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Transcutaneous vagus nerve stimulation (tVNS) in borderline personality disorder (tVNS-BPD): study protocol for a randomized, single-blind, sham-controlled trial

GIUSEPPE GUERRIERO, MD, MSC, PHD STUDENT

Background

Background (1) - BPD



Emotional instability

Interpersonal, identity, cognitive,
behavioral disturbances (e.g., NSSI)





Background (2) – Biosocial theory

BPD = disorder of emotion regulation

Emotional vulnerability (EV)

- heightened sensitivity to emotion
- increased emotional intensity
- slow return to emotional baseline



Invalidating environment



(Linehan, 1993)



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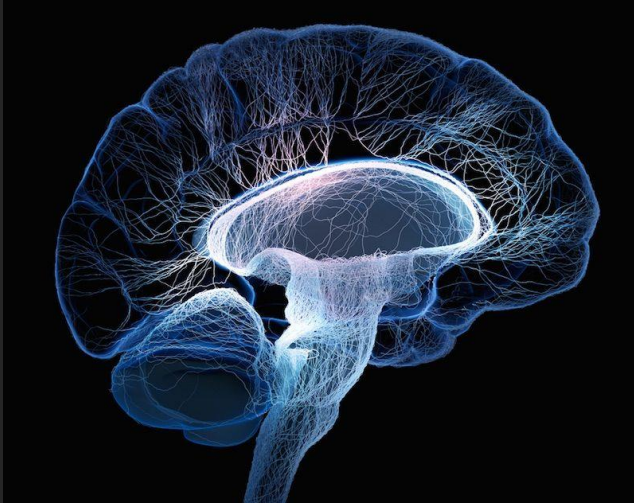


Invalidating environment

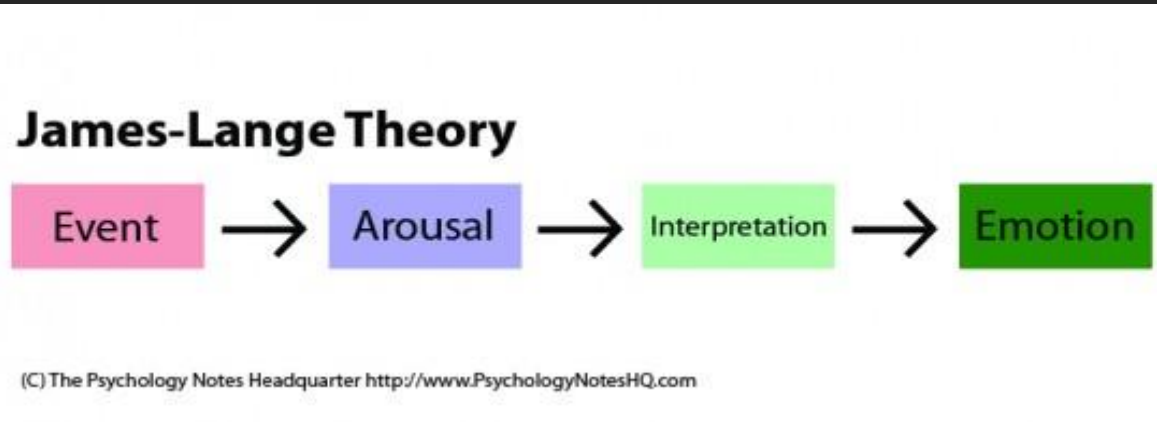


(Linehan, 1993)

Where do emotions start?

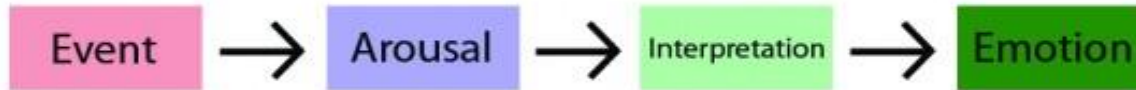


Background (3)



Background (3)

