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The Relationship Between Heart Rate Variability, Psychological Flexibility, and Pain in Neurofibromatosis Type 1

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Abstract

Individuals with neurofibromatosis type 1 (NF1) and plexiform neurofibromas (PNs) can experience chronic pain. Previous research has examined the relationship between heart rate variability (HRV) and persistent pain. HRV is an index of autonomic nervous system functioning, and reflects the variability in time elapsed between heartbeats. Patients with chronic pain tend to exhibit lower HRV, which has been associated with poor adaptability, or psychological flexibility, to stress. The aim of the current study was to examine relationships between HRV, psychological flexibility, and pain in a sample of adolescents and young adults (AYAs) with NF1 and PNs. AYA participants ($n = 40$) 16 to 34 years of age with NF1 completed baseline measures of pain and psychological functioning, and underwent a 5-minute electrocardiogram (ECG). A subset of 20 participants completed follow-up questionnaires and a second ECG 8 weeks later. Spectral analyses of ECGs yielded a measure of high-frequency heart rate variability (HF-HRV). Baseline correlations revealed that lower HF-HRV is related to greater inflexibility and more pain interference, but not pain intensity. Moreover, psychological inflexibility significantly mediated the relationship between HF-HRV and pain interference. Finally, regression models indicated that baseline psychological inflexibility is a significant predictor of HF-HRV at follow-up and, separately, that baseline HF-HRV significantly predicted pain intensity at follow-up. These findings suggest complex mind–body processes in the experience of pain in NF1, which have not been studied previously. Implications for pain-related interventions and future research are discussed.

Keywords

heart rate variability; psychological flexibility; neurofibromatosis type 1; pain; adolescents/young adults

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CONFLICT OF INTEREST

The authors state that they don't have any conflict of interest.

INTRODUCTION

Neurofibromatosis type 1 (NF1) is a genetic condition caused by a mutation on chromosome 17, which affects about 1 in 3,500 individuals.¹ It is associated with a high risk for chronic pain due to multiple morbidities, including plexiform neurofibromas (PNs; benign tumors composed of a proliferation of cells in the nerve sheath), chronic headaches, pseudoarthrosis, scoliosis, and gastrointestinal complications.² In particular, PN-related pain is neuropathic in nature, occurring in about 30% to 50% of patients,^{3,4} and is associated with worse everyday functioning and quality of life.^{5–7} Despite this, there has been limited research into factors related to pain in this population. Initial research suggests that depression and social support mediate the relationship between pain interference and quality of life among patients with PNs;⁷ however, further exploration of biopsychosocial variables is needed to better understand the experience of pain in NF1.

Among other chronic pain populations, there is increasing recognition of the importance of self-regulation in successful pain adaptation.⁸ In particular, psychological flexibility is a self-regulatory skill relevant to individuals with chronic pain.^{9,10} It is defined as the ability to purposefully persist in, or adapt, behavior while remaining accepting of internal experiences in order to pursue chosen values. High flexibility enables individuals to relate to their pain in a more accepting and adaptable manner, which is contrasted by traditional urges to ignore sensations or suppress thoughts about pain.¹¹ Individuals who demonstrate psychological inflexibility, on the other hand, exhibit a rigid cognitive and behavioral repertoire in the face of pain (eg, avoiding activities that may cause/exacerbate pain; social withdrawal; catastrophic thinking). Although considerable evidence cites the importance of psychological flexibility in pain adaptation,^{12,13} less research has investigated the relationship between psychological flexibility and physiological factors in chronic pain, and this has been entirely unexplored in patients with NF1.

In particular, heart rate variability (HRV) is a physiological measure of autonomic functioning known to be affected by pain. It reflects the sequence of time intervals between heart beats. Under healthy conditions, heart rate fluctuates in response to environmental demands, which is modulated by inhibitory parasympathetic (ie, vagal) and excitatory sympathetic nerves of the autonomic nervous system (ANS). Greater HRV suggests adaptive autonomic flexibility and emotional self-regulation in response to physical and psychological stress.^{14,15} In contrast, lower HRV is indicative of worse autonomic health and psychological rigidity during stress.¹⁶

Lower HRV is observed across persistent pain conditions;^{8,17} it has been conceptualized as a physiological marker of self-regulatory fatigue^{14,18} and may reflect poor psychological flexibility in response to nociceptive threat. While the latter has not been studied directly, research suggests that, among patients with chronic pain, low HRV is associated with poor emotional reactivity,⁸ poor adaptability to internal and external demands,¹⁹ and weak behavioral persistence,¹⁸ which are proximate behaviors associated with psychological flexibility.²⁰

Building on previous literature, the current study aimed to further and more directly explore the relationship between psychological flexibility, high-frequency heart rate variability (HF-HRV), and pain in a sample of adolescents and young adults (AYAs) with NF1 and chronic pain due to PNs. More specifically, the current study sought not only to better understand the relationship between psychological inflexibility and HF-HRV among individuals with NF1 and chronic pain, but also the impact of these psychophysiological processes on the experience of pain in this population.

