Chapter

# Exploring Cardiac Responses of Pain and Distress

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## Abstract

Pain and distress stand at the intersection of multiple health crises and are leading contributors to disability. Current pain assessments rely on self-reports—which assume a capacity to understand and verbalize mental/emotional states—and behavioral observation which can be subject to limitations and misinterpretation. Methods to evaluate pain/distress can be substantially enhanced with biometrics that incorporate the physiological aspects of the full pain experience. This chapter explores how induced pressure pain influences cardiac activity elicited via the autonomic nervous system. We aim to uncover signatures in cardiac responses via personalized analysis of the frequencies and the timings of the heart's inter-beat-interval. Autonomic responses such as cardiac activity serve as inevitable processes, which cannot be volitionally controlled—they exhibit a narrow range of dynamics, helping provide robust signatures of the body's responses to pain/distress. We find that pain elicits shifts in the heart rate variability metrics of the cardiac signal, alluding to changes in sympathetic and parasympathetic nervous system activation. Unique relationships are also observed between metrics obtained from the physiological data and self-reported pain ratings. The implications of this work are discussed in the context of precision medicine with possible applications in clinical populations such as autism.

**Keywords:** cardiac, pain, distress, sympathetic, biometric, ECG, HRV, autism, ASD

## 1. Introduction

Pain and distress are intrinsically undesirable experiences that are implicated in a variety of physical and mental illnesses. Pain stands at the intersection of multiple health crises, contributing to the opioid epidemic, health disparities, disability, and chronic pain [1, 2]. At least 125 million Americans suffer from acute or chronic pain, and this epidemic has been the root cause of the opioid crisis that arose in the late 1990s [2]. The increased use and misuse of opioids has led to over 47,000 deaths in the United States between 2013 and 2017 alone [3]. Thus, gaining a complete understanding of the neurobiological underpinnings of pain can lead to the most effective solutions to this epidemic [2].

Pain is yet to be explored and digitally characterized in terms of its effects on the autonomic nervous system (ANS). Aside from potential tissue damage, pain is associated with sensory, motor, cognitive, and social components [1]. Investigating pain thus requires multidisciplinary approaches that can integrate insights from

psychology (behavior, cognition, sensation, perception), neuroscience (nervous system physiology), and psychiatry (social/clinical research). An objective and noninvasive assessment of pain is also yet to be discovered and utilized in the clinical realm.

Traditional self-report techniques to assess pain are useful and convenient in the clinical realm however, they should be complemented with more objective approaches. Current pain assessments rely on surveys and questionnaires such as numerical rating scales, illustrative visual analog scales, and verbal rating scales which rely on semantic descriptors such as 'moderate' and 'severe' [4, 5]. Such assessments often assume the individual has the capacity to understand and verbalize mental/emotional states, making them disadvantageous for minimally verbal individuals or those with disabilities or neurodevelopmental disorders such as Autism Spectrum Disorder (ASD). Autistic children may experience difficulties in expressing their internal emotional states (hunger, pain, fatigue, etc.), leading to increased stress, tantrums/outbursts, and meltdowns. While external behavioral measures may be helpful in understanding such states, internal states may easily be masked or differently expressed across individuals, leading to interpretation errors. Thus, evaluating nervous system physiology in such populations can greatly enhance approaches that only rely on self-report measures and/or observing external behaviors.

In this work we evaluate the effect of pain on autonomic cardiac regulation, an inevitable process that cannot be consciously controlled during experimental tasks. The current study ultimately aims to develop digital biomarkers that can be used to detect pain and distress from cardiac activity elicited via the autonomic system. With the advent of wearable sensing technologies, it is possible to track physiologically relevant signals (electrocardiography/ECG) to help assess an individual's autonomic states. This study will utilize a multifaceted approach that investigates the effects of pain on cardiac reactivity in relation to self-reports of pain and pain sensitivity. With ECG sensors, we track the dynamics of heart signals and characterize how pain influences autonomic regulation. Pain-related biosignatures obtained via wearable sensors as the person

