*Autonomic Nervous System Function Among Individuals With Acute Musculoskeletal Injury*

David R. Grimm, EdD, Brian M. Cunningham, DC, MS, and Jeanmarie R. Burke, PhD

**Abstract**

**Objective:** To determine differences in peripheral and cardiovascular autonomic function between individuals with acute musculoskeletal injury (<1 week) and healthy controls.

**Methods:** Autonomic cardiovascular modulation, baroreceptor sensitivity, skin conductance, and peripheral skin temperature were obtained in 6 subjects with acute musculoskeletal injury and 6 age- and sex-matched controls. Power spectral analysis was performed on both beat-to-beat R-R intervals and continuous systolic blood pressure (SBP) peaks. Baroreceptor sensitivity was derived using both heart rate and blood pressure spectral analysis components.

**Results:** The SD of R-R intervals was significantly different for the acute injury group relative to controls (49.8 ± 10.5 vs 76.8 ± 12.7 ms; *P* < .01). Continuous SBP peaks and skin conductance (sympathetic vasomotor and sudomotor indices, respectively) were significantly higher (59.6 ± 6.7 vs 23.8 ± 6.4 mm Hg/Hz, and 3.87 ± 1.04 vs 2.19 ± 0.3 mhos; *P* < .01, respectively) and baroreceptor sensitivity lower (0.97 ± 0.07 vs 1.10 ± 0.08 mm Hg; *P* < .02) in the acute injury group compared with controls. Regression analysis revealed a significant relationship between skin conductance and continuous SBP peaks (*r* = 0.75; *P* < .01).

**Conclusions:** These findings suggest that interaction between cutaneous and vasomotor sympathetic neurons in response to acute musculoskeletal injury, reflected as increased afferent input from sensitized nociceptors and other sensory neurons, results in alterations in autonomic function. (J Manipulative Physiol Ther 2005;28:44-51)

**Key Indexing Terms:** Autonomic Nervous System; Musculoskeletal Physiological Phenomena; Musculoskeletal Injury; Power Spectral Analysis

One of the central hypotheses of traditional chiropractic is that dysfunction of somatic structures, chiefly the musculoskeletal components of the human vertebral column, may have significant impact on regulation of the nervous system, specifically the autonomic nervous system, and hence influence visceral function and health. Although the historical origins of this tenet are rooted in less scientific theories, the foundation of its modern interpretation was based on research performed by the osteopathic investigator Irvin M. Korr. More recent references lend support to the above statement including chiropractic textbooks used at many chiropractic colleges today.

Although often the emphasis is placed on the treatment of the spine in chiropractic health care, it is well established that nociceptive and other aberrant neurological input from dysfunctional musculoskeletal structures of any component of the human frame influences the autonomic nervous system. While it has been shown that noxious as well as innocuous stimuli of somatic structures results in changes in the autonomic nervous system, no definitive human research has shown a clear relationship between articular and muscular dysfunction of the spine and other musculoskeletal structures and autonomic perturbations (particularly beyond the immediate insult). Evaluation of autonomic nervous system function in subjects presenting with acute musculoskeletal soft tissue injury may shed light on such relationships.

It is generally understood that consequences of somatic tissue injury extend beyond the site of insult and include both spinal and supraspinal changes in neuron excitability and activity.

Injury to the somatic tissues of the musculoskeletal system results in heightened afferent input from sensitized nociceptors and other sensory neurons, and in some chronic conditions (ie, those associated with nerve damage), remodeling of the spinal dorsal horn has been reported. Although supraspinal pain modulatory systems were originally considered solely inhibitory of spinal nociceptive sensory input, stimulation of supraspinal sites can also facilitate spinal nociceptive transmission, both of which have...
been shown to produce autonomic and behavioral effects such as those associated with the ‘fight or flight’ response.\(^8\)

