Original Reports

The Role of Heart Rate Variability in Mindfulness-Based Pain Relief

Adrienne L. Adler-Neal,* Christian E. Waugh,† Eric L. Garland,‡ Hossam A. Shaltout,* Debra I. Diz,§ and Fadel Zeidan*∥

*Department of Neurobiology and Anatomy, Wake Forest School of Medicine, Winston-Salem, North Carolina, †Department of Psychology, Wake Forest University, Winston-Salem, North Carolina, ‡College of Social Work & Center on Mindfulness and Integrative Health Intervention Development, University of Utah, Salt Lake City, Utah, †Department of Surgery/Hypertension and Vascular Research, Cardiovascular Sciences Center, Winston-Salem, North Carolina, §Department of Obstetrics and Gynecology, Wake Forest School of Medicine, Winston-Salem, North Carolina, ∥Department of Anesthesiology, University of California San Diego, San Diego, California

Abstract: Mindfulness meditation is a self-regulatory practice premised on sustaining nonreactive awareness of arising sensory events that reliably reduces pain. Yet, the specific analgesic mechanisms supporting mindfulness have not been comprehensively disentangled from the potential nonspecific factors supporting this technique. Increased parasympathetic nervous system (PNS) activity is associated with pain relief corresponding to a number of cognitive manipulations. However, the relationship between the PNS and mindfulness-based pain attenuation remains unknown. The primary objective of the present study was to determine the role of high-frequency heart rate variability (HF HRV), a marker of PNS activity, during mindfulness-based pain relief as compared to a validated, sham-mindfulness meditation technique that served as a breathing-based control. Sixty-two healthy volunteers (31 females; 31 males) were randomized to a 4-session (25 min/session) mindfulness or sham-mindfulness training regimen. Before and after each group’s respective training, participants were administered noxious (49 °C) and innocuous (35 °C) heat to the right calf. HF HRV and respiration rate were recorded during thermal stimulation and pain intensity and unpleasantness ratings were collected after each stimulation series. The primary analysis revealed that during mindfulness meditation, higher HF HRV was more strongly associated with lower pain unpleasantness ratings when compared to sham-mindfulness meditation (B = -0.82, P = .04). This finding is in line with the prediction that mindfulness-based meditation engages distinct mechanisms from sham-mindfulness meditation to reduce pain. However, the same prediction was not confirmed for pain intensity ratings (B = -0.41). Secondary analyses determined that mindfulness and sham-mindfulness meditation similarly reduced pain ratings, decreased respiration rate, and increased HF HRV (between group ps < .05). More mechanistic work is needed to reliably determine the role of parasympathetic activation in mindfulness-based pain relief as compared to other meditative techniques.

Perspective: Mindfulness has been shown to engage multiple mechanisms to reduce pain. The present study extends on this work to show that higher HRV is associated with mindfulness-induced reductions in pain unpleasantness, but not pain intensity ratings, when compared to sham-mindfulness meditation. These findings warrant further investigation into the mechanisms engaged by mindfulness as compared to placebo.

© 2019 by the American Pain Society

Key words: Mindfulness meditation, heart rate variability, pain, placebo.
Nonpharmacological therapies, such as mindfulness-based regimens, are often characterized as safe and effective approaches to treat clinical pain. Mindfulness meditation is a self-regulatory practice premised on sustaining nonreactive attention to arising sensory events that reproducibly reduces pain symptomology in response to clinical and experimentally induced pain. Yet, the corresponding mechanistic underpinnings of mindfulness-based practices remain poorly characterized. In spite of the commonly held assumption that meditation engages mechanisms supporting placebo, placebo-controlled mindfulness studies have been limited. Benefits related to participating in mindfulness interventions may simply be associated with a spectrum of nonspecific factors (conditioning, facilitator attention, social support, body posture, and/or demand characteristics). To better address this issue, we recently developed and validated a sham-mindfulness meditation comparison condition to control for these nonspecific factors. This breathing control condition did not include the specific cognitive stance supporting mindfulness. In brief (see Methods for more details), the sham-mindfulness meditation condition consists of a self-facilitated technique practiced by sitting with the eyes closed and taking deep breaths every few minutes. This practice significantly lowers pain, anxiety, and respiration rate. Preliminary evidence shows that mindfulness engages distinct mechanisms from this sham-mindfulness meditation condition to reduce pain. As adapted in our laboratory, mindfulness meditation-based pain relief is associated with multiple neural mechanisms supporting the cognitive regulation of ascending nociceptive processing [↑prefrontal (PFC) and ↑perigenual anterior cingulate cortex (pgACC); ↓thalamus] and engages nonopioidergic endogenous systems. In contrast, this sham-mindfulness meditation comparison condition employs neural mechanisms reflecting lower cognitive control (↓pgACC) and higher sensory processing (↑thalamus) during noxious heat. Lower pain reports during sham-mindfulness meditation are associated with lower respiration rates, consistent with mechanisms involved in relaxation. However, we have yet to determine if mindfulness-based pain relief engages physiological processes that are distinct from placebo-based pain reductions.

In particular, the mechanistic role of the autonomic nervous system (ANS) in mindfulness-based pain relief remains unknown. The ANS is critical for homeostatic control of heart rate, blood pressure, and body temperature, among other physiologic functions. Heart rate variability (HRV), defined as the variability in the time between adjacent heartbeats, is an index of parasympathetic and sympathetic activity and autonomic flexibility. Parasympathetic input to the heart is mediated by the vagus nerve, which exerts its effects on cardiac rhythm more rapidly than sympathetic fibers. Thus, high-frequency changes in heart rate ([0.15–0.40 Hz; HF HRV]) are largely driven by parasympathetic activation. Importantly, lower HF HRV is a corollary marker of higher pain ratings during experimentally induced pain and clinical pain. In contrast, slow, rhythmic breathing, a pain relieving practice associated with some meditative practices, lowers pain and increases HF HRV. During normal breathing, changes in blood pressure activate the baroreceptor reflex, producing vagally mediated decreases in heart rate. Progressive breathing reductions increase baroreceptor reflex sensitivity, resulting in higher HF HRV. Mindfulness meditation engages neural mechanisms supporting cortical control of vagal activity and increases HF HRV. However, it is not known if heightened parasympathetic tone is related to the pain-relieving effects of mindfulness meditation.

