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Autonomic dysregulation and impairments in the recognition of facial emotional expressions in patients with chronic musculoskeletal pain

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Abstract

Objectives: Emotions are involved in the identification of safety cues in the environment, and are also related to social interaction through recognition of emotional facial expressions. Heart rate variability (HRV) can be an indicator of the adaptive response of the autonomic nervous system to stressful conditions, including pain. This study aimed to investigate the emotional processing in a sample of patients with chronic musculoskeletal by measuring the resting-state HRV and the ability to recognize facial emotion expressions.

Methods: This cross-sectional study was composed of 40 participants with chronic musculoskeletal pain and 40 asymptomatic participants. Resting HRV was measured for 10 min. The facial emotion recognition task was presented in videos and included modification from a neutral expression to faces of fear, anger, sadness, happiness, and disgust. For the facial emotion recognition task, the hit rate (%) and response time for each emotional category were measured.

Results: The symptomatic group had a mean high frequency (HF) lower (mean = 34.14; SD = 16.95; p<0.001) than the asymptomatic group (mean = 51.11; SD = 13.01; p<0.001). The emotional facial expressions of disgust (H (1, 80)=7.82; p<0.01), anger (H (1, 80)=13.56; p<0.01), sadness (H (1, 80)=6.58; p=0.01), and happiness (H (1, 80) =12.68; p<0.01) were those for which volunteers from the symptomatic group had a lower hit rate of correct answers compared to the asymptomatic group. The response time to corrected answers showed a major group effect (F (1.77) =21.11; p<0.001) and emotional category (F (4.308) =174.21; p<0.001), without presenting any interaction between the factors (F (4.308)=0.446; p=0.775). The symptomatic group was slower to perform the task of identifying facial emotional expression (7.066 s; SD = 1.188) than the participants in the asymptomatic group (6.298 s; SD = 1.203) for all emotional categories.

Conclusions: Participants with chronic musculoskeletal pain presented a lower vagal activity evidenced by HRV. Participants in the symptomatic group showed lower ability to recognize faces of disgust, anger, and sadness when compared to asymptomatic participants. Considering that individuals with low resting HF-HRV have difficulties with regulating their emotions, the lower vagal activity and lower ability to recognize faces of emotional expressions observed in chronic musculoskeletal pain may suggest alterations in emotional processing. This study may shed light on changes in the emotional processing and in the autonomic nervous system in this population.

Keywords: chronic pain; face recognition; heart rate variability; pain.

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Introduction

Emotion and pain are fundamental for survival [1]. Emotions can be understood as synchronized changes in

multiple physiological systems in response to the identification of salient stimuli in the environment, including those in facial expression [2–5]. The neurovisceral integration model describes a complex neural system that integrates signals from inside and outside the body and adaptively regulate physiological cognitive and behavioral responses, perception, and action including sensory and motor changes [6]. This model proposes that the amygdala, which has its control mediated by the prefrontal cortex and outputs to the autonomic nervous system (ANS), can be influenced during threat and uncertainty [7–9].

Despite the complexity of this neural system, it is possible that physiological measures, such as heart rate variability (HRV), can serve as indices of the degree to which this system provides flexible, adaptive regulation in the presence of challenges (i.e. environmental, and also pain) [10–14]. HRV provides a measure of the interaction of autonomic, humoral, and intrinsic influences on heart rate. In other words, HRV may serve as an objective index of emotional processing by demonstrating that affective states are integrated with a degree of physiological arousal that prepares the body to respond to stimuli present in the environment [15]. Although individuals with higher levels of resting HRV indicates a highly adaptative context emotional responses, low HRV is associated with a multitude of negative long-term health outcomes, including cardiovascular disease, mood disorders, and increased morbidity [15]. ANS dysregulation and low HRV have been reported in several health conditions, including chronic pain [16, 17].

