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Heart Rate Variability in Acute and Chronic Pain: A Systematic Review of Autonomic Function and Pain Mechanisms

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Authors' contributions

This work was carried out in collaboration among all authors. Author RAAMQ designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors GCMN and SDAN managed the analyses of the study. Author LMDMT managed the literature searches. All authors read and approved the final manuscript.

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Review Article

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ABSTRACT

Aims: To investigate the relationship between heart rate variability (HRV) and acute and chronic pain, focusing on its potential as an objective tool for pain assessment.
Study Design: Integrative literature review.
Place and Duration of Study: The study was conducted through database searches (SCIELO, PUBMED, LILACS, BVS, and MEDLINE) between July 2024 and october 2024.
Methodology: The results indicate a significant reduction in HRV in patients with chronic pain, suggesting dysfunction in the parasympathetic nervous system. In acute pain contexts, HRV also decreases, reflecting an increase in sympathetic activity and a decrease in parasympathetic response. HRV differences were observed based on age and gender, with young adults showing greater autonomic reactivity compared to older adults, and men exhibiting a greater reduction in HRV in response to acute pain compared to women. These findings suggest that HRV could serve as an objective tool for assessing pain, especially in non-communicative patients.
Results: A significant reduction in HRV was observed in patients experiencing chronic pain, which indicates parasympathetic nervous system dysfunction. In acute pain scenarios, HRV typically decreases, reflecting increased sympathetic activity and reduced parasympathetic response. Differences in HRV changes were also noted based on age and gender, with young adults experiencing greater autonomic reactivity compared to older individuals, and men showing more substantial HRV reduction in response to acute pain compared to women.
Conclusion: HRV shows promise as an objective pain indicator, providing healthcare professionals with an additional tool for assessing pain intensity and intervention effectiveness. However, there is a need for standardization in HRV measurement techniques and further studies to explore its clinical applications across various populations and health conditions. Variability in pain induction methods and HRV measurement approaches in the analyzed studies also represents a limitation, highlighting the need for more uniform methodologies to consolidate HRV use in pain contexts.

Keywords: Heart rate variability; acute pain; chronic pain; autonomic nervous system; pain assessment; sympathetic activation; parasympathetic dysfunction.

1. INTRODUCTION

The International Association for the Study of Pain (IASP) recently revised the definition of pain, describing it as "a distressing experience associated with actual or potential tissue damage, encompassing sensory, emotional, cognitive, and social components" [1]. Thus, pain is characterized as a subjective symptom that is difficult to measure, traditionally assessed through self-reporting.

Uncontrolled pain results in respiratory, hemodynamic, and metabolic changes, predisposing the patient to cardiovascular instability, increased energy and protein consumption, difficulty in early ambulation, and increased risk of deep vein thrombosis (DVT), especially in elderly patients undergoing extensive surgeries [2,3]. Furthermore, uncontrolled pain can impair sleep, leading to greater physical wear, fatigue, and reduced motivation to cooperate with treatment.

The measurement of pain experience is a challenging task due to the complexity of the phenomenon and the lack of an ideal measurement tool that allows precise and accurate access to what the patient is feeling. The American Pain Society defines pain as the fifth vital sign, which must always be assessed along with other vital signs, such as temperature, respiratory rate, heart rate, and blood pressure, at the time of patient admission [4]. Pain assessment assists in diagnosing the presented problem and is crucial for continued care and treatment during consultations or hospitalization [5].

It is known that the activity of the sympathetic and parasympathetic nervous systems is altered in conditions of chronic pain, such as chronic low back pain, pain in the neck and shoulder region, fibromyalgia, complex regional pain syndrome, and phantom limb pain. In this regard, dysregulation of autonomic balance can be measured using Heart Rate Variability (HRV), a marker of vagal components of the sinoatrial node of the heart that measures changes in beat-to-beat intervals [6].

Heart Rate Variability (HRV) is a vital sign that can be used to assess pain, especially in non-communicative patients. Pain causes

modifications in vital signs such as blood pressure, respiratory rate, and heart rate, as well as significantly influencing body temperature [7]. Thus, HRV, which reflects changes in heart rate, may be a potentially useful tool for healthcare professionals in pain assessment, as its variations indicate the body's physiological responses to pain, allowing for a more accurate analysis of pain sensitivity and its effects on vital signs [8].

However, the quantification of pain is subjective since it relies on analog scales and depends on each individual's perception of pain. This leads to subjective and often inaccurate diagnoses. Therefore, it is essential to quantify pain correctly, in a non-subjective manner, based on physiological signs.