James-Lange Theory



James-Lange Theory



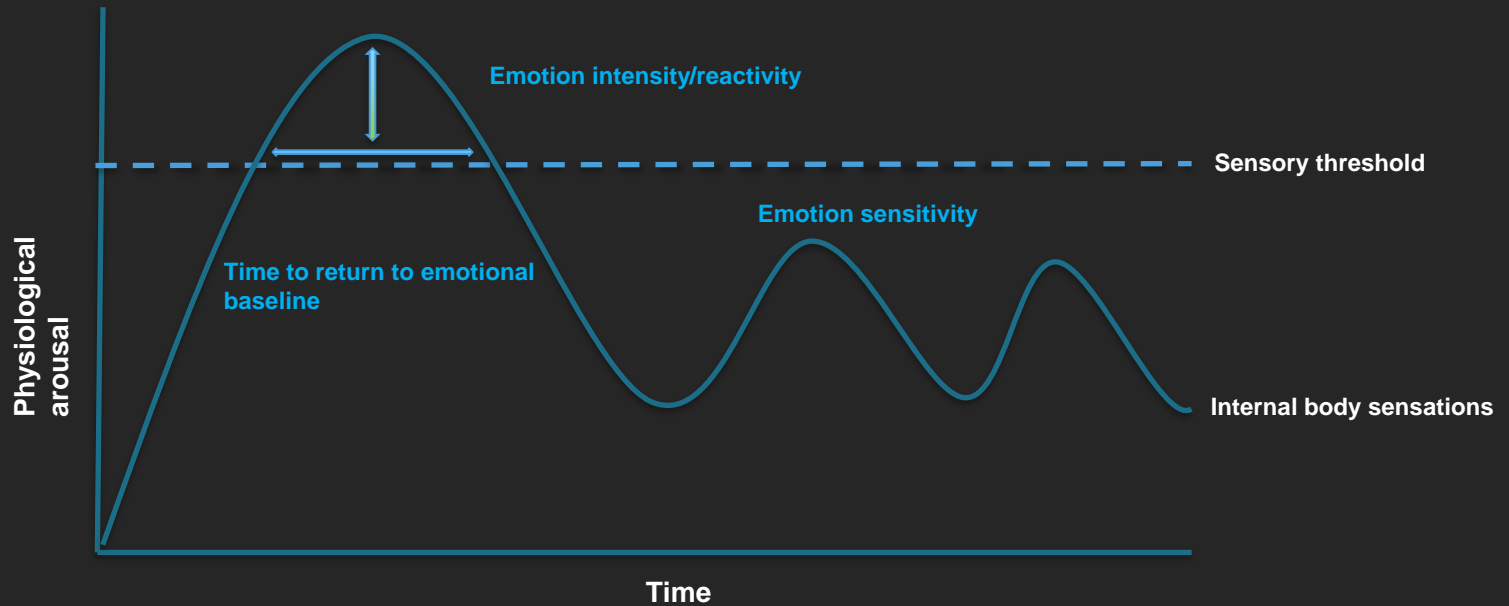
Heart pounding,
trembling, sweating,
running away



Fear

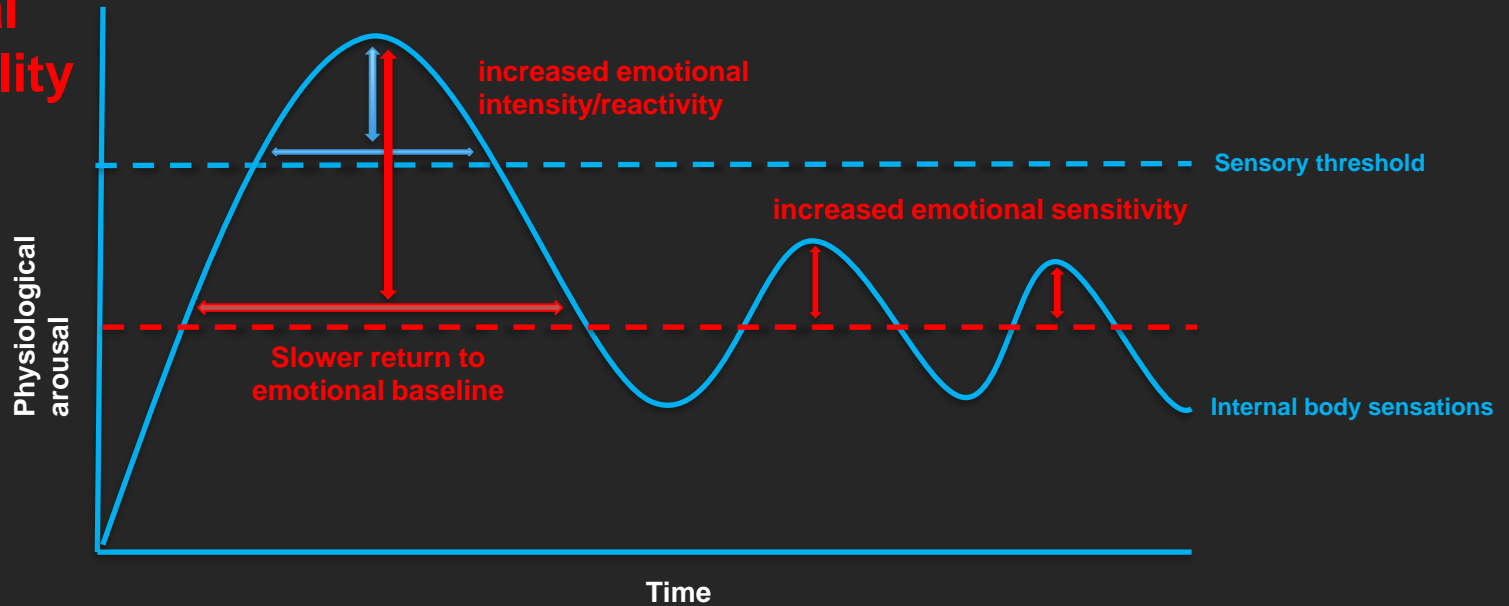
Background (4) – A sensory hypothesis of EV

