The Impact of Emotion-Related Autonomic Nervous System Responsiveness on Pain Sensitivity in Female Patients With Fibromyalgia

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Objective: Patients with fibromyalgia have shown hyporeactive autonomic nervous system (ANS) responses to physical stressors, augmented pain to ANS changes, and heightened negative emotions, which can increase pain. This study examined ANS reactivity to negative emotions and its association with pain in fibromyalgia and control participants. **Methods:** Sixty-two women with fibromyalgia and 59 women in a control group recalled neutral, and anger- and sadness-eliciting experiences while ANS activity was monitored. Clinical and experimental pain were assessed in response to each emotion. **Results:** Compared with neutral recall, heart rate ($p = .050$), mean arterial pressure ($p < .001$), and high-frequency heart rate variability ($p = .012$) increased in response to sadness, whereas heart rate decreased ($p = .002$) and mean arterial pressure increased ($p < .001$) in response to anger; however, ANS responses did not differ between patients and control participants (all $p > .29$). Among patients only, decreased preejection period (anger-pain threshold: $r = 0.31$, $p = .018$) and total peripheral resistance in response to negative emotions (anger-pain tolerance: $r = 0.35$, $p = .025$; sadness-pain threshold: $r = 0.51$, $p < .001$; sadness-pain tolerance: $r = 0.61$, $p < .001$) correlated with more pain. **Conclusions:** These data suggest that the ANS is not hyporesponsive to elicited emotions in fibromyalgia; however, patients with a larger pain response showed an ANS response pattern reflecting heightened β-adrenergic and reduced α-adrenergic reactivity. Future research should test whether a specific ANS response pattern to emotions is a consequence of increased pain or whether it amplifies pain. **Key words:** autonomic nervous system, cardiovascular responsiveness, emotions, fibromyalgia, pain, stress.

ANS = autonomic nervous system; **BP** = blood pressure; **DBP** = diastolic blood pressure; **DWT** = Discrete Wavelet Transformation; **ECG** = electrocardiogram; **HF-HRV** = high-frequency heart rate variability; **HR** = heart rate; **IBI** = interbeat interval; **MAP** = mean arterial pressure; **PEP** = preejection period; **SBP** = systolic blood pressure; **TPR** = total peripheral resistance.

INTRODUCTION

Negative emotions such as anger and sadness can increase pain (1,2), which may be explained by emotion-related changes in autonomic nervous system (ANS) functioning (2–4). For instance, depression and anxiety are linked to increased sympathetic and reduced parasympathetic activity (5–7), and experimentally induced negative moods cause specific (phasic) physiological responses (8–10). In particular, anger is linked to increased reactivity of the sympathetic nervous system, which is mediated by both α- and β-adrenergic pathways, as well as reduced parasympathetic activity (9–12). Sadness elicits a heterogeneous pattern of sympathetic-parasympathetic coactivation (9).

ANS functioning has been linked not only to emotions but also to pain sensitivity. For example, elevated blood pressure (BP) and parasympathetically mediated heart rate variability in the high-frequency band (HF-HRV) are linked to reduced pain sensitivity (12–15). A few studies have explicitly examined the role of ANS responsiveness in the emotion-pain link in healthy individuals. These studies showed that emotion-related increases in the cardiac response were related to increases in pain unpleasantness (2,16) and that anger-induced increases in BP led to pain inhibition (12). Thus, the role of physiological reactivity in the association between emotional stressors and pain remains unclear, but this link may be relevant particularly for patients with chronic pain.

Fibromyalgia is characterized by widespread pain and other symptoms (17). People with fibromyalgia experience heightened levels of negative emotions (18,19), which increase pain both in daily life and when induced experimentally (20,21). Along with physical deconditioning and disturbed sleep, negative emotions in people with fibromyalgia may alter their basal ANS activity (22), such as increasing sympathetic and decreasing parasympathetic activity, which have been noted in some (23,24) but not all (25) studies of patients with fibromyalgia or widespread pain. According to general adaptation syndrome theory, after being hyperreactive initially, the ANS may become hyporesponsive after prolonged stress exposure, such as with chronic pain (26). In support of this hyporesponsiveness hypothesis, studies of the chronic condition fibromyalgia have observed a hyporeactive ANS response to a range of physical stressors, including vasoconstrictor responses to cold pressor, norepinephrine and heart rate (HR) responses to exhausting physical exercise, ANS responses to orthostatic stress, and epinephrine responses to induced hypoglycemia (27). Much less is known, however, about ANS responses to psychosocial stressors in people with fibromyalgia (24,28,29). Regarding emotional stressors, one study in chronic low back pain found HR and BP increases in response to both recalled anger and sadness, but did not compare these responses to a control group without pain (30). A study that did compare patients with low back pain and controls found that both groups had a similar sympathetic response to anger, but patients had a smaller response to sadness (31).

