Characterizing Activity and Muscle Atrophy Changes in Rats With Neuropathic Pain: A Pilot Study

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Abstract
The study of neuropathic pain has focused on changes within the nervous system, but little research has described systemic changes that may accompany neuropathic pain. Objective: As part of a larger project characterizing the metabolic, activity, and musculoskeletal changes associated with neuropathic pain, the objective of the current study was to characterize changes in spontaneous activity and skeletal muscle mass using an established animal model of neuropathic pain, the chronic constriction injury (CCI) model. Method: Male Sprague-Dawley rats were used in this pre- and posttest quasi-experimental study. The experimental group (n = 13) received CCI surgery, while age- and weight-matched rats received sham surgery (SHAM; n = 5). Thermal testing verified the presence of neuropathic pain. Spontaneous cage activity was measured gravimetrically prior to and following CCI (n = 4). Animals were euthanized and skeletal muscle was dissected and weighed to determine muscle atrophy. Results: Shorter foot withdrawal latency of the ipsilateral hind limb confirmed the presence of thermal hyperalgesia in CCI rats, a sign of neuropathic pain. Weight increased in both CCI and SHAM rats. Spontaneous activity decreased following CCI ligation. Muscles of the ipsilateral hind limb weighed significantly less than contralateral hind limb muscles in CCI rats 2 and 6 weeks after surgery. In addition, CCI rats had smaller ipsilateral hind limb muscles than SHAM rats. Conclusion: Neuropathic pain contributes to skeletal muscle atrophy and decreases in activity in rats.

Keywords
neuropathic pain, activity, muscle atrophy

Neuropathic pain, a form of chronic pain, affects an estimated 76.2 million people in the United States (U.S. Department of Health and Human Services, National Center for Health Statistics, 2006). Neuropathic pain is defined as, “Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system” (Treede et al., 2008, p. 1631) and has several key manifestations: allodynia, hyperalgesia, and spontaneous pain. Allodynia occurs when a stimulus that is not normally painful evokes a painful response (Castro-Lopez, Raja, & Schmelz, 2008). Hyperalgesia is an amplified or exaggerated response to stimuli that are normally only mildly painful (Basić-Kes et al., 2009). Spontaneous pain occurs in the absence of a peripheral stimulus, resulting from ectopic action potential generation within nociceptive pathways (Costigan, Scholz, & Woolf, 2009).

In addition to changes within the nervous system and characteristic physical pain, neuropathic pain can have detrimental effects on activity and ambulation. Individuals with neuropathic pain have restrictions in mobility (Smith, Torrance, Bennett, & Lee, 2007; Toth, Lander, & Wiebe, 2009), activities of daily living, and leisure activity (De Souza & Frank, 2007). Inadequately treated neuropathic pain may cause an overall hypoactive lifestyle and contribute to a reduction in physical fitness, deconditioning, and decreased exercise tolerance, thus leading to further hypoactivity (Barkin, Barkin, & Barkin, 2005; van den Berg-Emons, Schasfoort, de Vos, Bussmann, & Stam, 2007).

Neuropathic pain may also directly and indirectly affect muscle structure and function via muscle atrophy (Daemen et al., 1998) or “loss of skeletal muscle mass and function” (Evans, 2010, p. 1125). Muscle mass is maintained by a balance between protein synthesis and degradation. In the absence of physical injury, immobility and activity restriction can contribute to muscle atrophy via decreased protein synthesis, increased degradation, or a combination of both (Evans, 2010). Previous research has shown that decreased protein synthesis is the primary contributor to decreases in muscle mass.

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mass following periods of bed rest in humans (Ferrando, Lane, Stuart, Davis-Street, & Wolfe, 1996; Symons, Sheffield-Moore, Chinkes, Ferrando, & Paddon-Jones, 2009). Muscle atrophy also develops in rats following limb immobilization (Frimel, 2005; Han, Zhu, Ma, & Du, 2007) and whole-body suspension (Musacchia, Steffen, Fell, & Dombrowski, 1990).

Nerve injury can also lead to muscle atrophy, as Beehler, Sleph, Bemmassaoud, and Grover (2006) reported in their study on sciatic nerve crush injury. The authors found atrophy of both the soleus (SOL) and the extensor digitorum longus (EDL) muscles. Hutchinson, Linderman, and Basso (2001) found that muscle atrophy is present in animals with induced spinal cord injury. Others have demonstrated muscle atrophy in various preclinical models of neuropathic pain (Bennett & Xie, 1988; Choe, Kim, An, Lee, & Heitkemper, 2011; Daemen et al., 1998). However, the relative contributions of nerve injury and decreased activity on muscle atrophy remain uncertain.

