

Preprints are preliminary reports that have not undergone peer review. They should not be considered conclusive, used to inform clinical practice, or referenced by the media as validated information.

# Experienced Meditators Show Enhanced Interaction between Brain and Heart Functioning

#### Michael Yufeng Wang ( michael.wang4@monash.edu )

Central Clinical School Department of Psychiatry, Monash University, Camberwell, Victoria, Australia https://orcid.org/0000-0002-8981-6385

#### Andrew W Corcoran

The Turner Institute for Brain and Mental Health, School of Psychological Sciences, Monash University, Victoria, Australia

#### **Brittany McQueen**

Central Clinical School Department of Psychiatry, Monash University, Camberwell, Victoria, Australia

#### Gabrielle Freedman

Central Clinical School Department of Psychiatry, Monash University, Camberwell, Victoria, Australia

#### **Gregory Humble**

Central Clinical School Department of Psychiatry, Monash University, Camberwell, Victoria, Australia

#### **Bernadette Mary Fitzgibbon**

Central Clinical School Department of Psychiatry, Monash University, Camberwell, Victoria, Australia

#### Paul B Fitzgerald

Monarch Research Institute, Monarch Mental Health Group, Sydney, NSW

#### **Neil W Bailey**

4. Monarch Research Institute, Monarch Mental Health Group, Sydney, NSW

#### **Research Article**

Keywords: mindfulness, fm-theta, HEP, HRV, Entropy

Posted Date: October 18th, 2023

#### DOI: https://doi.org/10.21203/rs.3.rs-3454617/v1

License: (c) (f) This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License

## Abstract Objectives

Regulation of the heart by the brain is a vital function of the autonomic nervous system (ANS), and healthy ANS function has been linked to a wide range of well-being measures. Although there is evidence of mindfulness-meditation related changes to brain functioning and heart functioning independently, few studies have examined the interaction between the brain and heart in experienced meditators.

## Methods

This study compared measures of the brain-heart relationship between 37 experienced meditators and 35 non-meditators (healthy controls) using three different analysis methods: 1) the heartbeat evoked potential (HEP; thought to reflect neural sensitivity to interoceptive feedback); 2) the relationship between fronto-midline theta neural oscillations (fm-theta) and the root mean square of successive differences (RMSSD) in electrocardiogram activity (an estimate of vagally-mediated heart rate variability); and 3) the correlation between heart rate wavelet entropy and electroencephalographic wavelet entropy – a measure of signal complexity.

## Results

The HEP analysis indicated that meditators showed a more central-posterior distribution of neural activity time-locked to the heartbeat (p < .001, partial  $\eta^2 = .06$ ) than controls. A significant positive relationship was also found between fm-theta and RMSSD in meditators (F(2,34) = 4.18, p = .02,  $R^2 = .2$ ) but not controls. No significant relationship was found between EEG entropy and ECG entropy in either group.

## Conclusions

The altered distribution of evoked neural activity, and the correlation between brain and heart biomarkers of vagal activity suggests greater neural regulation and perhaps greater sensitivity to interoceptive signals in experienced meditators.

### 1. Introduction

Mindfulness-meditation is a practice of non-judgemental awareness centred on the present moment, with the goal of harnessing a sense of openness and acceptance in attitude toward one's experiences (Kabat-Zinn, 2013). Regular mindfulness practice has been associated with both neurological and physiological changes. For example, neuroimaging studies of meditators have revealed altered brain structure and activation patterns in regions associated with exteroceptive and interoceptive awareness, emotion, memory, and attention (Fox et al., 2014, 2016). Meditation-related changes have also been observed in heart rate variability (HRV), and these HRV changes have been associated with improvements in attention (Burg et al., 2012), pain perception (Adler-Neal et al., 2020), and emotion regulation (Mankus et al., 2013). Although evidence has pointed to the effects of mindfulness on the brain and heart independently, less is known about the impact of mindfulness on the *relationship* between the brain and heart. The nervous and cardiovascular systems are inextricably linked in a synergistic and interdependent relationship (Ardell et al., 2016; Pereira et al., 2013). Modulation of the brain-heart interaction can improve cardiovascular functioning, reduce stress, and enhance pain regulation (Alshami, 2019; Samuels, 2007; Silvani et al., 2016). Thus, a greater understanding of the influence mindfulness has on brain-heart interaction could offer insights into the unique and multidimensional health benefits of mindfulness-meditation.

One method to investigate the effects of mindfulness on the brain-heart relationship is to examine the association between electrophysiological signals from the brain using electroencephalography (EEG) and from the heart using electrocardiography (ECG). Analysis of EEG and ECG signals often involves an approach focused on only a single measure, whereby unique features from each signal that are known markers of neurological and/or physiological functioning are analysed in isolation (Biel et al., 2001; Subha et al., 2010). However, a range of perspectives have proposed several possible mechanisms of action related to mindfulness practice, and some of these theoretical frameworks suggest the potential for distinct effects of mindfulness on the relationship between the brain and heart. Although analysis of either ECG or EEG modalities independently can extract specific measures of interest that are associated with potential mechanisms of change related to mindfulness practice, the single analysis approach only offers a limited understanding of underlying mechanisms. Moving beyond this conventional approach, the present study sought to investigate the brain-heart relationship through the lens of three unique conceptual frameworks using three different analysis methods, all of which examined the relationship between the ECG and EEG signals. This approach allows for a comprehensive understanding of the impact mindfulness has on the brain-heart relationship and mitigates the constraints of a single methodological framework. In the following sections, we briefly introduce the three conceptual frameworks that we examine in this study.

# 1.1 The Bayesian Brain: Heartbeat Evoked Potentials and Interoceptive Precision

The 'Bayesian brain' hypothesis proposes that the brain infers probabilistic beliefs about the world in accordance with Bayes' theorem (Doya, 2011; Knill & Pouget, 2004). In short, Bayes' theorem prescribes a method of probabilistic reasoning that specifies how much one's beliefs should change based on new information (Puga et al., 2015). Bayesian brain theories thus suggest that the brain functions by integrating *a priori* knowledge (prior beliefs) with sensory evidence in a way that mimics or approximates Bayesian inference. From this perspective, subjective perception is not necessarily a reflection of the world as it is, but the 'best guess' of a predictive model based on the functional integration of incoming stimuli, past experience, and contextual evidence (Friston, 2012; Ongaro & Kaptchuk, 2019). In the

Bayesian view, the brain generates hypotheses about the world and our place in it, and these hypotheses – based on beliefs formed through prior experiences – are met by sensory inputs which confirm or disconfirm predicted inputs (Manjaly & Iglesias, 2020). If the hypothesis does not align with the incoming stimuli, a prediction error occurs, creating an opportunity for the brain to update its beliefs by integrating new information (Friston, 2012; Kwee, 1995; Manjaly & Iglesias, 2020; Ongaro & Kaptchuk, 2019; O'Reilly et al., 2012).

However, prediction errors do not guarantee belief updates. In some situations, existing beliefs can be prioritised and outweigh the importance of sensory signals, thereby reducing the degree of belief updating prompted by prediction errors (Ongaro & Kaptchuk, 2019). For example, chronic conditions involving pain can lead to hypersensitivity, increased anxiety, threat detection, and catastrophic beliefs about pain (Latremoliere & Woolf, 2009; Linton & Shaw, 2011; Vlaeyen & Linton, 2000). Within the Bayesian brain framework, these factors are thought to undermine the reliability of sensory input, placing more weight (i.e., greater precision) on existing beliefs and contextual cues and thus diminishing the extent of belief updating in response to sensory signals (Ongaro & Kaptchuk, 2019). Non-judgmental awareness – a principle of mindfulness-meditation that involves directing attention to sensations while holding a neutral attitude (Bishop et al., 2004) - may influence the magnitude of belief updates following a prediction error. Non-judgemental awareness has been proposed to lessen the influence of existing beliefs while promoting the salience of sensory signals, thus increasing the amount of belief updating that occurs in response to a prediction error (Manjaly & Iglesias, 2020).

One method to explore the influence of mindfulness practice on the brain using the Bayesian brain perspective was proposed by Manjaly and Iglesias (2020), who suggested that heartbeat evoked potentials (HEP) could be utilised to examine the effects of meditation on precision-weighted prediction error and belief updates. The HEP is an event-related cortical response synchronised to the heartbeat that occurs between 200ms to 600ms after the R-peak (highest amplitude of the R wave in the QRS complex; Raj et al., 2018). Greater HEP amplitudes have been associated with increased interoceptive accuracy (Coll et al, 2021; Mai et al., 2018). For example, in two separate studies (Montoya et al., 1993; Petzschner et al., 2019), HEP amplitudes were measured while participants directed attention toward an external stimulus compared to an internal stimulus (heartbeat). Both studies reported greater HEP amplitudes when attention was directed internally compared to externally. Based on these results, the authors reasoned that HEP amplitude provides a quantitative measure of neural sensitivity to interoceptive feedback (Petzschner et al., 2019). Similarly, if mindfulness shifts the balance of precision towards sensory signals (and away from prior expectations), one would expect stronger HEPs on average as a consequence of the increased weighting of interoceptive inputs. Further, as mindfulness-related improvements in interoceptive awareness have been shown outside of active mindfulness practice (Mehling et al., 2018) enhanced interoceptive accuracy as reflected by stronger HEPs are thus likely to also be apparent while meditators are at rest, indicating enhanced interoception outside of active meditation practice periods as a result of prolonged interoceptive training.

## 1.2 Parasympathetic Regulation: Relationship between Frontal-Midline Theta and Heart Rate Variability

The parasympathetic nervous system is a subdivision of the autonomic nervous system (ANS) that regulates bodily functions (e.g., heart rate; Mankus et al., 2013; Wu & Lo, 2008) and is associated with top-down self-regulation (Silvani et al., 2016). Mindfulness practice has been shown to modulate brain and heart correlates of parasympathetic functioning (Jinich-Diamant et al., 2020; Mankus et al., 2013). For example, frontal midline theta activity (fm-theta), a neural oscillation within the 4Hz to 8Hz range detected predominantly over the medial prefrontal areas, has been observed to increase during meditation compared to rest (Baijal & Srinivasan, 2010; Brandmeyer & Delorme, 2018; Clayton et al., 2015). Fm-theta activity is thought to be associated with sustained and internalised attention and has been found to be increased by long-term meditation practice (Lee et al., 2018; Mitchell et al., 2008). In a study investigating the relationship between meditation, fm-theta, and cardiac dynamics, fm-theta activity during the mindfulness meditative state was anti-correlated with sympathetic activity, suggesting that participants were perhaps less distracted and more relaxed (Kubota et al., 2001). Fm-theta is also generated by the anterior cingulate cortex (ACC), which is linked with emotion and cognitive control processes, as well as autonomic nervous system regulation, providing further evidence that fm-theta is associated with parasympathetic function (Matthews et al., 2004).

Meditation practice has also been shown to enhance HRV metrics of vagally-mediated parasympathetic activity, such as the root mean square of successive differences (RMSSD; Joo et al., 2010; Kirk & Axelsen, 2020) and high frequency heart rate variability (HF-HRV; Mankus et al., 2013; Nagendra & Sasidharan, 2017; Wu & Lo, 2008). RMSSD is a measure of heart beat activity in the time-domain, while HF-HRV reflects activity in the frequency-domain; both measures are highly correlated, reflect parasympathetic reactivity, and both measures can be modulated by changes in breathing patterns (Minarini, 2020; Thomas et al., 2019).

While extensive research has been conducted on the effects of mindfulness on brain and heart metrics of parasympathetic functioning independently, few studies have investigated the relationship between fm-theta and HRV. One such study by Tang et al. (2009), investigated the relationship between the percentage of change between fm-theta and nuHF - a normalised form of HF-HRV that compares the ratio of low and high frequency HRV (Burr, 2007) - before and after meditation training. After five days of short-term meditation training, novice meditators showed a correlation between the percentage change in fm-theta power and nuHF, while no correlation was found in the control group. Tang et al. (2009) argued that these results indicated greater interaction and coupling between the autonomic and central nervous systems following meditation training, suggesting that mindfulness practice may improve self-regulation by enhancing ACC control of parasympathetic activity. However, Tang et al. (2009) measured fm-theta without accounting for the contribution of non-oscillatory EEG activity (commonly referred to as 1/f activity because the distribution of power values across different frequencies shows a 1/f slope). Recent research has demonstrated that 1/f non-oscillatory activity can contribute more power to power-

frequency measures than oscillatory activity and thus may confound analyses of oscillatory activity (Donoghue et al., 2020). Hence, unless the 1/f non-oscillatory confound is removed prior to analysis, conclusions might not relate to a relationship between fm-theta and HRV but could instead reflect a relationship between 1/f non-oscillatory activity and HRV. Furthermore, HF-HRV can be more susceptible to differences in respiratory rates than RMSSD, and RMSSD is a more accurate marker of vagal activity with changes in natural breathing patterns (Penttilä et al., 2001; Schmid & Thomas, 2021). Changes in respiratory rates have been associated with long term meditation (Peressutti et al., 2012; Steinhubl et al., 2015) and may confound the observed effects of mindfulness on HF-HRV. Thus, further investigation of the relationship between fm-theta activity (after the subtraction of 1/f non-oscillatory activity) and RMSSD may expand the existing understanding of mindfulness-related practice effects on parasympathetic functioning – a reflection of the coupling between brain and heart.

