Replication and extension of the link between the cardiovascular system and sensitivity to social pain in healthy adults

Masataka Umeda, Teresa M. Leutze and Tristen K. Inagaki

*Department of Kinesiology, University of Texas at San Antonio, San Antonio, TX, USA; †Department of Psychology, San Diego State University, San Diego, CA, USA

ABSTRACT

Resting blood pressure (BP) and heart rate variability (HRV) are linked to physical pain. Research also shows a link between social pain and physical pain, and an inverse association between resting BP and social pain. However, little is known regarding the relationship between resting HRV and social pain. Therefore, the present study aimed to replicate the link between social pain and physical pain, and the inverse relationship between resting BP and social pain, and to explore the relationship between resting HRV and social pain. One-hundred twenty three healthy adults completed 1) resting cardiovascular measurements of BP and low-frequency (LF) and high-frequency (HF) HRV powers, 2) social pain sensitivity assessment via the Brief Fear of Negative Evaluation (BFNE) and Mehrabian’s Sensitivity to Rejection (MSR) scales, and 3) physical pain sensitivity assessment via subjective pain responses during cold pressor test. The results indicated that no association was observed between social pain and physical pain, whereas resting BP was inversely associated with the MSR scores. Resting LF-HRV was inversely associated with social pain, whereas resting HF-HRV was positively associated with social pain. These findings suggest that physical pain and social pain may share biological substrates that are involved in BP regulation and pain control.

1. Introduction

A well-known, but sometimes puzzling, finding from the physical pain literature is the relationship between resting blood pressure (BP) and sensitivity to physical pain – defined as sensitivity to laboratory noxious stimuli (e.g., mechanical, electrical, thermal stimuli, etc.). Those who exhibit higher resting BP typically show reduced sensitivity to physical pain compared to those who exhibit lower resting BP (e.g., hypertensive individuals vs. normotensive individuals) (Bruehl & Chung, 2004; France, 1999; Ghione, 1996). Research suggests that the inverse relationship between resting BP and sensitivity to physical pain may be explained by chronic activation of a descending pain modulatory system, where elevated BP first stimulates the baroreceptor, a receptor that responds to stretching of arterial wall, and then sends neural signals to neuroanatomical areas in the brain that are involved in both descending control of physical pain and regulation of BP (e.g., nucleus tractus solitarius, periaqueductal gray area, etc.) (Bruehl & Chung, 2004; Ghione, 1996). These observations indicate that baroreceptor stimulation initiates the descending pain inhibitory mechanism, along with BP regulation. Consistent with such a mechanistic role of baroreceptor stimulation in physical pain regulation, there is evidence that experimental stimulation of the baroreceptor in a laboratory environment and spontaneous baroreceptor stimulation during the cardiac cycle are associated with reduced sensitivity to physical pain stimuli, whereas resting baroreceptor sensitivity is inversely associated with sensitivity to physical pain (Duschek et al., 2013).

While these findings demonstrate the close neurophysiological link between the cardiovascular system and sensitivity to physical pain, our everyday experiences suggest that pain hurts us not only physically (e.g., sprained ankle during a sport game), but also psychologically in our social life (e.g., after social rejection from peers at school). Indeed, physical and social pain – the unpleasant experience evoked by actual or potential damage to one’s sense of social connection or social value – may be experienced as aversive because they share similar neurobiological mechanisms (Eisenberger, 2015; Macdonald & Leary, 2005; Panksepp et al., 1980). In the same way that monitoring and maintaining one’s physical safety is important for well-being and survival, so too is it critical to monitor and maintain social relationships. Therefore, mechanisms that process and enable responses to the dangers from physical pain,
including alerting one to and helping one regulate pain, may also process and enable responses to the dangers from social rejection and loss.

As preliminary evidence for similarities between physical and social pain, language used to describe physical pain is also commonly used to describe social pain (e.g., my heart is broken, my feelings are hurt). Brain imaging research demonstrates that some of the same brain regions that activate in response to acute experiences of physical pain also activate in response to acute experiences of social pain (e.g., dorsal anterior cingulate cortex, anterior insula) (Eisenberger et al., 2011, 2003). In regard to sensitivity to both forms of pain, there is some empirical evidence suggesting that patients with chronic pain are more sensitive to social pain, and those who are more sensitive to experimental physical pain are also more sensitive to experimental social pain (Eisenberger, 2015; Sturgeon & Zautra, 2016).

