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RESEARCH ARTICLE

Induction of muscle cramps by nociceptive stimulation of latent myofascial trigger points

Hong-You Ge · Yang Zhang · Shellie Boudreau · Shou-Wei Yue · Lars Arendt-Nielsen

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Abstract The aim of this present study is to test the hypothesis that nociceptive stimulation of latent myofascial trigger points (MTrPs) increases the occurrence of local muscle cramps. Nociceptive muscle stimulation was obtained by a bolus injection of glutamate (0.1 ml, 0.5 M) into a latent MTrP and a control point (a non-MTrP) located in the right or left gastrocnemius medialis muscles in 14 healthy subjects. A bolus of isotonic saline (0.9%, 0.1 ml) injection served as a control. The injections were guided by intramuscular electromyography (EMG) showing resting spontaneous electrical activity at a latent MTrP and no such activity at a non-MTrP. Intramuscular and surface EMG activities in the gastrocnemius medialis muscle were recorded pre-, during-, and post-injection for a period of 8 min to monitor the occurrence of muscle cramps, which are characterized by a brief episodic burst of high levels of EMG activity. The results showed that glutamate and isotonic saline injections into the latent MTrPs induced higher peak pain intensity than into the non-MTrPs (both $P < 0.05$). Glutamate injection induced higher peak pain intensity than isotonic saline injection into either latent MTrPs or non-MTrPs (both $P < 0.05$). Muscle camps were observed in 92.86% of the subjects following glutamate injection into the latent MTrPs, but not into the non-MTrPs ($P < 0.001$). No muscle cramps were recorded following isotonic saline injection into either the latent MTrPs or the non-MTrPs. These results suggest that latent MTrPs could be involved in the genesis of muscle cramps. Focal increase in nociceptive sensitivity at MTrPs constitutes one of the mechanisms underlying muscle cramps.

Keywords Pain · EMG-guided injection · Nocturnal leg cramp · Glutamate · Myofascial trigger points

H.-Y. Ge (✉) · Y. Zhang · S. Boudreau · L. Arendt-Nielsen
Laboratory for Experimental Pain Research,
Center for Sensory–Motor Interaction (SMI),
Department of Health Science and Technology,
Aalborg University, Fredrik Bajers Vej 7 D-3,
9220 Aalborg, Denmark
e-mail: ghy@hst.aau.dk
URL: www.smi.auc.dk

Y. Zhang · S.-W. Yue
Department of Physical Medicine and Rehabilitation,
Qilu Hospital, Medical School of Shandong University,
250012 Jinan, People's Republic of China

Introduction

Muscle cramps are a common medical problem with an estimated 1-year incidence of 36% in the general adult population (Jansen et al. 1991). Muscle cramps are characterized by involuntary, painful, and spasmodic contractions associated with high levels of electrical activity in the skeletal muscle (Parisi et al. 2003; Miller and Layzer 2005). Muscle cramps may occur in healthy adults during voluntary muscle contractions, sleep, sports, and pregnancy. However, muscle cramps have also been associated with myopathies, neuropathies, motor neuron diseases, and metabolic disorders, although nocturnal calf cramps are the most common form of muscle cramps (Miller and Layzer 2005).

Injection of lidocaine into myofascial trigger points (MTrPs) has been shown to be equally effective to the current treatment (oral quinine) for nocturnal calf cramps (Prateepavanich et al. 1999). Interestingly, this study revealed an association between active MTrPs and muscle cramps, although the mechanisms underlying this association are not clear. MTrPs may be active or latent. An active MTrP is characterized by spontaneous pain and tenderness

on a taut muscle band. In addition, an active MTrP will reproduce familiar and/or referred pain and will induce a local twitch response when stimulated manually or with a needle. A latent MTrP does not produce spontaneous pain but pain may be induced when stimulated manually or with a needle. The main difference between an active and latent MTrP is that an active MTrP reproduces familiar pain (i.e. pain that is recognized by the patient) (Gerwin et al. 2004; Simons 2004; Cummings and Baldry 2007) when stimulated manually or with a needle. However, the presence of latent MTrPs in pain-free subjects has been shown to modulate muscle activation patterns during a motor task when compared to subjects without latent MTrPs (Lucas et al. 2004). It has been proposed that changes in muscle activation patterns could lead to motor dysfunctions, even in healthy subjects with latent MTrPs (Simons 2004).