## 1.3 Wavelet Entropy and the Brain-Heart Synchronisation Measured via Signal Complexity

In biomedical research, power-frequency spectrum analyses are typically used to examine bodily signals such as EEG and ECG activity (Li et al., 2019; Lomas et al., 2015; Shaffer & Ginsberg, 2017). Spectral analyses are linear models based in the time-frequency domain which can be used to isolate specific frequency features of biomedical signals (such as EEG waveforms) (Gao et al., 2016; Rosso et al., 2001). However, biomedical signals are complex, with non-linear properties, and while linear models provide some insights to neural or bodily functioning, they are unable to capture non-linear features (Bachmann et al., 2018; He et al., 2014). To better understand the nonlinear properties of biomedical signals, nonlinear methods such as entropy analyses have been adopted (Borowska, 2015). Entropy is a measurement of the degree of uncertainty or information content within a system (Quiroga et al., 2001), where higher entropy corresponds to a less predictable, more informative signal (Deolindo et al., 2020; Gao et al., 2016; Rosso et al., 2006). For example, cardiovascular control via sympathetic and vagal regulation is a dynamic and nonlinear process influenced by a multitude of factors, and although linear method are typically used to analyse HRV, nonlinear methods such as entropy analysis have been argued to better represent the dynamic and complex nature of heart rate control (Byun et al., 2019).

In mindfulness research, reduced (permutation) entropy has been found in the EEG activity of experienced meditators compared to novices during both rest and meditation practice (Kakumanu et al., 2018; Vyšata et al., 2014). This result suggests greater synchronisation of the EEG signal in meditators, perhaps indicating reduced information processing associated with an increase in single-pointed attention focus (Kakumanu et al., 2018; Vyšata et al., 2014; Young et al., 2021). In an extension of this research designed to examine how the brain-heart relationship is affected by mindfulness, Gao et al. (2016) and Sik et al. (2017) used the discrete wavelet transform (DWT) to calculate the wavelet entropy of both EEG and heart rate data. DWT decomposes a time series into sets of average or low pass components, where each set of components reflects the evolution of each frequency component across time (Bajaj, 2020; Jacob et al., 2021). The DWT method thus incorporates temporal information with spectral-frequency analysis, thereby taking into account transient fluctuations of electrophysiological signals (Bajaj, 2020; Jacob et al.)

al., 2021). Hence, wavelet entropy measures the uncertainty, information content, and complexity of signals in both the time and frequency domain, providing additional insights into the dynamics of EEG and heart rate activity (see Rosso et al., 2006 for a detailed review).

Gao et al. (2016) and Sik et al. (2017) reported reduced Wavelet entropy in EEG and heart rate data during meditation compared to rest in novice meditators. Moreover, both studies also reported a stronger correlation between EEG and heart rate entropy during mindfulness breathing compared to rest. These authors speculated that this result might indicate a greater detachment from visual sensory input and may reflect mindfulness-related effects on the synchronisation of body and mind, suggesting improved coherence of the parasympathetic nervous system.

## 1.4 Contrasting the Three Theoretical Frameworks

While empirical support for any of the three theoretical frameworks described above would provide evidence to substantiate an increase in mindfulness-related connectivity between the brain and heart activity, the implication of the results from each framework has discernible differences. For instance, under the Bayesian brain framework, significant differences in HEP amplitude between meditators and non-meditators could suggest enhanced bottom-up sensory processing. A significant correlation between fm-theta and RMSSD among meditators would indicate practice related enhancements in top-down parasympathetic regulation. Lastly, a stronger relationship for meditators between EEG and heart rate entropy could provide evidence for greater detachment from external stimuli in meditators than controls.

## 1.5 Aims and Hypotheses

Results from the studies outlined above (Gao et al., 2016; Manjaly & Iglesias, 2020; Sik et al., 2017; Tang et al., 2009) show evidence of mindfulness-related effects on brain-heart interaction; however, two constraints limit the generalisability of the findings. First, participants primarily involved novice meditators with short-term training. Mindfulness-meditation can affect individuals differently over time, with stronger effects found in meditators with long-term experience (Falcone & Jerram, 2018; Marchand, 2014; Wang et al., 2021). Secondly, comparison conditions within previous research tended to focus on state differences between meditation and rest, rather than a comparison between experienced meditators and non-meditators. While the effects detected during meditation are informative, it is unclear from studies focused only on the meditation state whether effects found during mindfulness practice continue outside of practice sessions. Thus, the present study sought to determine whether mindfulness related changes in brain-heart interaction are evident in experienced meditators while participants are at rest (rather than during active meditation practice). In particular, it was hypothesised that: 1) experienced meditators would show greater neural sensitivity to interoceptive information (as reflected by larger HEP amplitudes) at rest compared to controls; 2) experienced meditators would demonstrate higher levels of autonomic self-regulation, reflected by a significant positive relationship between fm-theta minus 1/f nonoscillatory activity and RMSSD, while no relationship was expected in controls; and 3) experienced meditators would show a significant positive correlation between EEG and ECG entropy while nosignificant correlation would be found for controls.

## 2. Methods 2.1 Participants

The data presented here was collected across two separate broader studies that examined differences in neural activity between meditators and non-meditators at rest and while attending to cognitive tasks (previous publications include:Bailey et al., 2023; Bailey et al., 2020; Bailey, Freedman, et al., 2019; Bailey, Raj, et al., 2019; Payne et al., 2020; Wang et al., 2020). The current study included a subset of 103 participants from those two studies who had ECG recorded concurrently with their EEG recordings. Participants in the current study had ages ranging from 18 to 65 years and included a total of 49 mindfulness-meditators and 54 healthy non-meditators. Participants were recruited via advertising in the local community and meditation centres. Each participant was reimbursed \$30 at the end of their participation for parking and travelling expenses.

Inclusion criteria for meditators were (1) more than two years of meditation experience, (2) current weekly practice of two or more hours, (3) meditation practice aligned with either body-scan or focused attention on the breath, and that (4) practice was congruent with Kabat-Zinn's (1994) definition of mindfulness – "paying attention in a particular way: on purpose, in the present moment, and nonjudgmentally". Non-meditators (controls) were defined as participants with no more than two hours of lifetime meditation experience. Experienced mindfulness researchers (GF, GH, NWB) screened participants on the phone and in person, and screening ambiguities were discussed and resolved via consensus between the principal researcher (NWB) and a second researcher.

Exclusion criteria included (1) current use of recreational drugs or psychoactive medication, (2) current or previous diagnosis of mental or neurological illness, (3) meeting diagnostic criteria for any psychiatric disorders on the DSM-IV assessed using the Mini International Neuropsychiatric Interview for DSM-IV (Sheehan et al., 1998), and (4) scoring in the mild or above range on the Beck Depression Inventory-II (BDI-II) or Beck Anxiety Inventory (Beck & Clark, 1997; Beck & Steer, 1990). Two meditators were excluded, with one participant reporting a history of mental illness and another reporting less than two hours of weekly mindfulness practice. Four controls were excluded after three participants scored within the clinical range on the BDI, and one control participant did not complete EEG recording. Further exclusions of select data were made for EEG and ECG analysis. Four controls were excluded from the analysis due to insufficient data length after EEG cleaning. A further ten meditators and ten controls were excluded due to unusable ECG data.

Thus, final analyses were run on 37 meditators and 35 controls (see Table 1). A significant difference in age was found between groups (t(70) = -2.214, p = .03), with meditators significantly older than controls. Both fm-theta and HRV have been shown to decline with age and thus could potentially confound the results (Kardos et al., 2014; Umetani et al., 1998). This is addressed in the results section by including age as a covariate in the analysis and the potential limitations of this are considered in the discussion. No

other demographic characteristics differed between meditators and controls (all p > 0.05). Key demographic characteristics of participants are presented in Table 1.

Demographic characteristics of participants		
	Meditators	Controls
N	37	35
Gender	23 females, 14 males	21 females, 14 males
	M (SD)	M (SD)
Age*	39.03 (12.83)	32.49 (12.21)
Years of Education	16.84 (2.14)	16.41 (2.86)
BAI	4.98 (5.15)	5.03 (4.84)
BDI	1.38 (2.19)	4.06 (5.15)
FFMQ**	153.33 (15.11)	134.37 (13.67)
<i>Note</i> : <i>N</i> = number of participants; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; FFMQ = The Five Facet Mindfulness Questionnaire.		
* <i>p</i> <.05, ** <i>p</i> <.001.		

Table 1

### 2.2 Procedure

A 64-channel Neuroscan EEG Ag/AgCl Quick Cap acquired EEG data to Neuroscan software through a SynAmps2 amplifier (Compumedics, Melbourne, Australia). Electrodes were referenced online to an electrode between Cz and CPz, and the ground electrode was AFz. Impedances were maintained at less than  $5k\Omega$ . Recordings were sampled at 1000 Hz and bandpass filtered from 0.05 to 200Hz (24 dB/octave roll off). ECG data were also acquired with Neuroscan software and SynAmps2 amplifier sampled at 1000 Hz. Using bipolar referenced EMG measurement, two adjacent EMG electrodes were placed below each clavicle (in line with the middle of the clavicle) to simultaneously record ECG activity into the same datafile as the EEG activity.

The recording length for each participant ranged from 2.5 to 3.5 hours depending on the study. In the first study, tasks included Go/No-Go task, the colour Stroop task, the emotional Stroop task, the 2-back task, and the Sternberg working memory task, with resting recordings taken after the Go/No-Go task (second task in the sequence of tasks presented). The second study included the Go/No-Go task, auditory oddball task, and attentional blink task, with resting recordings taken after the auditory oddball task (first task). Resting EEG and ECG data were recorded for each participant across two conditions: eyes opened (EO) and eyes closed (EC). The duration of recording for each condition across both EEG and ECG was approximately three minutes (six minutes in total including both the EO and EC conditions). Data were

collected from all electrodes except CB1, CB2, M1 and M2 for both conditions, so recorded data included 60 active electrodes in total.

## 2.3 Data Analysis

## 2.3.1 Pre-Processing

MATLAB (R2018b and R2020a; the MathWorks, USA) toolboxes EEGLAB (Delorme & Makeig, 2004) and FieldTrip (Oostenveld et al., 2011) were used to process EEG data. The procedure for cleaning EEG data was to apply the RELAX pipeline (Bailey, Biabani, et al., 2022; Bailey, Hill, et al., 2022). A summary of the cleaning process performed by the RELAX pipeline is as follows: fourth-order Butterworth filtering was applied to the data with a bandpass filter from 1 to 80Hz and a band stop filter from 47 to 53Hz. Noisy electrodes were then removed with the "Pre-processing" (PREP) pipeline (Bigdely-Shamlo et al., 2015) and RELAX's default electrode exclusion settings which are based on robust outlier detection methods (full details can be found in Bailey, Biabani, et al., 2022). No more than twenty percent of electrodes were removed for each participant. On average, 55 EEG channels remained for both Meditators (SD = 4.15) in the EO condition after rejection and 57 EEG channels remained for both Meditators (SD = 2.52) and Controls (SD = 2.36) in the EC condition after rejection. No significant differences were found between groups in the number of electrodes removed (all p < .05).

