Heliyon

Commercial mindfulness aid does not aid short-term stress reduction compared to unassisted relaxation

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Abstract

Increased public interest in mindfulness has generated a burgeoning market in new consumer technologies. Two exploratory studies examined effects of InteraXon's "Muse" electroencephalography (EEG)-based neurofeedback device and mobile application on mindfulness-based relaxation activities. Psychophysiological outcomes (heart rate variability (HRV), electro-dermal activity (EDA), saliva amylase activity (sAA) and Muse application EEG "calm percent") were collected for two 7-minute conditions: Muse-assisted relaxation exercise (MARE), and unassisted relaxation exercise (URE). In the first study, participants (n = 99) performed both conditions in a randomized sequential design. A follow-up study used a randomized parallel condition (n = 44) to test for differences in HRV effects between the two conditions and extended follow-up observation. Generalized estimating equation models demonstrated a moderate increase in HRV following relaxation exercises, with no observable difference between MARE and URE conditions. Both MARE and URE conditions produced equally effective short-term increases in heart rate variability, without additional benefit from neurofeedback.

1. Introduction

"Stress" refers to the subjective experience of sympathetic nervous system activation in response to adverse stimuli. Situations that are novel, unpredictable, or appear to be outside the subject's control elicit this "fight, flight, or freeze" response. Repeated or prolonged activation of the stress response has been associated with numerous harmful effects (Brosschot et al., 2005; Salleh, 2008), including cardiovascular and immune dysfunction, psychiatric disorders, and suicide risk. According to the American Psychological Association's 2017 Stress in America™ survey results (n = 3,440 adults), nearly half of Americans reported sleeplessness due to stress (45%), one-third of adults reported experiencing feeling nervous or anxious (36%), irritability or anger (35%), and fatigue (34%) due to their stress (APA, 2017). Stress-related illness and injury are estimated to cost the United States more than $300 billion per year, including costs related to stress-related accidents, absenteeism, employee turnover, diminished productivity, and direct medical, legal, and insurance costs (American Institute of Stress, 2013).

Physiologically, stress activates the body's autonomic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis in the brain by releasing adrenaline, corticotropin-releasing hormone, and cortisol. The degree of activation depends on the severity of the stressor, but also the individual's genetic background and life experiences. As individuals experience more symptoms of stress, they employ various stress-management methods. For example, more than half of Americans (53%) exercise or take part in physical activity to cope with stress, a significant increase in 2017 compared to each of the past three years (APA, 2017). The use of yoga and meditation is rising, with 12 percent of people using these activities to manage their stress, the highest percentage since the survey first asked about these activities in 2008 (APA, 2017).

Mindfulness is an umbrella term that describes many self-awareness practices, including some forms of meditation and yoga. While the term has its historical footing in Buddhism (Bodhi, 2011), it has achieved popularity in psychology, psychiatry, medicine, neuroscience, and education through its central role in mindfulness-based stress reduction (MBSR)—a structured training program from the University of Massachusetts Medical School researchers (Kabat-Zinn, 2003, 2011) The eight-week workshops incorporate weekly group instruction, daily individual practice, and a single day-long intensive to provide instruction in three formal techniques: mindfulness meditation, body scanning and simple yoga postures.

A robust meta-analysis of meditation programs for psychological stress and well-being examined 47 randomized control trials with active controls for placebo effects

and a total of 3,515 participants (Goyal et al., 2014). Meditation programs had moderate evidence of reduced anxiety (d = 0.38), depression (d = 0.30), and pain (d = 0.33) at 8 weeks, resulting in moderate reductions of multiple negative dimensions of psychological stress. A recent literature review did not find correlations between mindfulness program length and effect size for psychological outcomes, concluding that shorter programs using 1.5 h of instruction over 7 weeks may also be effective for reducing distress (Carmody and Baer, 2009). A recent study suggests that daily 10-minute online MBSR interventions over two weeks may offer benefits for non-clinical groups seeking stress-reduction strategies (Cavanagh et al., 2013). Regarding dose-response relationship between mindfulness practice and outcomes, post hoc analyses of practice time or attendance and symptoms or self-reported measures yield inconsistent results, with some studies showing a dose-dependency (Carmody and Baer, 2008; Collard et al., 2008; Farb et al., 2013; Rosenzweig et al., 2010; Shapiro et al., 2012), but other not (Carlson et al., 2004; Dobkin and Zhao, 2011; Hopkins and Proeve, 2013; MacCoon et al., 2012). The actual length of the intervention might not matter as much as attendance and the quality of the practice (DeVibe et al., 2012; Del Re et al., 2013). Several MBSR programs have implemented online and mobile applications for treatment delivery to extend the reach of mindfulness training, demonstrating improvements in psychological parameters with medium effect sizes (Cavanagh et al., 2013; Glück and Maercker, 2011). The effects of technology-supported mindfulness programs have been explored further in human-computer interaction research. Recognizing that novices often have trouble maintaining focus during a mindfulness session, Pisa et al. (2017) found the act of audibly amplifying a person's sound of breathing during meditation can help them regain and maintain focus on their breathing, leading to a more effective mindfulness session. A novel interactive biofeedback mobile application (Pause™, ustwo studio Ltd., London, England) was used by Ahmed et al. (2017) to explore the effects of three modalities - audio, vision, touch - and their combinations on perceived stress and the physiological indicator of relaxation measured by delta heart rate. The Touch condition required participants to slowly draw circular movements on the touch screen. In the Vision condition participants were asked to focus on the dynamic changing shape of the floating bubbles. The Audio condition had the participants listen to the audio of instrumental music with nature sounds and close their eyes whenever they felt like it. Each participant performed all conditions in a randomized crossover design and all measures in this study provided convergent results, though the study lacked a control condition. Participants performed best in the Audio condition and when Vision and Touch conditions were combined with Audio, participant performance in those conditions improved, suggesting that Audio is a significant contributor to overall relaxation. Conversely, Ahmed and associates (2017) found that when Audio was combined with other senses, the positive effect was less pronounced than when Audio was used on its own.