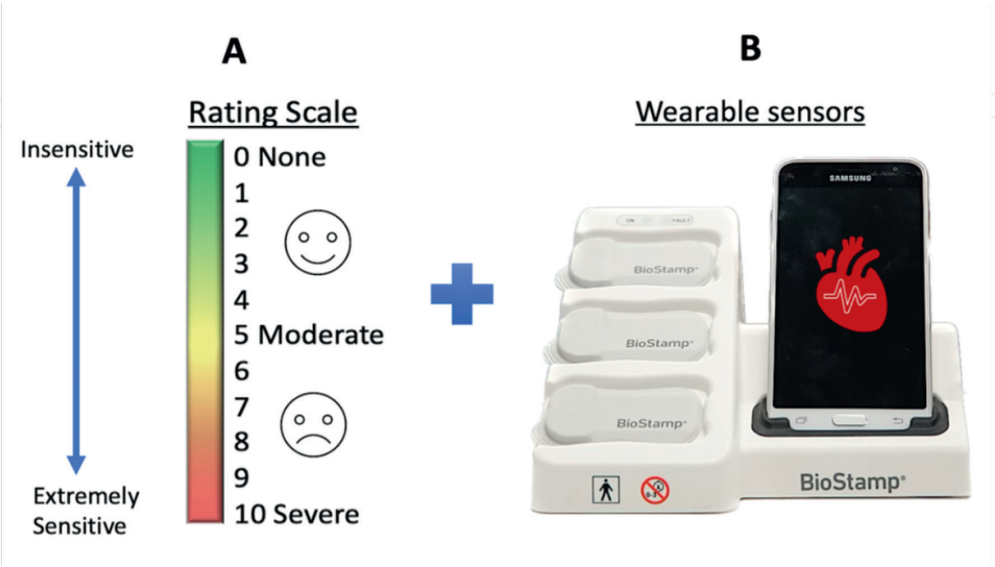


**Figure 1.**
*Integration of subjective and objective metrics to assess states of pain and distress. (A) Self-reports of pain and pain sensitivity levels are assessed by numeric rating scales traditionally used in healthcare settings to assess pain. (B) Wearable sensors that can track heart signals serve as a proxy for autonomic nervous system activity.*

experiences physical pain are compared to the results of pain assessments self-reported by the individual. This integrative approach (**Figure 1**) leverages information from the autonomic systems to help in developing a clearer psychophysiological understanding of pain and ultimately aims to create robust techniques to assess pain and distress in those who have difficulty expressing it and in the general population.

## 2. Cardiac signals as a proxy for autonomic nervous system (ANS) regulation

Heart activity is under the dynamic control of the sympathetic cardiac nerves and the parasympathetic vagus nerve via the autonomic branches of the peripheral nervous system (NS). The ANS is largely responsible for maintaining the body's overall homeostasis [5]. The sympathetic NS works to increase heart rate while the parasympathetic NS serves as the brakes that turn the cardiac activity back to normal functioning. Sensory neurons between the brain, spinal cord, and cardiac muscles engage in continuous feedback loops, consistently influencing each other via re-afferent signals (**Figure 2A**).

Fluctuations in sympathetic and parasympathetic activity can allude to unique physiological responses related to stress and anxiety. Exposure to painful stimuli and/or discomfort and distress can activate the sympathetic NS which elicits the excitatory fight-or-flight response [6]. Previous studies on stress and autonomic responses such as cardiac reactivities provide insight into the physiology of pain sensation [7, 8]. Heart rate variability (HRV) analyses have proven reliable and advantageous in evaluating autonomic functions in this regard [9, 10]. HRV metrics represent the various statistics of the inter-beat- interval (IBI), the timing between beats in a cardiac signal (**Figure 2B**). HRV is widely used to evaluate sympathetic and parasympathetic

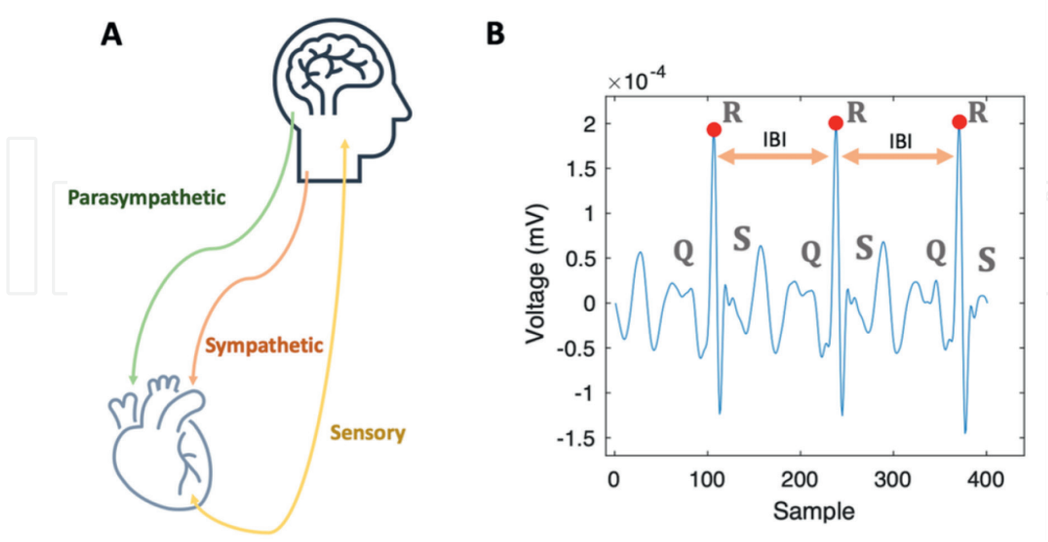


**Figure 2.**
*Cardiac responses as a proxy for autonomic nervous system function. (A) The sympathetic nervous system is responsible for increasing cardiac contractions during states of distress/anxiety while the parasympathetic nervous system serves as the brakes on the sympathetic system, modulating cardiac activity during resting states. Parasympathetic activity is guided by the vagal nerve, which governs heart rate variability (HRV) and allows for adaptive behaviors. Sensory neurons via the spinal cord allow for two-way communication between the heart and the brain. (B) Cardiac signals exhibit a unique QRS pattern where the timing between R-peaks (IBI) can serve as a proxy for sympathetic and parasympathetic activity.*

NS activity via various time and frequency-domain parameters. Improper balance between these two systems is often associated with cardiac pathologies such as strokes and heart attacks [9].