Should physical and social pain share similar processing streams, resting BP may also relate to sensitivity to social pain. Consistent with such a neurophysiological link, a recent study extended the established link between resting BP and sensitivity to physical pain to the domain of social pain. Resting (tonic) BP was inversely associated with individual differences in sensitivity to social pain (Inagaki et al., 2018). Further, the association was replicated across three separate samples and held after adjusting for covariates known to also relate to resting BP. Beyond social pain, higher resting BP has also been associated with reduced sensitivity to stimuli with emotional content (McCubbin et al., 2014; Purdy et al., 2004), further suggesting that resting cardiovascular measures are relevant for socio-emotional experiences such as social pain. Though promising for the hypothesis that social pain and physical pain share similar mechanisms, to date there is a limited amount of data demonstrating a link between sensitivity to both social and physical pain. Therefore, there is a need to replicate previous findings, as well as further explore the link between the cardiovascular system at rest and individual differences in sensitivity to social pain using additional cardiovascular measures.

Heart rate variability (HRV) is a physiological index to evaluate autonomic tone of cardiac function, and can be obtained via a noninvasive test (Laborde et al., 2017). While BP measures reflect pressure values during the contraction and relaxation phases of the cardiac cycle, HRV reflects neural activities that underlie BP, such as baroreflex and vagal nerve activities, which are also linked to sensitivity to physical pain. The HRV analysis typically produces a number of HRV parameters, and one of the well-accepted HRV parameters, known as low-frequency (LF)-HRV, represents baroreflex function (Goldstein et al., 2011). The other well-accepted HRV parameters include time-domain HRV and high-frequency (HF) HRV, and those HRV parameters represent parasympathetic/vagal nerve activity (Laborde et al., 2017). Research has demonstrated a link between vagal nerve activity and physical pain, such that chronic pain patients typically show reduced resting vagal nerve activity, evaluated via time-domain and/or HF-HRV parameters, compared to healthy controls (Koenig, Falvay et al., 2016; Koenig, Williams et al., 2016; Meeus et al., 2013; Tracy et al., 2016). In contrast, it is currently unclear whether resting vagal nerve activity is associated with sensitivity to social pain. However, there is some evidence that resting vagal nerve activity is inversely associated with experiences related to social pain, such as social rejection (Gyurak & Ayduk, 2008) and psychosocial stress (Lischke et al., 2018). Additionally, the impact of an acute experience of social pain (negative socioevaluative feedback) on physiological stress reactivity is better preserved in individuals with higher resting vagal nerve activity (Casad & Petzel, 2018). These observations lead to a hypothesis that vagal nerve activity, as reflected in time-domain/HF-HRV, may be inversely associated with sensitivity to social pain, but examination of the hypothesis is warranted.

Therefore, the present study aimed to replicate the link between individual differences in sensitivity to social pain and physical pain, and the inverse relationship between resting BP and sensitivity to social pain in healthy adults. The present study then aimed to assess whether such a link between the cardiovascular system and sensitivity to social pain extends to HRV parameters. Based on available evidence in the relevant areas, we hypothesized that 1) individual differences in sensitivity to social pain would be positively associated with sensitivity to physical pain, 2) resting BP would be inversely associated with sensitivity to social pain, 3) resting LF-HRV parameters, which represents baroreflex sensitivity, would be inversely associated with sensitivity to social pain, and 4) resting time-domain/HF-HRV parameters would be inversely associated with sensitivity to social pain.

2. Methods

2.1. Participants

Healthy men and women, at the age of 18–35, were recruited for this study via collegial classroom announcements, posting up study flyers on college campus, and social media postings targeting the San Antonio, Texas community. Individuals were excluded from the study if they 1) had any formal diagnosis of
any medical condition or 2) were taking any medication for pain or cardiovascular conditions. Additionally, women who were pregnant or breastfeeding at the time of recruitment were excluded from this study. The study was conducted in a research laboratory at a state university that is designated as a Hispanic serving institution in South Texas. The study protocol was fully approved by IRB, and all participants signed a consent form before their study session began.