Specifically, it was hypothesized that HF-HRV would be negatively associated with psychological inflexibility, pain interference, and pain intensity. Moreover, based on experimental research demonstrating direct and indirect relationships between autonomic functioning, executive skills, and behavioral persistence in individuals with pain,¹⁸ it was hypothesized that HF-HRV would have a significant indirect effect on pain interference, mediated by psychological inflexibility. Finally, it was hypothesized that psychological inflexibility would have a significant impact on HF-HRV, and separately, that HF-HRV would significantly predict pain intensity over time. Ultimately, a better understanding of these relationships can provide a more holistic picture of the complex physiological and psychological processes implicated in persistent pain in NF1, beyond the well-understood structural basis for pain related to PNs.

METHODS

Participants and Procedures

This investigation of HRV was a substudy of a larger randomized waitlist-controlled trial of an acceptance-based intervention for chronic pain. The institutional review board of a government institution approved this study. AYA participants between 16 and 34 years of age with NF1 and at least 1 PN were recruited from the NF1 program at the investigators' home institution; in addition, e-mails and/or fliers were sent to NF clinics around the country and to a national NF registry hosted by the Children's Tumor Foundation. All participants had a diagnosis of NF1 according to National Institute of Health Consensus Conference criteria²¹ or a confirmed germline NF1 mutation. PNs were confirmed clinically or through magnetic resonance imaging. Eligible participants reported chronic pain for at least 3 months. All participants could speak and read English.

Patients who did not live locally were reimbursed for travel, and all participants were paid \$30 to thank them for completing questionnaires. Following written informed consent and assent, a brief history was compiled and a physical examination was conducted for each participant by a provider specializing in NF1, and all participants completed baseline questionnaires (Time 1) to assess pain and psychological functioning as part of the larger intervention trial. Participants also underwent a 5-minute electrocardiogram (ECG), from which a measure of HF-HRV was obtained. The randomly assigned waitlist participants ($n = 20$) underwent a follow-up appointment approximately 8 weeks after baseline, and completed the same questionnaires and a second ECG (Time 2). All data were collected prior to initiating the acceptance-based intervention.

Electrocardiogram and HRV

HF-HRV was obtained in accordance with recommendations from the European Society of Cardiology and North American Society of Pacing and Electrophysiology Task Force.²² With MP150 equipment (Biopac Systems, Inc., Goleta, CA, U.S.A.) and using a lead II 3-electrode arrangement on the chest, a resting ECG was recorded for 5 minutes with participants in the supine position. ECGs were preprocessed and a band pass filter of 0.5 to 35 Hz was applied. QRS peaks were identified using Acqknowledge software (Biopac Systems) and manually inspected and corrected when necessary. Spectral analysis of the RR intervals was completed using automated parameters in Acqknowledge, which yielded high-frequency and low-frequency bands. The high-frequency band is a measure of parasympathetically mediated HRV and was utilized in this study.

Questionnaires

Background Information.—Demographic information was collected through a background questionnaire completed at baseline, in addition to medical record review.

Disease Severity.—An 18-item NF1 symptom checklist was used to obtain a discrete measure of disease severity, based on data obtained from history and physical data obtained by a physician or nurse practitioner. The checklist was completed by a study investigator. The total symptom score was used for each participant.²³

Pain Intensity.—The numeric rating scale–11 (NRS-11) consists of 1 question that assesses the intensity of the patient's overall pain over the past week. The investigators modified the item to specifically assess tumor pain. Responses are marked on a scale of 0 to 10. This measure is widely used and is recommended for use in clinical trials for patients with chronic pain, including NF1.^{24,25}

Pain Interference.—The PROMIS Pain Interference scales (adult and pediatric short forms) were administered to assess how much pain has interfered with things like sleep, mood, and leisure activities in the past week.^{26,27} Items are formatted on a 5-point Likert scale, and raw scores are converted to *T*-scores. Higher scores indicate more interference. In the current sample, internal consistency for the adult form was $\alpha = 0.92$ and for the pediatric form $\alpha = 0.73$.