Previous work on HRV and stress have shown that when humans experience mental/physical strain, the parasympathetic NS's control over the heart decreases while sympathetic NS activity increases [11–13]. In such studies, physical strain was induced by having subjects perform intensive exercises [12], and mental strain was induced by asking subjects to solve difficult puzzles or arithmetic problems [13]. From these studies we find a clear interaction between the ANS and the nociceptive system as pain may often induce both mental and/or physical strain and distress [5, 6].

### 2.1 Autonomic dysregulation: social and emotional components

The autonomic nervous system plays an important role in socio-emotional learning and control [14]. Balanced vagal tone via the parasympathetic NS (responsible for modulating heart-rate) allows for swift engagement and disengagement with people, which is important for building social communication skills [15]. Social skills development during early childhood predicts a range of positive outcomes (in communication, assertiveness, role transitions, etc.) along with the formation and management of family and peer relationships throughout the lifespan [16]. Increased vagal tone is also associated with higher facial expressivity levels [17]. Decreased vagal tone can lead to dysregulated heart-rate (HR) modulation which may in turn lead to social interaction difficulties [15]. Imbalanced autonomic activity can also contribute to socio-emotional dysregulation during dyadic interactions in children diagnosed or at-risk for psychopathologies [18].

Symptoms of ASD are proposed to be associated with autonomic dysfunctions. Previous studies show that children with ASD and Intellectual Disability (ID) exhibit low parasympathetic activity during high anxiety conditions [19]. Autonomic dysregulation is also apparent in autistic children compared to typically developing (TD) controls [20]. When comparing the cardiac and electrodermal activity of autistics and neurotypicals, those with ASD exhibited dampened HR reactivity and skin conductance responses to visual and auditory social stimuli (face images and speech sounds) and during social interactions (role play) [21, 22]. More recent work demonstrated that the non-linear metrics of HRV show decreased autonomic modulation in autistic individuals compared to controls during resting conditions [23]. During facial expression tasks where subjects were asked to draw, interpret, and recognize different emotions, the ASD group showed lower parasympathetic modulation compared to controls, alluding to the elicitation of cognitive stress. Such autonomic dysregulation was also correlated with autism severity [24]. During social attention tasks, autistic subjects similarly showed reduced parasympathetic modulation, suggesting that autonomic dysregulation may underly social deficits in ASD [25].

Such findings are in line with the Polyvagal Theory which suggests that social behaviors may arise from the autonomic nervous system, with efficient vagal/parasympathetic control preventing sympathetic overactivation and thus contributing to better socio-emotional skills [26]. In ASD, the 'vagal brakes' on the sympathetic system may be compromised, leading to sympathetic hyperarousal and increased distress, which may impair behavioral adaptation/control and the ability to satisfactorily reciprocate social interactions [27]. Thus, assessing autonomic modulation may prove useful in understanding social–emotional responses, adaptive behaviors, and ultimately in screening and tracking symptoms associated with ASD.

## 3. Experimental approach: autonomic biomarkers

In this work, we explore the cardiac activity of neurotypical (TD) and autistic (ASD) individuals. Autonomic responses were proxied via the electrical activity of the heart. Electrocardiographic (ECG) activity was captured via wearable biosensors placed on the chest at the standardized lead II position via gel adhesives.

At the beginning of the study, TD participants were asked to rate their perceived pain sensitivity (PPS) relative to other people on a scale of 0–10, where zero represents complete insensitivity and a 10 represents extreme sensitivity [28].

Participants were seated at a table where they performed a Resting Task under control and experimental conditions. In the control condition of the study, the participants performed the Resting Task by sitting in a relaxed position and avoiding excess movement for about two minutes. This task was used to establish baseline autonomic NS activity as no movement or cognitive effort was required. During the experimental/pain condition of the study (only conducted with TD subjects), sustained pressure pain was introduced via a manual blood pressure cuff. This pain induction method serves as a modified version of the submaximal effort tourniquet test [28] which is found to mimic pathological pain [29]. In this procedure, the blood pressure cuff (standard sphygmomanometer/tourniquet) was placed around the non-dominant arm of the participant (above the elbow) and was gradually inflated to a pressure level of about 200 mmHg [30]. The cuff was inflated at this level for the entirety of the task and was deflated right after task completion. Right before cuff deflation, TD subjects verbally reported their pain level using a Numeric Rating Scale (NRS) ranging from 1 to 10, where a 1 indicates minimal to no pain, 4–6 indicates moderate pain, and a 10 indicates extreme pain [31]. Participants in the ASD group performed the Resting Task only under the control condition.