The studies on mindfulness effects reviewed above have employed both subjective and objective measures of stress and relaxation. Due to the known relationship between stress and the body, there is interest in exploring more objective metrics regarding how the body's stress response functions in response to intervention. Studies show consistent physiological responses across multiple methods when attention tasks involve controlled breathing (Krygier et al., 2013; Lehrer et al., 1999; Tang et al., 2015). Parasympathetic vagal nerve control maintains heart rhythm in pace with breathing, also known as respiratory sinus arrhythmia (RSA; Porges, 2007). During mindful breathing practices, RSA predominates over sympathetic control of heart rhythm, and participants demonstrate a consistent interval between heartbeats (inter-beat-interval, IBI), which corresponds with a significant decrease in heart rate variability (HRV), with significantly greater decrease observed in experienced practitioners (Krygier et al., 2013; Peressutti et al., 2010). Post-intervention HRV is increased, which is associated with lower sympathetic activity and positive health outcomes (Kristal-Boneh et al., 1995), this change is also more pronounced with practice. Mindfulness states are associated with enhanced EEG alpha (8−12 Hz) and theta (4−8 Hz) power, compared to resting state (Takahashi et al., 2005). Generalizability and interpretation distinct EEG features, such as blocking or further decomposition into fast and slow components, is complicated by differing methodologies in spectral analysis and variety of meditation styles examined (Ivanovski and Malhi, 2007). Acute stressors are known to increase perspiration and skin conductance (electrodermal activity, EDA). Several studies show reduction in EDA during mindfulness tasks, lower baseline EDA following MBSR training, and lower EDA responsiveness to aversive stimuli (Delmonte, 1985; Grecucci et al., 2015; Lush et al., 2009). Acute stressors increase salivary activity of digestive enzyme α-amylase (sAA; Kirschbaum et al., 1993), which is regulated by sympathetic and parasympathetic innervation of its secretory glands, though no studies of the sAA biomarker following a "stress reducing" condition have been published.

Increased public interest in the beneficial effects of mindfulness practices has created an emerging market in mindfulness aids. These include mobile applications for instruction and managing practice, or electronic devices providing cues to increased stress or mindfulness practice enhancement using psychophysiological measurements associated with mindfulness practice and the stress response, such as respiration, heart rate variability (HRV), electrodermal activity (EDA), or electroencephalography (EEG). Such devices include the "Spire" (Spire Inc., San Francisco, California), which continuously monitors movement associated with respiration to cue the user and prompt awareness of increased stress, and products enabling cues from HRV sensors on the wrist, such as the Apple Watch (Apple Inc., Cupertino, California). Biofeedback methodologies using electromyography, electroencephalography, or cardiac measures have demonstrated efficacy in management of anxiety, attention deficit, and multiple psychosomatic conditions (Wenck, et al., 1996; Kaiser and Othmer,

2000; McKee, 2008). Potential applications of these methodologies in stress management has been examined for decades (Brown, 1977).