Psychological Inflexibility.—The Psychological Inflexibility in Pain Scale (PIPS)²⁸ is a 12-item measure that assesses how much an individual avoids activities due to pain (experiential avoidance) and thinks inflexibly about their pain (cognitive fusion). Items are summed to yield Avoidance and Fusion subscales, and a total score; the total score was used in this study. Higher scores suggest greater inflexibility. Internal consistency for the total scale was $\alpha = 0.90$.

Depression.—The Center for Epidemiological Studies–Depression scale (CES-D)²⁹ is a 20-item measure that has been validated with adolescents³⁰ and adults.³¹ Respondents rate the frequency of symptoms on a Likert scale of 0 to 3. Higher scores represent worse symptoms, and a score above 27 indicates concern for clinical levels of depression. This tool

is valid for use in medical patients, including those with chronic pain.^{32,33} Internal consistency for the CES-D in the current sample was $\alpha = 0.76$.

Pain Anxiety.—The Pain Anxiety Sensitivity Scale–20 (PASS-20)³⁴ is a 20-item measure assessing pain-related anxiety in individuals with medical problems. Responses are rated on a 6-point Likert scale from “never” to “always.” The PASS-20 is reliable and valid across samples.^{34,35} Internal consistency in the current sample is strong ($\alpha = 0.93$).

Statistical Methods

Statistical analyses were completed in SPSS version 24.³⁶ Descriptive statistics analyzed demographic and medical variables, and measures of psychological functioning, quality of life, and pain. Skewness and kurtosis were assessed and a log transformation was applied to HFHRV at Time 2, due to non-normality. Cross-sectional bivariate correlations of Time 1 data measured associations between HF-HRV and (1) psychological variables (inflexibility, pain anxiety, depression) and (2) pain (pain intensity and pain interference). Correlations also examined relationships between pain intensity, pain interference, depression, pain anxiety, and psychological flexibility. All correlations were 2-tailed, with $\alpha = 0.05$. In addition, given the potential for opioid use to affect parasympathetic tone, an independent-samples *t*-test assessed differences in HF-HRV (both at Time 1 and Time 2) for participants who were prescribed opioids for pain management compared to participants who were not prescribed opioids. This was done to evaluate the utility of including opioid use as a covariate in subsequent analyses.

The indirect effect of Time 1 HF-HRV on Time 2 pain interference was assessed, with psychological inflexibility at Time 2 as a mediator. To test this, Model 4 of the PROCESS macro for SPSS³⁷ was used, which produced 95% confidence intervals (CIs) for 5,000 bootstrapped samples. Bootstrapping is an analytical approach to mediation in which data are repeatedly resampled, thereby creating an empirical representation of the sampling distribution of the indirect effect.³⁸ This process yields a CI for the indirect effect, which is considered significant when it does not contain 0.³⁸ This approach to mediation is commonly employed in social and behavioral sciences, and aims to remedy some of the limitations of Baron and Kenny’s approach to mediation. In particular, it allows for detection of indirect effects when power is limited, or commonly, when the sampling distribution of the indirect effect is non-normal (which is an assumption of the Sobel test).^{39,40} Given the small sample here, bootstrapping provided a viable statistical model to test a theoretically driven mediation model.

In addition, 2 linear regression models explored Time 1 predictors of (1) HF-HRV at Time 2 and (2) pain intensity at Time 2. Continuous variables were mean-centered and multicollinearity was assessed. For each model, all variables were entered into a single step based on known and theoretical relationships. The model of HF-HRV included age, sex, pain intensity, and psychological inflexibility; the model of pain intensity included age, disease severity, pain anxiety, and HF-HRV.

RESULTS

Descriptive Statistics

Participants included 40 AYAs with NF1. One participant had an outlying Time 1 HF-HRV value, nearly 5 standard deviations above the mean, and was therefore excluded from all analyses. Of the remaining 39 participants, 59% were female. The majority of participants were White and non-Hispanic and completed high school. The mean pain intensity rating on the NRS-11 was 7.4 out of 10. Most participants (82.1%) managed pain with medication, of which nearly a third were prescribed narcotics. Table 1 depicts participant characteristics.