### 3.1 Analytical approach to assess cardiac activity

Electrocardiographic (ECG) data typically includes consecutive QRS complexes representing each heartbeat in the cardiac signal (**Figure 2B**). The R-peaks (sharp spikes) within QRS complexes are traditionally used to assess the timing between consecutive heartbeats (known as the R-R or inter-beat interval). Accurately detecting R-peaks is essential for assessing the fluctuations in the inter-beat interval (IBI) signal and in computing various heart rate variability (HRV) parameters. ECG signals may easily be corrupted by various artifacts such as baseline wandering and electrode movement [32]. To clean the raw ECG data, signal-processing filters were used to minimize excess noise/frequencies outside the range of a typical ECG recording [33]. After preprocessing of the ECG data, R-peaks were detected via a simple peak detection algorithm in MATLAB (MathWorks) software, and the IBI signal was obtained by computing the time between consecutive R-peaks. The statistics of the IBI signal were then evaluated via various frequency and time-domain metrics.

### 3.2 Cardiac activity metrics of the autonomic system

Changes in heart rate are the result of autonomic control via the sympathetic (excitatory) and parasympathetic (inhibitory) nervous systems (NS), which are informative in assessing how pain and distress influence the autonomic system [5]. HRV describes fluctuations in instantaneous heart rate (the oscillations between two consecutive heartbeats), where greater variability often reflects

enhanced vagal tone (heart rate regulation). The activities of the parasympathetic and sympathetic NS can be inferred from the Power Spectral Density (PSD) and Poincaré plots of the HRV signal (**Figure 3**). The high frequency (HF) component of the PSD (150–400 mHz range) is associated with parasympathetic activity and a general decrease in heart rate [34]. The low frequency (LF) component of the PSD (40–150 mHz range) is associated with sympathetic NS activity and blood pressure control [34]. The LF/HF ratio reflects the sympatho-vagal balance – the contribution of the sympathetic NS in controlling the heart compared to the parasympathetic NS [9]. Increases in the ratio between the LF and HF components (LF/HF ratio) have been previously associated with stress and intense exercise [12, 13]. The LF and HF components were computed by integrating the PSD over the associated frequency range.

Poincaré plots are also used to assess sympathetic and parasympathetic activation via time-domain metrics. Pioncaré plots serve as a geometrical and nonlinear method to assess the dynamics of HRV and are formed via a scatter of the IBI interval against the preceding IBI interval [35]. The width of the scatter is used to determine the SD1 parameter, which reflects parasympathetic NS activity and is correlated with HF power [36, 37]. The length of the scatter is used to determine the SD2 parameter, which reflects sympathetic NS activity and is correlated with LF power [36].

The PhysioNet Cardiovascular Signal Toolbox was also used to assess the ECG time series. This open-source toolbox is designed to assess HRV via standardized algorithms [38]. With this toolbox we windowed the IBI series and obtained a distribution of LF, HF, LF/HF, SD1, SD2, and SD2/SD1 parameters. To better visualize which frequencies (in the LF and HF ranges) dominated the cardiac signal across time, continuous wavelet transforms (CWT) or magnitude scalograms were used to visualize and evaluate temporal changes in frequency power and provide a personalized assessment of the autonomic activity (**Figure 4A**).

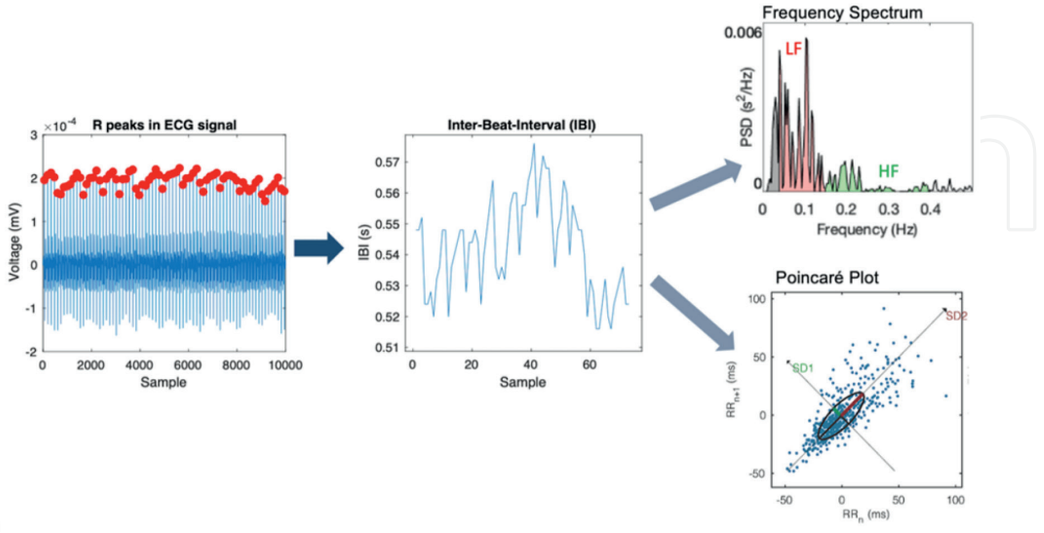


**Figure 3.**
*Analytical pipeline to assess autonomic activity via cardiac signals. The timing between R peaks (red markers) of the original ECG data are extracted to obtain the IBI signal. The IBI signal is then assessed in the frequency domain (power spectrum) to obtain LF (sympathetic) and HF (parasympathetic) components. The same IBI signal is assessed in the time domain (Poincaré plot) to obtain the SD2 (sympathetic) and SD1 (parasympathetic) parameters.*

