

# Noninvasive Vagus Nerve Stimulation Enhances the Response to Self-Compassion Training: Toward Electroceutical Enhancement of Meditation-Capabilities.

## Abstract

**Background:** Mind-body practices like mindfulness- and compassion-oriented meditation, rely on interoceptive attunement and a capacity to regulate interoceptive signals. The vagus nerve (VN) modulates and conveys these bodily signals to and from the brain and may, therefore, have a role in generating physiological states favourable to contemplative practices. We tested the putative role of the VN in modulating self-compassion (and related outcomes) using transcutaneous Vagus Nerve Stimulation (tVNS).

**Methods:** In a factorial randomized controlled clinical trial (NCT05441774), community-dwelling adults (n=120) were evenly assigned to eight daily sessions of tVNS *or* sham stimulation, *plus* Self-Compassion Mental Imagery Training (SC-MIT) *or* closely matched control training. Acute effects of stimulation and training were assessed in the lab on days 1 and 8, and remotely, between the lab sessions (days 2-7).

**Results:** In contrast to the other experimental conditions, tVNS-plus-SC-MIT showed large acute increases in state self-compassion ( $d=0.99$ ,  $p<0.001$ ) and state mindfulness ( $d=0.68$ ,  $p=0.003$ ) on day 1, and further increases in state mindfulness between days 1 and 8 ( $d=0.84$ ,  $p<0.001$ ). Irrespective of stimulation condition, SC-MIT was associated with an increase in oculomotor attentional bias to compassionate faces, and reductions in self-criticism and heart rate, but no change in heart rate variability.

**Conclusion:** tVNS may augment contemplative capabilities and may therefore have utility as a method for enhancing the efficacy of meditation-based therapies. However, the specific role of the VN in augmenting these competencies remains uncertain given the absence of an easily employed and reliable positive control for vagal stimulation.

## Introduction

The vagus nerve (VN) is the primary conveyor of parasympathetic signals from the brainstem to the main bodily organs. In addition, the predominating sensory afferents of the VN report changes in bodily state to the brain via the nucleus of the solitary tract (NST) (Butt, Albusoda, Farmer, & Aziz, 2020; Ruffoli et al., 2011). This bidirectional signalling allows for exquisite control of various physiological processes, including the phasic co-ordination of heart rate and respiration (respiratory sinus arrhythmia; RSA). Beyond controlling basic physiological processes, the VN may also indirectly regulate cognitive functions (Ridgewell et al., 2021) and motivational-affective states (Neuser et al., 2020) via ascending vagal projections from the NST to limbic and forebrain structures implicated in social-regulatory processes (Geller & Porges, 2014) (Porges, 2021).

Maladaptations in vagal function are proposed to contribute to a range of neurological (e.g. (Martins et al., 2021)), somatoform (e.g. (Bonaz, Sinniger, & Pellissier, 2017)) and psychiatric conditions (e.g. (Koenig, Kemp, Feeling, Thayer, & Kaess, 2016) (Koch, Wilhelm, Salzmann, Rief, & Euteneuer, 2019) (Schneider & Schwerdtfeger, 2020)). Invasive techniques for modulating the VN in these conditions have been superseded by non-invasive methods for stimulating the superficial fibres of the VN that innervate the outer ear (Butt et al., 2020). Thus, ‘transcutaneous vagus nerve stimulation’

(tVNS) of the auricular branch of the VN activates afferent fibres that terminate at the NST, which then projects to higher brain areas (Câmara & Griessenauer, 2015). Neuroimaging studies have confirmed activity in various brainstem nuclei (including NST), as well as forebrain and limbic areas following auricular tVNS (e.g. (Frangos, Ellrich, & Komisaruk, 2015) (Sharon, Fahoum, & Nir, 2021) (Wienke, Grueschow, Haghikia, & Zaehle, 2023) (Keatch, Lambert, Woods, & Kameneva, 2022)).

Preliminary evidence supports the therapeutic use of tVNS in depression (Tan et al., 2023), PTSD (Gurel et al., 2020) and other neuropsychiatric conditions (Thompson et al., 2021). Because tVNS is inexpensive, safe, well-tolerated and easily self-administered, it has high implementation potential (Kim et al., 2022) (Redgrave et al., 2018). However, successful clinical application and optimisation of novel technologies like tVNS requires a thorough-going understanding of their mechanisms of action at the neurobiological and psychological levels (Ford & Young, 2021). The growing literature investigating the modulation of multiple physiological systems (neuroendocrine, microbiomic, immunological, neuroanatomical and peripheral physiological) and basic psychological processes by tVNS (and hence potentially causally implicating the VN in these processes) is therefore an important complement to clinical trials of tVNS treatments.

These mechanistic experimental studies suggest that tVNS modifies (generally, improves) performance across a variety of cognitive (memory, attention, executive function (Ridgewell et al., 2021)) and self-regulatory domains (De Smet et al., 2021) and has wide-ranging effects on social-affiliative processes, including emotion recognition (Steenbergen, Maraver, Actis-Grosso, Ricciardelli, & Colzato, 2021), interpersonal cooperation (Oehrns et al., 2022), oxytocin release (Zhu et al., 2022) and even spiritual self-concept (Finisguerra, Crescentini, & Urgesi, 2019). These findings comport with long-standing ideas about the VN's modulatory role in higher-order cognitive-affective capabilities. For example, Porges (Porges, 2017) has outlined a role for the ventral vagal system in generating a quiescent physiological state that engenders a sense of 'safety' and may underlie contemplative mental states.