### 2.2. Resting cardiovascular measures

#### 2.2.1. HRV

HRV was evaluated to examine autonomic tone of cardiac function. The participants were asked to wear a heart rate (HR) monitor around the chest under the chest muscles that would communicate with the Polar wristwatch (Polar V800, Polar Electro Inc., NY), and then remain seated quietly for 10 minutes to record an R-R interval of heartbeat, a time interval between two successive R-waves of cardiac cycle on electrocardiogram. During the quiet rest, the participants were asked to sit straight in a chair, with hands on the thighs, palms facing up, eyes open, feet flat on the floor, and knees at a 90° angle, and keep their normal breathing. The recording protocol is very similar to published recommendation of HRV assessment (Laborde et al., 2017). The research staff also recorded frequency of the participants’ spontaneous breathing rate by counting the rise of their chest for 30 seconds during the first five minutes, and multiplied it by two to estimate their normal breathing rate per minute. The R-R interval data were uploaded from the wristwatch to the Polar Flow website (https://flow.polar.com/), and downloaded from the website in a text file for data analysis using the Kubios HRV analysis software (https://www.kubios.com) to calculate HRV parameters. A time-domain HRV parameter includes root mean square of successive differences (RMSSD), whereas frequency-domain HRV parameters include LF- and HF-HRV powers, expressed as normalized unit that allows comparison of frequency-domain HRV parameters among individuals (Shaffer & Ginsberg, 2017). The LF- and HF-HRV powers were derived using autoregressive analysis, with the frequency band identified between 0.04 and 0.15 Hz and 0.15–0.40 Hz for LF-HRV and HF-HRV powers, respectively (Laborde et al., 2017). Moderate artifact correction, which is available in the software, was applied to the R-R interval data that were obtained from the second half of five minutes to calculate the above HRV parameters (Laborde et al., 2017). Using a threshold-based method, R-R intervals were detected as artifacts if the values were smaller than the average R-R interval value – 0.25 sec or larger than the average R-R interval value +0.25 sec. The artifact correction was then made by replacing the identified R-R interval values with the interpolated values using a cubic spline interpolation (https://www.kubioa.com).

#### 2.2.2. BP and HR

BP and HR were assessed using a commercially available BP monitor (Omron HEM-907XL, Omron Healthcare Inc., IL) after the R-R interval recording. An appropriately sized BP cuff was attached to the participants’ left upper arm, and BP and HR were evaluated once while the participants sat quietly in a chair.

### 2.3. Self-report measures

#### 2.3.1. General information questionnaire

The participants were asked to answer several demographic questions (e.g., sex, age, race/ethnicity) in the questionnaire, which were used to describe the study sample.

#### 2.3.2. Sensitivity to social pain

Individual differences in sensitivity to social pain were assessed with two of the most common, widely used measures to assess sensitivity to social rejection: 1) Brief Fear of Negative Evaluation scale (BFNE) (Leary, 1983) and, p. 2) Mehrabian’s Sensitivity to Rejection (MSR) scale (Mehrabian, 1970). Resting BP has previously been shown to relate to individual differences in both the BFNE and MSR (Inagaki et al., 2018). The BFNE scale assesses the degree to which a person is sensitive to negative evaluation by others, and consists of 12 statements that describe various social interactions with others, including four positively worded statements and eight negatively worded statements. For each statement, the participants endorsed one response out of five (1: Not at all characteristic of me to 5: Extremely characteristic of me) that best characterized them. After the numeric responses to the negatively worded statements were reversed, all responses were summed up to represent a total score of the BFNE scale, with higher scores indicative of being more sensitive to social pain (score range: 12–60).

The MSR scale evaluates perceptions of negative social expectations, including fear that interactions will result in social rejection or discomfort, and consists of 24 items that consist of 12 positively worded and 12 negatively worded items. For each item, the participants were asked to endorse one response out of nine (1: Strongly disagree to 9: Strongly agree) that best described them. The numeric responses were then summed up separately for positively worded and negatively worded
items. Next, the scores from the negatively worded items were subtracted from scores from the positively worded items to determine the MSR scores, with higher scores indicative of higher sensitivity to social pain (score range: −96-96).

2.3.3. Anxiety
In order to assess the specificity of any associations with sensitivity to social pain, additional mental health measures that have also been shown to relate to resting cardiovascular measures (Gallo & Matthews, 2003), including anxiety and depression, were collected. Anxiety levels were evaluated using the Trait Anxiety Inventory (Spielberger et al., 1983) that consists of 20 items to assess trait anxiety. Each item is rated on a 4-point scale ranging from 1 to 4, and the participants endorsed one out of the four responses that best described themselves. Several responses were reverse-scored, and all endorsed responses were then summed up to make a total score, with higher scores indicative of higher levels of trait anxiety (score range 20–80).

2.3.4. Depression
Severity of depression symptoms was evaluated using the Beck Depression Inventory II (BDI-II) (Beck et al., 1996). The BDI-II consists of 21 items that assess various domains of the depressive symptoms. Each item is rated on a 4-point scale ranging from 0 to 3, and the participants marked one out of the four responses that best described their symptom. The marked responses were then summed up to make a total score, with higher scores indicating more severe depressive symptoms (score range 0–63).

