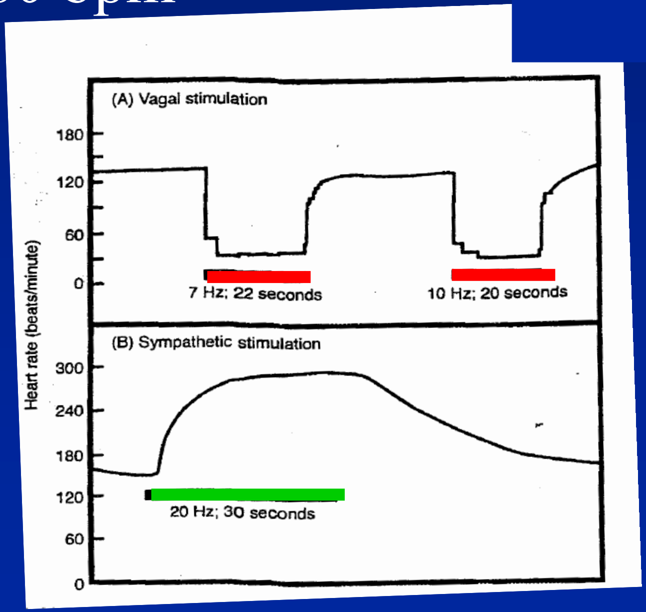
Vagus
Sympathetic


10 sec
Vagus
Sympathetics
Adrenergic Pathway
Low f roll-off with a delay
Acetylcholine
Fast with no delay (but inverted)
+
Heart Rate
Saul, 1990


R. VAGUS
L. VAGUS
SYMPATHETIC
GANGLIA
ACCELERATOR
NERVES
SINOATRIAL
NODE
ATRIOVENTRICULAR NODE

PNS influences:
"what happens in vagus …"

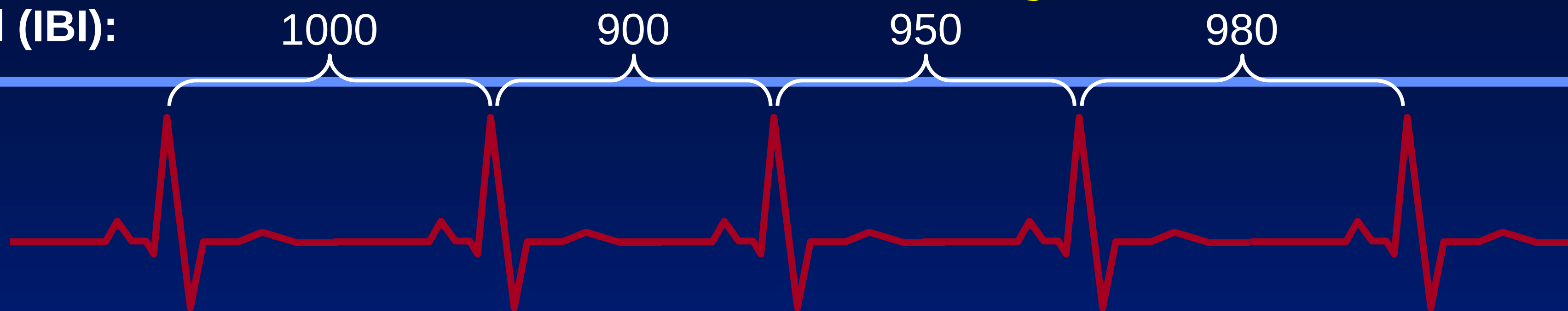
- PNS influences dominate: "vagal tone"[1]
  - intrinsic firing rate of S-A cells: 105 bpm
  - normal resting heart rate: 60–80 bpm [2]
- PNS mediation faster than SNS
  - PNS mediation (ACh): milliseconds
    - rapid action and hydrolysis
  - SNS mediation (NE): seconds

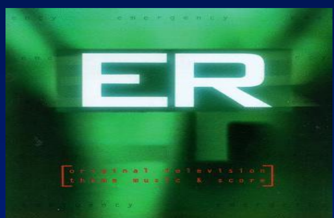


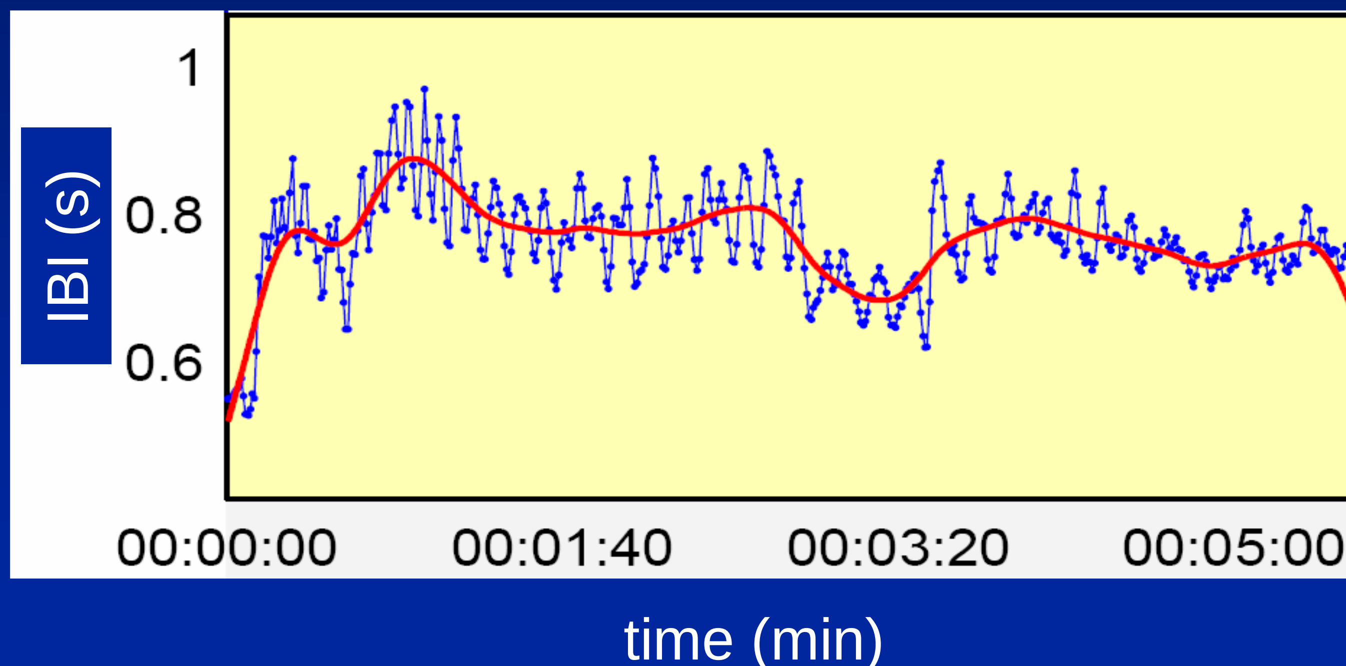
Warner & Cox, 1962

Heart Rate Variability

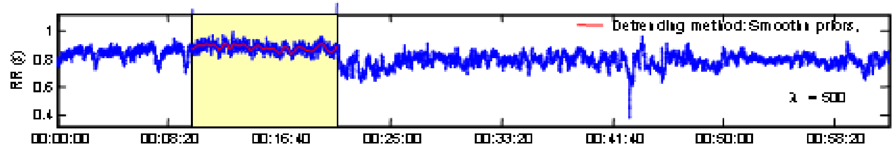
inter-beat interval (IBI):

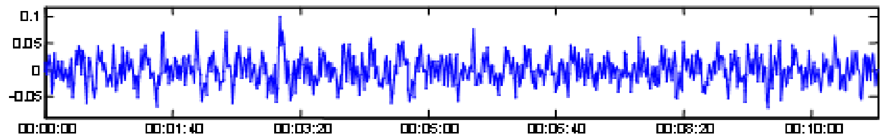


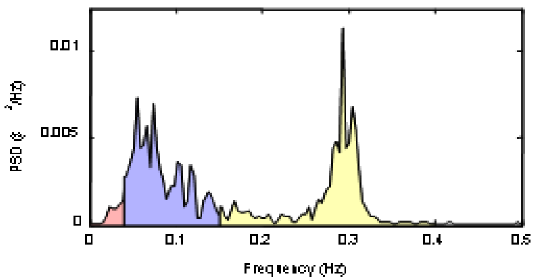


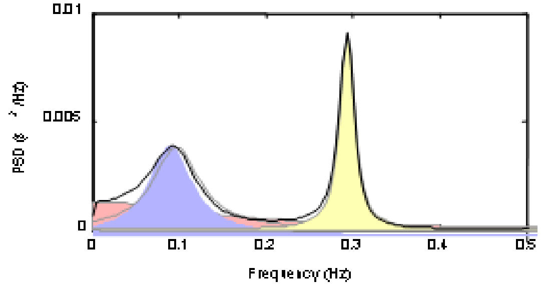


QEKG Methods







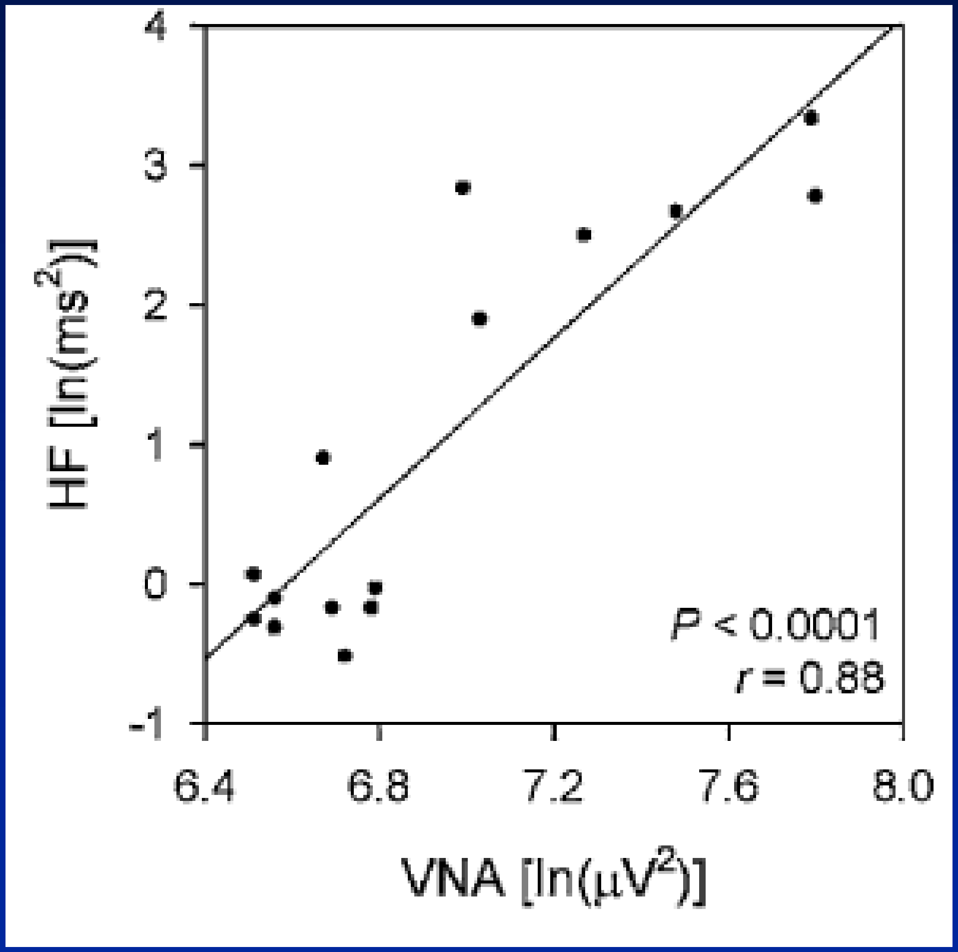


Frequency Band	Peak (Hz)	Power (ms^2)	Power (%)	Power (n.u.)
VLF (0-0.04 Hz)	0.0391	23	3.5	
LF (0.04-0.15 Hz)	0.0547	321	49.6	51.4
HF (0.15-0.4 Hz)	0.2930	304	46.9	48.6
Total		648		
LF/HF		1.058		

Frequency Band	Peak (Hz)	Power (ms^2)	Power (%)	Power (n.u.)
VLF (0-0.04 Hz)	0.0000	318	33.4	
LF (0.04-0.15 Hz)	0.0977	354	37.2	55.8
HF (0.15-0.4 Hz)	0.2930	281	29.4	44.2
Total		953		
LF/HF		1.263		

Regression Analysis Between Heart Rate Variability and Baroreflex-Related Vagus Nerve Activity in Rats

TERRY B. J. KUO, M.D., PH.D.,*,†,‡ CHING J. LAI, PH.D.,*,† YU-TING HUANG, M.S.,* and CHERYL C. H. YANG, PH.D.*,†

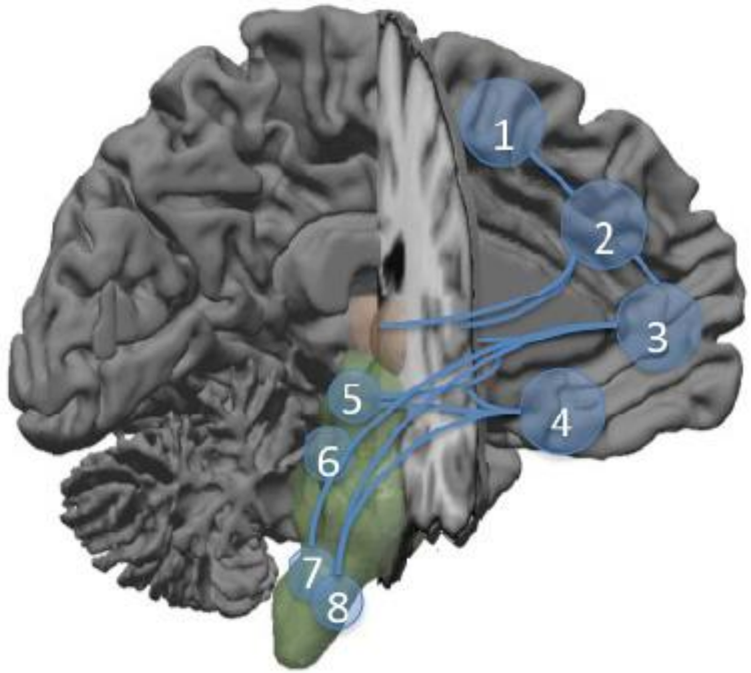


HRV and organism health

- An index of physiological health[4]
  - ↓ HRV_{rest} assoc. with ↑ levels of: hypertension, diabetes, cholesterol, obesity, arthritis, cancers
  - Independent predictor of all-cause mortality
- An index of emotional health[5]
  - ↓ HRV_{rest} associated with ↑ depression, anxiety
- An index of attentional processes[6,7,8]
  - HRV ↓ as attentional demands ↑
- An index of cognitive health[6]
  - ↑ HRV_{rest} linked with ↑ accuracy and faster RTs during working memory task

Figure 1.

Schematic illustration of the medial prefrontal-brainstem "axis"



Neuroscience and Biobehavioral Reviews 36 (2012) 747–756

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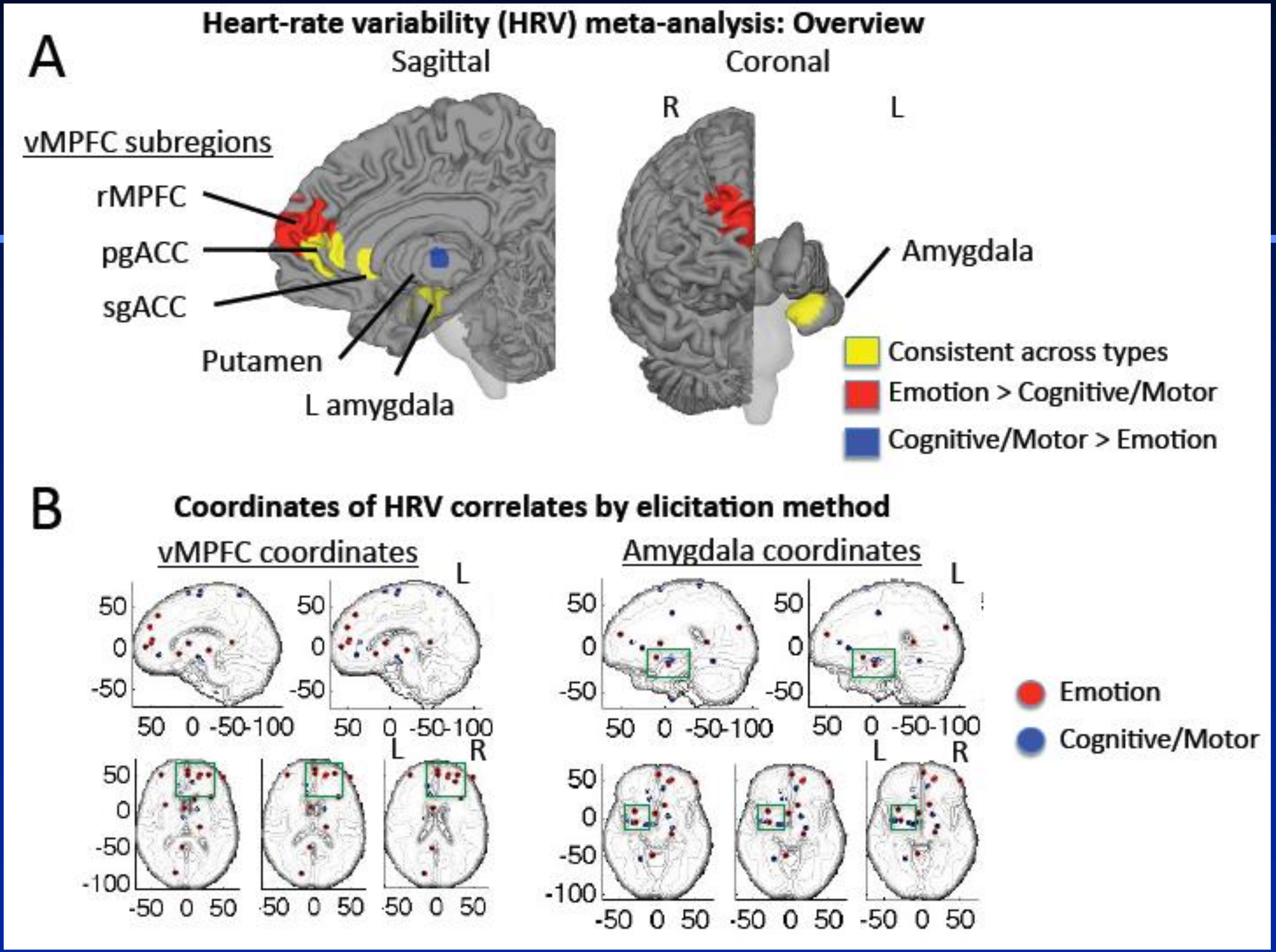
Neuroscience and Biobehavioral Reviews

journal homepage: www.elsevier.com/locate/neubiorev

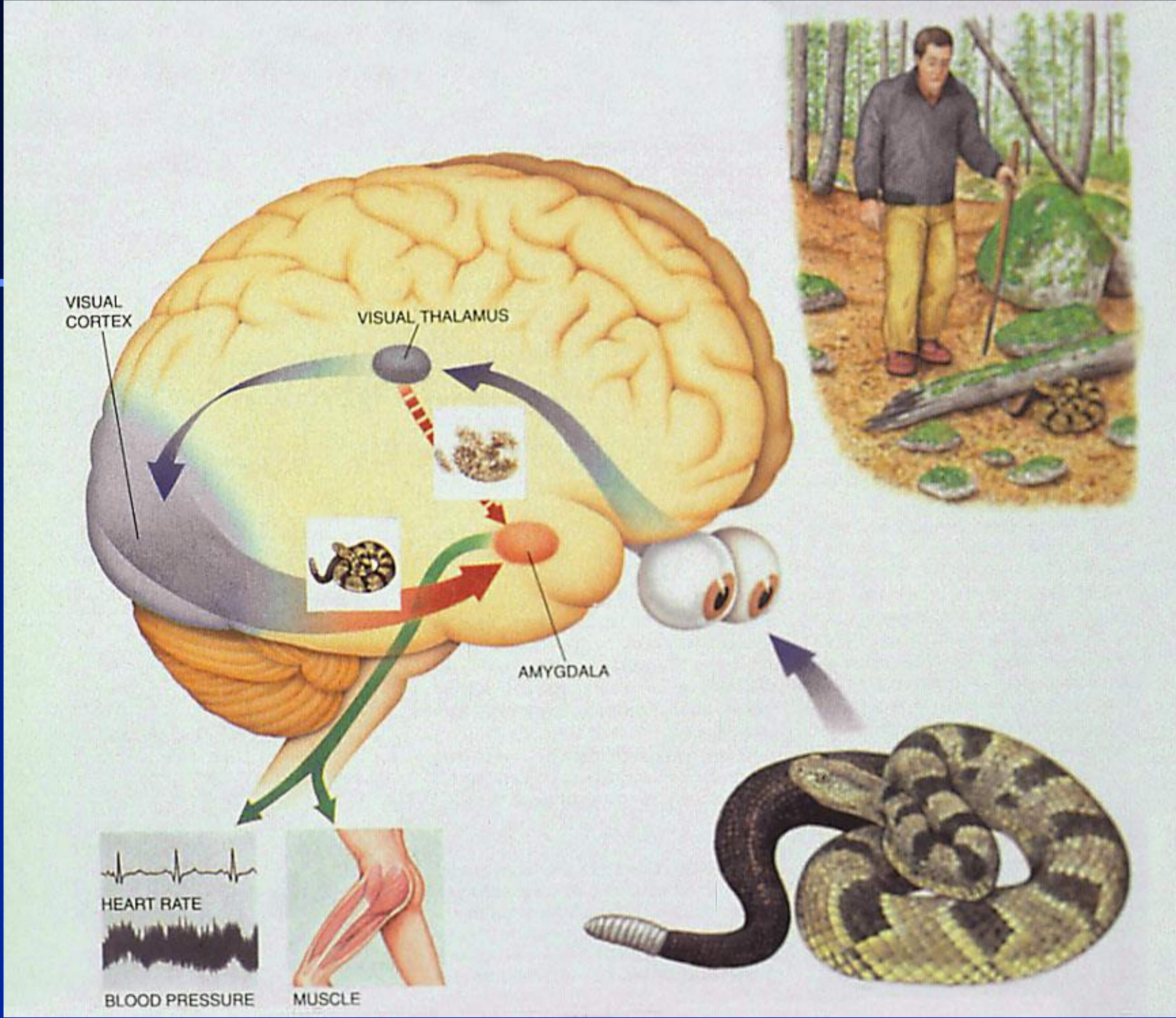
Review

A meta-analysis of heart rate variability and neuroimaging studies: Implications for heart rate variability as a marker of stress and health

Julian F. Thayer [a,b,*], Fredrik Åhs [c], Mats Fredrikson [c], John J. Sollers III [d], Tor D. Wager [e]



Heart-rate variability (HRV) meta-analysis: Overview
A
Sagittal
Coronal
R
L
vMPFC subregions
rMPFC
pgACC
sgACC
Putamen
L amygdala
Amygdala
Consistent across types
Emotion > Cognitive/Motor
Cognitive/Motor > Emotion
B
Coordinates of HRV correlates by elicitation method
vMPFC coordinates
Amygdala coordinates
Emotion
Cognitive/Motor



VISUAL
CORTEX
VISUAL THALAMUS
AMYGDALA
HEART RATE
BLOOD PRESSURE
MUSCLE

THE DEFENSE REACTION: A COMMON DENOMINATOR OF CORONARY RISK AND BLOOD PRESSURE IN NEUROGENIC HYPERTENSION?

Stevo Julius, M.D., Sc.D.
Department of Internal Medicine, Division of Hypertension
University of Michigan Medical School
Ann Arbor, Michigan 48109-0356

CLIN. AND EXPER. HYPERTENSION, 17(1&2), 375–386 (1995)

observed dyslipidemia in hypertension. The sympathetic overactivity in hypertension reflects a chronic activation of defense/vigilance reaction. The

The defense reaction may have been useful in evolution and may have offered survival advantage. In modern times with prolonged life expectancy the previously useful response (in evolutionary terms) contributes to a faster and deleterious wear and tear of the cardiovascular system.