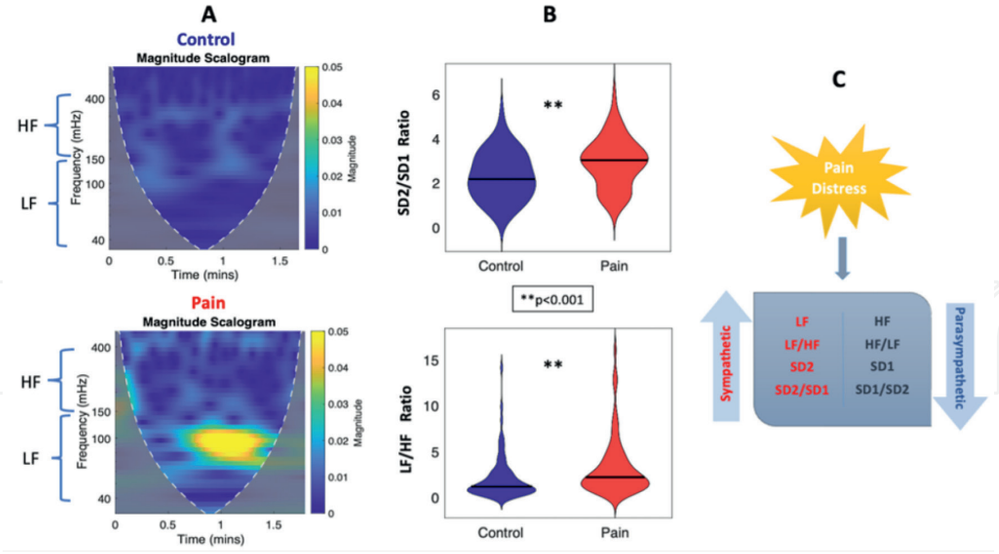


**Figure 4.**
*Cardiac responses across control and pain conditions in TD subjects. (A) CWT plots (or magnitude scalograms of the frequencies present in the heart signal across time) demonstrate higher magnitudes in the LF range corresponding to sympathetic nervous system activation in the pain compared to the control condition. (B) Violin plots from data accumulated across subjects demonstrate that the LF/HF and SD2/SD1 ratios (indicative of sympathetic NS arousal and/or parasympathetic NS inhibition) of the control vs. pain condition arise from different distributions, with the median for these ratios being higher for the pain condition. (C) Schematic of the effects of pain and pain-related distress on the autonomic system and the corresponding changes observed in the HRV metrics in the time (SD2 and SD1) and frequency (LF and HF) domains.*

### 3.3 Integrating cardiac biometrics with self-report data

To explore the relationship between self-reported responses and the cardiac biometric data, scatter plots were made comparing each subject's ratings against the absolute difference between the HRV metrics (obtained from the experimental and control conditions). Numeric scale pain ratings of the experimentally induced pressure pain were also compared to the perceived pain sensitivity (PPS) ratings. Scatterplots were used to assess possible relationships between PPS ratings and changes in the biometrics obtained from the cardiac signal. Such methods allow us to evaluate the correspondence between physiological metrics and common psychological assessments of pain.

## 4. Results: autonomic responses of distress

### 4.1 Heart rate variability (frequency + time-domain metrics)

HRV results were compared across control and pain conditions for TD subjects (**Figure 4**). Frequency-domain analysis of the IBI data demonstrated that the pain condition often elicited an increase in LF power (corresponding to sympathetic NS activation) and/or a decrease in HF power (corresponding to parasympathetic NS activity) for TD subjects. Such frequency changes can be visualized qualitatively across the entirety of the task via CWT plots (**Figure 4A**). The LF/HF and SD2/SD1 ratios (where an increase represents sympathetic NS activation or parasympathetic NS inhibition) were also computed across the control and pain conditions. Violin plots demonstrated changes in the shape of the probability density of these

parameters across participants (**Figure 4B**). For the pain condition, there was a general increase in both ratios based on data accumulated across TD subjects. Nonparametric Kruskal-Wallis tests indicated that the LF/HF and SD2/SD1 ratios across the control and pain conditions come from significantly different distributions: $\chi^2(1,175) = 14.37$, $p < 0.001$ and $\chi^2(1,179) = 12.44$, $p < 0.001$, respectively.

*4.1.1 The unique case of a subject with chronic pain*

Heart data analyses for a subject known to experience chronic pain led to unique findings compared to the remaining participants. The CWT plots of this subject consistently exhibited high LF power specifically in the 100–150 mHz range (**Figure 5**). This pattern was observed across both control and pain conditions. It is important to note that while this participant did experience the experimentally induced pressure sensation during the pain condition, they were accustomed to experiencing a consistent level of pain throughout their daily life. These results emphasize the importance of analyzing at the biophysical data in a personalized manner before calculating summary statistics or assessing trends based on the entire sample.

