



Boosting extinction learning during exposure with Vagal Nerve Stimulation

Prof. Dr. Ilse Van Diest

Hoogleraar Gezondheidspsychologie

Faculty of Psychology and Educational Sciences

KULeuven, Belgium

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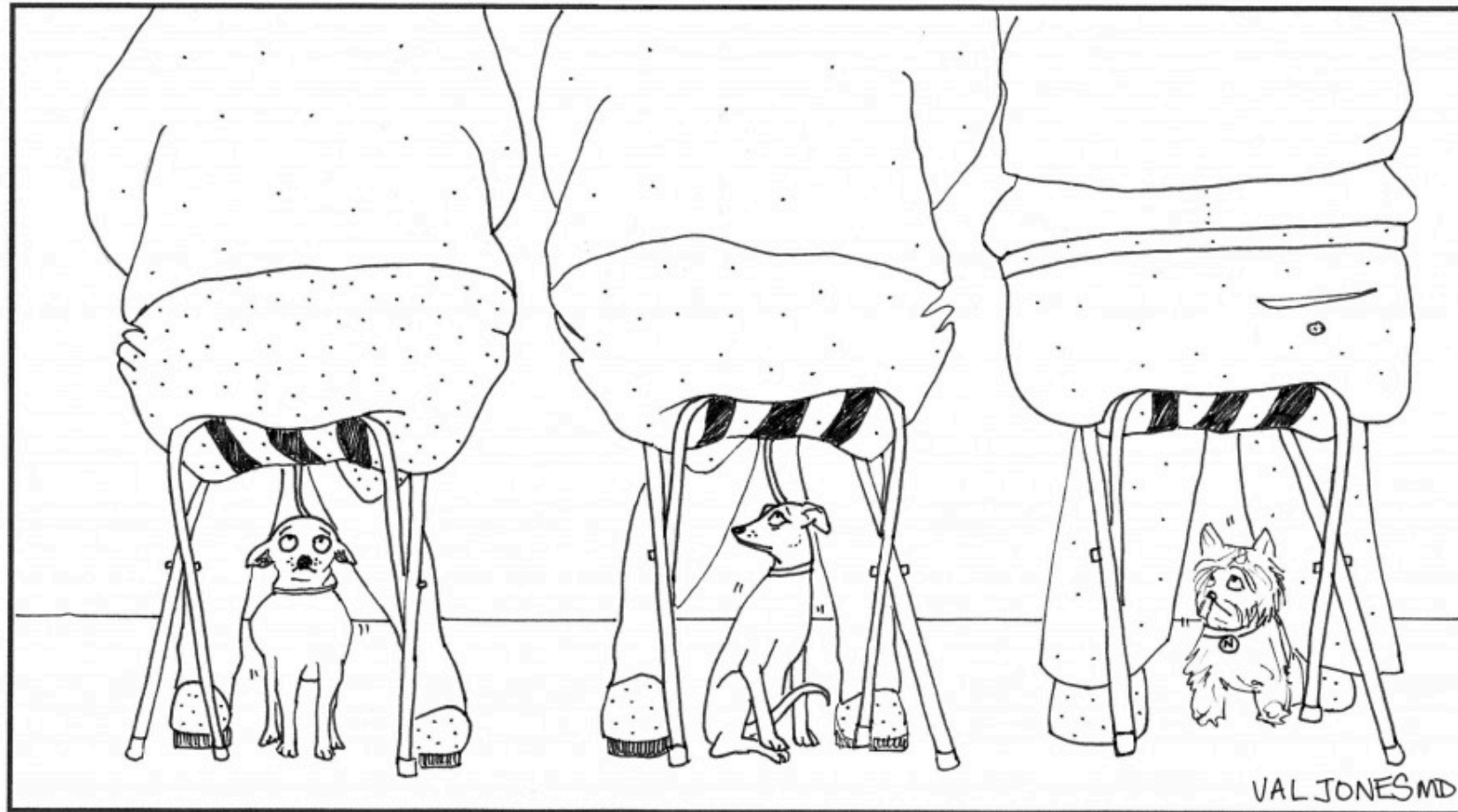
Conclusion

Stimulating the vagus nerve accelerates the extinction of fear and may therefore improve treatment effectiveness of exposure therapy for anxiety in otherwise difficult-to-treat persons

Content

- Background
 - Exposure therapy, Extinction learning
 - Vagus Nerve Stimulation
- Empirical Studies
 - Transcutaneous vagal nerve stimulation (tVNS)
 - Nutrients

EXPOSURE THERAPY for ANXIETY



"Nervous little dogs 'face their fears' at an anxiety management seminar."

What Is Exposure Therapy?

Exposure therapy is a psychological treatment that was developed to help people confront their fears. When people are fearful of something, they tend to avoid the feared objects, activities or situations. Although this avoidance might help reduce feelings of fear in the short term, over the long term it can make the fear become even worse. In such situations, a psychologist might recommend a program of exposure therapy in order to help break the pattern of avoidance and fear. In this form of therapy, psychologists create a safe environment in which to “expose” individuals to the things they fear and avoid. The exposure to the feared objects, activities or situations in a safe environment helps reduce fear and decrease avoidance.