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Consistent with findings in healthy individuals, a link between tonic ANS activity and pain has been reported in studies of fibromyalgia (24,28) and chronic widespread pain (25). Moreover, a pilot study suggested greater pain sensitivity to injected norepinephrine, the neurotransmitter of the sympathetic nervous system, in patients with fibromyalgia than in healthy people or patients with rheumatoid arthritis (32). Overall, these findings on the prevalence of negative emotions, their adverse pain effects, and tonic and stressor-responsive ANS deviations in fibromyalgia highlight the importance of studying the physiological effects of emotions and the potential impact of emotion-induced ANS changes on pain in fibromyalgia.

In a previous study, we found that inducing the negative emotions of anger and sadness increased pain in both participants with fibromyalgia and control participants (20). We now examine the role of cardiovascular reactivity to anger and sadness and the association of both baseline ANS activity and emotion-induced ANS reactivity to clinical and experimental pain. We assessed both general cardiovascular measures that integrate sympathetic and parasympathetic activity (HR and BP) and cardiovascular measures that are specific to parasympathetic activity (HF-HRV), β-adrenergic sympathetic activity (preejection period [PEP]), and α-adrenergic sympathetic activity (total peripheral resistance [TPR]). On the basis of findings from ANS responses to physical stressors, we hypothesized that patients with fibromyalgia would show ANS hyporeactivity to anger and sadness compared with control participants and that ANS hyporeactivity would be related to increased clinical and experimental pain in the fibromyalgia group.

METHODS

Participants

Participants were 62 women with fibromyalgia and 59 control women aged 21 to 72 years. Patients were diagnosed by rheumatologists at hospitals in Utrecht and Almere, the Netherlands, according to established criteria (33). Control participants were recruited from the community excluding fibromyalgia. Both groups were recruited from larger samples that participated in a questionnaire study (18). For the present study, we excluded participants on β-blockers or angiotensin-converting enzyme inhibitors for high BP ($n = 13$), who were pregnant ($n = 3$), or who underwent thyroidectomy ($n = 1$). No participants had serious medical or psychiatric diseases that could interfere with ANS assessments. Patients had symptoms for a mean of 10 years (range, 1½-50 years). The patient and control groups did not differ on demographic characteristics, except that patients were less likely to be fully employed ($\chi^2 = 40.99$, $p < .001$). Participant characteristics are described in Table 1. Other details about recruitment, demographics, and health-related characteristics of the participants are presented elsewhere (20).

To prevent withdrawal influences on physiological and pain responses, participants used their regular medications. Patients with fibromyalgia did not differ during the experiment from controls in their use of antidiuretics (3% versus 5%), glucocorticoids (3% versus 2%), or thyroid medication (8% versus 2%), but were more likely to use analgesics (52% versus 10%, $\chi^2 = 24.10$, $p < .001$), antidepressants (27% versus 3%, $\chi^2 = 13.19$, $p < .001$), or other medications (e.g., cholesterol or allergy medication; 29% versus 10%, $\chi^2 = 6.77$, $p = .009$).

TABLE 1. Demographic and Health-Related Characteristics of Participants With Fibromyalgia ($n = 62$) and Control Participants ($n = 59$)

Characteristics	Fibromyalgia	Controls
Demographic		
Age, M (SD), y	46.3 (10.8)	48.9 (11.4)
With partner, *n* (%)	48 (77)	51 (86)
Ethnicity (indigenous), *n* (%)	56 (90)	57 (97)
Secondary education level, *n* (%)	44 (71)	35 (59)
Tertiary education level, *n* (%)	15 (24)	23 (39)
Health-related		
Fibromyalgia symptoms, M (SD), y	9.6 (7.7)	
Fibromyalgia diagnosis, M (SD), y	3.5 (4.1)	
Work status, *n* (%)***		
Employed full time	2 (3)	15 (24)
Employed part time	30 (48)	31 (53)
Not employed (including [early] retirement and being a homemaker or student)	15 (24)	14 (24)
Workmen's Compensation Act or receiving benefit	24 (39)	0 (0)
Reduced work status because of health, *n* (%)***	35 (57)	3 (5)
Comorbidity, *n* (%)		
Chronic somatic condition (besides fibromyalgia, e.g., lung disease)	13 (21)	4 (7)
Psychological or psychiatric problems (e.g., depression)*	11 (18)	2 (3)
Prescribed medication use, *n* (%)***	45 (73)	16 (27)
Unprescribed medication use (e.g., analgesics), *n* (%)**	39 (64)	20 (34)
Nonpharmacological treatments (e.g., physiotherapy, psychotherapy, alternative medicine), *n* (%)***	38 (61)	10 (17)