The "Muse" is a consumer device and mobile application (InteraXon Inc., Toronto, Canada) that aims to enhance mindfulness meditation practice, combining instruction and tracking with EEG sensor biofeedback (or neurofeedback) during mindfulness relaxation exercise. The device has been validated in a study of EEG event-related potentials (ERP), compared with research-grade EEG hardware (Krigolson et al., 2017). Participants performed multiple trials of standard oddball and reward-learning tasks, with reward positivity, N200, and P300 ERP components recorded using either the Muse device or ActiChamp 10−20 EEG system (Brain Products GmbH, Gilching, Germany). EEG system data were reduced to match the Fpz, AF7, AF8, TP9, and TP10 channels available with the Muse device. ERP components were observed and quantifiable with both the Muse and reduced ActiChamp EEG systems, with equivalent mean peak amplitudes. Controlled studies of EEG-neurofeedback demonstrate enhanced performance in varied psychometric tests, including sustained attention, executive function, memory, psychomotor skills, and well-being. In the following studies, we evaluated the neurophysiological concomitants and proprietary brain activity measure of the "Muse" mindfulness device and relaxation exercise instruction. Considering the documented performance enhancement in diverse cognitive tasks using biofeedback methodologies, we hypothesized that the auditory EEG neurofeedback during a Muse assisted relaxation exercise (MARE) would result in greater changes of physiological measures of relaxation and stress compared to an unassisted relaxation exercise (URE). Specifically, this study sought to test the following research hypotheses:

Hypothesis 1: The MARE condition will result in greater changes in short-term HRV, EDA, and sAA activity than the URE condition.

Hypothesis 2: The MARE condition will result in greater percentage of time spent in the "Calm" mode, Muse's EEG-derived measure of relaxation, than the URE condition.

We also sought to answer the following exploratory research questions: Is the subjective perception of Muse audio feedback as distracting or irritating associated with HRV and EDA changes during the MARE condition?

2. Method

2.1. Participants

Both studies were approved by the University of Florida Institutional Review Board, and participants were recruited through an undergraduate research study

participation program and word of mouth. All participants completed the informed consent process prior to participation. Eligible participants were between 18 and 72 years old. In Study 1, interim power analysis of Baseline and Endpoint HRV (95% CI for difference = [0.03, 0.21], n = 40, d = 0.37) indicated 97 participants would need to be enrolled for sufficient power (1 - β < 0.20), therefore 99 participants were enrolled, and 96 completed both conditions. Study 2 enrolled 46 participants to further evaluate HRV, 23 and 21 participants completed MARE and URE with follow-up observation.

2.2. Procedure

2.2.1. Study 1: Randomized sequential study

The randomized sequential condition study was designed to evaluate the effects of MARE and URE relaxation conditions on HRV and EDA during relaxation, saliva samples following each condition, and Muse application "Calm %" metric during the relaxation. It also evaluated changes in HRV and EDA following both conditions and effect of condition order (see Fig. 1 for further detail). MARE or URE were administered in a counterbalanced order. In both conditions, participants engaged in a 1-min mental word association exercise to calibrate the Muse brain activity sensor prior to relaxation. The application provides a randomly chosen category every 20 s, such as "tools", "actors", or "fruit", and instructs the participant to think of as many examples in that category as possible. The application then provides auditory instructions for the relaxation condition. After both conditions were complete, follow-up HRV was recorded for 7 min while participants completed a post-questionnaire on their perceptions of the relaxation experience.

2.2.2. Study 2: Randomized parallel study

The randomized parallel study compared the effect of a single MARE or URE on post-intervention HRV over three observation periods following the intervention. In either condition, participants calibrate the Muse brain activity sensor using the same word association task as in the first study, followed by auditory instructions for the relaxation condition (MARE or URE). Participants then engaged in the relaxation exercise for 7 min. HRV was subsequently collected for three additional 7-minute intervals (see Fig. 2).

2.3. Experimental conditions

2.3.1. Muse assisted relaxation exercise (MARE)

Prior to the MARE condition, the Muse application orally explained the audio neurofeedback mechanism to participants: as more focused and relaxed brain states are
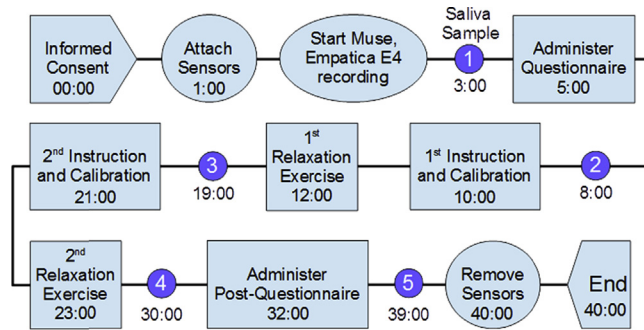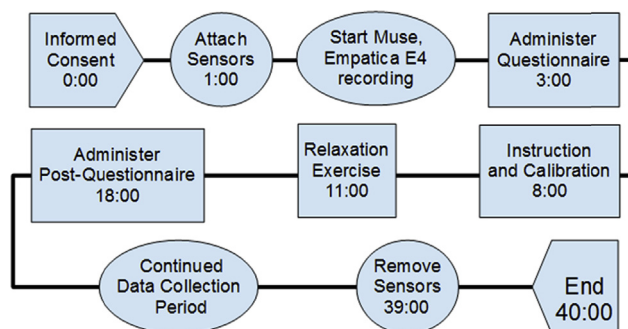
Fig. 1. Initial study procedure flowchart.