Exposure therapy has been scientifically demonstrated to be a helpful treatment or treatment component for a range of problems, including:

- Phobias
- Panic Disorder
- Social Anxiety Disorder
- Obsessive-Compulsive Disorder
- Posttraumatic Stress Disorder
- Generalized Anxiety Disorder

Effect size estimates (Hedges' g) and 95% confidence intervals (CI) for acute efficacy of CBT relative to placebo on diagnosis-specific symptom measures

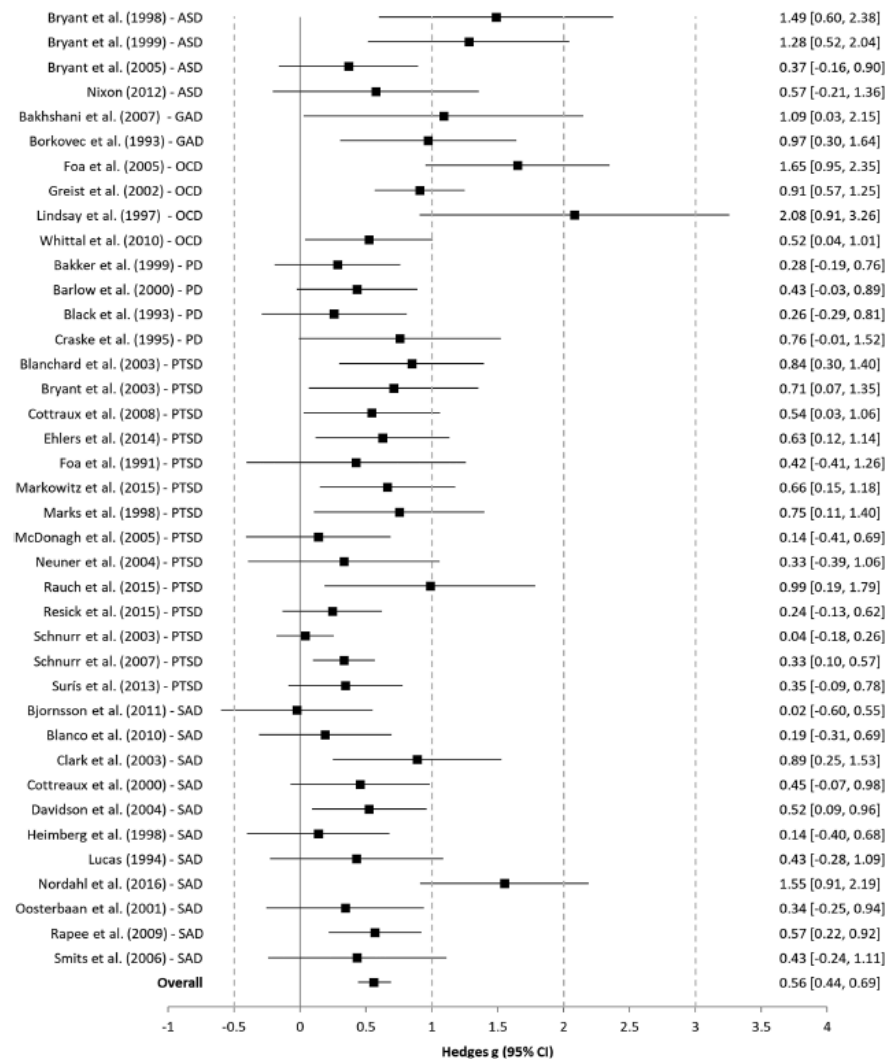


FIGURE 2 Effect size estimates (Hedges' g) and 95% confidence intervals (CI) for acute efficacy of CBT relative to placebo on diagnosis-specific symptom measures. ASD, acute stress disorder; GAD, generalized anxiety disorder; OCD, obsessive compulsive disorder; PD, panic disorder; PTSD, posttraumatic stress disorder; SAD, social anxiety disorder

Exposure Therapy - Challenges

- Relapse: return of fear
- 50 % of the patients who enter Exposure Therapy fail to achieve clinically significant improvements
- Anxiety patients with comorbid depression benefit less
(Higher chronicity, severity, disability, early life adversity)

Carpenter, J. K., et al. (2018). *Depres anxiety*, 35(6), 502-514.; Hofmeijer-Sevink, M. K., et al. (2012). *J Affect Disord*, 137(1–3), 106–112.; Huppert, J. D. (2009). In A. M. Martin & M.B. Stein (Eds.), *Oxford handbook of anxiety and related disorders* (pp. 576–586). New York, NY: Oxford University Press.; Kessler, R. C., et al. (2015). *Epidemol Psychiatr Sci*, 24(03), 210–226. Loerinc, A. G., et al. (2015). *Clin Psychol Rev*, 42, 72–82.; Pittig, A., et al. (2018). *Neurosci Biobehav Rev*, 88, 117-140.

Exposure therapy: Mechanism of Action ?

- **Extinction learning**
- Self-Efficacy
- Acceptance
- Emotional processing
- Cognitive restructuring
- ...