Placebo-based pain reductions are not mediated by increased parasympathetic activity. As adapted in our laboratory, the sham-mindfulness meditation comparison condition engages mechanisms supporting placebo. Thus, we postulated that increases in HF HRV would not be associated with sham-mindfulness meditation-induced pain relief after controlling for the influence of respiration rate on HF HRV. HF HRV is associated with higher cognitive control and an outcome that is enhanced by mindfulness training. The primary hypothesis was explicitly powered to test if pain relief is more strongly associated with HF HRV during mindfulness meditation than during sham-mindfulness meditation (Hypothesis 1). Secondary analyses tested between-group differences in HF HRV, respiration rate, pain relief, and perceived meditative efficacy. We predicted that the two meditation techniques would increase HF HRV (Hypothesis 2a) and lower respiration rate (Hypothesis 3a) and there would be no between-group differences on HRV (Hypothesis 2b) and respiration rate (Hypothesis 3b).

Materials and Methods

Participants

Study exclusion criteria included individuals with mental illnesses, personality disorders, hypertension, chronic heart, lung, or ongoing pain condition, and those using psychotropic, pain, cardiac medications, or any nicotine products. Participants were instructed to refrain from caffeine and alcohol for 12 hours and exercise for 24 hours prior to participation in the preintervention and postintervention sessions due to the influence of these variables on autonomic activity. Two participants reported prior experience with meditation practices (1 mindfulness meditation group member; 1 sham-mindfulness meditation group member). Wake Forest School of Medicine’s Institutional Review Board approved all study procedures. All subjects provided written, informed consent recognizing that they would experience painful heat stimuli, that all methods were clearly explained, and that they were free to withdraw from the study at any time without prejudice. Outlier
Sample Size Determination

To test the primary hypothesis, sample size determination (G*Power, 3.1.9.4; Test family: F tests; statistical test: Linear multiple regression, Fixed Model, $R^2$ increase; Effect size: Partial $R^2 = .13$; $f^2 = .15$; Alpha error probability: .05; power = .848; Number of tested predictors = 1; Total number of predictors = 8) was based on our previous studies’ effect sizes assessing changes in respiration rate and pain during mindfulness meditation.129,131,136 Sixty-two participants ($n = 31$/group) were estimated to provide 85% power ($P < .05$) to detect a medium effect size ($R^2 = .13$) to determine if mindfulness-based pain relief would be associated with greater HF HRV when compared to sham-mindfulness meditation.

We planned to recruit 70 participants to better account for statistical power due interindividual HRV variability98 but did not reach the target sample size due to the departure of key study personnel, necessitating the early closure of the study. Nevertheless, 66 participants successfully completed the study. Four participants completed the study but were subsequently removed from the final analysis due to HRV-related outliers ($n = 3$) and improper procedural adherence ($n = 1$) (see Participants for more details). Thus, there were a total of 62 participants analyzed in the present study.

Randomization Procedure

All participants were recruited, screened, and randomized to 1 of the 2 mental training regimen groups by a study coordinator not involved in any data collection after the first study session. The randomization sequence was determined before study recruitment was initiated and all participants provided consent. The 2 arms (mindfulness meditation = A; sham-mindfulness meditation = B) were permuted with respect to treatment assignment and stratified across cohort-block sizes of 2, 4, and 6. Due to the influence of age on HF HRV,56,72,103 randomization was stratified, using an Excel-based random number generator, by age (within 5 years) between the 2 groups employing their respective list of randomization codes. All participants were randomized into 1 of the 2 groups regardless of when they were screened and entered the study. After successful completion of the pre-intervention session (experimental session 1), the experimenter was informed of the respective participant’s group assignment by study coordinator via an email and all participants were told that they had been randomly assigned to the mindfulness meditation intervention (regardless of group assignment). As such, the experimenter was not aware of the participant’s group assignment until after completion of experimental session 1. If a participant was dismissed from the study (for whatever reason), we made a record of the reason and proceeded with the randomization procedure for the next cohort(s). Participants were debriefed as to the differences in sham-mindfulness versus mindfulness meditation in an email after the conclusion of the study.

Stimuli

A TSA-II device (Medoc Inc.) was used to deliver all thermal stimuli using a 16 mm² surface area thermal probe to the left arm (psychophysical training session) or back of the right leg (experimental sessions). This modest stimulus area allows a relatively wide range of noxious stimuli to be delivered. All stimulus temperatures were ≤49°C. Subjects placed the back of their right calf on the thermal probe and were free to lift their limb at any time. No stimuli produced any tissue damage. For the present study, innocuous stimulation was characterized by neutral series consisting of continual 35°C stimulation. Noxious stimulation were labeled heat series that included 10 alternating, 12-second plateaus of 49°C interleaved with 8 seconds of 35°C.129,131,136

Psychophysical Assessment of Pain

Pain intensity and unpleasantness ratings were assessed separately using a 15 cm, 11-point plastic sliding visual analog scale (VAS).95 The minimum rating (“0”) was designated as “no pain sensation” or “not at all unpleasant,” whereas the maximum rating (“10”) was labeled as “most intense pain imaginable” or “most unpleasant pain imaginable,” respectively. Participants were instructed that “the distinction between the two aspects of pain might be made clearer if you think of listening to a sound, such as a radio. The intensity of pain is like loudness; the unpleasantness of pain depends not only on intensity, but also on other factors which may affect you.”97 These scales provide reliably separate assessments of pain intensity and unpleasantness, are internally consistent, and approximate ratio scale measurement accuracy.94

Psychological Measures

Perceived Intervention Effectiveness

As previously,131 “perceived meditative effectiveness” was assessed with an 11-point plastic sliding VAS (“0” = not effective at all; “10” = most effective imaginable) after the completion of each of the mental training sessions. Participants were asked to provide VAS responses to the following question: “How effectively did you meditate?” This measure served as a manipulation check of the sham-mindfulness meditation regimen by verifying that training led participants to believe they were practicing mindfulness meditation.131

Physiological Measures

Physiological Acquisition

All participants were fitted with electrocardiography (ECG) sensors using a lead I configuration, where the
positive electrode is placed on the left upper chest under the clavicle and the negative electrode is placed on the right upper chest directly under the clavicle. Respiration was measured with a respiratory transducer that was placed around the participant’s chest close to the diaphragm (Biopac MP100, AcqKnowledge; Biopac Systems, Goleta, CA). Subjects were fitted with these instruments before heat testing. All physiological activities were recorded at a rate of 1 kHz with an integrated software system (Biopac MP100, AcqKnowledge; Biopac Systems, Goleta, CA).