More broadly, the relationships among neuropathic pain, activity, and muscle atrophy have yet to be fully characterized. A more thorough understanding of these complex relationships would allow for more effective pain reduction and physical activity interventions for individuals with neuropathic pain. The present pilot study was part of a larger study examining the effects of neuropathic pain on metabolism, activity, and muscle atrophy. The purpose of this pilot study was to characterize the activity and musculoskeletal changes in rats with neuropathic pain induced by ligation of the sciatic nerve. We used the chronic constriction injury (CCI) model, a form of neuropathic pain (Bennett & Xie, 1988). In their original study, Bennett and Xie (1988) characterized nociceptive, locomotive, and postural changes in response to the induced neuropathic pain. However, they combined the weight of the gastrocnemius and SOL muscles to describe muscle atrophy. In the present study, we measured the effect of sciatic nerve ligation on individual muscle weights (SOL and EDL) to characterize possible differential effects of neuropathic pain and activity on muscle atrophy. Additionally, we quantified activity following CCI.

**Material and Method**

**Animals**

We used male Sprague-Dawley rats (225–250 g; Charles River, Portage, USA) in this pre- and posttest quasi-experimental designed pilot study. Rats were housed in pairs in a humidity- and temperature-controlled room with a 12:12 light–dark cycle (lights on at 07:00) and were acclimated to the facility before any procedures were performed. Rats were allowed access to standard rat chow and water ad libitum. The University Committee for the Use and Care of Animals approved all procedures, and the study met the standards of the Association for Assessment and Accreditation of Laboratory Animal Care.

**Procedure**

The study involved three groups of rats: Eight received CCI surgery and underwent thermal hyperalgesic testing and skeletal muscle dissection 2 weeks later (CCI), five received CCI surgery and underwent testing and dissection 6 weeks later (CCI), and five age- and weight-matched rats received identical anesthesia, surgical procedure, and postoperative analgesia as CCI rats with the exception of sciatic nerve ligation, with thermal hyperalgesic testing and skeletal muscle dissection conducted 6 weeks after surgery (SHAM). The first CCI group was further divided into two subgroups: One (n = 4) was monitored for home-cage activity before and after surgery (CCI + activity), while the other (n = 4) underwent no activity monitoring (CCI + no activity). All animals were monitored for surgical healing and infection. No animals exhibited impaired wound healing or infection.

**Neuropathic Pain**

The CCI model was used to induce neuropathic injury, as described in Bennett and Xie (1988). While the rat was under isoflurane anesthesia, an incision was made through the left thigh (ipsilateral hind limb) exposing the common sciatic nerve. Four chromic gut ligatures were tied around the nerve proximal to the trifurcation with sufficient tension to produce a leg twitch. The wound was closed with sutures and sterile skin clips. A single injection of buprenorphine (0.05 mg/kg, intraperitoneal [IP]) was given immediately after CCI to minimize postoperative procedural pain (n=8). We did not provide additional analgesia in order to allow neuropathic pain to develop through anatomical, physiological, and genomic aspects of the spinal cord dorsal horn—which are well known—resulting from excessive nociceptive input.

**Thermal Hyperalgesic Testing**

The characterization of neuropathic pain in the CCI model is well known. Time of onset of thermal hyperalgesia, a sign of neuropathic pain, ranges from the first postoperative day through 2 months, with peak incidence occurring within the first 7 (± 3) days (Bennett & Xie, 1988; Dowdall, Robinson, & Meert, 2005; Jaggi, Jain, & Singh, 2009; Jarvis & Boyce-Rustay, 2009). To determine whether hyperalgesia changed over time, we conducted thermal hyperalgesic testing at 2 and 6 weeks after CCI (n = 8; n = 5, respectively) in two different groups of rats, as described above. We conducted thermal hyperalgesic testing 6 weeks after surgery in SHAM rats (n=5) to maintain treatment conditions consistent with those of CCI rats tested at 6 weeks. Based on data previously collected in our lab, SHAM rats do not display thermal hyperalgesia 2 weeks after surgery compared to CCI rats.