M = mean; SD = standard deviation.
Group differences tested by χ^2 tests, except for age (independent-samples *t* test).
*$p < .05$, **$p < .01$, ***$p < .001$.

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Measures

Emotions

Anger and sadness "now, at this moment" in response to the neutral, anger, and sadness conditions were assessed with two items each of the Positive and Negative Affect Schedule–Expanded Form (34): anger with "angry" and "irritable" and sadness with "sad" and "blue." Items were rated from 1 (*very slightly or not at all*) to 5 (*extremely*). Ratings for the two items for each emotion were summed (range, 2-10). Each pair of items showed excellent internal consistency (both α values = .85) in a previous study (21).

ANS Functioning

Biopac systems MP150 (Goleta, CA) with the software program AcqKnowledge 4.0 was used with ECG100C, NICO100C, and NIBP100A modules to collect continuous data (1000 Hz). The electrocardiogram (ECG) was assessed with a lead II configuration with two AgCl electrodes. For impedance cardiography, four strip electrodes were attached to the back, two close to the neck with a separation of 3 cm and two located 20 cm below, again separated 3 cm. BP was assessed by a wrist cuff.

HR was assessed from the ECG.

Mean arterial pressure (MAP) was determined from diastolic (DBP) and systolic (BP), which were monitored every 15 seconds, applying the formula DBP + ⅓[SBP − DBP].

Interbeat intervals (IBIs) were determined from ECG waveforms. IBI artifacts were corrected automatically based on a user-predefined percentage of the standard deviation from the moving mean of a particular segment or by visual inspection, according to described procedures (35–37). Next, HF-HRV power values (in the 0.125 to 0.5 Hz frequency band) were derived from the IBI time series using Discrete Wavelet Transformation (DWT), as described (36). The HF-HRV frequency band differs slightly from the guidelines (38) because of the use of DWT instead of fast Fourier transformation. DWT results in similar power values for relatively short stationary IBI data segments compared with fast Fourier transformation, but it is superior for nonstationary data segments. The HF-HRV power values were 10-log transformed to obtain a normal distribution.

PEP was assessed from analysis of the combined ECG and dZ/dt samples that make up the impedance cardiography waveforms within an interactive program from Data Analysis and Management Software for an ambulatory monitoring device called the VU-AMS device (VU University, Amsterdam, the Netherlands; http://www.vu-ams.nl/vu-ams/software/).

TPR was assessed by applying the formula MAP/cardiac output * 80, with cardiac output being derived from the VU-AMS software.

Clinical and Experimental Pain

Clinical pain assessments consisted of reporting current pain levels ("now, at this moment") on a 100-mm visual analog scale with anchors of "no pain at all" to "intolerable pain." Clinical pain assessments were analyzed only for patients with fibromyalgia because control participants had uniformly low ratings.

Experimental pain was evoked by means of electrical pain induction because we wanted to assess short-lived pain repeatedly in the same person. Pain was induced with a Tursky concentric electrode attached to the inner side of the nondominant forearm (39). For 40 seconds, an electric current was gradually increased from 0 mA to a maximum of 6 mA. Participants pressed a button when they felt the current (sensory threshold) and when it became painful (pain threshold) and intolerable (pain tolerance) at which time the stimulus was terminated immediately and the next trial started. Four experimental pain trials were conducted per condition, thus lasting a maximum of 160 seconds. Very high internal consistencies were obtained (Cronbach α from .94 to .99). Pain threshold and tolerance showed a consistent increase across the four trials in all three conditions (p values <.001) but did not differ between the anger and sadness recall conditions (p values >.30). Median values rather than means were analyzed to deal with occasional outliers.

Procedure

The protocol of the study was approved by the research and ethics committee of the University Medical Center Utrecht, and all participants provided written informed consent. Data were collected between December 2006 and January 2008.