2.3.5. Sensitivity to physical pain
Cold pressor test (CPT) was used to evaluate sensitivity to physical pain. CPT consisted of storing water and ice in a cooler box, and the research staff stirred water with ice until water temperature was decreased to approximately 7°C within a range of 6.5°C to 7.4°C. Once the target temperature was achieved, remaining ice in the water was removed, and the cold water was kept still. The participants were then asked to immerse their right hand into the cold water bath up to their wrist just under the head of ulna, with their fingers open up but without touching the bottom of the cooler box, for a maximum of 2 minutes. However, the participants were also instructed to remove their hands if cold pain sensation became intolerable before the end of the 2 minutes. During CPT, the participants were asked to indicate when the cold sensation changed from non-painful, cold sensation into painful sensation by saying “now”, and the research staff recorded the time in seconds that was required for the participants to feel the change in the sensations as pain threshold. Additionally, the research staff asked the participants to rate an intensity of cold pain sensation using a 0–10 numeric rating scale, where 0 indicates no pain, and 10 indicates the worst possible pain, every 30 seconds during CPT. The average cold pain ratings across the time points were calculated as pain rating. Together, cold pain threshold and cold pain rating during CPT were used to quantify sensitivity to physical pain. Previous research shows that CPT, as administered in this protocol, produces moderate-to-strong cold pain sensation in the immersed hand (Umeda & Okifuji, 2020).

2.4. Procedure
The participants were asked to visit our research laboratory to complete one study session with research staff. Prior to the study session, the participants were instructed to 1) follow a normal sleep routine at night, 2) avoid strenuous physical activity and alcohol intake for 24 hours, 3) avoid caffeine intake and smoking for three hours, and 4) avoid heavy meal intake for two hours, as behavioral preparations for HRV assessment (Laborde et al., 2017). After confirming that the individuals followed the preparations, physiological data were first collected as outlined in the Resting Cardiovascular Measures section above. Next, CPT was administered to evaluate sensitivity to physical pain as outlined in the Sensitivity to Physical Pain section above. Following CPT, the participants were asked to complete a set of questionnaires described in the Self-report Measures section above, which concluded their study participation. It took approximately 45–60 minutes for the participants to complete a study session.

2.5. Statistical analysis
A power analysis was performed to estimate an optimal sample size to examine the association between resting BP and sensitivity to social pain, with an alpha = 0.05, a power = 0.80, and a small-to-medium correlation (r = 0.25) that was reported in the previous study in healthy adults (Inagaki et al., 2018). The power analysis then indicated that approximately 125 individuals would be needed to replicate the inverse association between resting BP and sensitivity to social pain. After removing two cases due to error in the physiological measurements, data from a total of 123 individuals were analyzed for the present study.

Self-report questionnaires were scored based on the published guidelines. As for data from CPT, two individuals failed to report pain threshold, leaving the study
sample for pain threshold data 121. Additionally, two individuals removed their hand from the cold water bath before the 30-second time point of pain rating assessment, leaving the study sample for pain rating data 121. Among 123 individuals, 97 individuals completed the full 2-minute protocol of CPT. Means and standard deviations were then calculated for the outcome measures to describe the study participants.

Pearson’s correlation analysis was performed to examine the relationship 1) between sensitivity to social pain (BFNE and MSR scores separately) and sensitivity to physical pain (pain threshold and pain rating separately), 2) between resting BP and sensitivity to social pain and physical pain, 3) between LF-HRV, which represents baroreflex function, and sensitivity to social pain and physical pain, and 4) between time-domain/HF-HRV, which represent vagal nerve activity, and sensitivity to social pain and physical pain. Associations between cardiovascular and pain measures that were found to be statistically significant were considered for the follow-up analysis, with potential covariates included in the analytical model. To identify the covariates, correlational analysis was performed to examine the association between mental health (trait anxiety and depression) and outcome measures (cardiovascular and pain measures). Mental health variables that were significantly associated with either cardiovascular or pain measures were submitted to the follow-up analysis as covariates.

The follow-up analysis was performed using a hierarchical multiple regression to examine the independent association of resting cardiovascular measures with pain measures after statistically controlling for mental health variables as covariates. Specifically, the covariates were entered into the regression model as the first block of independent variables, whereas the resting cardiovascular measure was entered into the regression model as the second block of independent variable.

All statistical analyses were performed using SPSS version 25. The significance level was set at a familywise α = 0.05 for all analyses.

3. Results

3.1. Participants

One hundred twenty three participants (48 men and 75 women) completed the study. The participants were mostly in their twenties (mean age = 22.43, SD = 2.94), and consisted of individuals of various racial/ethnic backgrounds (74 Hispanics/Latinos, 27 Whites, 10 Asians, 9 African Americans, 1 American Indian/Alaskan Native, and 2 other/multiracial/ethnic individuals). Descriptive statistics of the outcome measures are presented in Table 1.

3.2. Results from correlation analyses

3.2.1. Relationship between sensitivity to pain measures

As expected, the BFNE and MSR scores were positively correlated with each other (r = 0.42, p < 0.01), whereas pain threshold and pain rating were inversely associated with each other (r = −0.48, p < 0.01). However, the results indicated no significant correlations between individual differences in sensitivity to social pain and sensitivity to an acute experience of physical pain (rs = −0.02 ~ 0.05, ps > 0.05).