identified by the device, the application provided more pleasant peaceful natural sounds, such as wind, water, trees, and birds; conversely, as users drift out of mindful states, turbulent and more intense sounds of wind give a clue to return their attention to their breathing. The mindful breathing instruction tells participants to focus attention on sensations caused by movements of the breath in the body over the course of the relaxation exercise and to re-assert the focus as they identify changes in the audio feedback. The basic instruction is consistent with traditional breath-focused mindfulness practices. During MARE, the Muse application uses a pair of headphones to provide audio neurofeedback to participants based on registered brain activity. The user then received neurofeedback through auditory cues derived from EEG activity analyzed based on proprietary algorithms while completing the mindfulness relaxation exercise. After the 7-minute MARE, the Muse device provided information regarding what percentage of time had been spent in a "calm" state as well as a graph depicting brain activity over time, with brain activity classified as "calm," "neutral," or "active."

2.3.2. Unassisted relaxation exercise (URE)

Prior to beginning the URE condition, each participant listened to the Muse application instructions as in the MARE condition but was then instructed by the study

Fig. 2. Follow-up study procedure flowchart.

facilitator to close their eyes and "relax using whatever method you find comfortable or intuitive". Instead of audio neurofeedback from the Muse application, participants listened to sham sound, a continuous recording of audio from the Muse application when registering maximally "calm" state. The Muse application registered brain activity for the "Calm %" metric.

2.3.3. Muse "Calm" mode percentage

The Muse device uses proprietary algorithms to register and analyze brain activity sensor data. The application then calculates the amount of time spent in the "calm" state. The Muse manufacturer provides a software developer kit and documentation, detailing hardware and streaming data specifications for the unmodified consumer Muse 2014 device and version 7.8.0 firmware used in this study (InteraXon, Inc. 2018). Activity is registered in four 240hz channels using static, dry electrodes on a flexible "headband" device. Two silver electrodes correspond to AF7 and AF8 frontal lobe positions, two conductive silicone-rubber electrodes are placed at TP9 and TP10 temporoparietal lobe positions, and a Fpz reference electrode is located between AF7/AF8 electrodes at the prefrontal cortex midline. Additionally, a three-axis accelerometer registers the users head movements. InteraXon provides access and documentation to a software developer kit which allows streaming and saving data from the Muse device, including multiple real time measures. Continuous accelerometer, real time voltage, raw fast Fourier transform, absolute power, and spectrum power relative to total power is provided for Delta (1−4Hz), Theta (4−8Hz), Alpha (7.5−13Hz), Beta (13−30Hz), and Gamma (30−44Hz) EEG frequency spectrums in each channel. Other scale measures include electrode contact quality, connection quality, blinking, and jaw clench. Experimental Boolean state measures "Concentration" and "Mellow" are sampled at 10Hz based on ratio of Gamma and Alpha powers, with additional proprietary processing. Session "Calm" percentage value is only available through the mobile Muse application and specific information regarding its processing is not provided. In the researchers' experience, a combination of the above measures is used. Head, eye, and jaw movements during relaxation exercise reliably result in lower Calm % values. Intentionally interfering with the word-association calibration step before relaxation exercise appears to shift baseline upper/lower thresholds for activity and reliably affect the subsequent session Calm %: not performing word association and calibrating during a resting, meditative state decreases session Calm %, while an effortful disordered state results in higher Calm %.

2.3.4. Electro-dermal activity and heart rate variability (Empatica E4)

The Empatica E4 (Empatica Inc., Cambridge, Massachusetts) is a photoplethysmography (PPG) biosensor device placed around the participant's wrist on the non-

dominant hand, providing similar data quality to portable clinical ECG devices (McCarthy et al., 2016). By measuring absorption of emitted light, it calculates heart rate, inter-beat-interval (IBI), and skin temperature, used as indices of the body's physiological stress and relaxation response. Time domain heart rate variability (HRV) in the 7-minute observation intervals was calculated using the root mean square of the successive differences (RMSSD) of IBI. The RMSSD HRV measure captures high-frequency activity, of which parasympathetic vagal nerve activity is a primary component (Electrophysiology TF, 1996). The E4 uses proprietary algorithms to filter PPG data artifacts and report only valid IBIs, observation intervals containing >120 valid IBIs were used for analysis (90.6% in Study 1, 99.1% in Study 2).

The E4 also measures electrodermal activity (EDA) using impedance from two dry electrodes on the wrist. For 40 participants in the sequential study and all 44 participants analyzed in the parallel study, the EDA sensor was modified by attaching external leads and adhesive paste electrodes on the middle and ring fingers of their non-dominant hand, which provided the greater dynamic range necessary for analysis. EDA is recorded as mean impedance in microSiemens for each 7-minute time domain interval used in HRV. Positively skewed HRV and EDA data were normality transformed using the natural log of HRV and square root of EDA prior to analysis.