Fear Acquisition

- Learning to predict & prepare for danger



CS - US

Dental drill - sharp pain

- °FEAR MEMORY
- fear response to CS
- motivation to avoid

Fear Extinction

- Learning the CS is no longer predictive of US

CS – noUS

- °EXTINCTION MEMORY
- inhibition of fear response to CS

- Exposure therapy
 - disconfirmation of beliefs
 - opportunities to learn inhibiting fear response to CS

Competing Memories

(fragile)

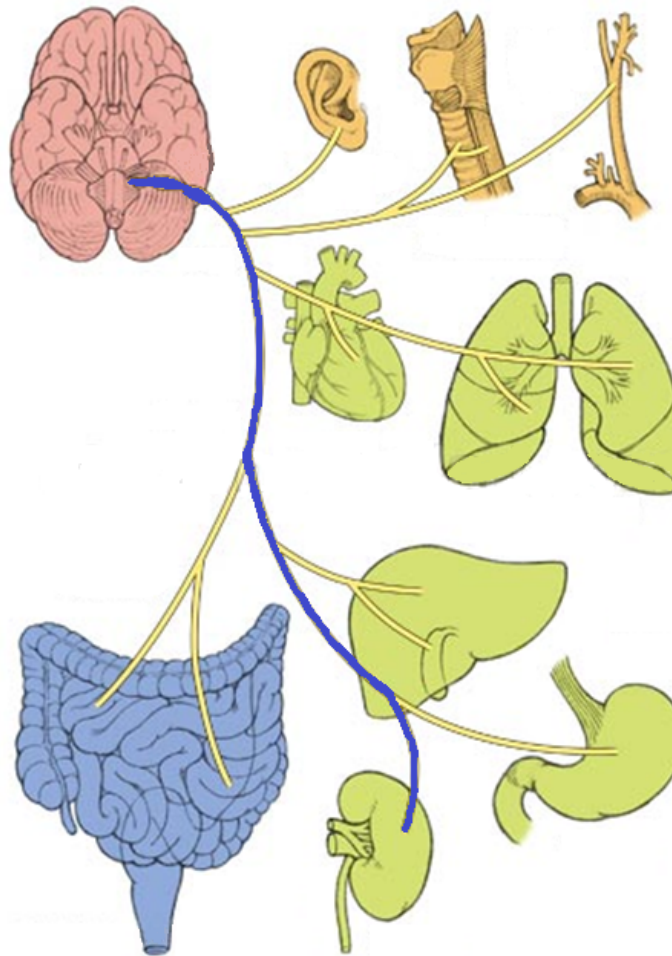
EXTINCTION MEMORY

CS - no US

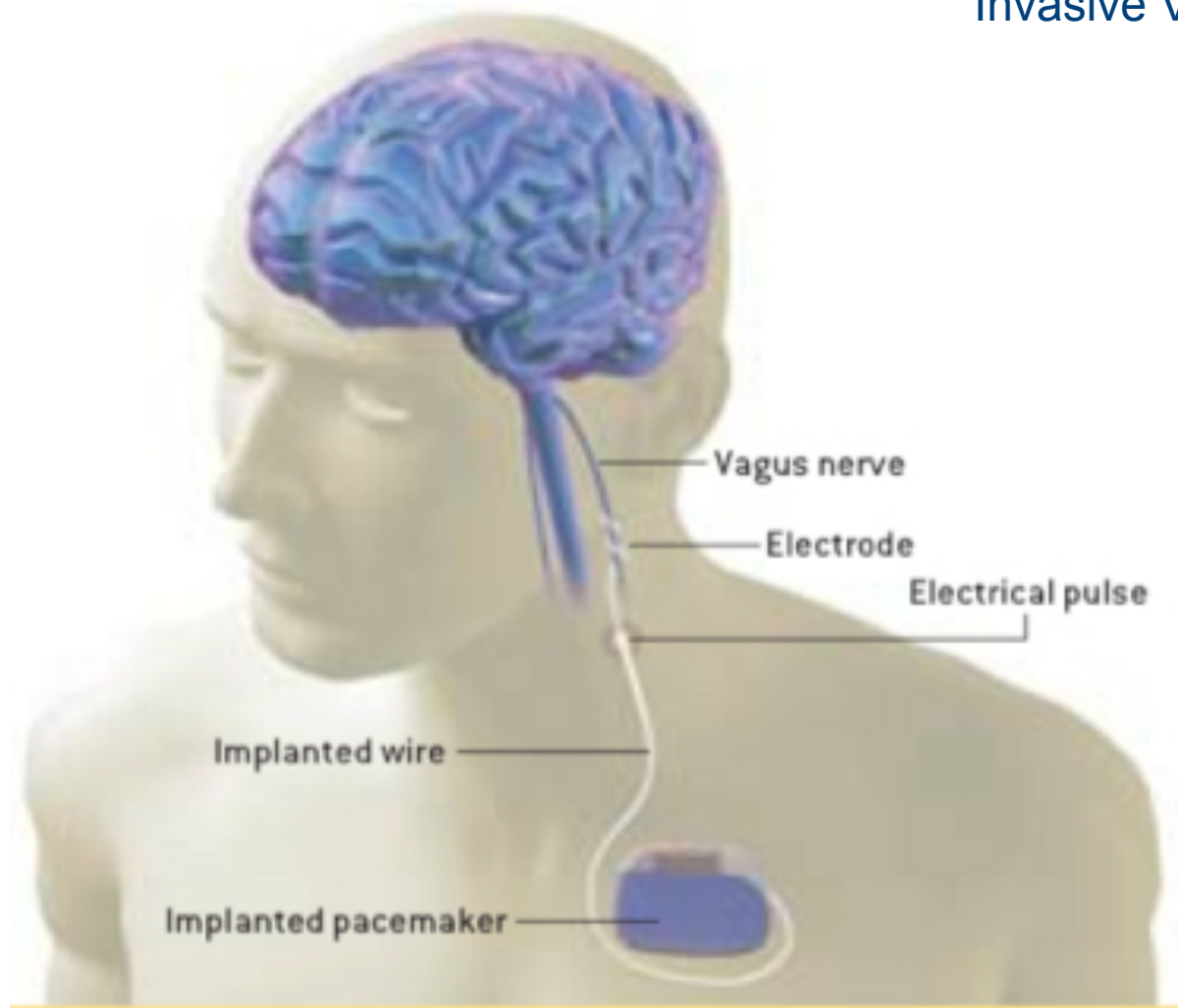