3.2.2. Relationship between cardiovascular and sensitivity to pain measures

Results from the correlational analysis between cardiovascular and sensitivity to pain measures are presented in Table 2. In replication of previous findings, resting BP was inversely associated with the scores on the MSR scale (SBP: r = −0.24, p < 0.01 & DBP: r = −0.26, p < 0.01). However, resting BP was not significantly associated with the scores on the BFNE scale (SBP: r = −0.08, p > 0.05 & DBP: r = −0.06, p > 0.05) nor with sensitivity to physical pain (rs = −0.07 ~ 0.14, p > 0.05).

RMSDD was not significantly associated with the scores on either BFNE (r = 0.04, p > 0.05) or MSR

<table>
<thead>
<tr>
<th>Table 1. Primary characteristics of the participants.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular Measures</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
</tr>
<tr>
<td>110.24 (15.42)</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
</tr>
<tr>
<td>68.89 (11.58)</td>
</tr>
<tr>
<td>HR (beat per minute)</td>
</tr>
<tr>
<td>72.98 (12.78)</td>
</tr>
<tr>
<td>Breathing Rate (rate per minute)</td>
</tr>
<tr>
<td>14.39 (3.15)</td>
</tr>
<tr>
<td>RMSDD (millisecond)</td>
</tr>
<tr>
<td>39.97 (27.06)</td>
</tr>
<tr>
<td>LF-HRV (normalized unit)</td>
</tr>
<tr>
<td>60.72 (20.00)</td>
</tr>
<tr>
<td>HF-HRV (normalized unit)</td>
</tr>
<tr>
<td>39.21 (19.95)</td>
</tr>
<tr>
<td>Pain Sensitivity Measures</td>
</tr>
<tr>
<td>BFNE</td>
</tr>
<tr>
<td>32.57 (8.60)</td>
</tr>
<tr>
<td>MSR</td>
</tr>
<tr>
<td>3.87 (21.72)</td>
</tr>
<tr>
<td>Pain Threshold (second)</td>
</tr>
<tr>
<td>41.09 (28.02)</td>
</tr>
<tr>
<td>Pain Rating</td>
</tr>
<tr>
<td>5.90 (1.84)</td>
</tr>
<tr>
<td>Mental Health Measures</td>
</tr>
<tr>
<td>Trait Anxiety</td>
</tr>
<tr>
<td>36.52 (9.47)</td>
</tr>
<tr>
<td>Depression</td>
</tr>
<tr>
<td>8.24 (6.62)</td>
</tr>
</tbody>
</table>

Data are means and standard deviations
SBP: Systolic blood pressure
DBP: Diastolic blood pressure
HR: Heart rate
RMSDD: Root mean square of successive RR interval differences
LF-HRV: Low-frequency heart rate variability
HF-HRV: High-frequency heart rate variability
BFNE: Brief Fear of Negative Evaluation
MSR: Mehrabian’s Sensitivity to Rejection
scales \((r = 0.00, p > 0.05)\). On the other hand, RMSSD was positively associated with pain threshold \((r = 0.21, p < 0.05)\), but not with pain rating \((r = -0.17, p > 0.05)\).

LF-HRV was inversely associated with the scores on both BFNE \((r = -0.24, p < 0.01)\) and MSR scales \((r = -0.19, p < 0.05)\), consistent with our hypothesis regarding the link between baroreflex sensitivity and sensitivity to social pain (Figure 1). In contrast, correlations between LF-HRV and sensitivity to physical pain were not statistically significant \((rs = -0.05 \sim -0.02, p > 0.05)\).

In contrast to our hypotheses that vagal nerve activity would be negatively associated with sensitivity to social pain, HF-HRV was positively associated with the scores on both BFNE \((r = 0.24, p < 0.01)\) and MSR scales \((r = 0.19, p < 0.05)\). These associations are presented in Figure 2. There were no statistically significant correlations between HF-HRV and sensitivity to physical pain \((rs = 0.02 \sim 0.05, p > 0.05)\).