Multiple approaches were then applied to reject extreme outlying data and identify voltage drifts, eye movements, and blinks, as well as muscle activity (details are reported in (Bailey, Biabani, et al., 2022; Bailey, Hill, et al., 2022). Following this, a multi-channel Weiner filter (MWF) was used to separately reduce muscle activity, blinks, and then horizontal eye movement and voltage drift artifacts sequentially in three separately-applied MWFs (Somers et al., 2018). The MWF filter was selected for its effectiveness in cleaning a wide variety of artifacts while preserving a high signal-to-error ratio, and a low risk of the algorithm creating overcorrection artifacts (Somers et al., 2018; Somers & Bertrand, 2016). Data was then re-referenced using PREP's robust average re-referencing procedure which ensures data are not biased by the removal of bad electrodes (Bigdely-Shamlo et al., 2015). Wavelet-enhanced ICA was then applied to reduce any remaining artifactual components identified by ICLabel (Castellanos & Makarov, 2006; Pion-Tonachini et al., 2019). Electrodes that were removed after being identified as bad in the initial extreme outlying rejection step were then interpolated using spherical spline interpolation (Perrin et al., 1989). Finally, for frequency-power and wavelet entropy analyses, the EEG data were split into epochs of 5 seconds in length with a 1.5 second overlap on each side (providing 2 unique seconds within each epoch for frequency-power computation and a sufficient buffer on each side of the epoch to prevent edge effects from influencing computations). Epochs that showed improbable voltage distributions or kurtosis values exceeding 5SD for any single electrode or 3SD for all electrodes were rejected. The percentage of rejected epochs from each participant was consistent with prior research and remained below 15% (Kosciessa et al., 2020). Epoching for the HEP analysis is reported below.

Pre-processing of ECG data was conducted using the software HRVanalysis (Pichot et al., 2016). The program automatically detects R-peaks and constructs beat-to-beat (RR) signals as a series of time

differences between successive heartbeats (Pichot et al., 2016). The software allows for the automatic correction of invalid or missing beats using a formula developed by Kamath et al. (2013). Although these corrections generally result in a clean RR signal, they can still produce inconsistent values when the original ECG signal is too corrupted. Thus, R peaks were also visually inspected and corrected when necessary.

## 2.3.2 EEG Processing

HEP data was analysed using EEGLAB (Delorme & Makeig, 2004) and HEPlab (Perakakis, 2019). HEPLAB is an EEGLAB plugin able to automatically detect R peaks in raw ECG signals using a peak detection algorithm developed by Azevedo De Carvalho et al. (2002). Detected R peaks (events) were visually inspected, and artifacts were corrected when necessary. R peak events were then saved to EEGLAB's EEG structure. EEG data were epoched around the R peaks (-100 to 650ms). Epochs with two R-peaks within 700ms of each other were excluded from the analysis to ensure that the cardiac field artifact of the following heartbeat could not drive any observed effects (Petzschner et al., 2019). On average, in the EC condition, 189.43 (SD = 24.48) epochs were included in the analysis for Controls and 194.06 (SD = 33.64) epochs were included for Meditators. In the EO condition, on average 196.53 (SD = 28.62) epochs were included for Controls and 197.3 (SD = 34.7) epochs were included for Meditators. No significant differences were found between groups in the number of epochs included (all p > 0.05). Previous studies on HEPs have avoided performing baseline corrections of the data (which are typically applied in eventrelated potential analyses) to avoid introducing artefactual biases from preceding heartbeats (e.g., Petzschner et al., 2019). However, electrode voltages can slowly drift, and baseline correction is typically performed to normalise voltages and address this potential confound. Without baseline correction, there is the potential for differences to be explained by slow electrode drift. To correct for potential voltage drifts, a regression baseline correction (rather than the traditional subtraction baseline correction) was used (Alday, 2019). The regression baseline correction method averages the amplitude of voltage within the baseline period and records the value for each trial separately. The regression baseline correction is then performed on each channel separately by regressing out the variance in the HEP from the baseline period. This approach does not introduce differences from the baseline into the HEP (in contrast to the subtraction baseline correction method, which transposes baseline differences into the active period of interest; Bailey et al., 2023). The specific implementation of the regression baseline correction method used is provided in (Bailey, Hill, et al., 2022). Separate analysis was also conducted without baseline correction to directly replicate previous research, the results of which are reported in supplementary materials 1.

Frontal-midline theta activity was computed at electrodes Fz, FCz, and Cz using a Mortlet Wavelet multitaper convolution transform with a 6-cycle width and a Hanning taper to provide a measure of power in the 3–8 Hz frequency range. Wavelet transforms calculate the power spectrum accounting for variation in both the frequency and time domains, and thus this transform is more appropriate for analysing signals with transient or non-stationary characteristics (which are commonly present in EEG data) than Fourier transforms (Bulnes, 2022). To extend the methods reported by Tang et al., (2009) and reduce the potential for confounds, 1/f non-oscillatory activity was subtracted from theta power calculations using the methods provided by the eBOSC toolbox (Kosciessa et al., 2020). These power values were then averaged, resulting in a single value of theta power at each electrode.

Wavelet entropy for EEG was calculated based on methods by (Gao et al., 2016). The calculation gives a summary estimate of signal complexity at each EEG channel. The procedure for computation was as follows (Gao et al., 2016, supplementary materials, p. 2):

Given a signal, the wavelet coefficients are calculated as  $c_i = \langle x, \varphi_i \rangle$ , where  $\varphi_i$  is an orthonormal basis of the Harr wavelet family and  $i = 1, 2, \ldots, N$  denoting the decomposition levels. The relative energy is defined as  $p_i = c_i^2 / \sum_{i=1}^N c_i^2$ , with  $\sum_{i=1}^N p_i = 1$  and the wavelet entropy is calculated as .

## 2.3.3 ECG Processing

RMSSD was obtained by first calculating the squared value of the time difference (in ms) between each adjacent RR interval (RRI). This value was then averaged, and a square root of the total was calculated (Pichot et al., 2016; Shaffer & Ginsberg, 2017). Frequency domain HRV metrics were also calculated for comparison with RMSSD. The power spectral density (PSD) for the RRI time series was calculated using Welch's periodogram algorithm with a Hamming window of 256 points, an overlap of 50%, and a precision of 256 points/Hz. From the resulting PSD estimate, very low frequency (VLF, 0.003–0.04Hz), low-frequency (LF, 0.04–0.15Hz), and high-frequency (HF, 0.15–0.4Hz) spectral powers, their ratio (LF/HF ratio), as well as the normalized units of both LF and HF components (nuLF and nuHF) were calculated. Calculations for nuLF and nuHF are as follows: nuLF = 100 x LF/ (total power – VLF) and nuHF = 100 x HF / (total power - VLF). Total power for short recordings is calculated as the sum of VLF, LF, and HF bands (Shaffer & Ginsberg, 2017). RMSSD and HF-HRV were highly correlated (all r > .8, p < .001) within all groups and conditions. Descriptive metrics for the HRV measures are presented in supplementary materials 2.

The wavelet entropy of heart rate activity was calculated from the RRI time series across both EO and EC conditions. Following Gao et al. (2016)'s methods, a sliding window of 200 RRIs and a step length of 10 was applied to derive entropy estimates using the same method as described above for EEG entropy. These estimates were then averaged to yield a summary statistic of individual RRI entropy for each participant per condition.

## 2.4 Statistical Comparisons

Statistical comparisons of HEP differences between groups were conducted using the Randomization Graphical User Interface (RAGU), which uses rank order randomization statistics to compare global scalp field differences from all electrodes and epoch time points between groups, assessing differences in overall neural response (Koenig et al., 2011). For the primary analysis, a Global Field Power (GFP) test was performed to assess whether overall HEP amplitude differed between groups irrespective of scalp distribution differences. GFP is a reference-free EEG measure, which avoids an arbitrary choice of an EEG

reference montage (Koenig et al., 2011). RAGU uses the spatial standard deviation of the electric field from all electrodes simultaneously to obtain a single GFP value for each point in time across the epoch, thus controlling for multiple comparisons across space. A Topographic Analysis of Variance (TANOVA) was also performed on the baseline corrected data using the recommended L2 normalisation to determine whether groups differed in the distribution of HEP activity across all electrodes. This L2 normalisation of the data accounts for differences in the variance between maps and is calculated through the division of all possible values of a map by its GFP (Habermann et al., 2018)

Additionally, the topographical Consistency Test (TCT) was performed to assess the consistency of topographical activation within groups, in order to confirm that any between group differences were not simply due to inconsistency within one of the groups (Koenig & Melie-García, 2010). Inconsistent topographical activation can be interpreted as within group variability and supports the null hypothesis of no difference from 0 signal within a group/condition, whereas consistent topographical activation within groups allows valid TANOVA comparisons between groups and conditions (Koenig & Melie-García, 2010). The TCT analysis is presented in supplementary materials 3.

Comparisons of HEP data were made for a 200 to 650ms window following the R-peak (Petzschner et al., 2019). GFP and TANOVA tests used a 2 group × 2 conditions (EC and EO) design. The recommended 5000 randomization runs were employed for each statistical test. Global duration statistics were used to control for multiple comparisons across time points within the epoch. Global duration statistics calculate the duration of significant effects within the epoch that are longer than 95% of significant periods in the randomized data. This ensures that significant differences in the real data last longer than the random comparison data with our alpha level of 0.05 (Grieder et al., 2012). In order to determine whether the difference between groups in age affected the results, the Topographical Analysis of Covariance (TANCOVA) was used to test the relationship between age and the HEP data. TANCOVA functions the same as TANOVA except it tests the relationship between a continuous numerical predictor and the neural data (rather than testing a between groups comparison).

For the second primary analysis, an average of the theta values across the three frontal-midline electrodes was calculated for the EC condition separately for each group. Lower within group variability was observed for EEG data in the EC condition and thus tests of the relationship between RMSSD and fm-theta activity in the EC condition were chosen as the primary analysis. Using the software JASP (Version 0.14.1; JASP Team, 2021), a regression analysis was performed to examine the relationship betweenthe averaged fm-theta (after the removal of 1/f activity) and RMSSD in both groups, with age included as a covariate. To examine the relationship between EEG and ECG wavelet entropy values, a regression analysis was performed between the average EEG entropy values and RRI entropy values for each group, again with age included as a covariate (Shaffer et al., 2014).

Lastly, the Benjamini and Hochberg false discovery rate (FDR; Benjamini & Hochberg, 1995) was used to control for multiple comparisons across all primary statistical tests. The correction was implemented on

the global count p-values from each main effect or interaction in RAGU, and on the overall p-values from the regression analyses.

### 3. Results

# 3.1 Heartbeat Evoked Potentials

# 3.1.1 **TANOVA**

TANOVA using the recommended L2 normalisation for variation in amplitude was performed to examine whether groups differed in the distribution of HEP activity across all electrodes (independently of overall amplitude). A significant main effect of group was found from 200 to 294ms that survived global duration controls (33ms) for multiple comparisons, and also passed the global count statistic (global count statistics across the whole epoch p = .01, FDR p = .04). This result was also significant when activity was averaged across a window showing the significant effect, from 200 to 294ms (p = .001, partial  $\eta^2 = .06$ ), with meditators showing HEP with a more central posterior distribution of positive voltages during this window. No interaction between group and condition (EC and EO) was present (p > .05), except for a few brief time periods that did not last longer than duration control multiple comparisons (global count statistics across the whole epoch p = .79). Figure 1 depicts topographical differences between groups for the significant window from 200 to 294ms.

# 3.1.2 GFP

An exploratory GFP randomization test was performed to assess whether the strength of HEP amplitude differed between groups irrespective of scalp distribution differences. There was no significant main effect of Group, with no periods of significance lasting longer than the duration control of 43ms (global count statistics across the whole epoch p = .45, FDR p = .5), nor interaction for Group x Condition (EC and EO; global count statistics across the whole epoch p = .72). See Fig. 2.

To assess whether age influenced the altered distribution of HEP activity shown in the TANOVA test, a TANCOVA was performed between the averaged activity within the significant period shown in the TANOVA and participant age. TANCOVA between age and topographies averaged across the significant HEP window (200 to 294ms) were not significant within both meditator (p = 1) and control groups (p = 1) across both EC and EO conditions, suggesting those HEP topographies were not related to age.

## 3.2 Frontal-Midline Theta and Heart Rate Variability

A linear regression was performed to assess whether RMSSD could be predicted from averaged fm-theta (after the subtraction of 1/f activity) in the EC conditions for both groups with age included as a covariate. The relationship between fm-theta and RMSSD was significant within the meditator group (F(2,34) = 4.18, p = .02, FDR p = .04,  $R^2 = .2$ ). fm-theta significantly predicted RMSSD ( $\beta = 3.11$ , p = .02); no significant relationship was found between age and RMSSD ( $\beta = -0.54$ , p = .07). For the control group, the

overall regression was significant with age included in the analysis (F(2,32) = 3.72, p = .04,  $R^2 = .19$ ). Age significantly predicted RMSSD ( $\beta = -.82$ , p = .01); however, fm-theta did not significantly predict RMSSD ( $\beta = -.6.67$ , p = .53).