We measured changes in nociceptive threshold (pain sensitivity) using the tail flick analgesiometer (Ugo Basile, Collegeville, Pennsylvania) to confirm the presence of neuropathic pain. The foot withdrawal latency (FWL) indicates the reflexive withdrawal of the (ipsilateral) hind foot in response to noxious thermal infrared heat stimulus. With rats under light sodium pentobarbital anesthesia (35 mg/kg, IP), we exposed the dorsal surface of the paw to the focused infrared heat
stimulus. A computer recorded the time it took for the rat to withdraw its foot from the heat source in seconds. Rats were tested every 5 min for 45 min (Jeong & Holden, 2009; Jeong, Moes, Wagner, & Holden, 2012). Shorter latencies demonstrate increased sensitivity to heat or thermal hyperalgesia. Testing occurred in the morning (10 a.m.). Rats were monitored for 1 hr after testing and returned to their home cage.

**Activity Monitoring**

Home-cage activity was measured in a subgroup of rats from the CCI group that underwent testing at 2 weeks. Rats were individually housed and served as their own controls (n = 4; CCI + activity). Activity monitoring occurred in two continuous 48-hr bouts with minimal activity interruptions, the first immediately prior to CCI surgery and the second immediately prior to thermal hyperalgesic testing. Spontaneous home-cage activity was measured gravimetrically, as described previously (Biesiadecki, Brand, Koch, & Britton, 1999). Briefly, the rat remained in its home cage, which was placed on an electronic precision balance (Sartorius BP6100) that was interfaced with a computer. Rat movements produced changes in weight (samples) that were transmitted to the computer at 10 Hz. Data were analyzed using a laboratory data acquisition software (DASYLab 9.0) to derive the absolute value of the difference in weight between consecutive samples, and the 1-s averages of the absolute values were calculated. Raw data were consolidated into 30-min intervals, and area under the curve for pre- and postoperative measurements was calculated for analysis.

Activity monitoring was conducted in a different facility than the other study procedures. Animals were transported by the animal husbandry staff in an approved transport vehicle with covered cages to minimize stress. Light–dark cycle, humidity, temperature, and access to food and water conditions were the same in the activity-monitoring facility as in our housing facility. In addition to the activity monitoring described above, rats were observed daily for behavioral changes in activity, such as limping, guarding, and altered gait, but we did not collect data on the frequency of these behaviors.

**Muscle Atrophy**

Muscle atrophy was defined as a loss of skeletal muscle mass (Evans, 2010). Muscle weight was examined 2 weeks after surgery (CCI, n = 71) to coincide with changes in thermal sensitivity (Jeong & Holden, 2009) and metabolic outcomes collected for a future study. We examined muscle weight in the two remaining groups of rats (CCI and SHAM, n = 5 in both groups) 6 weeks after surgery to coincide with thermal hyperalgesic testing in these rats and, again, with metabolic outcomes collected for a future study.

Rats were euthanized 48 hr after thermal hyperalgesic testing using 50-mg/kg sodium pentobarbital, IP, followed by exsanguination, and the EDL and SOL muscles were removed and weighed. We selected these muscles based on their anatomical and physiological properties: SOL is involved in posture, while the EDL is a nonload-bearing muscle used in locomotion. Rats euthanized 6 weeks after surgery had significantly heavier total body weight than rats euthanized 2 weeks after surgery. To account for this difference in total body weight, individual muscle weight (mg) was divided by 100 g body weight. Baseline weight was obtained immediately prior to CCI or SHAM surgery. All rats were weighed on a calibrated scale between 9 a.m. and 11 a.m.

**Statistical Analysis**

Data are presented as mean ± standard error of the mean. Two-way repeated measures analysis of variation (ANOVA) with Bonferroni post hoc tests was used to compare means for thermal hyperalgesic testing and weight data. ANOVA with Bonferroni post hoc tests was used to compare mean muscle weight. Paired t-test was used to compare spontaneous activity. An α level of p < .1 was established for significance because of the exploratory nature of this pilot study.

**Results**

Rats with CCI-induced neuropathic pain had a significantly shorter FWL of the ipsilateral hind limb (n = 5; 5.04 ± 0.99 s) compared to SHAM rats (n = 5; 8.17 ± 0.4 s; F(1, 8) = 29.5, p < .05; see Figure 1) 6 weeks after surgery, indicating increased sensitivity to thermal stimulus. CCI rats tested 6 weeks after surgery (n = 5; 5.04 ± 0.99 s) had a longer FWL than CCI rats tested 2 weeks after surgery (n = 8; 4.02 ± 0.19 s; p = .099).