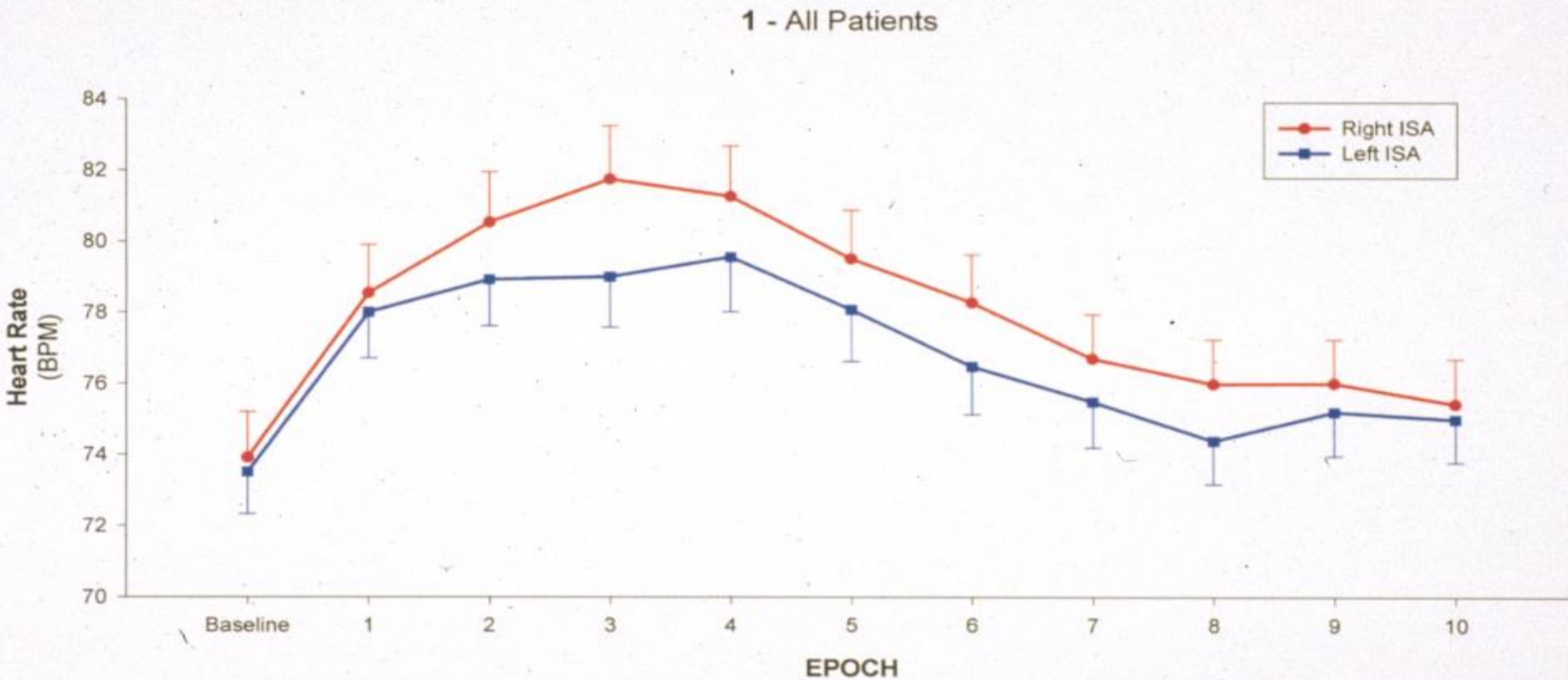
If these anticipatory reactions have offered a survival advantage, in the course of evolution they may have become a selection factor. A proportion of individuals with an efficient and prompt defense reaction could have selectively survived to pass on their genes to the next generation. In evolutionary terms these mechanisms are geared to preserve the organism until the times of sexual maturity. What could have provided a relatively short term advantage for the passage of genes across generations may have under the contemporary conditions of a prolonged life become deleterious to the organism [37]. If we wish to further extend the life under modern circumstances, it may be necessary to dampen the defense response. A

The “Default” Stress Response

- When in doubt prepare for the worst
- Adaptive response
- Fast, automatic?
- The negativity bias

HR and HRV Response to Pharmacological Blockade of the Prefrontal Cortex

- Approximately 80 patients undergoing pre-operative evaluation for epilepsy surgery
- Approximately half male and half female
- Approximately half left sided loci and half right sided loci
- Prediction: Inactivation of PFC associated with increase in HR and decrease in HRV


1 - All Patients
Right ISA
Left ISA
Heart Rate
(BPM)
84
82
80
78
76
74
72
70
Baseline
1
2
3
4
5
6
7
8
9
10
EPOCH

Cortical thickness and resting-state cardiac function across the lifespan: A cross-sectional pooled mega-analysis

Psychophysiology. 2020;00:1–16.

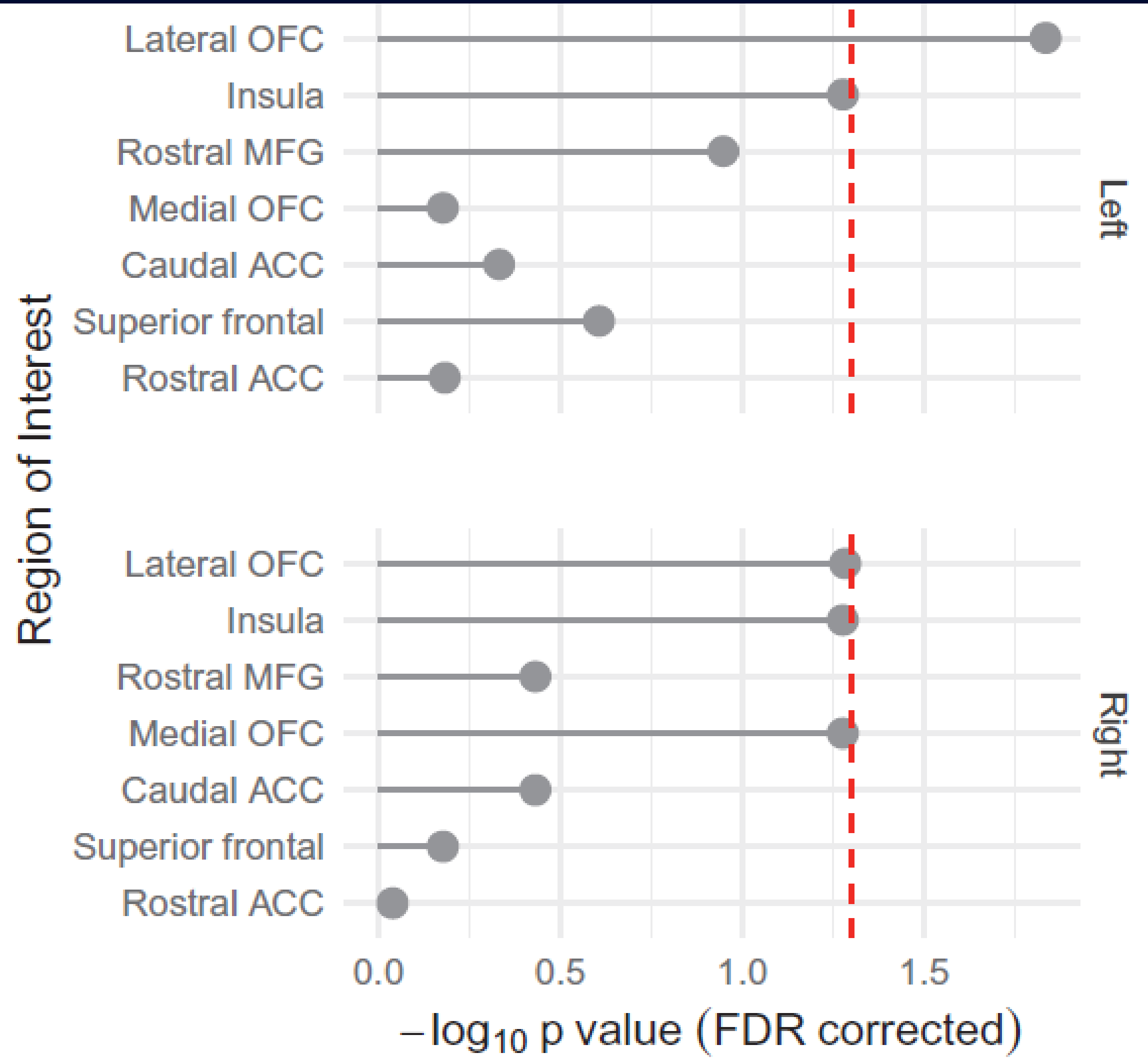
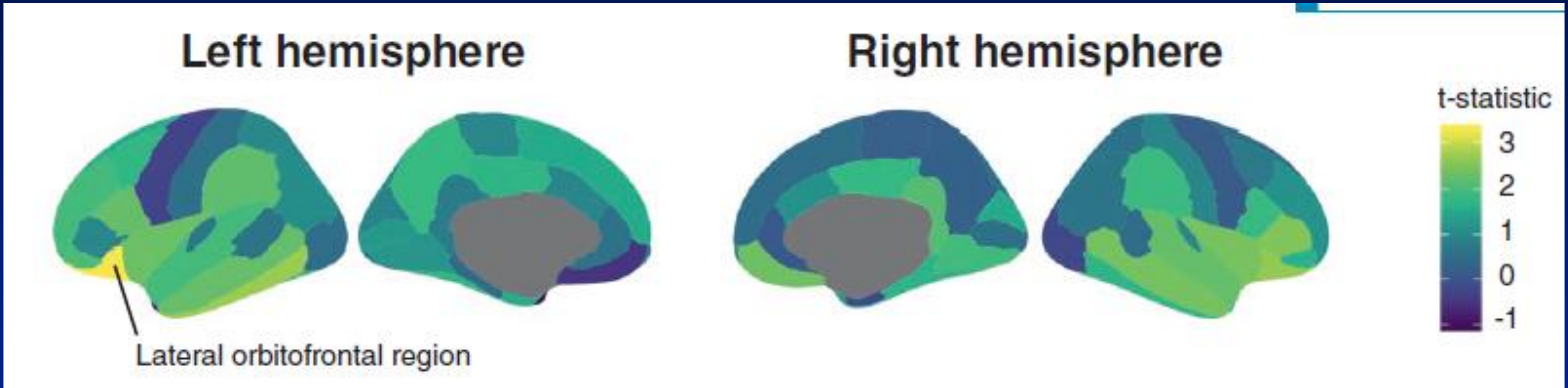


FIGURE 2 Association between heart rate variability and cortical thickness in pre-specified ROI accounting for research group, BMI, age, sex, and sex × age. Grey dots represent the FDR corrected


Left hemisphere
Right hemisphere
t-statistic
3
2
1
0
-1
Lateral orbitofrontal region

RESEARCH ARTICLE

Self-domestication in *Homo sapiens*: Insights from comparative genomics

Constantina Theofanopoulou[1,2☯], Simone Gastaldon[1,3☯], Thomas O'Rourke[1], Bridget D. Samuels[4], Angela Messner[1], Pedro Tiago Martins[1], Francesco Delogu[5], Saleh Alamri[1], Cedric Boeckx[1,2,6*]

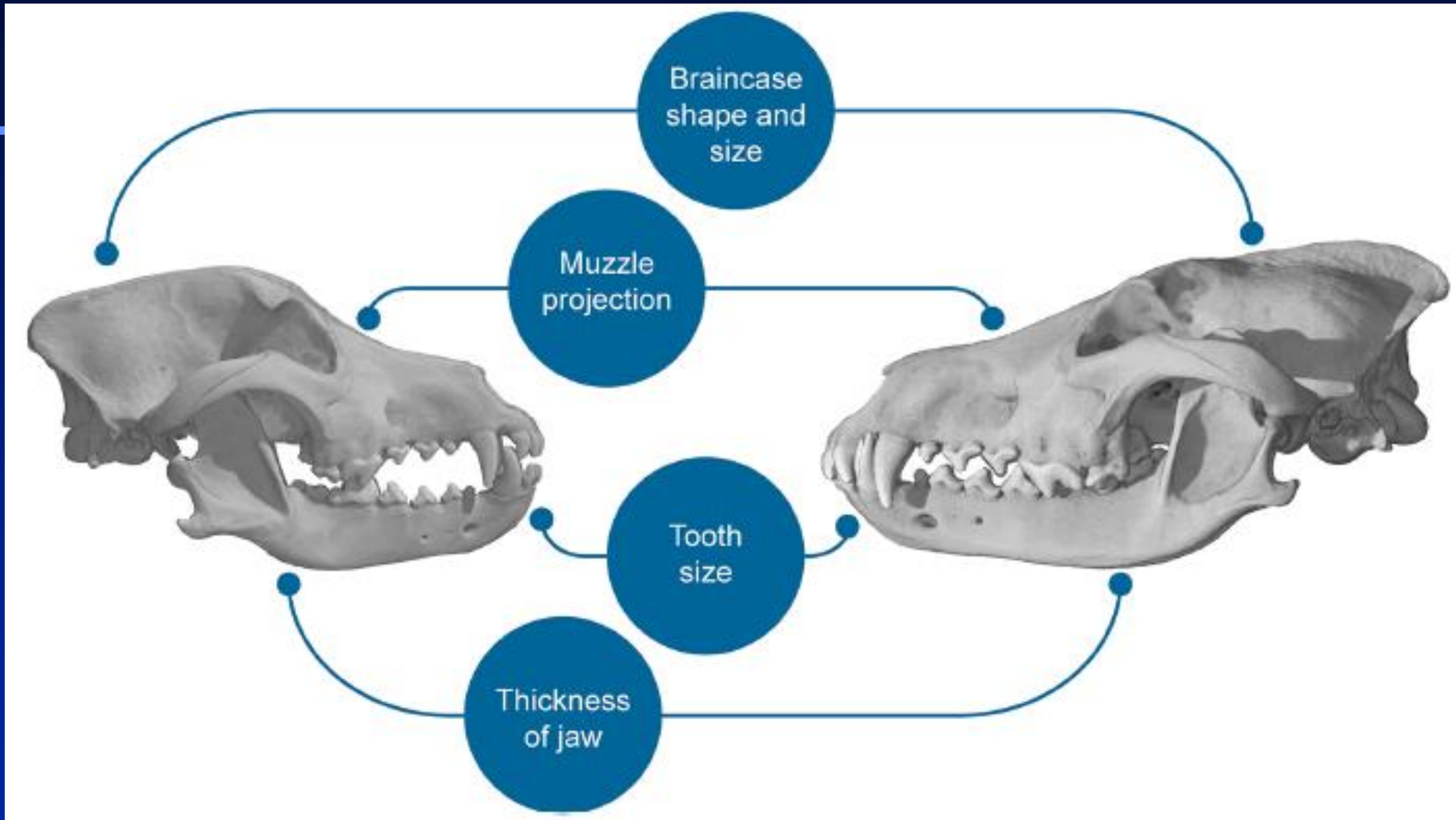
PLOS ONE | https://doi.org/10.1371/journal.pone.0185306 October 18, 2017

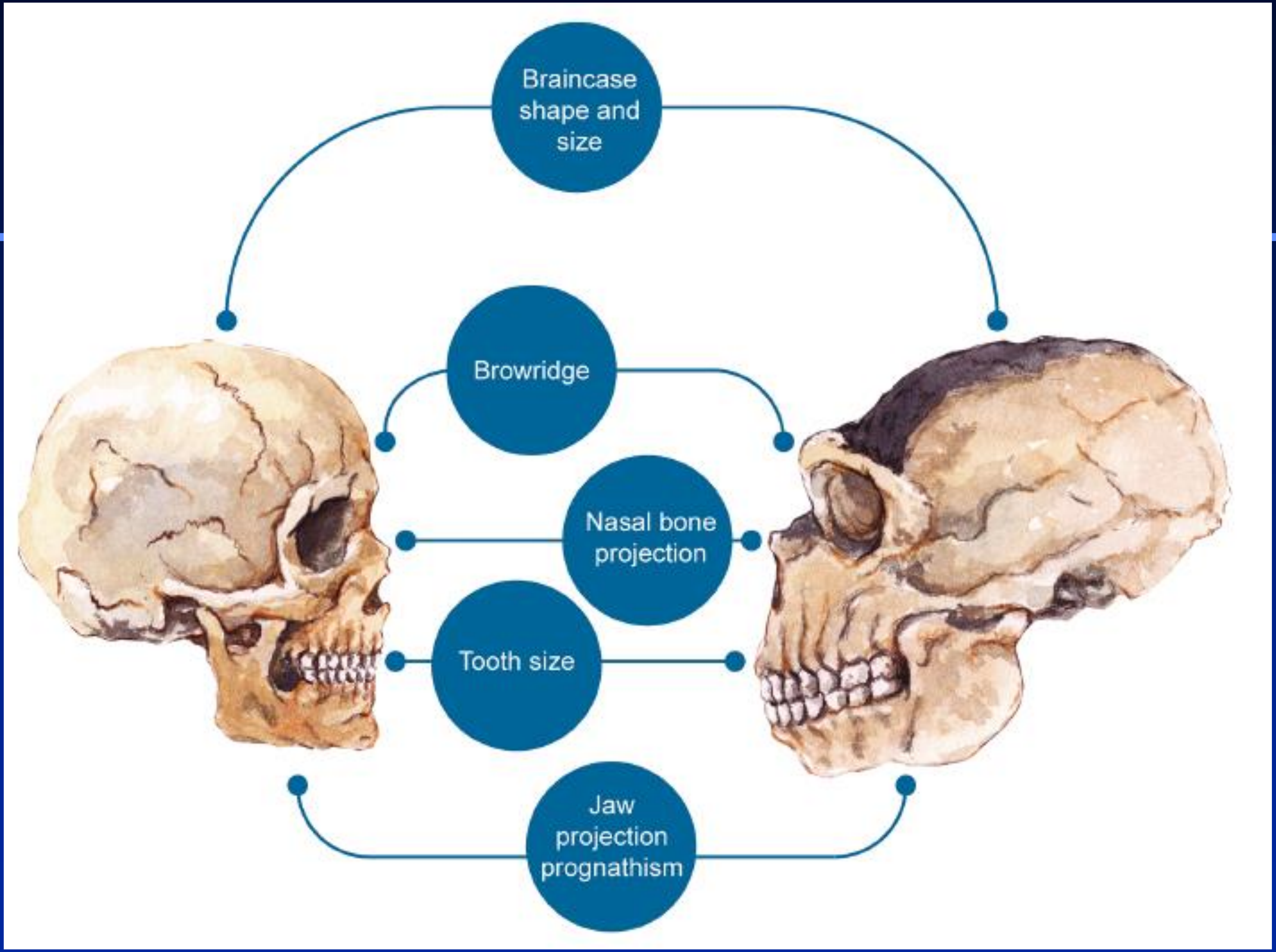
of self-domestication. As has been well documented elsewhere [1, 2], the idea that anatomically modern humans (AMH) are a domesticated species has long been entertained by preeminent scholars in biological and human sciences (in passing by Charles Darwin [3] and more seriously by Franz Boas [4]). We argue that such characterizations are accurate, not merely as which humans share. The domesticated traits exhibited by AMH plausibly emerged following similar intraspecific selective pressures for prosocial behaviors: in other words, tameness towards fellow humans. Similarly, it has been claimed that reduced emotional reactivity and increased prosociality among humans were keys to our self-domestication [34]. So, what, if

The self-domestication hypothesis is, then, a strong contender to account for key aspects of modern human cognition. The central claim of the present paper is that (paleo-)genomic data

Intriguingly, there is evidence that domestication can enable the development of complex behaviors beyond those discussed so far for the domestication syndrome. For example, both dogs and domesticated foxes outperform all non-human primates in tests of cooperative communication [34]. The Bengalese finch, domesticated from its wild ancestor, the white-rumped munia [35, 36], has developed a complex song that is preferred by both female finches and munias over the stereotyped song of the male munia [37]. There are tempting parallels to be

The self-domestication hypothesis is, then, a strong contender to account for key aspects of modern human cognition. The central claim of the present paper is that (paleo-)genomic data


Braincase shape and size
Muzzle projection
Tooth size
Thickness of jaw

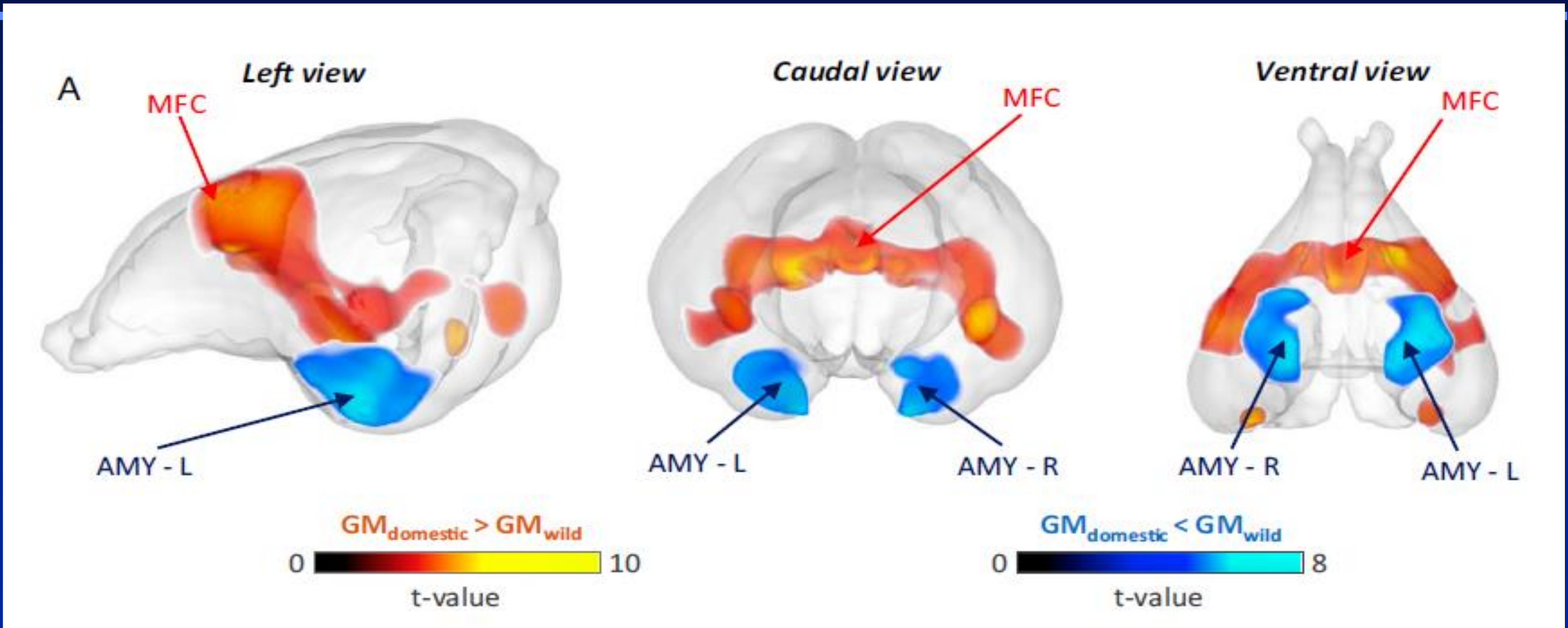

Braincase shape and size
Browridge
Nasal bone projection
Tooth size
Jaw projection prognathism

Changes in brain architecture are consistent with altered fear processing in domestic rabbits

Irene Brusini[a,1], Miguel Carneiro[b,c,1], Chunliang Wang[a,1], Carl-Johan Rubin[d], Henrik Ring[e], Sandra Afonso[b], José A. Blanco-Aguiar[b,f], Nuno Ferrand[b,c,g], Nima Rafati[d], Rafael Villafuerte[h], Örjan Smedby[a], Peter Damberg[i], Finn Hallböök[e], Mats Fredrikson[j,k,1], and Leif Andersson[d,l,m,1,2]

7380–7385 | PNAS | July 10, 2018 | vol. 115 | no. 28

The most characteristic feature of domestic animals is their change in behavior associated with selection for tameness. Here we show, using high-resolution brain magnetic resonance imaging in wild and domestic rabbits, that domestication reduced amygdala volume and enlarged medial prefrontal cortex volume, supporting that areas driving fear have lost volume while areas modulating negative affect have gained volume during domestication. In contrast to the localized gray matter alterations, white matter anisotropy was reduced in the corona radiata, corpus callosum, and the subcortical white matter. This suggests a compromised white matter structural integrity in projection and association fibers affecting both afferent and efferent neural flow, consistent with reduced neural processing. We propose that compared with their wild ancestors, domestic rabbits are less fearful and have an attenuated flight response because of these changes in brain architecture.

