General Section
Research Paper

OPEN

PAIN REPORTS

Night time heart rate predicts next-day pain in fibromyalgia and primary back pain

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Abstract

Introduction: Primary chronic pain is pain that persists for over 3 months without associated measurable tissue damage. One of the most consistent findings in primary chronic pain is its association with autonomic hyperactivation. Yet whether the autonomic hyperactivation causes the pain or results from it is still unclear. It is also unclear to what extent autonomic hyperactivation is related to experienced pain intensity in different subtypes or primary chronic pain.

Objectives: Our first aim was to test lagged relationships between the markers of autonomic activation (heart rate) and pain intensity to determine its directionality. The main question here was whether autonomic biomarkers predict pain intensity or whether pain intensity predicts autonomic biomarkers. The second aim was to test whether this relationship is different between people with primary back pain and people with fibromyalgia.

Methods: Sixty-six patients with chronic pain were observed over an average of 81 days. Sleep heart rate and heart rate variability were measured with a wearable sensor, and pain intensity was assessed from daily subjective reports.

Results: The results showed a predictive relationship between sleep heart rate and next-day pain intensity ($P < 0.05$), but not between daily pain intensity and next night heart rate. There was no interaction with the type of chronic pain.

Conclusions: These findings suggest that autonomic hyperactivation, whether stress-driven or arising from other causes, *precedes* increases in primary chronic pain. Moreover, the present results suggest that autonomic hyperactivation is a common mechanism underlying the pain experience in fibromyalgia and chronic back pain.

Keywords: Wearable sensors, Primary chronic pain, Heart rate, Heart rate variability, Autonomic hyperactivation

1. Introduction

Primary chronic pain is pain that persists for over 3 months without associated measurable tissue damage. The mechanisms underlying this mysterious condition are still debated[25,51] and so is the question of whether different subtypes of primary chronic pain share similar underlying causes.[23]

Numerous findings link primary chronic pain to increased sensitivity of the central nervous system to stimulation[17,53,57] or decreased ability to downregulate pain.[7,9] In healthy people, hypersensitivity to pain is observed during negative emotional experiences.[2,13,54,56] It is then plausible to suggest that primary chronic pain is caused or exacerbated by experiences of stress and other negative emotions.[46] And indeed, multiple studies link predisposition to stress to presence of chronic pain,[29] increased stress to higher pain sensitivity in people with chronic pain,[10] and acquisition of stress-management techniques to decreased severity of chronic pain.[45] Yet on the other hand, psychosocial challenges associated with chronic pain are generally assumed to be a result of pain itself.[23,49]

The experience of stress is regulated by the autonomic nervous system (ANS), which also regulates bodily functions such as heart rate, digestion, and pupil size. Historically, the ANS has been conceptualized as 2 branches: sympathetic and parasympathetic, although the separability of these branches is increasingly being questioned.[52,60,65] Within the traditional view, ongoing negative emotional states such as chronic stress can be induced by sympathetic hyperactivation. However, the same outcome can come about through decreased activity of the

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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PR9 9 (2024) e1119

http://dx.doi.org/10.1097/PR9.0000000000001119

parasympathetic system. In fact, several accounts[55,59] emphasize the role of parasympathetic system underreactivity in states of chronic stress and poor mental health.[3,37,67]

Heart rate variability (HRV) and heart rate (HR) are often presented as markers of parasympathetic and sympathetic systems, respectively.[43] Heart rate is indexed as the number of heart beats per minute. Heart rate is regulated by multiple systems, including the heart's internal pacemaker. The most direct way in which the brain regulates the heart is by slowing its rate through activation of the vagus nerve.[55] Vagal activation produces slower and, most importantly, uneven heart beats. This is why parasympathetic activation is conceptualized as variability in the time that elapses between heart beats.

Decreased HRV is commonly observed in people with chronic pain,[26,66] especially in fibromyalgia,[6,66] as is an increase in HR.[33,58,62,64] These findings support the notion that chronic pain is associated with a dysregulated ANS, likely caused by an insufficiently active parasympathetic system. To investigate the directionality of this association, the present study examined the lagged relationships between the state of the ANS and primary chronic pain intensity. In addition, we compared 2 primary chronic pain conditions that provided the most consistent evidence (fibromyalgia[66]) and the least consistent evidence (chronic back pain[4]) of ANS dysregulation.

1.1. The present study

In this study, we focused on fluctuations of ANS and changes in pain intensity within 2 chronic pain cohorts, people with primary back pain and people with fibromyalgia. Previous studies have established that both ANS markers[12,41] and chronic pain intensity fluctuate from day to day.[47,63] In this study, we used wearable technology to track autonomic markers, allowing us to test the association of these markers with subjective pain reports over an extended period.

In a previous study testing the reliability of autonomic markers taken from wrist-worn sensors, we reported that high reliability of HR and HRV measurements can be achieved during sleep.[19] However, only HR, but not HRV, correlated with next-day mood. In a second pilot study, pain intensity was predicted by sleep HR in people with primary chronic pain of various subtypes, but not in pain-free controls.[21]

Here, we aim to test these associations again, in a larger group of people and over a longer time. We now also focus specifically on primary back pain and fibromyalgia to test whether the association varies for these 2 types of chronic pain. By measuring HR and HRV during sleep and pain intensity during the day, this study aims to determine whether changes in ANS markers precede or follow changes in reported pain intensity.

2. Methods

2.1. Participants

Using a safeguard approach, we estimated the target effect as the lower limit of the 80% CI on the effect size obtained in Ref. 21. We then used simulation approach to power analysis for generalized linear mixed models implemented as the simr package for R.[30,31] To address HR, HRV, and potential-moderating effect of painkillers, our target sample size was 35 participants per group (fibromyalgia vs back pain) with observational data for 2 months. Anticipating dropouts, we aimed to recruit up to 80 participants. Seventy-five people took part in the study. Of them, 66 provided at least 14 days of subjective metrics and sufficient amount of biometric data (see below) and were included in the analyses.