Normal



Background (4) – A sensory hypothesis of EV

Emotional vulnerability





Background (5) – interoception studies

Impairment processing interoceptive stimuli in BPD suggested

EEG-HEPs (100-700 ms following ECG-R wave)

Results inconsistent

Possible cognition (e.g., attention) bias

(Schmitz et al., 2020)



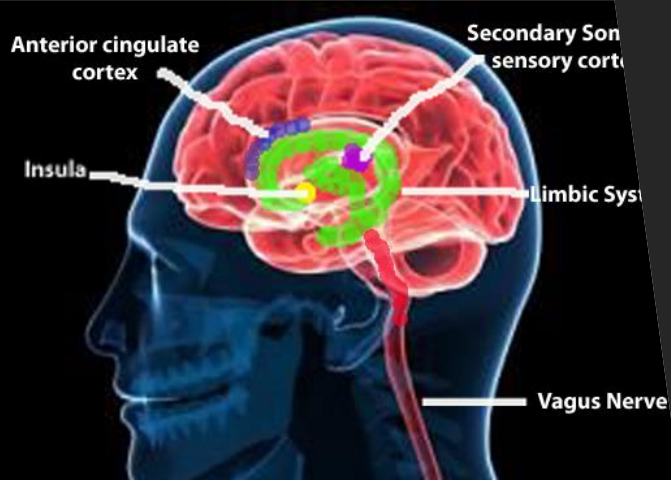
Background (6) - Vagus nerve

"Wandering" from brain stem to abdomen

80% are afferent fibers from head, neck, thorax, abdomen to the brain

Vagal tone associated with executive functions and emotional regulation (two theories)

low vagal tone observed in a variety of psychiatric disorders and in BPD



(Porges, 2009; Thayer and Friedman, 2002; Koenig, 2016).

Background (7) - Vagus nerve and sensory processing

Rapid Effects of Vagus Nerve Stimulation on Sensory Processing Through Activation of Neuromodulatory Systems

Charles Rodenkirch^{1,2}, Jason B. Carmel³ and Qi Wang^{1*}*

¹ Department of Biomedical Engineering, Columbia University, New York, NY, United States, ² Jacobs Technion-Cornell Institute, Cornell Tech, New York, NY, United States, ³ Department of Neurology and Orthopedics, Columbia University Medical Center, New York, NY, United States

Vagus Nerve Stimulation

- Tactile, auditory, olfactory and gustatory processing
- Modulates NA, Ach, 5-HT, DA Systems

(Rodenkirch et al., 2022)

How to stimulate vagus nerve?