# 3.3 Wavelet Entropy

To examine the relationship between EEG and RRI wavelet entropy values, a linear regression was performed with age included as a covariate. No significant relationship between EEG and RRI wavelet entropy values was present in either the meditator group (F(2,34) = .71, p = .5, FDR p = .5) or the control group (F(2,32) = 3.11, p = .06). For comparison with previous research, exploratory group comparisons were made for EEG entropy and RRI entropy separately. A significant difference in RRI entropy (F(1,57) = 5.02, p = .03,  $\eta^2 = .08$ ) was found between meditators and controls, with controls exhibiting higher RRI wavelet entropy values (see Fig. 3). No significant difference was found in EEG wavelet entropy between groups (F(1, 70) = .01, p = .93). See supplementary materials 4 for mean and standard error of EEG and ECG Entropy.

#### 4. Discussion

To our knowledge, the present study is the first to examine resting-state differences in the interaction between brain activity and heart activity between healthy controls and experienced meditators (while participants were not actively meditating). Meditators showed a HEP with more central posterior positivity compared to the control group. A significant relationship was also found between fm-theta activity and RMSSD, indicating stronger coupling between brain and heart activity within the meditator group than in the control group. Finally, an exploratory analysis showed lower heartbeat entropy values in meditators compared to controls, suggesting lower complexity (or less uncertainty / lower information content) in their heart activity signals. These results provide evidence of differences in neural processing of heartbeat signals and greater coupling between brain and heart functioning in long term meditators, and that these effects were present outside of active meditation practice.

# 4.1 More Central Posterior Distribution of HEPs in Meditators

The inclusion of both the TANOVA with L2 normalisation and GFP analysis provides evidence that, while neural responses to the heartbeat signal were equal in strength between the groups (no difference in GFP amplitude), there was a between group difference related to the distribution of neural activity during the HEPs. As this study was the first to examine the effects of long-term mindfulness-meditation experience on HEPs at rest, there is scant literature available to directly compare our results. When examined in light of existing HEP literature, the differences in neural distribution of activity between groups during the HEP window could suggest enhanced susceptivity to physiological signals and thus greater brain-heart coupling in meditators. For instance, Pollatos and Schandry (2004) examined differences in the topographical distribution of the neural HEP between individuals who were accurate heartbeat perceivers

and individuals who showed poor accuracy in their heartbeat perception. To test for the accuracy of heartbeat perception, participants were given a time window to count their own heartbeats in silence while an ECG recorded their actual heart beats. The authors noted a significant difference between the accurate heartbeat perceivers and inaccurate heartbeat perceivers in the distribution of neural HEP activity. Results revealed that those with high scores on the heartbeat detection task (considered good heartbeat perceivers) showed a HEP distribution with positive voltage maximums predominantly over the parietal and fronto-central regions, an effect that is similar to the distribution found in our meditation group.

Fronto-central activity during the HEP window is thought to be modulated by attention (Canales-Johnson et al., 2015; García-Cordero et al., 2017; Marshall et al., 2018), while HEPs over the parietal region are thought to be influenced by external sensory stimulation (Al et al., 2020, 2021). In two studies by (Al et al., 2020, 2021), participants undertook a sensory detection task where they were instructed to attend to electrical stimulation over the finger and asked whether they felt the stimulation after each trial while their EEG was simultaneously recorded. The authors found that HEP amplitudes over centro-parietal regions were greater when participants missed the stimulation compared to when they felt the stimulation. This could suggest that centro-parietal HEPs index the depth of interoceptive (as opposed to exteroceptive) processing. Similarly, the greater HEP amplitudes observed over the parietal region in the current study might suggest that meditators were less distracted by external sensory stimulation while at rest and were more attuned to their interoceptive signals.

Relating to the Bayesian brain hypothesis, the difference in HEP distribution over the parietal region might imply enhanced neural sensitivity to interoceptive feedback. In a study by (Baranauskas et al., 2021), HEP amplitudes were found to be more positive at the centro-parietal areas when the current RRIs was longer than the preceding RRI, suggesting that increased parietal processing of heart rate information is associated with a longer postponement of the next heartbeat. Under the Bayesian Brain framework, increased activation in these regions when RRIs are prolonged could be indicative of reduced weighting of existing beliefs and increased processing of interoceptive prediction errors based on sensory input (Baranauskas et al., 2021; Smith, 2017) an effect that a Bayesian brain perspective on mindfulness has suggested is likely to be present (Manjaly & Iglesias, 2020).

Taken together, group differences in the topographic distribution of HEPs in our study might indicate that meditators were more sensitive to bottom-up sensory feedback and less distracted by external sensory stimuli than the control group. Future studies could test for corroborating evidence for this interpretation by including a separate heartbeat detection task to examine whether increased heartbeat-evoked activity over parietal-occipital regions correlates with higher heartrate detection scores in experienced meditators while they are at rest. This could provide further evidence of mindfulness-related enhancements in interoceptive accuracy (however, note that the validity of heartrate detection scores is still being debated; Ring et al., 2015; Ring & Brener, 2018; Zamariola et al., 2018).

In contrast to the hypothesis that experienced meditators would show greater HEP amplitudes than the control group, no significant group differences were found in global HEP amplitudes. Our prediction for a difference in global HEP amplitudes was based on the assumption that HEP amplitude across the whole brain would reflect increased weighting of the interoceptive signal, as HEP amplitude in past studies has been associated with greater interoceptive sensitivity to the heartbeat (Canales-Johnson et al., 2015; Judah et al., 2018; Petzschner et al., 2019). The contrast between our finding and previous research might not be indicative of a lack of difference in interoceptive sensitivity in meditators in our study, but instead could be due to differences in the analysis methods employed. Previous studies that have demonstrated differences in HEP amplitude between conditions or groups have tended to focus on either single electrode analyses (Judah et al., 2018; Schulz et al., 2015) or brain region of interest differences in HEP amplitudes (Canales-Johnson et al., 2015; García-Cordero et al., 2017; Marshall et al., 2018). Analysis of a single parietal or occipital electrode in the current study would likely show higher HEP amplitudes in the meditator group than the control group, as our test of the topographical distribution of activity during the HEP window show that these electrodes had increased positive voltages compared to controls. However, single electrode analyses are unable to discriminate between differences in the distribution of neural activity and differences in the strength of neural response (Koenig et al., 2011). Similar issues arise with comparisons of regional brain differences in HEP amplitude. By including all electrodes in our analysis, we were able to determine that the difference between groups was produced by a difference in the distribution of neural activity, and as such, we were able to more accurately characterise inter-individual differences in the activation patterns of event-related neural responses.

# 4.2 Association between fm-theta and HRV in Experienced Meditators

As predicted, a significant positive correlation was found between fm-theta and vagally-mediated HRV (RMSSD) in meditators, while no such relationship was found for the control group. These results extend those reported by Tang et al., (2009) who found a correlation between the percentage change in fm-theta power and nuHF in a sample of participants after 5 days of meditation training. First, we found additional evidence of a positive association between fm-theta and HRV in meditators, whereby meditators with higher RMSSD tended to demonstrate greater theta-band activity. Crucially, our estimates of theta-band power were corrected to eliminate the potential confounding effect of differences in1/f non-oscillatory activity (Donoghue et al., 2020). Secondly, the present study determined that the relationship between fm-theta and HRV was present in meditators at rest, indicating that mindfulness-meditation may alter brainheart interaction while participants were in a general state of relaxed awareness, and that effects are not limited to when meditators are actively meditating.

The results are in line with previous research linking theta activity to HRV, particularly RMSSD. For example, significant positive correlations between theta power and RMSSD have been observed in healthy participants while at rest and when participants were asked to take deep slow breaths (Sinha et al., 2020). In research using brain stimulation techniques, increases in fm-theta activity through intermittent theta-burst stimulation (iTBS) - a form of brain stimulation that modulates theta activity (see

Suppa et al. (2016) for a comprehensive review of iTBS) – have been found to relate to increased RMSSD post stimulation (Cosmo et al., 2022; Keerthy et al., 2021). Both fm-theta and RMSSD are also associated with vagal tone (Kubota et al., 2001; Shaffer et al., 2014). Vagal tone reflects parasympathetic control over heart rate and is sensitive to attentional demands (McLaughlin et al., 2015; Park et al., 2012). For example, increased working memory and attention demands have been shown to lower RMSSD, suggesting a cognition-related reduction in vagally-mediated cardiac activity (Hansen et al., 2003). Greater vagal activity has also been found in individuals with greater attentional control in attention demanding tasks (Park et al., 2012). Fm-theta has been implicated in mindfulness-related reduction in mind wandering and improved attentional functioning (Baijal & Srinivasan, 2010; Brandmeyer & Delorme, 2018; Cavanagh & Shackman, 2015; Clayton et al., 2015). Given the above points, the significant relationship between fm-theta activity and RMSSD in experienced meditators may suggest altered coordination of central and autonomic nervous system functioning and greater vagal tone due to increased attentional control (Shaffer & Ginsberg, 2017).

These findings are also congruent with mindfulness research that has identified changes in activity and volume in the ACC in experienced meditators (Fox et al., 2012, 2016; Zsadanyi et al., 2021). For example, in a fMRI study, Short et al., (2010) examined regional brain activation in meditators during a 12-minute meditation session. The authors found that during meditation, experienced meditators showed more stable and sustained activation in the ACC region than meditators without much experience in meditation. In a separate study, increased cortical thickness of the ACC has been demonstrated in experienced meditators compared to controls (Grant et al., 2010). Mindfulness techniques enhance attention and acceptance for one's inner and outer experiences reducing emotional reactivity (Kabat-Zinn, 1994). Enhanced attentional functioning and reduced emotional reactivity are both associated with modulation of the ACC in meditators (Tang et al., 2016; Wheeler et al., 2017; Zsadanyi et al., 2021). The ACC is also associated with parasympathetic regulation and thus is directly related to the modulation of HRV (Beissner et al., 2013). Together, findings from the present study demonstrate that long term mindfulness practice might enhance parasympathetic modulation, an effect illustrated by the increased connection between fm-theta and RMSSD, and that these effects are retained outside of active meditation practice.

## 4.3 No Significant Correlation in EEG and RRI Wavelet Entropy in Meditators and Controls

Unlike findings reported by Gao et al. (2016) and Sik et al. (2017), EEG and RRI wavelet entropies were not significantly correlated in the meditator group, nor in the control group. Nor were there differences between the groups in EEG measures of wavelet entropy. The inconsistency between our finding and the previous research could be attributed to a number of factors. Entropy values measured in the EEG are sensitive to attentional state, and entropy values have been shown to be correlated with changes in mental focus, attention, and cognitive fatigue (Azarnoosh et al., 2011; Wang et al., 2015). Both EEG and RRI wavelet entropy has also been associated with alertness levels in participants (Lin et al., 2018). In the research by Gao et al. (2016) and Sik et al. (2017), EEG and RRI wavelet entropy were significantly

correlated during active meditation practice, and were not significantly correlated while participants were at rest. As such, our null result may indicate that the relationship between RRI and EEG wavelet entropy may be dependent on whether participants are actively engaged in an attention-related exercise, and as such the resting state recordings in our study did not reveal any relationship. Thus, coherence between EEG and RRI wavelet entropies may be state-dependent, manifesting when participants are meditating but not at rest.

A notable finding in our study was the higher RRI wavelet entropy in controls relative to experienced meditators. As discussed, wavelet entropy indexes the amount of information within the signal, with greater entropy values indicating more signal irregularity (Natwong et al., 2006). This technique has been adopted to investigate and detect abnormal heart activity (Natwong et al., 2006; Ródenas et al., 2015). For example,Natwong et al. (2006) found that patients with ventricular late potentials (VLP; a marker of heart disease) showed higher RRI wavelet entropy than patients without VLPs. Additionally, in testing for confounding variables, we also investigated the relationship between age and RMSSD. The results revealed that for controls, RMSSD correlated significantly negatively with age, while for meditators, the relationship between age and RMSSD was not significant. RMSSD has been consistently shown to decrease with age, signaling a decline in top-down parasympathetic modulation of HR (Umetani et al., 1998; Voss et al., 2012). Our results for the control group are thus in line with past research, while for meditators ageing appears to have less impact on top-down parasympathetic modulation of HR. Together with the wavelet entropy findings, the results could suggest that mindfulness practice may decelerate age-related decline in top-down parasympathetic modulation, thus helping to preserve better heart health as demonstrated by lower RRI entropy values.