As a prototype of such states, 'compassion' refers a cognitive, affective and behavioural responsiveness towards - and motivation to alleviate - suffering. Through sustained contemplative practice (Galante, Galante, Bekkers, & Gallacher, 2014)) or favourable developmental conditions (Shiota, Keltner, & John, 2006), compassion can also be expressed as a trait-like competency, which, through the human capacity for self-representation, can be directed inward, as a form of emotion-regulation (i.e. *self-compassion*; (Neff & Germer, 2017)). 'Mindfulness' is similarly a self-regulatory capability (Rough & Strauss, 2023) that involves an expansive attentional stance towards, and non-judgementally noticing of, the present-moment contents of mind without attaching meaning or desire to any particular object of awareness. Again, dedicated meditation practice may establish mindful attention as a trait-like capability (Kiken, Garland, Bluth, Palsson, & Gaylord, 2015).

The meditation practices that help cultivate compassionate and mindful states belong to different (though closely related) contemplative traditions that are distinguished by the predominating cognitive processes that underlie them (Dahl, Lutz, & Davidson, 2015). Despite their distinctive phenomenological/subjective characteristics, self-reported mindfulness and (self-)compassion are reliably (though modestly) correlated (Miller & Verhaeghen, 2022) and mutually interdependent (Tirch, 2010) (Ferrari et al., 2019). For example, interventions designed to increase compassionate responding, also substantially increase trait mindfulness (Jazaieri et al., 2014). Relatedly, mindfulness-based interventions improve self-compassion (Kuyken et al., 2010). Either as dispositional traits (Tomlinson, Yousaf, Vittersø, & Jones, 2018), or competencies acquired through

meditation practice (Galante et al., 2014), (self-)compassion and mindfulness are associated with improvements in well-being and positive physical and mental health outcomes (e.g. (MacBeth & Gumley, 2012)). Conversely, maladaptations in attentional and self-regulation processes that underlie (a capacity for) mindfulness and (self-)compassion may contribute to psychopathology (e.g. (Bradley & Mathews, 1983)).

Secular psychosocial interventions that strengthen these capabilities are therefore an important therapeutic innovation, forming part of the ‘new wave’ of cognitive therapies which emphasise psychological flexibility and (self-)acceptance. However, despite their promise, certain psychobiological indicators (e.g. attachment security, capacity for self-soothing, differences in oxytocin gene expression (Bakker et al., 2014) (Gilbert, 2010, 2014; Wang et al., 2019)) may moderate the efficacy of contemplative therapies, such that some patients are less able to respond positively to such interventions. Recent advances in the neurobiology of contemplative states have contributed to the notion that biological interventions might interact additively or supra-additively (synergistically) with psychosocial interventions to enhance self-compassion (e.g. (Di Bello et al., 2023; Kamboj et al., 2018; Rockliff et al., 2011)). One target for such biomodulatory interventions might be the VN.

Although not yet demonstrated experimentally, activity of the VN is thought to be a biological mediator of contemplative states ((Stellar & Keltner, 2017) (Di Bello et al., 2020) (Porges, 2017)). To date, empirical studies examining the relationship between vagal activity and compassionate states/behaviours (and prosocial behaviour more generally, e.g. (Beffara, Bret, Vermeulen, & Mermillod, 2016; Bornemann, Kok, Boeckler, & Singer, 2016)) have either examined the correlation between resting state heart rate variability (HRV) and compassionate responding, or have compared HRV metrics as a ‘readout’ of vagal tone in participants who performed a compassion-inducing or control behavioural task (Di Bello et al., 2020). However, these indirect approaches have limitations. For example, they entirely rely on the assumption that (high frequency) HRV is a reliable (replicable) and valid indicator of the influence of vagal tone on higher-order cognitive processes, rather than a more circumscribed index of the cardioinhibitory effects of VN activity (Grossman, 2023, 2024). Even if high frequency HRV is a valid indicator of vagal influences on psychological processes, the conditions under which associations between HRV and prosocial/affiliative states (e.g. compassion) are operative remain poorly understood (Smith, Deits-Lebehn, Williams, Baucom, & Uchino, 2020) and might be quite circumscribed (e.g. (Beffara et al., 2016)). This potentially explains the highly variable - but generally weak - relationship between HRV and compassion (Di Bello et al., 2020).