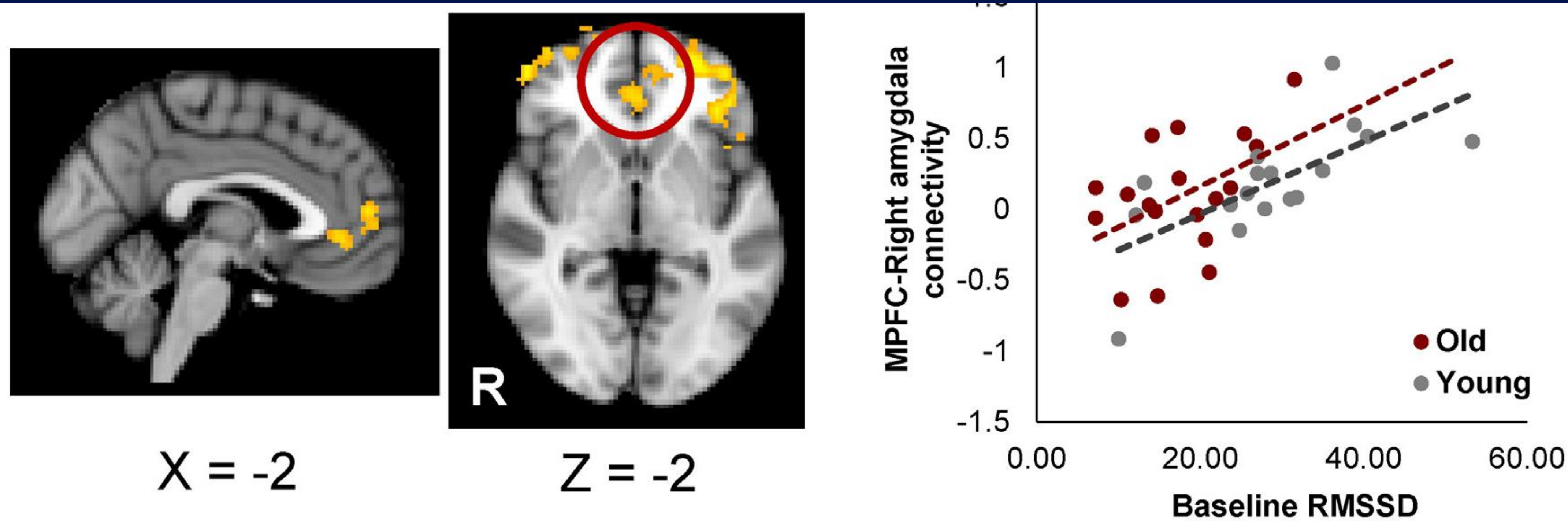


A
Left view
Caudal view
Ventral view
MFC
MFC
MFC
AMY - L
AMY - L
AMY - R
AMY - R
AMY - L
GMdomestic > GMwild
0
10
t-value
GMdomestic < GMwild
0
8
t-value

Heart rate variability is associated with amygdala functional connectivity with MPFC across younger and older adults

Michiko Sakaki [a,b,*], Hyun Joo Yoo [c], Lin Nga [c], Tae-Ho Lee [d], Julian F. Thayer [e], &, Mara Mather [c]

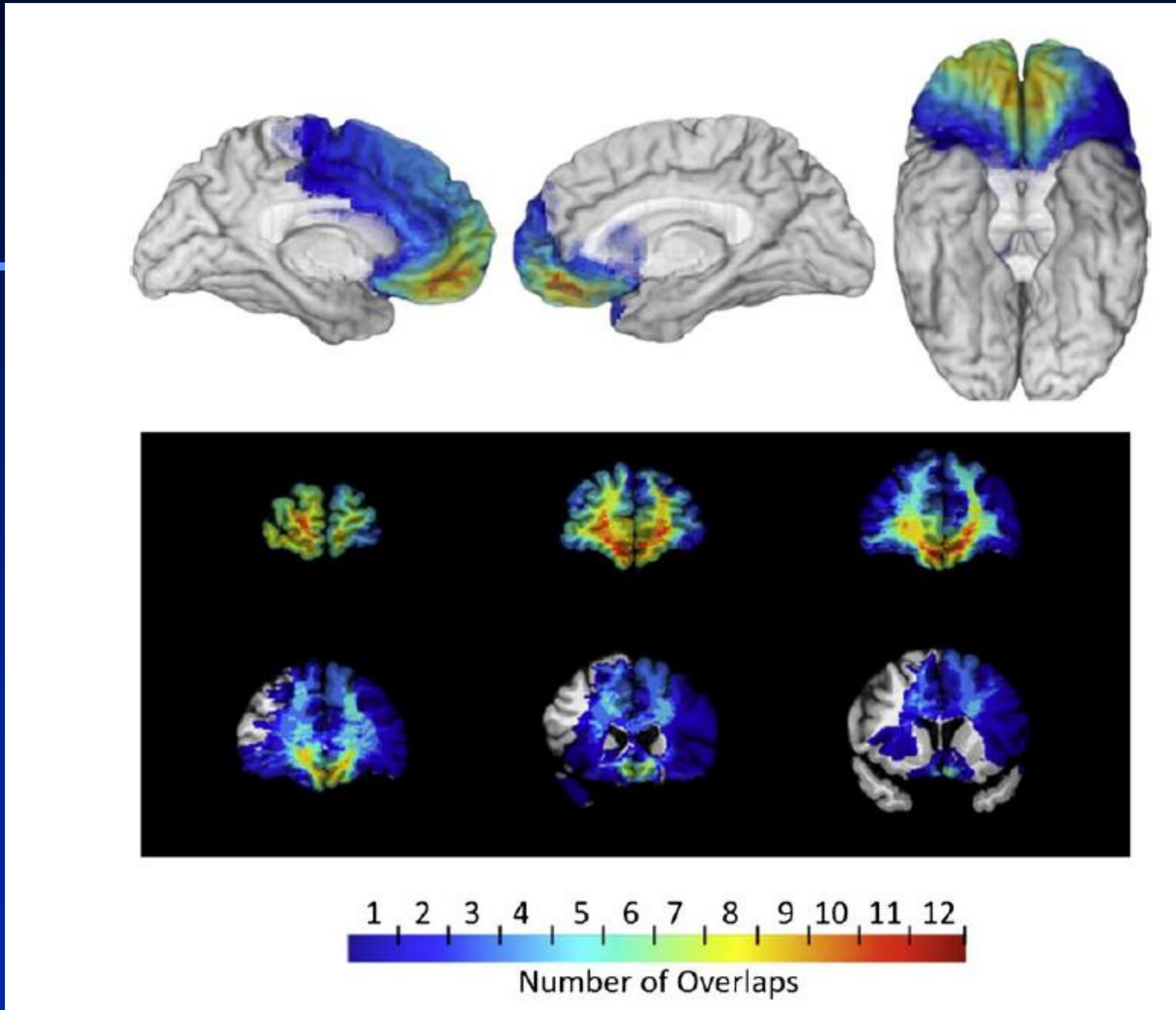
NeuroImage 139 (2016) 44–52

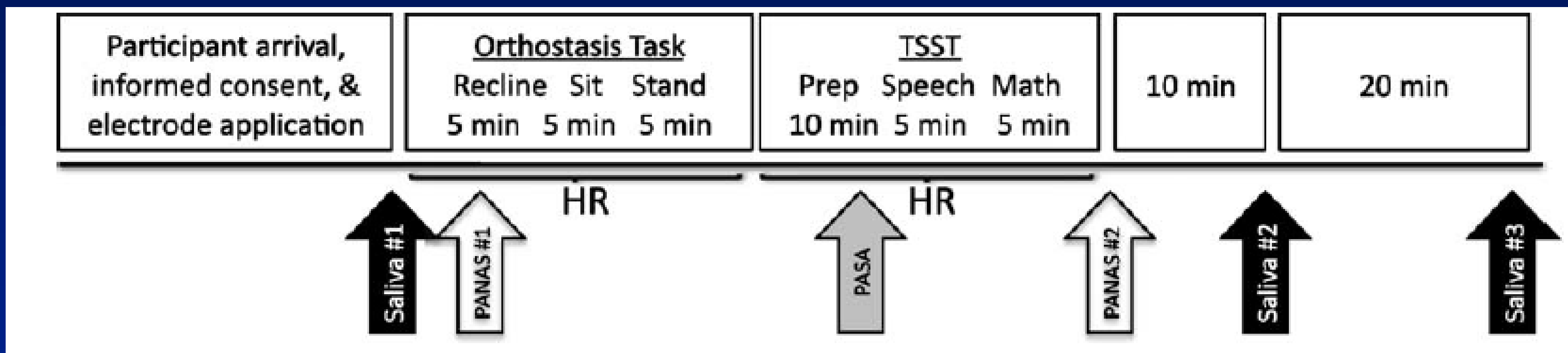

R
X = -2
Z = -2
MPFC-Right amygdala connectivity
1
0.5
0
-0.5
-1
-1.5
0.00
20.00
40.00
60.00
Baseline RMSSD
Old
Young

Medial prefrontal cortex damage affects physiological and psychological stress responses differently in men and women

Tony W. Buchanan[a,*], David Driscoll[b], Samantha M. Mowrer[c], John J. Sollers III[c], Julian F. Thayer[c,d], Clemens Kirschbaum[e], Daniel Tranel[b]

Psychoneuroendocrinology (2010) 35, 56—66

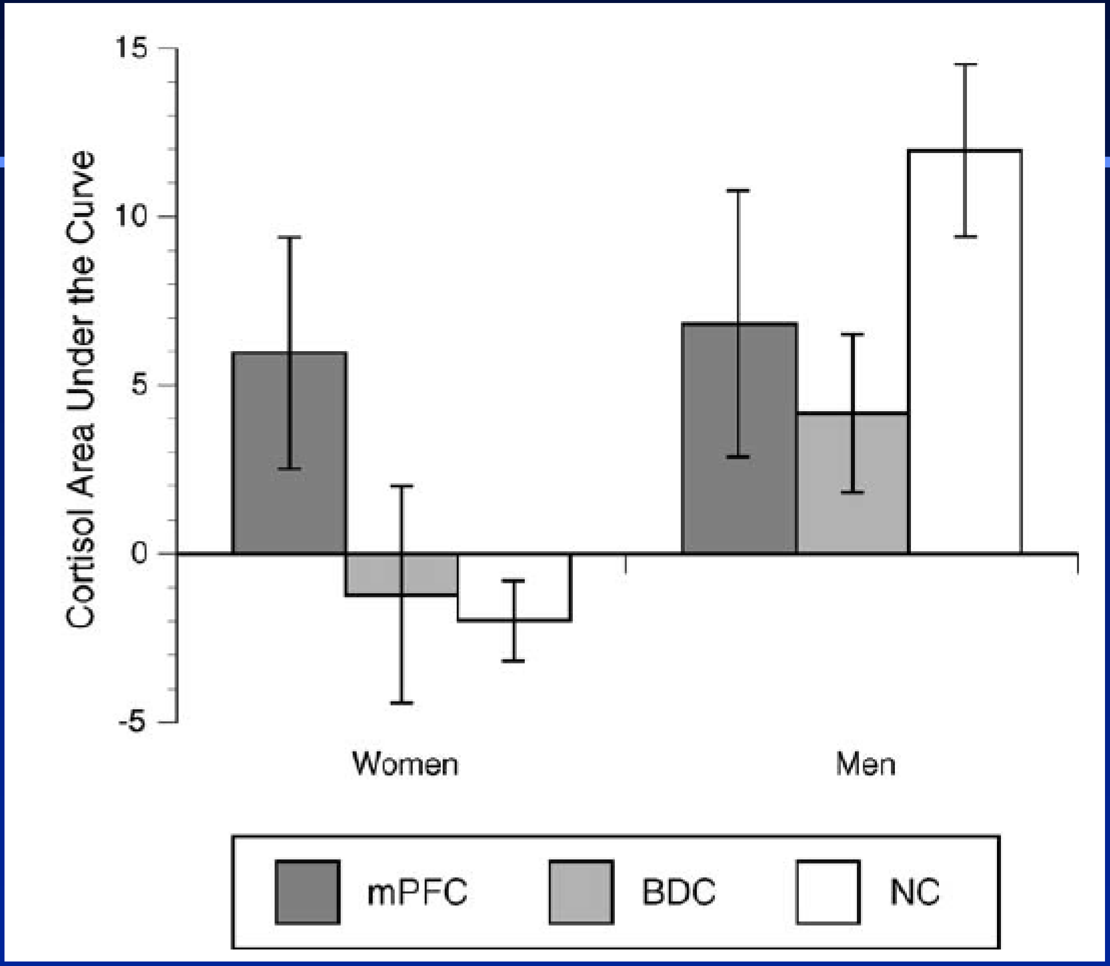

1 2 3 4 5 6 7 8 9 10 11 12
Number of Overlaps



Participant arrival, informed consent, & electrode application
Orthostasis Task
Recline 5 min
Sit 5 min
Stand 5 min
TSST
Prep 10 min
Speech 5 min
Math 5 min
10 min
20 min
HR
HR
Saliva #1
PANAS #1
PASA
PANAS #2
Saliva #2
Saliva #3

Table 1 Demographics. Mean age and education in years ± standard deviation.

Participant	Mean age	Mean education	Sex	Side of lesion
mPFC group (*N* = 18)	53.6 ± 13.9	13.8 ± 1.9	9M/9F	11B/3L/4R
Brain damaged comparison (*N* = 12)	56.3 ± 10.4	13.9 ± 3.1	6M/6F	2B/7L/3R
Healthy comparison participants (*N* = 54)	50.2 ± 10.7	16.0 ± 2.5	27M/27F	–



15
10
5
0
-5
Cortisol Area Under the Curve
Women
Men
mPFC
BDC
NC

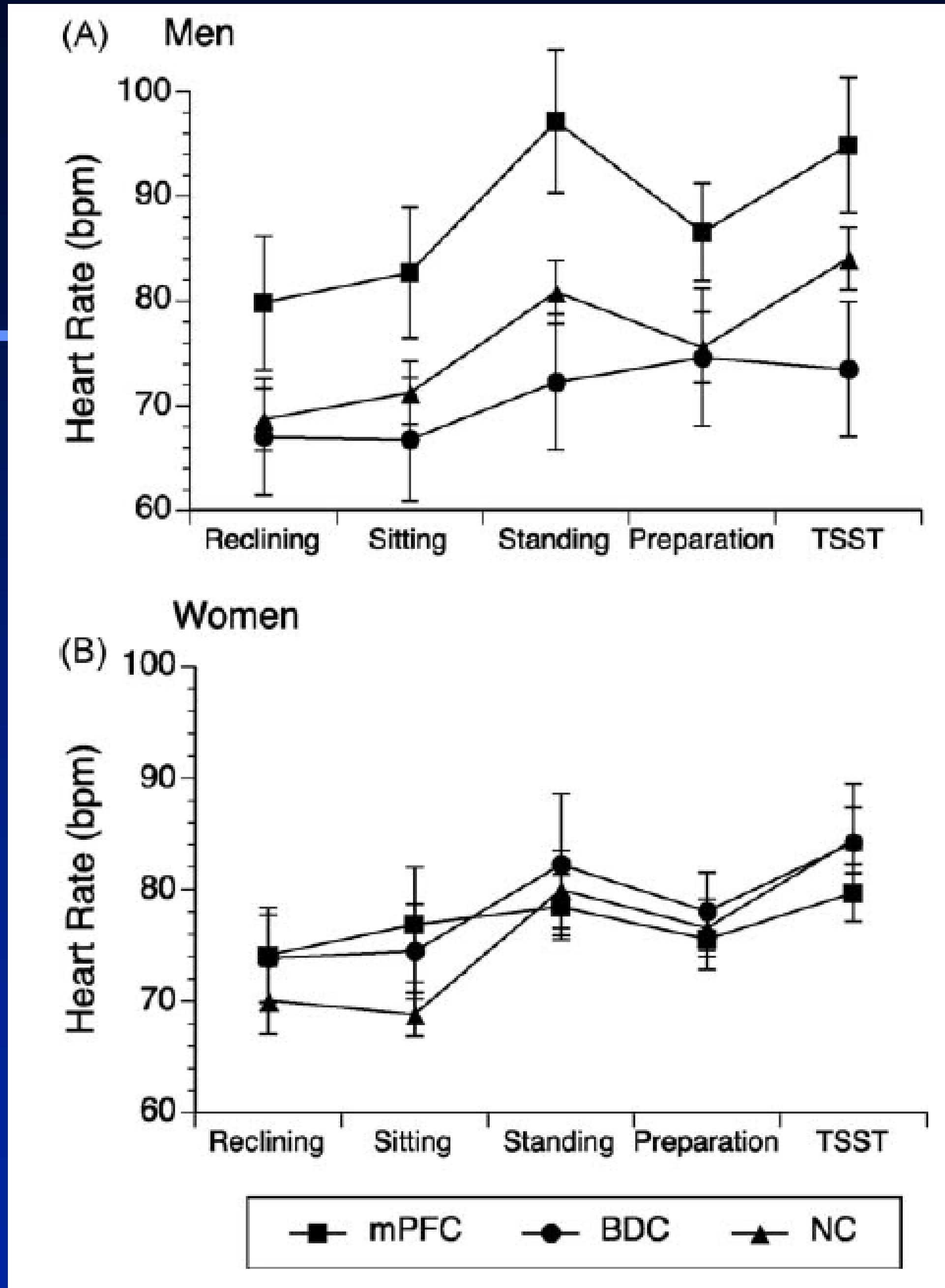

(A) Men
Heart Rate (bpm)
100
90
80
70
60
Reclining
Sitting
Standing
Preparation
TSST
Women
(B)
Heart Rate (bpm)
100
90
80
70
60
Reclining
Sitting
Standing
Preparation
TSST
mPFC
BDC
NC

Table 4 Affective responses to TSST. Entries show mean ± S.E.M.

Sex	Group	Change in positive affect	Change in negative affect	Threat	Challenge	Self-concept	Control expectancy
Female	mPFC	−4.7 (2.3)*	13.4 (2.2)*	3.4 (0.3)*	3.6 (0.2)	3.4 (0.3)*	4.2 (0.3)
	BDC	0.3 (2.2)	4.0 (2.3)	2.7 (0.4)	4.0 (0.2)	3.5 (0.4)	4.3 (0.3)
	Healthy comparison	−0.4 (1.2)	4.0 (0.8)	2.1 (0.2)	3.6 (0.2)	4.0 (0.2)	4.2 (0.2)
Male	mPFC	−4.1 (1.9)*	10.7 (2.4)*	2.6 (0.4)*	3.3 (0.4)	3.7 (0.2)*	4.4 (0.2)
	BDC	0.7 (3.5)	6.5 (4.2)	1.0 (0.4)	3.3 (0.7)	3.9 (0.4)	3.8 (0.3)
	Healthy comparison	0.4 (1.1)	2.4 (0.7)	2.2 (0.2)	3.7 (0.2)	4.1 (0.2)	4.3 (0.2)

* Significant difference from comparison participants using Bonferroni corrected multiple comparison procedure.

Stress Regulation

is

Emotion Regulation

Emotion regulation moderates the association between chronic stress and cardiovascular disease risk in humans: a cross-sectional study

Brita Roy, Carley Riley & Rajita Sinha

STRESS
2018, VOL. 21, NO. 6, 548–555
https://doi.org/10.1080/10253890.2018.1490724

Table 4. Association between stress scores and composite CV risk score, stratified by median emotion regulation score, Yale Stress Center cohort 2007–2012, $N = 528$.

	Full sample		High emotion regulation		Low emotion regulation	
	ß	*p* Value	ß	*p* Value	ß	*p* Value
Cumulative life events						
Unadjusted	0.054	<.001	0.056	.002	0.049	.003
Adjusted[a]	0.034	.005	0.033	.064	0.033	.052
Chronic Stress Score						
Unadjusted	0.034	.009	0.036	.083	0.033	.064
Adjusted[a]	0.028	.029	0.018	.38	0.042	.021
Perceived Stress Scale						
Unadjusted	0.020	.027	−0.004	.80	0.038	.004
Adjusted[a]	0.020	.021	0.007	.67	0.032	.014
Composite Stress Score						
Unadjusted	0.145	<.001	0.081	.36	0.185	.006
Adjusted[a]	0.116	.003	0.048	.59	0.206	.005

[a]Adjusted model includes age, sex, race, educational attainment, and smoking.

In the full sample, all stress measures were significantly associated with our composite CV risk score (Table 4). The interaction term between DERS and our composite chronic stress score was significant in predicting the composite and modified CV risk scores ($p = .007$), and marginal effects of DERS ranged from −0.017 (95% CI: −0.027, −0.006) to 0.012 (95% CI: 0.004, 0.20), signifying the DERS modifies the association between chronic stress and CV risk. Stratified analyses

Resting heart rate variability predicts self-reported difficulties in emotion regulation: a focus on different facets of emotion regulation

DeWayne P. Williams [1], Claudia Cash [1, 2], Cameron Rankin [1], Anthony Bernardi [1], Julian Koenig [1] and Julian F. Thayer [1]*

frontiers in Psychology

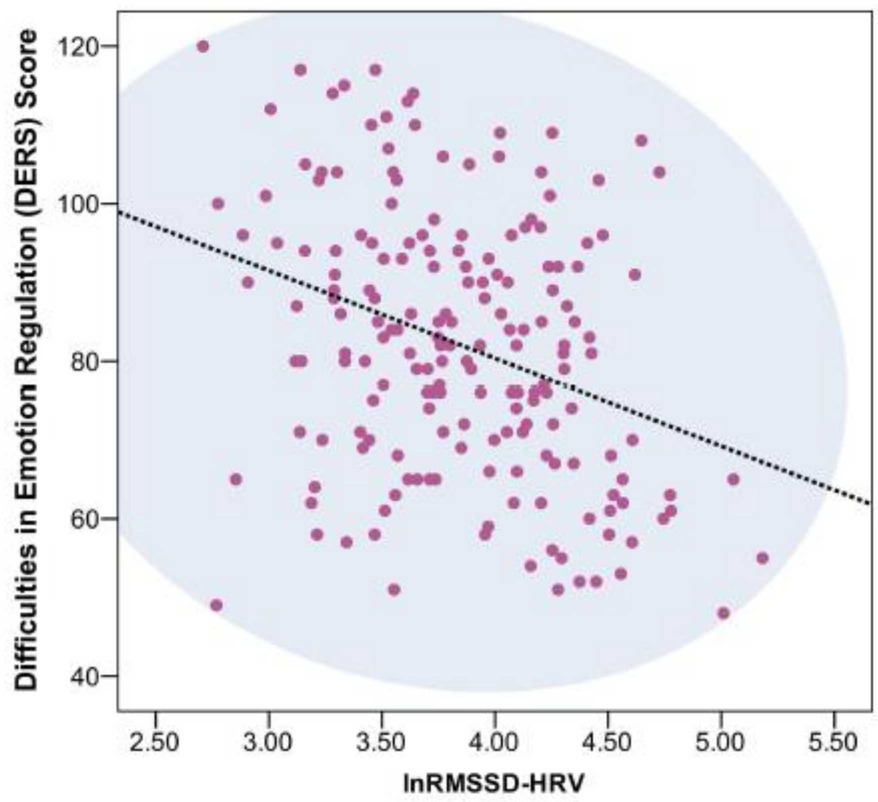


FIGURE 1 | Scatterplot of HRV and Difficulties in Emotion Regulation Scale (DERS) scores. This figure represents a scatterplot between RMSSD (in milliseconds and natural log (ln) transformed and difficulties in emotion regulation scale (DERS) total scale scores ($r = -0.325$, $p < 0.001$).

Heart rate variability as a transdiagnostic biomarker of psychopathology☆

Theodore P. Beauchaine *, Julian F. Thayer

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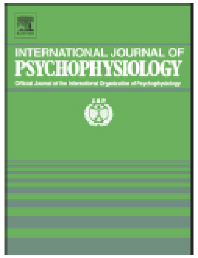
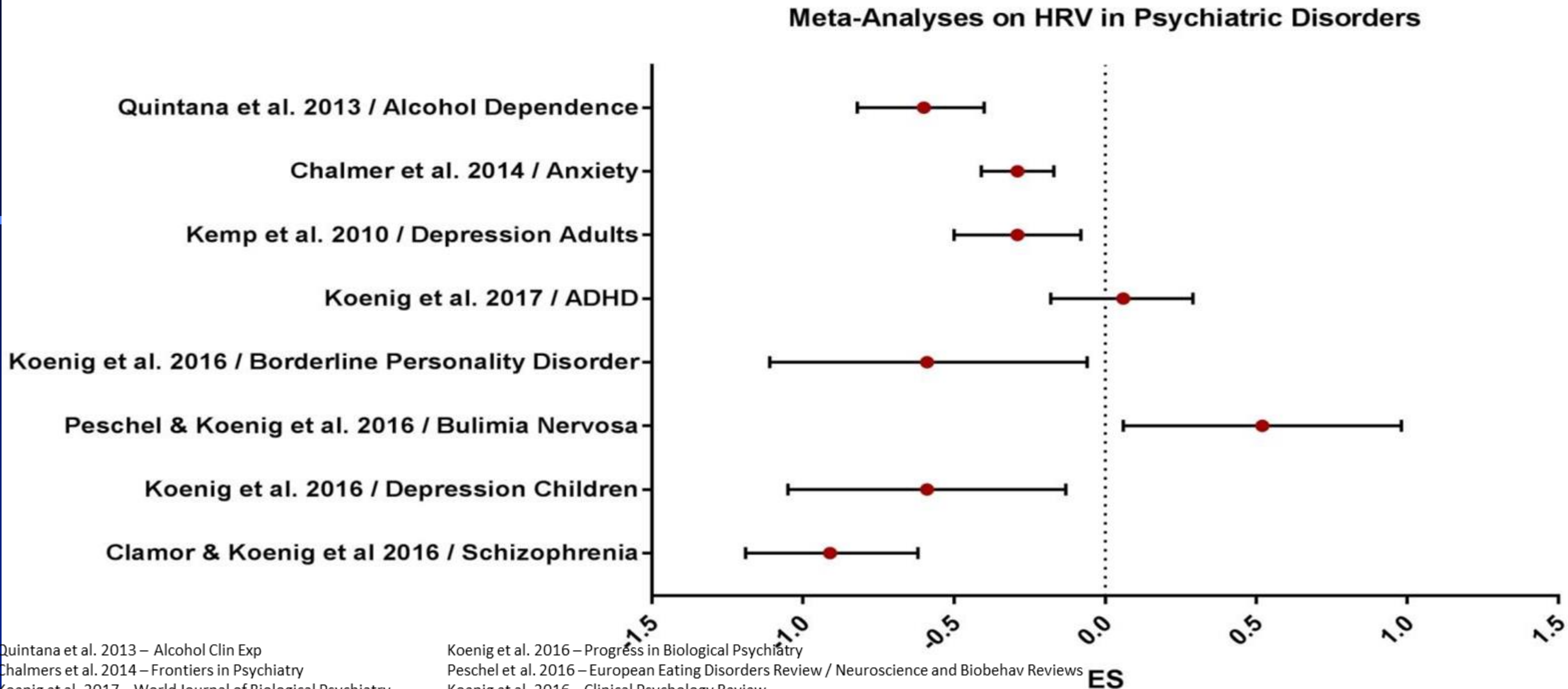
Contents lists available at ScienceDirect