2.3.5. Salivary α-amylase bio-assay

For collection of saliva samples in the repeated interventions study, the participant is asked to chew and dispense a small disposable swab at 5 time points, approximately 10 min apart for conditioned samples (see Fig. 1). These sampling intervals are consistent with Trier Social Stress Test protocols showing significant changes following psychosocial stressors (Kirschbaum et al., 1993). Samples were analyzed using an *in vitro* enzymatic activity assay of α-amylase (sAA), a physiological indicator of heightened psycho-social stress. Laboratory assay with 2mM CNP-G3 substrate was assembled using commercial components, comparable to standard protocol (Winn-Deen et al., 1988), and validated using commercial assay kit and standards (r = 1.00, p < 0.001; RE80111, IBL International GmbH). A requirement of the assay is that participants not eat or drink anything for 30 min prior to the study, individual samples with undiluted sAA concentration <1U/mL were treated as missed samples and excluded from analysis, with no imputation. Positively skewed sAA data was natural log transformed to normality prior to analysis.

2.3.6. Perceived Stress Scale

Participants completed the Perceived Stress Scale (PSS-10, Cohen et al., 1983), a 10-item self-report questionnaire that quantifies a participant's subjective stress

experience. It is comprised of a Perceived Helplessness (PH) factor with six items, such as "In the last month, how often have you been angered because of things that were outside of your control?", and a Perceived Self-Efficacy (PSE) factor with four items, such as "In the last month, how often have you been able to control irritations in your life?". Responses are graded on a Likert-type scale ranging from 0 (never) to 4 (very often). PSE responses are reverse-coded and added to PH to produce the PSS-10 score. Internal consistency of the measure reached $\alpha = .86$ in the current study.

2.3.7. Post-questionnaire

Participants also completed a post-questionnaire at the end of the studies. Two free-response questions asked for participants' prior experience with mindfulness or stress-reduction practice and a description of the relaxation method they implemented during the URE condition. It also included eight Likert Scale questions with five options: "Strongly Agree", "Agree", Neither Agree nor Disagree", "Disagree", and "Strongly Disagree". Four Likert Scale items assessed participants' perception of relaxation state and effort during MARE and/or URE, such as "I felt calm or relaxed during the unassisted exercise" and "I found the Muse audio feedback distracting or irritating." An additional four items assessed their interest in MBSR and mindfulness research, such as "I am interested in the subject of mindfulness, meditation, or stress reduction" and "I would consider using the Muse application outside of the study". These responses allowed us to evaluate the participants' results based on experience with meditation or other relaxation techniques, self-report of effort and relaxation, and interest in the study topic.

2.4. Data analysis

E4 session data was imported and processed to mean impedance EDA and RMSSD HRV for individually variable 7-minute observation intervals using the Python Pandas data analysis library. Prior to analysis, HRV, sAA, and EDA data were transformed to achieve normality using natural logarithm transformation for HRV and sAA, square root transformation for EDA.

Statistical analysis was performed using IBM SPSS 23.0 software and the R 'gee' package v4.19. Generalized Estimating Equations (GEE) were used for HRV, sAA, EDA, and Calm % (in the initial study) to determine main and interaction effects of observation interval, questionnaire responses, intervention order (in the sequential interventions study), and relaxation condition. Bonferroni corrected post-hoc multiple comparisons and Independent-Samples Kruskal-Wallis tests were used when significant effects were observed.

To compare Calm % measures in the parallel study, Independent-Samples Mann-Whitney U and Independent-Samples Kruskal-Wallis tests were used. Kolmogorov-Smirnov test was used to compare distributions of Likert Scale responses. Pearson Product-Moment and Spearman Rank-Order correlations were used to evaluate correlations between measures collected in each study.

Neither of the experiments reported in this article was formally preregistered. Neither the data nor the materials have been made available on a permanent third-party archive; requests for the data or materials can be sent via email to the corresponding author at rbussing@ufl.edu.

3. Results

3.1. Study 1: Randomized sequential condition study

3.1.1. HRV analysis

In this study, HRV was modeled as a response variable using GEE with AR(1) correlation structure, normal distribution, and identity link function (Table 1). Significant effect of interval on HRV was found, $X^2(3, N = 362) = 70.16$, $p < 0.001$, with no significant effect of condition order or significant interaction effect (Table 2).

Corrected multiple comparisons of intervals showed a significant decrease in HRV in Exercise #1 vs Baseline, $p = 0.001$, $d = 0.26$, followed by a significant increase in the Endpoint interval, $p < 0.001$, $d = 0.53$ (Table 3). These results indicate a beneficial increase in HRV following both relaxation conditions, regardless of order of MARE and URE conditions.