Emotion Induction

An autobiographical recall procedure was used to induce the intended emotion. The participant recalled an event in which she felt neutral (a general everyday event, such as taking a walk), angry (an event that still evoked angry feelings), or sad (such as a death of a family member). This procedure has high ecological validity and strongly elicits the intended emotions (40,41). Participants were asked to describe every detail and to continue talking until they felt the emotion strongly and then to think silently about their experience for 2 minutes, to obtain physiological measures that were not contaminated by talking. The neutral condition was always presented first, to provide a baseline assessment of emotion, physiology, and pain and to reduce the occurrence of carryover effects between conditions. Next, either anger was elicited followed by sadness or sadness was elicited followed by anger. The order was determined randomly, stratified by patient versus control status.

Cardiovascular Measures

Electrodes, BP cuff, and the electrical pain stimulus device were attached and tested. To reduce artifacts (e.g., of movement), the most reliable 90-second period of all physiological indices during the 120 seconds of silent recall was selected for analyses.

Self-Rated Measures

Immediately after each of the three conditions (neutral, anger, sadness), participants completed the state emotion and pain questions followed by the experimental pain assessment.

Return to Baseline

Between each of the conditions, participants counted backward from 25 to 0, read a neutral magazine for 5 minutes, and watched a relaxing nature video for 5 minutes to distract attention away from the emotion that was evoked and to induce relaxation. ANS activity returned to baseline after each condition. After the third condition, participants were debriefed, received reimbursement for travel expenses, and completed an evaluation questionnaire. The experimental session lasted approximately 2 hours.

Data Analyses

Analyses included between-person (fibromyalgia versus control) and within-person (neutral induction followed by anger and sadness inductions) comparisons. The neutral condition was used as the comparison condition to control for the effects of engaging in a recall task, thus studying the unique contribution of the negative emotions to ANS and pain responses (42).

Baseline differences in ANS activity during the neutral condition were examined with independent-samples t tests. However, consistent with recommendations (43), PEP and TPR were compared only within group because of large interindividual differences in scoring of the b-point. Physiological reactivity to anger and sadness was examined using repeated-measures analyses of variance for each physiological variable separately, with group (patients versus controls) and order (anger-sadness versus sadness-anger) as between-participant factors and condition (neutral, anger, sadness) as a within-participant factor. Significant condition effects were followed by post hoc Bonferroni tests between each of two conditions (neutral-anger, neutral-sadness, anger-sadness). Analyses were repeated including disease duration as a covariate. For measures of effect size, partial eta squared (η_p^2) or Cohen d coefficients were used (44). Pearson correlations were calculated between physiological (re)activity scores and changes in clinical and experimental pain. Correlational analyses were performed for the two groups separately, with exclusion of multivariate outliers of the correlated variables (based on Cook distance >1 in regression analyses).

Sample size was based on a power analysis conducted with the program G*Power 3.1 (45). A total sample of 120 were needed to detect a small difference (f = 0.10) between two groups (the group * condition interaction for one emotion [experimental versus neutral], α = .05, 1 − β = 0.80, r = 0.70). The achieved power (1 − β) with a more conservative α of .01 and the smallest

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sample size of 79 is 0.37 for a small effect size and 0.99 for a medium effect size ($f = 0.25$).

RESULTS

Emotion Induction and Pain

Both groups had substantial anger and sadness increases from the neutral condition in response to the induction of anger and sadness (see our previous article (20)) The emotionality of the participant to both anger and sadness recall as judged by the researcher during recall, and the self-reported ability of the participant to think of and to imagine a previous anger- and sadness-provoking situation did not differ between patients and controls (all p values >.25). In response to the anger and sadness induction, clinical pain reports increased in the patients with fibromyalgia; pain threshold and tolerance decreased in both groups equally (20).

ANS (Re)Activity

Owing to equipment problems, there were occasional missing data on some physiological measures. Below, we report results for each measure with all available data. However, repeating the analyses only for those participants who had complete data across all measures (patient group: $n = 40$, control group: $n = 39$) did not meaningfully change the results.

Emotion-Induced HR and MAP Reactivity

Figure 1 presents the HR and MAP levels during silent recall. Patients with fibromyalgia had a higher HR ($t(115) = -3.12$, $p = .002$, $d = 0.58$) and a lower MAP ($t(97) = 2.20$, $p = .030$, $d = 0.44$) than did controls.