## 4.4 Limitations and Future Direction

Engagement in mindfulness-meditation can be influenced by various socio-demographic factors such as education level, with those of higher education more likely to practice mindfulness-meditation (Olano et al., 2015). While the present study matched participants across groups with similar education level, differences in personality characteristics, life experiences, and even neurobiological traits that motivate mindfulness practice remain as limitations in cross-sectional studies (Mascaro et al., 2013). The lack of standardisation of meditation practices across the meditators included in our study could also present as a limitation. Meditators were identified based on a set of inclusion criteria that were consistent with Kabat-Zinn. (1994, p.4)'s description of "*paying attention in a particular way: on purpose, in the present moment, and nonjudgmentally*". However, the school and tradition of their practice varied and thus our meditator group were not uniform in the techniques practiced. This presents a barrier to the conclusions we have drawn, as our conclusions are not limited to a set of clear definitive practice techniques. This factor does however allow for the generalisation of the result across different mindfulness-meditation practices with techniques resembling those set out in our inclusion criteria. A potential confounding variable in our study was the significant age difference between groups. However, since age did not correlate significantly with any of the outcome variables of interest in our primary analyses (except with

RMSSD in the control group) the difference between groups in age does not affect our interpretation of the results.

#### Summary

Our results showed that long-term mindfulness-meditation practice can enhance brain-heart integration, supporting both a Bayesian Brain model that suggests mindfulness affects the brain-heart relationship by increasing bottom-up processing of sensory signals, and a model that suggests mindfulness increases top-down regulation of the heart by fm-theta activity. The detection of differences in the brain-heart connection is particularly significant for understanding mindfulness-specific effects on ANS function (Tracy et al., 2016; Wu & Lo, 2008). Overall, the study's results promote a greater understanding of the mechanisms underlying mindfulness-related effects on the brain-heart connection and offer insights to the potential health consequences of long-term mindfulness practice.

#### Declarations

#### Data Availability Statement

Data sharing was not approved by the ethics committee as participants did not provide consent to sharing the data with third party researchers.

#### **Declaration of Interests**

In the last 3 years PBF has received equipment for research from Medtronic Ltd, Neurosoft, Nexstim and Brainsway Ltd. He has served on scientific advisory boards for Magstim and LivaNova and acted as a founder and board member for TMS Clinics Australia and Resonance Therapeutics. All other authors have no conflicts to report.

#### Funding Information

AWC is supported by the Three Springs Foundation. PBF is supported by a National Health and Medical Research Council of Australia Investigator grant (1193596). The study received no direct funding.

#### References

- Adler-Neal, A. L., Waugh, C. E., Garland, E. L., Shaltout, H. A., Diz, D. I., & Zeidan, F. (2020). The Role of Heart Rate Variability in Mindfulness-Based Pain Relief. Journal of Pain, 21(3–4), 306–323. https://doi.org/10.1016/j.jpain.2019.07.003
- Al, E., Iliopoulos, F., Forschack, N., Nierhaus, T., Grund, M., Motyka, P., Gaebler, M., Nikulin, V. v., & Villringer, A. (2020). Heart-brain interactions shape somatosensory perception and evoked potentials. Proceedings of the National Academy of Sciences of the United States of America, *117*(19), 10575– 10584. https://doi.org/10.1073/PNAS.1915629117/SUPPL\_FILE/PNAS.1915629117.SAPP.PDF

- 3. Al, E., Iliopoulos, F., Nikulin, V. v., & Villringer, A. (2021). Heartbeat and somatosensory perception. NeuroImage, *238*, 118247. https://doi.org/10.1016/J.NEUROIMAGE.2021.118247
- 4. Alday, P. M. (2019). How much baseline correction do we need in ERP research? Extended GLM model can replace baseline correction while lifting its limits. Psychophysiology, *56*(12), e13451. https://doi.org/10.1111/PSYP.13451
- 5. Alshami, A. M. (2019). Pain: Is It All in the Brain or the Heart? *Current Pain and Headache Reports* 2019 23:12, 23(12), 1–4. https://doi.org/10.1007/S11916-019-0827-4
- Ardell, J. L., Andresen, M. C., Armour, J. A., Billman, G. E., Chen, P. S., Foreman, R. D., Herring, N., O'Leary, D. S., Sabbah, H. N., Schultz, H. D., Sunagawa, K., & Zucker, I. H. (2016). Translational neurocardiology: preclinical models and cardioneural integrative aspects. Journal of Physiology, 594(14), 3877–3909. https://doi.org/10.1113/JP271869
- Azarnoosh, M., Motie Nasrabadi, A., Mohammadi, M. R., & Firoozabadi, M. (2011). Investigation of mental fatigue through EEG signal processing based on nonlinear analysis: Symbolic dynamics. Chaos, Solitons & Fractals, 44(12), 1054–1062. https://doi.org/10.1016/J.CHAOS.2011.08.012
- Azevedo De Carvalho, J. L., Da Rocha, A. F., De Oliveira Nascimento, F. A., Neto, J. S., & Junqueira, L. F. (2002). Development of a matlab software for analysis of heart rate variability. *International Conference on Signal Processing Proceedings, ICSP*, *2*, 1488–1491. https://doi.org/10.1109/ICOSP.2002.1180076
- Bachmann, M., Päeske, L., Kalev, K., Aarma, K., Lehtmets, A., Ööpik, P., Lass, J., & Hinrikus, H. (2018). Methods for classifying depression in single channel EEG using linear and nonlinear signal analysis. Computer Methods and Programs in Biomedicine, *155*, 11–17. https://doi.org/10.1016/J.CMPB.2017.11.023
- Baijal, S., & Srinivasan, N. (2010). Theta activity and meditative states: Spectral changes during concentrative meditation. Cognitive Processing, *11*(1), 31–38. https://doi.org/10.1007/s10339-009-0272-0
- Bailey, N., Biabani, M., Hill, A., Miljevic, A., Rogasch, N., McQueen, B., Murphy, O., & Fitzgerald, P. (2022). Introducing RELAX (the Reduction of Electroencephalographic Artifacts): A fully automated pre-processing pipeline for cleaning EEG data - Part 1: Algorithm and Application to Oscillations. *BioRxiv*, 2022.

03.08.483548

. https://doi.org/10.1101/2022.03.08.483548

 Bailey, N., Hill, A., Biabani, M., Murphy, O., Rogasch, N., McQueen, B., Miljevic, A., & Fitzgerald, P. (2022). Introducing RELAX (the Reduction of Electroencephalographic Artifacts): A fully automated pre-processing pipeline for cleaning EEG data – Part 2: Application to Event-Related Potentials. *BioRxiv*, 2022.

03.08.483554

. https://doi.org/10.1101/2022.03.08.483554

- Bailey, N. W., Baell, O., Payne, J. E., Humble, G., Geddes, H., Cahill, I., Hill, A. T., Chung, S. W., Emonson, M., Murphy, O. W., & Fitzgerald, P. B. (2023). Experienced Meditators Show Multifaceted Attention-Related Differences in Neural Activity. *BioRxiv*, 2023. 02.10.527999
  https://doi.org/10.1101/2023.02.10.527999
- Bailey, N. W., Freedman, G., Raj, K., Spierings, K. N., Piccoli, L. R., Sullivan, C. M., Chung, S. W., Hill, A. T., Rogasch, N. C., & Fitzgerald, P. B. (2020). Mindfulness Meditators Show Enhanced Accuracy and Different Neural Activity During Working Memory. Mindfulness, *11*(7), 1762–1781. https://doi.org/10.1007/S12671-020-01393-8/FIGURES/8
- Bailey, N. W., Freedman, G., Raj, K., Sullivan, C. M., Rogasch, N. C., Chung, S. W., Hoy, K. E., Chambers, R., Hassed, C., Van Dam, N. T., Koenig, T., & Fitzgerald, P. B. (2019). Mindfulness meditators show altered distributions of early and late neural activity markers of attention in a response inhibition task. PLOS ONE, *14*(8), e0203096. https://doi.org/10.1371/JOURNAL.PONE.0203096
- 16. Bailey, N. W., Geddes, H., Zannettino, I., Humble, G., Payne, J., Baell, O., Emonson, M., Chung, S. W., Hill, A. T., Rogasch, N. C., Hohwy, J., & Fitzgerald, P. B. (2023). Meditators Probably Show Increased Behaviour-Monitoring Related Neural Activity. Mindfulness, *14*(1), 33–49. https://doi.org/10.1007/S12671-022-02052-W/FIGURES/3
- Bailey, N. W., Raj, K., Freedman, G., Fitzgibbon, B. M., Rogasch, N. C., Van Dam, N. T., & Fitzgerald, P. B. (2019). Mindfulness Meditators Do Not Show Differences in Electrophysiological Measures of Error Processing. Mindfulness, *10*(7), 1360–1380. https://doi.org/10.1007/s12671-019-1096-3
- 18. Bajaj, N. (2020). Wavelets for EEG Analysis. Wavelet Theory. https://doi.org/10.5772/INTECHOPEN.94398
- Baranauskas, M., Grabauskaitė, A., Griškova-Bulanova, I., Lataitytė-Šimkevičienė, B., & Stanikūnas, R. (2021). Heartbeat evoked potentials (HEP) capture brain activity affecting subsequent heartbeat. Biomedical Signal Processing and Control, *68*, 102731. https://doi.org/10.1016/J.BSPC.2021.102731
- Beck, A. T., & Clark, D. A. (1997). An information processing model of anxiety: Automatic and strategic processes. Behaviour Research and Therapy, *35*(1), 49–58. https://doi.org/10.1016/S0005-7967(96)00069-1
- 21. Beck, A. T., & Steer, R. A. (1990). Manual for the Beck anxiety inventory. *San Antonio, TX: Psychological Corporation.*
- Beissner, F., Meissner, K., Bär, K. J., & Napadow, V. (2013). The Autonomic Brain: An Activation Likelihood Estimation Meta-Analysis for Central Processing of Autonomic Function. Journal of Neuroscience, *33*(25), 10503–10511. https://doi.org/10.1523/JNEUROSCI.1103-13.2013
- 23. Benjamini, Y., & Hochberg, Y. (1995). Controlling the False Discovery Rate: A Practical and Powerful Approach to Multiple Testing. Journal of the Royal Statistical Society. Series B, Methodological, *57*(1), 289–300. https://doi.org/10.1111/j.2517-6161.1995.tb02031.x