In the current pre-registered trial, we therefore aimed to take a more direct approach to examining the causal link between experiences of self-compassion and vagal activation by stimulating the VN using tVNS. According to Porges (Porges, 2017) “[the] physiological state mediated via vagal pathways is a necessary, but not sufficient, condition for an individual to experience compassion” (p189). This suggests that vagal activation via tVNS would interact with meditation-like training intended to increase self-compassion, but not generate self-compassion by itself. We tested this using a factorial randomised controlled design, with appropriate controls for stimulation and compassion-meditation training. The effects of tVNS plus ‘Self-Compassion Mental Imagery Training’ (SC-MIT) were tested acutely within a single lab session, as well as across sessions using measures of self-compassion, self-criticism, HRV and (secondarily), mindfulness (among other outcomes). Our primary focus on *self*-compassion (rather than compassion more generally) was motivated by its relevance to clinical psychology and psychiatry, as well as the availability of experimental methods

for inducing (Ferrari et al., 2019) and reliably assessing this construct as a trait and state (Falconer, King, & Brewin, 2015).

## Methods

Full methodological details are provided elsewhere (Kamboj, Peniket, & Simeonov, 2023). The study was prospectively registered on the Open Science Framework (<https://osf.io/4t9ha>) and on ClinicalTrials.gov (Trial Identifier: NCT05441774) as a clinical trial.

### *Participants*

Participants (n=120) were eligible if they were healthy, 18-35 years old, fluent in English and with normal (corrected) vision and hearing (please refer to (Kamboj et al., 2023)).

### *Design*

This was a single-site randomized controlled experimental medicine trial. Participants were randomized evenly to one of four conditions in a 2 x 2 between-subjects factorial design (randomization and other methodological and procedural details in (Kamboj et al., 2023)), with repeated assessment of outcomes occurring within and between two lab sessions (Figure 1). The between-subjects factors were stimulation (sham *versus* active tVNS) and training condition (control mental imagery training *versus* Self-Compassion Mental Imagery Training; SC-MIT), with n=30/condition. Two separate within-subjects time-related factors were used in the data analysis: (i) *timepoint* (t<sub>1</sub>=pre-stimulation, t<sub>2</sub>=peri-stimulation, t<sub>3</sub>=post-training) for acute within-session effects and (ii) *day* (day 1-8) which used baseline/pre-stimulation assessments on day 1 and post-training assessments on each subsequent day to analyse sustained between-session effects.

### *Interventions*

The stimulation and training conditions are outlined in detail in Kamboj et al 2023. To minimize expectancy effects and conceal the true nature of the study, the participant information sheet only provided general details about the procedure and study aims.

### *Self-report 'state' measures*

State questionnaires were administered at t<sub>1</sub>, t<sub>2</sub>, and t<sub>3</sub> during the lab sessions on days 1 and 8 (Figure 1). Each block of state questionnaires consisted of the Self-Compassion-Self-Criticism scale (SCSC, (Falconer et al., 2015)), State Mindfulness Scale (SMS; 5-items as described in (Shoham, Goldstein, Oren, Spivak, & Bernstein, 2017)) and Types of Positive Affect Scale ((TPAS (Gilbert et al., 2008)).