Participants were recruited using newsletters serving the local patient population with chronic pain (Pain BC) and the provincial platform for recruitment of participants into health research in British Columbia (Reach BC). Inclusion criteria were (1) aged at least 18 years, (2) presence of fibromyalgia or primary chronic back pain, (3) fluent English, (4) no history of heart disease, and (5) no injury or surgery in the 3 months before the study and no surgeries planned for the time of the study. The diagnosis of fibromyalgia or chronic back pain (or both, see below) was self-reported. Volunteers were also asked to report any other conditions that could be related to pain, and people with such conditions (eg, cancer, rheumatoid arthritis, osteoarthritis, or spondylosis) were not included in the study.

2.2. Procedure

Participants were asked to track their emotional state, pain intensity, and heart biometrics for 2 to 3 months. **Figure 1** shows the daily study procedures. Participants were instructed to wear the wristband sensor for sleep only (main sleep period of the day, not naps). Subjective state was reported during participants' waking time.

2.2.1. Subjective experience

We used the Ecological Momentary Assessment tool to track daily subjective experience.[38] Using RealLifeData app (https://www.lifedatacorp.com), participants were prompted 3 times a day at random times between 7 AM and 9:30 PM with 5 to 7 questions each time. The questions assessed, in this order: (1) emotional experience (reported elsewhere) and (2) pain intensity assessed using the standard 11-point pain scale.[35] At the end of each day, participants were asked whether they used any symptomatic pain medication (yes/no question) and nonmedical pain modulators (yes/no question), and if yes, when they took it for the first time during that day. Information about regular and symptomatic pain medication brand names and dosages was collected in the intake survey (see below).

2.2.2. Objective state

Heart rate and heart rate variability were tracked using the Biostrap wearable sensor (www.biostrap.com), which captures beat-to-beat intervals by using photoplethysmography (PPG). From it, HR is computed as beats per minute (BPM), HRV is computed as root mean square of successive differences (rMSSD) between heart beats. Root mean square of successive difference is the most reliable and widely used time domain measure of vagal tone.[43] It is the measure provided by most wearable sensors of HRV.[5,27,36] Beat-to-beat intervals are sampled for 60 seconds, with 86 Hz frequency, automatically on 2-minute cycles. The data collected by the device are then passed to a smartphone app, which transfers it to the Biostrap servers for filtering and processing.[22] Dur et al. (2018) demonstrated that BPM and rMSSD measured with Biostrap correlated with those assessed with ECG at $r = 0.994$ and $r = 0.924$, respectively.

The sensor also detects oxygen saturation and respiration rate, making it possible to control for these biometrics when assessing HRV. In addition, the Biostrap device contains an accelerometer to detect movement, and HRV values obtained during movement are automatically discarded.[39]

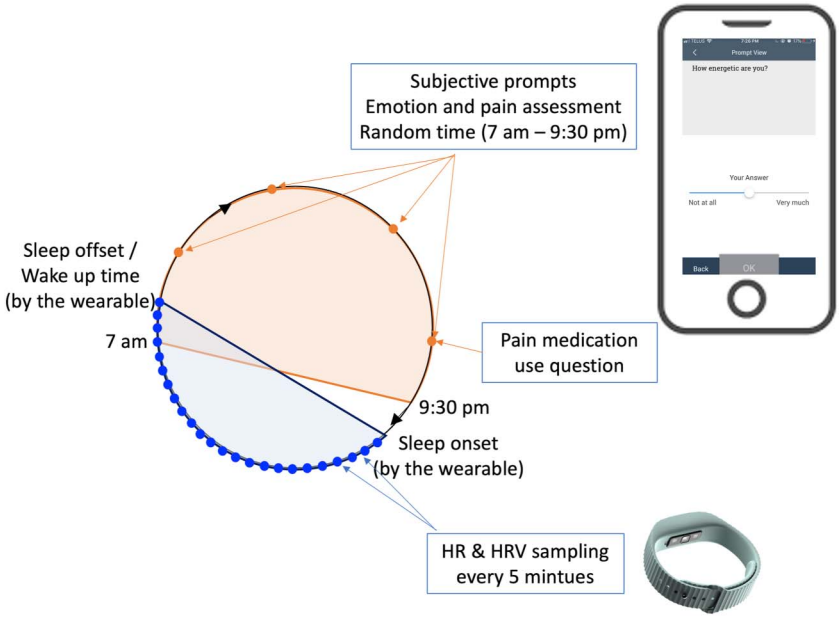

Figure 1. Overview of daily study procedures. The circle represents a day of study. Each dot on the circle represents data collection point: blue dots for biometric data collected with a wearable sensor during sleep and orange dots for subjective data collected using RealLife app during wakeful hours. HR, heart rate; HRV, heart rate variability.

Participants could not see their biometrics or subjective state measures for the duration of the study, and only saw their results on completion.

2.2.3. Additional information

Participant demographic and medical information was collected at the time of recruitment: age, sex, medical diagnoses (pain-related and pain-unrelated), regularly and symptomatically used medications, and duration of chronic pain. The questionnaires were administered through RealLifeData app. In addition, participants filled out questionnaires assessing pain interference (Pain Disability Index[11]), depression, anxiety, alexithymia, emotion regulation, interoceptive awareness, psychological well-being, and physical activity (reported elsewhere).

All aspects of this study were approved by the Behavioral Research Ethics Board of the University of British Columbia (approval number H19-03824). All participants gave informed consent to participate in the study.

2.3. Data processing

Heart rate was assessed as BPM and HRV was indexed as the root mean square difference between successive beats (rMSSD), and both measures were determined by Biostrap on recording PPG and processing it with Biostrap proprietary algorithms.[22] Heart rate and HRV recording samples were screened by removing 0 values. Heart rate and HRV values for the samples where SPO_2 was 0 or 100 were also excluded.