- 24. Biel, L., Pettersson, O., Philipson, L., & Wide, P. (2001). ECG analysis: A new approach in human identification. IEEE Transactions on Instrumentation and Measurement, *50*(3), 808–812. https://doi.org/10.1109/19.930458
- Bigdely-Shamlo, N., Mullen, T., Kothe, C., Su, K.-M., & Robbins, K. A. (2015). The PREP pipeline: standardized preprocessing for large-scale EEG analysis. Frontiers in Neuroinformatics, 9(JUNE), 1– 19. https://doi.org/10.3389/FNINF.2015.00016
- 26. Bishop, S. R., Lau, M., Shapiro, S., Carlson, L., Anderson, N. D., Carmody, J., Segal, Z. V., Abbey, S., Speca, M., Velting, D., & Devins, G. (2004). Mindfulness: A proposed operational definition. Clinical Psychology: Science and Practice, *11*(3), 230–241. https://doi.org/10.1093/clipsy.bph077
- 27. Borowska, M. (2015). Entropy-based algorithms in the analysis of biomedical signals. Studies in Logic, Grammar and Rhetoric, *43*(56), 21–32. https://doi.org/10.1515/SLGR-2015-0039
- Brandmeyer, T., & Delorme, A. (2018). Reduced mind wandering in experienced meditators and associated EEG correlates. Experimental Brain Research, *236*(9), 2519–2528. https://doi.org/10.1007/s00221-016-4811-5
- Bulnes, F., & Bulnes, F. (2022). A Modern Review of Wavelet Transform in Its Spectral Analysis. *Recent Advances in Wavelet Transforms and Their Applications*. https://doi.org/10.5772/INTECHOPEN.105559
- Burg, J. M., Wolf, O. T., & Michalak, J. (2012). Mindfulness as self-regulated attention: Associations with heart rate variability. Swiss Journal of Psychology, *71*(3), 135–139. https://doi.org/10.1024/1421-0185/a000080
- 31. Burr, R. L. (2007). Interpretation of Normalized Spectral Heart Rate Variability Indices In Sleep Research: A Critical Review. Sleep, *30*(7), 913. https://doi.org/10.1093/SLEEP/30.7.913
- 32. Byun, S., Kim, A. Y., Jang, E. H., Kim, S., Choi, K. W., Yu, H. Y., & Jeon, H. J. (2019). Entropy analysis of heart rate variability and its application to recognize major depressive disorder: A pilot study. Technology and Health Care: Official Journal of the European Society for Engineering and Medicine, 27(S1), S407–S424. https://doi.org/10.3233/THC-199037
- 33. Canales-Johnson, A., Silva, C., Huepe, D., Rivera-Rei, Á., Noreika, V., del Carmen Garcia, M., Silva, W., Ciraolo, C., Vaucheret, E., Sedeño, L., Couto, B., Kargieman, L., Baglivo, F., Sigman, M., Chennu, S., Ibáñez, A., Rodríguez, E., & Bekinschtein, T. A. (2015). Auditory Feedback Differentially Modulates Behavioral and Neural Markers of Objective and Subjective Performance When Tapping to Your Heartbeat. *Cerebral Cortex (New York, N.Y.: 1991)*, *25*(11), 4490–4503. https://doi.org/10.1093/CERCOR/BHV076
- Castellanos, N. P., & Makarov, V. A. (2006). Recovering EEG brain signals: artifact suppression with wavelet enhanced independent component analysis. Journal of Neuroscience Methods, *158*(2), 300– 312. https://doi.org/10.1016/J.JNEUMETH.2006.05.033
- 35. Cavanagh, J. F., & Shackman, A. J. (2015). Frontal midline theta reflects anxiety and cognitive control: Meta-analytic evidence. Journal of Physiology Paris, *109*(1–3), 3–15. https://doi.org/10.1016/j.jphysparis.2014.04.003

- 36. Clayton, M. S., Yeung, N., & Cohen Kadosh, R. (2015). The roles of cortical oscillations in sustained attention. In *Trends in Cognitive Sciences* (Vol. 19, Issue 4, pp. 188–195). https://doi.org/10.1016/j.tics.2015.02.004
- 37. Systematic review and meta-analysis of the relationship between the heartbeat-evoked potential and *interoception*, 122 190 (2021) (testimony of Michel Pierre Coll, Hannah Hobson, Geoffrey Bird, & Jennifer Murphy).
- 38. Cosmo, C., Seligowski, A. V., Aiken, E. M., van't Wout-Frank, M., & Philip, N. S. (2022). Heart Rate Variability Features as Predictors of Intermittent Theta-Burst Stimulation Response in Posttraumatic Stress Disorder. *Neuromodulation: Technology at the Neural Interface*. https://doi.org/10.1111/NER.13529
- Delorme, A., & Makeig, S. (2004a). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. Journal of Neuroscience Methods, *134*(1), 9– 21. https://doi.org/10.1016/j.jneumeth.2003.10.009
- 40. Delorme, A., & Makeig, S. (2004b). EEGLAB: An open source toolbox for analysis of single-trial EEG dynamics including independent component analysis. Journal of Neuroscience Methods, *134*(1), 9–21. https://doi.org/10.1016/j.jneumeth.2003.10.009
- 41. Deolindo, C. S., Ribeiro, M. W., Aratanha, M. A., Afonso, R. F., Irrmischer, M., & Kozasa, E. H. (2020). A Critical Analysis on Characterizing the Meditation Experience Through the Electroencephalogram. Frontiers in Systems Neuroscience, *14*, 53. https://doi.org/10.3389/FNSYS.2020.00053/BIBTEX
- Donoghue, T., Haller, M., Peterson, E. J., Varma, P., Sebastian, P., Gao, R., Noto, T., Lara, A. H., Wallis, J. D., Knight, R. T., Shestyuk, A., & Voytek, B. (2020). Parameterizing neural power spectra into periodic and aperiodic components. Nature Neuroscience, *23*(12), 1655–1666. https://doi.org/10.1038/S41593-020-00744-X
- 43. Doya, Kenji. (2011). Bayesian brain: probabilistic approaches to neural coding. 326.
- Falcone, G., & Jerram, M. (2018). Brain Activity in Mindfulness Depends on Experience: a Meta-Analysis of fMRI Studies. Mindfulness, 9(5), 1319–1329. https://doi.org/10.1007/s12671-018-0884-5
- 45. Fox, K. C. R., Dixon, M. L., Nijeboer, S., Girn, M., Floman, J. L., Lifshitz, M., Ellamil, M., Sedlmeier, P., & Christoff, K. (2016). Functional neuroanatomy of meditation: A review and meta-analysis of 78 functional neuroimaging investigations. In *Neuroscience and Biobehavioral Reviews* (Vol. 65, pp. 208–228). https://doi.org/10.1016/j.neubiorev.2016.03.021
- 46. Fox, K. C. R., Nijeboer, S., Dixon, M. L., Floman, J. L., Ellamil, M., Rumak, S. P., Sedlmeier, P., & Christoff, K. (2014). Is meditation associated with altered brain structure? A systematic review and meta-analysis of morphometric neuroimaging in meditation practitioners. In *Neuroscience and Biobehavioral Reviews* (Vol. 43, pp. 48–73). https://doi.org/10.1016/j.neubiorev.2014.03.016
- 47. Fox, K. C. R., Zakarauskas, P., Dixon, M., Ellamil, M., Thompson, E., & Christoff, K. (2012). Meditation Experience Predicts Introspective Accuracy. PLOS ONE, 7(9), e45370. https://doi.org/10.1371/JOURNAL.PONE.0045370

- 48. Friston, K. (2012). The history of the future of the Bayesian brain. In *NeuroImage* (Vol. 62, Issue 2, pp. 1230–1233). Academic Press. https://doi.org/10.1016/j.neuroimage.2011.10.004
- 49. Gao, J., Fan, J., Wu, B. W. Y., Zhang, Z., Chang, C., Hung, Y. S., Fung, P. C. W., & Sik, H. hung. (2016). Entrainment of chaotic activities in brain and heart during MBSR mindfulness training. *Neuroscience Letters*, *616*, 218–223. https://doi.org/10.1016/j.neulet.2016.01.001
- 50. García-Cordero, I., Esteves, S., Mikulan, E. P., Hesse, E., Baglivo, F. H., Silva, W., García, M. del C., Vaucheret, E., Ciraolo, C., García, H. S., Adolfi, F., Pietto, M., Herrera, E., Legaz, A., Manes, F., García, A. M., Sigman, M., Bekinschtein, T. A., Ibáñez, A., & Sedeño, L. (2017). Attention, in and out: Scalp-level and intracranial EEG correlates of interoception and exteroception. Frontiers in Neuroscience, *11*(JUL), 411. https://doi.org/10.3389/FNINS.2017.00411/BIBTEX
- 51. Grant, J. A., Courtemanche, J., Duerden, E. G., Duncan, G. H., & Rainville, P. (2010). Cortical Thickness and Pain Sensitivity in Zen Meditators. Emotion, *10*(1), 43–53. https://doi.org/10.1037/a0018334
- 52. Grieder, M., Crinelli, R. M., Koenig, T., Wahlund, L. O., Dierks, T., & Wirth, M. (2012). Electrophysiological and behavioral correlates of stable automatic semantic retrieval in aging. Neuropsychologia, *50*(1), 160–171. https://doi.org/10.1016/j.neuropsychologia.2011.11.014
- 53. Habermann, M., Weusmann, D., Stein, M., & Koenig, T. (2018). A student's guide to randomization statistics for multichannel event-related potentials using Ragu. Frontiers in Neuroscience, *12*(JUN). https://doi.org/10.3389/fnins.2018.00355
- 54. Hansen, A. L., Johnsen, B. H., & Thayer, J. F. (2003). Vagal influence on working memory and attention. International Journal of Psychophysiology, *48*(3), 263–274. https://doi.org/10.1016/S0167-8760(03)00073-4
- 55. He, F., Billings, S. A., Wei, H. L., & Sarrigiannis, P. G. (2014). A nonlinear causality measure in the frequency domain: Nonlinear partial directed coherence with applications to EEG. Journal of Neuroscience Methods, *225*, 71–80. https://doi.org/10.1016/J.JNEUMETH.2014.01.013
- 56. Jacob, J. E., Chandrasekharan, S., Nair, G. K., Cherian, A., & Iype, T. (2021). Effect of combining features generated through non-linear analysis and wavelet transform of EEG signals for the diagnosis of encephalopathy. Neuroscience Letters, *765*, 136269. https://doi.org/10.1016/J.NEULET.2021.136269
- 57. Jinich-Diamant, A., Garland, E., Baumgartner, J., Gonzalez, N., Riegner, G., Birenbaum, J., Case, L., & Zeidan, F. (2020). Neurophysiological Mechanisms Supporting Mindfulness Meditation–Based Pain Relief: an Updated Review. Current Pain and Headache Reports 2020 *24:10*, *24*(10), 1–10. https://doi.org/10.1007/S11916-020-00890-8
- 58. Joo, H. M., Lee, S. J., Chung, Y. G., & Shin, I. Y. (2010). Effects of Mindfulness Based Stress Reduction Program on Depression, Anxiety and Stress in Patients with Aneurysmal Subarachnoid Hemorrhage. Journal of Korean Neurosurgical Society, 47(5), 345. https://doi.org/10.3340/JKNS.2010.47.5.345
- 59. Judah, M. R., Shurkova, E. Y., Hager, N. M., White, E. J., Taylor, D. L., & Grant, D. M. M. (2018). The relationship between social anxiety and heartbeat evoked potential amplitude. Biological Psychology, *139*, 1–7. https://doi.org/10.1016/J.BIOPSYCH0.2018.09.013

- 60. Kabat-Zinn, J. (n.d.). *Full catastrophe living: using the wisdom of your body and mind to face stress, pain, and illness.*
- 61. Kabat-Zinn, J. (1994). Wherever you go, there you are: mindfulness meditation in everyday life. In *Mindfulness meditation in everyday life* (1st ed.). New York: Hyperion.
- 62. Kakumanu, R. J., Nair, A. K., Venugopal, R., Sasidharan, A., Ghosh, P. K., John, J. P., Mehrotra, S., Panth, R., & Kutty, B. M. (2018). Dissociating meditation proficiency and experience dependent EEG changes during traditional Vipassana meditation practice. Biological Psychology, *135*, 65–75. https://doi.org/10.1016/J.BIOPSYCH0.2018.03.004
- 63. Kamath, M. V, Watanabe, M. A., & Upton, A. R. M. (2013). *Heart rate variability (HRV) signal analysis: clinical applications*. Boca Raton: Taylor & Francis. https://doi.org/10.1201/b12756
- 64. Kardos, Z., Tóth, B., Boha, R., File, B., & Molnár, M. (2014). Age-related changes of frontal-midline theta is predictive of efficient memory maintenance. Neuroscience, *273*, 152–162. https://doi.org/10.1016/J.NEUROSCIENCE.2014.04.071
- 65. Keerthy, B. N., Sreepada, S. S. S., Naik, S. S., Bose, A., Hanumegowda, R., Mehta, U. M., Venkatasubramanian, G., Thirthalli, J., Sathyaprabha, T. N., Udupa, K., Keerthy, B. N., Sreepada, S. S. S., Naik, S. S., Bose, A., Hanumegowda, R., Mehta, U. M., Venkatasubramanian, G., Thirthalli, J., Sathyaprabha, T. N., & Udupa, K. (2021). Effects of a single session of cathodal transcranial direct current stimulation primed intermittent theta-burst stimulation on heart rate variability and cortical excitability measures. Indian Journal of Physiology and Pharmacology, *65*(3), 162–166. https://doi.org/10.25259/IJPP\_339\_2020
- 66. Kirk, U., & Axelsen, J. L. (2020). Heart rate variability is enhanced during mindfulness practice: A randomized controlled trial involving a 10-day online-based mindfulness intervention. PLoS ONE, *15*(12). https://doi.org/10.1371/JOURNAL.PONE.0243488
- 67. Knill, D. C., & Pouget, A. (2004). The Bayesian brain: the role of uncertainty in neural coding and computation. Trends in Neurosciences, *27*(12), 712–719. https://doi.org/10.1016/J.TINS.2004.10.007
- 68. Koenig, T., Kottlow, M., Stein, M., & Melie-García, L. (2011). Ragu: A free tool for the analysis of EEG and MEG event-related scalp field data using global randomization statistics. *Computational Intelligence and Neuroscience*, *2011*. https://doi.org/10.1155/2011/938925
- 69. Koenig, T., & Melie-García, L. (2010). A method to determine the presence of averaged event-related fields using randomization tests. Brain Topography, *23*(3), 233–242. https://doi.org/10.1007/s10548-010-0142-1
- 70. Kosciessa, J. Q., Grandy, T. H., Garrett, D. D., & Werkle-Bergner, M. (2020). Single-trial characterization of neural rhythms: Potential and challenges. NeuroImage, 206, 116331. https://doi.org/10.1016/J.NEUROIMAGE.2019.116331
- 71. Kubota, Y., Sato, W., Toichi, M., Murai, T., Okada, T., Hayashi, A., & Sengoku, A. (2001). Frontal midline theta rhythm is correlated with cardiac autonomic activities during the performance of an attention

demanding meditation procedure. Brain Research. Cognitive Brain Research, *11*(2), 281–287. https://doi.org/10.1016/S0926-6410(00)00086-0

