



Cardiovascular activity and chronic pain severity



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HIGHLIGHTS

- Chronic pain sensation severity affects orienting cardiovascular response.
- Severity of pain sensitization affects early orthostatic cardiovascular response.
- Severity of emotional distress affects late orthostatic cardiovascular response.
- MMPI-2 results demonstrate three-cluster solution for the cardiovascular activities.

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ABSTRACT

Objective: Objective markers of chronic pain severity are needed when examining and treating patients with chronic pain whose suffering may be overstated or underestimated. This study tested a hypothesis that the strength of cardiovascular (CV) reactivity in response to a social evaluative threat and orthostatic challenge is a reliable index of severity of pain-related complaints.

Methods: Measurement of CV reactivity and response styles in 34 men and 16 women with chronic pain from different bodily injuries, were retrieved from a larger database of patients. Measurement of CV reactivity in response to a postural challenge was repeated twice (sessions 1 and 2) on the same day of a medical examination which includes a psychosocial evaluation.

Results: A decrease in systolic blood pressure (SBP) from session 1 to session 2 was found in subjects with low pain severity scores, but not in those with high pain severity scores. High scores for pain catastrophizing/magnification and pain-related emotional distress were independently associated respectively with a SBP increase at an early-point in time and a SBP decrease at a mid-point in time after standing up from lying down. Stronger heart rate reactivity responses to orthostatic challenge indicated greater protection against the presence of these chronic pain symptoms.

Conclusions: This biobehavioral protocol enables measurement of chronic pain suffering and protection in three dimensions: physical, emotional, and cognitive.

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1. Introduction

Clinical indices of disease severity, body impairment, and nociception using traditional physical, morphologic, imaging, or serologic examination protocols are only weakly related to self-reports of chronic pain severity, frequency and number of pain episodes, and disabling functional impairments [1–3]. The challenge is especially relevant in children, older adults, and persons with limited education or ability to communicate [4,5] and in individuals with traumatic brain injuries, residual post-concussive syndromes and PTSD, dementia, post-stroke syndromes, neuropathic pain syndromes, somatoform pain disorders, and personality

disorders [6–11] whose self-reported suffering related to chronic pain may be intentionally or unintentionally misrepresented as a consequence of “illness behavior” [12].

Prior studies have emphasized the importance of pain in blood pressure (BP) regulation [13–17]. They show that pain modulates the activity of neurons responsible for controlling baroreceptor responses and that pain may increase hypertension risk in people with chronic pain. Neural components mediating baroreceptor and nociceptive signals are functionally intertwined within the nervous system [18–20]. Evidence suggests that nociceptive stimulation increases BP by attenuating the cardiac baroreflex and by increasing sympathetic nervous system activity [21–23]. Resting systolic BP (SBP) and baroreceptor sensitivity were positively related to pain threshold and tolerance in healthy people [24,25]. However, these relationships are not present in young patients with chronic pain [26]. In older patients with chronic pain, the relationships

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between resting SBP and the pain sensation measures are already negative, and higher resting SBP is already associated with lower baroreceptor sensitivity [25]. Taken together, these findings suggest that pain chronicity may moderate the relationship between baroreflex mechanisms regulating BP and pain sensation intensity.

Postural (orthostatic) change from lying to standing is a gravity induced biological challenge that triggers several successive evolutionary-developed physiological processes for maintaining BP level. It corresponds to alertness behavior most activated when standing up to protect against light-headedness and fainting [27–29]. Baroreceptors play a primary role in controlling these processes by causing both parasympathetic withdrawal and sympathetic activation [30–32]. Systolic blood pressure fluctuations in earlier response to orthostatic challenge (around the 1st minute after standing up) were found to correlate with pharmacological and non-pharmacological indicators of baroreflex functioning [33]. Deeper and delayed orthostatic fall was associated with lower baroreceptor sensitivity or transfer gain function. Other baroreflex mechanisms like cardiac and vascular baroreflex resetting (vagal withdrawal and sympathetic activation) can also be involved in blood pressure regulation during orthostasis [32] and all these mechanisms may be impaired in patients with chronic pain [34].

A study of orthostatic cardiovascular (CV) responses in chronic pain patients found that the ability to enhance sympathetic activation of blood vessels and the withdrawal of vagal modulation of the sinoatrial node for maintaining BP level is significantly reduced [35]. Poor orthostatic CV reactivity (CVR) is considered to result from inadequate triggering of baroreflex mechanisms that regulate common arousal- and pain-related (analgesic/sedative) systems in those experiencing greater chronic pain [36–38]. A weak orthostatic CVR and its inversion due to (de)conditioning (i.e., higher CV activity when lying down compared with standing posture) is found to be a reliable marker or predictor of difference and change in both somatic and mental health [27,39,40]. This CVR regulated by baroreflex activity may also be associated with the emotional component of chronic pain as a general physiological response to the negative affect associated with stressful events [27,41,42]. A weak or flattened CVR in response to psychological challenges like mental concentrations and social evaluative threat in patients with chronic pain may also use the same baroreflex mechanisms coupling its impairment with severity and/or duration of chronic pain [43,44].