### 3.3. Results from follow-up analyses

#### 3.3.1. Relationship between mental health and primary outcome measures

The results indicated that trait anxiety and depression were positively associated with the scores on the BFNE

<table>
<thead>
<tr>
<th>BFNE</th>
<th>MSR</th>
<th>Pain Threshold</th>
<th>Pain Rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>-0.08</td>
<td>-0.24**</td>
<td>0.12</td>
</tr>
<tr>
<td>DBP</td>
<td>-0.06</td>
<td>-0.26**</td>
<td>0.14</td>
</tr>
<tr>
<td>RMSSD</td>
<td>0.04</td>
<td>0.00</td>
<td>0.21*</td>
</tr>
<tr>
<td>LF-HRV</td>
<td>-0.24**</td>
<td>-0.19*</td>
<td>-0.05</td>
</tr>
<tr>
<td>HF-HRV</td>
<td>0.24**</td>
<td>0.19*</td>
<td>0.05</td>
</tr>
</tbody>
</table>

BFNE: Brief Fear of Negative Evaluation  
MSR: Mehrabian’s Sensitivity to Rejection  
SBP: Systolic blood pressure  
DBP: Diastolic blood pressure  
RMSSD: Root mean square of successive RR interval differences  
LF-HRV: Low-frequency heart rate variability  
HF-HRV: High-frequency heart rate variability  
**: \(p < 0.01\)  
*: \(p < 0.05\)

**Figure 1.** The inverse link between LF-HRV and sensitivity to social pain. Higher values from the LF-HRV measure was associated with lower scores on the BFNE (Panel A: \(r = -0.24, p < 0.01\)) and MSR scales (Panel B: \(r = -0.19, p < 0.05\)). Lower numbers on the BFNE and MSR scales indicate lower sensitivity to social pain. LF-HRV: Low-frequency heart rate variability. BFNE: brief fear of negative evaluation. MSR: Mehrabian’s sensitivity to rejection.
scale (trait anxiety: $r = 0.54, p < 0.01$ & depression: $r = 0.46, p < 0.01$) and the MSR scale (trait anxiety: $r = 0.31, p < 0.01$ & depression: $r = 0.23, p = 0.01$). In contrast, neither of the mental health variables was significantly associated with cardiovascular measures (trait anxiety: $rs = -0.14 \sim 0.10, p > 0.05$ & depression: $rs = -0.12 \sim 0.02, p > 0.05$) or sensitivity to physical pain (trait anxiety: $rs = 0.06 \sim 0.10, p > 0.05$ & depression: $rs = -0.03 \sim 0.17, p > 0.05$). Those mental health variables that were significantly associated with social pain measures were then entered into the follow-up analysis as covariates to test the relationship between cardiovascular and social pain measures. On the other hand, the follow-up analysis was not performed for the association between RMSSD and pain threshold because mental health variables were not associated with either of them.

### 3.3.2. Hierarchical regression analysis

Results from the analysis are presented in Table 3. In general, adding cardiovascular measure to the regression model as the second block of independent variable helped explain an additional, small portion of the variance in social pain measures after statistically controlling for the covariates ($R^2$ changes $= 0.02 \sim 0.04$).

In general, inclusion of covariates in the analysis made a very minimal impact on the associations between cardiovascular and social pain measures: Even after statistically controlling for the covariates, the association between resting BP and MSR scores remained significant (SBP: $\beta = -0.20, t = -2.32, p < 0.05$ & DBP: $\beta = -0.22, t = -2.60, p < 0.05$). Also, accounting for covariates did not change the significance of the associations between resting HRV and BFNE scores (LF-HRV:

---

**Figure 2.** The positive link between HF-HRV and sensitivity to social pain. Higher values from the HF-HRV measure were associated with higher scores on the BFNE (Panel A: $r = 0.24, p < 0.01$) and MSR scales (Panel B: $r = 0.19, p < 0.05$). Lower numbers on the BFNE and MSR scales indicate lower sensitivity to social pain. HF-HRV: high-frequency heart rate variability. BFNE: brief fear of negative evaluation. MSR: Mehrabian’s sensitivity to rejection.
Table 3. Summary of hierarchical regression analysis for cardiovascular and pain measures with covariates.

<table>
<thead>
<tr>
<th></th>
<th>Block 1</th>
<th>Block 2</th>
<th>Block 1</th>
<th>Block 2</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SBP-MSR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait Anxiety Depression</td>
<td>0.30</td>
<td>0.03</td>
<td>0.24</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>2.38*</td>
<td>0.20</td>
<td>1.95#</td>
<td>0.43</td>
</tr>
<tr>
<td>DBP</td>
<td>0.20</td>
<td>-2.32*</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>HF-HRV-Depression</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait Anxiety Depression</td>
<td>0.30</td>
<td>0.02</td>
<td>0.24</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>2.38*</td>
<td>0.14</td>
<td>1.89#</td>
<td>0.38</td>
</tr>
<tr>
<td>DBP</td>
<td>-0.22</td>
<td>-2.60#</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LF-HRV-DBP</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait Anxiety Depression</td>
<td>0.26</td>
<td>0.05</td>
<td>0.26</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>2.80*</td>
<td>0.38</td>
<td>2.80*</td>
<td>0.38</td>
</tr>
<tr>
<td>HF-HRV</td>
<td>-0.16</td>
<td>-1.86#</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LF-HRV-BFNE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trait Anxiety Depression</td>
<td>0.42</td>
<td>0.16</td>
<td>0.37</td>
<td>0.20</td>
</tr>
<tr>
<td></td>
<td>3.84**</td>
<td>1.43</td>
<td>3.46**</td>
<td>1.82**</td>
</tr>
<tr>
<td>HF-HRV</td>
<td>-0.21</td>
<td>-2.81**</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BFNE: Brief Fear of Negative Evaluation
MSR: Mehrabian’s Sensitivity to Rejection
SBP: Systolic blood pressure
DBP: Diastolic blood pressure
LF-HRV: Low-frequency heart rate variability
HF-HRV: High-frequency heart rate variability