**FEAR
MEMORY
CS - US**



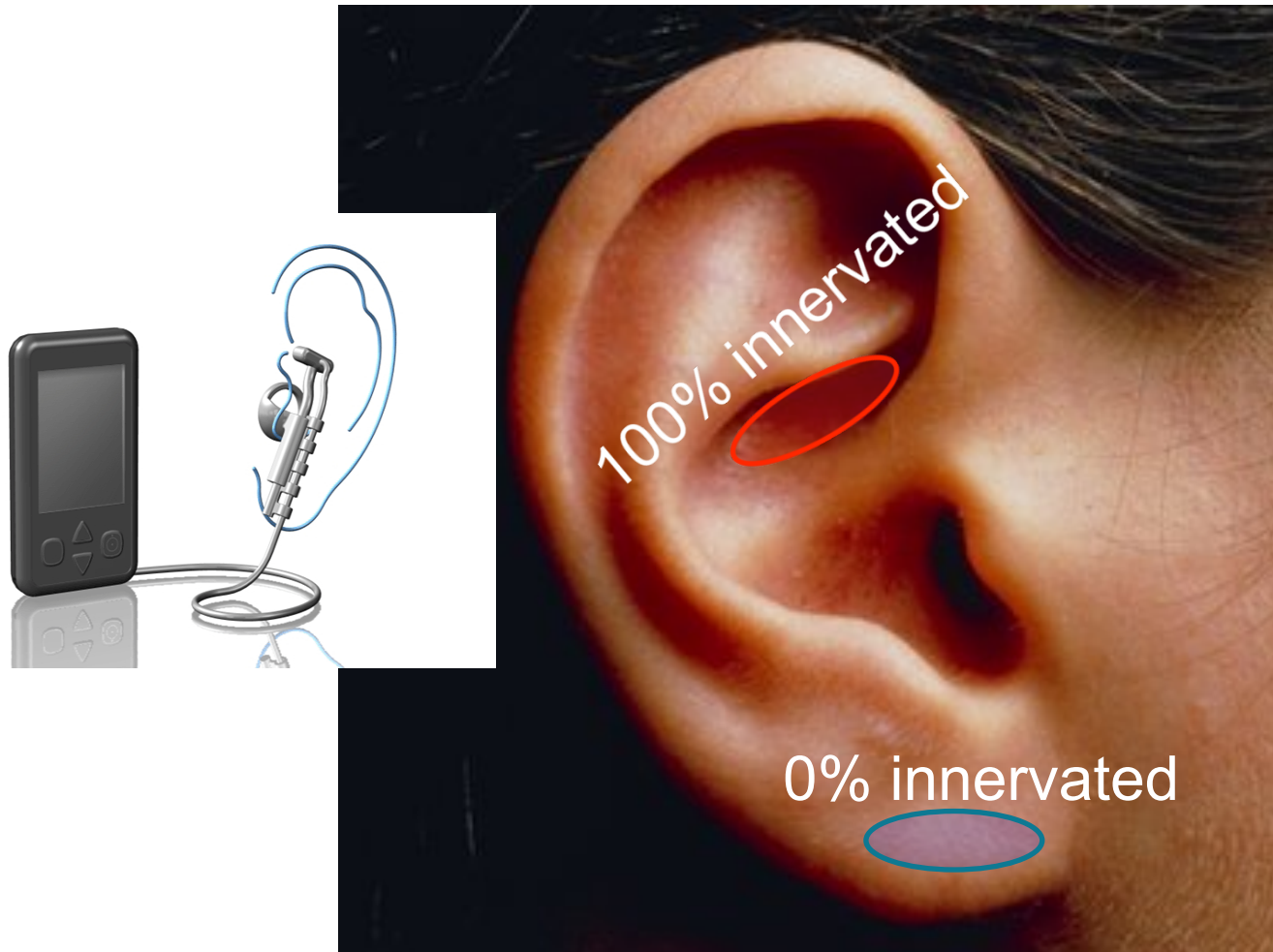


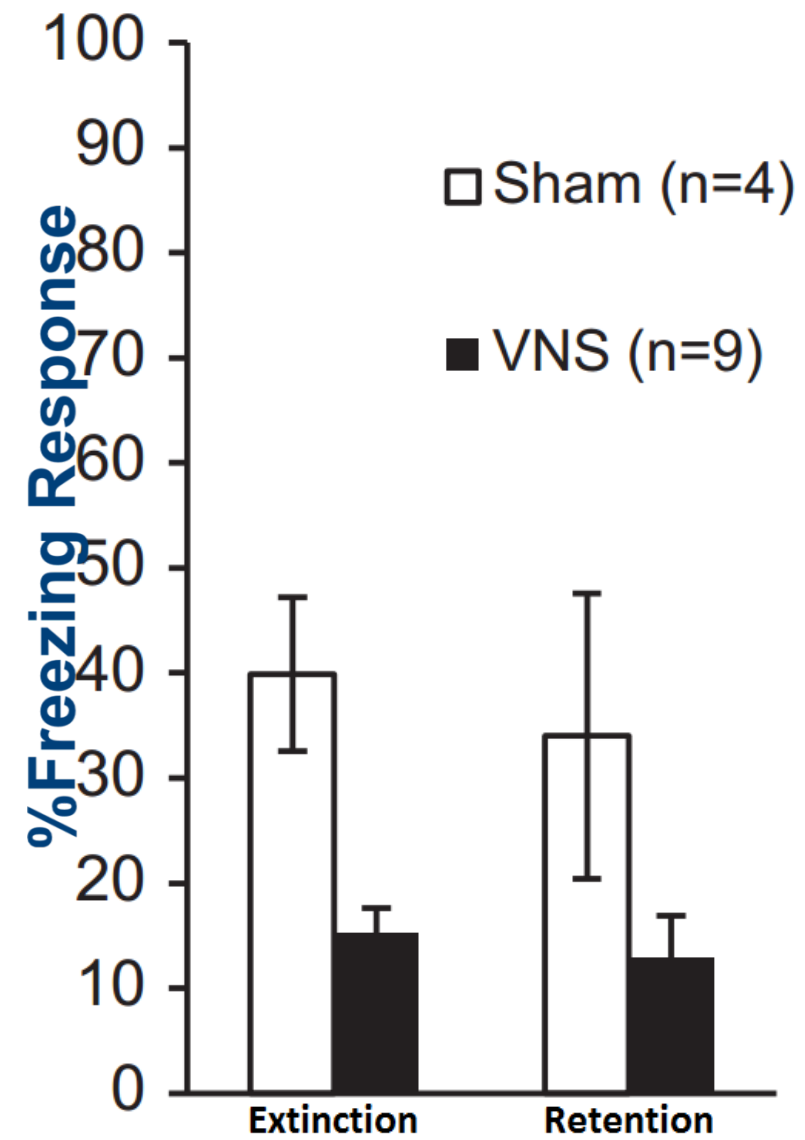
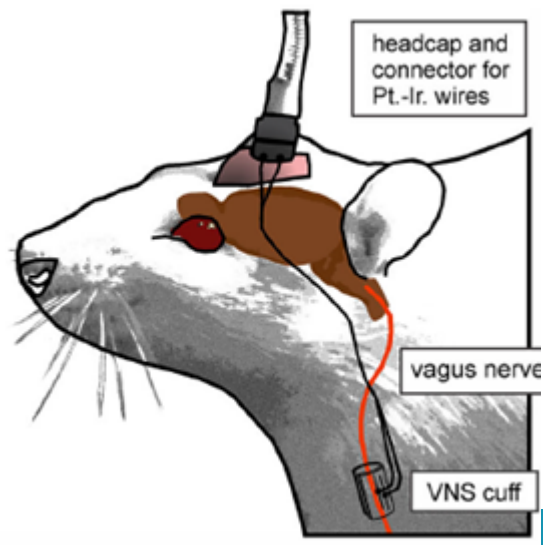
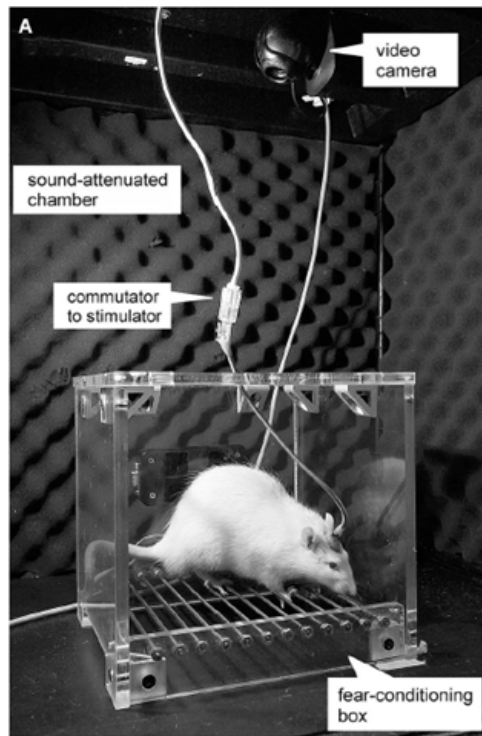


Invasive VNS



Non-invasive VNS





What about Humans?