Sleep periods were determined by removing datapoints that were more than 5 hours away from a next and previous recorded measurement. This is based on an observation that during periods of immobility (sleep or watching a movie) most measurements which are automatically attempted every 2 minutes are successful. In contrast to that, during wakeful activity very few datapoints survive artifact and movement monitoring, and the successful recordings are very sparce in time. Sleep periods shorter than 2 hours were removed. Within the remaining sleep periods, BPM and HRV values more than 2 standard deviations above each participant's average were removed. Finally, nights with less than 20 BPM samples were discarded. This resulted in one participant losing all their biometric data.

For regression analyses, we used HR and HRV averaged per sleeping period per participant and subjective pain ratings averaged per day per participant. Missing data were not interpolated. Sixty-six participants with on average 81 days/nights (not necessarily consecutive) provided sufficient data for mixed model regressions. Day count was included in all regressions to account for the near-consecutive character of the data.

2.4. Analyses

The focus of the study was testing the predictive association between sleep heart rate and daytime pain intensity. The preregistered analysis[20] was an multilevel model (MLM) regression predicting pain intensity from (1) sleep HR (preceding the day of pain), (2) day of study, (3) proportion of day with painkiller, and (4) pain type, and all possible interactions as fixed factors, and participant as the random factor. In addition to this analysis, we report the same analysis as used in Ref. 21: MLM regression predicting pain intensity from sleep HR, HRV, day of study, and pain on the previous day as fixed factors to account for autocorrelation of pain. MLM regressions were conducted in R using package lmerTest.[42] Additional analyses (t-tests) were performed to compare the 2 pain groups in pain intensity, HR, and HRV.

3. Results

Sixty-seven participants provided at least 14 days of subjective responses, and over 70 days on average (average age 47.7, range 22-79, sex: 4 male, 60 female). One participant kept responding to daily questions after they returned the sensor to the study team and reached 176 days of participation. For this

participant, only days until returning the sensor were included in the analyses (n = 115). One participant had no biometric data left after data cleaning (see Section 2.3).

The final sample included 66 participants: 28 with chronic back pain and 38 with fibromyalgia. We aimed to recruit equal number of people with fibromyalgia and chronic back pain and performed prescreening (by subjective reports) to achieve that. However, some people recruited into the chronic back pain group endorsed fibromyalgia diagnosis in the intake survey. We use endorsed diagnoses in all following assignments, classifying people with fibromyalgia (with or without back pain) as the fibromyalgia group and those with back pain only as the back pain group.

Of all participants, 9 reported an injury or surgery within 3 months before the study and 3 people had emergency hospital admissions during the study. Exclusion of these participants does not change the patterns of the results or their significance.

3.1. Between-participant comparisons

Patients with fibromyalgia and back pain did not differ on age, average HR, HRV, or number of days with biometrics, all $P's > 0.1$. However, participants with fibromyalgia experienced more years with chronic pain, higher pain intensity, and interference (**Table 1**, **Fig. 2**), suggesting higher severity of their chronic pain condition. In addition, participants with fibromyalgia provided significantly more days with subjective reports. To balance the amount of data for the 2 groups, we limited all analyses to the first 60 days for everyone.

3.2. Within-participant correlations

3.2.1. Predicting daily pain intensity

Within-participant reliability[19] was high for both HR and HRV, 0.99 and 0.88, respectively. Normality and homoscedasticity assumptions for all the models reported below were assessed by visual inspection of the residual and Q-Q plots. The absence of any correlation in these plots, along with no other apparent systematicity, indicated that no violations of the assumptions were evident. After,[21] we performed MLM regression predicting pain intensity from sleep HR, HRV, pain intensity on the previous day, and day of study as fixed factors. Daily pain intensity was predicted by HR on the previous night, $b = 0.012$, $t(2474) = 2.78$, $P = 0.005$, and pain on the previous day, $b = 0.36$, $t(2478) = 20.03$, $P < 0.001$. This pattern of results suggests that daily pain is autocorrelative, ie, current pain is best predicted by pain on the previous day, which is not surprising. Importantly, above and beyond autocorrelative predictiveness, daily pain is also predicted by sleep HR.

Does use of symptomatic painkillers moderate this result? We computed proportion of days when painkillers were used, for each participant, and added this as a factor to the model described above, as well as the interactions between painkiller use and each of the biometrics. Painkiller was associated with higher pain, $b = 2.27$, $t(959.7) = 2.22$, $P = 0.027$, suggesting that participants with higher pain intensity were taking symptomatic painkillers more often. Above and beyond this effect, pain intensity was still predicted by sleep HR, $b = 0.004$, $t(2421) = 2.90$, $P = 0.004$, and pain on the previous day, $b = 0.36$, $t(2470) = 20.05$, $P < 0.001$. There was no interaction between sleep HR and painkiller, $P = 0.09$.

Does pain type moderate this association? MLM predicting pain intensity from sleep HR, HRV, pain type, the 2-way interactions between pain type and the 2 biometrics, pain on the previous day, and day of study as fixed factors revealed only 2 significant effects: that of pain on the previous day, $b = 0.36$, $t(2486) = 19.91$, $P < 0.001$, and that of HR, $b = 0.011$, $t(2134) = 2.67$, $P = 0.008$. Heart rate variability and its interaction with pain type did not yield significant effects, $P's > 0.4$. Crucially, pain type had neither main effect nor interaction with cardiac biometrics, all $P's > 0.2$ (**Fig. 3**).