Pain is a complex experience associated with sensory events, emotions, thoughts, and physical and interpersonal actions; and with no valid and reliable method of 'objective' quantification at present [45]. Therefore, we relied mainly on self-report measures as the 'gold standard' to determine the relationships between chronic pain and physiological measures. Sensory or nociceptive experience (pain severity including pain intensity and frequency), experience of negative affect (pain distress or unpleasantness associated with anxiety, depression, irritation, and overall negative mood), experience of negative cognition or thought disorganization (e.g., pain catastrophizing including helplessness, rumination, and magnification), and experience of physical (functional) and psychosocial (interpersonal) behavioral problems have been considered as core experiential dimensions caused by chronic pain [45,46]. Thus the pain experience should be assessed in a complex way and subjective scales should be selected specifically relevant for the subjects and objectives of study. Most recommendations for chronic pain assessment tools have been provided for clinical trials and vary depending on specific patient populations and objectives [47,48]. Instruments that are legally encouraged for use, have a normative database in the specific population of injured workers with chronic pain, and cover all the above mentioned core experiential dimensions of chronic pain were included in this study [49–52]. Some of these instruments measure several dimensions of pain with differing combinations of intensity, affect, interference with functioning and thoughts and certain overlapping was expected, assessed, and controlled for.

This study evaluates group data from injured workers with chronic pain. It aims to test the hypothesis that an altered (reduced,

inverted, or unstable) CVR in response to physical (orthostatic) and mental (psychosocial evaluation) stress conditions are related to greater severity of chronic pain-related complaints, i.e., its sensational, emotional, cognitive, and behavioral components. The second objective of this study is to evaluate the independence or uniqueness of these chronic pain's components in their impact on these CV responses. Scales that measure behavior, emotional response styles, and maladaptive behavioral responses in this clinical population are evaluated as possible mediators and moderators of these relationships.

2. Materials and methods

2.1. Data source

This study relies on clinical and laboratory data obtained from mandated medical-legal examinations (MLEs) of injured workers with litigated disability claims. The selected population has several salient characteristics [53], which provide researchers with several advantages in achieving previously mentioned objectives: (i) the litigating process gives unsolicited access to people with remarkably diverse etiological and pathological sources of chronic pain and its severity. This helps generalize the expected findings of a common biomarker of severity, i.e. the CVR indicator of maladaptive neuroplastic change in pain control, to different patients with chronic noncancer pain [18,54]; (ii) the examining doctor is a neutral panel qualified medical examiner (PQME) typically given carte blanche authority to perform whatever diagnostic tests are required short of authorizing hospitalization; and (iii) injured workers are legally required to attend this examination but nonetheless asked to initially give written informed consent regarding no privacy, confidentiality, or future treatment relationship. The MLEs were performed by a PQME according to the California Labor Code mandates for medical-legal examinations. At no point in time was the injured worker ever identified as a research subject participating in a research study. MLEs of injured workers with a litigated injury claim are not voluntary.

The situation under which all subjects were being examined could bias self-reports of pain severity. Validity MMPI-2 scales were used (see below) to control for this bias as recommended in this population [55]. We used these validity scores in mediation and moderation analyses for assessing if an over- or under-reporting strategy of subjects produces/mediates or biases/modifies the expected relationships between CVR and pain scores. It allowed us to additionally evaluate the reliability of CVR metrics when assessing chronic pain severity.

Survey data of MLEs over the past 3 years are retrospectively analyzed to study relationships between subjective measures of pain and functional disability with orthostatic CV measures. The CV measures were included in the PQME's assessment protocol to provide a physiological measure of individual resilience to adversity, i.e., occupational injuries [27,28,56]. The CV measurement procedure was not considered at the time for studying or evaluating chronic pain. The approval for publishing this study was received from the institutional review board (IRB) of the University of California, Los Angeles (UCLA).

2.2. Procedures.

All the data examined in this study are from injured workers with litigated disputed injury claims mandated to be examined by SP as a PQME. 100% presented with chronic pain. MLEs are typically conducted over the course of two days, usually several weeks apart. This enabled a test-retest clinical assessment protocol. Day one (D-1) assessments were conducted by a trained technician who supervised administration of self-report standardized depression, anxiety, and pain questionnaires including self-reports of functional impairments. The trained technician also administered the CV measurement protocol and supervised completion of computer-administered psychodiagnostic and neurocognitive tests by subjects. Day two (D-2) assessments were conducted by the PQME. They included an extensive face-to-face medical-legal neuropsychiatric

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