Figure 2A and B shows HR and MAP reactivity to anger and sadness compared with neutral recall. For the entire sample, HR decreased in response to anger ($p = .002$, $d = 0.31$) and increased in response to sadness ($p = .050$, $d = 0.23$) compared with the neutral condition; HR was significantly lower during anger than during sadness ($p < .001$, $d = 0.41$; condition effect: $F(2,226) = 12.95$, $p < .001$, $\eta_p^2 = 0.10$). A significant condition * order effect ($F(2,226) = 9.54$, $p < .001$, $\eta_p^2 = .08$) reflected no significant changes in HR when the anger situation was recalled before the sadness situation ($d = 0.07$ and 0.10 for anger and sadness compared with neutral), whereas HR decreased in response to anger ($d = 0.61$) and increased in response to sadness ($d = 0.34$) when sadness was recalled before anger.

For the entire sample, MAP increased in response to both anger ($p < .001$, $d = 0.41$) and sadness ($p < .001$, $d = 0.75$) compared with the neutral condition; MAP was significantly higher during sadness than anger ($p = .001$, $d = 0.39$) (condition effect: $F(2,178) = 29.02$, $p < .001$, $\eta_p^2 = 0.25$). Order did not affect these outcomes (condition * order effect: $p = .64$).

Emotion-induced HR and MAP reactivity did not differ between patients and controls (condition * group effect: $p = .41$ and .30). In patients with fibromyalgia, there was no interaction of emotion-induced HR and MAP reactivity with disease duration.

Emotion-Induced HF-HRV, PEP, and TPR Reactivity

Patients and controls did not differ in HF-HRV during neutral recall ($p = .46$). Figure 2C shows the HF-HRV reactivity to anger and sadness compared with neutral recall. For the entire sample, compared with the neutral condition, HF-HRV increased in response to sadness ($p = .012$, $d = 0.28$) but did not in response to anger ($p > .99$). Also, HF-HRV was higher during sadness than during anger ($p = .004$, $d = 0.31$) (condition effect: $F(2,226) = 6.34$, $p = .002$, $\eta_p^2 = 0.05$). Results did not differ by order (condition * order effect: $p = .86$).

Figure 2D and E shows the reactivity of PEP and TPR in response to anger and sadness compared with neutral recall. For the entire sample, the recall of anger and sadness did not affect PEP (condition effect: $p = .15$) or TPR ($p = .97$). Also, reactivity did not differ as a function of the order of emotion recall (condition * order effect: $p = .090$ and .56 for PEP and TPR).

Emotion-induced HF-HRV, PEP, and TPR reactivity did not differ between patients and controls (condition * group effect: $p = .29$, .80, and .17). In patients with fibromyalgia, no interaction of emotion-induced HF-HRV, PEP, and TPR reactivity with disease duration was found.

Association Between Baseline and Emotion-Induced ANS (Re)Activity and Pain

In patients, a lower MAP during neutral recall was associated with higher clinical pain ($r = -0.27$, $p = .051$); none of

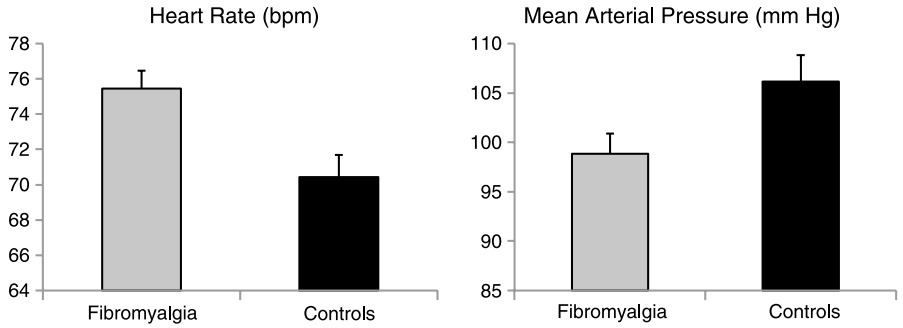

Figure 1. Baseline differences (with standard errors of the mean) in heart rate and mean arterial pressure between participants with fibromyalgia and control participants. bpm = beats per minute.