Cross-Sectional Analyses

Consistent with hypotheses, bivariate correlations of Time 1 data revealed that HRV was negatively correlated with psychological inflexibility ($r = -0.50$, $P < 0.01$) and pain interference ($r = -0.34$, $P < 0.05$). However, contrary to hypotheses, HF-HRV was not significantly associated with pain intensity at Time 1. In addition, exploratory analyses of cross-sectional data (ie, Time 1) revealed that pain interference shared a significant positive association with psychological inflexibility ($r = 0.54$, $P < 0.01$). There were no significant associations between HF-HRV and depression ($r = -0.14$, $P = \text{not significant [NS]}$), pain anxiety ($r = -0.08$, $P = \text{NS}$), or disease severity ($r = 0.10$, $P = \text{NS}$). Further, pain intensity was not correlated with psychological variables (depression $r = -0.05$, $P = \text{NS}$; pain anxiety $r = 0.05$, $P = \text{NS}$; psychological inflexibility $r = -0.05$, $P = \text{NS}$), disease severity ($r = -0.02$, $P = \text{NS}$), or pain interference ($r = 0.12$, $P = \text{NS}$). There were no differences in HF-HRV at Time 1 or Time 2 among participants taking opioids for pain management compared to those who did not take opioids ($t(36) = 1.29$, $P = \text{NS}$ and $t(16) = 0.09$, $P = \text{NS}$, respectively). As a result, opioid use was not included as a predictor or covariate in longitudinal analyses.

Longitudinal Analyses

Testing of Indirect Effects.—As shown in Figure 1, Time 1 HF-HRV was associated with psychological inflexibility at Time 2 (path a: $t(16) = 2.32$, $P < 0.05$), and psychological inflexibility was significantly associated with Time 2 pain interference (path b: $t(15) = 3.01$, $P < 0.05$); however, the total effect of HF-HRV on pain interference was not significant (path c: $t(16) = 1.42$; $P = \text{NS}$). When psychological flexibility was added to the model as a mediator, the direct effect between HF-HRV and pain interference remained nonsignificant (path c': $t(15) = 0.01$, $P = \text{NS}$). The test of the indirect effect of HF-HRV on pain interference through psychological inflexibility was significant (path ab: 95% CI -0.09 to -0.1 ; $F(2, 15) = 6.05$, $P < 0.05$), which is consistent with hypotheses. In other words, psychological inflexibility significantly mediated the relationship between HF-HRV and pain interference.

Linear Regression Model of HF-HRV.—The proposed model examining the influence of Time 1 psychological flexibility on Time 2 HF-HRV explained approximately 39% of the variance (adjusted $R^2 = 0.39$, $F(4, 11) = 3.43$, $P < 0.05$). As hypothesized, above and beyond the effects of demographic variables (ie, age and sex) and pain intensity, psychological inflexibility significantly predicted HRV ($\beta = -0.58$, $t = -2.83$, $P < 0.05$). Other independent predictors were nonsignificant. Results of this model are provided in Table 2.

Linear Regression Model of Pain Intensity.—The proposed model examining HF-HRV's influence at Time 1 on pain intensity at Time 2 explained approximately 58% of the variance (adjusted $R^2 = 0.57$, $F(4,12) = 6.40$, $P < 0.01$). Age was a significant independent predictor of pain intensity ($\beta = 0.46$, $t = 2.57$, $P < 0.05$). In addition, as hypothesized, while controlling for age, disease severity, and pain anxiety, HF-HRV significantly predicted pain intensity ($\beta = -0.51$, $t = -2.85$, $P < 0.05$). Other independent predictors were nonsignificant. See Table 3 for results.

DISCUSSION

This is the first known study to account for psychophysiological factors in the experience of pain in NF1. It builds on a strong body of literature demonstrating the interplay between psychological self-regulation, broadly speaking, and physiological processes in persistent pain. Consistent with hypothesized relationships, correlational analyses demonstrated a significant association between HF-HRV and psychological flexibility. Specifically, individuals with lower HF-HRV exhibited more psychological inflexibility in the context of their pain. In addition, lower HF-HRV was associated with greater pain interference, although not pain intensity, while greater pain interference was associated with greater psychological inflexibility.

The correlational data are consistent with previous research suggesting a relationship between self-regulatory capability (indexed by HF-HRV and the level of psychological inflexibility in this study) and behavioral persistence (measured by pain interference here) in patients with chronic pain.¹⁸ Research has demonstrated that patients with chronic pain experience self-regulatory depletion,^{9,19} which has been theorized to limit the availability of other personal resources (eg, motivation, planning) needed to persist with daily activities or respond adaptively to stress.^{18,41} This relationship is exemplified in the current data through a mediational model in which HF-HRV directly influences psychological flexibility, and that, in turn, affects everyday behavior in the context of pain.