Cold Exposure

Deep and Slow Breathing

Singing, Humming, Chanting and Gargling

Acupuncture

Yoga and Tai Chi

Probiotics

Meditation and Neurofeedback

Omega-3 Fatty Acids

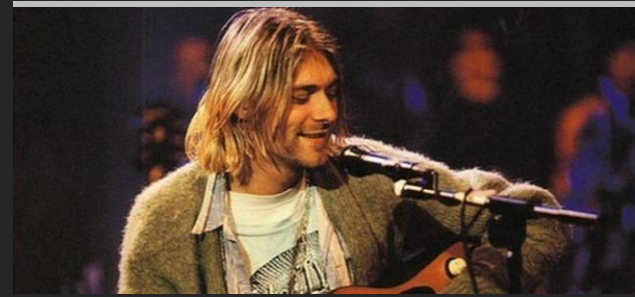
Exercise

Zinc

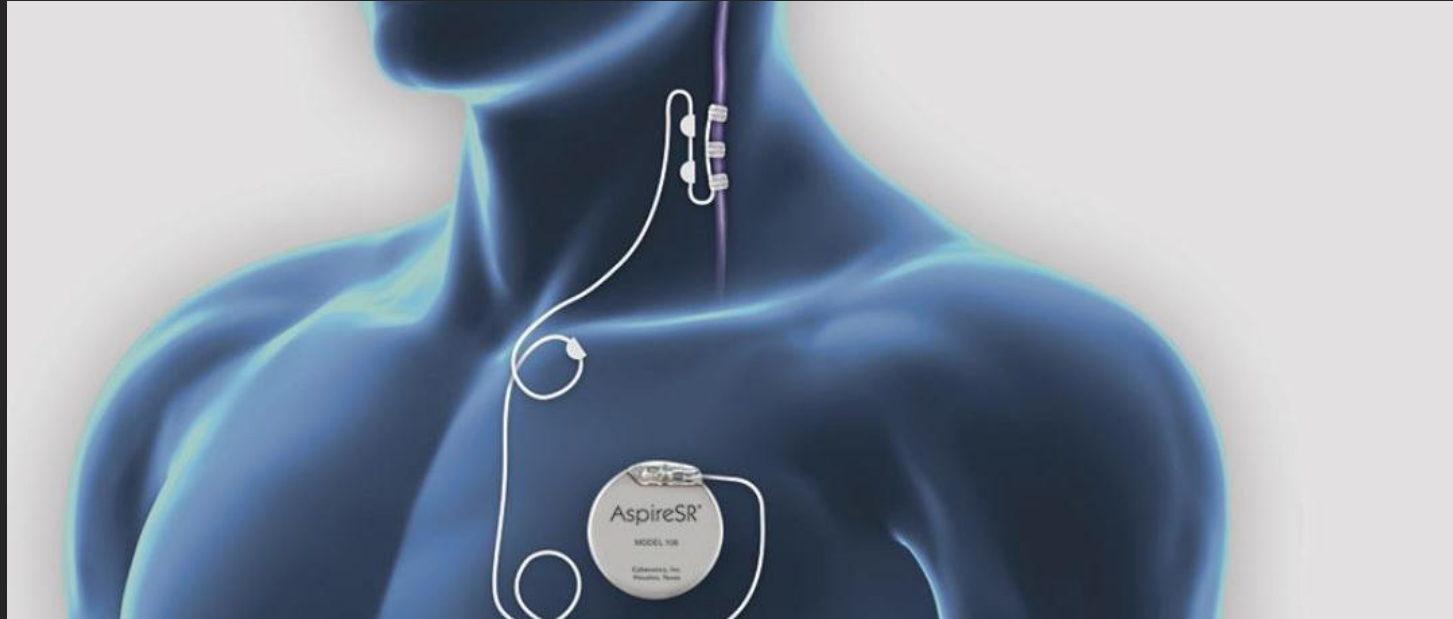
Massage

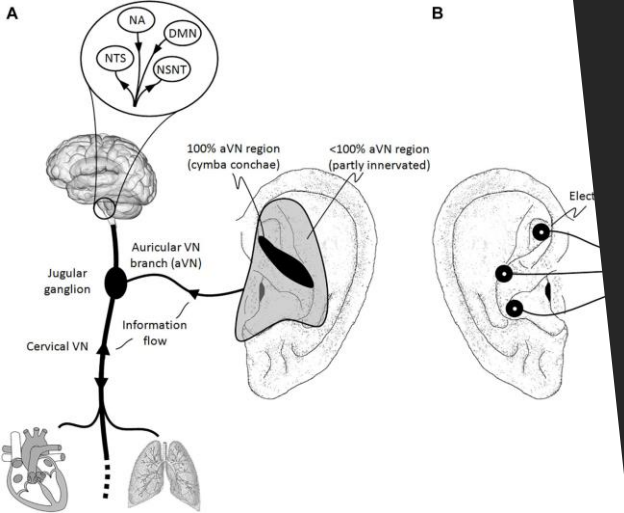
Socializing and Laughing

Intermittent Fasting



Electrical Vagus Nerve Stimulation (VNS)





Background (8) - tVNS

Non-invasive transcutaneous vagus nerve stimulation (tVNS)