Fear extinction in healthy humans

3 collaborative studies



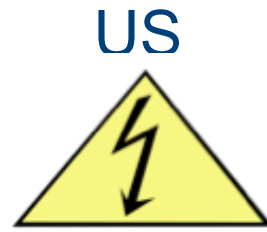
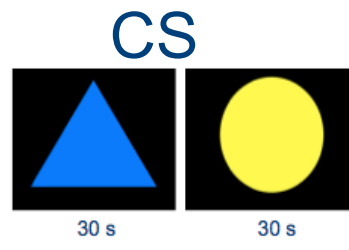
General Design 3 studies

Burger, et al. (2016). *Neurobiol Learn Mem*, 132, 49–56

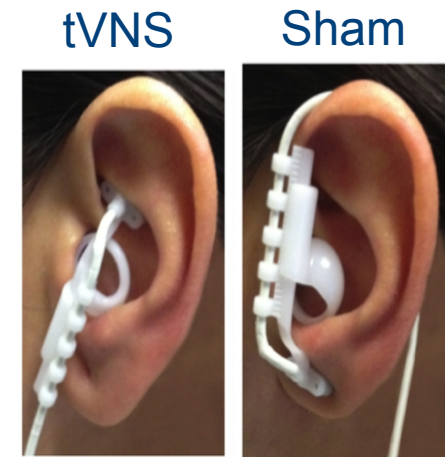
Burger, A. M., et al. (2017). *Beh Res Ther*, 97, 64–74.

Burger, et al. (2018). *Sci. Rep.*, 8, 1–1

- Acquisition



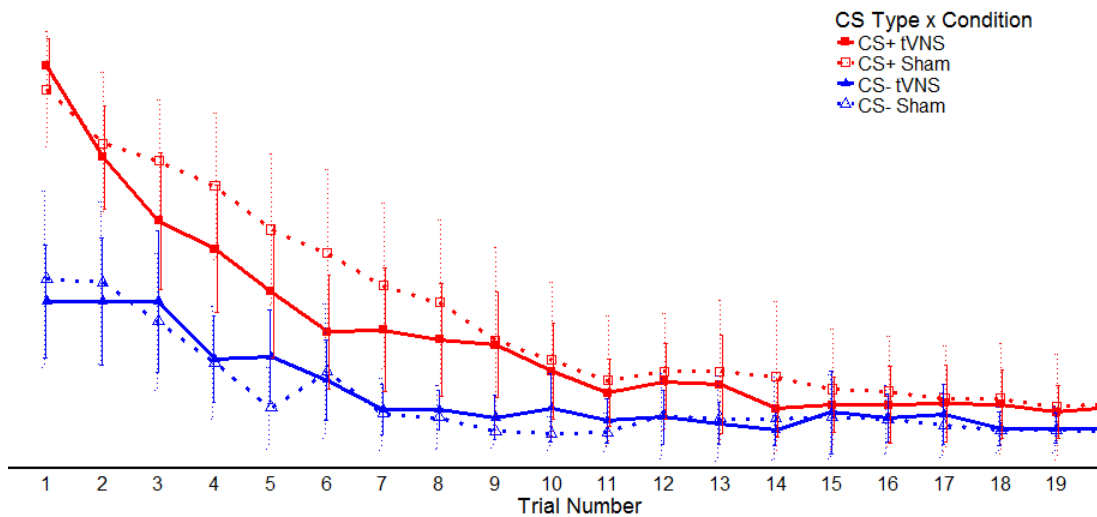
- Extinction: CS - no US
 - 1 group: tVNS
 - 1 group: sham



EXTINCTION learning findings

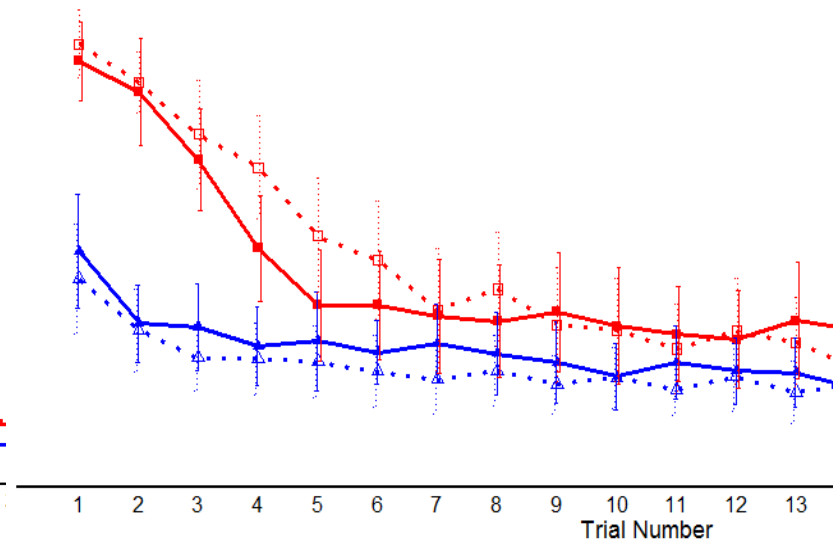
Study 1

Burger, et al. (2016). *Neurobiol Learn Mem*, 132, 49–56



Study 2

Burger, A. M., et al. (2017). *Beh Res Ther*, 97, 64–74.