Physiological Signal Processing

All physiological data were processed using Autonomic Nervous System Laboratory software (ANSLab v2.51). The following standardized procedures were employed to collect and analyze ECG data and HF HRV values. First, cardiovascular data were visually inspected for artifacts and missing R-peaks. Missing R-peaks were determined based upon intervals between adjacent R-peaks that appeared too long or too short. If an R-peak was missing, an R-peak was inserted at a time-point halfway between the 2 adjacent R-peaks (to preserve variability this insertion was not done more than once per minute). Fast Fourier Transformation was then performed on ECG data. HF HRV was calculated as the natural log of the high-frequency power (0.15 – 0.40 Hz), a measurement shown to indicate vagal input to the heart. Respiration rate was calculated as the average number of breaths per minute (min).

Study Design

Experimental sessions 1 to 6 were conducted on separate days (Fig 1).

Experimental Session 1: Preintervention Session

Seven-minute physiological recording. After obtaining consent, all subjects were fitted with a respiratory transducer and ECG sensors. Participants then were instructed to “rest comfortably” in a supine position during physiological measurement recordings (7 minutes 39 seconds). The first 3 minutes of this time period were collected as an acclimation period to allow participants to adapt to the experimental set-up. The first 3 minutes of this time period were collected as an acclimation period to allow participants to adapt to the experimental set-up. The heart rate variability was measured for the first 3 minutes (120 seconds). Fast Fourier Transformation was then performed on ECG data. HF HRV was calculated as the natural log of the high-frequency power (0.15 – 0.40 Hz), a measurement shown to indicate vagal input to the heart. Respiration rate was calculated as the average number of breaths per minute (min).

Psychophysical training. All participants then underwent psychophysical training (PT), where they were familiarized with 32, 5-second stimuli (35–49°C) and trained to use the VAS. During PT, stimuli were delivered to the ventral aspect of the left forearm. The thermal probe was moved to a new location after each stimulus to reduce habituation and/or sensitization. No physiological data were collected during PT.

Baseline heat testing (Rest + Heat). Two neutral and 2 heat series were administered in the following order (neutral-1, heat-1, neutral-2, heat-2; each series = 4 minutes 39 seconds) to all participants. VAS pain intensity and unpleasantness ratings were collected after each series. After each series, participants were instructed to “rate the feeling of pain (pain intensity and unpleasantness, respectively) for the overall experience” of each heat and neutral series. Physiological data were collected throughout each thermal stimulation series. The thermal probe was moved to a new location on the right calf after each series to reduce stimulus habituation and sensitization. Care was taken to place the thermal probe within the middle of the lower leg (ie, on the calf muscle) as to avoid individual variability related to probe placement.

Intervention Training

Three trained mindfulness and sham-mindfulness interventionists facilitated the mindfulness and sham-mindfulness meditation interventions to better attenuate intervention variability.
Experimental Session 2 to 5: Mindfulness Meditation Training

As previously described, subjects in the mindfulness meditation group participated in 4 separate sessions (25 min/session) of mindfulness-based mental training within 7 days. Meditation training was introduced to subjects as a secular practice. While the majority of training sessions occurred in group settings (2–5 people), 3 mindfulness meditators were trained in a one-on-one setting due to scheduling conflicts and/or participant drop-outs. Across all training sessions, subjects were trained to focus on the changing sensations of the breath and to nonreactively appraise arising sensations, thoughts, and feelings. Time spent providing guided meditation instructions were progressively reduced across meditation training days to allow subjects to meditate in silence. As previously, subjects in the mindfulness meditation group were taught that perceived sensory/affective events were “to close their eyes and to take a deep breath” every 2

Experimental Session 6: Postintervention Session

Rest + Stimulation. Similar to the preintervention session, participants were instructed to “rest comfortably” in a supine position and “not to meditate” during physiological recording (7 minutes 39 seconds). The first 3 minutes of this time period was not analyzed because it was used to allow participants to acclimate to the sensors and testing environment. The remaining time was used to test respiration rate and HF HRV after participation in the intervention sessions.

Subsequently, participants were fitted with the thermal probe on the right calf and were administered 2 neutral and 2 heat series in the following order (neutral-1, heat-1, neutral-2, heat-2). Participants provided VAS pain intensity and unpleasantness ratings after each series. The thermal probe was moved to a new location on the right calf after each series. Physiological data were collected during all thermal stimulation series in the postintervention session.

Meditation. After the first 4 thermal stimulation series, participants in both groups were instructed to “begin meditating and continue meditating for the remainder of the experiment.” They were provided 10 minutes to meditate before the initiation of the noxious heat stimulation. Physiological data were collected continuously throughout “meditation.”

Meditation + Stimulation. After 10 minutes of mindfulness meditation or sham-mindfulness meditation, 2 neutral and 2 heat series (neutral-3, heat-3, neutral-4, heat-4) were administered. In order to not disturb participants’ meditation practice, subjects were not entertained that they would be administered a thermal stimulus immediately prior to neutral-3. The thermal probe was moved to a new location on the right calf after each series. Participants provided VAS ratings of pain intensity and pain unpleasantness after each thermal series.

Analysis of Behavioral and Physiological Data

In all ANOVAs (SPSS 19.0 IBM, Armonk, New York), significant (P < .05) main effects and interactions were investigated with a priori simple effects tests. For all references pertaining to the postintervention session and both groups, (1) the delineation “rest” corresponds to data collected before subjects practiced mindfulness
mortality.

**Primary Analysis:** Is mindfulness-based pain relief associated with greater HF HRV when compared to sham-mindfulness meditation?

Two separate moderated analyses with pain intensity and pain unpleasantness ratings designated as the dependent variables, respectively, were conducted to test the primary hypothesis. Pain ratings during rest and heat series and meditation and heat series were averaged separately. Rest and meditation-related respiration rate and HF HRV were averaged across neutral and heat series values, respectively. Significant interactions were investigated with a priori within group analyses to determine if the strength of the association between HRV and pain differed between mindfulness and sham-mindfulness meditation.

**Secondary Analyses: Preintervention HRV and Respiration Rate**

For preintervention session analyses, two separate 2 (group: mindfulness vs sham-mindfulness) X 2 (stimulation: heat vs neutral) mixed ANOVAs were conducted on HF HRV and respiration rate across heat and neutral series, respectively. This was performed to verify that there were no group differences in HF HRV or respiration rate at baseline.