A close interaction between pain and emotion should be expected since pain is inherently salient, aiming to protect our body from actual or potential tissue damage [18]. Neuroimaging studies present evidence of anatomical and functional maladaptive brain modifications in several areas involved in pain, cognitive and emotional processing such as the amygdala, anterior cingulate cortex, prefrontal cortex, and insula [19–23]. In humans, emotions are also crucial for social interactions. The ability to perceive, process, and interpret social information is achieved mainly by the understanding of nonverbal facial expressions of emotions in others. This ability informs us about the emotional states of other individuals and guides the way we interact [4, 24]. Deficits in face recognition of emotional expressions have been reported in patients with regional complex pain syndrome [25], orofacial pain [26], and fibromyalgia [27].

Until now, few studies have evaluated the resting HRV as well as the ability to recognize facial emotional expressions in patients with chronic pain. The aim of this study was to investigate the emotional processing in a sample of patients with chronic musculoskeletal pain by measuring the resting HRV and the ability to recognize faces of emotional expressions (fear, anger, disgust, surprise, happiness, and sadness) [28].

We hypothesize that participants with chronic pain present ANS dysregulation and impairment in recognizing faces of emotional expressions when compared to asymptomatic participants.

Methods

Ethical considerations and sample characteristics

This cross-sectional study was approved by the Ethical Board Committee of the Federal Institute of Rio de Janeiro (CAAE 53993616.4.0000.5268). Study participants were assigned to symptomatic and asymptomatic groups. The study protocol followed the recommendations of the strengthening the reporting of observational studies in epidemiology (STROBE) Statement [29]. Data was collected from October 2018 to April 2019.

Participants

We recruited participants of both genders and aged between 18 and 60 years. The symptomatic group included participants with chronic musculoskeletal pain [30] (discomfort stemming from muscles, ligaments, tendons, and bones for more than three months) with moderate and severe pain intensity. Participants were recruited consecutively during their medical appointment at the Orthopedics and Traumatology Service of the Clementino Fraga Filho University Hospital (HUCFF). The asymptomatic group was composed of participants who did not have pain in any part of the body recruited by advertisement in the University and on the social media (Facebook and Instagram). Exclusion criteria were: regular intake of psychiatric medication (for example antidepressants, anticonvulsants), radiculopathies, diagnosis of psychiatric disorders, major cognitive impairment, heart diseases, history of heart infarction, hypertension, and diabetes.

Instruments

Initially, demographic and health-related data was collected using an assessment form. The following instruments were used to characterize the group with chronic musculoskeletal pain:

(1) Pain intensity and pain interference: The brief pain inventory (BPI) was used to measure mean pain intensity, current pain, and pain interference. BPI is an 11-point numerical rating scale, where zero indicates 'no pain' and 10 indicates 'worst pain possible'. The pain interference subscale consists of seven items to measure to what extent pain interferes in various aspects of life, including general activity, mood, mobility, normal work, relationships with others, sleep, and life pleasure. Items are also rated on an 11-point numerical rating scale where zero indicates 'does not interfere' and ten indicates 'completely interferes' [31].
(2) Symptoms of anxiety and depression: The symptoms of anxiety and depression were investigated using the hospital anxiety and depression scale (HADS). This scale has 14 items, of which seven are anxiety related statements, and seven are depression related

statements. Responses can be scored from zero to three points for a total of 21 points for each scale division and a total of 42 points [32].

(3) Alexithymia: Alexithymia is a personality trait characterized by difficulty in experiencing and expressing emotions. The Alexithymia Toronto Scale (TAS) is a self-report instrument composed of 26 items and is designed to measure the degree of alexithymia. Items are answered on a five-point Likert scale ranging from 1 (strongly disagree), 2 (disagree), 3 (don't know), 4 (agree), and 5 (strongly agree). Total scores range from 26 to 130. For scores above 75 the participant is considered to have alexithymia, and below 62 is considered as not having alexithymia [33].

(4) Kinesiophobia: The Tampa Kinesiophobia scale is a self-reported 17-item scale that is used to measure fear of movement/re-injury. All items are rated on a four-point Likert scale (1 = strongly disagree, 4 = strongly agree). The total score ranges from 17 to 68. Higher scores indicate higher levels of kinesiophobia [34].