2. MATERIALS AND METHODS

For a comprehensive and accurate understanding of the relationship between Heart Rate Variability (HRV) and pain in acute and chronic contexts, this study conducted a systematic literature review using widely recognized databases (SCIELO, PUBMED, LILACS, BVS, MEDLINE). Studies published between January 2010 and March 2023 were considered, covering HRV experiments in the context of autonomic modulation and pain response.

2.1 Inclusion and Exclusion Criteria

The inclusion criteria were restricted to studies with robust methodology, such as systematic reviews, meta-analyses, and randomized clinical trials investigating HRV in response to pain. Studies with advanced methodological approaches were considered essential for interpreting the relationship between autonomic modulation and pain, particularly due to the consolidated evidence of parasympathetic dysfunction in chronic pain cases and the use of HRV as a tool to evaluate the autonomic response to experimentally induced pain stimuli.

Exclusion criteria included articles unavailable in full text, uncontrolled observational studies due to high risk of bias, and studies without a representative sample. This review also faced limitations related to publication bias, as studies with negative or null results are less frequently published. However, efforts were made to minimize these biases through a rigorous screening methodology.

2.2 Study Selection and Analysis

The initial search identified 25 studies, of which 15 were included in the final qualitative synthesis. Studies examining the applicability of HRV as an objective marker of pain in populations with chronic pain, and analyzing the association between resting HRV and pain sensitivity, were considered due to the high relevance of their contributions. Additionally, to expand the analysis of specific subpopulations, a study using HRV to assess pain in neonates was included, highlighting HRV's utility across different age groups and health conditions.

Data from each study were extracted to evaluate the influence of pain on HRV and the changes in autonomic balance between the sympathetic and parasympathetic nervous systems. To ensure consistency and quality in data collection, each article was reviewed according to PRISMA guidelines, and relevant information was categorized based on the impact of acute and chronic pain on HRV.

2.3 Synthesis and Interpretation of Results

The results were interpreted in terms of autonomic response, acknowledging limitations in specific studies, such as methodological variability in HRV measures and differences in pain induction approaches. Studies providing insights into the limitations of HRV in different contexts of stress and pain highlighted autonomic variations and their potential influences on pain assessment. The analysis emphasized autonomic responses during acute pain, such as increased sympathetic activity, and chronic responses reflecting parasympathetic dysfunction.

2.4 Limitations and Potential Biases

Limitations of this review include lack of access to some full-text articles and publication bias, which could limit the representation of findings on HRV and pain. Variability in pain induction techniques and HRV measurement methodologies may also contribute to methodological biases. Nonetheless, the inclusion of recent and robust studies provided a solid basis for analyzing specific subgroups, such as postoperative patients and individuals with neurofibromatosis, expanding the understanding of the relationship between pain and HRV in different clinical contexts.

3. RESULTS AND DISCUSSION

3.1 Heart Rate Variability (HRV) and Pain

In chronic pain conditions, a significant reduction in Heart Rate Variability (HRV) is observed in patients with persistent pain, indicating dysfunction in the parasympathetic nervous system. This alteration is particularly evident in conditions such as fibromyalgia and chronic fatigue syndrome, in which sympathovagal imbalance is recurrent, reflecting a state of sympathetic hyperactivity and reduced parasympathetic activity [9,10]. In acute pain contexts, HRV also tends to decrease, accompanied by an increase in sympathetic activity and a reduction in parasympathetic response, which reflects a heightened reactivity of the autonomic nervous system (ANS) to painful stimuli [11,12]. These HRV response patterns in pain contexts indicate that this measure can be used as an index of autonomic reactivity to noxious stimuli [9-12].

The modulation of acute pain is generally associated with an increase in heart rate (HR) and a reduction in HRV, reflecting an ANS stress response [13]. Studies demonstrate that HRV is a reliable method for assessing autonomic modulation during episodes of acute pain, with significant changes indicating increased sympathetic activity and decreased parasympathetic activity [14]. HRV alterations, such as sympathetic predominance observed in patients with chronic pain, also suggest a possible impairment in the pain modulation system [15].

Furthermore, evidence indicates that higher resting HRV is associated with a better capacity for pain modulation, whereas reduced HRV may reflect a deficient pain modulation system, especially in chronic conditions such as fibromyalgia [10,13]. Recent studies have expanded this understanding by suggesting that HRV, associated with psychological flexibility, is a relevant factor in chronic pain conditions, as observed in patients with neurofibromatosis type 1, where reduced HRV reflects greater pain interference and lower stress adaptability [16].