The preregistered analysis was an MLM predicting pain intensity from sleep HR, day of study, pain type, proportion of days when symptomatic pain medications were taken per participant, and all possible interactions between them as fixed factors, with participant as the random factor. The results yielded a significant main effect of sleep HR, $b = 0.016$, $t(2575) = 2.22$, $P = 0.027$, and an interaction between sleep HR and day of study, $b = 0.011$, $t(2541) = 3.22$, $P = 0.001$. There was also a main effect of the painkiller, $b = 2.27$, $t(479.4) = 2.08$, $P = 0.038$, and day of study, $b = -0.66$, $t(2541) = -2.99$, $P = 0.003$. Pain type had no significant effect nor interactions, all $P's > 0.2$.

To summarize, the data show that daily pain intensity was predicted by sleep HR even controlling for multiple contributing factors such as pain on the previous day and use of symptomatic painkillers. The type of chronic pain did not moderate this association. As in our previous study, sleep HRV did not contribute to prediction of daily pain.

3.2.2. Predicting heart rate metrics

Two MLM models were tested, predicting each biometric (HR and HRV) from pain on the previous day, same biometric on the previous night, the other biometric on the same night, and day of study, with participant as the random factor. Only autocorrelations and correlations between HR and HRV were significant, with pain having no predictive effect on either HR or HRV, $P's > 0.1$.

Table 1

Characteristics of participants with primary back pain and participants with fibromyalgia.

	Back pain M (SD)	Fibromyalgia M (SD)	Comparison *t* test
Age	43.58 (11.6)	48.8 (12.9)	$t(63) = 1.66$, $P = 0.1$
Duration of chronic pain (y)	**9.31 (7)**	**18.8 (15.7)**	**$t(63) = 2.91$, $P = 0.005$**
Pain interference	**2.04 (1.78)**	**5.87 (1.85)**	**$t(63) = 2.53$, $P = 0.014$**
Pain intensity (average across all days)	**3.39 (1.74)**	**5.39 (1.53)**	**$t(65) = 5.0$, $P < 0.001$**
BPM (average across all nights)	64.73 (8.4)	68.13 (8.66)	$t(64) = 1.60$, $P = 0.115$
HRV (average across all nights)	43.52 (13.6)	44.38 (15.14)	$t(64) = 0.24$, $P = 0.81$
Number of days with biometric data	49.8 (22.7)	58.7 (22.9)	$t(65) = 1.58$, $P = 0.12$
Number of days with subjective data	**70.04 (23.6)**	**83.1 (18.7)**	**$t(65) = 2.51$, $P = 0.014$**

Bold font highlights significant differences between the groups.
BPM, beats per minute; HRV, heart rate variability.

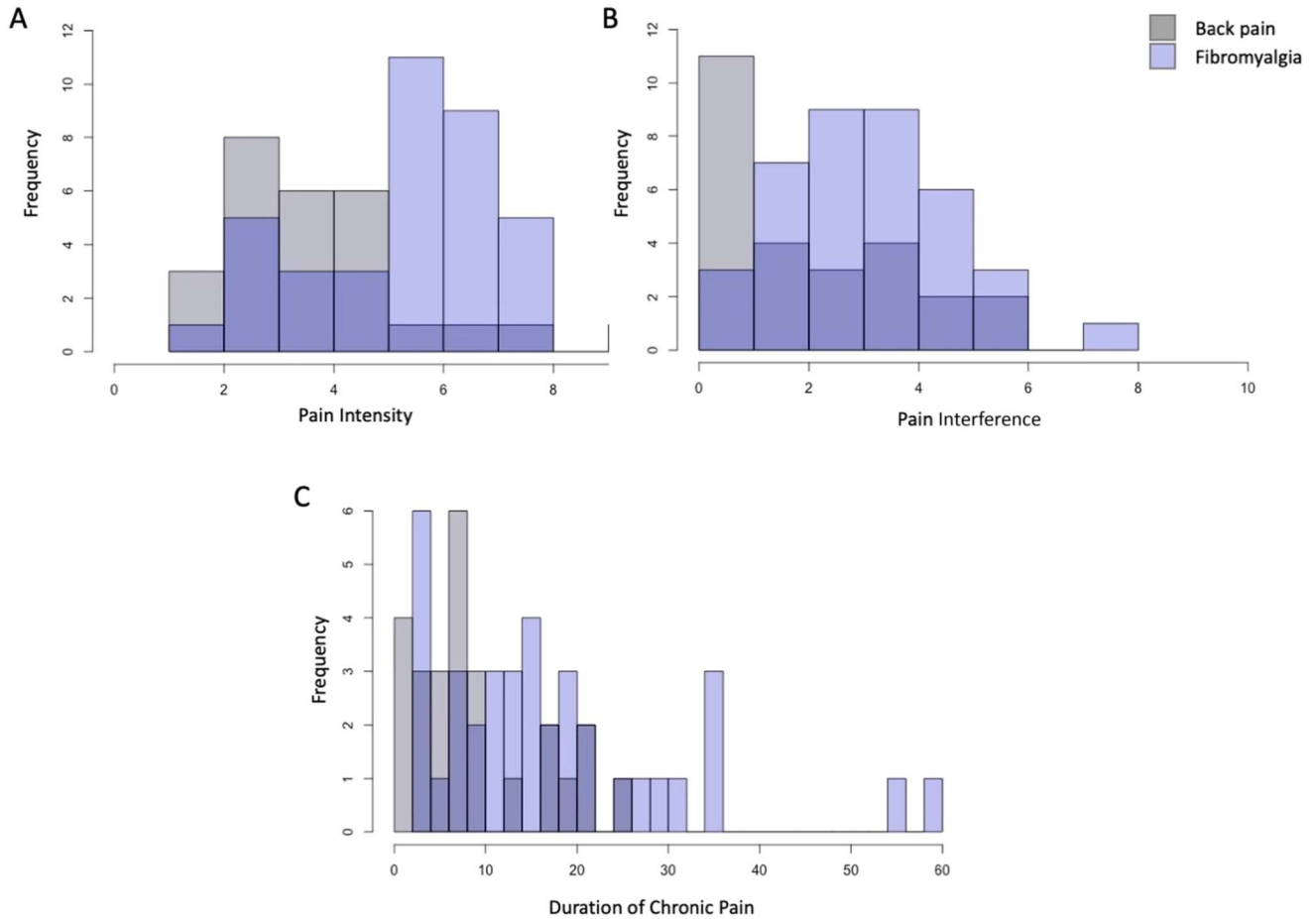

Figure 2. Pain intensity (A), interference (B), and duration (C) in participants with chronic back pain (gray) and in participants with fibromyalgia (with or without back pain, purple). The vertical axis shows the number of participants. Pain intensity in this figure is based on participants' rating of their pain on the NRS scale (from 0 to 10) at the beginning of the study. Pain interference is the total score of the Pain Disability Index. Duration of pain was reported in years at the beginning of the study.