(5) Catastrophizing: The pain catastrophizing scale (PCS) was used to measure pain catastrophizing thoughts. Catastrophizing pain can be defined as an exaggerated negative perception of pain and is well established as an important psychological risk factor for pain-related outcomes. The PCS consists of 13 items that refer to an expanded perception of pain-related threats, ruminant thoughts about pain, and feelings of helplessness. The frequency of thoughts associated with each item is rated on a five-point Likert scale, where zero indicates 'not all' and four indicates 'all the time'. The total score is calculated as the sum of all items. Higher scores in the PCS indicate higher levels of catastrophizing. The PCS is the most common measure used for pain catastrophizing and has been shown to have strong reliability and predictive value among people with musculoskeletal pain [35].

HRV measurement and analysis

Volunteers attended a single visit in the laboratory between 8:00 a.m. and 10:00 a.m. for anamnesis, HRV recordings and facial emotion recognition task measurements. The experimental protocol was carried out in a quiet room with noise, temperature, and humidity controlled. Before starting the HRV measurement, participants were instructed to remain seated on a chair with armrests in front of a computer screen, and to breath normally for 5 min. During the HRV acquisition, participants were instructed to look at a white fixation cross in a black background, displayed on a 15-in. computer screen. For HRV acquisition, a portable heart rate monitor, Polar H7 Bluetooth (Bethpage, NY, USA), fitted just below the sternum, was used to register the RR intervals. Portable HRV methods are reliable and consistent with an electrocardiogram [36]. Participants were asked to avoid talking, performing large and sudden movements, and sleep. After the 5 min resting phase, HRV was measured for 10 min. The collected HRV was reviewed by visual inspection and data analysis was performed using the open-source software Kubios (http://www.kubios.com). HRV was analyzed in frequency domain including low frequency [LF (ms^2), 0.04–0.15 Hz] (reflects a mix between sympathetic and vagal influences that shows an influence of both sympathetic and parasympathetic branches), high frequency [HF, (ms^2) 0.15–0.4 Hz] (reflects vagal tone), and low frequency-to-high frequency ratio [LF (ms^2)/HF (ms^2 130)] components of the RR interval time series.

Recognition of facial expressions of emotion

The stimuli were composed of high-resolution monochrome digital photographs selected from the standardized set pictures of facial affect [37]. Male and female faces of emotional expressions (neutral, anger, disgust, fear, happiness, and sadness) were selected for the task. The morphing technique (i.e. gradual transition from one image to another until reaching the final image) was used to convert pictures into videos. The morphing was generated in Facemorpher lite (Luxand Development) and then transferred to E-prime 2.0 software (Psychology Software Tools USA). For all stimuli, the initial face consisted of a neutral face that changed to another face of emotional expression as follows: neutral–happiness; neutral–fear; neutral–