Building on these findings, and consistent with our hypotheses, the current results also indicate that greater psychological inflexibility predicts lower HF-HRV in patients with NF1, which is aligned with previous research in chronic pain populations.⁴² Moreover, along with older age, lower resting HF-HRV predicts higher levels of pain intensity. Taken together, these data point toward the possibility of a top-down process in which psychological self-regulatory capacities, such as one's level of mental flexibility or inflexibility, influence autonomic functioning, which is associated with pain intensity over time.⁴³

Ultimately, the precise mechanisms underlying the relationships between psychological flexibility, HF-HRV, and pain in NF1 cannot be discerned from this study. Nonetheless, the data provide preliminary support for a model wherein bidirectional mind–body processes influence the experience of pain. In particular, drawing from theoretical and empirical models of neurovisceral integration,^{44–46} it has been shown that normal environmental stress leads to an increased activation of prefrontal regions—responsible for perceiving and interpreting emotionally valent stimuli, constructing context, self-monitoring thoughts and

behavior, and organizing goal-directed responses—which disinhibit subcortical circuits that share efferents with the heart. The disinhibitory effect results in increased activation of sympathetic nerves and a cascade of temporary physiological changes, followed by a return to parasympathetic dominance. Under adaptive health states, this homeostatic system is designed to dynamically and flexibly respond to the environment, resulting in beat-to-beat variability in heart rate (high HRV). However, prolonged psychological or physical stress, including chronic pain, can lead to an overactivation of prefrontal networks and persistent disinhibition of subcortical circuits, resulting in excess and prolonged sympathetic activity.⁴⁷ Over time, this increases allostatic load in the periphery, which feeds back and contributes to neurobiological changes that maintain a maladaptive response pattern.

Specifically, research in other populations suggests that long-term persistent pain can cause central and peripheral centers to become more sensitized to nociceptive threat on a physiological level,⁴⁸ which is coupled with changes in psychological (eg, cognitive-evaluative, emotional) processing of stimuli.⁴⁹ Taken together, these changes can lead pain to generalize and/or become more intense.⁵⁰ Because some of the neural regions (eg, prefrontal-limbic circuits) that process pain also underlie multiple executive and self-regulatory skills, including psychological flexibility, chronic pain depletes the psychological resources needed to respond adaptively to physical discomfort.⁵¹ This makes it harder for individuals to consistently engage in everyday activities (eg, work, school, socialization) or shift habitual patterns of responding (eg, withdraw, lie down) when pain arises.

Patients with NF1 may be particularly susceptible to the persistent effects of pain due to the impact of this condition on multiple systems of the body. Specifically, the NF1 mutation can lead to overt and subtle neuro-biological changes, which affect the same prefrontal networks that process nociceptive input and are taxed by chronic pain. Although this has not yet been explored by research, it is possible that premorbid prefrontal vulnerabilities in NF1 (eg, executive deficits, weak attention) increase patients' risk for chronic pain. In addition, natural history data suggest that tumor burden and pain increase with age in patients with NF1,^{52,53} alongside potential concomitant psychological stress of living with pain.⁵¹ That is, there are concurrent pathophysiological processes that, over time, may increase nociceptive stress on a structural level and pain-related vulnerability on a psychological level. All of this is compounded by the fact that PN pain is difficult to treat using conventional medical intervention (eg, pharmacotherapies, surgery), leaving patients with limited options for full pain relief. Indeed, research suggests that over 90% of youth taking medication for PNs continue to report significant pain interference.⁷

Implications for Treatment

The current results pinpoint a role for pain-related therapies in NF1 that target dysregulated psychophysiological processes. Acceptance-based therapies such as acceptance and commitment therapy (ACT) or mindfulness-based interventions may be well suited for this population. Broadly, these interventions help individuals connect with the present moment, and aim to enhance psychological flexibility and acceptance of experiences, whether enjoyable or difficult. In this way, acceptance-based therapies shift the focus from

ameliorating pain directly, and help individuals better attune to their experiences so they can modify their behavior in a manner that is consistent with their values.