4. Discussion

A longstanding finding from the physical pain literature is that resting cardiovascular activity, in particular BP, predicts sensitivity to physical pain. Recently, this link has been extended to the domain of social pain. The present study aimed to replicate past findings regarding the link between physical pain and social pain, and the inverse relationship between resting BP and sensitivity to social pain. In addition, the present study was the first to explore the relationship between additional cardiovascular measures (HRV) and sensitivity to social pain. The results not only successfully replicated the inverse association between resting BP and sensitivity to social pain, but also demonstrated an inverse association between LF-HRV and sensitivity to social pain. These findings add to a broader literature suggesting that physical pain and social pain share biological substrates.

In agreement with previous findings (Inagaki et al., 2018), resting BP was inversely associated with individual differences in sensitivity to social pain. Importantly, the present study extended this finding by demonstrating a similar inverse association between LF-HRV and sensitivity to social pain. Thus, higher resting LF-HRV was associated with lower sensitivity to social pain. It has been shown that LF-HRV implicates baroreflex function, and correlates positively to baroreflex sensitivity (Goldstein et al., 2011). Baroreflex sensitivity, in turn, reflects neural activities that contribute to BP control, with greater sensitivity indicative of greater afferent neural inputs to the brain regions that are involved in the regulation of BP and physical pain (e.g., nucleus tractus solitarius, periaqueductal gray area, etc.) (Bruehl & Chung, 2004; Ghione, 1996). Consistent with the role of the baroreflex sensitivity in physical pain regulation, there is evidence that baroreflex sensitivity is inversely associated with sensitivity to physical pain (Duschek et al., 2013), which is likely mediated by activation of the descending inhibition of physical pain in response to baroreceptor stimulation that is caused by elevation of BP (Bruehl & Chung, 2004; Ghione, 1996). Therefore, the present study collectively suggests that the descending inhibitory mechanism of pain that is linked to the cardiovascular system may be a shared regulatory mechanism for both physical pain and social pain.

Contrary to our hypotheses, higher HF-HRV was related to greater sensitivity to social pain. We hypothesized an inverse association based on observations that chronic pain patients typically show reduced resting HRV compared to healthy controls (Koenig, Falvay et al., 2016; Koenig, Williams et al., 2016; Meeus et al., 2013; Tracy et al., 2016). Unfortunately, there is only a limited
amount of data regarding the relationship between resting HF-HRV and sensitivity to laboratory physical pain. Further, the findings are inconsistent: some studies report an inverse association between resting HF-HRV and sensitivity to physical pain (Tracy, Jarczok et al., 2018; Tracy, Koenig et al., 2018), whereas other studies report no correlation between them (Appelhans & Luecken, 2008; Meuse et al., 2013). In contrast, the present study showed a positive association between resting HF-HRV and sensitivity to social pain. Together, the relationship between resting HF-HRV and sensitivity to social pain is currently unclear. We evaluated sensitivity to social pain using self-report questionnaires in the present study, but others have used an experimental paradigm, called “Cyberball”, to manipulate social exclusion in a computer-game environment (Hartgerink et al., 2015; Williams et al., 2000). A recent study then shows that individuals generally exhibit increased HF-HRV compared to their baseline in response to social exclusion created by the Cyberball paradigm (Liddell & Courtney, 2018). Although the study shows the increased HF-HRV as a result of social exclusion rather than predictive role of increased HF-HRV in social pain experiences, the study suggests that a positive link may potentially exist between HF-HRV and social pain. However, sensitivity to social pain, which was evaluated at the trait level using the questionnaires in the present study (e.g., fear that social interactions, in general, will result in rejection or discomfort), may not be equivalent to acute experience of experimental social exclusion. More research is needed to determine the relationship between resting HF-HRV and social pain.