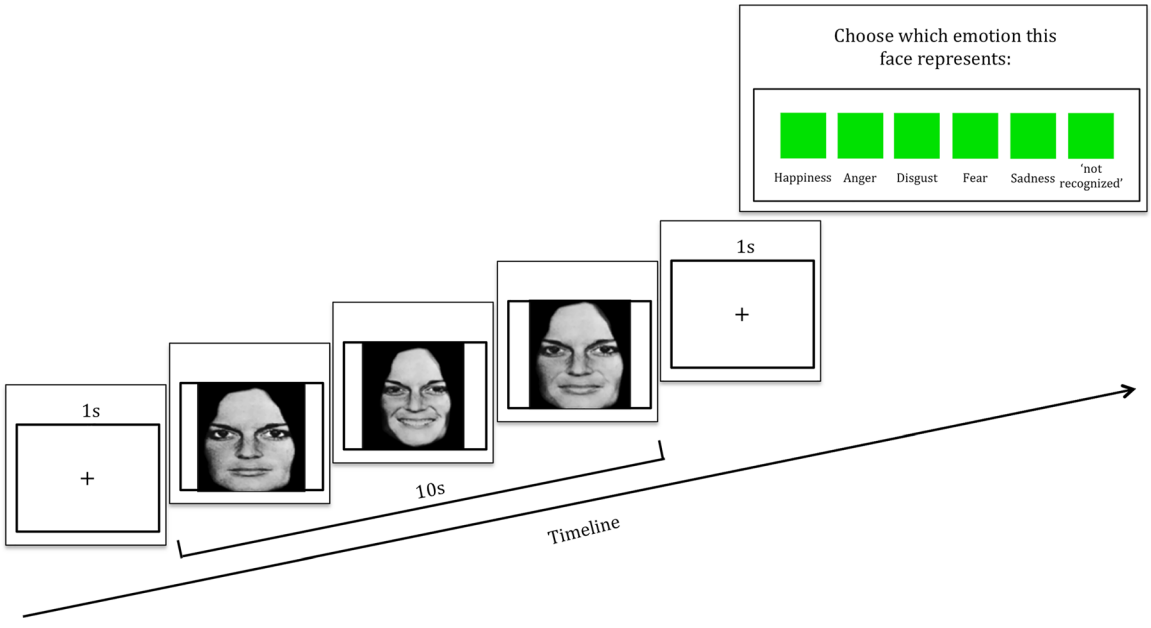

Figure 1: A timeline showing the recognition of facial expressions of emotion task. Pictures were converted into videos using a morphing technique.

disgust; neutral–sadness; neutral–anger. Faces of neutral emotional expression were used to neutralize the stimulus [38]. Videos were presented for ten seconds on a 15-in. computer screen in a randomized sequence, followed by a white fixation cross (1 s) and then a screen with response options with six options (anger, disgust, fear, happiness, sadness, and 'not recognized'). Participants were instructed to press the left mouse button quickly (response time) and accurately as soon as they had identified the emotion during the video presentation. Figure 1 represents the timeline of the recognition of facial expressions task.

Data analysis

An a priori sample size calculation showed that a total of 74 individuals would be necessary to detect 30% difference on LF and on facial expressions of emotion task with a statistical power of 80%, alpha of 5%. The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 22 for Windows (IBM Corporation, Armonk, New York, USA). The demographic and clinical variables of the study population were presented as means and standard deviations for continuous variables. Categorical variables were presented as absolute values and frequencies. Data normality was tested through visual inspection of histograms and Shapiro–Wilk Test. For the HRV means within-group difference, we used the paired Student's *t*-test and the Student's *t*-test for independent samples for the mean difference between groups. Mean difference and confidence interval (95%) were presented. For facial emotion recognition tasks, the number of correct responses (hit rate) was computed for each volunteer from percentage correct classification out of the total number of stimuli for each emotional category (percentage relative to the videos presented). A non-parametric test, Friedman's analysis of variance (ANOVA) was performed to test the hit rate for each emotion category, and the Kruskal–Wallis test was applied to assess the effect of the groups. Additionally, the unbiased hit rates (Hu) were calculated for each emotion using the formula proposed by Wagner et al. [39], and each response option was added to the calculation (five emotions and the 'not recognized' option). For each volunteer, the median and standard deviation of the valid response time (RT) for each emotional category were calculated. The valid RT considered the correct classification of emotional faces, and the anticipatory (below 100 ms), slow response (above 10 s), and incorrect or 'not recognized' classifications were excluded from RT calculation. These data were analyzed using repeated-measures ANOVA: the first factor was a group of volunteers with two sublevels (symptomatic and asymptomatic) and the second factor was the emotional category of the video with five sublevels (anger, disgust, fear, happiness, and sadness). The significance level adopted in the study was 95%.

Results

Eighty-three volunteers were evaluated. We excluded one volunteer for not responding to the recognition of facial expressions of emotion task and two due to sleepiness. The total sample consisted of 80 participants, 40 in the symptomatic group and 40 in the asymptomatic group, matched by gender and age (Table 1).

Table 1: Sociodemographic and clinical characteristics of participants in the symptomatic and asymptomatic group.