3.1.2. EDA analysis

EDA was modeled as a response variable using GEE with AR (1) correlation structure, normal distribution, and identity link function. Significant effect of interval on EDA was found, $X^2(3, N = 139) = 95.81$, $p < 0.001$, with no significant effect of condition order or significant interaction effect (Table 4).

Table 1. Estimated marginal means of HRV for Study 1 by observation Interval.

Interval	Mean	Std. Error	95% Wald Confidence Interval	
			Lower Bound	**Upper Bound**
Baseline	4.0581	.03642	3.9868	4.1295
Exercise #1	3.9679	.03575	3.8978	4.0379
Exercise #2	4.0486	.03879	3.9725	4.1246
Endpoint	4.2372	.03742	4.1639	4.3106

Table 2. GEE model effects of Interval and Condition Order on HRV in Study 1.

Source	Type		
	df	Wald Chi-Square	Sig.
(Intercept)	1	16582.608	.000***
Interval	3	70.161	.000***
Condition Order	1	2.821	.093
Interval * Condition Order	3	1.138	.768

Note: ***$p < .001$.

Corrected multiple comparisons of intervals showed a significant decrease in EDA in the first relaxation condition vs baseline, $p = 0.01$, $d = 0.10$, followed by a significant increase in EDA in the final interval, $p < 0.001$, $d = 0.26$ (Table 5). These results indicate a significant reduction in EDA initially when beginning the relaxation conditions, with an increase once both have been completed, with no effect of intervention order.

3.1.3. Percentage of time in muse "Calm" mode

In the Randomized Sequential Condition study, Calm % was modeled using GEE with exchangeable correlation structure, Gamma distribution, and Log link. Condition interval was used as a within-subject variable and condition order (MARE first or URE first) as a factor. Significant effect of condition interval on Calm % was found, $X^2(1, N = 186) = 5.61$, $p = 0.02$, with no significant effect of condition order (Table 6).

Table 3. Pairwise comparisons of HRV by observation Interval with corrected significance in Study 1.

(I) Interval	(J) Interval	Mean Difference (I-J)	Std. Error	df	Bonferroni Sig.	95% Wald Confidence Interval for Difference	
						Lower	Upper
Baseline	Exercise #1	.0902[a]	.02396	1	.001***	.0270	.1535
	Exercise #2	.0096	.03180	1	1.000	-.0743	.0935
	Endpoint	-.1791[a]	.03553	1	.000***	-.2728	-.0854
Exercise #1	Baseline	-.0902[a]	.02396	1	.001***	-.1535	-.0270
	Exercise #2	-.0807[a]	.02561	1	.010**	-.1482	-.0131
	Endpoint	-.2693[a]	.03320	1	.000***	-.3569	-.1817
Exercise #2	Baseline	-.0096	.03180	1	1.000	-.0935	.0743
	Exercise #1	.0807[a]	.02561	1	.010**	.0131	.1482
	Endpoint	-.1887[a]	.03720	1	.000***	-.2868	-.0905
Endpoint	Baseline	.1791[a]	.03553	1	.000***	.0854	.2728
	Exercise #1	.2693[a]	.03320	1	.000***	.1817	.3569
	Exercise #2	.1887[a]	.03720	1	.000***	.0905	.2868

Note: ([a]) — Significant difference at $p < .05$; *$p < .05$; **$p \leq .01$; ***$p \leq .001$.

Table 4. GEE model effects of Interval and Condition Order on EDA in Study 1.

Source	Type III		
	df	**Wald Chi-Square**	**Sig.**
(Intercept)	1	251.759	.000***
Interval	3	95.809	.000***
Condition Order	1	.843	.359
Interval * Condition Order	3	1.983	.576

Note: ***p < .001.

Table 5. Pairwise comparisons of EDA by interval with corrected significance in Study 1.

(I) Interval	(J) Interval	Mean Difference (I-J)	Std. Error	df	Bonferroni Sig.	95% Wald Confidence Interval for Difference	
						Lower	**Upper**
Baseline	Exercise #1	.1805[a]	.05922	1	.014*	.0243	.3368
	Exercise #2	.0600	.08106	1	1.000	-.1538	.2739
	Endpoint	-.4867[a]	.06344	1	.000***	-.6541	-.3194
Exercise #1	Baseline	-.1805[a]	.05922	1	.014*	-.3368	-.0243
	Exercise #2	-.1205	.06505	1	.384	-.2921	.0512
	Endpoint	-.6673[a]	.08651	1	.000***	-.8955	-.4390
Exercise #2	Baseline	-.0600	.08106	1	1.000	-.2739	.1538
	Exercise #1	.1205	.06505	1	.384	-.0512	.2921
	Endpoint	-.5468[a]	.07072	1	.000***	-.7334	-.3602
Endpoint	Baseline	.4867[a]	.06344	1	.000***	.3194	.6541
	Exercise #1	.6673[a]	.08651	1	.000***	.4390	.8955
	Exercise #2	.5468[a]	.07072	1	.000***	.3602	.7334

Note: ([a]) − Significant difference at p < .05; *p < .05; ***p < .001.