International Journal of Psychophysiology

journal homepage: www.elsevier.com/locate/ijpsycho



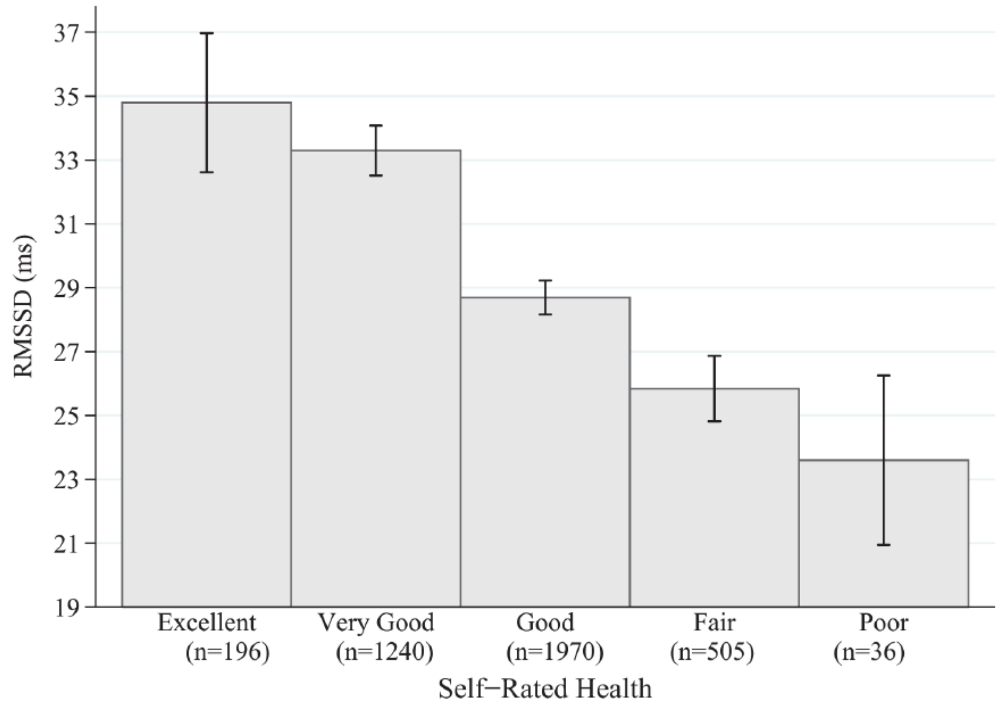


Quintana et al. 2013 – Alcohol Clin Exp
Chalmers et al. 2014 – Frontiers in Psychiatry
Koenig et al. 2017 – World Journal of Biological Psychiatry
Clamor et al. 2016 – British Journal of Psychiatry
Koenig et al. 2016 – Progress in Biological Psychiatry
Peschel et al. 2016 – European Eating Disorders Review / Neuroscience and Biobehav Reviews
Koenig et al. 2016 – Clinical Psychology Review
Kemp et al. 2010 – Biological Psychiatry

Investigating the Associations of Self-Rated Health: Heart Rate Variability Is More Strongly Associated than Inflammatory and Other Frequently Used Biomarkers in a Cross Sectional Occupational Sample

Marc N. Jarczok[1], Marcus E. Kleber[1], Julian Koenig[2]*, Adrian Loerbroks[3], Raphael M. Herr[4,1], Kristina Hoffmann[1], Joachim E. Fischer[1], Yael Benyamini[5], Julian F. Thayer[2,1]

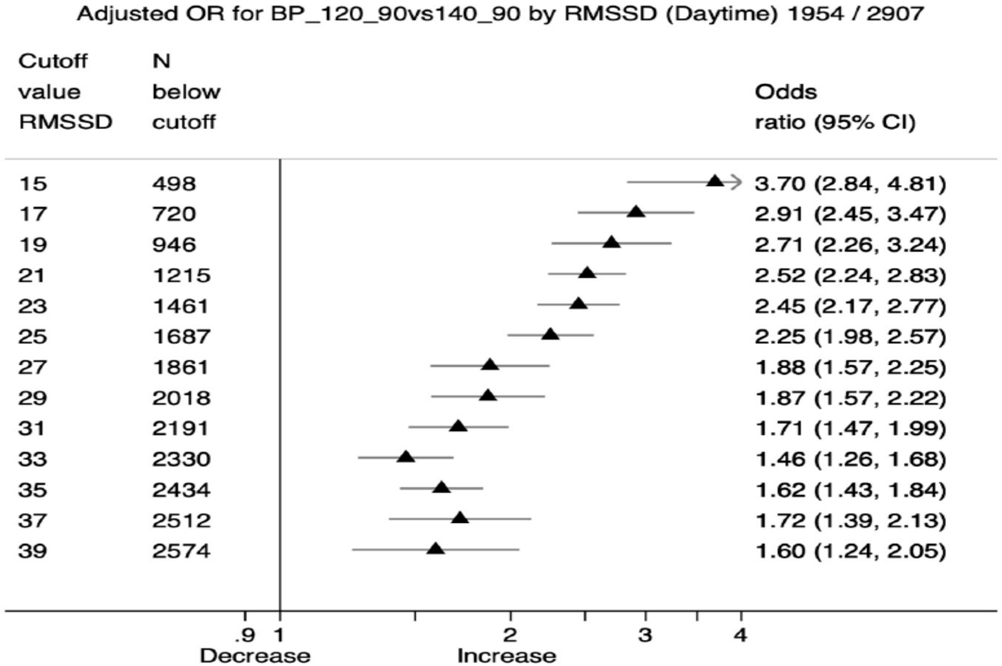
PLOS ONE | DOI:10.1371/journal.pone.0117196 February 18, 2015



First Evaluation of an Index of Low Vagally-Mediated Heart Rate Variability as a Marker of Health Risks in Human Adults: Proof of Concept

Marc N. Jarczok [1,2,*], Julian Koenig [3,4], Arne Wittling [5], Joachim E. Fischer [2] and Julian F. Thayer [6]

J. Clin. Med. 2019, *8*, 1940; doi:10.3390/jcm8111940

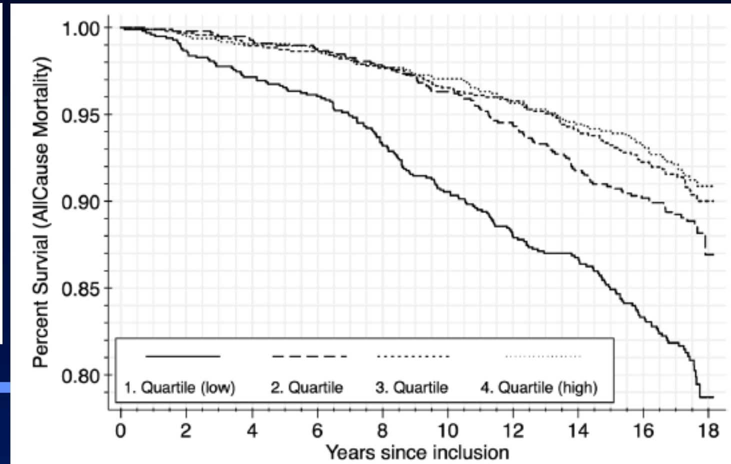


RMSSD, values below 25 ± 4 indicated elevated risk (odds ratios (OR) 1.5–3.5 across risk factors)

Lower values of a novel index of Vagal-Neuroimmunomodulation are associated to higher all-cause mortality in two large general population samples with 18 year follow up

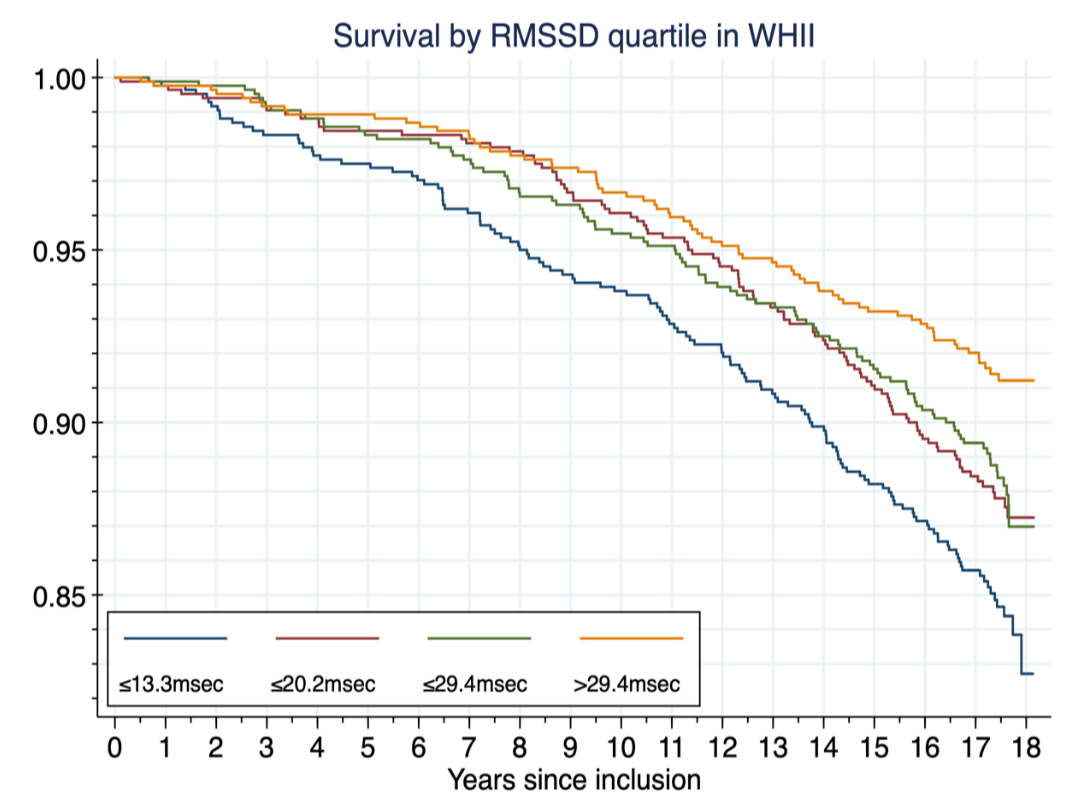
Marc N. Jarczok[1], Julian Koenig[2,3] & Julian F. Thayer[4]

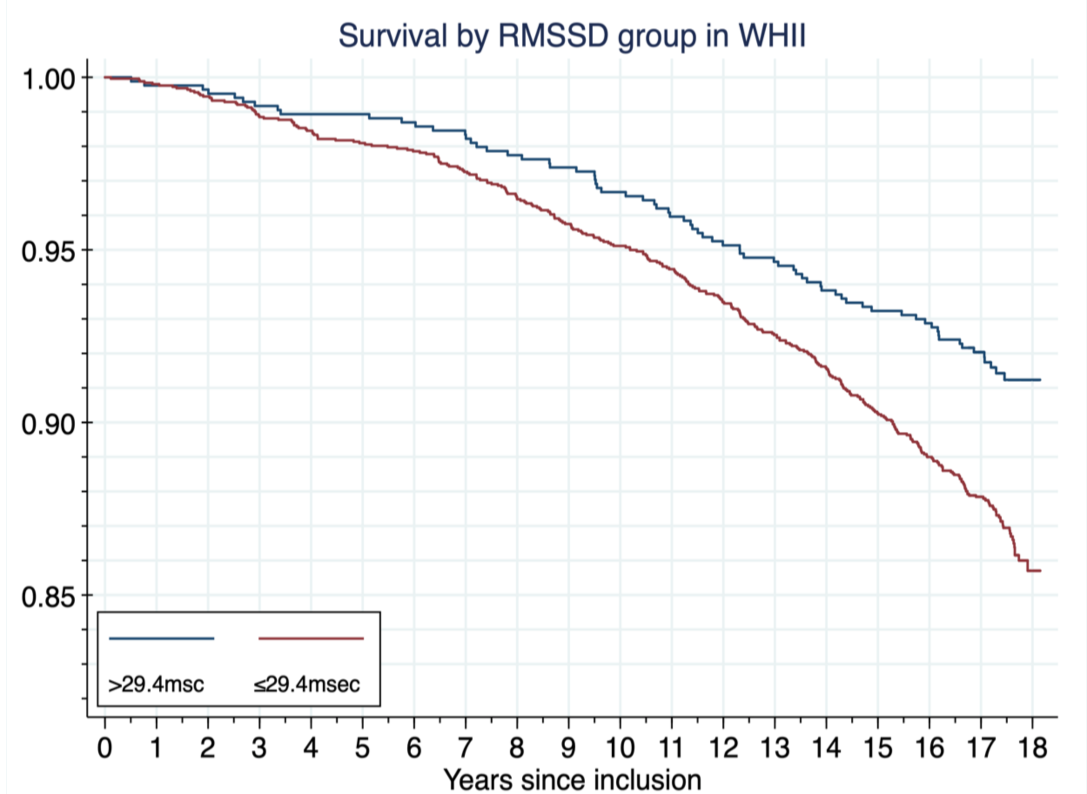
Scientific Reports | (2021) 11:2554

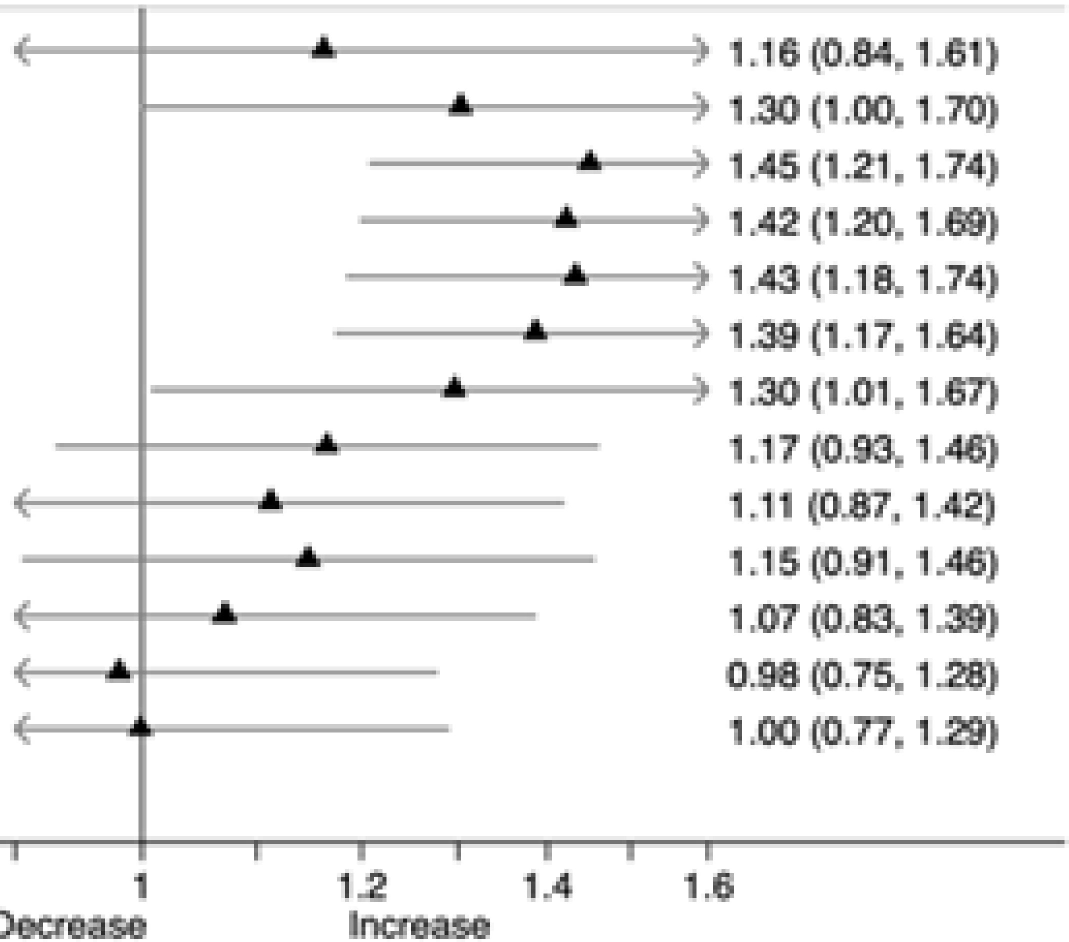


mber at risk

1. Quartile	983	(13)	970	(15)	955	(11)	944	(28)	916	(26)	890	(24)	801	(11)	688	(26)	623	(21)	24
2. Quartile	976	(2)	974	(5)	969	(5)	964	(10)	954	(14)	940	(18)	859	(23)	746	(12)	672	(12)	47
3. Quartile	950	(3)	947	(7)	940	(3)	937	(9)	928	(11)	917	(7)	831	(14)	723	(13)	666	(12)	52
4. Quartile	951	(4)	947	(5)	942	(3)	939	(10)	929	(6)	923	(13)	836	(10)	736	(9)	688	(14)	65







Cutoff value RMSSD	N below cutoff	Odds ratio (95% CI)
15	1117	1.16 (0.84, 1.61)
17	1754	1.30 (1.00, 1.70)
19	2462	1.45 (1.21, 1.74)
21	3289	1.42 (1.20, 1.69)
23	4102	1.43 (1.18, 1.74)
25	4835	1.39 (1.17, 1.64)
27	5558	1.30 (1.01, 1.67)
29	6195	1.17 (0.93, 1.46)
31	6839	1.11 (0.87, 1.42)
33	7359	1.15 (0.91, 1.46)
35	7813	1.07 (0.83, 1.39)
37	8182	0.98 (0.75, 1.28)
39	8486	1.00 (0.77, 1.29)

The p Factor: One General Psychopathology Factor in the Structure of Psychiatric Disorders?

Avshalom Caspi[1,2,3,4], Renate M. Houts[1], Daniel W. Belsky[5], Sidra J. Goldman-Mellor[6], HonaLee Harrington[1], Salomon Israel[1], Madeline H. Meier[1], Sandhya Ramrakha[7], Idan Shalev[1], Richie Poulton[7], and Terrie E. Moffitt[1,2,3,4]

Clinical Psychological Science
2014, Vol. 2(2) 119–137

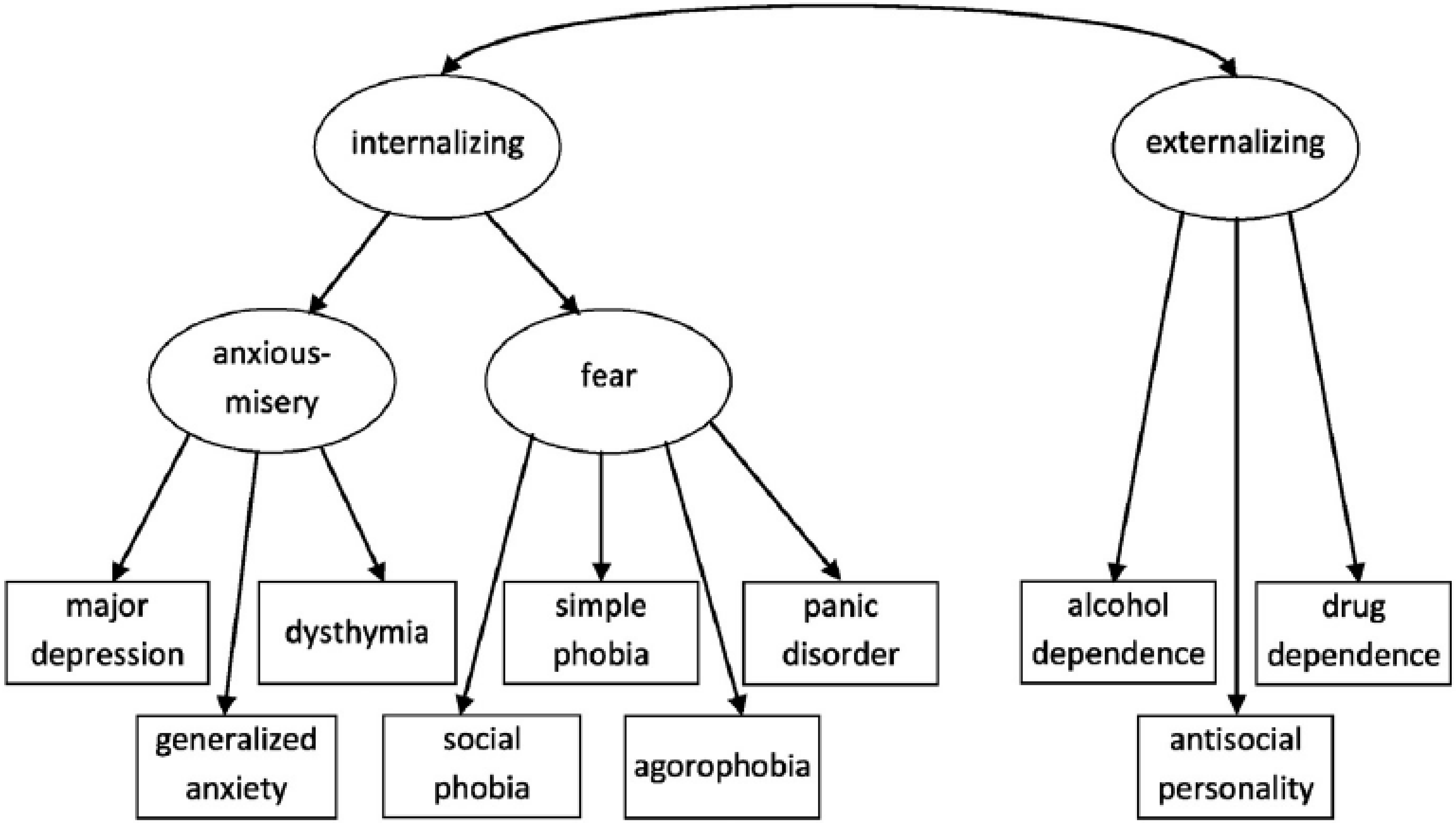
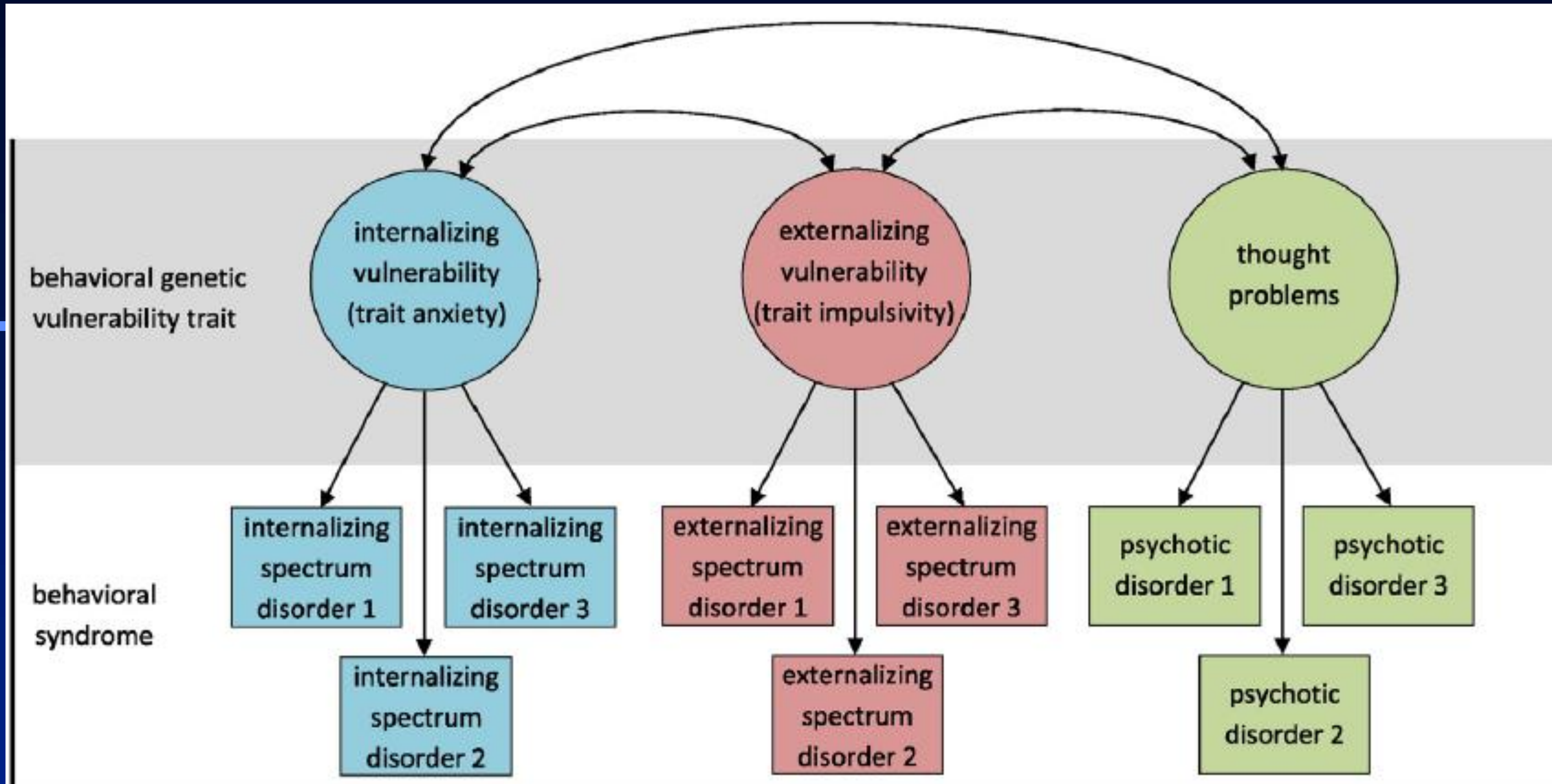
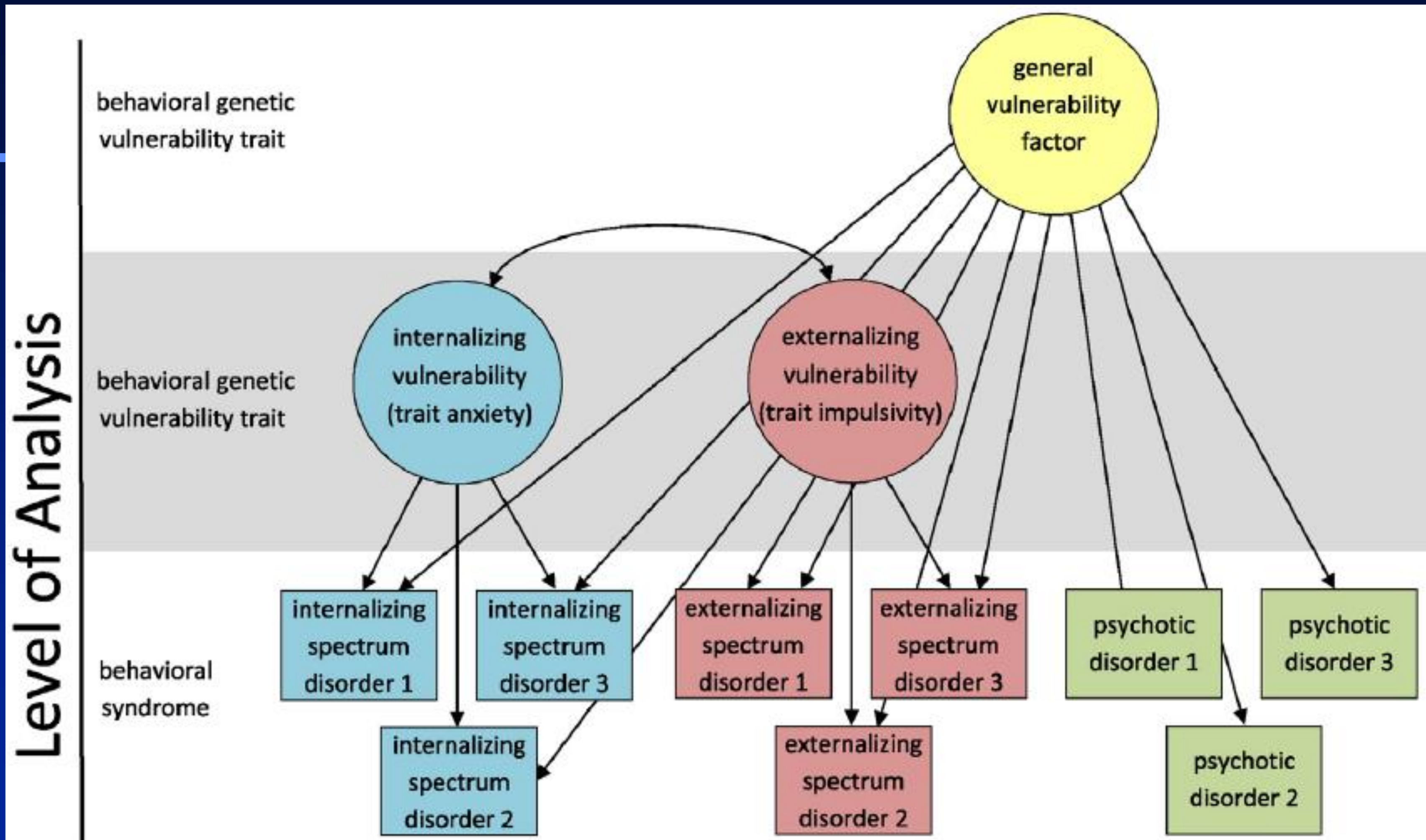


Fig. 1. The general latent structure of psychopathology.
Adapted from Krueger (1999).