Characteristics	Asymptomatic group	Symptomatic group
Age (years), mean (SD)	43.18 (11.0)	43.15 (11.58)
Gender, n (%)		
Female	32 (80.0%)	32 (80.0%)
Male	8 (20.0%)	8 (20.0%)
Relationship, n (%)		
Single	30 (75.0%)	15 (37.5%)
Married	10 (25.0%)	22 (55.0%)
Divorced		3 (7.5%)
Educational level, n, %		
Elementary	1 (2.5%)	6 (15.0%)
Medium	15 (37.5%)	17 (42.5%)
Higher	24 (60.0%)	17 (42.5%)
Pain, mean, SD		
Mean pain intensity (0–10)*		5.7 (1.50)
Pain intensity (at the moment) (0–10)		3.98 (2.41)
Pain interference (0–10)		4.72 (2.40)
Kinesiophobia (0–68), mean (SD)		44.02 (7.96)
Catastrophizing (0–52), mean (SD)		25.32 (10.6)
Anxiety (0–21), mean (SD)	5.65 (3.47)	9.52 (3.90)
Depression (0–21), mean (SD)	3.18 (2.14)	6.55 (3.69)
Alexithymia (0–100), mean (SD)	70.28 (9.67)	80.08 (12.14)

Comparison of resting HRV

In the HRV frequency domain, the mean of LF and LF/HF were higher for the symptomatic group when compared to the asymptomatic group. The symptomatic group had a mean HF lower (mean = 34.14; SD = 16.95; $p<0.001$) than the asymptomatic group (mean = 51.11; SD = 13.01; $p<0.001$) (Table 2).

Recognition of facial expressions of emotion

The results of video classification by Friedman's ANOVA showed a significant effect of emotion category (Chi-squared (80, 4)=142.86; $p<0.01$). For both groups a lower hit rate was found for disgust (mean = 68.20 sd = 18.04), anger (mean = 72.75 sd = 13.63) and sadness (mean = 78.42 sd = 16.13), and a higher hit rate was found to happiness (mean = 97.33 sd = 4.70), and fearful (mean = 86.25 sd = 14.50) facial expressions (Figure 2). The results of the classification of each emotion by group are presented in a confusion matrix (Figure 3).

Table 2: Mean resting heart rate variability (HRV) parameters and mean HRV difference between symptomatic and asymptomatic groups.

Variables	Mean, SD		Mean difference (95% CI)	p-Value
	Asymptomatic (n=40)	Symptomatic (n=40)	Asymptomatic vs. symptomatic	
Frequency domain				
LF (n.u)	48.73 (13.4)	64.46 (16.27)	−15.72 (−22.29 to −9.16)	<0.001
HF (n.u)	51.11 (13.01)	34.14 (16.95)	16.97 (10.24–23.70)	<0.001
LF/HF, ms^2	1.21 (1.30)	2.68 (1.97)	−1.46 (−2.21 a −0.72)	<0.001

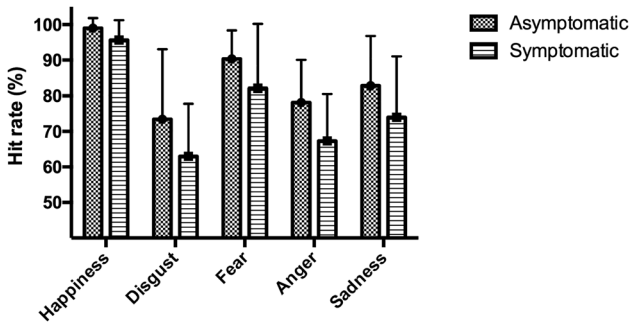

Figure 2: Hit rate (%) responses for each facial expressions of emotion by group.

The Kruskal–Wallis ANOVA revealed that the emotional facial expressions of disgust (H (1, 80)=7.82; p<0.01), anger (H (1, 80)=13.56; p<0.01), sadness (H (1, 80)=6.58; p=0.01), and happiness (H (1, 80)=12.68; p<0.01) were those for which volunteers from the symptomatic group had a lower hit rate of correct answers compared to the asymptomatic group. No significant group differences were observed to fearful faces expression (H (1, 80)=2.04; p=0.15). The participants in the symptomatic group presented a lower number of correct responses when compared to the asymptomatic group (Table 3).

The RT to corrected answers showed a major group effect (F (1.77) = 21.11; p<0.001) and emotional category (F (4.308) = 174.21; p<0.001), without presenting any interaction between the factors (F (4.308) = 0.446; p=0.775). In general, the symptomatic group was slower to perform the task of identifying facial emotional expression (7.066 s; SD = 1.188) than the participants in the asymptomatic group (6.298 s; SD = 1.203) for all emotional categories. The emotional categories that presented the highest differences in RT between the symptomatic and asymptomatic groups were the facial expressions of sadness (919.70 ms), fearful (866.98 ms), and disgust (818.69 ms) (Table 3).