Pairwise comparisons of estimated marginal means of Calm % showed significantly higher Calm % in the second relaxation exercise than the first (95% CI = [1.15,11.70], p = 0.017, d = 0.27), regardless of order of MARE and URE. MARE Calm % was significantly, moderately positively correlated with URE Calm % ($r_s = 0.45$, $p < 0.001$).

3.1.4. Salivary bio-assay analysis

No significant differences in sAA were found between saliva samples at the 5 time points (Baseline: N = 85, M = 3.87, SD = 1.01; Sample 2: N = 86, M = 3.96, SD = 1.03; Sample 3: N = 86, M = 4.00, SD = 1.04; Sample 4: N = 86, M = 4.07, SD = 0.95; Endpoint: N = 87, M = 3.92, SD = 1.00). Results are consistent with those observed in unstimulated saliva samples from healthy adults (Mandel, et al., 2010).

Table 6. GEE model for Muse Calm % by Condition Interval and Condition order in Study 1.

Source	Type III		
	df	Wald Chi-Square	Sig.
(Intercept)	1	4543.252	.000***
Condition Interval	1	5.610	.018*
Condition Order	1	.652	.420
Condition Interval * Condition Order	1	.176	.675

Note: *p < .05; ***p < .001.

3.1.5. Perceived stress scale analysis

Participants reported overall perceived stress scores consistent with normative statistics (PSS-10 $M = 16.13$, $SD = 5.61$; Perceived Helplessness $M = 11.00$, SD = 4.12; Perceived Self-Efficacy $M = 5.13$, $SD = 2.20$). Internal consistency was acceptable for Helplessness ($\alpha = .84$), Self-Efficacy ($\alpha = 0.69$), and the overall PSS-10 ($\alpha = 0.86$). No significant GEE model effects of PSS score or correlations with other measures collected in the study were found.

3.1.6. Post-questionnaire analysis

Only responses to "I found the Muse audio feedback distracting or irritating" showed significant effects on other measures in the study, with 2 (2.1%) responding "Strongly Agree" and 24 (25.0%) Agree", while 34 (35.4%) responded "Disagree" and 12 (12.5%) "Strongly Disagree". Those who found Muse audio feedback more distracting were lower performers in Calm % in the first relaxation condition, though demonstrated higher HRV following both conditions. Perception of effort during the MARE condition had significant effect when included as a factor in GEE model of HRV, $X^2(4, N = 362) = 86.63$, $p < 0.001$, and Calm % $X^2(4, N = 186) = 18.80$, $p < 0.001$, with no significant interaction effects with condition or order of MARE/URE. Corrected multiple comparisons demonstrated statistically significant difference between HRV in follow-up observation interval groups responding "Agree" (n = 20) and "Neither agree nor disagree" (n = 23), (*95% CI = [0.02,0.57]*, *p* = 0.027, d = .86), and "Agree" and "Strongly Disagree" (n = 11), (95% CI = *[0.04, 0.71]*, *p* = 0.02, d = 1.15). Corrected non-parametric multiple comparisons of Calm % demonstrated significant difference in Calm % performance between those responding "Agree" and "Strongly Disagree" (Z = -2.77, p = 0.03) in the first relaxation condition only. No other significant effects of Post-Questionnaire responses on measures collected in this study were found.

3.2. Study 2: Randomized parallel conditions

3.2.1. HRV analysis

A similar effect of interval on GEE model of HRV was identified in the parallel study. Significant effect of interval on HRV was found, $X^2(4, N = 218) = 54.71$, $p < 0.001$, with no significant effect of Condition or significant interaction effect. Corrected multiple comparisons of intervals showed a significant decrease in HRV during the relaxation condition vs baseline, 95% CI = [-0.11-0.22], t(43) = 6.19, p < 0.001, d = 0.42. Similar to Study 1, HRV results in Study 2 indicate a beneficial increase in HRV in the first follow-up observation period vs baseline (95% CI = [0.00, 0.16], t(43) = 2.03, p = 0.049, d = 0.22), with no difference between MARE and URE or in additional observation periods.

3.2.2. EDA analysis

Significant effect of interval on GEE model of EDA was found, $X^2(4, N = 203) = 47.495$, p < 0.001, and a significant interaction effect between interval and condition, $X^2(4, N = 203) = 12.86$, p = 0.012. Condition remains an insignificant factor in EDA in GEE model without interaction effect. Multiple comparisons in Study 2 display the same overall trend of increase in skin conductivity in follow-up observation, unrelated to the study conditions.