Functional NIMH RDoC Domains				
Negative Valence System	**Positive Valence System**	**Cognitive System**	**Systems for Social Processes**	**Arousal and Regulatory System**
e.g. fear, anxiety, loss	e.g. reward, learning, habit	e.g. attention, perception, memory	e.g. attachment, communication, perception of self & others	e.g. arousal circadian rhythms


Level of Analysis
behavioral genetic vulnerability trait
behavioral genetic vulnerability trait
behavioral syndrome
general vulnerability factor
internalizing vulnerability (trait anxiety)
externalizing vulnerability (trait impulsivity)
internalizing spectrum disorder 1
internalizing spectrum disorder 3
internalizing spectrum disorder 2
externalizing spectrum disorder 1
externalizing spectrum disorder 3
externalizing spectrum disorder 2
psychotic disorder 1
psychotic disorder 3
psychotic disorder 2

ing, shows that adults with higher levels of p fared less well on tests requiring attention, concentration, mental control, visual-perceptual speed, and visual-motor coordination. Attesting to the ecological validity of these deficits, people who knew them well said that individuals with high levels of p experienced cognitive problems in their everyday lives.

ann. behav. med. (2009) 37:141–153
DOI 10.1007/s12160-009-9101-z

ORIGINAL ARTICLE

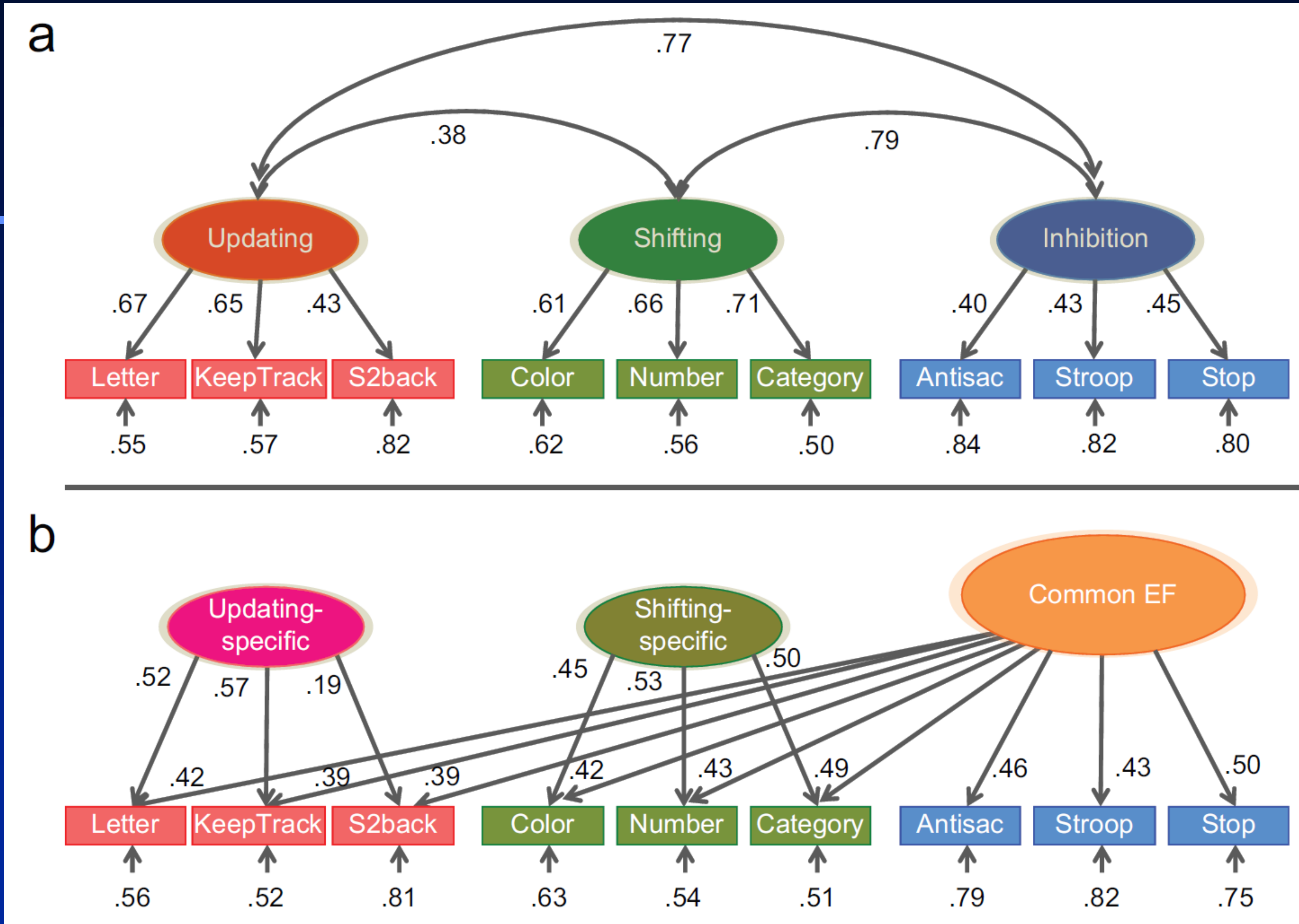
Heart Rate Variability, Prefrontal Neural Function, and Cognitive Performance: The Neurovisceral Integration Perspective on Self-regulation, Adaptation, and Health

Julian F. Thayer, Ph.D. · Anita L. Hansen, Ph.D. · Evelyn Saus-Rose, Cand. Psychol. · Bjorn Helge Johnsen, Ph.D.

Published online: 8 May 2009

Abstract
Background In the present paper, we describe a model of

navigation simulation. Finally, we review our studies in anxiety patients, as well as studies examining psychopathy.



a
.77
.38
.79
Updating
Shifting
Inhibition
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.65
.43
.61
.66
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.43
.45
Letter
KeepTrack
S2back
Color
Number
Category
Antisac
Stroop
Stop
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.57
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.62
.56
.50
.84
.82
.80
b
Updating-specific
Shifting-specific
Common EF
.52
.57
.19
.45
.53
.50
.42
.39
.39
.42
.43
.49
.46
.43
.50
Letter
KeepTrack
S2back
Color
Number
Category
Antisac
Stroop
Stop
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.52
.81
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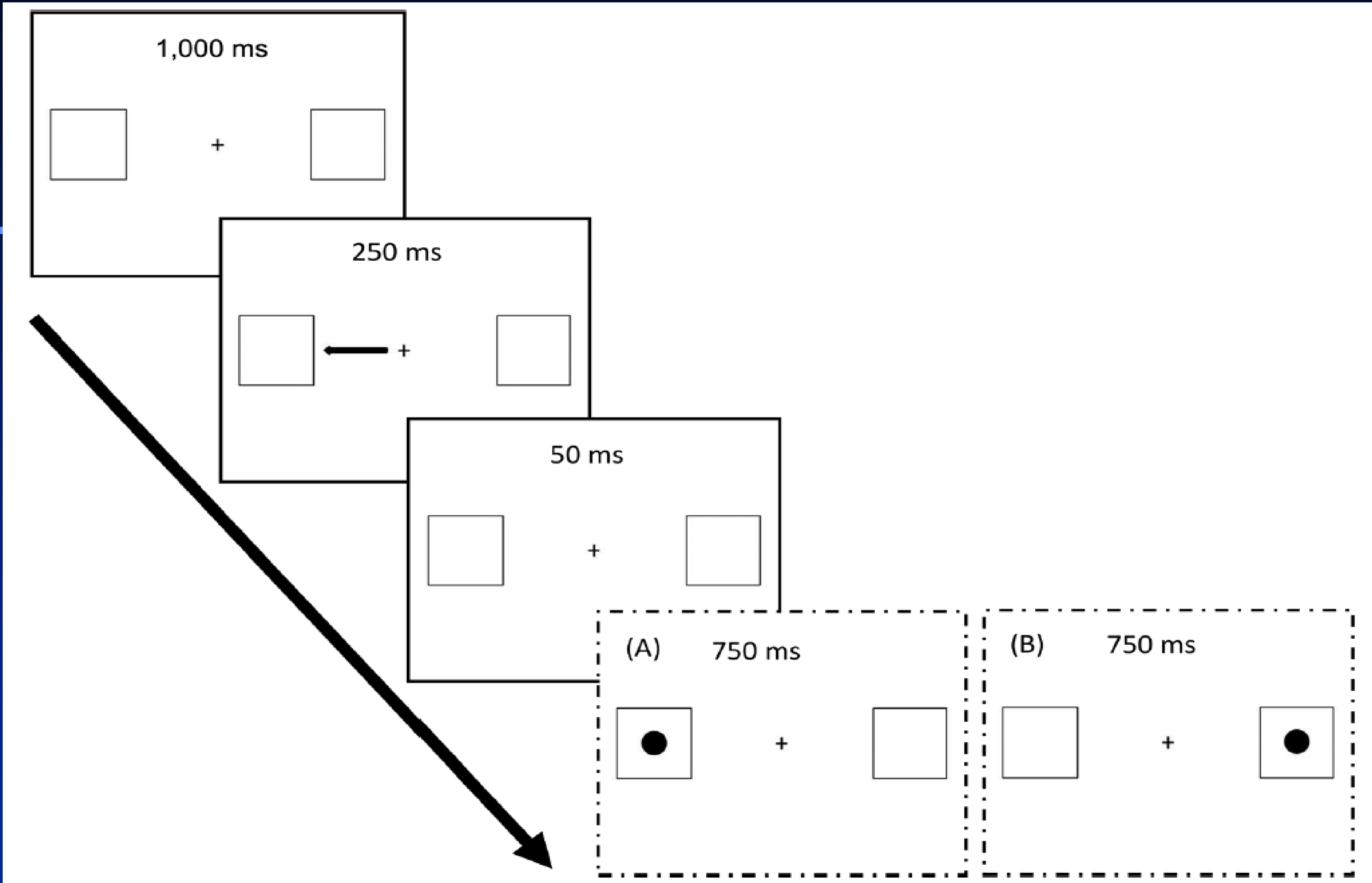
.51
.79
.82
.75

Resting cardiac vagal tone predicts intraindividual reaction time variability during an attention task in a sample of young and healthy adults

DEWAYNE P. WILLIAMS,[a] JULIAN F. THAYER,[a] AND JULIAN KOENIG[a,b]

Psychophysiology, 53 (2016), 1843–1851.



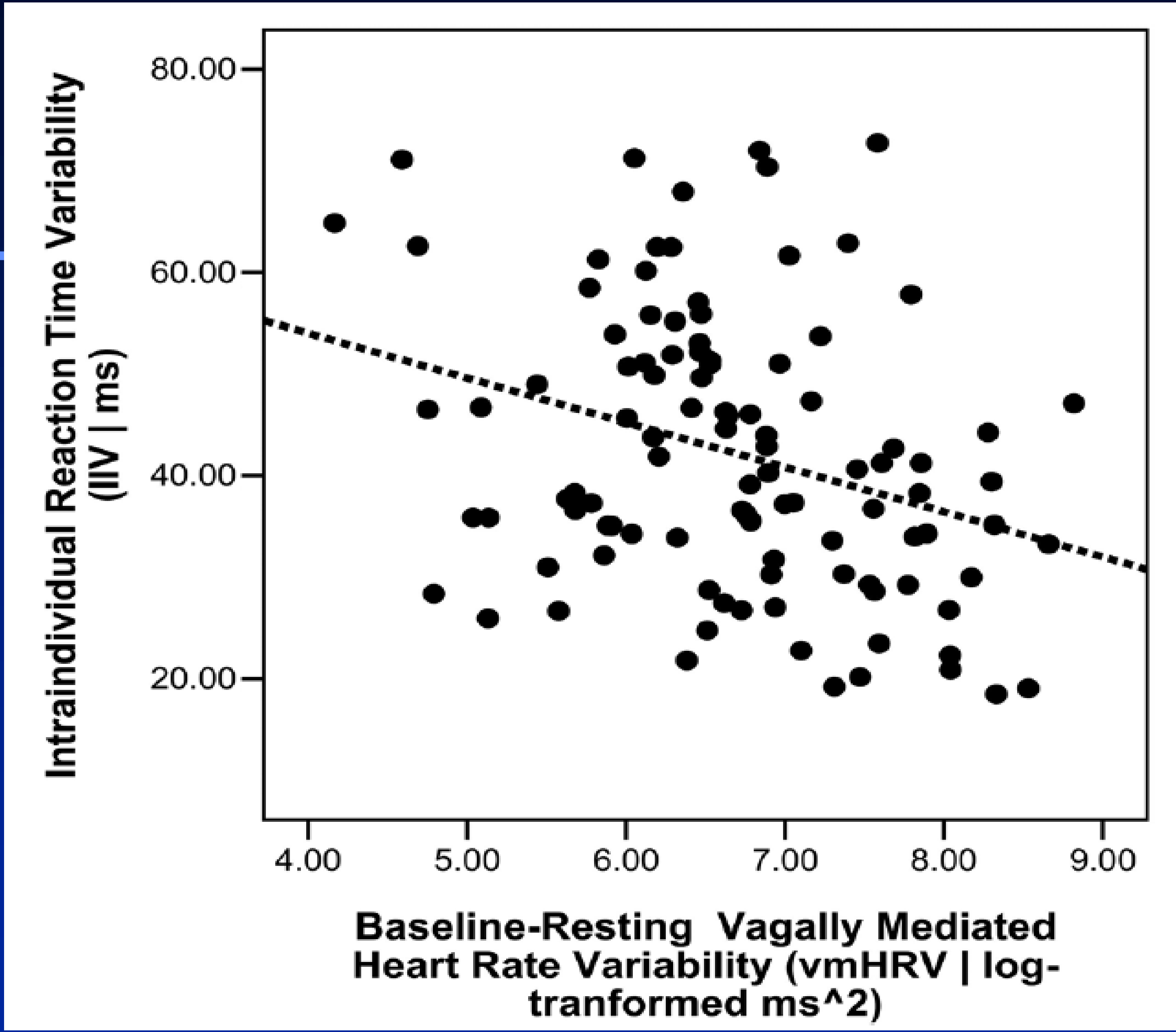
1,000 ms
250 ms
50 ms
(A)
750 ms
(B)
750 ms

Table 2. *Correlations of All Variables by Trial Type*

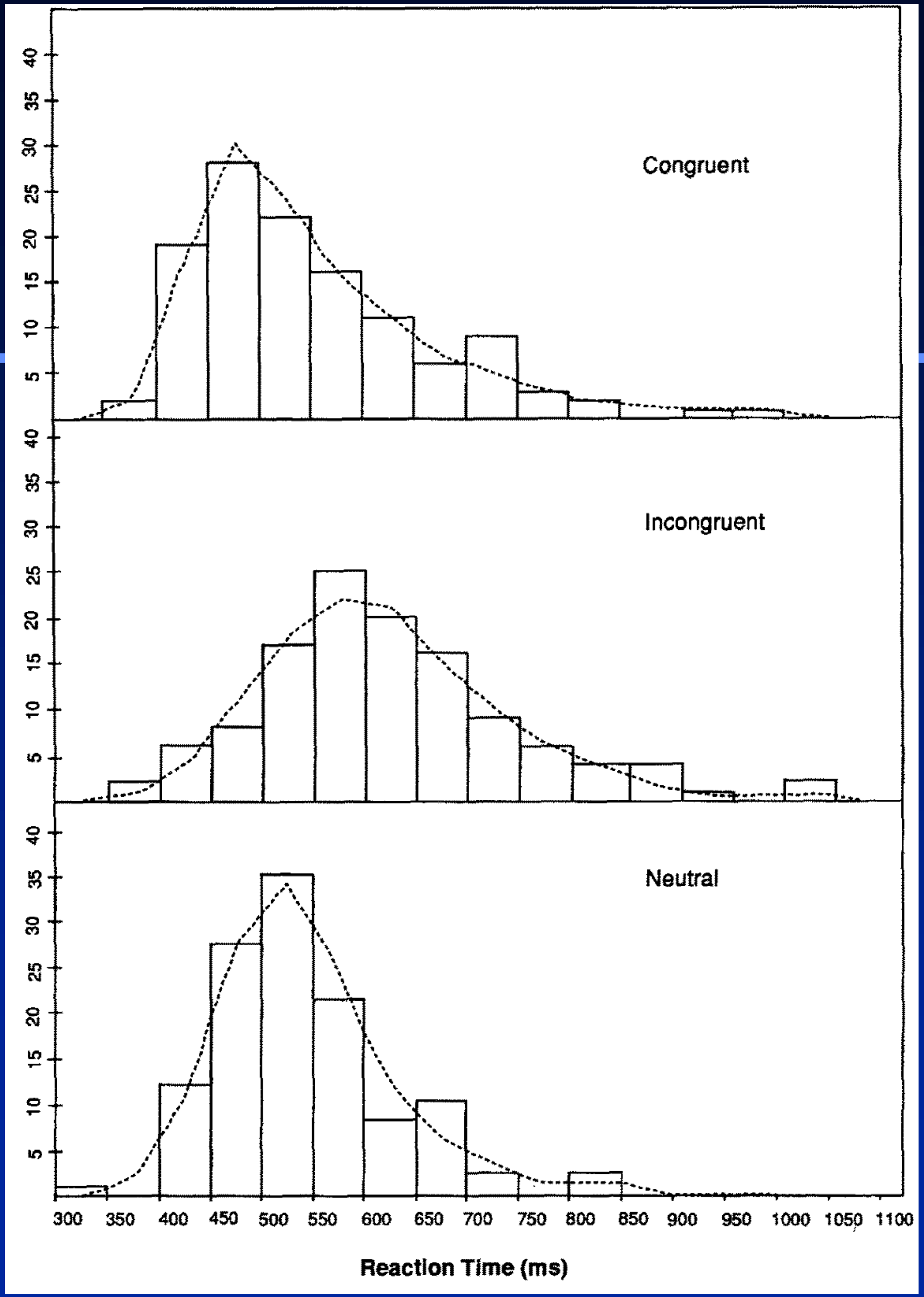
(A) Congruent	1	2	3	4
1. lnHF-HRV	–	–	–	–
2. Accuracy	.071	–	–	–
3. RT	−.034	.109	–	–
4. SD-RT	**−.301****	−.013	**.360*****	–

(B) Incongruent	1	2	3	4
1. lnHF-HRV	–	–	–	–
2. Accuracy	.086	–	–	–
3. RT	−.150	.123	–	–
4. SD-RT	**−.255****	.014	**.688*****	–

(C) Combined	1	2	3	4
1. lnHF-HRV	–	–	–	–
2. Accuracy	.093	–	–	–
3. RT	−.105	**.204***	–	–
4. SD-RT	**−.313****	−.151	**.646*****	–



Intraindividual Reaction Time Variability
(IIV | ms)
80.00
60.00
40.00
20.00
4.00
5.00
6.00
7.00
8.00
9.00
Baseline-Resting Vagally Mediated
Heart Rate Variability (vmHRV | log-
tranformed ms^2)



Congruent
Incongruent
Neutral
5
10
15
20
25
30
35
40
300
350
400
450
500
550
600
650
700
750
800
850
900
950
1000
1050
1100
Reaction Time (ms)

Registered Reports

Resting heart rate variability is associated with ex-Gaussian metrics of intra-individual reaction time variability☆,☆☆

Derek P. Spangler[a,*,1], DeWayne P. Williams[b], Lassiter F. Speller[b], Justin R. Brooks[a,c,2], Julian F. Thayer[b]

International Journal of Psychophysiology 125 (2018) 10–16

Table 2. Zero-order Correlations Among vmHRV and Performance Metrics Combined Across Stroop Conditions

	1	2	3	4	5	6
1. RMSSD	-					
2. Accuracy	.27*	-				
3. Mean RT	-.07	-.12	-			
4. SD-RT	-.06	-.44**	.16	-		
5. Mu	.08	-.13	.87**	.13	-	
6. Sigma	.14	-.27*	.38**	.74**	.55**	-
7. Tau	-.26*	.08	-.32**	-.004	-.74**	-.52**

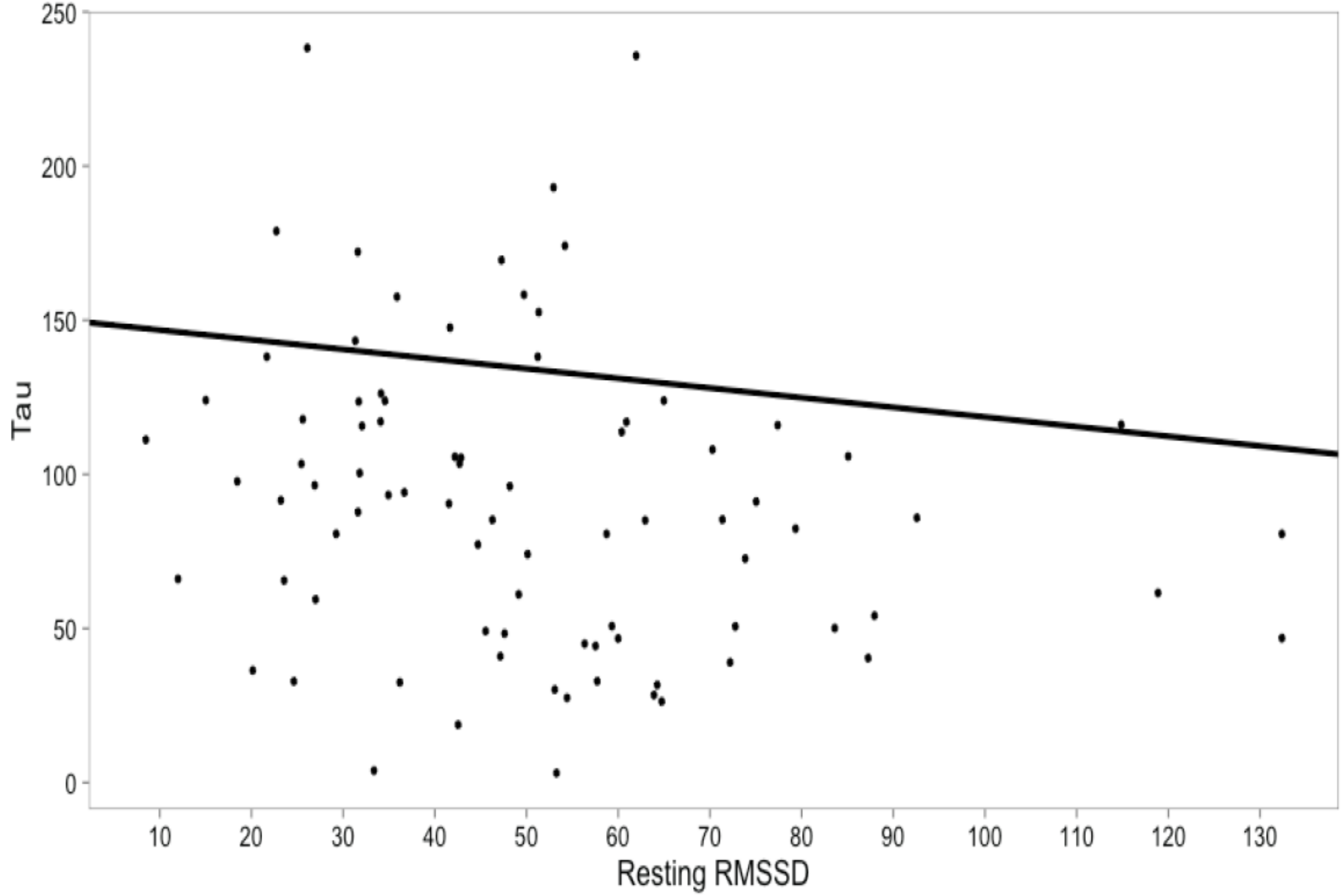


***Figure 2.* Relationship between resting RMSSD and tau.**

Scatter points represent individual subjects. Line represents the relationship between tau and RMSSD adjusted for gender, BMI, ethnicity, HF peak, depletion condition, and mu. RMSSD= root mean square of successive differences (metric or resting vmHRV in ms units).