**Secondary Analyses: Postintervention HRV and Respiration Rate**

Two separate 2 (group: mindfulness vs sham-mindfulness) X 2 (manipulation: rest vs meditation) X 2 (stimulation: heat vs neutral) mixed ANOVAs were performed on HF HRV and respiration rate, respectively, to determine if both groups would increase HF HRV (Hypothesis 2a) and lower respiration rate (Hypothesis 3a). We predicted that there would be no between-group differences on these outcomes (Hypothesis 2b & 3b).

**Secondary Analyses: Pain Ratings**

Pain intensity and unpleasantness ratings were examined separately. A 2 (group: mindfulness vs sham-mindfulness) X 2 (manipulation: rest vs. meditation) mixed ANOVA was conducted on postintervention session pain ratings with “manipulation” as the within-subjects factor to assess if mindfulness and sham-mindfulness meditation lowered pain ratings. Preintervention pain intensity and unpleasantness ratings were entered as a covariate to control for preintervention pain ratings, respectively.

**Secondary Analyses: Perceived Intervention Effectiveness**

A 2 (group: mindfulness vs sham-mindfulness) X 4 (session: meditation training sessions 1, 2, 3, and 4) mixed ANOVA was conducted on “perceived mediative effectiveness” scores with “group” designated as the between-subjects factor and “session” as the within-subjects factor. This was performed as a manipulation check of our sham-mindfulness meditation technique. However, in order to provide a more complete assessment of our observed data’s support for the null hypothesis (ie, no difference between groups) versus the alternative hypothesis (ie, group differences on this outcome), we estimated Bayesian factors for the findings of interest. We used JASP software JASP Team114 with Cauchy null distributions as priors. For the interaction terms, the ratio of the Bayesian factors for the model with and without the interaction term is presented (BF_{I,R}). To interpret the Bayesian factors, values below 1 support the null hypothesis, whereas values above 1 are considered stronger evidence for the alternative hypothesis. Values over 3 represent positive evidence for the alternative hypothesis.66

**Results**

**Participants**

Seventy-five healthy, pain-free volunteers (age range: 18–55 years) provided informed consent in the present study. Nine subjects were dismissed from the study due to scheduling conflicts (n = 8) and a psychiatric disorder disclosure (Fig 2). Sixty-six participants successfully completed all study procedures (Fig 2).

Before we tested our hypotheses or analyzed any of our data, routine Tukey outlier hinges detection methods were conducted122 to identify individuals exhibiting extreme HF HRV values. Subsequently, 3 individuals (1 female and 1 male sham-mindfulness meditation; 1 male mindfulness meditation group member) were identified as outliers and removed from the final analyses. Each of these 3 participants exhibited HF HRV values that were less than 1.5 times the interquartile range below the first quartile122 and were 2.6 to 3 standard deviations (SD) below the mean for each HF HRV value measured in both physiological experimental sessions (ie, pre/postintervention sessions, across heat + neutral stimulation series). After all, HF HRV values obtained were averaged across both experimental sessions, the 3 outliers exhibited a mean HF HRV value of 4.66 (SD = .16). In contrast, the other 62 participants (included in the final analysis) exhibited a mean HF HRV value of 8.11 (SD = .97). All analyses were also performed without excluding outliers (see Supplement A).

Data from 1 participant (female mindfulness group
member) were removed from the final analysis because the research technician inadvertently miscommunicated with the subject and was directed to and subsequently practiced meditation during the postintervention session’s Rest + Stimulation condition. Sixty-two participants (mean age [SD] = 31 ± 10 years; 41 = white, 18 = black, and 3 = Asian; 31 females; 31 males; Table 1) were included in the final analyses. There were no significant differences between groups on age (F(1, 60) = .03; P = .86, η²p = 0.00) or gender (F(1, 60) = .57; P = .45, η²p = .01; Table 1).

Primary Analysis

Mindfulness-induced pain unpleasantness reductions were associated with higher HF HRV when compared to sham-mindfulness meditation. The significant group X HF HRV interaction (β = −.82, SE = .39, t(57) = −2.07, P = .04; Table 3) demonstrated that mindfulness-based pain relief was associated with higher HF HRV when compared to the relationship between sham-mindfulness meditation-induced pain relief and lower HF HRV (Fig 3). Follow-up within group analyses revealed a trending to significance association (β = −.46, P = .07; Fig 3A; Table 4) between mindfulness-induced pain relief and higher HF HRV. In contrast, there was not a significant relationship between sham-mindfulness-induced pain relief and lower HF HRV (β = .42, P = .11; Fig 3B; Table 5). There was no significant group X HF HRV interaction on pain intensity ratings during meditation (t(57) = −1.45, P = .15 (Table 2).

Secondary Analyses

Preintervention Session HF HRV: There was a significant increase in HF HRV during noxious heat when compared to neutral series (F(1, 59) = 9.53, P = .003, η²p = .14; Table 1), and there were no significant between-group differences (F(1, 59) = 1.01, P = .32, η²p = .02) or a group X stimulation type interaction (F(1, 59) = .02, P = .88, η²p = 0.00).

Preintervention Session Respiration Rate: Respiration rate did not significantly vary by stimulation type (heat; neutral) (F(1, 59) = 3.34, P = .07, η²p = .05) or by group
Table 1. Participant Demographic, VAS Pain Intensity and Unpleasantness Ratings, Respiration Rate (RR), High-Frequency Heart Rate Variability (HF HRV), and Perceived Intervention Effectiveness Ratings (Mean ± SEM)