From auricular branch to NTS

Produces similar therapeutic effects as iVNS





Background (9) - tVNS

tVNS has been shown to


- increase vagal tone.
- reduce temper outbursts in adults with Prader-Willi Syndrome
- enhance recognition of emotions
- modulates amygdala functional connectivity in patients with depression
- Increases pain threshold and decreases pain sensitivity

(Manning et al., 2019; Sellaro et al., 2019; Koenig et al., 2019)

Background (10)

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Review Article

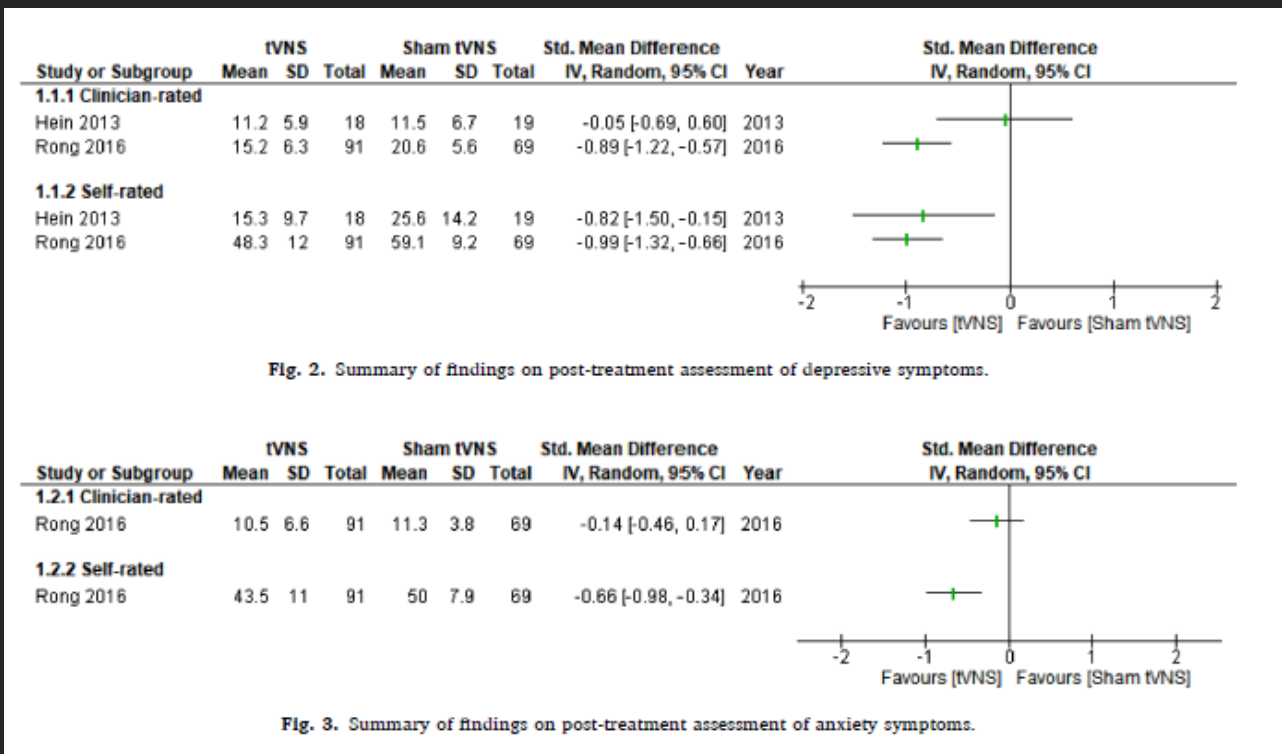


Efficacy of transcutaneous vagus nerve stimulation as treatment for depression: A systematic review

Giuseppe Guerriero^{a,b,c,*}, Constanze Wartenberg^d, Susanne Bernhardsson^{a,d,e}, Sara Gunnarsson^b, Michael Ioannou^{a,b}, Sophie I. Liljedahl^{a,b,c}, Kajsa Magnusson^f, Therese Svanberg^f, Steinn Steingrimsdóttir^{a,b}

Methods: A systematic review to systematically evaluate the efficacy of tVNS for the treatment of depression was conducted according to PRISMA guidelines. Primary outcomes were mortality, self-harm, depressive symptoms, and health-related quality of life (HRQoL). Secondary outcomes were anxiety symptoms, medication use, everyday functioning, complications, and patients' experiences of treatment. Five databases were searched systematically. The included articles were critically appraised and certainty of evidence was assessed using GRADE.