Resting Heart Rate Variability Predicts Inhibitory Control Above and Beyond Impulsivity

Cristina Ottaviani,[1,2] Pietro Zingaretti,[3] Anna Maria Petta,[2] Gabriella Antonucci,[1,2]
Julian F. Thayer,[4] and Grazia Fernanda Spitoni[1,2]

Journal of Psychophysiology (2018)
https://doi.org/10.1027/0269-8803/a000222

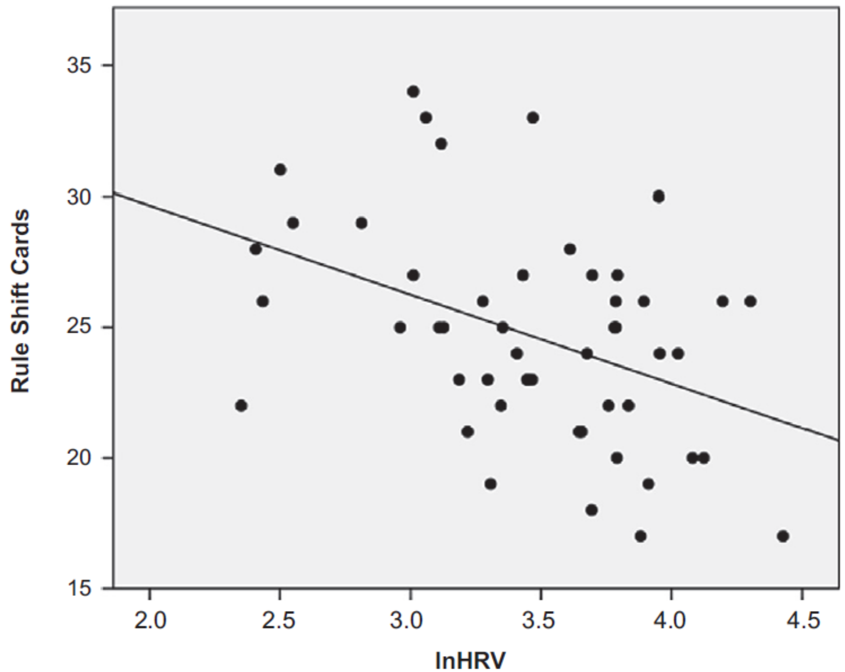


Figure 1. Scatterplots of Heart Rate Variability and time taken on the second section of the Rule Shift Cards. lnHRV = log transformation of root mean square of successive beat-to-beat interval differences.

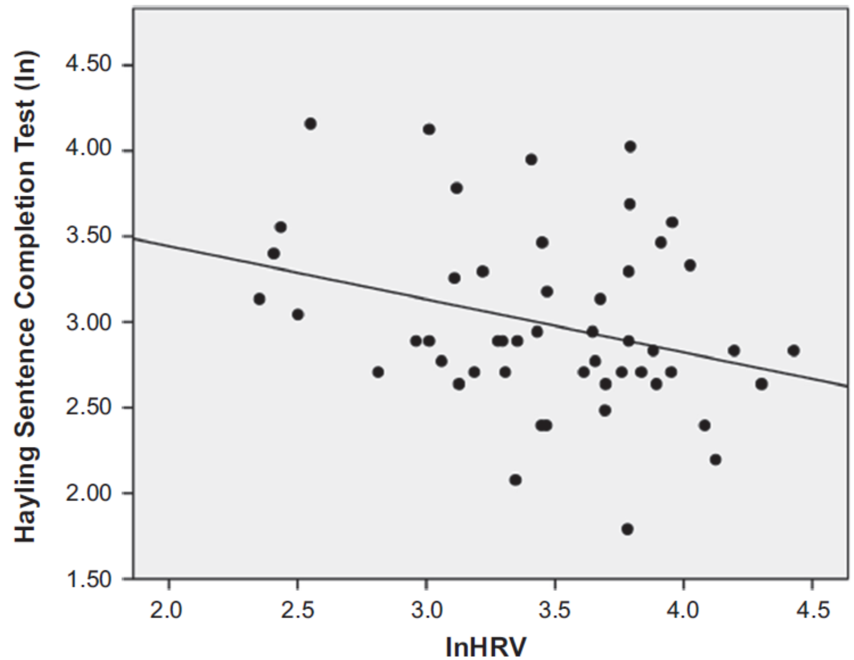


Figure 2. Scatterplots of Heart Rate Variability (ln) and response latencies on the second section of the Hayling Sentence Completion Test (ln). lnHRV = log transformation of root mean square of successive beat-to-beat interval differences.

The association between individual differences in executive functioning and resting high-frequency heart rate variability

Paula G. Williams[a,*], Matthew R. Cribbet[b], Ruben Tinajero[a], Holly K. Rau[c], Julian F. Thayer[d], Yana Suchy[a]

Biological Psychology 148 (2019) 107772

Table 2

Zero-Order Correlations Among Study Variables.

Variable	1	2	3	4	5	6	7
1. EF residual							
2. Resting HF-HRV	.39***						
3. Resting PEP	−.06	.11					
4. DKEFS-Non-EF	−.03	.12	−.04				
5. WAIS-WM	.40***	.14	.05	.19			
6. ACS	−.12	.05	−.04	−.02	−.19		
7. DERS total	−.15	.10	−.03	.16	.08	−.30**	
8. Daily SR ratings	.04	.16	−.05	.04	−.09	−.16	.36**

Note: DKEFS = Delis-Kaplan Executive Function Scales; EF = Executive Functioning; HF-HRV = high frequency-heart rate variability; PEP = pre-ejection period; WAIS = Wechsler Adult Intelligence Scale; WM = working memory; ACS = Attentional Control Scale; DERS = Difficulties in Emotion Regulation Scale; SR = self-regulation

IV: Baseline HF-HRV

DV: Executive Functioning

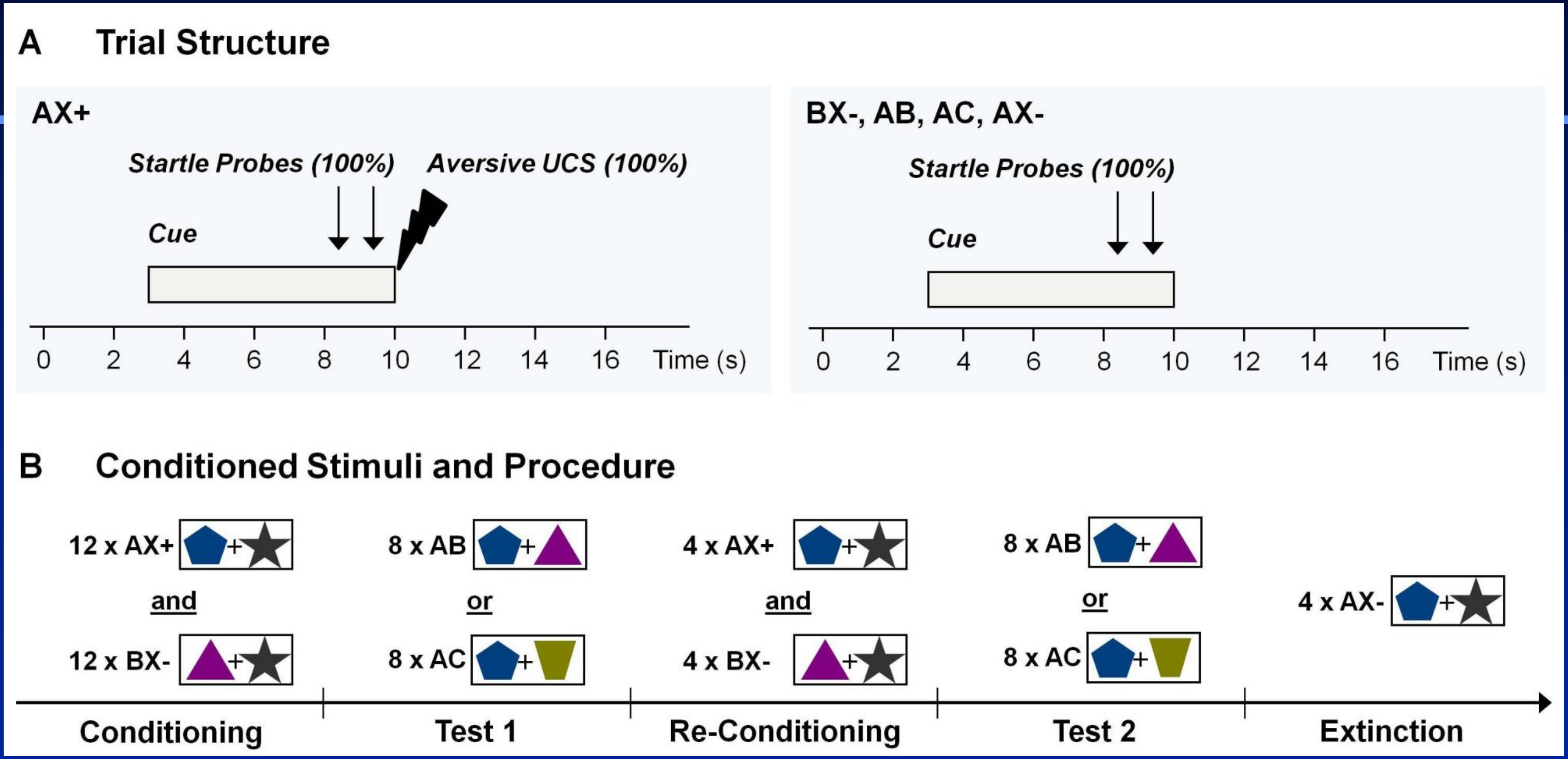
Age	−0.04	−0.34	$p > 0.05$	
Sex	−0.06	−0.501	$p > 0.05$	
Years of Education	−0.31	−2.14	$p = 0.04$	
Physical Activity	−0.05	−0.317	$p > 0.05$	
BMI	−0.06	−0.451	$p > 0.05$	
Baseline HF-HRV	0.31	2.53	$p = 0.01$	0.09

Total $R^2 = 0.21$; Adj $R^2 = 0.13$

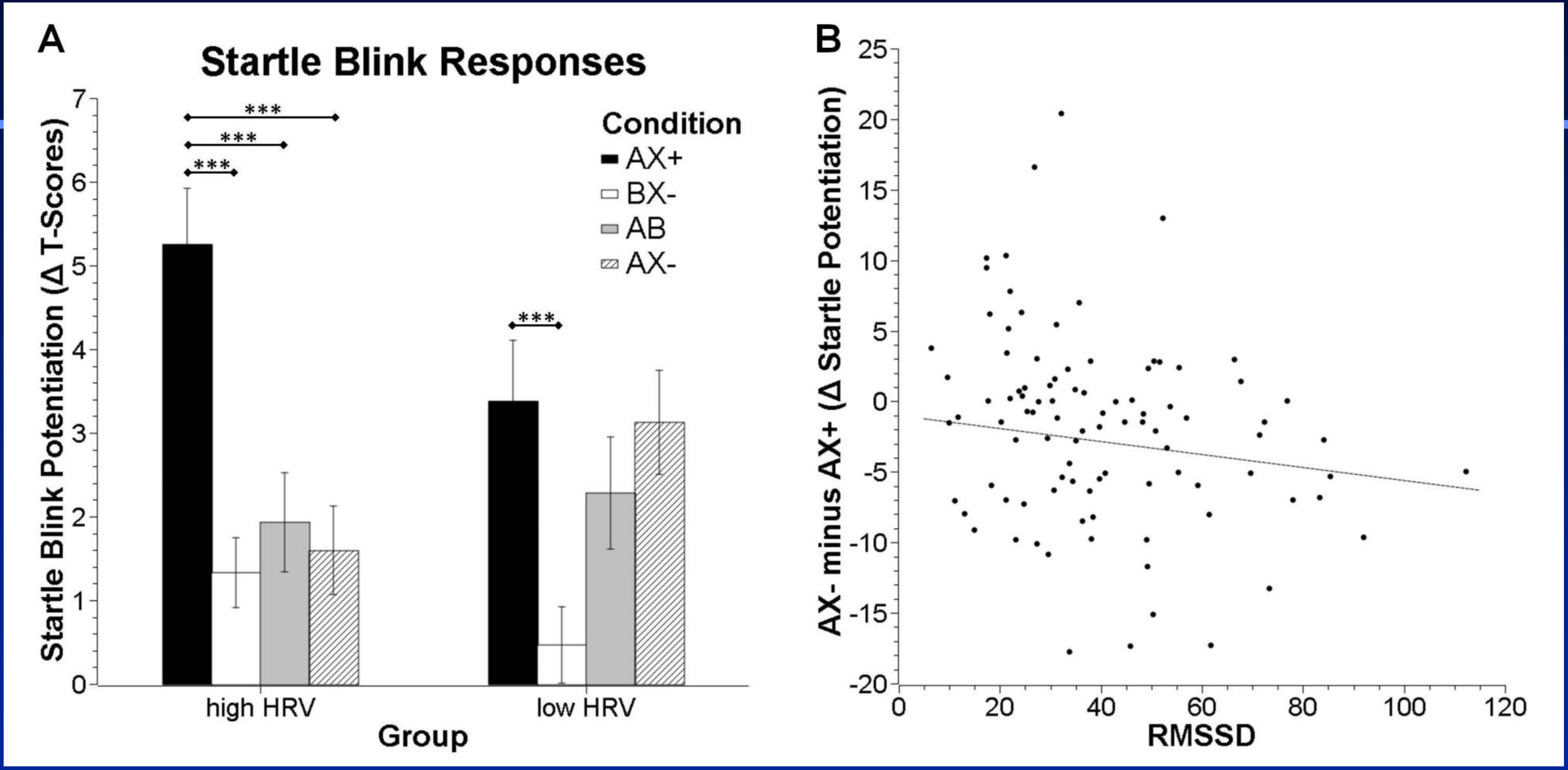
Resting heart rate variability is associated with inhibition of conditioned fear

JULIA WENDT,[a] JÖRG NEUBERT,[a] JULIAN KOENIG,[b,c] JULIAN F. THAYER,[b] AND ALFONS O. HAMM[a]
[a]Department of Psychology, University of Greifswald, Greifswald, Germany
[b]Department of Psychology, The Ohio State University, Columbus, Ohio, USA
[c]Department of Child and Adolescent Psychiatry, Centre for Psychosocial Medicine, University of Heidelberg, Heidelberg, Germany

Psychophysiology, 00 (2015).



A Trial Structure
AX+
Startle Probes (100%)
Aversive UCS (100%)
Cue
0 2 4 6 8 10 12 14 16 Time (s)
BX-, AB, AC, AX-
Startle Probes (100%)
Cue
0 2 4 6 8 10 12 14 16 Time (s)
B Conditioned Stimuli and Procedure
12 x AX+
and
12 x BX-
8 x AB
or
8 x AC
4 x AX+
and
4 x BX-
8 x AB
or
8 x AC
4 x AX-
Conditioning
Test 1
Re-Conditioning
Test 2
Extinction

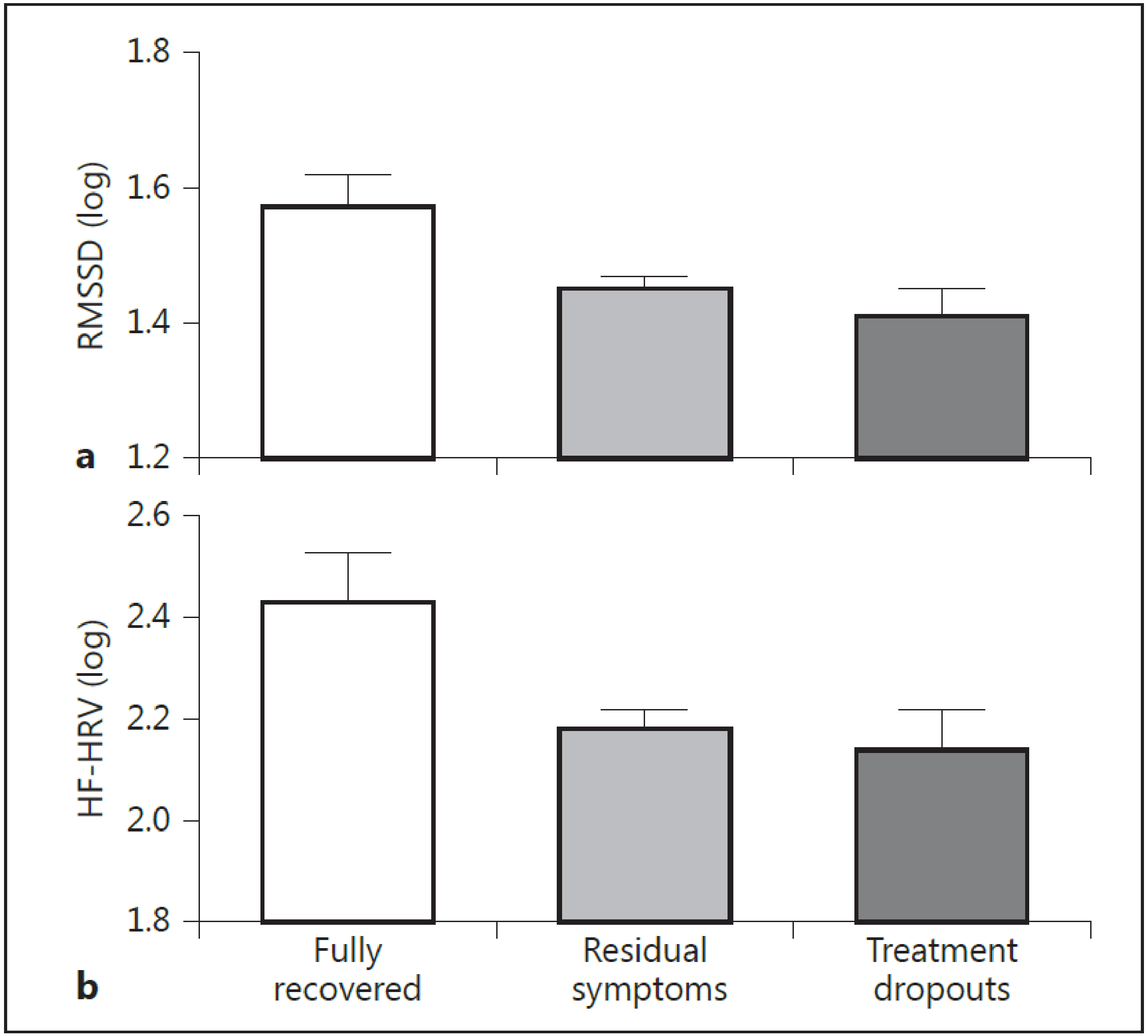

A
Startle Blink Responses
Startle Blink Potentiation (Δ T-Scores)
Condition
AX+
BX-
AB
AX-
***
***
***
***
0
1
2
3
4
5
6
7
high HRV
low HRV
Group
B
AX- minus AX+ (Δ Startle Potentiation)
25
20
15
10
5
0
-5
-10
-15
-20
0
20
40
60
80
100
120
RMSSD

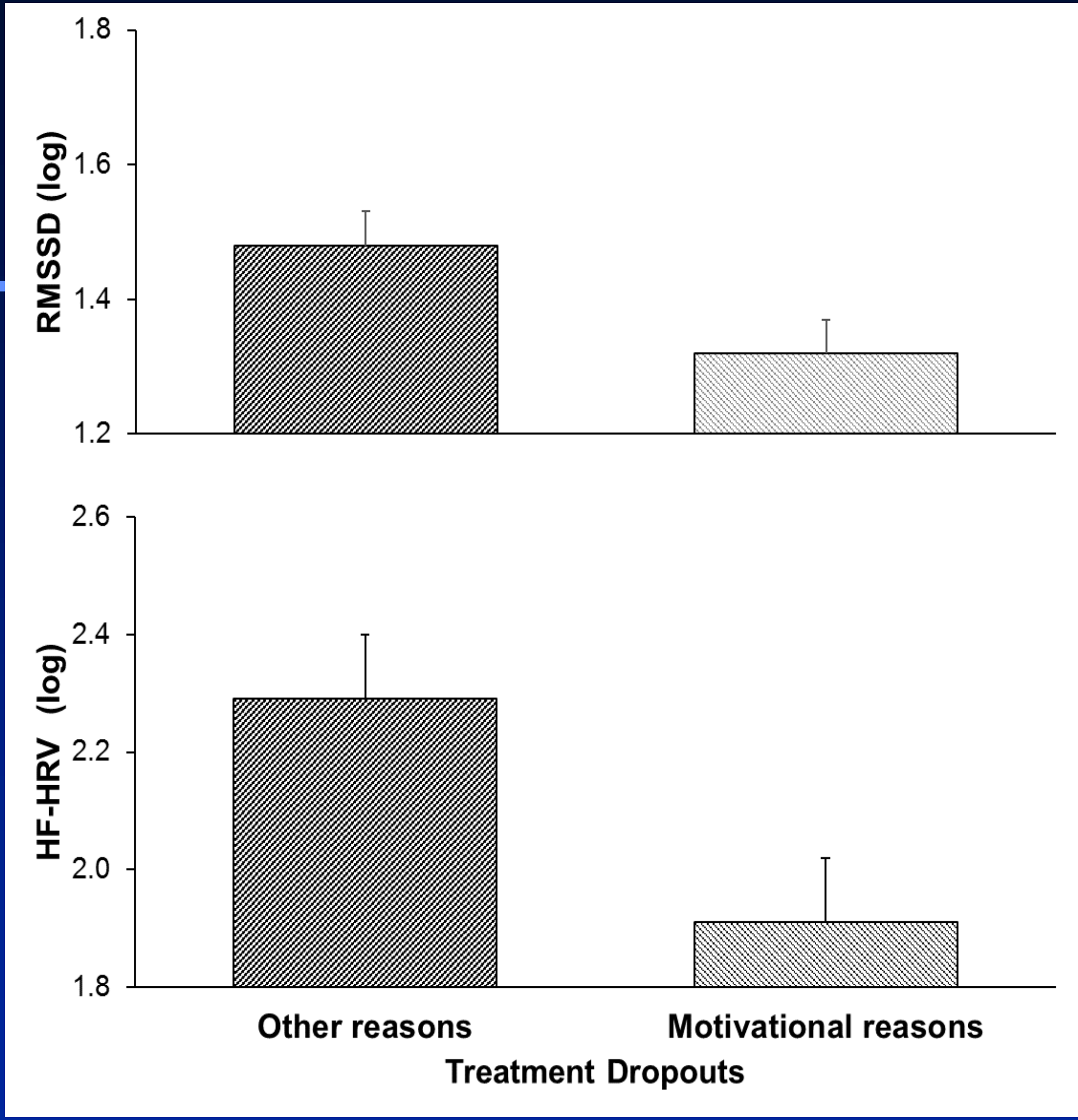
Pretreatment Cardiac Vagal Tone Predicts Dropout from and Residual Symptoms after Exposure Therapy in Patients with Panic Disorder and Agoraphobia

Julia Wendt[a] *Alfons O. Hamm*[a] *Christiane A. Pané-Farré*[a]
Julian F. Thayer[b] *Alexander Gerlach*[c] *Andrew T. Gloster*[d]
Thomas Lang[e, f] *Sylvia Helbig-Lang*[f] *Paul Pauli*[g]
Thomas Fydrich[h] *Andreas Ströhle*[i] *Tilo Kircher*[j] *Volker Arolt*[k]
Jürgen Deckert[l] *Hans-Ulrich Wittchen*[m] *Jan Richter*[a]

Psychotherapy and Psychosomatics

DOI: 10.1159/000487599


1.8
1.6
1.4
1.2
RMSSD (log)
a
2.6
2.4
2.2
2.0
1.8
HF-HRV (log)
b
Fully recovered
Residual symptoms
Treatment dropouts


1.8
1.6
1.4
1.2
RMSSD (log)
2.6
2.4
2.2
2.0
1.8
HF-HRV (log)
Other reasons
Motivational reasons
Treatment Dropouts

Emotion & Cognition Lab Contributors

Mara Mather, Ph.D.
Professor and Principal Investigator

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+ an amazing team of RA's!

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Effects of slow breathing on heart rate variability: A meta-analysis

Laborde, S., Allen, M.S., Borges, U., Dosseville, F., Hosang. T. J., Mosley, E., Salvotti, C., Spolverato, L., Zammit, N., Javelle, F.