Rats gained weight after surgery regardless of group [F(1, 15) = 242.78, p < .05; see Figure 2]. CCI rats that were monitored for activity (CCI + activity; n = 4) were significantly heavier than CCI rats that did not receive activity monitoring (CCI + no activity) and SHAM rats at baseline [F(2, 17) = 137.32, p < .05]. Rats gained weight between baseline and 2 weeks after surgery [F(2, 15) = 25.62, p < .05]. However, SHAM and CCI + no activity rats gained more weight (89.7 ± 10.1 g and 69.6 ± 3.7 g, respectively) than did CCI + activity rats (19.6 ± 4.8 g) between baseline and 2 weeks after surgery. Rats continued to gain weight regardless of group up to 6 weeks after surgery [F(1, 8) = 183.42, p < .05]. Weight did not differ significantly between CCI and SHAM rats 6 weeks after surgery.

Spontaneous activity decreased in CCI + activity rats (n=4) from presurgery to 2 weeks postsurgery [r(3) = 2.93; p = .06; see Figure 3]. Rats were more active during the nocturnal phase (off) of the light cycle.

CCI rats euthanized 2 and 6 weeks after surgery had lighter (p < .05) ipsilateral hind limb SOL and EDL muscles compared to the same muscles in their contralateral hind limbs. Ipsilateral hind limb SOL and EDL muscles were lighter (p < .05) in CCI compared to SHAM rats euthanized 6 weeks after surgery. Ipsilateral hind limb SOL and EDL muscles were not significantly different in weight between CCI rats 2 and 6 weeks after surgery. Contralateral hind limb muscles were not significantly different among CCI and SHAM rats at 6 weeks after surgery (see Table 1).
Figure 1. Foot withdrawal latency (FWL) during thermal hyperalgesic testing in rats with chronic constriction injury (CCI)-induced neuropathic pain and a SHAM control group. Testing was conducted 2 weeks after surgery in one group of CCI rats \((n = 8)\) and 6 weeks after surgery in the remaining group of CCI rats \((n = 5)\) and the SHAM group \((n = 5)\). Measures were taken every 5 min for 45 min. Data are mean ± SEM. SEM = standard error of the mean.

Figure 3. Spontaneous activity in rats \((n = 4)\) pre- and postchronic 2 weeks constriction injury (CCI) surgery. Data are means. Rats were kept on a 12:12 light–dark schedule, with lights on at 06:00 and off at 18:00.

Table 1. Hind limb Muscle Weights (mg/100 g Body Weight) in Rats With CCI-Induced Neuropathic Pain and SHAM Rats.

<table>
<thead>
<tr>
<th>Group</th>
<th>Ipsilateral</th>
<th>Contralateral</th>
<th>Ipsilateral</th>
<th>Contralateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCI 2 weeks ((n = 7))</td>
<td>18.2 (6.2)*</td>
<td>41.3 (5.8)</td>
<td>16.8 (9.4)*</td>
<td>34.0 (5.4)</td>
</tr>
<tr>
<td>CCI 6 weeks ((n = 5))</td>
<td>13.2 (3.6)*</td>
<td>47.5 (5.2)</td>
<td>10.9 (7.1)*</td>
<td>41.4 (4.1)</td>
</tr>
<tr>
<td>SHAM ((n = 5))</td>
<td>43.0 (2.9)</td>
<td>44.0 (2.2)</td>
<td>35.6 (4.1)</td>
<td>38.6 (2.7)</td>
</tr>
</tbody>
</table>

Note. CCI = chronic constriction injury; EDL = extensor digitorum longus muscle; SOL = soleus muscle. Data are reported as mean (standard error of the mean). CCI rats were euthanized and their muscles weighed 2 or 6 weeks after surgery, as indicated. SHAM rats were euthanized 6 weeks after surgery. *\(p < .05\) versus Contralateral. †\(p < .05\) versus ipsilateral SHAM at 6 weeks.