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>MINDFULNESS MEDITATION</th>
<th>SHAM-MINDFULNESS</th>
<th>COMBINED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>30.77 (1.98)</td>
<td>30.29 (1.78)</td>
<td>30.53 (1.32)</td>
</tr>
<tr>
<td>Sex</td>
<td>M = 14; F = 17</td>
<td>M = 17; F = 14</td>
<td>M = 31; F = 31</td>
</tr>
<tr>
<td>Preintervention pain intensity</td>
<td>5.43 (.40)</td>
<td>4.77 (.29)</td>
<td>5.10 (.25)</td>
</tr>
<tr>
<td>Preintervention unpleasantness</td>
<td>6.03 (.45)</td>
<td>5.10 (.37)</td>
<td>5.56 (.29)</td>
</tr>
<tr>
<td>Postintervention rest pain intensity</td>
<td>5.31 (.41)</td>
<td>4.82 (.20)</td>
<td>5.06 (.23)</td>
</tr>
<tr>
<td>Postintervention meditation pain intensity</td>
<td>4.09 (.31)</td>
<td>3.81 (.27)</td>
<td>3.95 (.20)*</td>
</tr>
<tr>
<td>Postintervention rest unpleasantness</td>
<td>5.48 (.43)</td>
<td>5.18 (.28)</td>
<td>5.33 (.26)</td>
</tr>
<tr>
<td>Postintervention meditation pain unpleasantness</td>
<td>3.48 (.33)</td>
<td>3.38 (.35)</td>
<td>3.43 (.24)*</td>
</tr>
<tr>
<td>Preintervention heat RR</td>
<td>16.65 (.85)</td>
<td>15.70 (.63)</td>
<td>16.17 (.53)</td>
</tr>
<tr>
<td>Preintervention neutral RR</td>
<td>17.14 (.65)</td>
<td>16.54 (.64)</td>
<td>16.83 (.45)</td>
</tr>
<tr>
<td>Preintervention heat HF HRV</td>
<td>8.15 (.20)</td>
<td>8.43 (.23)</td>
<td>8.29 (.15)*</td>
</tr>
<tr>
<td>Preintervention neutral HF HRV</td>
<td>7.96 (.17)</td>
<td>8.25 (.21)</td>
<td>8.11 (.14)</td>
</tr>
<tr>
<td>Postintervention Rest RR heat</td>
<td>17.31 (.72)</td>
<td>15.89 (.48)</td>
<td>16.60 (.44)</td>
</tr>
<tr>
<td>Postintervention Rest RR neutral</td>
<td>17.79 (.74)</td>
<td>17.18 (.49)</td>
<td>17.48 (.44)</td>
</tr>
<tr>
<td>Postintervention meditation RR heat</td>
<td>11.04 (.86)</td>
<td>9.96 (.72)</td>
<td>10.50 (.56)</td>
</tr>
<tr>
<td>Postintervention meditation RR neutral</td>
<td>13.83 (.85)</td>
<td>13.34 (.64)</td>
<td>13.58 (.53)</td>
</tr>
<tr>
<td>Postintervention rest HF HRV heat</td>
<td>7.75 (.20)</td>
<td>8.27 (.18)</td>
<td>8.01 (.14)</td>
</tr>
<tr>
<td>Postintervention rest HF HRV neutral</td>
<td>7.60 (.21)</td>
<td>8.07 (.18)</td>
<td>7.83 (.14)</td>
</tr>
<tr>
<td>Postintervention meditation HF HRV heat</td>
<td>8.05 (.21)</td>
<td>8.45 (.17)</td>
<td>8.25 (.13)</td>
</tr>
<tr>
<td>Postintervention meditation HF HRV neutral</td>
<td>8.14 (.18)</td>
<td>8.45 (.17)</td>
<td>8.29 (.13)</td>
</tr>
<tr>
<td>TS 1 perceived meditative effectiveness</td>
<td>5.16 (.36)</td>
<td>4.43 (.32)</td>
<td>4.80 (.24)</td>
</tr>
<tr>
<td>TS 2 perceived meditative effectiveness</td>
<td>5.47 (.34)</td>
<td>4.87 (.36)</td>
<td>5.17 (.25)</td>
</tr>
<tr>
<td>TS 3 perceived meditative effectiveness</td>
<td>5.81 (.44)</td>
<td>4.78 (.41)</td>
<td>5.30 (.30)</td>
</tr>
<tr>
<td>TS 4 perceived meditative effectiveness</td>
<td>6.23 (.46)</td>
<td>6.07 (.33)</td>
<td>6.15 (.28)</td>
</tr>
</tbody>
</table>

During session 6, both groups significantly (P < .05) reduced pain intensity (−22%) and pain unpleasantness ratings (−36%) when compared to rest when controlling for pain ratings at session 1. There were no between-group differences on pain intensity or unpleasantness ratings (ps > .05). At session 1, HF HRV during heat was higher for both groups when compared to neutral stimulation (P < .05).

*P < .05.

Figure 3. The relationship between HF HRV and pain unpleasantness ratings. There was a significant (P = .04) group difference on the relationship between HF HRV and pain unpleasantness. (A) Post hoc analyses revealed that there was a marginally significant relationship between increased HF HRV and decreased pain unpleasantness ratings (r = −.46; P = .07) for the mindfulness meditation group after controlling for age, pain ratings during rest, respiration rate, and HF HRV during rest. (B) HF HRV was not significantly (r = .42; P = .11) associated with pain unpleasantness after accounting for age, pain ratings during rest, respiration rate, and HF HRV during rest in the sham-mindfulness meditation group.
Table 2. Moderated Regression Analysis on HF HRV and Pain Intensity Ratings in the Postintervention Session

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>B</th>
<th>SE B</th>
<th>β</th>
<th>sr²</th>
<th>MODEL R²</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>.01</td>
<td>.02</td>
<td>.06</td>
<td>0.00</td>
<td>.66</td>
<td>13.11**</td>
</tr>
<tr>
<td>Rest pain intensity</td>
<td>.70</td>
<td>.08</td>
<td>.78</td>
<td>.52**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest RR</td>
<td>-.03</td>
<td>.05</td>
<td>-.07</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest HF HRV</td>
<td>-.07</td>
<td>.26</td>
<td>-.04</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation RR</td>
<td>.04</td>
<td>.04</td>
<td>.09</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation HF HRV</td>
<td>.80</td>
<td>.51</td>
<td>.49</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group</td>
<td>3.35</td>
<td>2.35</td>
<td>1.05</td>
<td>.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group X Meditation HF HRV</td>
<td>-.41</td>
<td>.28</td>
<td>-1.07</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B, unstandardized beta coefficient; SE B, standard error of unstandardized beta coefficient; β, standardized beta coefficient; sr², semipartial coefficient squared. Rest pain intensity, averages of pain intensity ratings during the Rest + Stimulation condition; Rest RR, averages of heat and neutral respiration rate during the Rest + Stimulation condition; Rest HF HRV, averages of heat and neutral HF HRV during the Rest + Stimulation condition; Meditation RR, averages of heat and neutral respiration rate during the Meditation + Stimulation condition; Meditation HF HRV, averages of heat and neutral HF HRV during the Meditation + Stimulation condition; Group, value depicting assignment to the sham-mindfulness or mindfulness meditation group; Group X HF HRV, interaction between Group values and Meditation HF HRV values.

**P < .001.

(F₁, 59) = .73, P = .40, η²_p = .01), and there was no significant group X stimulation interaction (F₁, 59) = .45, P = .51, η²_p = .01; Table 1).