Discussion

The results of the present study showed that the symptomatic group presented a lower mean for the HF band and a higher mean for LF and LF/HF characterizing lower vagal activity. For the facial emotion recognition task, the symptomatic group had a lower hit rate for classification for all emotions, especially negative emotions (disgust, anger, and sadness), and slower RT. Altogether, these results are indicating autonomic and emotional impairments in the symptomatic group that could also include cognitive and motor alterations.

The autonomic dysregulation measured by HRV in people with chronic pain has been reported in previous studies in the literature. A recent systematic review

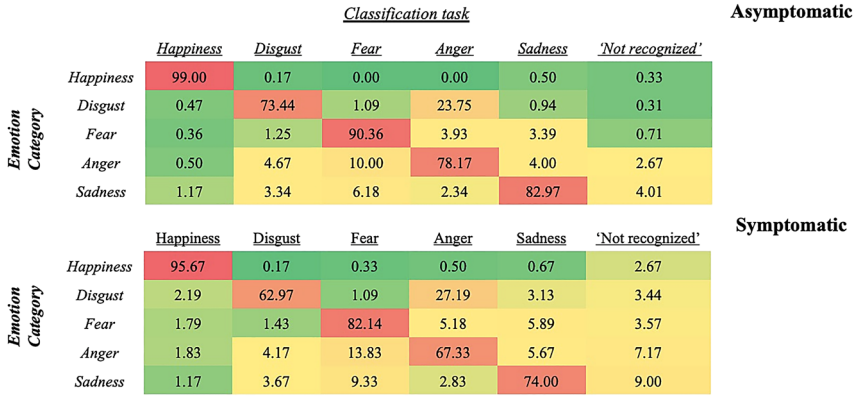

Figure 3: Confusion matrix presenting the results of the recognition of facial expressions of emotion task by group.

Table 3: Comparison between asymptomatic and symptomatic participants in the recognition of facial expressions of emotion task.

Recognition of facial expressions of emotion task	Asymptomatic n=40	Symptomatic group n=40
Correct answers, % (DP)		
Happiness	99.0% (2.84)	95.67% (5.56)
Disgust	73.44% (19.60)	62.97% (14.80)
Fear	90.36% (8.01)	82.14% (18.08)
Anger	78.17% (11.89)	67.33% (13.23)
Sadness	82.83% (13.99)	74.00% (17.07)
Response time, mean, SD[a]		
Happiness	4,942.50 (844.30)	5,706.85 (877.47)
Disgust	6,492.74 (1,027.05)	7,311.43 (974.09)
Fear	6,138.21 (871.70)	7,005.19 (926.08)
Anger	7,139.96 (895.24)	7,873.58 (877.49)
Sadness	6,777.36 (1,067.90)	7,697.06 (908.23)

[a]Response time in milliseconds.

including a broad range of chronic pain conditions identified that HF was lower in people with chronic pain compared to healthy controls, with a moderate effect size of 0.39 (95% CI = 20.60–20.19). The authors also found a higher LF/HF ratio compared to healthy controls, with a significant effect size of 0.99 (95% CI = 0.45–1.53] [40]. However, no differences were observed in LF values. These findings are in accordance with the current study representing changes in sympathovagal balance in participants with chronic musculoskeletal pain.

There are some hypotheses to explain sympathetic-excitatory responses in people with chronic pain. The most plausible mechanism may be based on the relationship between descending pain inhibitory pathways and ascending vagal pathways [41, 42]. Our results provide evidence that the changes in sympathovagal balance may be related to the continuous presence of a stressor (pain) in the body [43] or even a consequence of shared neural network dysfunctions involved in the processing of pain, emotion, cognition, perception, and physiological responses [44, 45]. This autonomic dysfunction, in particular cardiac sympathetic regulation and vagal tone, may be partially involved in health problems associated with chronic pain, such as poor sleep quality [46, 47].