Long-term activation of spinal and extraspinal nociceptive afferents contributes to stimulation of the autonomic nervous system that may in turn have a deleterious effect over time on visceral function and homeostasis with the potential to negatively impact health and wellness.\(^9-11\) Experimental evidence exists demonstrating a relationship between somatic structures and the autonomic nervous system, mainly via neurological reflex mechanisms.\(^12,13\) In contrast, no relationship has been shown between short-term activation of spinal afferents, as found in nonexperimental human subjects with acute musculoskeletal injury, and the autonomic nervous system. The intent of this observational study was therefore to determine whether differences exist in peripheral and cardiovascular autonomic function between individuals with acute musculoskeletal injury and healthy controls.

**Materials and Methods**

**Subjects**

Twelve subjects participated in this study, 6 with acute musculoskeletal injury and 6 age- and sex-matched healthy controls. Inclusion criteria for the injury group were acute musculoskeletal injury to the low back or 1 of the extraspinal articulations less than 1 week in duration and level of pain assessed using a Visual Analogue Scale (VAS) between 3 and 6 (Table 1). Before testing, the musculoskeletal injury group received a routine chiropractic physical examination. For both groups, exclusion conditions included known coronary heart and/or artery disease, hypertension, renal function abnormalities, diabetes mellitus, obesity, current cigarette smoking, and medications known to affect the autonomic and/or cardiovascular systems. The institutional review board of New York Chiropractic College granted approval for the study, and informed consent of each subject was obtained before the investigation.

Testing occurred between 2:00 and 4:00 PM in a private and thermo-controlled autonomic laboratory. Subjects were required to rest quietly (prone position) for 30 minutes followed by 5 minutes of peripheral and cardiovascular autonomic data collection. All subjects refrained from beverages containing caffeine and alcohol during the day of the study, and data were collected 2 hours postprandial. Control subjects abstained from exercise 24 hours before study.

**Data Collection**

Dependent variables obtained included cardiovascular autonomic modulation: beat-by-beat systolic blood pressure (SBP) and R-R intervals (RRIs) of the electrocardiograph (ECG) QRS complex both measured using power spectral analysis, baroreceptor sensitivity, skin conductance, and peripheral skin temperature (Fig 1). To assess peripheral and cardiovascular autonomic modulation, data acquisition was performed on cardiovascular autonomic data, skin conductance, and peripheral skin temperature at a sampling rate of 250 Hz per channel with a 12-bit analog-to-digital converter. R-R intervals and SBP were measured beat-by-beat using lead V\(_5\) of the ECG and a continuous tonometry and oscillometric blood pressure instrument (Colin, Medical Instruments Corp, San Antonio, Tex). R-R intervals and SBP data were acquired and spectral decomposition performed using a customized program created with LabVIEW software (National Instruments, Austin, Tex) as previously described\(^14\); a more detailed description of the methodology, physiological interpretation, and clinical use is provided in Ref. 16.

For peripheral autonomic assessment skin conductance was recorded by using a pair of Ag/AgCl electrodes, approximately 0.8 cm\(^2\) in contact area, filled with conductivity gel placed on the volar surface of the distal phalanges of digits I and II of the hand and then attached with a Velcro strip.\(^15\) Data was collected with a Grass model CSA1 Skin Conductance Adaptor then channeled into a Grass P122 amplifier (Astro-Med Inc, W Warwick, RI) and sampled and digitized as previously described. Peripheral skin temperature was obtained by a thermocoupled temperature probe (YSI, Yellow Springs, OH) secured with medical tape to the volar surface of the distal phalanges of digit IV of the hand. The signal was channeled into the computer via an interface module converter (Deban Enterprises, Yellow Springs, OH), and data for all measurements were analyzed off-line.