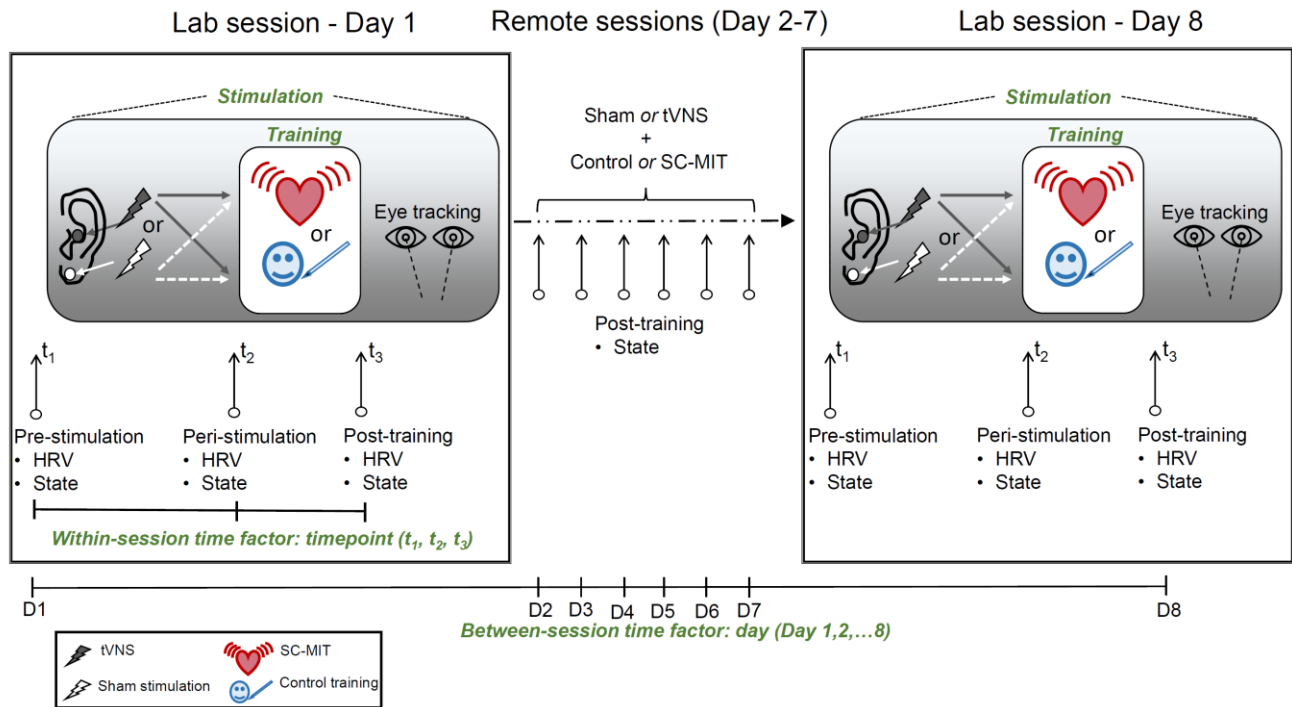
### *Additional measures*

Three credibility/expectancy questions (adapted from (Deville & Borkovec, 2000)) were administered on day 1 after the rationale for stimulation + imagery was provided, each rated on a 9-point Likert scale (0=not at all; 8=very) enquiring about logic, likely success and likelihood of use of vagal stimulation to improve mental imagery (the main component of each training condition). In addition, on day 8, general (tingling, pulsing, discomfort) and adverse effects of stimulation across the preceding week were evaluated.

### *Psychophysiology*

A Bodyguard-2 (Firstbeat, Finland) device was used to acquire RR interval data during the two lab sessions (day 1 and 8). Three 5-min sampling periods corresponding to t<sub>1</sub>, t<sub>2</sub> and t<sub>3</sub> were analysed

using Kubios software (Tarvainen, Niskanen, Lipponen, Ranta-Aho, & Karjalainen, 2014) to obtain RMSSD and high frequency power (Kamboj et al., 2023).



**Figure 1: Design and procedure.** The procedure for each of the two lab sessions (Day 1 and 8) is bounded by a square box showing the timeline of experimental manipulations and assessment episodes within session (‘timepoint’) and across sessions (‘day’). These experimentally controlled factors (bold dark green text) were the key independent variables used in the analyses described in the results. The grey-gradient shaded boxes indicate the procedures carried out *during* (*sham* or *tVNS*) stimulation. The white unshaded boxes indicate the period of ‘online’ training (control=face/pencil symbols or SC-MIT=heart symbol), which was followed by the eye-tracking/attentional bias task. HRV and self-reported outcomes (‘State’), namely self-compassion/-criticism (SCSC), mindfulness (SMS), general affect (PANAS), soothing positive affect (TPAS) and vividness of facial imagery (VFIQ; see text), were sampled at three timepoints. Pre-stimulation ( $t_1$ ) refers to the assessment period before any intervention, peri-stimulation assessment ( $t_2$ ) occurred after 30-min of continuous stimulation in the absence of any concurrent task (offline stimulation) and post-training assessment ( $t_3$ ) occurred immediately after participants had practiced their assigned training (before eye-tracking task). Remote sessions (Days 2-7) were conducted with guided audio-instructions and monitored through meta-data collected from the study website. On Day 2-7 state measures were only administered post-training (corresponding to  $t_3$  in the lab session). Mixed effects models with eight levels of the ‘day’ factor used the values obtained during the latter, and the post-training  $t_1$  values on day 1 (corresponding to baseline, prior to any intervention) and  $t_3$  values on day 8 (the final assessment of the trial).

### Statistical Analysis

The statistics plan is outlined in Kamboj et al (2023). Briefly, we tested the within- and between-session effects of the fixed *stimulation* (sham, active tVNS) and *training condition* (control training, SC-MIT) factors across time using linear mixed models (LMMs). According to the preregistration, self-compassion, self-criticism and HRV were pre-specified as primary outcomes. Therefore, analyses of other variables should be considered exploratory.

## Results

Note: due to space limitations, some effects are not described (e.g. eyetracking results). These will be published in the peer-reviewed paper describing the findings.

### *Participant characteristics*

Baseline sample characteristics are described for the 2 x 2 conditions in Table 1.

**Table 1: Demographics and baseline characteristics.** Values are means (SD) or n(%) across 2 x 2 levels of stimulation (sham=earlobe; active=tragus) and training (control training; SC-MIT).

	Control training + Sham	SC-MIT + Sham	Control training + tVNS	SC-MIT + tVNS
Age	22.63 (4.59)	23.20 (4.16)	22.73 (3.19)	23.00 (4.36)
Male : Female	8:22	8:22	8:22	8:22
Education (yr)	15.07 (1.82)	16.00 (1.68)	16.07 (1.55)	16.03 (1.59)
Ethnicity (white)	9 (30%)	7 (23%)	13 (43%)	10 (33%)
DASS (Total)	17.33 (18.82)	13.20 (11.84)	18.07 (13.16)	18.53 (14.06)
FoSC	17.07 (13.82)	12.27 (9.02)	15.27 (12.46)	15.97 (9.48)
SOC-Self	74.90 (12.12)	77.43 (10.96)	73.63 (8.92)	73.77 (10.78)
FFMQ	50.20 (6.62)	52.27 (6.56)	51.27 (6.09)	50.67 (6.75)
Resting HRV; HF-HRV (nu) <sup>‡</sup>	41.33 (20.11)	43.19 (16.43)	37.77 (17.08)	42.41 (19.90)
Resting HRV; RMSSD (ms) <sup>‡</sup>	37.80 (19.63)	43.72 (22.86)	38.58 (22.04)	37.80 (19.63)
Meditates – Yes (n; %)	3 (10%)	7 (23%)	11 (37%)	6 (20%)