### 4.2 Self-reported pain ratings and HRV parameters

When exploring the self-reported measures, we find that perceived pain sensitivity (PPS) generally corresponded with the pain ratings reported during the study (**Figure 6A**). This indicated that participants could accurately approximate their pain sensitivity levels compared to others. To assess the relationship between objective and self-reported measures, we compared the HRV parameters of the cardiac signal with each subject's ratings during the pain condition of the Resting Task. The absolute difference (Diff) in the SD2 parameter (indicative of sympathetic NS activity) was computed to assess how much each subjects' cardiac signatures during the pain experience deviated from those of the control condition (SD2 Diff). This deviation in the SD2 parameter appeared to positively correlate with self-reported pain ratings and

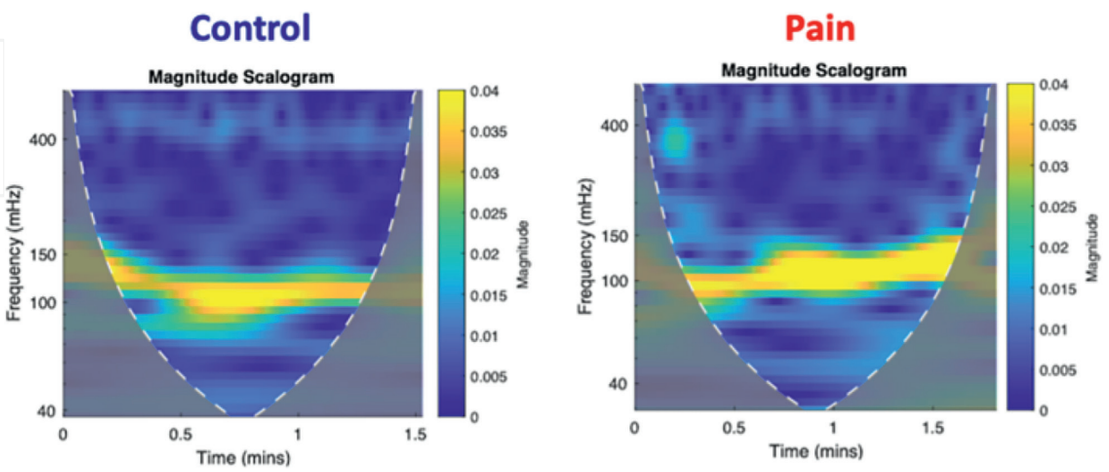


**Figure 5.**
*Cardiac activity of a participant with chronic pain. CWT plots consistently showed high magnitude in the 100–150 mHZ range (corresponding to LF power) regardless of whether pressure pain was or was not (control condition) introduced during the resting task.*

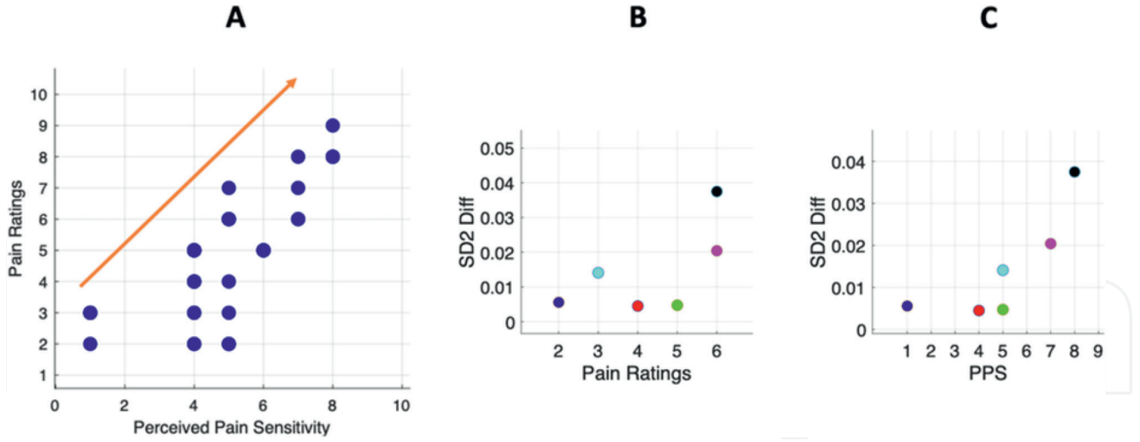


**Figure 6.**
*Integrating self-reported measures with autonomic HRV biometrics. (A) Participants with higher perceived pain sensitivity (PPS) levels typically reported the induced pressure pain to be of a higher intensity on the 1–10 numeric rating scale. (B) The absolute difference in the SD2 biometric between the control and pain condition (SD2 Diff) generally corresponded with higher self-reported pain ratings and perceived pain sensitivity levels.*