**Signal Processing**

All signals were visually inspected for artifact and anomalies and peak detection was performed on all QRS complexes and systolic peaks. The standard deviation (SD) of RRIs (a time domain variable representing global cardiac parasympathetic input\(^16\)) was calculated. R-R intervals and systolic peaks were then interpolated to provide continuous wave forms. The data were transformed into frequency spectra using discrete Fourier algorithms, and the spectral estimates smoothed by applying a Hamming window function to produce the power spectra. The standard spectral bandwidths for RRI and SBP parameters each

<table>
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<th>Table 1. Profile: acute injury group</th>
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R, right; L, left.
Fig 1. Represents signal processing of RRIs and SBP for 1 subject. Graphs a and b show raw digitized (sampling rate 250 Hz per channel) ECG and blood pressure data. Graphs c and d depict histogram of RRIs and SBP, and graphs e and f show interpolated data providing continuous waveforms for both RRIs and systolic peaks.
consist of a low-frequency (LF) component in the 0.04 to 0.15 Hz range and a high-frequency (HF) component between 0.15 to 0.40 Hz. Power spectral analysis was performed on both beat-to-beat RRIs (RRIHF and RRILF) and continuous SBP peaks (SBPLF) depicting 5 minutes of autonomic nervous system modulation. The area under the power spectrum, both the LF and HF bands, is determined through integration. Both LF and HF components are presented as normalized units (percentage) by dividing by the difference between the total power and the very low frequency component and multiplying the result by 100.19

The index $\alpha$ was calculated to assess baroreceptor sensitivity. This index is a closed-loop model based on the simultaneous analysis of beat-by-beat changes in RRIs and SBP frequency domain measures and is used to estimate the overall gain of the neural feedback from baroreceptor mechanisms.20,21 This is computed both in correspondence to LF and HF oscillatory components, and an average index is derived from the power spectral density analysis data and calculated as:

$$\alpha = \frac{1}{2} \left[ \frac{(RRI_{LF}/SBP_{LF})^{1/2} + (RRI_{HF}/SBP_{HF})^{1/2}}{2} \right]$$

where RRI and SBP represent the spectral power for heart rate and blood pressure variability, and the subscripts LF and HF represent the low-frequency and high-frequency components, respectively. The validity of the index $\alpha$ requires that the coherence (a measure of the linear association between 2 signals in the frequency domain—equivalent to the squared correlation coefficient) between the 2 variability signals is greater than 0.5. The magnitude squared coherence and phase functions between RRIs and SBP were evaluated by cross-spectral analysis for final determination of the index $\alpha$.22

### Table 2. Results: Subject Characteristics

<table>
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<tr>
<th>Group</th>
<th>Sex (m/f)</th>
<th>Age (y)</th>
<th>Height (cm)</th>
<th>Weight (kg)</th>
<th>HR (beats/min)</th>
<th>SBP (mm Hg)</th>
<th>DBP (mm Hg)</th>
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</thead>
<tbody>
<tr>
<td>Acute</td>
<td>5/1</td>
<td>25 ± 3.2</td>
<td>175 ± 8.1</td>
<td>88 ± 17.8</td>
<td>64 ± 11.2</td>
<td>128 ± 11.4</td>
<td>71 ± 8.3</td>
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<tr>
<td>Control</td>
<td>5/1</td>
<td>26 ± 2.5</td>
<td>180 ± 5.1</td>
<td>86 ± 15.7</td>
<td>56 ± 7.4</td>
<td>129 ± 9.7</td>
<td>78 ± 7.3</td>
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Results are expressed as mean values ± SD; m/f, Male-to-female ratio; HR, heart rate; DBP, diastolic blood pressure.
Statistical Analysis

An unpaired Student’s $t$ test was applied to determine differences for dependent variables between groups, and results are presented as mean values ± SD. Simple regression analysis was used to describe relationships between sudomotor function (skin conductance) and sympathetic vasomotor modulation with the level of significance for all analyses set at $P < .05$.