4. Discussion

This study investigated the relationship between sleep heart rate metrics and daily pain intensity in people with primary back pain and fibromyalgia. In a previous study,[21] we reported that night-time HR predicted next-day pain intensity in people with primary chronic pain, but not in pain-free controls matched by age and sex. This relationship implies that sympathetic activation precedes rather than follows increases in pain, suggesting that autonomic hyperactivation plays a causal role in chronic pain.

Figure 3. Daily pain predicted by heart rate and group (back pain vs fibromyalgia), controlling for the autocorrelation and HRV. HRV, heart rate variability.

The method of this study was designed to replicate and extend the previous study in 4 ways. First, it included a larger group of people (N = 66) than the previous study (N = 54, 30 with chronic pain). Second, it observed participants for longer time (mean = 81 days) than the previous study (mean = 33 days). Third, it documented the use of symptomatic painkillers. Fourth, it tested whether the finding held equally for back pain and fibromyalgia.

The finding of a predictive relationship between sleep heart rate and next-day pain intensity was replicated in this study with an effect size (b = 0.012, 95% CI [0.004, 0.020]) that was similar to the previous study (b = 0.024, 95% CI [0.012, 0.036]). This relationship held even after controlling for previous day pain intensity and for concurrent HRV. More frequent painkiller use was also associated with higher pain intensity, although this effect did not modulate the association between sleep HR and pain intensity.

We were surprised to find, in both this and in our previous study, that there was no evidence for an association between HRV and pain reports. These null findings stand in striking contrast to a body of literature outlining multiple pathways by which the vagus nerve regulates pain perception[14] and studies showing decreased HRV in people with chronic pain.[26,66] We offer 2 possible interpretations of this null result. The first is that the Biostrap measurement of HRV may not have sufficient precision to support finding a relatively small correlation with next-day pain reports. We discuss this possibility in the upcoming Limitations section. However, a second interpretation also deserves careful consideration. If the absent HRV–pain correlation does not reflect a measurement problem, it begs for further study of the timelines of sympathetic and parasympathetic mechanisms of chronic pain. For example, if the intensity of chronic pain fluctuates over time, then pain regulation by sympathetic and parasympathetic pathways is also variable. At the timescale used in this study (night to next day), the HR measure may have had a better opportunity to reveal the sympathetic impact.[8] It could be that parasympathetic influence, linked more closely to HRV, changes on a different timescale and thus evaded our analyses. This, in turn, begs for more detailed longitudinal studies.

The 2 pain conditions that were tested—fibromyalgia and back pain—offered an opportunity to compare involvement of autonomic hyperactivation in these 2 different manifestations of chronic pain. Fibromyalgia is a classic example of nociplastic pain: widespread pain with a multitude of additional symptoms, such as fatigue, sleep, mood, and memory problems. Fibromyalgia patients show most distinct signs of central sensitization[16] and autonomic hyperactivation.[6,66] Chronic back pain, on the other hand, represents a very diverse category, with pain occurrence, resurgence, intensity, and pain-related disability varying widely. Studies show that 75% of adults have experienced back pain at least once in their lives, with pain becoming chronic in about a quarter of them.[15] People who have experience back pain are also more likely to develop fibromyalgia.[44] The mechanisms and categorization of chronic back pain are still debated,[24,48] yet there is growing evidence of involvement of central sensitization in this type of pain.[28,40,48,50] However, the data on involvement of autonomic mechanisms in chronic back pain are still mixed.[4,32,61]

In this study, participants with fibromyalgia and those with chronic back pain presented distinguishable profiles of pain intensity, interference, and duration, all these being higher in fibromyalgia. In addition, it is notable that our attempt to recruit equal number of participants with fibromyalgia and back pain was not successful because many participants recruited with chronic back pain also endorsed a fibromyalgia diagnosis. Most importantly, sleep heart rate was predictive of next-day pain intensity for both participants with fibromyalgia and chronic back pain, even despite the differences in pain intensity between these groups. This supports the interpretation of central sensitization—specifically ANS activation—being a common mechanism in the pain experience of both groups.

Interventions that reduce autonomic hyperactivation, eg, exercise and cognitive behavioural therapy, are widely recommended for people with fibromyalgia.[1,34] Yet for chronic back pain both doctors and patients consider them as a second or even third line of treatment.[18,68] The evidence presented here suggests that biopsychosocial approaches and interventions aimed at restoring autonomic balance should be prioritized for both conditions. One way of implementing these approaches in the context of our novel finding is to target interventions specifically for the mornings after elevated HR values.

4.1. Limitations and strengths

Longitudinal observation of biomarkers of ANS undertaken in this study was made possible by the use of wearable technology, which is both a strength and a limitation. Although consumers and markets are rushing to adopt wearable sensors of different physiological indexes, the research community is concerned about the validity of the data acquired from wearables. Not only is the resolution of commercially available wearables generally much lower than that of laboratory equipment but wearable devices are also likely to be affected more by circumstances of the measurement, such as movement, chemical intake, etc. In a previous study, we found that both HR and HRV were highly reliable during sleep,[19] yet HR was more reliable numerically, and it was the only biometric that correlated with mood on the next day. In that article, we discuss how reduced measurement precision is expected to weaken predictions based on HRV more than those based on HR because HR estimates are more robust to missing or extreme intervals between heartbeats. It is therefore possible that HRV correlations are more vulnerable to being masked by noise when looking for weak relationships measured in real-life environment across time lags from night to day. In this interpretation, wearable technology is simply not of sufficient fidelity to measure HRV and its associations with other outcomes.