Extensive literature supports acceptance-based therapies for chronic pain,⁵⁴ in addition to pilot research supporting the benefits of ACT for treating pain in adolescents with NF1.²³ Studies suggest that the beneficial effects of acceptance-based therapies for chronic pain are mediated partly through changes in pain acceptance⁵⁵ and psychological flexibility.^{11,13,56} These findings are highly relevant given the current data, which provide preliminary evidence that the level of psychological (in)flexibility can influence, and is influenced by, autonomic functioning and that autonomic functioning is associated with pain in NF1. Further, the neurobiological literature implicates adaptive changes in the very neural regions (eg, prefrontal cortex, anterior cingulate) negatively affected by chronic pain following acceptance-based therapies.⁵⁷ This is in addition to improvements in multiple homeostatic functions including HRV following acceptance-based therapies.⁵⁸ Taken together, there is strong evidence to suggest beneficial impact of these behavioral interventions for patients with NF1. Future research should continue to investigate their efficacy through behavioral and biological measures.

LIMITATIONS AND FUTURE DIRECTIONS

The current results should be considered with several limitations in mind. First, our relatively small sample, particularly among participants with longitudinal data, constrained our ability to explore more complex analytical models related to the experience of pain in NF1. While the small sample is certainly a limiting factor, it is also in the context of a rare disease, which makes these preliminary data important. It also bears noting that the current sample is restricted to patients who self-report chronic pain related to PNs and, therefore, results may not reflect all patients with NF1 and may not generalize to patients with non-neuropathic pain-related conditions.

Although this study utilized a well-validated measure of pain intensity—consistent with the standard in the field—there are inherent limitations to this approach. In particular, although patients were asked to consider their pain experience over a week-long period, this may not have fully captured the chronicity and fluctuating nature of pain experienced by patients with NF1. Further, while this study utilized multiple modes of measurement (ie, self-report, biological data)—which is a strength—it did not examine tumor volume or location or the role of medications. These considerations are important for future research and will offer a more comprehensive picture of the experience of pain among individuals with NF1.

CONCLUSIONS

This study adds to the small body of literature focused on the relationship between psychological flexibility and physiological factors in the context of chronic pain. It also extends the very limited research on the pain experience in NF1. Collectively, the current findings suggest a strong rationale for acceptance-based therapies in patients with NF1, which should be investigated in the future. Research should also continue to explore the relationship between psychological factors—particularly those relevant in the context of

behavioral interventions (eg, psychological flexibility, dispositional mindfulness)—and physiological markers of pain across affected populations. This knowledge would help further our understanding of the multiple systems involved in the development and maintenance of pain, and will help guide efforts toward more effective and sorely needed interventions.

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Abbreviations: HRV=Heart rate variability; ^aunstandardized beta value with standard errors in parentheses; * $p < 0.05$

Figure 1.

Psychological inflexibility with pain significantly mediates the relationship between heart rate variability (HRV) and pain interference. Values are unstandardized beta values with standard errors in parentheses. * $P < 0.05$.

Table 1.

Participant Characteristics

	Mean $\pm$ SD	n (%)
Age (years)	23.9 $\pm$ 2.1	
Gender		
Male		16 (41.0)
Female		23 (59.0)
Race		
Caucasian		29 (74.4)
African American		6 (15.3)
Other		4 (10.3)
Education (years)	13.0 $\pm$ 2.08	
NRS-11 Pain Rating	7.4 $\pm$ 1.9	
Pain interference score *	60.6 $\pm$ 5.9	
CES-D score	23.8 $\pm$ 12.1	

* Pain interference score is from the PROMIS and reflects a T-score with mean = 50 and SD = 10; CES-D clinical cutoff is > 27. CES-D, Center for Epidemiological Studies– Depression; NRS, numeric rating scale–11.

Table 2.

Linear Regression Model Examining Predictors of Heart Rate Variability

Variable	Statistics by Variable			
	Partial R^2	Beta	t	P
Sex	0.26	0.19	0.88	0.40
Age	0.19	0.13	0.64	0.53
Pain intensity (NRS-11)	−0.43	−0.48	−2.12	0.06
Psychological inflexibility (PIPS)	−0.65	−0.58	−2.84	< 0.02

Boldface values indicate statistically significant independent predictors. NRS-11, numeric rating scale–11; PIPS, Psychological Inflexibility in Pain Scale.

Table 3.

Linear Regression Model Examining Predictors of Pain Intensity

Variable	Statistics by Variable			
	Partial R^2	Beta	t	P
Age	0.60	0.46	2.57	< 0.03
Disease severity	0.34	0.21	1.25	0.23
Pain anxiety (PASS)	-0.30	-0.19	-1.09	0.30
HRV	-0.64	-0.51	-2.85	< 0.02

Boldface values indicate statistically significant independent predictors. HRV, heart rate variability; PASS, Pain Anxiety Sensitivity Scale.