Postintervention SessionHF HRV: There was a significant increase in HF HRV from rest to meditation across both groups (F₁, 60) = 27.96, P < .001, η²_p = .32; Table 1). The significant manipulation X stimulation interaction (F₁, 60) = 7.64, P = .008, η²_p = .11) revealed higher HF HRV values during heat and rest (F₁, 60) = 7.88, P < .007, η²_p = .12) compared to neutral and rest (F₁, 58) = .35; P = .56, η²_p = .01). There was no significant main effect of stimulation (F₁, 60) = 1.46, P = .23, η²_p = .02) and no between-group differences on HF HRV (F₁, 60) = 2.93, P = .09, η²_p = .05).

Table 3. Moderated Regression Analysis on HRV and Pain Unpleasantness Ratings During the Postintervention Session

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>B</th>
<th>SE B</th>
<th>β</th>
<th>sr²</th>
<th>MODEL R²</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>.03</td>
<td>.02</td>
<td>.15</td>
<td>.02</td>
<td>.51</td>
<td>6.83**</td>
</tr>
<tr>
<td>Rest pain unpleasantness</td>
<td>.57</td>
<td>.09</td>
<td>.61</td>
<td>.35**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest RR</td>
<td>-.01</td>
<td>.07</td>
<td>-.02</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest HF HRV</td>
<td>-.04</td>
<td>.36</td>
<td>-.02</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation RR</td>
<td>.07</td>
<td>.05</td>
<td>.16</td>
<td>.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation HF HRV</td>
<td>1.32</td>
<td>.72</td>
<td>.70</td>
<td>.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group</td>
<td>6.60</td>
<td>3.29</td>
<td>1.79</td>
<td>.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group X Meditation HF HRV</td>
<td>-.82</td>
<td>.39</td>
<td>-1.85</td>
<td>.04*</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B, unstandardized beta coefficient; SE B, standard error of unstandardized beta coefficient; β, standardized beta coefficient; sr², semipartial coefficient squared. Rest pain intensity, averages of pain unpleasantness ratings during the Rest + Stimulation condition; Rest RR, averages of heat and neutral respiration rate during the Rest + Stimulation condition; Rest HF HRV, averages of heat and neutral HF HRV during the Rest + Stimulation condition; Meditation RR, averages of heat and neutral respiration rate during the Meditation + Stimulation condition; Meditation HF HRV, averages of heat and neutral HF HRV during the Meditation + Stimulation condition; Group, value depicting assignment to the sham-mindfulness or mindfulness meditation group; Group X HF HRV, interaction between Group values and Meditation HF HRV values.

**P < .001.

Postintervention SessionRespiration Rate: There was a significant reduction in respiration rate from rest to meditation across both groups (–29.5%, 95% CI [–36.7%, –23.1%]; F₁, 60) = 90.82, P < .001, η²_p = .60; Table 1) and there was a significant manipulation X stimulation interaction (F₁, 60) = 22.09, P < .001, η²_p = .27). Post hoc analyses revealed that these respiration rate decreases were significantly greater during heat (–36.7%, 95% CI [–35.5%, –40.4%]; F₁, 60) = 106.69, P < .001, η²_p = .64) when compared to neutral series (–22.3%, 95% CI [–20.3%, –24.5%]; F₁, 60) = 48.80, P < .001, η²_p = .45). Respiration rate was significantly higher during neutral when compared to heat series (F₁, 60) = 68.40, P < .001, η²_p = .53) and there was no significant between-group differences (F₁, 60) = 1.38, P = .25, η²_p = .02).

Pre/Postintervention Session: Pain intensity: Across both groups, pain intensity ratings significantly

Table 4. Regression Analysis on HRV and Pain Unpleasantness Ratings for the Mindfulness Meditation Group

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>B</th>
<th>SE B</th>
<th>β</th>
<th>sr²</th>
<th>MODEL R²</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>.08</td>
<td>.02</td>
<td>.45</td>
<td>.13*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest pain unpleasantness</td>
<td>.34</td>
<td>.10</td>
<td>.45</td>
<td>.16*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest RR</td>
<td>-.01</td>
<td>.06</td>
<td>-.02</td>
<td>0.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest HF HRV</td>
<td>.56</td>
<td>.39</td>
<td>.34</td>
<td>.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation RR</td>
<td>.09</td>
<td>.05</td>
<td>.22</td>
<td>.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meditation HF HRV</td>
<td>-.81</td>
<td>.43</td>
<td>-.46</td>
<td>.04</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B, unstandardized beta coefficient; SE B, standard error of unstandardized beta coefficient; β, standardized beta coefficient; sr², semipartial coefficient squared. Rest pain unpleasantness, averages of pain unpleasantness ratings during the Rest + Stimulation condition; Rest RR, averages of heat and neutral respiration rate during the Rest + Stimulation condition; Rest HF HRV, averages of heat and neutral HF HRV during the Rest + Stimulation condition; Meditation RR, averages of heat and neutral respiration rate during the Meditation + Stimulation condition; Meditation HF HRV, averages of heat and neutral HF HRV during the Meditation + Stimulation condition; Group, value depicting assignment to the sham-mindfulness or mindfulness meditation group; Group X HF HRV, interaction between Group values and Meditation HF HRV values.

**P < .001.

*P < .04.
pain intensity ratings were significantly higher during the preintervention session when compared to the postintervention session \( (F_{(1, 59)} = 89.24, P < .001, \eta^2_p = .60) \). There was no significant main effect of group \( (F_{(1, 59)} = .03, P = .86, \eta^2_p = 0.00) \), group X manipulation interaction \( (F_{(1, 59)} = .44, P = .51, \eta^2_p = .01) \), or between-group differences in preintervention pain intensity ratings \( (F_{(1, 60)} = 1.82, P = .18, \eta^2_p = .03) \).

Pre/Postintervention Session: Pain unpleasantness:

Pain unpleasantness ratings significantly decreased by 35.6\% (95\% CI \([-33.2\%, -38.7\%]\)) across both groups during meditation when compared to rest \( (F_{(1, 59)} = 10.88, P = .002, \eta^2_p = .16; \text{Fig 4B; Table 1}) \). Preintervention pain unpleasantness ratings were significantly higher than postintervention pain ratings \( (F_{(1, 59)} = 51.32, P < .001, \eta^2_p = .47) \). There were no significant group differences \( (F_{(1, 60)} = .77, P = .39, \eta^2_p = .01) \), group X manipulation interaction \( (F_{(1, 59)} = .30, P = .64, \eta^2_p = 0.00) \), or between-group differences in preintervention pain unpleasantness ratings \( (F_{(1, 60)} = 2.63, P = .11, \eta^2_p = .04) \).