**Figure 2.** Body weight 2 and 6 weeks after chronic constriction injury (CCI) and SHAM surgery. CCI + activity rats received activity monitoring prior to CCI surgery and again prior to thermal hyperalgesic testing 2 weeks postsurgery \((n = 4)\). CCI + no activity rats did not receive activity monitoring and underwent thermal hyperalgesic testing 2 \((n = 4)\) or 6 \((n = 5)\) weeks postsurgery. Rats in the SHAM group \((n = 5)\) underwent thermal hyperalgesic testing 6 weeks postsurgery. Data are mean ± SEM for each group. *\(p < .05\) versus CCI + activity. †\(p < .05\) versus baseline. †‡\(p < .05\) versus 2-week measures. SEM = standard error of the mean.
Discussion

Our study findings confirm and extend the findings of Bennett and Xie (1988), contributing to the characterization of activity and muscle atrophy changes in rats with neuropathic pain. Similar to the rats in Bennett and Xie’s study, CCI rats in our study demonstrated increased sensitivity to a thermal stimulus following sciatic nerve ligation. Our data are consistent with previous findings that thermal hyperalgesia develops within 2 weeks of CCI surgery (Bennett & Xie, 1988; Jeong & Holden, 2009). This increased sensitivity to the thermal stimulus continued up to 6 weeks after sciatic nerve ligation. The longer FWL we found for CCI rats tested 6 versus 2 weeks after surgery may reflect a shift from hyper- to hypoalgesia, which develops over time in this model of neuropathic pain (Bennett & Xie, 1988). Values for FWL in the present study are similar to data collected previously in our lab for both CCI rats and SHAM rats (Jeong & Holden, 2009).

The development of thermal hyperalgesia in CCI rats was not accompanied by a change in overall weight gain. CCI and SHAM rats gained weight at a similar rate despite differences in sensitivity to thermal stimulus. The rate and amount of weight the rats gained aligns with weight gain expectations provided by the breeder (Charles River). Our results contradict those of Choe et al. (2011), who found that body weight in rats with neuropathic pain was less than that of control and sham groups over 14 days, including baseline. However, the spinal nerve ligation (SNL) model that Choe et al. used to induce neuropathic pain is more invasive than the CCI model we used, which may explain this difference between studies. SNL contributes to surrounding tissue damage, requires more extensive surgical procedures compared with the CCI, and has more widespread neurological effects than ligation of a peripheral nerve (Jaggi et al., 2009).

Activity monitoring may have contributed to altered weight gain in a subcohort of CCI rats. Rats that received activity monitoring weighed more at baseline than CCI + no activity rats but gained weight at a slower rate than the other two groups in the 2 weeks following surgery. It is possible that being transported between facilities may have affected the weight gained by CCI + activity rats. Weight did not differ significantly among the groups 2 weeks after surgery.

Spontaneous activity decreased in a small subcohort of CCI rats from just prior to CCI surgery to just prior to thermal hyperalgesic testing at 2 weeks postsurgery. We also observed limping, guarding, and altered gait in these CCI rats, which likely reflected changes in overall animal activity/movement (Bennett & Xie, 1988; Jaggi et al., 2009). Our findings support those of Choe et al. (2011), who found that rats with neuropathic pain had lower activity levels than controls, but contradict those of Bennett and Xie (1988), who found no decrease in general activity in the rats with neuropathic pain. The latter authors, however, described activity changes but did not quantify spontaneous activity, as we did. Unfortunately, the mechanism we used in the present study for measuring spontaneous activity did not allow us to differentiate type of movement. For example, if the animal moved its head, the scale was disrupted and a recording was made. Therefore, overall spontaneous activity does not necessarily reflect changes in recruitment or weight bearing of the ipsilateral hind limb muscles in CCI rats, and the use of a more specific measurement of weight-bearing activity would be useful in future studies. In addition, we did not conduct activity monitoring continuously or in SHAM rats. Future studies should use larger samples from both groups of rats (CCI and SHAM) and should conduct activity monitoring over longer periods of time to confirm that changes in activity levels could be attributed to neuropathic pain.