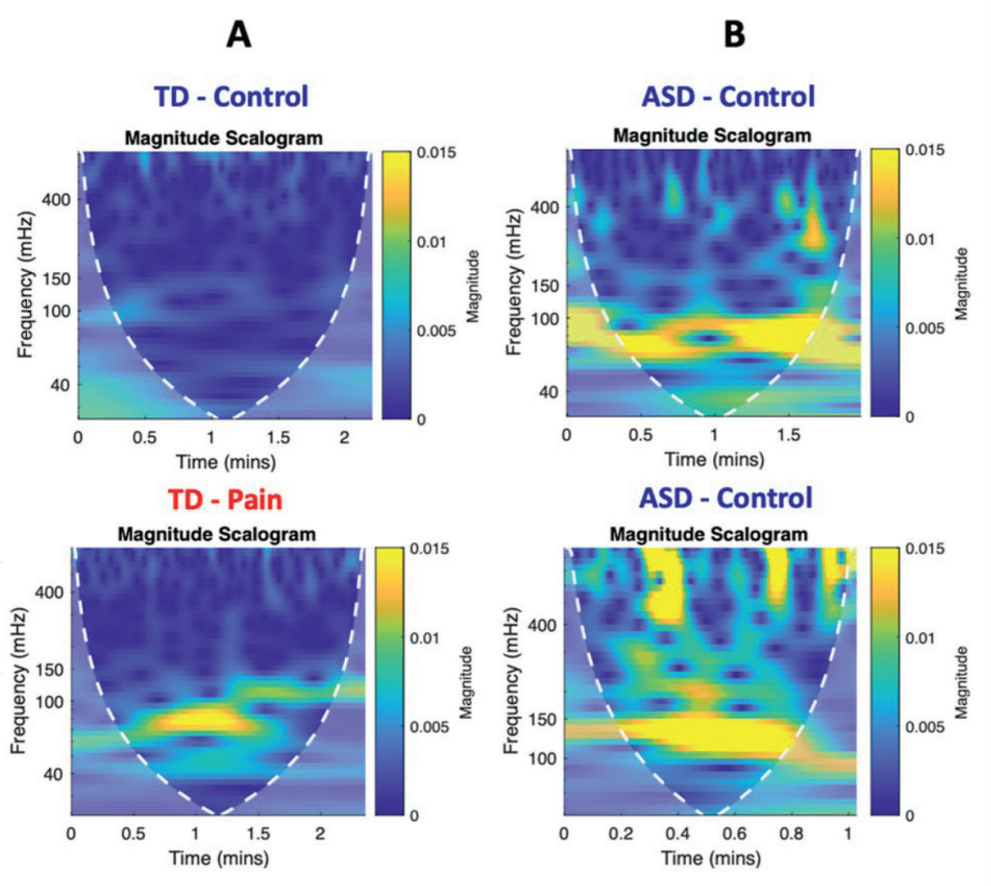


**Figure 7.**
*Comparing cardiac responses of TD and ASD participants. (A) Cardiac activity of neurotypical (TD) participants during the pain condition exhibited higher power in the LF range of the magnitude scalogram compared to the control condition where no pressure pain was induced. (B) For ASD participants at baseline, we observe a similar pattern of higher power in the LF range that mimics what is observed in TD participants during the pain condition.*

perceived pain sensitivity (**Figure 6B-C**). This indicates that it is possible to elucidate relationships between objective and subjective measures of pain sensation.

### 4.3 Autonomic responses in ASD subjects at baseline

When assessing the cardiac activity of autistic participants during the control condition of the Resting Task, we see a pattern in the CWT magnitude scalograms that mimics what was observed in TD participants at baseline (**Figure 7**). This indicated that autistic individuals may be experiencing sympathetic hyperarousal or have dampened parasympathetic nervous system regulation at baseline.

## 5. Discussion

The goal of this work was to assess changes in autonomic nervous system responses when the body experienced physical pain. We aimed to determine whether pain could be objectively characterized via heart rate variability metrics and how these metrics would compare to self-reported measures of pain. The pressure pain's influence on cardiac activity was apparent in the HRV metrics of the ECG signal. In the TD group, the induced pain led to increases in LF power. For most subjects, we also saw a corresponding decrease in HF power, which ultimately led to an increased LF/HF ratio. Such changes in the frequency-domain metrics suggest that the pressure pain led to sympathetic nervous system activation [25]. Interestingly, when assessing the cardiac activity of a participant who experienced chronic pain, we detected a consistent band of LF power (sympathetic activity) dominating the signal across both the control and pain conditions. This may indicate that the subject's chronic pain elicits a cardiac response that is impervious to the experimentally induced pressure pain. The finding that this subject's baseline cardiac activity resembles that of TD subjects under the pain condition helps provide some external validity to the pain induction procedure and provides further evidence for how pain can lead to increases in LF power and the LF/HF ratio. When evaluating HRV metrics in the time-domain via Poincaré plots, we generally observed an increase in the SD2, a decrease in the SD1, and an increase in the SD2/SD1 ratio, each of which are associated with sympathetic NS overdrive [35]. We find similar patterns of sympathetic hyperarousal in autistic individuals at baseline.