4. Discussion

4.1. Effect of neurofeedback on stress reduction

These study findings did not support the initial hypothesis that the EEG-based neurofeedback during the MARE condition would result in greater changes of physiological measures of relaxation and stress compared to the URE condition. Instead, the MARE and URE conditions were found to be equally effective in producing decreases in HRV during the exercises, followed by beneficial short-term increases in HRV that are associated with stress reduction. Observed changes in HRV are consistent with findings in prior mindfulness practice studies (e.g., Krygier et al., 2013; Peressutti et al., 2010).

Calm percentage was increased in the second relaxation exercise, regardless of the order of the MARE and URE conditions. Changing MARE and URE conditions had no effect on Calm percentage, and no effect of self-reported prior experience was found. MARE Calm percentage was significantly, moderately positively correlated with the URE Calm percentage ($r_s = 0.45$, $p < 0.001$). Interestingly, results of the post-intervention perceptions questionnaire revealed that those who agreed that the Muse audio feedback was "distracting or irritating" had substantially lower Calm % performance, supporting it as a measure of participant effort during the relaxation

exercise. However, this was only in the first relaxation condition, and the same group of participants also demonstrated higher HRV following the mindfulness exercise. It appears that the negative perception of Muse audio feedback in this subset of participants may have led to greater difficulty in initial engagement with the mindfulness exercise. The substantially larger HRV effects in participants who found it more distracting suggests that higher effort relaxation may produce more benefit.

Furthermore, against our initial hypothesis, no difference was found between MARE and URE conditions in the effects of relaxation on EDA. Several studies have demonstrated reduction in EDA during mindfulness exercises, lower baseline EDA following MBSR training, and lower EDA responsiveness to aversive stimuli (Delmonte, 1985; Erisman and Roemer, 2010; Grecucci et al., 2015; Lush et al., 2009). Reports on this measure are less consistent compared to the effects of mindfulness on HRV (Erisman and Roemer, 2010) and our sequence of two studies indicate that while a significant reduction in EDA was initially achieved by participants when beginning relaxation conditions, there was a significant increase once both interventions had been completed, with no effect of intervention order. This finding is consistent with the HRV results discussed above, suggesting that stress reduction is indeed achieved due to sustained focus and relaxation during mindfulness exercise, but this effect is not statistically different across the two experimental conditions and therefore shows no additional benefit of the EEG neurofeedback in this specific implementation of the technology.

Finally, another measure used in our studies to explore physiological changes in stress levels was salivary alpha amylase (sAA) activity. SAA is increased following stress inducing conditions (Kirschbaum et al., 1993), though our sequence of experiments failed to show a significant difference in sAA activity in response to either MARE or URE. This suggests that unlike HRV and EDA, sAA activity may not be sensitive enough as a physiological measure of stress to detect stress level changes, especially reductions in response to brief relaxation exercises.

4.2. Research contributions

Overall, the results of our study are consistent with results of prior research on mindfulness-based relaxation and its positive effects on stress reduction (Carmody and Baer, 2009). Importantly, even brief mindfulness-based interventions, such as the Muse-assisted and unassisted relaxation exercises, may offer short-term benefits in the form of increased HRV. Our findings contribute to the growing body of literature on technology-enabled relaxation approaches (Cavanagh et al., 2013; Glück and Maercker, 2011; Krusche et al., 2012) suggesting that while short-term stress reduction may indeed be achieved by engaging in simple, brief relaxation exercises, such benefits cab be achieved without externalizing or "outsourcing" primary cognitive awareness components of meditation and mindful awareness practices.

4.3. Research limitations

Limitations of this study include the single participation sessions, hardware, and analysis. A longitudinal study may observe persistent improvements in stress measures or training effects associated with neurofeedback that this study cannot detect (Zoefel et al., 2011). While simple to use, the Empatica E4 sensor limits quality and detailed spectral analysis of physiological signals compared to ECG methods, and analysis was limited to more accessible mean EDA and RMSSD HRV time domain measures. Future studies may explore the unexpected finding that increased difficulty in initially engaging attentional awareness may affect more positive physiological outcomes.

5. Conclusion

A growing body of literature shows that mindfulness-based exercises improve regulation of emotion and cognition. Biofeedback and other technologies have been recently introduced to assist individuals with mindfulness, mediation, and stress reduction by externalizing components of mindfulness practice. Our investigation of the effects of one such device — Interaxon's Muse — has failed to show incremental short-term stress reduction benefits above unassisted relaxation, using the physiological indices of heart rate variability, electro-dermal activity, and Muse's own EEG-based measure, percentage of time spent in Calm mode. Future studies should explore if longer, repeated mindfulness interventions with Muse or other devices would produce more pronounced incremental effects of EEG neurofeedback on stress reduction and well-being.

Declarations

Author contribution statement

Artem S. Svetlov: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper.

Melanie M. Nelson, Joseph P.H. McNamara: Conceived and designed the experiments; Wrote the paper.

Pavlo D. Antonenko: Analyzed and interpreted the data; Wrote the paper.

Regina Bussing: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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