CCI rats in the present study exhibited atrophy of both the SOL and the EDL muscles in the ipsilateral hind limb, both of which are innervated by branches of the sciatic nerve (Lehnert, Steudal, Marzi, & Mautes, 2003; Leterme & Tyc, 2004). These findings support those of previous studies on skeletal muscle atrophy in rats with induced nerve injury. Bennett and Xie (1988) described skeletal muscle atrophy 58 days after CCI, while in the present study we observed it occurring as early as 2 weeks following CCI. Other researchers have reported atrophy of the SOL (Choe et al., 2011) and gastrocnemius and rectus femoris muscles (Daemen et al., 1998) following spinal and peripheral nerve injury, respectively. In a study on sciatic nerve crush injury in rats, Beehler et al. (2006) found that the SOL and EDL muscles exhibited a degree of atrophy similar to what we found in the present study. Hutchinson et al. (2001) also found that muscle atrophy was present in animals with induced spinal cord injury.

The mechanisms underlying the findings of the present and previous studies on skeletal muscle atrophy in cases of induced nerve injury, however, remain unclear. Motor denervation or axonal disruption may contribute to muscle atrophy directly (Daemen et al., 1998). Daemen et al. (1998) attributed atrophy of muscles involved in locomotion to motor denervation of the sciatic (ligated) and femoral (nonligated) nerves. Our finding in the present study that the EDL muscle was atrophied following CCI supports their conclusion. Motor denervation may be a less likely cause of muscle atrophy, however, in the CCI model than in other models of nerve injury. Sciatic nerve ligation is a loose ligation that causes epineural swelling and inflammation while leaving the axons intact (Bennett & Xie, 1988; Jeong & Holden, 2008), so the amount of actual muscle denervation that occurs in CCI is less than in more severe injury models such as crush injury (Leterme & Tyc, 2004). Scarring, adhesions, and axonal disruption can occur in CCI, but improved axonal function can also occur relatively quickly because the nerve has not been severed or severely damaged (Smit, 2006). Based on these observations, the atrophy we observed in the EDL muscle in the present study may not have been directly attributable to sciatic nerve ligation, suggesting other causes. However, we cannot rule out denervation or axonal disruption, and further study is warranted.

Neuropathic pain that results from nerve damage may also contribute to muscle atrophy indirectly through hypokinesia. The reduced activity in CCI rats pre- to postsurgery suggests that hypokinesia may have played a role in the muscle atrophy
we observed in the present study. Previous research has shown that muscle atrophy occurs in both the SOL and the EDL muscles with cast immobilization in mice (Frimel, 2005) as well as with tail cast suspension (Han et al., 2007), space flight, and whole-body suspension in rats (Musacchia et al., 1990). We selected the SOL and EDL muscles for the present study based on their distinct functional properties: The EDL muscle is involved in ambulation, while the SOL muscle has a postural function. Rats may have experienced neuropathic pain differently depending on the type of activity in which they were engaged. Thus, if rats experienced increased pain during ambulation, they were likely to have ambulated less, leading to increased atrophy of the EDL muscle. However, if pain was elicited when rats were standing, the SOL muscle may have been more affected (Daemen et al., 1998).

Finally, decreased nutritional intake can also contribute to muscle atrophy. In a previous study, rats with neuropathic pain following SNL had significant decreases in total dietary intake 15 days after surgery (Choe et al., 2011), which may have contributed to the outcome of muscle atrophy. One limitation of the present study was that, while we did measure body weight daily, we did not record nutritional intake. While our finding that total body weight did not differ significantly between CCI and SHAM rats suggests that nutritional intake likely did not vary between groups, we cannot rule out the possibility that changes in nutritional intake may have contributed to muscle atrophy in CCI rats.

Conclusion
Our findings in the present study confirm that neuropathic pain contributes to changes in activity and muscle composition. Changes in activity, nerve injury, and nutritional intake can have significant effects on muscle atrophy (Lindboe & Presthus, 1985). While some muscles are more susceptible to nerve damage (Daemen et al., 1998), other muscles may tend to atrophy more from decreased mobility (Lindboe & Presthus, 1985). Future research exploring which muscles are being recruited during weight-bearing activities in ipsilateral hind limbs following sciatic nerve ligation would enable us to better elucidate the underlying mechanisms contributing to muscle atrophy in CCI rats.

Our findings also have implications for the care of individuals with neuropathic pain. In addition to ensuring adequate pain management and proper nutrition in these individuals, nurses must monitor for signs of muscle atrophy (Herr, 2004) and assist patients to gradually increase their physical activity to prevent further muscle injury and/or atrophy (Kasper, Talbot, & Gaines, 2002).

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Note
1. One chronic constriction injury rat died prior to muscle dissection and was not included in the analysis.

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