Another major feature of this study is that cardiac biometrics and pain intensity measurements were lagged, the former occurring during sleep and the latter during wakeful time. This was conducted to minimize extraneous influences on cardiac biometrics, and it allowed testing of the temporal directionality of the relationships between heart rate and pain intensity.

The comparison between fibromyalgia and chronic back pain was complicated by several factors. First, our effort to recruit equal number of participants into the 2 groups failed, as described above. This finding emphasizes the association between back pain and fibromyalgia and suggests that people whose primary complaint is back pain actually experience more widespread pain and/or other somatic symptoms. Second, participants with back pain had significantly lower pain intensity and interference than those with fibromyalgia, although no differences were detected in the cardiac metrics. Yet, despite that difference in pain intensity for these 2 groups, we did not find any modulation by pain type for the association between heart rate and pain. This null result should be treated with caution because the comparison between subgroups does not have the same statistical power as the measurement of a heart–pain correlation. However taken at face value, the null finding implies

that any difference in the heart–pain correlation for fibromyalgia and back pain is likely very small, if exists at all.

4.2. Conclusions

Two main findings are reported. First, sleep heart rate was predictive of next-day pain intensity, after controlling for concurrent HRV, pain on the previous day, and painkiller use. Pain reports, on the other hand, were not a reliable predictor for either HR or HRV on the next night. This pattern replicates our previous findings.[21] The 2 studies together strongly suggest that sympathetic tone precedes and possibly causes changes in pain intensity in primary chronic pain. The second finding is the absence of a measurable difference in the heart–pain correlation for fibromyalgia and primary chronic back pain. This finding suggests that autonomic hyperactivation is a common mechanism in the pain experience for both conditions.

Disclosures

G.D. is a CEO of HealthQb Technologies, and O.B., M.R., and V.D. are employees of same. J.T.E. has no conflict of interest to declare.

Acknowledgments

V.D.'s involvement in this research was funded by Mitacs Accelerate Postdoctoral fellowship (IT23473) and HealthQb Technologies. The research costs associated with this study were funded by a Discovery Grant to J.T.E. from the Natural Sciences and Engineering Council of Canada and by HealthQb Technologies, Inc.

Data and code generated in this study are available at https://zenodo.org/badge/latestdoi/638721947.

Article history:
Received 15 May 2023
Received in revised form 24 September 2023
Accepted 30 September 2023
Available online 1 February 2024