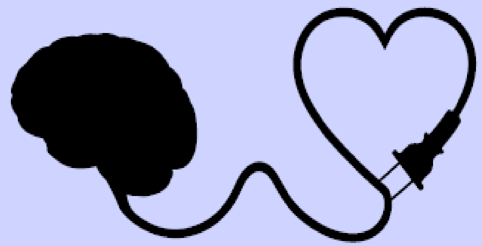
German Sport University Cologne
Institute of Psychology
Department of Performance Psychology

INTRODUCTION

The importance of breathing techniques

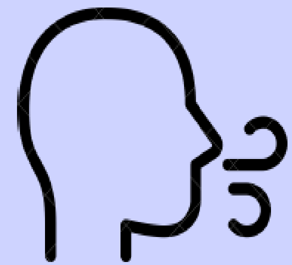
Benefits

Breathing has been used for centuries as part of meditation and relaxation techniques



Vagus nerve

Several papers propose a model that involves the vagus nerve to explain the therapheutic effects of slow paced breathing



Slow paced breathing

Voluntary slow breathing is performed at a pace of ~6 cpm; benefits found at many levels of health and stress-related physiology

Gerritsen & Band, 2018; Russo et al., 2017a; Zaccaro et al., 2018a; Brodal, 2016; Lehrer et al., 2020; Lehrer & Gevirtz, 2014; Mather & Thayer, 2018; Noble & Hochman. 2019a

SLOW VS SPONTANEOUS BREATHING

Voluntary slow breathing

↓

~ 6 cycles per minute

Spontaneous breathing

↓

12-20 cycles per minute

Sherwood, 2006

EFFECTS OF SPB

- Optimizing the functioning of the autonomic nervous system
- Optimizing the functioning of cardiopulmonary and neuroendocrine functions
- Decreasing anxiety and arousal

- Increasing relaxation
- Modest reductions in blood pressure

Chaddha et al., 2019; Herbell & Zauszniewski, 2019; Kennedy & Parker, 2019; Landman et al., 2014; Mahtani et al., 2012, 2016; Noble & Hochman, 2019b; Pinter et al., 2019; Russo et al., 2017b; Yu et al., 2018; Zaccaro et al., 2018b; Shaffer & Meehan 2020

RESULTS

EFFECTS DURING

DURING
while one is performing
the slow breathing technique

IM-AFTER1
immediately after 1 session

AFTER-INT
after a multi-sessions intervention

RMSSD

Effect size of 0.52

95% CI 0.43 - 0.62

$I^2 = 81\%$

12 studies missing (Egger's test not significant)

1 outlier

LF-HRV

Effect size of 1.49

95% CI 1.28 - 1.69

$I^2 = 93\%$

0 studies missing (Egger's test significant)

2 outliers

RESULTS

EFFECTS IM-AFTER1

DURING
while one is performing
the slow breathing technique

IM-AFTER1
immediately after 1 session

AFTER-INT
after a multi-sessions intervention

RMSSD

Effect size of 0.14

95% CI 0.03 - 0.24

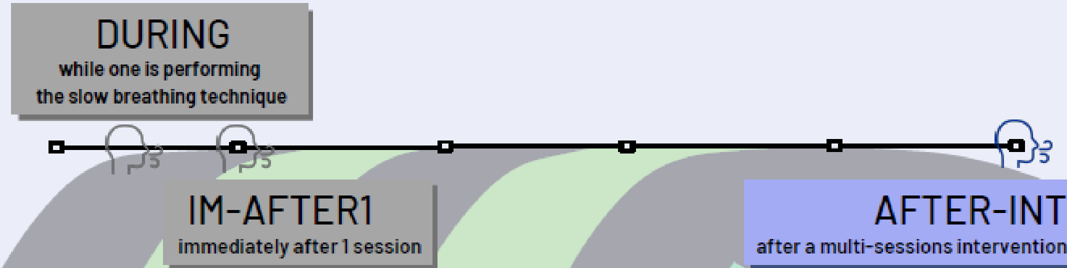
$I^2 = 0\%$

0 studies missing

1 outlier

RESULTS

EFFECTS AFTER-INT



RMSSD

Effect size of **0.32**

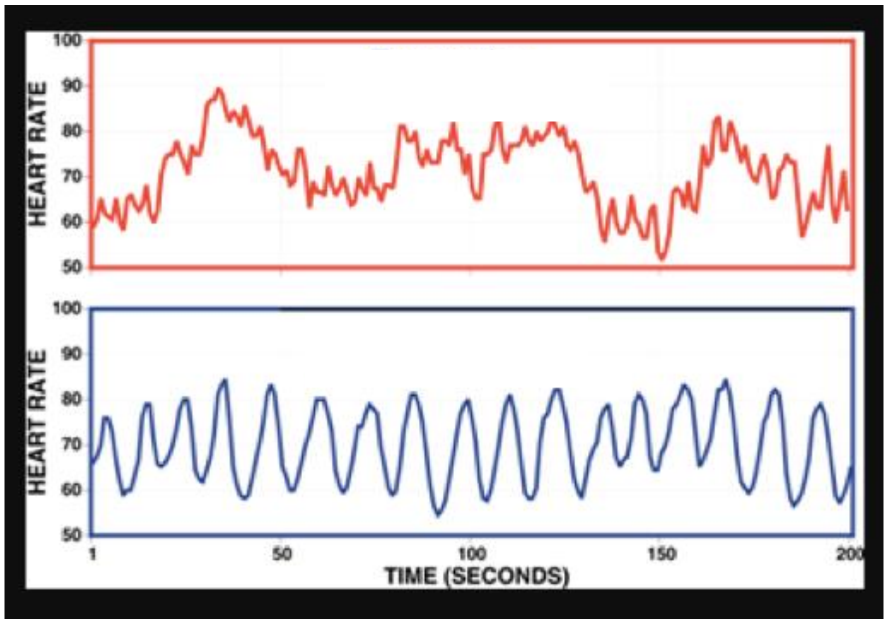
95% CI **0.08 - 0.56**

I^2 = **79%**

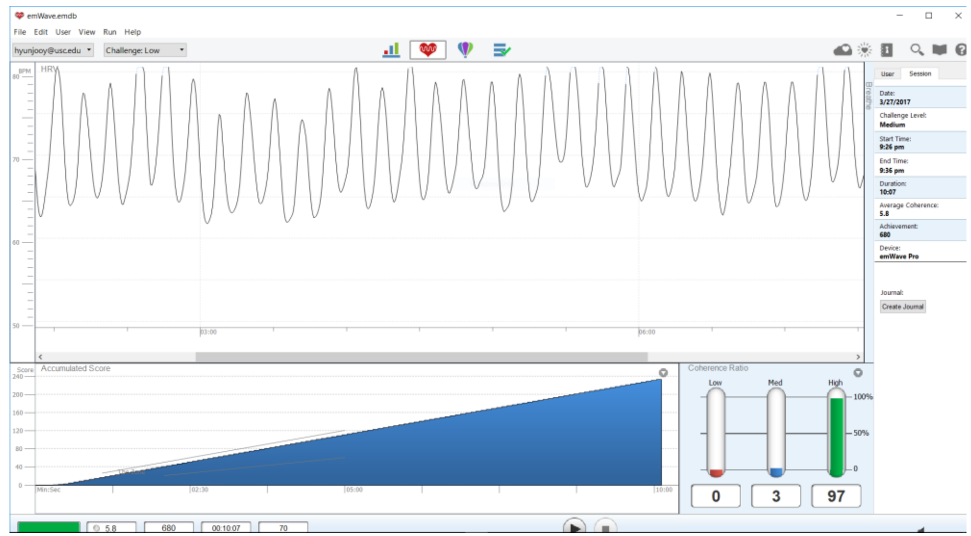
1 study missing (Egger's test not significant)

0 outliers

Biofeedback training : Increase group



Increase group: attempt increase HRV by paced breathing



Increasing coordination and responsivity of emotion-related brain regions with a heart rate variability biofeedback randomized trial

Kaoru Nashiro[1] · Jungwon Min[1] · Hyun Joo Yoo[1] · Christine Cho[1] · Shelby L. Bachman[1] · Shubir Dutt[1] · Julian F. Thayer[2] · Paul M. Lehrer[3] · Tiantian Feng[1] · Noah Mercer[1] · Padideh Nasseri[1] · Diana Wang[1] · Catie Chang[4] · Vasilis Z. Marmarelis[1] · Shri Narayanan[1] · Daniel A. Nation[2] · Mara Mather[1]

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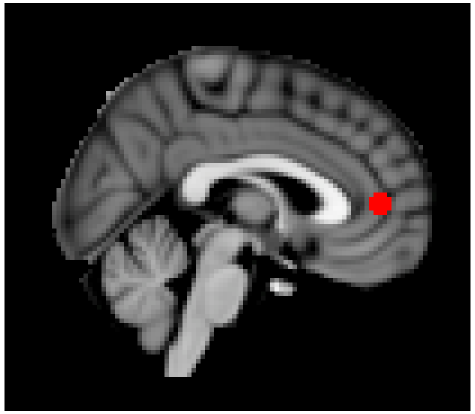
Cognitive, Affective, & Behavioral Neuroscience
https://doi.org/10.3758/s13415-022-01032-w

Resting-State fMRI Seed Regions

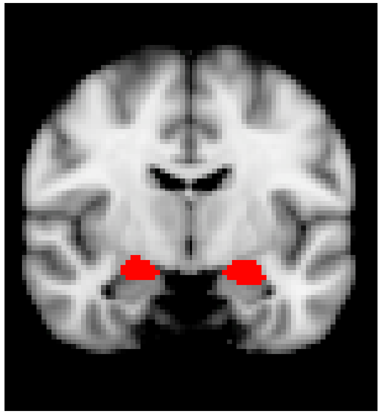
Kaoru Nashiro

mPFC

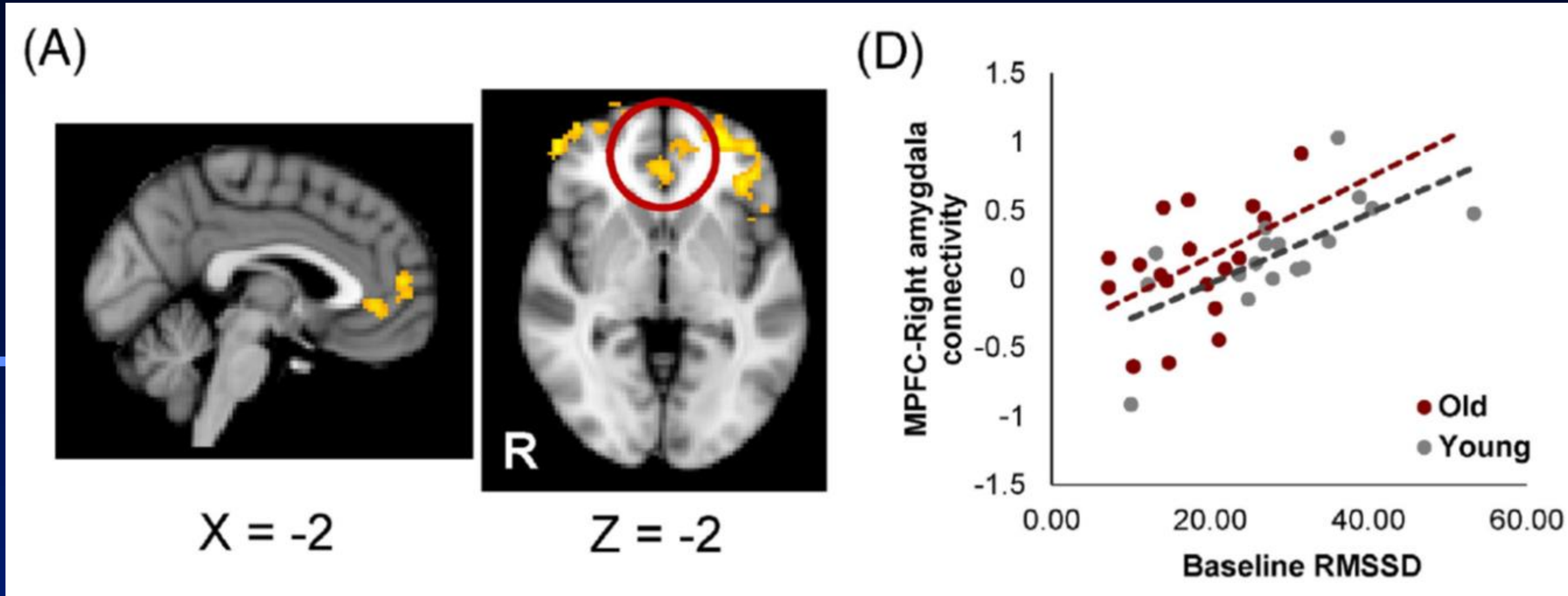


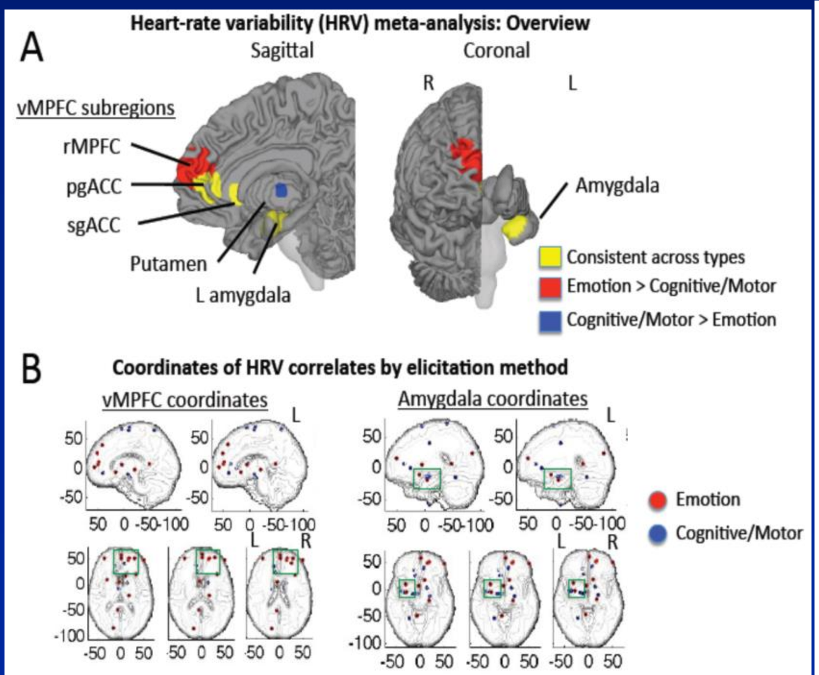
MPFC was defined based on a previous meta-analysis (i.e., a sphere of 5mm around the peak voxel [x=2, y=46, z=6] in Thayer et al., 2012).

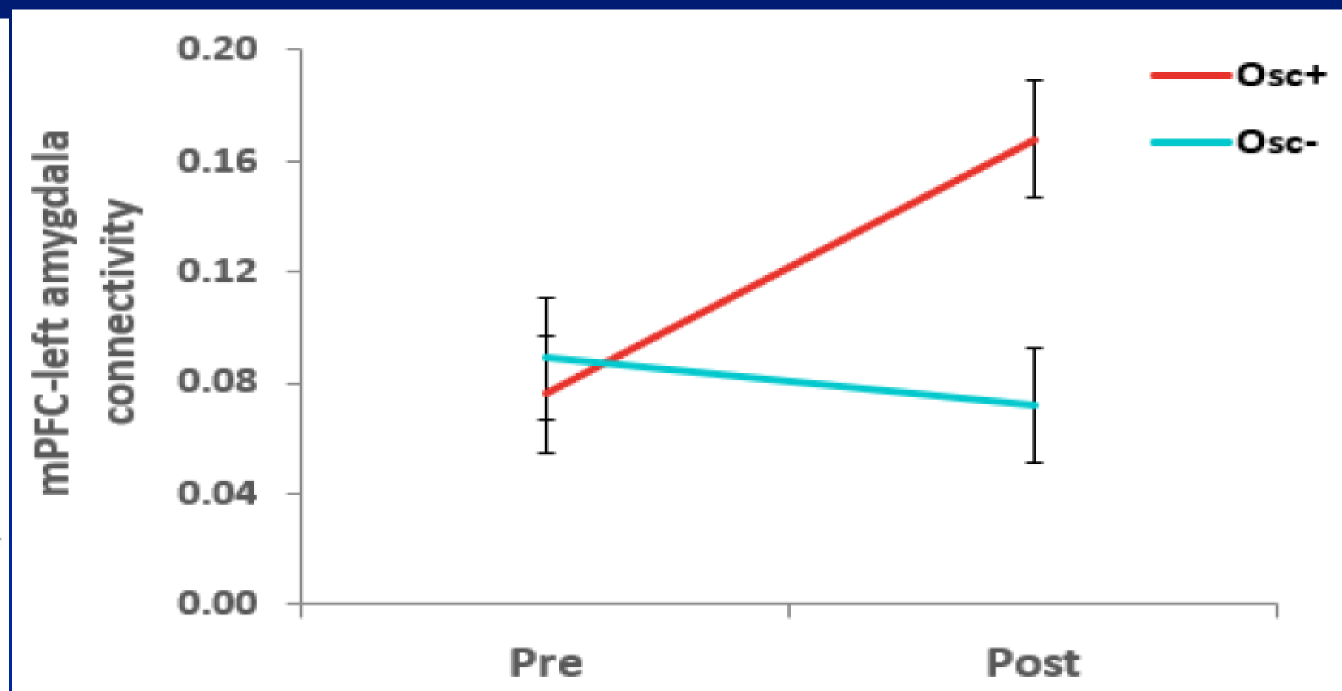
Amygdala



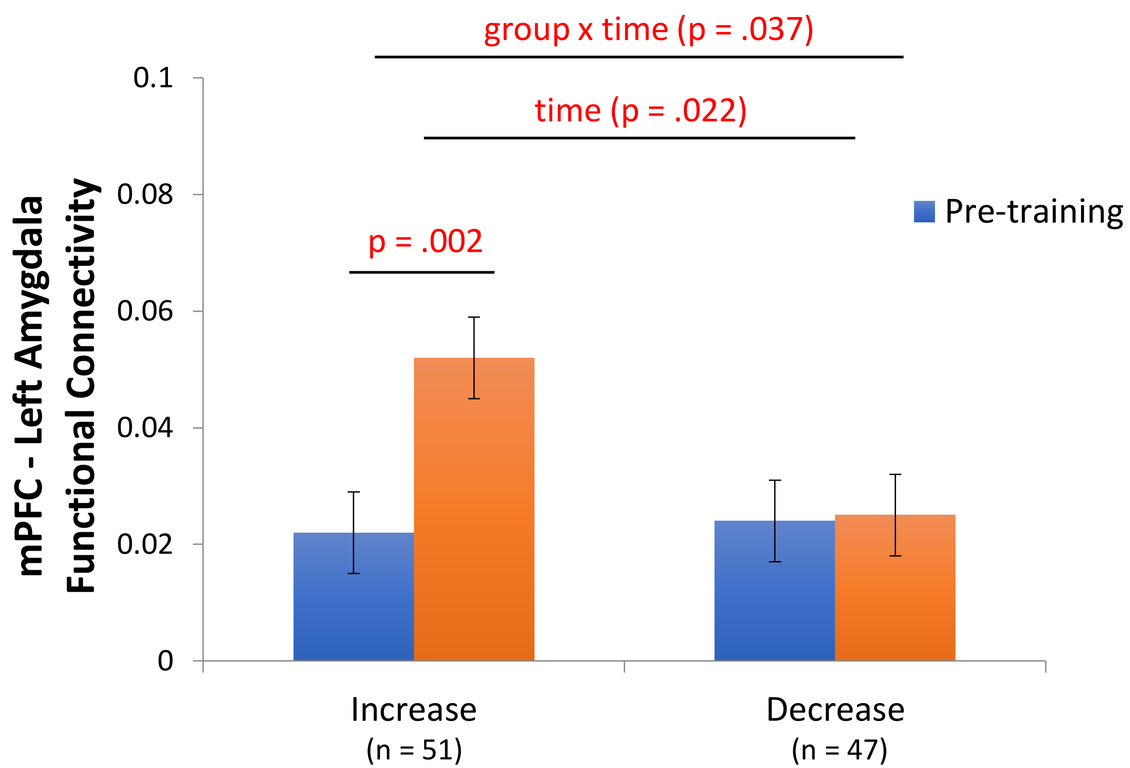
The right and left amygdala were defined using the Harvard-Oxford atlas.


(A)
R
X = -2
Z = -2
(D)
MPFC-Right amygdala connectivity
1.5
1
0.5
0
-0.5
-1
-1.5
0.00
20.00
40.00
60.00
Baseline RMSSD
Old
Young


Heart-rate variability (HRV) meta-analysis: Overview
A
Sagittal
Coronal
vMPFC subregions
rMPFC
pgACC
sgACC
Putamen
L amygdala
R
L
Amygdala
Consistent across types
Emotion > Cognitive/Motor
Cognitive/Motor > Emotion
B
Coordinates of HRV correlates by elicitation method
vMPFC coordinates
Amygdala coordinates
Emotion
Cognitive/Motor


mPFC-left amygdala connectivity
0.20
0.16
0.12
0.08
0.04
0.00
Pre
Post
Osc+
Osc-

[Resting State] The increase group showed greater left amygdala-mPFC functional connectivity in post-training compared with pre-training



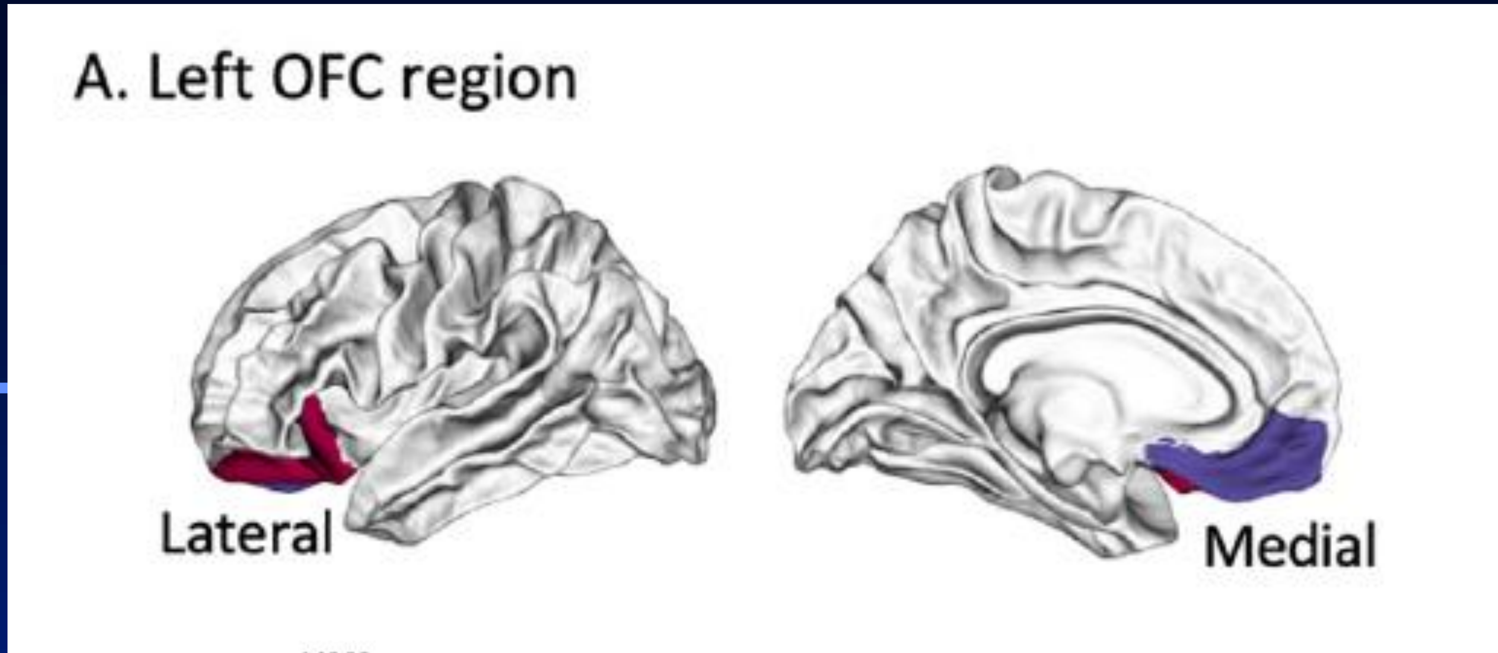
Structural brain changes

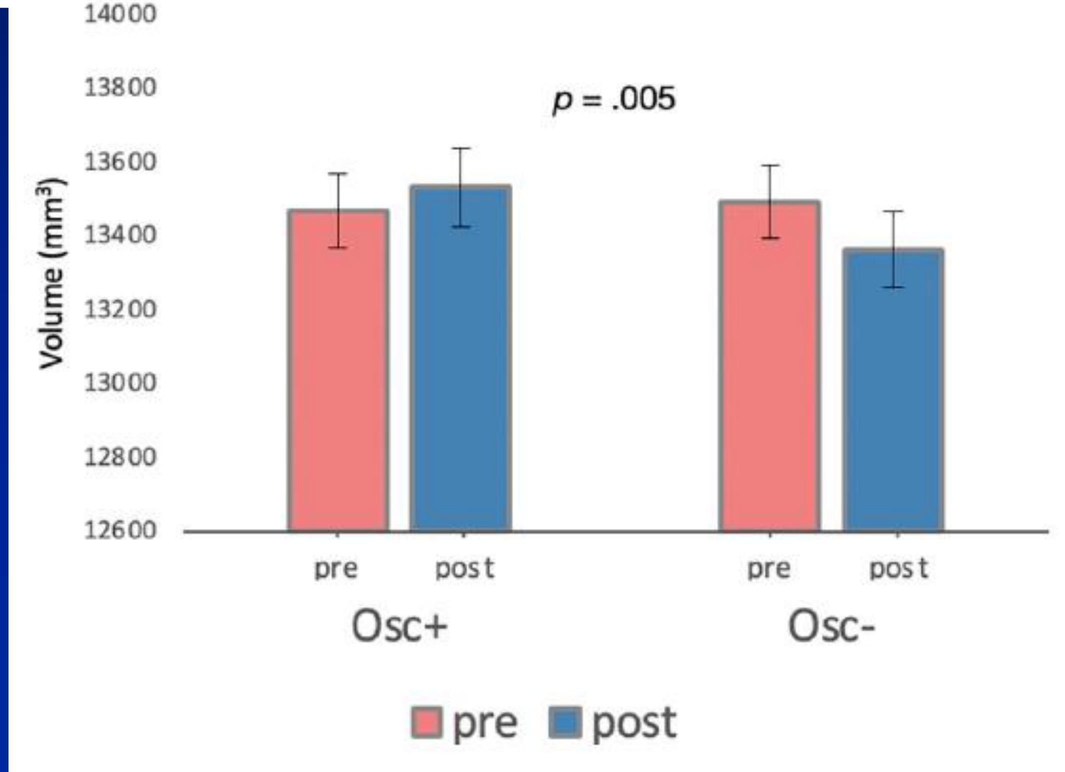
Hyun Joo Yoo

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

Hyun Joo Yoo [a], Kaoru Nashiro [a], Jungwon Min [a], Christine Cho [a], Shelby L. Bachman [a], Padideh Nasseri [a], Shai Porat [a], Shubir Dutt [a], Vardui Grigoryan [b], Paul Choi [a], Julian F. Thayer [c], Paul M. Lehrer [d], Catie Chang [e], Mara Mather [a,*]