Nine participants reported nonzero pain intensity and unpleasantness rating in response to neutral stimulation series (mean = .7 and .4, respectively). There were no group differences in pain intensity \( (F_{(1, 60)} = .13; P = .72, \eta^2_p = 0.00) \) or pain unpleasantness \( (F_{(1, 60)} = .03; P = .87, \eta^2_p = 0.00) \) in response to neutral series.
Perceived Intervention Effectiveness: Both groups reported significant increases in "perceived meditative effectiveness" across the 4 intervention sessions ($F_{(3, 58)} = 13.39, P < .001, \eta^2_p = .19, BF_{10} = 2.4 \times 10^{6}$; Table 1). There were no significant differences in perceived meditation effectiveness between groups ($F_{(3, 58)} = 1.46, P = .23, \eta^2_p = .03, BF_{10} = .61$) or a significant group X session interaction ($F_{(3, 58)} = 1.08, P = .36, \eta^2_p = .02, BF_{FR} = .15$), demonstrating that the sham-mindfulness meditation regimen effectively led participants to believe they were practicing mindfulness meditation.

**DISCUSSION**

**Primary Analysis**

Mindfulness-Induced Pain Unpleasantness Reductions Were Associated With Higher HF HRV When Compared to Sham-Mindfulness Meditation

The present study demonstrated that mindfulness-based pain unpleasantness relief was associated with a different parasympathetic pattern when compared to a robust, sham-mindfulness meditation condition. However, this relationship was not borne out with pain intensity ratings. Visual inspection of the data reveals that in the case of pain unpleasantness, pain relief in the sham-mindfulness group was associated with lower, not higher HF HRV when compared to mindfulness meditation (Fig 3). This finding is consistent with converging lines of evidence demonstrating that placebo-based pain relief does not increase (and may reduce) parasympathetic nervous system activity.$^{62,92,120}$ Although mindfulness and sham-mindfulness meditation were designed to have procedural similarities, these mind-body techniques differed by a number of cognitive features that may explicate the observed (Fig 3) differential relationship between HF HRV and pain unpleasantness. Unlike sham-mindfulness meditation, mindfulness practitioners were trained to pay direct attention to the sensations of the breath and to reduce cognitive and affective evaluations of distracting thoughts and feelings. Mindfulness-based pain relief is associated with behavioral and neural correlates of interoception.$^{50,49,68,104}$ and when compared to sham-mindfulness meditation, mindfulness produced greater activation (right anterior insula; subgenual ACC)$^{130}$ in brain regions implicated in the so-called interoception network.$^{15,22,24,51,60,69,127}$ Mindfulness meditation reliably increases cognitive flexibility$^{1,30,74,75,108,134}$ and affective resilience$^{49,63,88}$ factors that are also directly associated with higher HRV.$^{59,104}$ It is then fitting that mindfulness-based HF HRV increases were more aligned with modulating the affective (and not sensory) dimension of pain. Taken together, we stipulate that mindfulness-based cognitive reappraisal processes may uniquely regulate affective pain responses through executive level modulation and PNS processes, an integrative, multimodal process that may lead to improvements in pain and health outcomes. In that regard, affective regulation via cognitive reappraisal is associated with increases in HF HRV. Mindfulness-based relief of acute experimentally induced pain is a nonopioidergic process associated with effortful, corticothalamic–mediated regulation of ascending nociceptive information, a known neurophysiological correlate of higher HRV.$^{32,93,118}$ This reappraisal-based process engages supraspinal mechanisms presumably through the recruitment of GABA-ergically mediated corticothalamic interactions.$^{48,129,130,136,138}$

In the present study, we showed that mindfulness and sham-mindfulness lowered pain and increased HF HRV. However, there was a significant difference between the sham-mindfulness meditation group and the mindfulness mediation group in the relationship with HRV and pain unpleasantness. Visual inspection of the data reveals that in the case of pain unpleasantness, pain relief in the sham-mindfulness group was associated with lower, not higher HF HRV when compared to mindfulness meditation (Fig 3), a finding consistent with converging lines of evidence demonstrating that placebo-based pain relief does not increase (and may reduce) parasympathetic nervous system activity (ie, HF HRV).

**Secondary Analyses**

**Pain Ratings**

The sham-mindfulness meditation condition was employed to better characterize and disentangle the specific mechanisms supporting pain relief during mindfulness meditation. It is not particularly surprising that mindfulness and sham-mindfulness meditation produced pain intensity ($\eta^2_p = .09$) unpleasantness reductions ($\eta^2_p = .16$). However, there were no reliable between-group differences on pain intensity ($\eta^2_p = .03$) or unpleasantness ($\eta^2_p = .01$) ratings.

**HRV and Respiration Rate**

We were not explicitly powered to test the secondary hypotheses relating to respiration rate and HF HRV. However, our results signified large effect sizes relating to HF HRV and respiration rate and revealed both meditative techniques increased HF HRV ($\eta^2_p = .32$) and decreased respiration rate ($\eta^2_p = .60$), and there were no between-group differences on these outcomes ($\eta^2_p < .06$). Thus, if replicated, mindfulness and sham-mindfulness meditation may lower respiration rate and increase HF HRV.

**Considerations for Mindfulness-Based Pain Relief**

There are significant operational parallels between the 2, slow-breathing practices. Recent work from our laboratory revealed that the cognitive state of mindfulness meditation and sham-mindfulness meditation
Mindfulness meditation. Mindfulness is a nebulous construct that requires appropriate operational characterizations. Thus, the sham-mindfulness meditation condition in this experiment might be better described as a comparison mental training condition, especially in light of its similar analgesic effects to genuine mindfulness practice. Yet, sham-mindfulness meditation is an effective pain relieving technique and resembles other meditative techniques. Sham-mindfulness meditation is associated with significant deactivation of the rostral ACC and ventromedial PFC, suggesting that nonreactivity is also a mechanism engaged by sham-mindfulness meditation. However, it is likely that sham-mindfulness-based nonreactivity does not engage metacognitive states of awareness associated with mindfulness practices.

Consequently, it may not be appropriate to characterize this technique as a placebo manipulation, but rather an active, noninert practice. Sham-mindfulness meditation has been reported to be easier to exercise than mindfulness meditation suggesting that this technique is clinically viable and pragmatic to treat pain. Although we did not explicitly test this, pain conditions that exhibit comorbidities related to higher fatigue and cognitive deficits might then benefit from a less cognitively demanding practice (sham-mindfulness meditation).