- 72. Kwee, M. (1995). Wherever you go, there you are: Mindfulness meditation in everyday life. In *Behaviour Research and Therapy* (Vol. 33, Issue 8). https://doi.org/10.1016/0005-7967(95)90133-7
- 73. Latremoliere, A., & Woolf, C. J. (2009). Central Sensitization: A Generator of Pain Hypersensitivity by Central Neural Plasticity. In *Journal of Pain* (Vol. 10, Issue 9, pp. 895–926). NIH Public Access. https://doi.org/10.1016/j.jpain.2009.06.012
- 74. Lee, D. J., Kulubya, E., Goldin, P., Goodarzi, A., & Girgis, F. (2018). Review of the neural oscillations underlying meditation. Frontiers in Neuroscience, *12*(MAR), 178. https://doi.org/10.3389/FNINS.2018.00178/BIBTEX
- 75. Li, K., Rüdiger, H., & Ziemssen, T. (2019). Spectral analysis of heart rate variability: Time window matters. Frontiers in Neurology, *10*(MAY), 545. https://doi.org/10.3389/FNEUR.2019.00545/BIBTEX
- 76. Lin, C. T., Nascimben, M., King, J. T., & Wang, Y. K. (2018). Task-related EEG and HRV entropy factors under different real-world fatigue scenarios. Neurocomputing, *311*, 24–31. https://doi.org/10.1016/J.NEUCOM.2018.05.043
- 77. Linton, S. J., & Shaw, W. S. (2011). Impact of psychological factors in the experience of pain. Physical Therapy, *91*(5), 700–711. https://doi.org/10.2522/ptj.20100330
- 78. Lomas, T., Ivtzan, I., & Fu, C. H. Y. (2015). A systematic review of the neurophysiology of mindfulness on EEG oscillations. Neuroscience & Biobehavioral Reviews, 57, 401–410. https://doi.org/10.1016/J.NEUBIOREV.2015.09.018
- 79. Mai, S., Wong, C. K., Georgiou, E., & Pollatos, O. (2018). Interoception is associated with heartbeatevoked brain potentials (HEPs) in adolescents. Biological Psychology, *137*, 24–33. https://doi.org/10.1016/j.biopsycho.2018.06.007
- 80. Manjaly, Z. M., & Iglesias, S. (2020). A Computational Theory of Mindfulness Based Cognitive Therapy from the "Bayesian Brain" Perspective. *Frontiers in Psychiatry*, *11*, NA-NA. https://doi.org/10.3389/fpsyt.2020.00404
- 81. Mankus, A. M., Aldao, A., Kerns, C., Mayville, E. W., & Mennin, D. S. (2013). Mindfulness and heart rate variability in individuals with high and low generalized anxiety symptoms. Behaviour Research and Therapy, *51*(7), 386–391. https://doi.org/10.1016/j.brat.2013.03.005
- 82. Marchand, W. R. (2014). Neural mechanisms of mindfulness and meditation: Evidence from neuroimaging studies. World Journal of Radiology, *6*(7), 471. https://doi.org/10.4329/wjr.v6.i7.471
- Marshall, A. C., Gentsch, A., Schröder, L., & Schütz-Bosbach, S. (2018). Cardiac interoceptive learning is modulated by emotional valence perceived from facial expressions. Social Cognitive and Affective Neuroscience, *13*(7), 677–686. https://doi.org/10.1093/SCAN/NSY042
- Mascaro, J. S., Rilling, J. K., Negi, L. T., & Raison, C. L. (2013). Pre-existing brain function predicts subsequent practice of mindfulness and compassion meditation. NeuroImage, *69*, 35–42. https://doi.org/10.1016/j.neuroimage.2012.12.021

- 85. Matthews, S. C., Paulus, M. P., Simmons, A. N., Nelesen, R. A., & Dimsdale, J. E. (2004). Functional subdivisions within anterior cingulate cortex and their relationship to autonomic nervous system function. NeuroImage, 22(3), 1151–1156. https://doi.org/10.1016/j.neuroimage.2004.03.005
- 86. McLaughlin, K. A., Rith-Najarian, L., Dirks, M. A., & Sheridan, M. A. (2015). Low Vagal Tone Magnifies the Association Between Psychosocial Stress Exposure and Internalizing Psychopathology in Adolescents. Journal of Clinical Child and Adolescent Psychology: The Official Journal for the Society of Clinical Child and Adolescent Psychology, American Psychological Association, Division *53*, *44*(2), 314. https://doi.org/10.1080/15374416.2013.843464
- Mehling, W. E., Chesney, M. A., Metzler, T. J., Goldstein, L. A., Maguen, S., Geronimo, C., Agcaoili, G., Barnes, D. E., Hlavin, J. A., & Neylan, T. C. (2018). A 12-week integrative exercise program improves self-reported mindfulness and interoceptive awareness in war veterans with posttraumatic stress symptoms. Journal of Clinical Psychology, *74*(4), 554–565. https://doi.org/10.1002/JCLP.22549
- 88. Minarini, G. (2020). Root Mean Square of the Successive Differences as Marker of the Parasympathetic System and Difference in the Outcome after ANS Stimulation. Autonomic Nervous System Monitoring - Heart Rate Variability. https://doi.org/10.5772/INTECHOPEN.89827
- Mitchell, D. J., McNaughton, N., Flanagan, D., & Kirk, I. J. (2008). Frontal-midline theta from the perspective of hippocampal "theta." Progress in Neurobiology, *86*(3), 156–185. https://doi.org/10.1016/J.PNEUROBIO.2008.09.005
- 90. Montoya, P., Schandry, R., & Müller, A. (1993). Heartbeat evoked potentials (HEP): topography and influence of cardiac awareness and focus of attention. Electroencephalography and Clinical Neurophysiology/ Evoked Potentials, 88(3), 163–172. https://doi.org/10.1016/0168-5597(93)90001-6
- 91. Nagendra, R., & Sasidharan, A. (2017). *Vipassana Meditation Practices Enhance the Parasympathetic Activity during Sleep: a Case-Control Study of Heart Rate Variability across Sleep Cycles Improving P300-based Deception Detection using Deception Awareness View project Vipassana Meditation Pract*. https://doi.org/10.15406/ijcam.2016.05.00145
- 92. Natwong, B., Sooraksa, P., Pintavirooj, C., Bunluechokchai, S., & Ussawawongaraya, W. (2006). Wavelet entropy analysis of the high resolution ECG. 2006 1st IEEE Conference on Industrial Electronics and Applications. https://doi.org/10.1109/ICIEA.2006.257276
- 93. Olano, H. A., Kachan, D., Tannenbaum, S. L., Mehta, A., Annane, D., & Lee, D. J. (2015). Engagement in Mindfulness Practices by U.S. Adults: Sociodemographic Barriers. Journal of Alternative and Complementary Medicine, 21(2), 100. https://doi.org/10.1089/ACM.2014.0269
- 94. Ongaro, G., & Kaptchuk, T. J. (2019). Symptom perception, placebo effects, and the Bayesian brain. In *Pain* (Vol. 160, Issue 1, pp. 1–4). Lippincott Williams and Wilkins. https://doi.org/10.1097/j.pain.000000000001367
- 95. Oostenveld, R., Fries, P., Maris, E., & Schoffelen, J. M. (2011). FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data. *Computational Intelligence and Neuroscience*, *2011*. https://doi.org/10.1155/2011/156869

- 96. O'Reilly, J. X., Jbabdi, S., & Behrens, T. E. J. (2012). How can a Bayesian approach inform neuroscience? In *European Journal of Neuroscience* (Vol. 35, Issue 7, pp. 1169–1179). John Wiley & Sons, Ltd. https://doi.org/10.1111/j.1460-9568.2012.08010.x
- 97. Park, G., Van Bavel, J. J., Vasey, M. W., & Thayer, J. F. (2012). Cardiac vagal tone predicts inhibited attention to fearful faces. Emotion, *12*(6), 1292–1302. https://doi.org/10.1037/A0028528
- 98. Payne, J. R., Baell, O., Geddes, H., Fitzgibbon, B., Emonson, M., Hill, A. T., Van Dam, N. T., Humble, G., Fitzgerald, P. B., & Bailey, N. W. (2020). Experienced Meditators Exhibit No Differences to Demographically Matched Controls in Theta Phase Synchronization, P200, or P300 During an Auditory Oddball Task. Mindfulness, *11*(3), 643–659. https://doi.org/10.1007/S12671-019-01287-4/TABLES/4
- 99. Penttilä, J., Helminen, A., Jartti, T., Kuusela, T., Huikuri, H. V., Tulppo, M. P., Coffeng, R., & Scheinin, H. (2001). Time domain, geometrical and frequency domain analysis of cardiac vagal outflow: effects of various respiratory patterns. Clinical Physiology, *21*(3), 365–376. https://doi.org/10.1046/J.1365-2281.2001.00337.X
- 100. Perakakis, P. (2019). *HEPLAB: a Matlab graphical interface for the preprocessing of the heartbeatevoked potential*. https://doi.org/10.5281/ZENOD0.2649943
- 101. Pereira, V. H., Cerqueira, J. J., Palha, J. A., & Sousa, N. (2013). Stressed brain, diseased heart: A review on the pathophysiologic mechanisms of neurocardiology. In International Journal of Cardiology (Vol. 166, Issue 1, pp. 30–37). Elsevier. https://doi.org/10.1016/j.ijcard.2012.03.165
- 102. Peressutti, C., Martín-González, J. M., & García-Manso, J. M. (2012). Does mindfulness meditation shift the cardiac autonomic nervous system to a highly orderly operational state? International Journal of Cardiology, 154(2), 210–212. https://doi.org/10.1016/J.IJCARD.2011.10.054
- 103. Perrin, F., Pernier, J., Bertrand, O., & Echallier, J. F. (1989). Spherical splines for scalp potential and current density mapping. Electroencephalography and Clinical Neurophysiology, 72(2), 184–187. https://doi.org/10.1016/0013-4694(89)90180-6
- 104. Petzschner, F. H., Weber, L. A., Wellstein, K. v., Paolini, G., Do, C. T., & Stephan, K. E. (2019). Focus of attention modulates the heartbeat evoked potential. NeuroImage, *186*, 595–606. https://doi.org/10.1016/j.neuroimage.2018.11.037
- 105. Pichot, V., Roche, F., Celle, S., Barthélémy, J. C., & Chouchou, F. (2016). HRV analysis: A free software for analyzing cardiac autonomic activity. *Frontiers in Physiology*, 7(NOV). https://doi.org/10.3389/FPHYS.2016.00557
- 106. Pion-Tonachini, L., Kreutz-Delgado, K., & Makeig, S. (2019). ICLabel: An automated electroencephalographic independent component classifier, dataset, and website. NeuroImage, *198*, 181–197. https://doi.org/10.1016/J.NEUROIMAGE.2019.05.026
- 107. Pollatos, O., & Schandry, R. (2004). Accuracy of heartbeat perception is reflected in the amplitude of the heartbeat-evoked brain potential. Psychophysiology, 41(3), 476–482. https://doi.org/10.1111/1469-8986.2004.00170.X