References

[1] Andrade A, Vilarino GT, Serafim TT, Pereira Júnior AA, de Souza CA, Sieczkowska SM. Modulation of autonomic function by physical exercise in patients with fibromyalgia syndrome: a systematic review. PM R 2019;11:1121–31.
[2] Appelhans BM, Luecken LJ. Heart rate variability and pain: associations of two interrelated homeostatic processes. Biol Psychol 2008;77:174–82.
[3] Balzarotti S, Biassoni F, Colombo B, Ciceri MR. Cardiac vagal control as a marker of emotion regulation in healthy adults: a review. Biol Psychol 2017;130:54–66.
[4] Bandeira PM, Reis FJJ, Sequeira VCC, Chaves ACS, Fernandes O, Arruda-Sanchez T. Heart rate variability in patients with low back pain: a systematic review. Scand J Pain 2021;21:426–33.
[5] Barrios L, Oldrati P, Santini S, Lutterotti A. Evaluating the accuracy of heart rate sensors based on photoplethysmography for in-the-wild analysis. ACM Int Conf Proceeding Ser 2019:251–261.
[6] Beiner E, Lucas V, Reichert J, Buhai D-V, Jesinghaus M, Vock S, Drusko A, Baumeister D, Eich W, Friederich H-C, Tesarz J. Stress biomarkers in individuals with fibromyalgia syndrome: a systematic review with meta-analysis. PAIN 2023;164:1416–27.
[7] Benarroch EE. Pain-autonomic interactions. Neurol Sci 2006;27(suppl 2):130–3.
[8] Brosschot JF, Van Dijk E, Thayer JF. Daily worry is related to low heart rate variability during waking and the subsequent nocturnal sleep period. Int J Psychophysiol 2007;63:39–47.
[9] Bruehl S, Chung OY. Interactions between the cardiovascular and pain regulatory systems: an updated review of mechanisms and possible alterations in chronic pain. Neurosci Biobehavioral Rev 2004;28:395–414.
[10] Chalaye P, Lafrenaye S, Goffaux P, Marchand S. The role of cardiovascular activity in fibromyalgia and conditioned pain modulation. PAIN 2014;155:1064–9.
[11] Chibnall JT, Tait RC. The pain disability index: factor structure and normative data. Arch Phys Med Rehabil 1994;75:1082–6.
[12] Coutts LV, Plans D, Brown AW, Collomosse J. Deep learning with wearable based heart rate variability for prediction of mental and general health. J Biomed Inform 2020;112:103610.
[13] Craig AD. A new view of pain as a homeostatic emotion. Trends Neurosciences 2003;26:303–7.
[14] De Couck M, Nijs J, Gidron Y. You may need a nerve to treat pain: the neurobiological rationale for vagal nerve activation in pain management. Clin J Pain 2014;30:1099–105.
[15] de Girolamo G. Epidemiology and social costs of low back pain and fibromyalgia. Clin J Pain 1991;7(suppl 1):S1–S7.
[16] de la Coba P, Montoro CI, Reyes del Paso GA, Galvez-Sánchez CM. Algometry for the assessment of central sensitisation to pain in fibromyalgia patients: a systematic review. Ann Med 2022;54:1403–22.
[17] Descalzi G, Ikegami D, Ushijima T, Nestler EJ, Zachariou V, Narita M. Epigenetic mechanisms of chronic pain. Trends Neurosciences 2015;38:237–46.
[18] Deyo RA, Mirza SK, Turner JA, Martin BI. Overtreating chronic back pain: time to back off? J Am Board Fam Med 2009;22:62–8.
[19] Dudarev V, Barral O, Zhang C, Davis G, Enns JT. On the reliability of wearable technology: a tutorial on measuring heart rate and heart rate variability in the wild. Sensors 2023;23:5863.
[20] Dudarev V, Barral O, Zhang C, Davis G, Enns JT. Physiological correlates of pain in chronic pain conditions, 2022. doi: 10.17605/OSF.IO/WSQU5.
[21] Dudarev V, Zhang C, Barral O, Davis G, Enns JT. Night-time cardiac metrics from a wearable sensor predict intensity of next-day chronic pain. Proced Comput Sci 2022;206:34–44.
[22] Dur O, Rhoades C, Ng MS, Elsayed R, van Mourik R, Majmudar MD. Design rationale and performance evaluation of the wavelet health wristband: benchtop validation of a wrist-worn physiological signal recorder. JMIR mHealth and uHealth 2018;6:e11040.
[23] Finnern MM, Kleinböhl D, Flor H, Benrath J, Hölzl R. Differential sensory and clinical phenotypes of patients with chronic widespread and regional musculoskeletal pain. PAIN 2021;162:56–70.
[24] Fitzcharles MA, Cohen SP, Clauw DJ, Littlejohn G, Usui C, Häuser W. Nociplastic pain: towards an understanding of prevalent pain conditions. Lancet (London, England) 2021;397:2098–110.
[25] Fornasari D. Pain mechanisms in patients with chronic pain. Clin Drug Invest 2012;32(suppl 1):45–52.
[26] Forte G, Troisi G, Pazzaglia M, De Pascalis V, Casagrande M. Heart rate variability and pain: a systematic review. Brain Sci 2022;12:153.
[27] Georgiou K, Larentzakis AV, Khamis NN, Alsuhaibani GI, Alaska YA, Giallafos EJ. Can wearable devices accurately measure heart rate variability? A systematic review. Folia Med 2018;60:7–20.
[28] Gerhardt A, Eich W, Treede RD, Tesarz J. Conditioned pain modulation in patients with nonspecific chronic back pain with chronic local pain, chronic widespread pain, and fibromyalgia. PAIN 2017;158:430–9.
[29] Giusti EM, Lacerenza M, Manzoni GM, Castelnuovo G. Psychological and psychosocial predictors of chronic postsurgical pain: a systematic review and meta-analysis. PAIN 2021;162:10–30.
[30] Green P, Macleod CJ. SIMR: an R package for power analysis of generalized linear mixed models by simulation. Methods Ecol Evol 2016;7:493–8.
[31] Green P, MacLeod CJ, Alday P. Package 'simr'. R Package. 2016. Available at: https://cran.r-project.org/web/packages/simr
[32] Griep EN, Boersma JW, Lentjes EG, Prins AP, Van der Korst JK, de Kloet ER. Function of the hypothalamic-pituitary-adrenal axis in patients with fibromyalgia and low back pain. J Rheumatol 1998;25:1374–81.
[33] Hallman DM, Lyskov E. Autonomic regulation, physical activity and perceived stress in subjects with musculoskeletal pain: 24-hour ambulatory monitoring. Int J Psychophysiol 2012;86:276–82.
[34] Hassett AL, Gevirtz RN. Nonpharmacologic treatment for fibromyalgia: patient education, cognitive-behavioral therapy, relaxation techniques, and complementary and alternative medicine. Rheum Dis Clin North Am 2009;35:393–407.
[35] Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: visual analog scale for pain (VAS pain), numeric rating scale for pain (NRS pain), McGill pain questionnaire (MPQ), short-form McGill pain questionnaire (SF-MPQ), chronic pain grade scale (CPGS), short form-36 bodily pain scale (SF-36 BPS), and measure of intermittent and constant osteoarthritis pain (ICOAP). Arthritis Care Res 2011;63:240–52.
[36] Hinde K, White G, Armstrong N. Wearable devices suitable for monitoring twenty four hour heart rate variability in military populations. Sensors (Switzerland) 2021;21:1061.