DASS=Depression Anxiety and Stress Scale; total DASS scores are used here as a measure of general distress and derived from raw totals of 21 items multiplied by two (as recommended for the 21 item DASS). FoSC=Fear of self-compassion, SOC-self=Sussex Oxford Compassion Scale (self version). FFMQ=Five facet Mindfulness Questionnaire. Nu=6normalized units. <sup>‡</sup>HRV sampled at baseline (t<sub>1</sub>) on Day 1. N=30 per cell except HRV for SC-MIT + tVNS and SC-MIT + Sham stimulation (n=29 each) due to technical difficulties.

### *Manipulation checks.*

Participants' ratings of expectancy and credibility did not differ across conditions ( $p>0.1$ ). Nor did they differ in the occurrence of adverse effects or duration and intensity of stimulation across days ( $p>0.1$ )

### *State self-compassion and HRV*

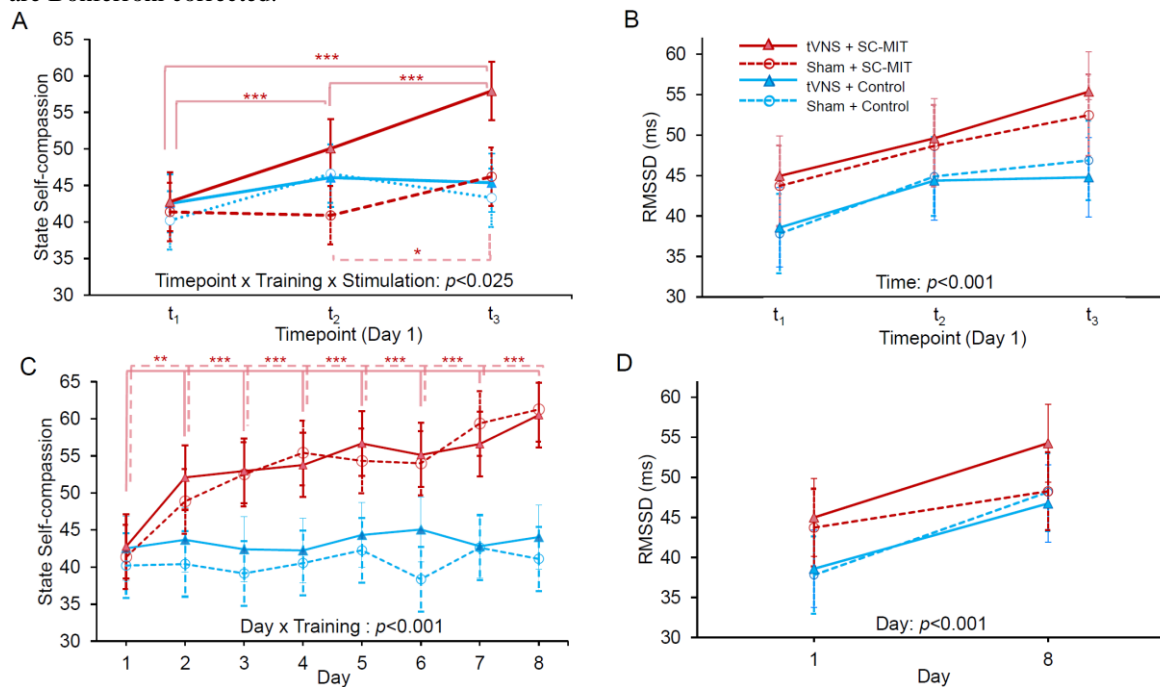
We found a significant Timepoint x Training x Stimulation interaction ( $\chi^2(2)=7.40, p=0.025$ , Figure 2A), which was first decomposed into two two-way analyses and then simple effects of timepoint. There was a significant effect of timepoint on state self-compassion in three of the four groups: sham + control training ( $\chi^2(2)=7.89, p=0.020$ ), sham + SC-MIT ( $\chi^2(2)=6.77, p=0.034$ ) and most clearly in the tVNS + SC-MIT group ( $\chi^2(2)=51.69, p<0.001$ ). Pairwise Bonferroni corrected tests showed a significant t<sub>2</sub> to t<sub>3</sub> increase in the sham + SC-MIT ( $p=0.029, d=0.51$ ) consistent with previously reported acute effects of brief self-compassion interventions. On the other hand, the t<sub>1</sub> versus t<sub>2</sub> comparison in the tVNS + SC-MIT group - putatively representing the effects of offline tVNS alone on state self-compassion - was significant ( $p<0.001$ ) and large ( $d=0.84$ ). Like sham + SC-MIT, the tVNS + SC-MIT group also showed a significant t<sub>2</sub> to t<sub>3</sub> increase in self-compassion, representing an additional large effect of SC-MIT ( $p<0.001; d=0.77$ ). The total additive effect of tVNS and SC-MIT (t<sub>1</sub> to t<sub>3</sub>) was again, large ( $p<0.001, d=0.99$ ).