In the present study, symptomatic participants had more difficulty in recognizing faces of sadness, disgust, and anger. The lower hit rate and the slower response implies that there is an impairment of emotional recognition of facial expression in the symptomatic group. This impairment has been presented in several studies that investigated patients with neurological disease [48, 49] and mental disorders, such as major depression [50, 51]. Some studies have demonstrated that patients with depression present a negative perceptual bias (i.e., recognizing significantly more sadness in facial expressions than healthy volunteers) in individuals with major depression [52–55]. This negative bias manifested by attentional displacement from negative faces, inaccurate labeling of negative emotions and enhanced recognition of negative facial displays was also observed in patients with social anxiety [56].

Until now, studies have used different protocols. Von Piekartz et al. [26] included participants with chronic orofacial pain and observed lower hit rate and a longer response time when compared to the asymptomatic group. Shin et al. [25] also observed a lower hit rate and a higher response time in a sample of participants with chronic complex regional pain syndrome. Di Tella et al. [57] included participants with fibromyalgia and identified greater difficulty in recognizing faces of anger and disgust when compared to the asymptomatic group.

One important difference in our study remains in our protocol, which used the morphing method to evaluate the ability to recognize faces of emotional expressions. Morphing presentation, rather than the use of static images, is closer to what occurs in social interactions where the expressions of emotions change rapidly (dynamic expressions) [58]. This protocol is not new and has already been used in previous studies [59–61], and it seems that dynamic expressions were recognized more accurately and faster than static expressions [61]. However, differences in tasks and procedures could lead to different results in terms of accuracy for discrimination and response time. According to our initial hypothesis, participants with chronic musculoskeletal pain have a lower hit rate to the recognition of emotional facial expressions and were slower to detect changes of neutral to emotional stimuli.

Social cognition is a relevant ability to interact with others. The inability to recognize faces of emotional expressions may contribute to impairment in social integration and consequent social isolation [45]. Deficits in the perception of facial emotion expressions are also associated with increased psychological and interpersonal stress through the reduction in or avoidance of peer interactions [43, 62]. The perception of social isolation can have a relevant impact on patients with pain [63]. Until now, few studies have investigated the social isolation in patients with chronic pain. Perceived social isolation was a significant predictor of disability at 6-month follow-up in a sample of patients with low back pain of any duration [64]. It is important to consider that the response time may be influenced not only by changes in the face recognition

ability of emotional expressions, but also by deficits in tasks that involve concentration and attention observed in people with chronic pain [60, 65].

Limitations

This study presents some limitations that need to be noted. First, other psychological comorbidities may influence HRV and also in the face recognition task. However, the patients included in this study represent those assessed in clinical practice. Second, we did not classify the patients according to the pain mechanism (nociceptive, neuropathic, or nociplastic). Participants with nociplastic pain may have different results regarding HRV and the recognition of faces of emotional expressions, since this population may have deficits in descending pain modulation. Clinical studies based on diagnostic criteria, incorporating an extensive pain examination, are needed to address this issue. Third, women were predominant in our sample. We tried to reduce the gender influence in the results by matching the samples by gender and age. The present results should be addressed with caution in terms of sex differences in autonomic measures of emotion reactivity [66]. Fourth, no information regarding the participants' perception of social isolation was collected to verify the association with the deficit of face recognition of emotional expression. Besides, the cross-sectional design of our study does not allow attributing causal relationships or temporal associations between HRV, face recognition, and pain. Longitudinal studies to investigate the potential temporal sequence between reductions in vagal control, changes in face recognition, and changes in pain processing are strongly encouraged. Finally, we did not analyze other domains of HRV such as time domain and non-linear methods since they need a longer acquisition duration. Future studies are required to address these limitations as longitudinal studies in acute/subacute pain conditions, 24-h HRV recording, and the relationship of clinical improvement with HRV and face recognition are recommended.

Conclusion

In the present study, it was demonstrated that participants with chronic musculoskeletal pain have a sympathetic-excitatory response and consequently lower vagal activity as evidenced by HRV. Participants in the symptomatic group also present lower ability to recognize faces of disgust, anger, and sadness when compared to asymptomatic participants. The changes observed in the present study may involve alterations in emotion processing in the brain due to modifications observed in chronic pain conditions.

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Informed consent: All participants signed the informed consent.
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