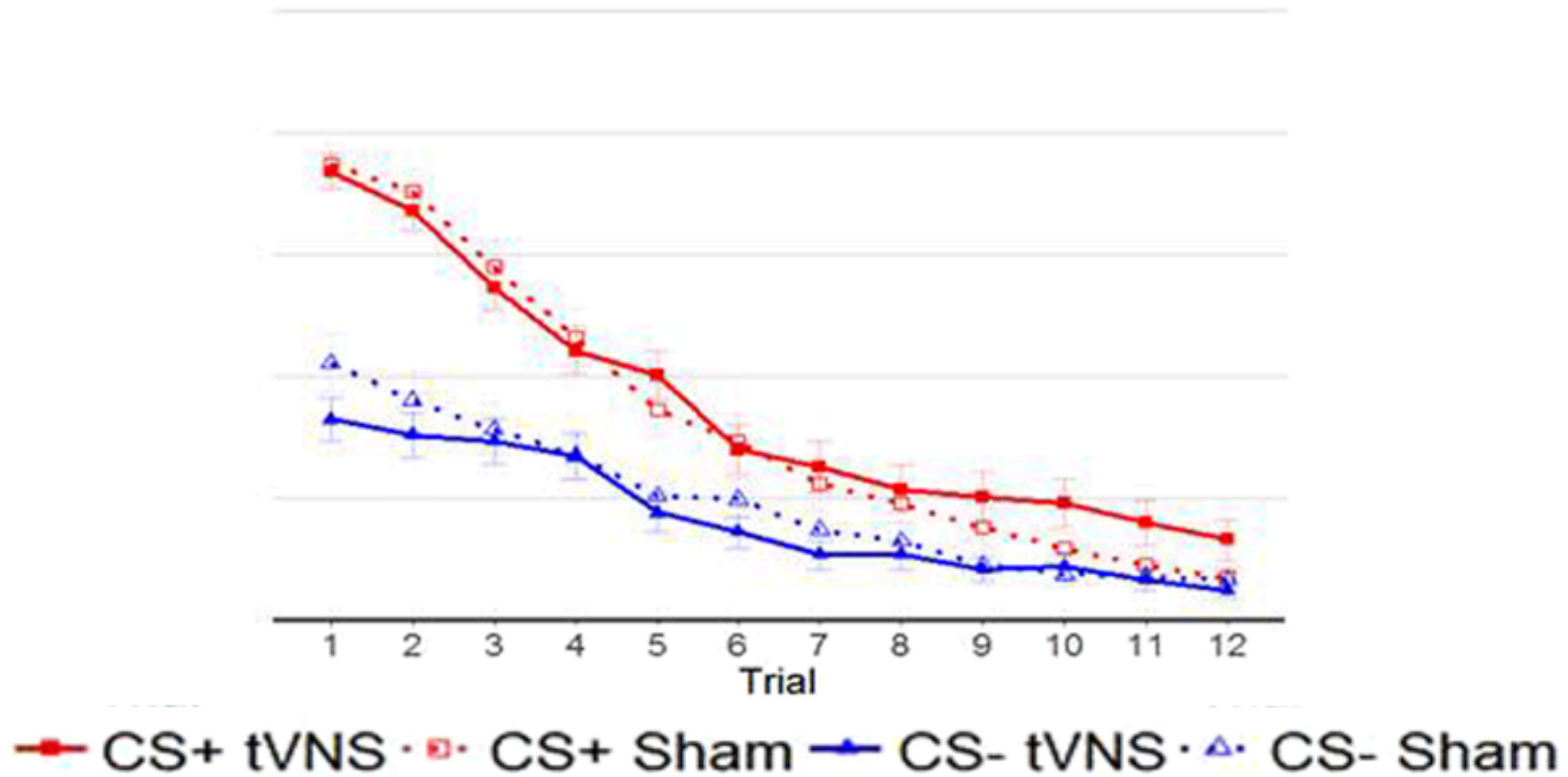


CS+ tVNS · CS+ Sham — CS- tVNS · CS- Sham

EXTINCTION learning findings

Study 3

Burger, et al. (2018). Sci. Rep., 8, 1–1



	CS	US	background noise
study 1	geometrical shape	electrical shock	no
study 2	geometrical shape	white noise 95dB	no
study 3	spider pictures	electrical shock	yes

- Higher arousal state in study 3 (ceiling effect)?
- Extinction is optimal at 'moderate' levels of arousal;
inverted U-shape (Giustino, T. F., & Maren, S. (2018). Front Behav Neurosci, 12(43), 1-20.)

Future studies

- Persons with depression and Early Life Adversity (ELA) show blunted physiological stress-reactivity (Carroll, D., et al. (2017). *Neurosci & Biobeh Rev*, 77, 74–86; McTeague, L. M., et al. (2010). *Biol Psychiatry*, 67(4), 346–356.)
- Arousal is needed for optimal extinction learning (Giustino, T. F., & Maren, S. (2018). *Front Behav Neurosci*, 12(43), 1-20.)

→ Especially patients with blunted stress reactivity may benefit from tVNS during exposure therapy?



How to stimulate the VN during exposure therapy/extinction learning ?

- Electrically (tVNS)
- Slow Deep Breathing
- Nutrients?