In this work, the physiological HRV metrics also complemented self-report measures. In general, we found that subjects have an accurate perception of their pain sensitivity level, as their PPS ratings appeared to positively correlate with their self-reported pain ratings. When assessing the relation between HRV metrics of the cardiac signal and the self-reported responses, we observed that higher deviations in the SD2 between the baseline and pain condition corresponded to higher PPS and numeric pain ratings. Such findings indicate that objective and nonlinear measures of HRV such as the SD2 parameter can be informative in understanding an individual's pain levels and their general pain sensitivity.

### 5.1 Study implications and future work

With this work we can begin to understand the relationship between pain, psychological responses, and physiological activity. This study demonstrated that the influence of pain on the body can be characterized via the statistics obtained from

cardiac signals and that such biometrics can inform current subjective approaches. The findings of this study have several clinical implications. Characterizing the effects of sustained pressure on cardiac functioning of healthy individuals can help in the development of accurate and objective digital biomarkers of pain sensation. Such objective assessments are vital to understanding whether and how individuals who may have difficulty communicating their pain – such as those with Autism Spectrum Disorder (1 of 59 in the US), Intellectual Disability, or impaired communication skills – experience pain under normal conditions [39–41]. Individuals with Intellectual Disability experience chronic pain that often goes unnoticed and untreated [41]. Autistic individuals often exhibit higher sensitivity to painful stimuli and generally have trouble communicating their emotional or mental states to others [39, 40]. During states of sympathetic overdrive (as commonly observed in ASD), it is difficult for the parasympathetic system to acquire the predictability needed for expressing internal mental and emotional states and reciprocating social interactions. Thus, there is an urgent need to develop objective methods to characterize and understand pain and distress in such individuals. Detecting any form of autonomic dysregulation may indeed help us understand the hypersensitivities and socio-emotional difficulties observed in ASD. Such assessments can ultimately contribute to early diagnoses and mitigated distress for families and non-speaking populations at large.

Pain is a multi-faceted construct, associated with multiple biological, sensory, cognitive, and social components [1]. Thus, it must be explored via a multidimensional psychophysiological approach. Future work aims to explore the sensory-motor and socio-emotional aspects of the pain experience. This can be done by assessing the facial expression and movement activity of participants as they perform motor-cognitive tasks while experiencing pain. While the autonomic system provides a bounty of information about the underlying physiology of pain and distress, we cannot forget about the contribution of the overarching peripheral nervous system that works to guide sensation, perception, decision-making, movement, and overall behavior. Recent work by Ryu and Torres has indeed connected voluntary control of motor output to the autonomic system in neurotypical individuals [42]. This work demonstrated that the heart plays a vital role in agency, highlighting the delicate balance between autonomy and control. From this previous work we learned that the cardiac signal leads the motor signal when a movement is intended but lags it when the movement is unintended [42]. Besides differentiating between deliberate and spontaneous motions, the cardiac code can help us begin the path of characterizing and distinguishing different types of afferent feedback, including those from kinesthetic and somatic pain signals. Further evaluating the autonomic system can help us deconvolve the continuous efferent stream of voluntary movements from the afferent consequences that they themselves cause. Understanding such relations will help us derive causal mechanisms of the nervous systems, beyond mere correlations. Such work highlights the importance of exploring the peripheral nervous system (including the autonomic branches) as a whole, as it can play key roles in the multi-faceted nature of pain and distress.

## 6. Conclusions

This work provides an innovative approach to better understand the mechanisms by which experimentally induced pain – that mimics pathological pain [28] – influences the autonomic nervous system via evaluating cardiac signals. From this work,

we learn that pain can interfere with autonomic regulation, eliciting sympathetic overdrive. The cardiac reactivities also appear to correspond with self-reports of pain and pain sensitivity. The observed patterns of autonomic dysregulation (sympathetic hyperarousal) during the physical pain experience in TD individuals mimic the cardiac responses observed in ASD participants at baseline. The unique results observed in ASD and chronic pain subjects highlight the importance of a personalized approach to assessing data. Such methodologies lend themselves to the Precision Medicine platform which helps inform the development of personalized treatments [43]. Our psychophysiological approach can ultimately help create robust techniques to detect pain and aid in the development of personalized interventions that are tailored to each individual's autonomic functioning. The added convenience of using wearable sensors makes this technique flexible and translatable for use in healthcare settings. The digital biometrics explored in this work open a new realm of research that can help us scientifically understand and characterize pain in a variety of neurodevelopmental disorders and in those with communication disabilities. Ultimately, such research can lead to new methods of identifying and alleviating pain and distress, improving the quality of life of individuals across the globe.

## Additional Information

Portions of this book chapter are derived from the thesis project titled "Characterization of Psychophysiological Responses to Pressure Pain" authored by Mona Elsayed, which is available on the Rutgers University repository platforms, dated October 2021. The thesis work has not been peer-reviewed nor published elsewhere.

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## Conflict of interest

The authors declare no conflict of interest.

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