RESULTS

No significant differences were observed between groups for subject characteristics or hemodynamic parameters (Table 2). Comparison of autonomic cardiovascular modulation data revealed a significantly higher SBP$_{LF}$ and a significantly lower baroreceptor sensitivity in the musculoskeletal injury group than the control group (59.6 ± 6.7 vs 23.8 ± 6.4 mm Hg/Hz; 0.97 ± 0.07 vs 1.10 ± 0.08 mm Hg, respectively, $P < .02$). The SD of RRI$_{s}$ was significantly attenuated in the injury group compared with controls (49.8 ± 10.5 vs 76.8 ± 12.7 ms; $P < .01$); however, no differences were observed for either RRI$_{LF}$ or RRI$_{HF}$ frequency domain variables. The peripheral autonomic measure skin conductance was statistically greater in the musculoskeletal injury group than in the control group (3.87 ± 1.04 vs 2.19 ± 0.3 mhos; $P < .01$), whereas no difference was found for peripheral skin temperature (Fig 2).

Regression analysis revealed a highly significant positive relationship between skin conductance and SBP$_{LF}$ ($R^2 = 0.57$, $P < .01$) as shown in Fig 3. The power spectral analysis (Fig 4) illustrates representative acute and control subjects. Note significantly greater power in the LF component (0.04-0.15 Hz range) of SBP in the acute subject relative to the control, suggesting heightened vasomotor sympathetic influence.

DISCUSSION

The results of this observational study showed that both sympathetic vasomotor influence (shown by SBP$_{LF}$) and sympathetic sudomotor control (skin conductance) are heightened, whereas the baroreflex mechanism (index $\alpha$) is attenuated, in subjects with acute musculoskeletal injury relative to age- and sex-matched healthy controls. Our findings suggest that activity of and interaction between cutaneous and vasomotor sympathetic neurons in response to acute musculoskeletal injury, potentially reflected as increased afferent input from sensitized nociceptors and other sensory neurons, can be noninvasively quantified as alterations in peripheral and cardiovascular autonomic modulation. Although this is a small preliminary study, there appears to be a relationship between acute musculoskeletal tissue injury and the autonomic nervous system in human subjects.
The low-frequency component of SBP has been used to characterize sympathetic vasomotor modulation and cardiovascular control, and changes in sympathetic outflow are controlled by various receptors (ie, arterial baroreceptors, chemoreceptors, and cardiopulmonary) combined with other direct mechanical or humoral influences and alterations in the activity of higher brain centers (ie, nucleus tractus solitarius). Evidence is available, however, to show that sympathetic neural outflow of a central or peripheral nature exerts a prominent role in selectively modifying and adjusting appropriately to the needs of the cardiovascular system. In view of the number and complexity of these regulatory mechanisms, caution should be exercised when interpreting results obtained from beat-to-beat SBP LF. With this consideration appreciated, our findings suggest that acute musculoskeletal injury results in a shift in the autonomic nervous system toward a sympathetic dominance, as reported with chronic pain.

Precise measurement of galvanic skin response (for this study we used skin conductance) relies on the ability of the autonomic nervous system to modulate sudomotor activity. This dependence is based on the anatomy of the skin, supplied abundantly by eccrine sweat glands that are innervated solely by efferent sympathetic fibers. Specifically, ventral root fibers originating from neurons in the intermediolateral cell column (lamina VII) of the spinal cord synapse on postganglionic sympathetic neurons in the periphery and innervate the exocrine portion of the sweat gland and the muscles controlling piloerection. In response to sympathetic stimulation, an increasing proportion of sweat glands in a given area become active resulting in a change in the skin’s conductivity (decreased resistance and thus an increase in its reciprocal conductance). Although regression analysis of skin conductance and SBP LF for the 2 groups separately yields no significant relationships, regression analysis of skin conductance and SBP LF for the combined groups reveals that in the injury group, those with heightened sympathetic vasomotor modulation also exhibited elevated sudomotor activity, lending further support to the notion that acute musculoskeletal injury results in heightened global sympathetic autonomic modulation. In addition, the scatter of data points clearly differentiates group membership, and thus future studies with a larger cohort may permit discriminate analysis to predict the independent variable (ie, group membership) based on differences in the dependent variables.