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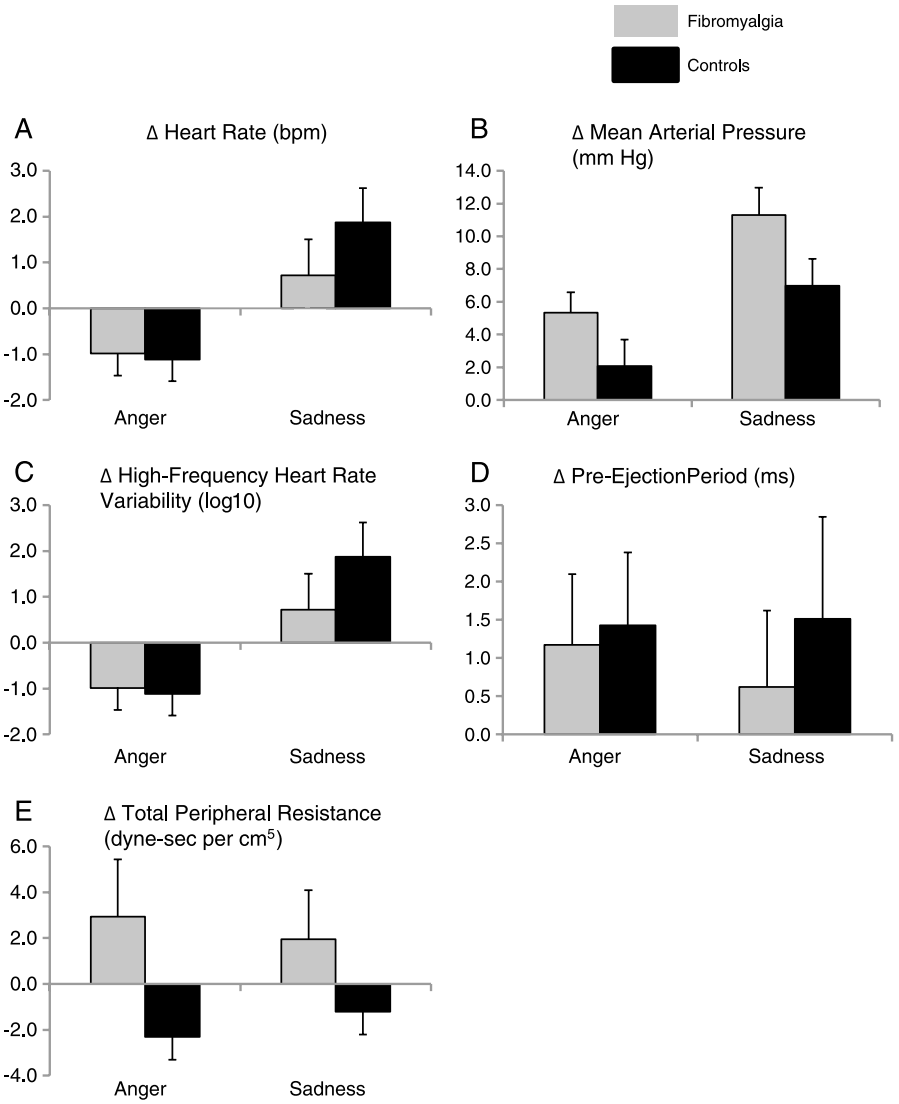

Figure 2. Reactivity in heart rate, mean arterial pressure, high-frequency heart rate variability, preejection period, and total peripheral resistance (with standard errors of the mean) in response to anger and sadness recall compared with neutral recall. bpm = beats per minute.

the other baseline ANS measures were associated with pain. Regarding reactivity, a larger decrease in pain threshold (i.e., more pain) was found in patients with a smaller decrease in HR reactivity to anger ($r = -0.33$, $p = .010$), which held after controlling for order ($r = -0.29$, $p = .027$). The same association was found for patients showing a larger reduction of PEP ($r = 0.31$, $p = .018$) to anger. A larger increase in pain threshold or pain tolerance (less pain) was found in patients showing a larger TPR increase in response to both anger (pain tolerance: $r = 0.35$, $p = .025$) and sadness (pain threshold: $r = 0.51$, $p < .001$; pain tolerance: $r = 0.61$, $p < .001$). These correlations were not significant in the control group. No associations were found between HF-HRV reactivity and pain.

DISCUSSION

This experimental study examined ANS reactivity to anger and sadness in women with fibromyalgia and from the general population, as well as the associations of baseline ANS activity and emotion-induced ANS reactivity with pain. The recall of anger and sadness elicited emotion-specific autonomic reactivity. In contrast to previous findings on ANS reactivity to physical stressors, we found no ANS hyporeactivity to emotional stressors in patients with fibromyalgia relative to controls. However, among patients, emotion-induced autonomic reactivity and pain were related. These findings are discussed in turn.