Alternatively, the positive relationship between resting HF-HRV and sensitivity to social pain may be explained by multi-dimensionality of social pain constructs. Although we conceptualized social pain as an emotional pain that shares underlying neurophysiological mechanisms with physical pain, others have argued that social pain reflects socio-emotional salience rather than emotional pain (Eisenberger, 2015; Iannetti et al., 2013). There is some evidence that resting HF-HRV is positively associated with the scores on an emotion recognition test (Quintana et al., 2012), suggesting a positive link between HF-HRV and socio-emotional salience. To the extent that social pain, as measured with the MRS scale, assesses salience, resting HF-HRV may be related to this part of the scale. However, more careful research is needed to tease apart the salience of an experience of social pain from sensitivity to being rejected in order to clarify the relationship between resting HF-HRV and sensitivity to social pain.

Based on past research that chronic pain patients are more sensitive to social pain, and those who are more sensitive to experimental physical pain are also more sensitive to experimental social pain (Eisenberger, 2015; Sturgeon & Zautra, 2016), we hypothesized a positive association between social pain and physical pain. However, sensitivity to social pain and physical pain was not related to one another in the present study. Although future research is needed to clarify why there was not an association in the present study, one explanation may be due to the way in which sensitivity to pain was assessed. Specifically, sensitivity to social pain was evaluated at the trait level, whereas sensitivity to physical pain was assessed at the state level (subjective responses to acute exposure to cold water). Had both sensitivity to pain measures been collected on the same scale, the expected correlation may have emerged. In support of this possibility, sensitivity to social pain was positively associated with similar trait-like mental health measures (anxiety and depression). No such correlations were observed between any of the trait measures and the state level sensitivity to physical pain measure. Future research that attempts to directly replicate previous correlational findings (i.e., between sensitivity in response to acute experiences of both social pain and physical pain) is needed to clarify the link between sensitivity to both forms of pain.

The present study also failed to support another hypothesis that resting BP was inversely associated with sensitivity to physical pain (Bruehl & Chung, 2004; France, 1999; Ghione, 1996). The inverse association between resting BP and physical pain was first examined with hypertensive adults in comparison to normotensive adults. Some studies have then shown that risk factors for hypertension, such as elevated resting BP (Bruehl et al., 1992; Dushek et al., 2009; McCubbin & Bruehl, 1994) and parental history of hypertension (Page & France, 1997; Stewart & France, 1996), are associated with decreased sensitivity to physical pain in normotensive adults. These findings suggest that a lack of information regarding parental history of hypertension may explain the null findings regarding resting BP and physical pain. Additionally, the other potential methodological issue that may explain the null findings is a physical pain modality that was used in the present study. Although CPT has been used widely as a laboratory pain measure in human research, our findings show that many individuals completed the 2-minute CPT, with large variability of pain threshold and moderate cold pain rating on average. The observations suggest that the null findings may be, at least partly, due to the floor effect of physical pain assessment. Together, although it is unclear why the present study failed to detect the expected association between resting BP and physical pain, it is possible that the methodological
issues may be responsible for the failure to replicate the previous findings.

There are several limitations to the present study. Current hypotheses are that resting cardiovascular measures will predict sensitivity to pain, but the cross-sectional design does not allow causal inference. Additional research, where resting cardiovascular measures in clinical pain populations are compared to healthy controls, or resting cardiovascular measures are experimentally manipulated, will provide more clarity regarding the causal influence of resting BP for sensitivity to social pain. Similarly, sensitivity to social pain was quantified using trait-level questionnaires. Future studies that experimentally manipulate social pain (e.g., via Cyberball) will further understandings of relationships between resting cardiovascular measures and sensitivity to social pain. Also, it is well known that sex differences exist in sensitivity to physical pain (Fillingim et al., 2009; Riley et al., 1998), as well as resting cardiovascular measures (Fu & Ogho, 2019; Koenig & Thayer, 2016; Oparil & Miller, 2005). However, the present study was not powered to test sex differences in those measures, as well as role of sex in the relationship between cardiovascular and pain measures. Future research is warranted to answer these questions.

In conclusion, the present study aimed to replicate past findings linking sensitivity to social pain and physical pain, and the inverse relationship between resting BP and sensitivity to social pain in healthy adults. The present study also aimed to explore the relationship between additional cardiovascular measures and sensitivity to social pain. The results indicated that while resting BP and LF-HRV were inversely associated with sensitivity to social pain, HF-HRV was positively associated with sensitivity to social pain. No significant associations between sensitivity to social pain and physical pain were observed in the present study. More research is warranted to further investigate the involvement of cardiovascular system in the processing of social pain.

**Acknowledgments**

The authors thank undergraduate and graduate research assistants who contributed to data collection for the present study. The study was supported by the institutional startup fund awarded to MU.

**Disclosure statement**

No potential conflict of interest was reported by the author.

**Funding**

The study was supported by the institutional startup fund awarded to MU.

**ORCID**

Masataka Umeda https://orcid.org/0000-0001-9420-6998

**References**