The present findings are particularly generalizable to healthy, pain-free individuals and are not directly applicable to chronic pain patients. Chronic pain patients exhibit an array of comorbidities that can confound specific mechanisms of action supporting mindfulness. We employed healthy subjects, experimentally induced pain, and an event-related design to better identify the specific physiological processes supporting mindfulness-based pain attenuation. It is also difficult to explicitly ascertain that changes in HRV were directly associated with noxious heat, due to the limitation that HRV measurements cannot be disentangled in an “on-off” block design. A third-arm, nonmanipulation regimen may have provided a more suitable control for potential habituation/sensitization effects, although our previous studies employing identical experimental paradigms show that nonmanipulation controls exhibit significant pain increases (+16%) in response to noxious heat. We were only statistically powered to test the primary aim of the study (ie, Hypothesis 1). Thus, we were not justified to determine if mindfulness-based analgesia is mediated by HRV. This analysis would also inform potential mechanistic differences between mindfulness and sham-mindfulness practices. We find that mindfulness, in this study, was not more effective than sham-mindfulness meditation in reducing pain. This suggests that mindfulness may not be more effective at reducing pain when compared to a robust and active sham-mindfulness meditative technique. It is also important to state that a technique labeled “mindfulness meditation” that is premised on lowering breathing rate could be an effective pain reliever. It would also be important to compare the mechanisms supporting mindfulness to other effective pain therapies, such as cognitive behavioral therapy (CBT). Mindfulness and CBT produce similar pain relieving effects and both techniques likely employ executive control processes to reduce pain, although CBT is premised on changing thoughts about pain, whereas mindfulness is based on accepting thoughts about pain.

Importantly, there were no significant differences in pain responses between the mindfulness and sham-mindfulness techniques. This could be due to the possibility that some participants had prior experience with mindfulness. That is, participants were not asked prior to participation in the study if they had any knowledge regarding the exact practices of mindfulness meditation based on their experiences or media exposure. As such,
some participants may have recognized that sham-mindfulness meditation was not true mindfulness meditation. Nevertheless, we have solid evidence that the 2 interventions have the same effect on pain intensity and unpleasantness, and the present study provides some indication that there might be a difference in how parasympathetic responses relate to this analgesic effect. Yet, we were not statistically powered to state that both of these techniques are mediated by different mechanisms. More mechanistic work is needed to reliably determine the role of parasympathetic activation in mindfulness-based pain relief as compared to other meditative techniques.

It is also possible that the facilitators were more motivated to promote relief for the mindfulness training as compared to the sham-mindfulness technique. Further, while participants were not asked to meditate between intervention sessions, we did not explicitly ask if they had done so. It should also be noted that the experimenter was not blinded to participants’ group assignments (ie, sham-mindfulness vs mindfulness) during the postintervention session, a factor that may have confounded our results. Of note, HF HRV was higher during the experience of a painful stimulus. It should also be considered that we were primarily powered to test Hypothesis 1, the regression analysis examining the between-group difference in the relationship between HF HRV and pain ratings. Consequently, our secondary analyses should be interpreted with caution and primarily utilized as a tool to guide future studies. We have restricted our interpretation of analyses to the manipulation checks and primary analysis. The process of age matching may have introduced bias into the study procedures and should be considered when interpreting the results. Specifically, if groups were unbalanced, it would be dictated that an individual of a certain age would be assigned to whichever group required matching. It is important to note that several fundamental principles are embedded in the treatment modality supporting mindfulness-based practices such as nonreactivity, attention regulation, meta-cognition, distraction, beliefs, conditioning, and other factors. Investment in demonstrating the clinical efficacy of a suite of these processes under the construct of mindfulness may hamper the comprehension and operationalization of mindfulness-based practices and the potential for therapeutic progress. Thus, future studies should be conducted to explicitly test the purported mechanisms and clinical efficacy supporting each of these factors across different patient populations to better tailor and target the use of these potential pain therapies. We also urge caution in using the term “sham-mindfulness meditation” in the clinical treatment of pain because there are likely active mechanisms that are shared by genuine and sham-mindfulness meditation that are therapeutic. Mindfulness-based regimens are premised on increasing one’s ability to self-regulate and accept maladaptive experiences. Growing evidence demonstrates that one’s ability to sustain nonreactive attention in the present moment (ie, mindfulness) uniquely modulates the elaboration of maladaptive pain-related appraisals and improves parasympathetic processes, factors that may serve as a buffer for the exacerbation of clinical pain.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jpain.2019.07.003.

References


25. Cushing H. VI: Concerning a possible “Parasympathetic Center” in the diencephalon. PNAS 17:253-264, 1931


52. Hassett AL, Cone JD, Patella SJ, Sigal LH: The role of catastrophizing in the pain and depression of women with fibromyalgia syndrome. Arthritis Rheum 43:2493-2500, 2000


The Role of Heart Rate Variability in Mindfulness-Based Pain Relief

classifying the properties of Zen meditation. Neuropsychobiology 50:189-194, 2004

85. O’Doherty JP, Buchanan TW, Seymour B, Dolan RJ: Predictive neural coding of reward preference involves disso-


87. Park G, Vasey MW, Van Bavel JJ, Thayer JF: Cardiac vagal tone is correlated with selective attention to neu-


89. Penfield W, Boldrey E: Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain 60:389, 1937


91. Pollatos O, Fustos J, Critchley HD: On the generalised embodiment of pain: How interoceptive sensitivity modu-

92. Pollo A, Vighetti S, Rainero I, Benedetti F: Placebo anal-


96. Price DD, Harksins SW, Baker C: Sensory-affective relationships among different types of clinical and experimen-

97. Price DD, McGrath PA, Rafii A, Buckingham B: The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. Pain 17:45-56, 1983

98. Quintana DS: Statistical considerations for reporting and planning heart rate variability case-control studies. Psychophysiology 54:344-349, 2017


114. Team J. JASP (Version 0.9.0.1). 2018


120. Tracy LM, Gibson SJ, Labuschagne I, Georgiou-Karistianis N, Giannarou MA: Intranasal oxytocin reduces heart rate variability during a mental arithmetic task: A randomised, double-blind, placebo-controlled cross-over study. Prog Neuropsychopharmacol Biol Psychiatry 81:408-415, 2018


122. Tukey JW: Exploratory Data Analysis. Reading, PA, Addison-Wesley, 1977