To determine whether the increases in state self-compassion described above were accompanied by increased HRV, fixed effects of stimulation, training and timepoint were evaluated on RMSSD and HF-HRV power. Although RMSSD increased across timepoints ( $\chi^2(2)=49.11, p<0.001$ ; Figure 2B), this timepoint effect was not moderated by training or stimulation condition ( $p\geq 0.357$ ). HF-HRV did

not show a significant increase across timepoints or any significant moderation by training or stimulation.

### Figure 2. State self-compassion and HRV within and across sessions

**A:** Within-session effects of stimulation and training between  $t_1$  (pre-stimulation),  $t_2$  (peri-stimulation) and  $t_3$  (post-training) on the first lab session (day 1), illustrating a significant Timepoint x Stimulation x Training interaction. Red lines represent effects of SC-MIT with tVNS (solid red, triangle symbols) or sham stimulation (dashed red, open circles). Blue lines represent the control training condition with tVNS (solid blue, triangles) or sham (dashed blue, open circles). Significant pairwise comparisons are indicated (\*\* $p < 0.001$ , Bonferroni corrected). The bracket linking  $t_2$  and  $t_3$  in the sham stimulation + SC-MIT group indicates a significant ( $*p < 0.05$ ) difference for that group. **B:** Within-session effects (day 1) on HRV (RMSSD) showing only a main effect of time ( $p < 0.001$ ). **C:** Patterns of change in state self-compassion across days in the different Stimulation x Training groups, illustrating a significant Day x Training interaction. Brackets (solid overlaid on dashed pink line) indicate pairwise differences between day 1 and all subsequent days: \*\* $p < 0.005$ ; \*\*\* $p < 0.001$ . **D:** Change in HRV (RMSSD; ms) across the two lab sessions (Day 1, 8), showing only a main effect day (HRV sampled at  $t_1$  on day 1 and  $t_3$  on day 8). All  $p$  values are Bonferroni corrected.



In contrast to the within-session effects of stimulation and training, we found no interactions involving stimulation when evaluating state self-compassion across *days* ( $p$  values  $\geq 0.560$ ), although a Day x Training interaction was clear (Figure 2C;  $\chi^2(7)=58.73$ ,  $p < 0.001$ ). RMSSD also showed a generalised increase across days (day 1 to 8;  $\chi^2(1)=18.25$ ,  $p < 0.001$ ), but again, day-dependent effects were not moderated by stimulation or training condition (Figure 2D;  $p \geq 0.390$ ).

#### Trait self-compassion

Trait self-compassion (SOCS-S) scores on days 1 and 8 showed a Stimulation x Day interaction ( $\chi^2(1)=4.16$ ,  $p=0.042$ ) but no interaction involving training condition ( $p \geq 0.40$ ). tVNS showed a larger increase in trait self-compassion than sham although the effect was modest ( $d=0.37$ ).

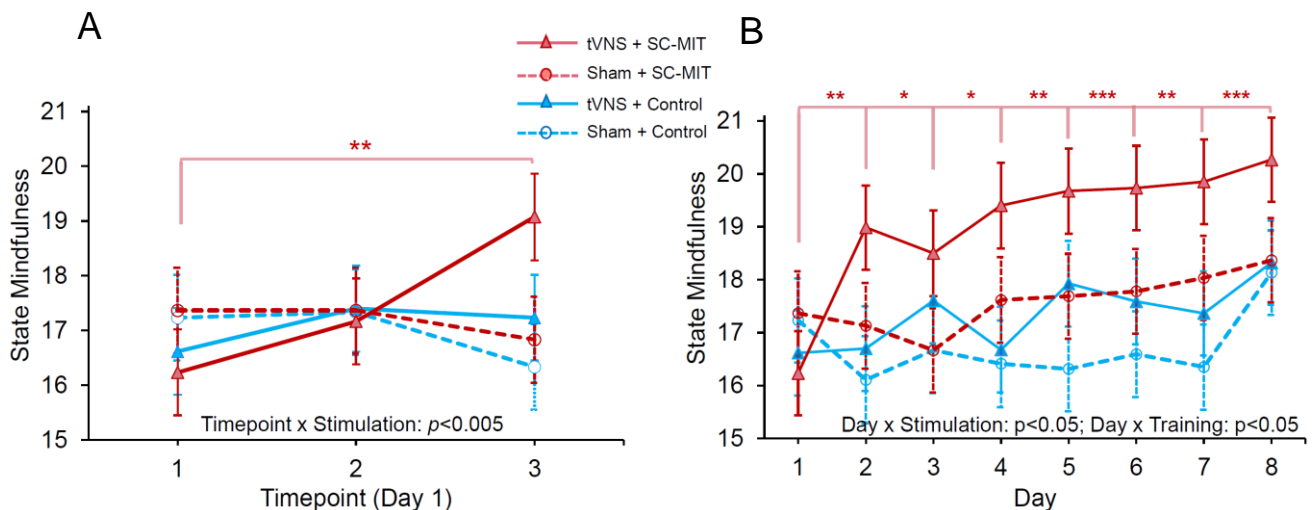
## Self-criticism

Self-criticism decreased more in the SC-MIT group than control training (Timepoint x Training;  $\chi^2(2)=15.16, p<0.001$ ) but there was no effect of not stimulation (Timepoint x Stimulation and Timepoint x Stimulation x Training  $p$  values  $\geq 0.273$ ). Similarly a Day X Training interaction was found ( $\chi^2(7)=24.43, p=0.001$ ) reflecting larger significant decreases in the SC-MIT condition, but no interactions involving stimulation ( $p$  values  $\geq 0.488$ ).