- 108. Puga, J. L., Krzywinski, M., & Altman, N. (2015). Bayes' theorem. Nature Methods, *12*(4), 277–278. https://doi.org/10.1038/nmeth.3335
- 109. Quian Quiroga, R., Rosso, O. A., Başar, E., & Schürmann, M. (2001). Wavelet entropy in event-related potentials: A new method shows ordering of EEG oscillations. Biological Cybernetics, 84(4), 291– 299. https://doi.org/10.1007/s004220000212
- 110. Raj, S., Kailash, , Ray, C., & Shankar, O. (2018). Development of robust, fast and efficient QRS complex detector: a methodological review. Australasian Physical & Engineering Sciences in Medicine, 41, 581–600. https://doi.org/10.1007/s13246-018-0670-7
- 111. Ring, C., & Brener, J. (2018). Heartbeat counting is unrelated to heartbeat detection: A comparison of methods to quantify interoception. Psychophysiology, 55(9), e13084. https://doi.org/10.1111/PSYP.13084
- 112. Ring, C., Brener, J., Knapp, K., & Mailloux, J. (2015). Effects of heartbeat feedback on beliefs about heart rate and heartbeat counting: a cautionary tale about interoceptive awareness. Biological Psychology, *104*, 193–198. https://doi.org/10.1016/J.BIOPSYCHO.2014.12.010
- 113. Ródenas, J., García, M., Alcaraz, R., & Rieta, J. J. (2015). Wavelet entropy automatically detects episodes of atrial fibrillation from single-lead electrocardiograms. Entropy, *17*(9), 6179–6199. https://doi.org/10.3390/E17096179
- 114. Rosso, O. A., Blanco, S., Yordanova, J., Kolev, V., Figliola, A., Schürmann, M., & Ba ar, E. (2001). Wavelet entropy: A new tool for analysis of short duration brain electrical signals. *Journal of Neuroscience Methods*, *105*(1), 65–75. https://doi.org/10.1016/S0165-0270(00)00356-3
- 115. Rosso, O. A., Martin, M. T., Figliola, A., Keller, K., & Plastino, A. (2006). EEG analysis using waveletbased information tools. Journal of Neuroscience Methods, *153*(2), 163–182. https://doi.org/10.1016/j.jneumeth.2005.10.009
- 116. Samuels, M. A. (2007). The brain-heart connection. Circulation, *116*(1), 77–84. https://doi.org/10.1161/CIRCULATIONAHA.106.678995
- 117. Schmid, R. F., & Thomas, J. (2021). The interactive effects of heart rate variability and mindfulness on indicators of well-being in healthcare professionals' daily working life. International Journal of Psychophysiology, *164*, 130–138. https://doi.org/10.1016/J.IJPSYCHO.2021.01.012
- Schulz, A., Ferreira de Sá, D. S., Dierolf, A. M., Lutz, A., van Dyck, Z., Vögele, C., & Schächinger, H. (2015). Short-term food deprivation increases amplitudes of heartbeat-evoked potentials. Psychophysiology, *52*(5), 695–703. https://doi.org/10.1111/PSYP.12388
- 119. Shaffer, F., & Ginsberg, J. P. (2017). An Overview of Heart Rate Variability Metrics and Norms. Frontiers in Public Health, *5*, 258. https://doi.org/10.3389/FPUBH.2017.00258
- 120. Shaffer, F., McCraty, R., & Zerr, C. L. (2014). A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability. *Frontiers in Psychology*, *5*. https://doi.org/10.3389/FPSYG.2014.01040
- 121. Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., & Dunbar, G. C. (1998). The Mini-International Neuropsychiatric Interview (M.I.N.I.): The development

and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. Journal of Clinical Psychiatry, *59*(SUPPL. 20), 22–33.

- 122. Short, E. B., Kose, S., Mu, Q., Borckardt, J., Newberg, A., George, M. S., & Kozel, F. A. (2010). Regional brain activation during meditation shows time and practice effects: An exploratory FMRI study. Evidence-Based Complementary and Alternative Medicine, 7(1), 121–127. https://doi.org/10.1093/ECAM/NEM163
- 123. Sik, H. H., Gao, J., Fan, J., Wu, B. W. Y., Leung, H. K., & Hung, Y. S. (2017). Using Wavelet Entropy to Demonstrate how Mindfulness Practice Increases Coordination between Irregular Cerebral and Cardiac Activities. Journal of Visualized Experiments: JoVE, 2017(123). https://doi.org/10.3791/55455
- 124. Silvani, A., Calandra-Buonaura, G., Dampney, R. A. L., & Cortelli, P. (2016). Brainheart interactions: physiology and clinical implications. *Philosophical Transactions of the Royal Society A: Mathematical, Physical and Engineering Sciences*, *374*(2067). https://doi.org/10.1098/RSTA.2015.0181
- 125. Sinha, M., Sinha, R., Ghate, J., & Sarnik, G. (2020). Impact of Altered Breathing Patterns on Interaction of EEG and Heart Rate Variability. Original Article Annals of Neurosciences, 27(2), 67–74. https://doi.org/10.1177/0972753120950075
- 126. Smith, M. (2017). Intuitionistc probability and the Bayesian objection to dogmatism. Synthese, *194*(10), 3997–4009. https://doi.org/10.1007/S11229-016-1120-2
- 127. Somers, B., & Bertrand, A. (2016). Removal of eye blink artifacts in wireless EEG sensor networks using reduced-bandwidth canonical correlation analysis. Journal of Neural Engineering, *13*(6), 066008. https://doi.org/10.1088/1741-2560/13/6/066008
- 128. Somers, B., Francart, T., & Bertrand, A. (2018). A generic EEG artifact removal algorithm based on the multi-channel Wiener filter. Journal of Neural Engineering, *15*(3), 036007. https://doi.org/10.1088/1741-2552/AAAC92
- 129. Steinhubl, S. R., Wineinger, N. E., Patel, S., Boeldt, D. L., Mackellar, G., Porter, V., Redmond, J. T., Muse, E. D., Nicholson, L., Chopra, D., & Topol, E. J. (2015). Cardiovascular and nervous system changes during meditation. Frontiers in Human Neuroscience, *9*(MAR), 145. https://doi.org/10.3389/FNHUM.2015.00145/BIBTEX
- 130. Subha, D. P., Joseph, P. K., Acharya U, R., & Lim, C. M. (2010). EEG signal analysis: a survey. Journal of Medical Systems, *34*(2), 195–212. https://doi.org/10.1007/S10916-008-9231-Z
- 131. Tang, Y. Y., Ma, Y., Fan, Y., Feng, H., Wang, J., Feng, S., Lu, Q., Hu, B., Lin, Y., Li, J., Zhang, Y., Wang, Y., Zhou, L., & Fan, M. (2009). Central and autonomic nervous system interaction is altered by short-term meditation. Proceedings of the National Academy of Sciences of the United States of America, 106(22), 8865–8870. https://doi.org/10.1073/pnas.0904031106
- 132. Tang, Y. Y., Tang, R., & Posner, M. I. (2016). Mindfulness meditation improves emotion regulation and reduces drug abuse. Drug and Alcohol Dependence, *163*, S13–S18. https://doi.org/10.1016/J.DRUGALCDEP.2015.11.041

- 133. Thomas, B. L., Claassen, N., Becker, P., & Viljoen, M. (2019). Validity of Commonly Used Heart Rate Variability Markers of Autonomic Nervous System Function. Neuropsychobiology, 78(1), 14–26. https://doi.org/10.1159/000495519
- 134. Tracy, L. M., Ioannou, L., Baker, K. S., Gibson, S. J., Georgiou-Karistianis, N., & Giummarra, M. J. (2016). Meta-analytic evidence for decreased heart rate variability in chronic pain implicating parasympathetic nervous system dysregulation. Pain, *157*(1), 7–29. https://doi.org/10.1097/J.PAIN.00000000000360
- 135. Umetani, K., Singer, D. H., McCraty, R., & Atkinson, M. (1998). Twenty-Four Hour Time Domain Heart Rate Variability and Heart Rate: Relations to Age and Gender Over Nine Decades. Journal of the American College of Cardiology, 31(3), 593–601. https://doi.org/10.1016/S0735-1097(97)00554-8
- 136. Vlaeyen, J. W. S., & Linton, S. J. (2000). Fear-avoidance and its consequences in chronic musculoskeletal pain: A state of the art. In *Pain* (Vol. 85, Issue 3, pp. 317–332). https://doi.org/10.1016/S0304-3959(99)00242-0
- 137. Voss, A., Heitmann, A., Schroeder, R., Peters, A., & Perz, S. (2012). Short-term heart rate variability age dependence in healthy subjects. Physiological Measurement, *33*(8), 1289. https://doi.org/10.1088/0967-3334/33/8/1289
- 138. Vyšata, O., Schätz, M., Kopal, J., Burian, J., Procházka, A., Jiří, K., Hort, J., Vali&scaron, M., Vyšata, O., Schätz, M., Kopal, J., Burian, J., Procházka, A., Jiří, K., Hort, J., & Vali&scaron, M. (2014). Non-Linear EEG Measures in Meditation. *Journal of Biomedical Science and Engineering*, 7(9), 731–738. https://doi.org/10.4236/JBISE.2014.79072
- 139. Wang, F., Lin, J., Wang, W., & Wang, H. (2015). EEG-based mental fatigue assessment during driving by using sample entropy and rhythm energy. 2015 IEEE International Conference on Cyber Technology in Automation, Control and Intelligent Systems, IEEE-CYBER 2015, 1906–1911. https://doi.org/10.1109/CYBER.2015.7288238
- 140. Wang, M. Y., Bailey, N. W., Payne, J. E., Fitzgerald, P. B., & Fitzgibbon, B. M. (2021). A Systematic Review of Pain-Related Neural Processes in Expert and Novice Meditator. In *Mindfulness* (Vol. 12, Issue 4, pp. 799–814). Springer. https://doi.org/10.1007/s12671-020-01558-5
- 141. Wang, M. Y., Freedman, G., Raj, K., Fitzgibbon, B. M., Sullivan, C., Tan, W. L., Van Dam, N., Fitzgerald, P. B., & Bailey, N. W. (2020). Mindfulness meditation alters neural activity underpinning working memory during tactile distraction. Cognitive, Affective and Behavioral Neuroscience, 20(6), 1216–1233. https://doi.org/10.3758/S13415-020-00828-Y/FIGURES/9
- 142. Wheeler, M. S., Arnkoff, D. B., & Glass, C. R. (2017). The Neuroscience of Mindfulness: How Mindfulness Alters the Brain and Facilitates Emotion Regulation. Mindfulness 2017 8:6, 8(6), 1471– 1487. https://doi.org/10.1007/S12671-017-0742-X
- 143. Wu, S.-D., & Lo, P.-C. (2008). Inward-attention meditation increases parasympathetic activity: a study based on heart rate variability. Biomedical Research, 29(5), 245–250. https://doi.org/10.2220/BIOMEDRES.29.245

- 144. Zamariola, G., Maurage, P., Luminet, O., & Corneille, O. (2018). Interoceptive accuracy scores from the heartbeat counting task are problematic: Evidence from simple bivariate correlations. Biological Psychology, *137*, 12–17. https://doi.org/10.1016/J.BIOPSYCHO.2018.06.006
- 145. Zsadanyi, S. E., Kurth, F., & Luders, E. (2021). The Effects of Mindfulness and Meditation on the Cingulate Cortex in the Healthy Human Brain: A Review. Mindfulness 2021 *12:10*, *12*(10), 2371– 2387. https://doi.org/10.1007/S12671-021-01712-7

#### **Figures**



#### Figure 1

a – TANOVA using L2 normalisation p-graph showing the significant main effect of group and *p*-values across the duration of the epoch (global count statistics across the whole epoch p = .01, FDR p = .04). Green bars reflect periods that exceeded the duration control for multiple comparisons across time (33ms). This period was a longer duration of significance than 95% of the 5000 randomizations. b – TANOVA with L2-normalisation topographic maps for each group and a t- map for meditators topography minus control topography during the 200 to 294ms time window (averaged across the significant period, p = .001, partial  $\eta^2 = .06$ )



#### Figure 2

a - Main effect of group in GFP test across the duration of the epoch (no significant periods lasted longer than the duration control of 43ms). b - Group effects by conditions (EC and EO) interaction in GFP test across the duration of the epoch. No significant main effect of Group, nor interaction for Group x Condition in GFP were present



#### Figure 3

Mean RRI entropy by group. Error bars represent standard error. \*p < .05

#### **Supplementary Files**

This is a list of supplementary files associated with this preprint. Click to download.

• SUPPWangM2023BrainHeartCouplingMed.docx