Dietary influences on extinction learning

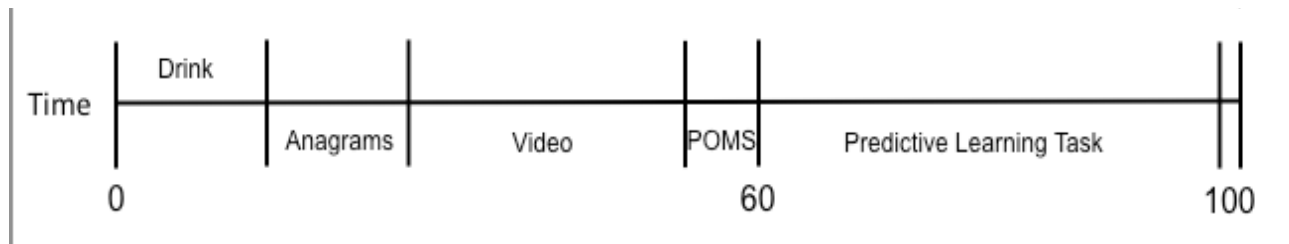
- Regular consumption of perilla oil (50% ALA) accelerates extinction learning in rats

(Yamamoto et al., 1988)

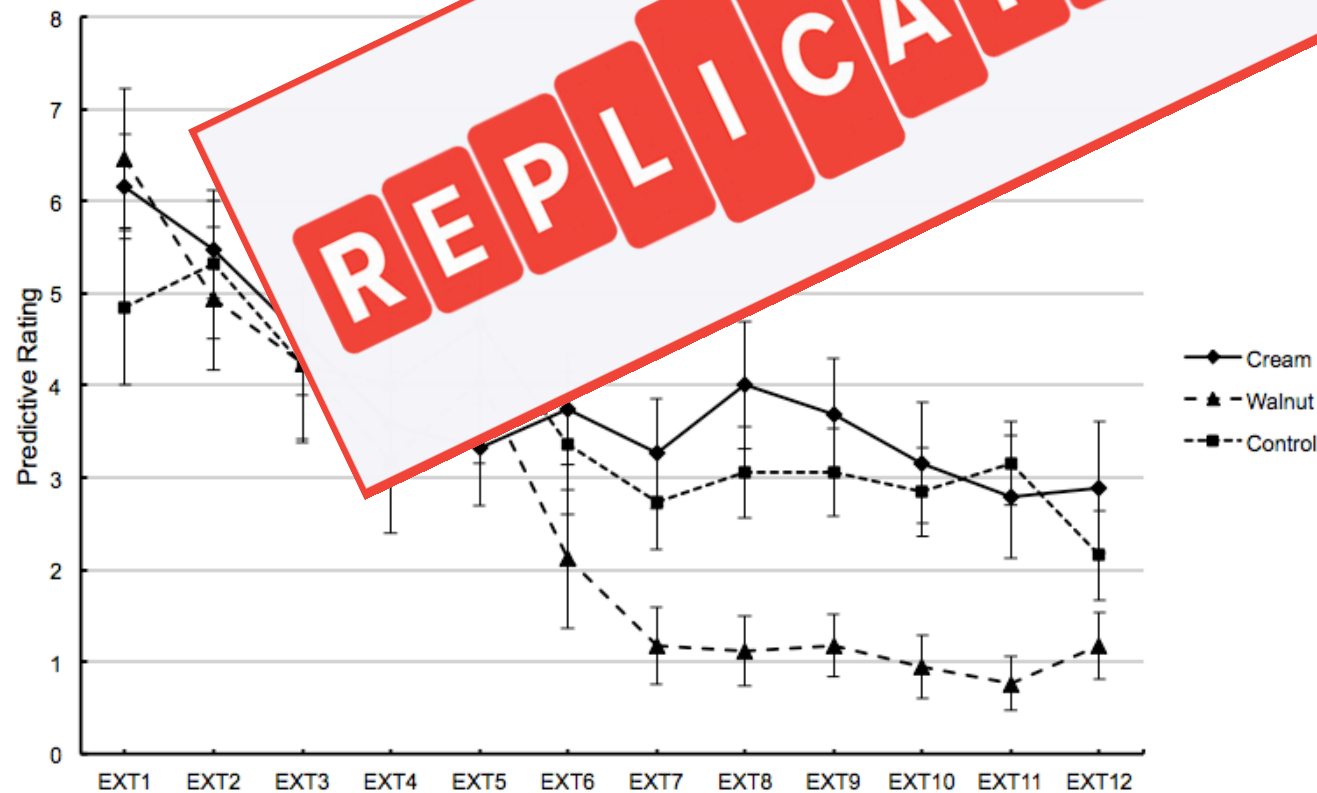
- Goal: to explore the effects of the acute consumption of polyunsaturated versus saturated fat on predictive learning in healthy humans

Method

- Randomized, double blind, placebo-controlled between subject design
- 3 milk shakes: Cream / Walnut oil / Control
- N = 59 students (22 men)



Extinction



Conclusion

Stimulating the vagus nerve accelerates the extinction of fear and may therefore improve treatment effectiveness of exposure therapy for anxiety in otherwise difficult-to-treat persons

Take home general statement

“Cognitive-affective processes at the core of mental health are modulated by bodily inputs that have a clear potential as add-ons to psychological treatment. “

Collaborators (past, current, future)

Faculty of Psychology & Educ Sciences, KULeuven:

- **Martina D'Agostini**
- **Prof. Bram Vervliet**
- **Dr. Holly C. Miller**

Faculty of Medicine, KULeuven

- **Prof. Stephan Claes**
- **Prof. Lukas Van Oudenhove**
- **Boushra Dalile**

Institute of Psychology, University of Leiden:

- **Andreas M Burger**
- **Prof. Bart Verkuil**

Thank YOU

For your attention