## Mindfulness

Within-session effects on day 1 for state mindfulness (Figure 4A) partially resemble those seen with state self-compassion (Figure 2A) but only a two-way Timepoint x Stimulation interaction (no other 2- or 3-way interactions) was significant ( $\chi^2(2)=10.37, p=0.006$ ). Simple effects analysis showed significant effect of timepoint only in the tVNS + SC-MIT group ( $\chi^2(2)=15.23, p<0.001$ ). Follow-up pairwise tests in the tVNS + SC-MIT group showed that only the  $t_1$  to  $t_3$  comparison – representing the additive effect of tVNS and SC-MIT was significant after multiplicity correction ( $p=0.003, d=0.68$ ; Figure 3A).

**Figure 3.** A: Within-session effects of stimulation and training on state mindfulness at  $t_1, t_2$  and  $t_3$  in at each combination of levels of stimulation and training on day 1; \*\*  $p<0.005$  for  $t_1$  v  $t_3$  in tVNS + SC-MIT. B: State mindfulness across days. Pairwise post hoc tests between day 1 and subsequent days: \* $p<0.05$ , \*\* $p<0.01$ , \*\*\* $p<0.001$ .



Changes in mindfulness across the eight daily sessions are shown in Figure 3B. Although the pattern of results suggests a differential effect (enhancement) across days in the tVNS + SC-MIT group, the three-way (Day x Training x Stimulation) interaction was not significant ( $\chi^2(7)=3.30, p=0.856$ ). However, only the tVNS + SC-MIT group showed a clear monotonic increase in state mindfulness across days ( $\chi^2(7)=47.93, p<0.001$ ). All pairwise comparisons (day 1 versus all subsequent days) were significant in that group ( $p$  values  $<0.05$ ; Figure 3B).

## Discussion

This study directly tested the causal role of the vagus nerve in generating or augmenting contemplative states using a combination of tVNS and a compassion-focused meditation (SC-MIT). Despite the likely weak (relative to invasive stimulation techniques) and imprecise stimulation of the



VN produced by transcutaneous electric stimulation of the tragus, we found support for the notion that experiences of self-compassion can be modulated by tVNS. Although there was some evidence that a 30-min period of off-line tVNS increased state self-compassion relative to sham, even in the absence of a concurrent relevant input, the clearest effects on self-compassion were evident when tVNS was delivered with concurrent SC-MIT. A descriptively similar pattern of acute effects was found with the tVNS + SC-MIT on state mindfulness, although this was not driven by a *three-way* interaction, but rather by a Timepoint x Stimulation interaction.

This pattern of results is most consistent with the idea that bottom up vagal signals are conducive to (rather than sufficient to generate) contemplative mental states, as previously proposed (Porges, 2017) (Stellar & Keltner, 2017) but not directly tested. Our findings therefore begin to clarify the specific role of components of the autonomic nervous system implicated in these complex cognitive-affective-motivational states to complement our growing understanding of the central nervous system structures and pathways activated during experiences of (self-)compassion and mindfulness.

### Conclusion and recommendations

We found support for a central pre-registered hypothesis, namely that tVNS could modulate self-compassion. In addition state mindfulness showed a similar pattern. However, the lack of effect on HRV presents significant interpretational challenges, especially in relation to the role of the VN in the observed effects. Further research is needed to identify a suitable positive control for tVNS. The findings however are promising in suggesting a method to augment contemplative capabilities.