HRV analysis in neonates also suggests that this indicator can be a useful tool for assessing pain in non-communicative groups. In newborns, HRV is sensitive to post-surgical discomfort, with significant variations in response to pain, reinforcing its potential as an objective indicator of pain perception in vulnerable populations [17]. HRV has also been investigated as a potential marker of pain intensity in post-operative patients, with studies observing a correlation between pain intensity and reduced HRV after abdominal surgeries, suggesting that HRV could complement subjective pain assessment scales [18].

3.2 Patterns and Trends Related to Acute and Chronic Pain

Most studies indicate a significant reduction in Heart Rate Variability (HRV) in patients with chronic pain. This reduction is associated with dysfunction in the parasympathetic nervous system, suggesting a predominance of sympathetic activity in persistent pain conditions [6,15]. Patients with conditions such as fibromyalgia, chronic fatigue syndrome, and chronic neck and shoulder pain consistently exhibit reduced HRV, indicating autonomic imbalance [6,12,19].

In acute pain contexts, HRV also tends to decrease, reflecting increased sympathetic activity. This pattern is observed in experiments with healthy individuals, where pain is induced, resulting in changes in HRV that reflect the reactivity of the autonomic nervous system (ANS) to painful stimuli [6, 13,20]. Endogenous pain modulation correlates with resting HRV, and studies suggest that higher HRV is associated with better pain modulation capacity [6].

Chronic pain may develop from an initial trauma that triggers episodes of acute pain, evolving into chronic pain. Degenerative changes have also been suggested as underlying causes, although tissue damage is not necessary for chronic pain to develop. Psychological factors, such as emotional trauma and stress, are also associated with the etiology of chronic pain [10]. In patients with chronic pain, central sensitization and reduced inhibitory mechanisms are frequently observed, indicating increased sympathetic activation and reduced parasympathetic activation [16,19].

Moreover, spinal surgeries are frequently associated with postoperative complications, including persistent chronic pain. It is estimated that approximately 10 to 40% of patients who undergo lumbar surgeries develop chronic pain, significantly impacting their quality of life [17,20]. Recent studies also suggest that patients who develop chronic pain post-surgery exhibit a

consistent reduction in HRV, which may serve as a potential prognostic marker for complications related to chronic pain [18,21].

3.3 Age Effects

In neonates and infants, the autonomic response to acute pain is more pronounced. Studies indicate that Heart Rate Variability (HRV) is a sensitive measure for assessing pain in these age groups, being particularly useful in premature neonates, who exhibit a differentiated autonomic response to pain, with lower HRV compared to full-term neonates [9,10,19]. Studies by Faye et al. further support the use of HRV to accurately identify discomfort in neonates, especially in post-surgical pain contexts, indicating HRV's efficacy as an objective pain indicator in vulnerable pediatric populations [15,17,22,18].

HRV tends to decrease with age, regardless of pain presence. In young adults, acute pain induces a more significant reduction in HRV compared to the elderly, suggesting greater autonomic reactivity in younger individuals [13,15,20,23]. This difference in autonomic response may be attributed to the adaptation capacity of the autonomic nervous system, which is more robust in younger age groups and tends to decline with aging. Studies indicate that young adults with higher autonomic flexibility demonstrate superior pain modulation in response to acute stimuli, while the response in the elderly is less pronounced, possibly due to decreased parasympathetic function with age [14,19].

3.4 Gender Effects

Autonomic modulation of pain may vary between men and women. Men tend to exhibit a more pronounced reduction in Heart Rate Variability (HRV) in response to acute pain compared to women, which may be associated with hormonal differences and variations in stress responses [10]. Studies suggest that the sympathetic response to pain may be more pronounced in men, indicating greater autonomic reactivity in acute pain contexts.

Interventions such as manual therapy may also produce gender-specific effects. For instance, men generally respond more quickly to spinal manipulation techniques, showing an increase in HRV, while women may display more variable responses influenced by factors such as the menstrual cycle, which directly impacts autonomic modulation [6].

Additionally, in experimental studies of induced pain, evidence indicates that men exhibit greater sensitivity to thermal pain compared to women, which may be associated with reduced parasympathetic activity observed in HRV during the pain stimulus. These differences underscore the importance of considering gender when evaluating autonomic modulation of pain and the efficacy of therapeutic interventions [11-13,15].

3.5 Health Condition Effects

Individuals with chronic pain conditions, such as fibromyalgia, exhibit a significant reduction in Heart Rate Variability (HRV), indicating autonomic imbalance. This reduction in HRV reflects a predominance of sympathetic activity and diminished parasympathetic activity, commonly observed in chronic pain cases. Interventions such as HRV biofeedback have shown efficacy in improving autonomic modulation and reducing pain symptoms in these patients [11-13,15,23].