International Journal of Psychophysiology 181 (2022) 50–63

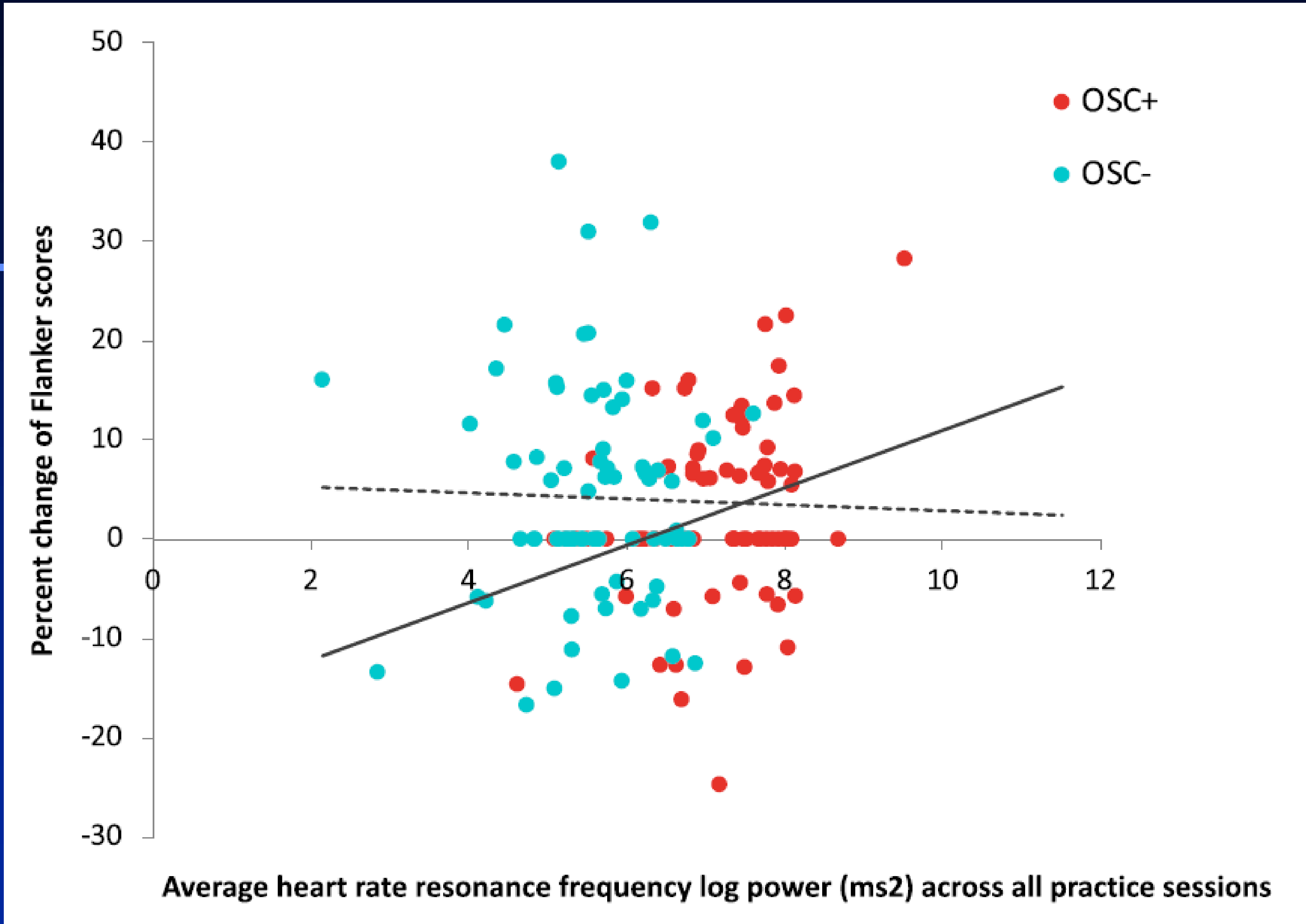

A. Left OFC region
Lateral
Medial


14000
13800
13600
13400
13200
13000
12800
12600
Volume (mm³)
p = .005
pre
post
pre
post
Osc+
Osc-
pre
post

Effects of a Randomised Trial of 5-Week Heart Rate Variability Biofeedback Intervention on Cognitive Function: Possible Benefits for Inhibitory Control

Kaoru Nashiro[1] · Hyun Joo Yoo[1] · Christine Cho[1] · Jungwon Min[1] · Tiantian Feng[1] · Padideh Nasseri[1] · Shelby L. Bachman[1] · Paul Lehrer[2] · Julian F. Thayer[3] · Mara Mather[1]

Applied Psychophysiology and Biofeedback
https://doi.org/10.1007/s10484-022-09558-y



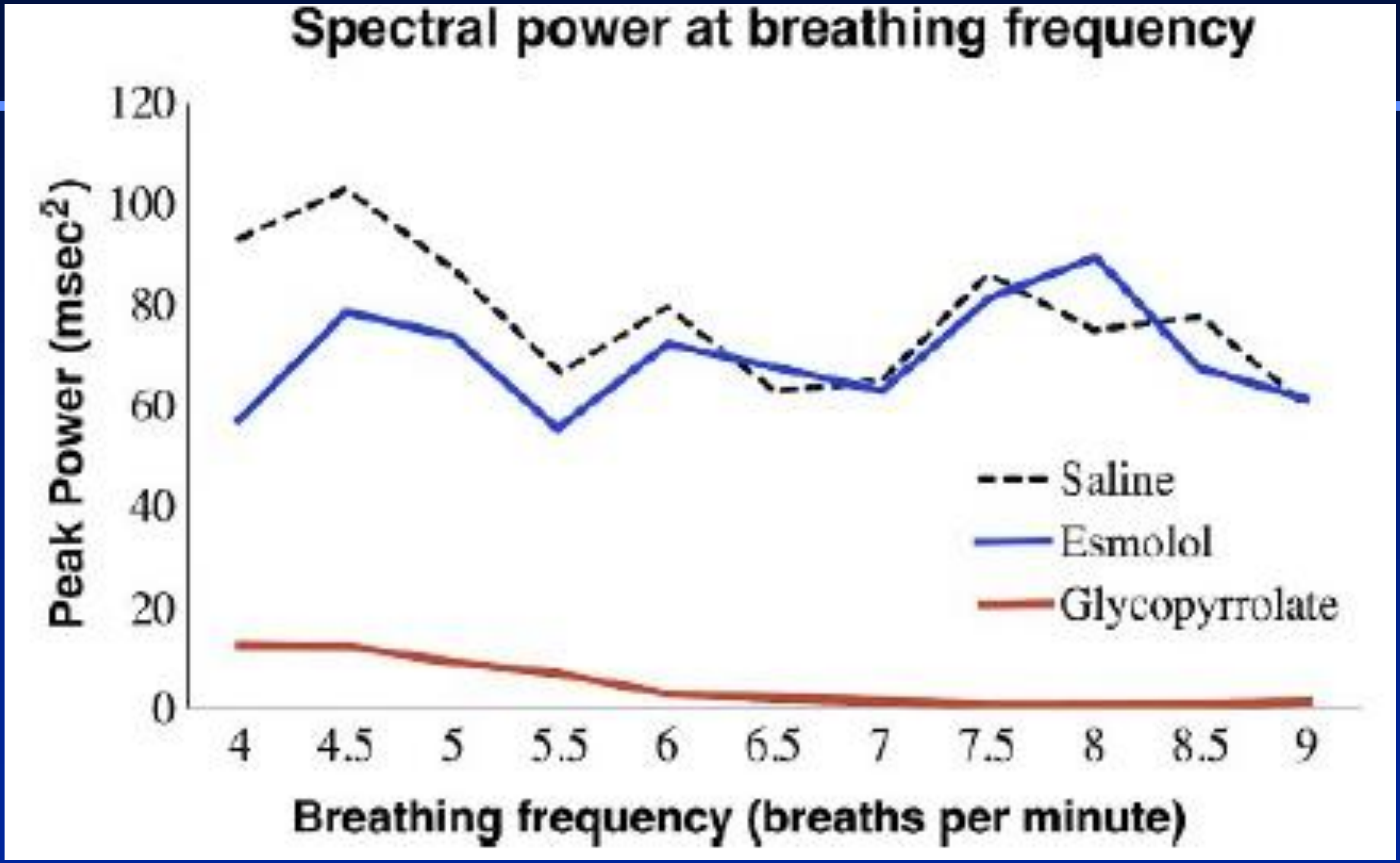
OSC+
OSC-
Percent change of Flanker scores
50
40
30
20
10
0
-10
-20
-30
0
2
4
6
8
10
12
Average heart rate resonance frequency log power (ms2) across all practice sessions

Vagal Mediation of Low-Frequency Heart Rate Variability During Slow Yogic Breathing

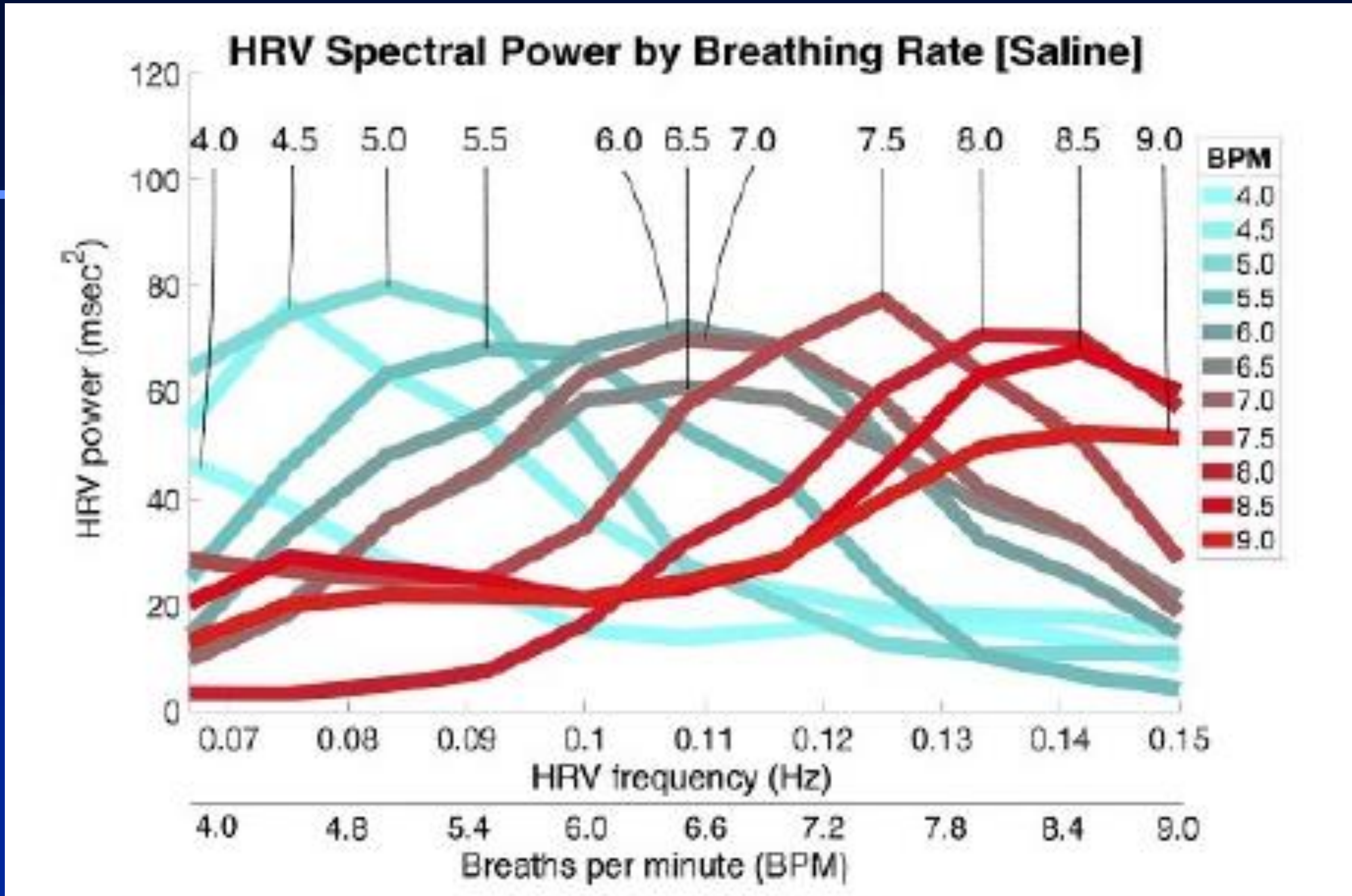
Bryan W. Kromenacker, MA, RN, Anna A. Sanova, BS, Frank I. Marcus, MD,
John J.B. Allen, PhD, and Richard D. Lane, MD, PhD

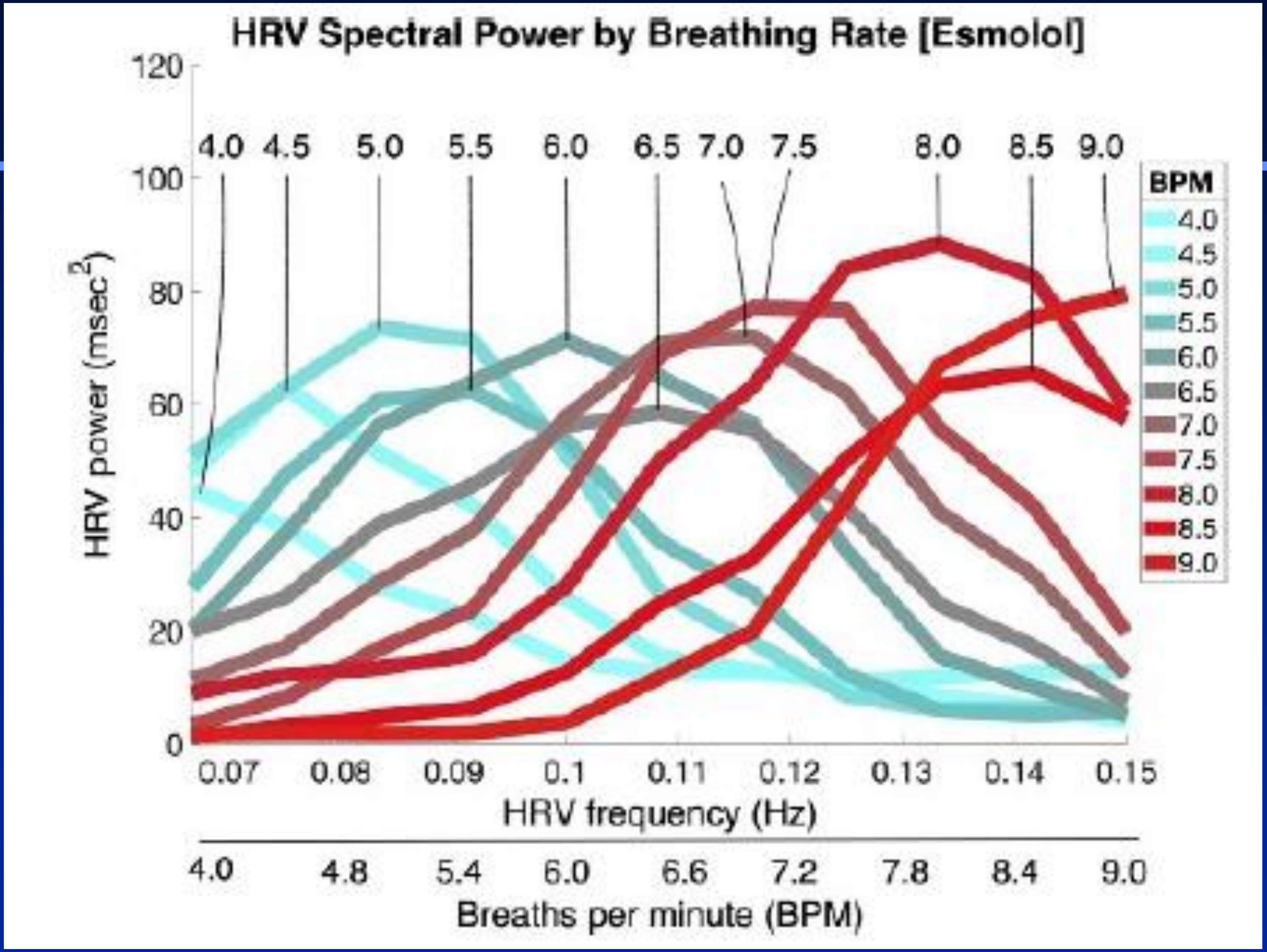
Psychosomatic Medicine, V 80 • 581-587

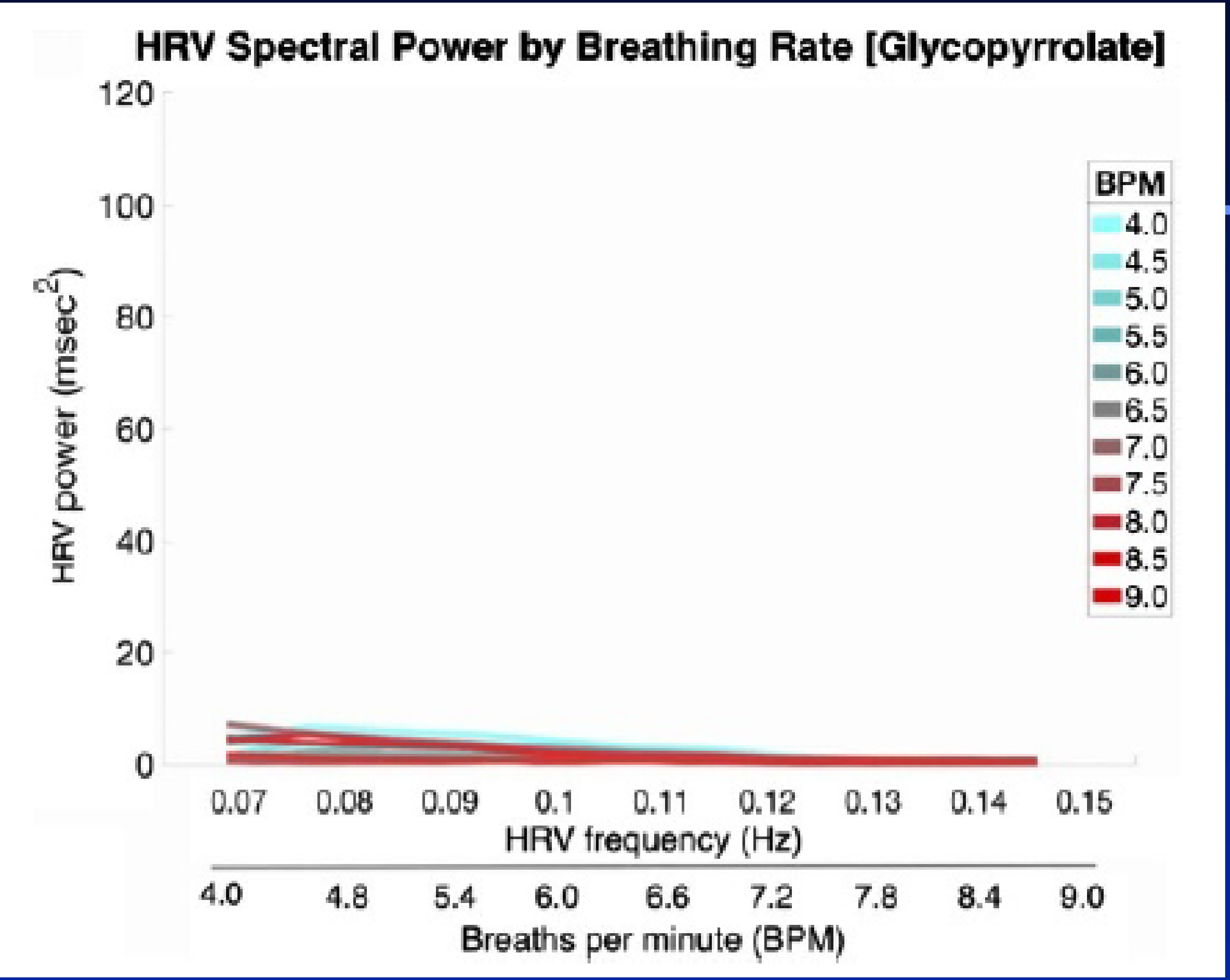
July/August 2018



Spectral power at breathing frequency
Peak Power (msec²)
120
100
80
60
40
20
0
4
4.5
5
5.5
6
6.5
7
7.5
8
8.5
9
Breathing frequency (breaths per minute)
Saline
Esmolol
Glycopyrrolate


HRV Spectral Power by Breathing Rate [Saline]
HRV power (msec^2)
0
20
40
60
80
100
120
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
BPM
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
0.07
0.08
0.09
0.1
0.11
0.12
0.13
0.14
0.15
HRV frequency (Hz)
4.0
4.8
5.4
6.0
6.6
7.2
7.8
8.4
9.0
Breaths per minute (BPM)

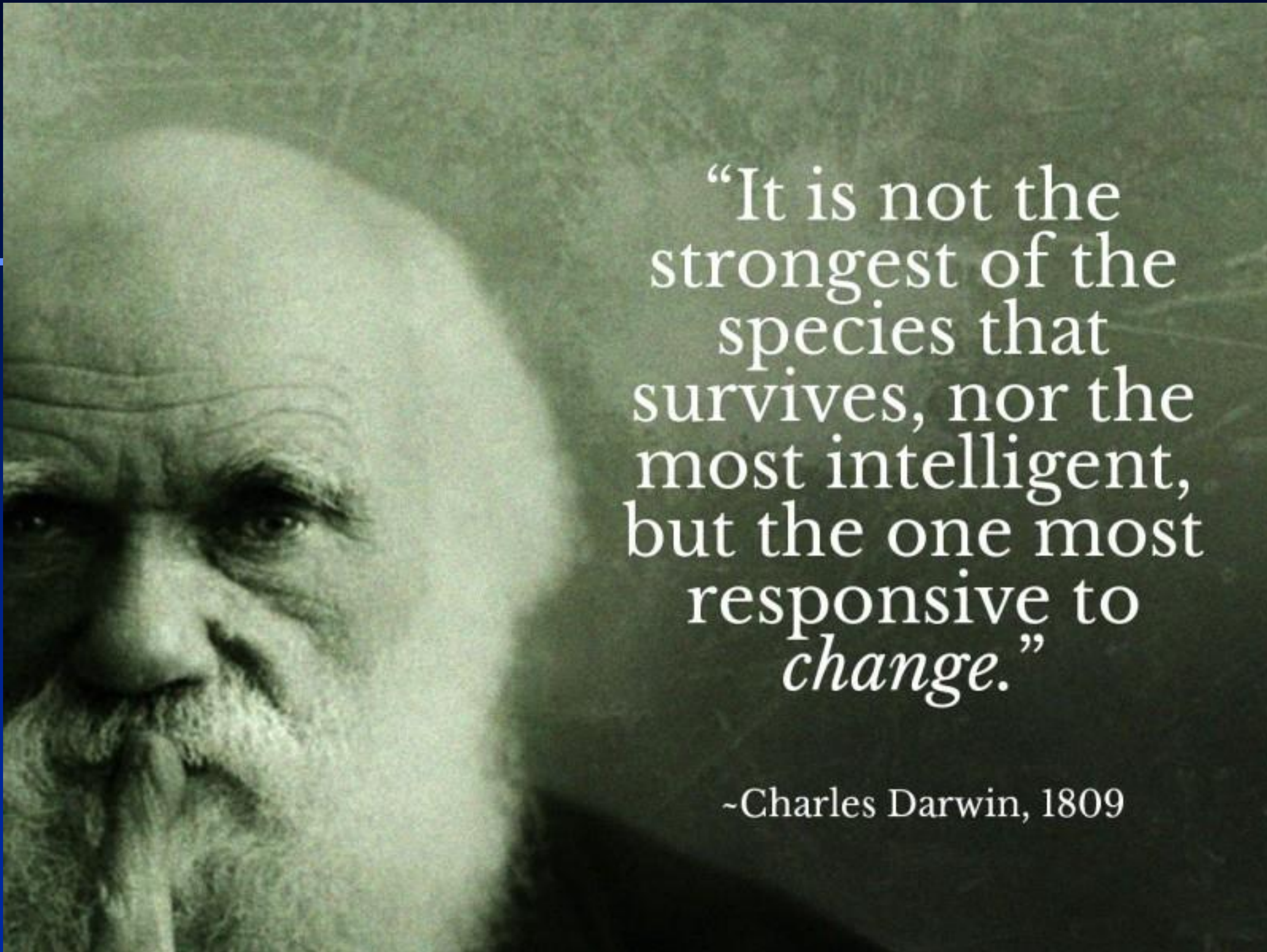

HRV Spectral Power by Breathing Rate [Esmolol]
HRV power (msec^2)
120
100
80
60
40
20
0
4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0 8.5 9.0
BPM
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
0.07 0.08 0.09 0.1 0.11 0.12 0.13 0.14 0.15
HRV frequency (Hz)
4.0 4.8 5.4 6.0 6.6 7.2 7.8 8.4 9.0
Breaths per minute (BPM)



HRV Spectral Power by Breathing Rate [Glycopyrrolate]
120
100
80
60
40
20
0
HRV power (msec^2)
BPM
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
8.0
8.5
9.0
0.07 0.08 0.09 0.1 0.11 0.12 0.13 0.14 0.15
HRV frequency (Hz)
4.0 4.8 5.4 6.0 6.6 7.2 7.8 8.4 9.0
Breaths per minute (BPM)

Conclusions

- The brain and the heart are intimately connected
- The prefrontal cortex is needed to feel safety
- HRV biofeedback influences the brain
- This effect is almost exclusively vagally mediated


"It is not the strongest of the species that survives, nor the most intelligent, but the one most responsive to *change*."
-Charles Darwin, 1809

Thank You!