## References

- Bakker, J. et al *Translational Psychiatry*, 4(4), e384-e384.  
Beffara, B., et al *Physiology & Behavior*, 164, 417-428.  
Bonaz, B. et al *Frontiers in Immunology*, 8, 1452.  
Bornemann, B., et al *Biological Psychology*, 119, 54-63.  
Bradley, B., & Mathews, A. (1983). *British Journal of Clinical Psychology*, 22(3), 173-181.  
Butt, M. et al *Journal of Anatomy*, 236(4), 588-611.  
Câmara, R., & Griessenauer, C. J. (2015). *Nerves and Nerve Injuries* (pp. 385-397). London: Academic Press.  
Dahl C et al (2015). *Trends in Cognitive Sciences*, 19(9), 515-523.  
De Smet, S., et al . (2021). *Behaviour Research and Therapy*, 145, 103933.  
Deville, G. J., & Borkovec, T. D. (2000). *J Behav Ther Exp Psychiatry*, 31(2), 73-86.  
Di Bello et al . *Neuroscience & Biobehavioral Reviews*, 116, 21-30.  
Di Bello, M. et al *International Journal of Clinical and Health Psychology*, 23(3), 100362.  
Falconer, C. J et al . *Psychology and Psychotherapy: Theory, Research and Practice*, 88(4), 351-365.  
Ferrari et al . *Mindfulness*, 10(8), 1455-1473.  
Finisguerra, A. et al (2019). *Neuroscience*, 412, 144-159.  
Ford, C. L., & Young, L. J. (2021). *Current opinion in neurobiology*, 68, 1-8.  
Frangos, E., et al (2015). *Brain stimulation*, 8(3), 624-636.  
Galante, J., *Journal of consulting and clinical psychology*, 82(6), 1101.  
Geller, S. M., & Porges, S. W. (2014). *Journal of Psychotherapy Integration*, 24(3), 178.  
Gilbert, P. (2010). *International Journal of Cognitive Therapy*, 3(2), 97-112.  
Gilbert, P. (2014). *British Journal of Clinical Psychology*, 53(1), 6-41.  
Gilbert, P., et al *The Journal of Positive Psychology*, 3(3), 182-191.  
Grossman, P. (2023). *Biological Psychology*, 180, 108589.  
Grossman, P. (2024). *Biological Psychology*, 108739.  
Gurel, N. Z et al (2020). *Neurobiology of Stress*, 13, 100264.  
Jazaieri et al *Motivation and emotion*, 38, 23-35.  
Kamboj, S. K et al . *Plos one*, 18(3), e0282861.

Kamboj, S. K. et al (2018). *Mindfulness*, 9(4), 1134-1145.

Keatch, C et al *Journal of Neural Engineering*, 19(2), 026038.

Kiken, L. G. et al (2015) . *Personality and Individual differences*, 81, 41-46.

Kim, A. Y. et al (2022) *Scientific Reports*, 12(1), 22055.

Kirschner, H., et al 2019. *Clinical Psychological Science*, 7(3), 545-565.

Koch, C. et al (2019). *Psychological Medicine*, 49(12), 1948-1957.

Koenig, et al (2016) *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 64, 18-26.

Kuyken, W., et al (2010) *Behaviour research and therapy*, 48(11), 1105-1112.

MacBeth, A., & Gumley, A. (2012). *Clinical psychology review*, 32(6), 545-552.

Martins, D. F. et al (2021) *Neuroscience & Biobehavioral Reviews*, 131, 1136-1149.

Miller, J. T., & Verhaeghen, P. (2022). *BMC psychology*, 10(1), 1-14.

Neff, K., & Germer, C. (2017). *The Oxford Handbook of Compassion Science*. (pp. 371-390). Oxford, UK: Oxford University Press.

Neuser, M. P et al (2020). *Nature Communications*, 11(1), 3555.

Oehrn, C. R., et al (2022) *Scientific Reports*, 12(1), 1-9.

Porges, S. W. (2017). *The Oxford handbook of compassion science* (pp. 189-202). Oxford: Oxford University Press.

Porges, S. W. (2021). *Comprehensive Psychoneuroendocrinology*, 7, 100069.

Raugh, I. M., & Strauss, G. P. (2023). *Emotion*. doi:<https://dx.doi.org/10.1037/emo0001308>

Redgrave, J. et al *Brain stimulation*, 11(6), 1225-1238.

Ridgewell, C., et al (2021). *Neuropsychology*, 35(4), 352.

Rockliff, H. et al (2011) *Emotion*, 11(6), 1388.

Ruffoli, R., et al (2011) *Journal of chemical neuroanatomy*, 42(4), 288-296.

Schneider, M., & Schwerdtfeger, A. (2020). *Psychological Medicine*, 50(12), 1937-1948.

Sharon, O., et al (2021) *Journal of Neuroscience*, 41(2), 320-330.

Shiota, M. N., et al (2006) *Journal of positive psychology*, 1(2), 61-71.

Shoham, A., et al (2017) *Journal of consulting and clinical psychology*, 85(2), 123.

Smith, T. W., et al (2020). *Social and Personality Psychology Compass*, 14(3), e12516.

Steenbergen, et al (2021). *Cognitive, Affective, & Behavioral Neuroscience*, 21, 1246-1261.

Stellar, J. E., & Keltner, D. (2017). *Compassion: Concepts, Research and Applications* (pp. 120-134): Routledge.

Tan, et al (2023). *Journal of Affective Disorders*(337), 37-49.

Tarvainen, M. P. et al (2014) *Computer methods and programs in biomedicine*, 113(1), 210-220. =

Thompson, S. L. et al (2021). *Frontiers in neuroscience*, 15, 709436.

Tirch, D. D. (2010). *International Journal of Cognitive Therapy*, 3(2), 113-123.

Tomlinson, E. R., et al (2018) *Mindfulness*, 9, 23-43.

Wang, Y. et al (2019) *Mindfulness*, 10, 1792-1802.

Wienke, C., et al (2023) *Journal of Neuroscience*, 43(36), 6306-6319.

Zhu, S., et al (2023) *Psychophysiology*, 59(11), e14107.