In patients with traumatic brain injuries, HRV can be used to monitor pain and stress. However, the autonomic response to pain may be blunted due to central nervous system damage, resulting in lower HRV compared to healthy individuals [9,10]. This profile is relevant for continuous health assessment in these patients and for personalized interventions, as nervous system damage may impair the capacity for autonomic modulation [12,20].

Furthermore, although Hypnotic Virtual Reality (HVR) has demonstrated significant changes in some physiological parameters, such as reduced respiratory rate and skin conductance response (SCR), no effect was observed on time-domain HRV measures. These findings suggest that HVR may not directly influence these cardiac parameters in acute and chronic pain contexts, as evidenced in the described experiments [15,17,18,20].

3.6 CONFLICTING OR DISCREPANT RESULTS

Some studies indicate that interventions, such as manual therapy, have an immediate effect on Heart Rate Variability (HRV), while others did not observe significant changes post-treatment. For instance, the addition of four sessions of spinal

manipulative therapy to a home-based stretching exercise program did not result in significant HRV changes. Conflicting results were also identified in studies examining the impact of different spinal manipulation techniques on HRV, with some systematic reviews reporting acute autonomic responses to various spinal manipulative therapy (SMT) techniques, while others found no robust evidence due to the low quality of the included studies [6,10,13].

HRV can be influenced by various factors beyond pain, such as emotional stress, physical activity, and pre-existing medical conditions, which can lead to variations in results. Studies that do not adequately control for these factors may present conflicting findings regarding the relationship between HRV and pain [6]. In individuals with chronic pain, these variables may interfere with the ability to accurately assess autonomic changes, as HRV reflects a combination of intrinsic and extrinsic factors that may not be directly related to the pain stimulus [11,12].

Furthermore, inconsistency in results is highlighted in studies involving Hypnotic Virtual Reality (HVR) interventions. While some physiological parameters, such as skin conductance, show significant responses, time-domain HRV does not exhibit robust changes. This suggests that HVR may not directly influence autonomic response in terms of HRV but affects other markers of stress and pain response [15,23].

3.7 Limtations of the Research

The limitations of this research include, firstly, methodological variability among the analyzed studies, with differing methods of pain induction and approaches to measuring Heart Rate Variability (HRV). This generates inconsistencies in results, making direct comparisons between findings challenging, as varied HRV measurement techniques and differences in pain intensity and type influence the outcomes. Additionally, not all relevant articles were available in full-text format, which limits the scope of evidence included in the analysis. Limited access to certain studies may introduce publication bias, as studies with negative or non-significant results are less frequently published and accessible.

Another important point is that external factors, such as emotional stress, physical activity, and pre-existing medical conditions, influence HRV and can interfere with results. In studies that do not adequately control these variables, interpreting data on the relationship between HRV and pain becomes conflicting. The low methodological quality of some studies, particularly those examining spinal manipulative therapy (SMT) and other autonomic interventions, also stands out. The inclusion of lower-rigor studies compromises the strength of conclusions and limits the reliability of the evidence in establishing a consistent relationship between interventions and HRV effects.

The generalization of results is limited, as the research mainly focuses on specific populations, such as patients with fibromyalgia, postoperative pain, and neonates, restricting the applicability of findings to other populations and chronic pain conditions. Populations with distinct neurological or metabolic conditions, which can influence autonomic modulation, are underrepresented in the analyzed studies. Additionally, the lack of standardization in using HRV as an objective marker of pain presents a significant limitation for its broader clinical application. Although HRV shows potential as a pain assessment tool, standardized protocols are still necessary to ensure consistency and accuracy in results. These limitations highlight the need for additional studies, with more uniform and rigorous methods, to consolidate the use of HRV in pain assessment across different clinical contexts and populations.

4. CONCLUSION

This study confirms that Heart Rate Variability (HRV) is significantly reduced in contexts of chronic pain, reflecting dysfunction in the parasympathetic nervous system. In acute pain situations, HRV decreases, indicating increased sympathetic activity, which characterizes the stress response of the autonomic nervous system. These findings suggest that HRV may be a useful and objective tool for pain assessment, especially in non-communicative patients.

The analysis revealed that the autonomic response to pain is influenced by factors such as age and sex, requiring an individualized approach to pain management. Additionally, it was observed that acute pain causes a more pronounced reduction in HRV in young adults compared to older adults, and that men tend to experience a greater reduction in HRV in

response to acute pain than women, possibly due to hormonal and stress response differences.

These findings underscore the need for standardizing HRV measurement methods and further research to explore its clinical applications across different populations and health conditions.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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