[37] Holzman JB, Bridgett DJ. Heart rate variability indices as bio-markers of top-down self-regulatory mechanisms: a meta-analytic review. Neurosci Biobehavioral Rev 2017;74:233–55.
[38] Hovsepian K, Al'Absi M, Ertin E, Kamarck T, Nakajima M, Kumar S. cStress: towards a gold standard for continuous stress assessment in the mobile environment. Proc ACM Int Conf Ubiquitous Comput 2015;2015: 493–504.
[39] Jarchi D, Salvi D, Velardo C, Mahdi A, Tarassenko L, Clifton DA. Estimation of HRV and SpO2 from wrist-worn commercial sensors for clinical settings. 2018 IEEE 15th international conference on wearable and implantable body sensor networks. Las Vegas, NV: BSN, 2018. p. 144–7.
[40] Kindler LL, Bennett RM, Jones KD. Central sensitivity syndromes: mounting pathophysiologic evidence to link fibromyalgia with other common chronic pain disorders. Pain Manag Nurs 2011;12:15–24.
[41] Koskimäki H, Kinnunen H, Rönkä S, Smarr B. Following the heart - What does variation of resting heart rate tell about us as individuals and as a population. UbiComp/ISWC 2019—Adjunct Proceedings of the 2019 ACM International Joint Conference on Pervasive and Ubiquitous Computing and Proceedings of the 2019 ACM International Symposium on Wearable Computers 2019. p. 1178–81.
[42] Kuznetsova A, Brockhoff PB, Christensen RHB. lmerTest package: tests in linear mixed effects models. J Stat Softw 2017;82:1–26.
[43] Laborde S, Mosley E, Thayer JF. Heart rate variability and cardiac vagal tone in psychophysiological research—recommendations for experiment planning, data analysis, and data reporting. Front Psychol 2017;8:213–8.
[44] Lápossy E, Maleitzke R, Hrycaj P, Mennet W, Müller W. The frequency of transition of chronic low back pain to fibromyalgia. Scand J Rheumatol 1995;24:29–33.
[45] Lauche R, Cramer H, Dobos G, Langhorst J, Schmidt S. A systematic review and meta-analysis of mindfulness-based stress reduction for the fibromyalgia syndrome. J Psychosomatic Res 2013;75:500–10.
[46] Marvizon JC, Walwyn W, Minasyan A, Chen W, Taylor BK. Latent sensitization: a model for stress-sensitive chronic pain. Curr Protoc Neurosci 2015;71:9.50.1–14.
[47] May M, Junghaenel DU, Ono M, Stone AA, Schneider S. Ecological momentary assessment methodology in chronic pain research: a systematic review. J Pain 2018;19:699–716.
[48] McPhee ME, Vaegter HB, Graven-Nielsen T. Alterations in pronociceptive and antinociceptive mechanisms in patients with low back pain: a systematic review with meta-analysis. PAIN 2020;161:464–75.
[49] Miettinen T, Mäntyselkä P, Hagelberg N, Mustola S, Kalso E, Lötsch J. Machine learning suggests sleep as a core factor in chronic pain. PAIN 2021;162:109–23.
[50] Nees F, Löffler M, Usai K, Flor H. Hypothalamic-pituitary-adrenal axis feedback sensitivity in different states of back pain. Psychoneuroendocrinology 2019;101:60–6.
[51] Nickel FT, Seifert F, Lanz S, Maihöfner C. Mechanisms of neuropathic pain. Eur Neuropsychopharmacol 2012;22:81–91.
[52] Ondicova K, Mravec B. Multilevel interactions between the sympathetic and parasympathetic nervous systems: a mini review. Endocr Regul 2010;44:69–75.
[53] Petersen KK, Vaegter HB, Stubhaug A, Wolff A, Scammell BE, Arendt-Nielsen L, Larsen DB. The predictive value of quantitative sensory testing: a systematic review on chronic postoperative pain and the analgesic effect of pharmacological therapies in patients with chronic pain. PAIN 2021;162:31–44.
[54] Phillips ML, Gregory LJ, Cullen S, Coen S, Ng V, Andrew C, Giampietro V, Bullmore E, Zelaya F, Amaro E, Thompson DG, Hobson AR, Williams SCR, Brammer M, Aziz Q. The effect of negative emotional context on neural and behavioural responses to oesophageal stimulation. Brain 2003;126:669–84.
[55] Porges SW. Cardiac vagal tone: a physiological index of stress. Neurosci Biobehavioral Rev 1995;19:225–33.
[56] Rainville P, Duncan GH, Price DD, Carrier B, Bushnell MC. Pain affect encoded in human anterior cingulate but not somatosensory cortex. Science 1997;277:968–71.
[57] Reichling DB, Levine JD. Critical role of nociceptor plasticity in chronic pain. Trends Neurosciences 2009;32:611–8.
[58] Riva R, Mork PJ, Westgaard RH, Okkenhaug Johansen T, Lundberg U. Catecholamines and heart rate in female fibromyalgia patients. J Psychosomatic Res 2012;72:51–7.
[59] Roos LE, Knight EL, Beauchamp KG, Berkman ET, Faraday K, Hyslop K, Fisher PA. Acute stress impairs inhibitory control based on individual differences in parasympathetic nervous system activity. Biol Psychol 2017;125:58–63.
[60] Schwartz PJ, De Ferrari GM. Sympathetic-parasympathetic interaction in health and disease: abnormalities and relevance in heart failure. Heart Fail Rev 2011;16:101–7.
[61] Sosa MK, Boorman DC, Keay KA. Sciatic nerve injury rebalances the hypothalamic–pituitary–adrenal axis in rats with persistent changes to their social behaviours. J Neuroendocrinology 2022;34:e13131.
[62] Staud R. Autonomic dysfunction in fibromyalgia syndrome: postural orthostatic tachycardia. Curr Rheumatol Rep 2008;10:463–6.
[63] Stone AA, Obbarius A, Junghaenel DU, Wen CKF, Schneider S. High-resolution, field approaches for assessing pain: ecological momentary assessment. PAIN 2021;162:4–9.
[64] Terkelsen AJ, Mølgaard H, Hansen J, Finnerup NB, Krøner K, Jensen TS. Heart rate variability in complex regional pain syndrome during rest and mental and orthostatic stress. Anesthesiology 2012;116:133–46.
[65] Tiwari R, Kumar R, Malik S, Raj T, Kumar P. Analysis of heart rate variability and implication of different factors on heart rate variability. Curr Cardiol Rev 2021;17:1–10.
[66] Tracy LM, Ioannou L, Baker KS, Gibson SJ, Georgiou-Karistianis N, Giummarra MJ. Meta-analytic evidence for decreased heart rate variability in chronic pain implicating parasympathetic nervous system dysregulation. PAIN 2016;157:7–29.
[67] Verkuil B, Brosschot JF, Tollenaar MS, Lane RD, Thayer JF. Prolonged non-metabolic heart rate variability reduction as a physiological marker of psychological stress in daily life. Ann Behav Med 2016;50:704–14.
[68] Weiner SS, Nordin M. Prevention and management of chronic back pain. Best Pract Res Clin Rheumatol 2010;24:267–79.