Patients with fibromyalgia had higher HR and lower BP tonic levels than did control participants, consistent with previous findings (23,24,28). This physiological alteration may be constitutional and potentially contributing to fibromyalgia or an epiphenomenon caused by pain, fatigue, psychological distress, sleep disturbance, physical inactivity, or low fitness (27). In our patient group, lower baseline BP was associated with more clinical pain, as has been found in the general, normotensive population (46,47). The observed tonic abnormalities and the inverse association of baseline BP with clinical

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pain support the relevance of examining emotion-induced ANS functioning in fibromyalgia.

Studies of ANS reactivity to emotional stressors in healthy individuals have been inconsistent regarding emotion specificity or generality (e.g., Refs. (9,10)). In our study, anger and sadness recall elicited emotion-specific autonomic reactivity patterns. Anger increased BP but decreased HR. The increased BP may have resulted from activation of α-adrenergic receptors reducing HR via the baroreceptor reflex (48), which may play a role in pain inhibition (49). In fibromyalgia, diminished baroreflex sensitivity has been associated with pain (24,50). However, patients did not differ from controls in this simultaneous decrease of HR and increase in BP during anger, and neither increased BP nor decreased HR or TPR in response to anger was related to pain. Thus, our results obtained with an emotional stressor instead of a physical stressor, such as the cold pressor, to activate the baroreflex system do not indicate a disturbance of this system in fibromyalgia. Sadness, in contrast to anger, elicited increases in HR, BP, and HF-HRV, which suggests a coactivation of the sympathetic and parasympathetic systems (51), in line with findings in healthy populations (9).

Consistent with other studies (9,10), BP increased in response to anger, but the HR response to anger seems inconsistent with some previous research, which may be partly explained by specifics of the emotion induction procedure. Although anger is generally conceived to be an activating emotion accompanied by α- and β-adrenergically mediated increased HR, MAP, and TPR, there are various types of anger that are differentiated by motivational direction and cardiovascular response (9). In contrast to approach-oriented anger, HR may decrease in withdrawal-oriented anger (52), which can occur when people are asked to recall a previous event from their lives, as in our study. Studies using stressful interviews or anger-arousing pictures or films have found no changes in HR (9). This lack of increase in HR may also stem from a unique aspect of our experimental design. Most studies showing an anger-induced cardiac acceleration have used a resting baseline as the comparison condition, and the anger induction was often accompanied by talking, a behavior that by itself increases HR. Indeed, one study showed an HR increase in response to storytelling, but not an additional increase in response to anger induction (53). We also note that HR decreased in response to anger recall only after sadness recall, but not when anger was the first negative emotion recalled. This order effect is difficult to explain; it could be an aftereffect of the large HR and MAP increases in response to sadness. Also, although the absolute decrease in HR was small, as can be seen in Figure 2A, the change in HR is significant because stable individual differences go with a small standard error. Finally, in addition to HR, HF-HRV increased in response to sadness recall and did not change in response to anger recall. These findings contradict most previous literature showing vagal withdrawal, or HF-HRV reduction, to both sadness and anger (9,10); nonetheless, unchanged HF-HRV has been found previously in response to anger (9,10).

Regarding sadness, HRV changes seem to depend on whether the sadness was anticipatory (about a future loss) or acute (experienced loss) and whether or not sadness was accompanied by crying (activating versus deactivating response). Many people in our experiment cried in response to the sadness recall (20), suggesting an activating response, which seems to be accompanied by increased HR and MAP and decreased, unchanged, or increased HF-HRV, with increased HF-HRV being observed mainly in increased sadness intensity and in sadness situations in which the loss has already occurred (9). Also, in our study, participants recalled a sad situation from their past that still made them very sad, and HF-HRV increased compared with the neutral situation.

Finally, unlike some studies that found low tonic HF-HRV in fibromyalgia (24,54), we found no alteration of vagal tone. A meta-analysis of parasympathetic activity indices in functional somatic disorders including fibromyalgia has shown that only 22% of all studies reported significantly lower parasympathetic activity, whereas the remaining 78% found no effect (55). To conclude, although the results of the current study are not always consistent with most previous research, the results are not unique and can potentially be explained by specifics of the design. Nonetheless, we found that both anger and sadness elicited ANS reactivity, which was an important precondition for examining the potential hyporeactivity in patients compared with controls and the relationship of emotion-induced physiological reactivity to pain.