We measured parasympathetic neural influence on cardiac function in both the time and frequency domains, and although no differences were found between groups for frequency domain values, differences were noted for the time domain variable, SD of the RRI. For continuous ECG recordings, each QRS complex is detected, and the normal-to-normal intervals are established. Therefore, the SD of the RRI, that is, the square root of variance that is mathematically equivalent to total power of the spectral analysis, represents all cyclic components responsible for variability in the raw signal. A rationale for the absence of a significant difference between groups for the RRI HF is not obvious; however, the large variability (ie, SD) observed in this measure may contribute. A potential explanation for differences between groups for the SD of the RRI is that it represents global involvement of the autonomic nervous system in cardiac function, whereas the RRI HF component depicts a more precise index of parasympathetic influence.

The index z is based on simultaneous beat-to-beat changes in SBP and RRI frequency domain measures, which interact in a closed-looped relationship, and represents an estimate of the overall gain of the neural feedback from baroreflex mechanisms without providing information on changes in tonic activity. In healthy control populations, the index z has been reported to be reduced during sympathetic activation (active standing) and enhanced during autonomic sympathetic blockade (atenolol). Other investigators have observed a lower index value in patients with uncomplicated essential hypertension suggesting a reduced gain of baroreflex mechanisms. We previously reported in normotensive individuals with paraplegia, relative to able-bodied controls, an attenuated index z value suggesting that the interaction between parasympathetic and baroreceptor feedback control mechanisms is impaired in this population. We postulate that a similar mechanism is responsible for the diminished baroreceptor sensitivity, instead of similar mechanism is responsible for the diminished QRS found in the study herein, such that acute musculoskeletal injury contributes to alterations in the autonomic nervous system in which a change in one system, augmented sympathetic efferent outflow, is accompanied by shifts in others resulting in resetting of the autonomic nervous system (ie, interaction between parasympathetic and sympathetic baroreceptor feedback control mechanisms).

From a clinical perspective, these results add to a growing body of evidence of both controlled and uncontrolled studies demonstrating a relationship between somatic nociceptive and other sensory afferent input and autonomic nervous system modulation, particularly within the sympathetic branch. One of the fundamental premises of chiropractic and osteopathy is that dysfunction in the somatic structures of the body, particularly within the spine, results in nociceptive input that influences autonomic nervous system function. Specifically, it has been hypothesized that such afferent input causes an increase in the thoracolumbar outflow of the sympathetic nervous system and that the efferent sympathetic nervous system can then be actively involved in the generation of pain. This small observational study using human subjects with acute musculoskeletal pain contributes to this hypothesis. Furthermore, if it could be definitively shown that such change in efferent sympathetic activity has a negative impact on health and wellness, the need to address painful dysfunction or injury to the musculoskeletal system using manipulation or...
other manual therapies would be indicated. Moreover, we feel it suggests the need for chiropractors to better recognize their role as primary-care portal-of-entry physicians specializing in the care and maintenance of the musculoskeletal system as a whole and not only the spine.

CONCLUSION

Sprains and strains produce mild forms of nociceptive pain, whereas the pain of arthritis or a tumor that invades soft tissue is chronic and much more intense. Patients with both acute musculoskeletal tissue injury (<1 week) and mild to moderate pain (3-6, VAS) were selected in an attempt to noninvasively quantify interactions between such injury types and the autonomic nervous system, as occurs in some chronic pain states. Our findings suggest that in acute injuries to somatic structures, the autonomic nervous system shifts to a predominance of cardiovascular and peripheral sympathetic modulation as shown by augmentation in sudomotor and vasomotor control and attenuation of baroreceptor sensitivity.

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REFERENCES