Background (11)



(Guerriero et al., 2021)

Objectives

Objectives

Efficacy of one session tVNS vs. sham control in BPD patients to acutely

- Reduce emotional reactivity (primary)
- Reduce baseline emotional arousal (secondary)
- Ease emotional recovery (secondary)
- Improve emotional regulation (secondary)

Methods

Methods (1)

Design: randomized, single-blind, sham-controlled trial

Intervention: tVNS vs. Sham-tVNS while undergoing affect induction

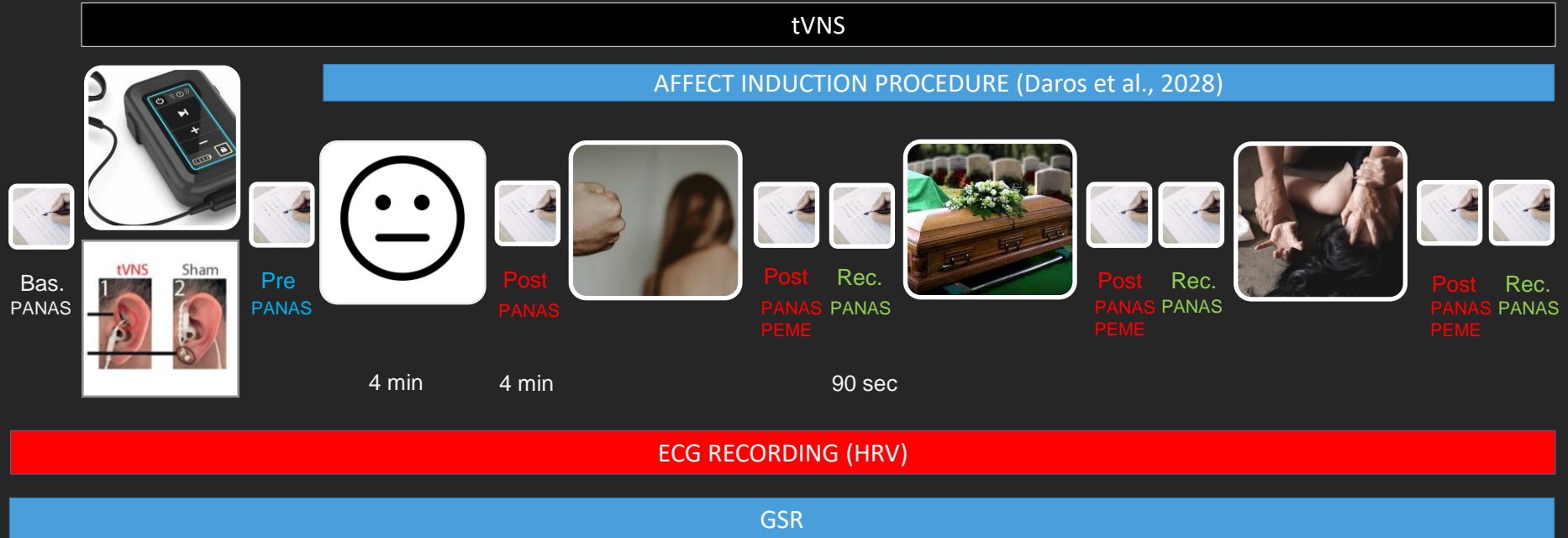
Inclusion: BPD, females, age 18-50

Exclusion: neurological, neuropsychiatric, sensory impairment, alcohol and substance use disorder (<1 month), bipolar/psychotic disorder, antiepileptics or BDZ

Sample size: 42 (ratio 1:1)

Statistical analysis: Mixed models

Methods (2) – Procedure



Primary Outcome: PANAS-N post-induction

Secondary Outcomes: PANAS-N pre-induction and recovery, PEME

Conclusions

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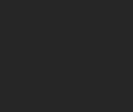
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- A new “bottom-up” sensory hypothesis or perspective for EV in BPD
- A low vagal tone is a potential core candidate
- New insights into the role of vagal tone in emotion vulnerability and dysregulation in BPD

Conclusions

- Mechanisms of emotional vulnerability not yet understood
- A new “bottom-up” sensory hypothesis or perspective for EV in BPD
- A low vagal tone is a potential core candidate
- New insights into the role of vagal tone in emotion vulnerability and dysregulation in BPD
- Preliminary data on the effectiveness of tVNS as a possible non-invasive brain stimulation to treat a core symptom of BPD.

References

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UNIVERSITY OF
GOTHENBURG

giuseppe.guerriero@gu.se