Patients with fibromyalgia did not differ from controls in their autonomic reactivity to personally relevant emotional events. We found no evidence that disease duration influenced this effect. Therefore, if we exclude ANS hyporesponsiveness as an explanation of the emotion-pain link, there are several alternative neural, physiological, and psychological mechanisms. Neurally, there is a close anatomical relationship between pain and emotion circuits in the brain (3,56,57), with emotional and physical pain sharing a common neural alarm system (58,59). Physiologically, reduced responsiveness of the hypothalamus-pituitary-adrenal axis in response to negative emotions might increase nociception (23,60). Psychologically, negative emotions may affect the processing of pain through altered attentional processes (3,12,61).

Although patients with fibromyalgia did not show different reactivity to emotional stressors than did controls, there were significant associations between emotion-induced ANS (re)-activity and pain among the patients. The data suggest that a stronger β-adrenergic (i.e., more PEP decrease) and a smaller α-adrenergic response (i.e., less TPR increase) to negative emotions is associated with increased pain in fibromyalgia. The health consequences of this pattern are hard to interpret. Whereas many cross-sectional studies have indicated that better physical fitness is associated with attenuated psychophysiological responses (62,63), randomized controlled trials shed doubt on this (64). The cumulative evidence of experimental studies does not support the idea that cardiorespiratory fitness is generally related to an attenuation of stress reactivity. Instead, fitness is related to slightly greater reactivity, but also better recovery with generally small

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and heterogeneous effect sizes (65). Thus, considering the inconsistencies in the literature, the health consequences of the stronger β-adrenergic response to emotions in our study are not clear. Moreover, the reduced TPR increase could be adaptive because typical tasks activating the α-adrenergic system (e.g., the cold pressor) aggravate pain (66,67). Because our study was not powered to do extensive covariate analyses, we were not able to examine the influence of possible moderators of the associations found between ANS (re)activity and pain in the fibromyalgia group such as medication use, physical fitness, and depression (22,25). Thus, we observed that the ANS response pattern of patients with fibromyalgia is related to pain, but we do not know whether this reaction is adaptive or maladaptive. Future research may focus on the possible mechanisms of the relations between pain and ANS reactivity found in fibromyalgia.

Our results indicate either that patients with fibromyalgia with more pain are more sensitive to emotion-induced ANS changes or that the emotion-induced ANS changes have consequences for pain in fibromyalgia. Patients with fibromyalgia experience negative emotions in their daily lives and use emotion avoidant strategies more often than controls (18,68,69), and expressing intensely experienced emotions may be associated with lower pain (70). Experimental trials targeting emotional functioning are needed to understand the cause-effect relationships among emotions, ANS reactivity, and pain in fibromyalgia.

Strengths of the present study include the specification of physiological subsystems instead of a focus solely on the global ANS indices of HR and BP, the inclusion of two distinct emotions, the use of a neutral condition without the confound of talking, and the inclusion of both clinical and experimental pain. Limitations of the study include the large number of correlational analyses because of the desire to provide insight into the specific disturbed cardiovascular mechanisms in fibromyalgia, some missing physiological data, the within-person order effects that make interpretation of our HR results more difficult, the lack of direct respiratory measures, and the inherent difficulty of interpreting the directionality of associations. In addition, emotion recall as a way to test emotional responsiveness assumes that patients and controls have equivalent ability to recall and experience emotions and that the memories are equivalently evocative. Although we cannot exclude a group difference in, for example, imaginative capacity or defensive avoidance of emotions, we did not find experimenter-rated or self-reported differences between patients and controls in emotionality during recall. The limitation of using recall as emotion stimulus might be reduced by using standardized external emotion-eliciting stimuli such as film clips or role plays (42); yet, such external stimuli may have less ecological validity.

In conclusion, the present study was the first to compare emotion-induced ANS reactivity by analyzing indicators of parasympathetic and sympathetic (β- and α-adrenergic) activity in patients with fibromyalgia and in controls. Although patients with fibromyalgia showed deviant tonic ANS functioning, they did not differ from controls in their ANS reactivity to negative emotions. However, among patients with fibromyalgia, physiological responses indicative of larger β-adrenergic and smaller α-adrenergic ANS reactivity were related to higher experimental pain responses. Future longitudinal or experimental research should test whether the specific physiological reactivity to emotions is an adaptive or maladaptive consequence of increased pain sensitivity or whether this physiological reactivity is a potential pathway explaining how negative emotions amplify pain.

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