Lower pressure pain thresholds have been shown to exist at active and latent MTrPs when compared to control points (Reeves et al. 1986; Ge et al. 2006; Fernandez-de-Las-Penas et al. 2007). Lower pain thresholds also exist at active MTrPs when compared to latent MTrPs, which suggests that nociceptive sensitivity has been dramatically increased at active MTrPs. Furthermore, higher concentrations of algogenic substances have been shown to exist at active MTrPs when compared to latent MTrPs (Shah et al. 2008).

We hypothesize that increased nociceptive sensitivity at MTrPs may underlie the association between MTrPs and muscle cramps. To test this hypothesis we injected the algesic chemical glutamate into latent MTrPs to increase nociceptive sensitivity at latent MTrPs. The aim of this present study was to determine if injection of glutamate into latent MTrPs in healthy subjects increases the occurrence of muscle cramps.

Materials and methods

Subjects

Fourteen healthy subjects (10 males and 4 females, mean age: 25.4 ± 2.5 years), with no signs or symptoms of musculoskeletal pain, volunteered for this study. This study was approved by the local Ethics Committee and conducted in accordance with the Helsinki Declaration. Informed consent was obtained from all the subjects.

Experimental protocol

Each subject participated in a two-session study in which glutamate or isotonic saline was injected into left or right gastrocnemius muscle. The glutamate and isotonic saline sessions were randomized and separated by at least 1 week. The left and right gastrocnemius muscle was also randomized between the two sessions. The subjects were asked to relax both legs for the duration of each experimental session. Each session consisted of two glutamate or isotonic saline injections. Glutamate or isotonic saline was injected into a latent MTrP and a non-MTrP in randomized order. In each session, the subjects were asked to take a prone position on a comfortable bed. A pillow was then placed under the subjects' ankle joint to elevate the lower leg and slightly flex the knee joint. The flexed knee joint resulted in a slight stretch of the gastrocnemius muscle. A latent MTrP was then identified in the gastrocnemius muscle, and a non-MTrP was then chosen on the opposite side of the gastrocnemius muscle. A latent MTrP was confirmed by a taut muscle band, local twitch response, and most tender point without referred pain upon digital palpation. A non-MTrP was confirmed by the absence of latent MTrP characteristics. An EMG-guided injection needle was then inserted into a latent MTrP or non-MTrP. A pair of bipolar surface electrodes were then placed 2 cm distal to the EMG-guided injection needle. A latent MTrP was then reconfirmed by the presence of spontaneous intramuscular electrical activity (Fig. 1, upper trace) in the EMG-guided injection needle and absence of surface EMG activity in the surface electrodes (Fig. 1, lower trace). Conversely a non-MTrP was reconfirmed by the absence of spontaneous intramuscular electrical activity in the EMG-guided injection needle and surface EMG in the surface electrodes. A bolus of glutamate or isotonic saline was then injected into a latent MTrP or non-MTrP. A 20 min hiatus followed after the first injection of glutamate or isotonic saline. A second injection of glutamate or isotonic saline was then delivered to the non-injected site (i.e. the latent MTrP or non-MTrP). Following each injection of glutamate or isotonic saline, pain ratings were continuously recorded on a visual analogue scale (VAS). Intramuscular electrical and surface EMG activity was recorded before, during, and after bolus injection.

EMG-guided intramuscular injection

A MTrP occupies an area approximately 1–2 mm^2 (Simons 2004), thus EMG-guided intramuscular injection was used in this present study to accurately deliver glutamate or isotonic saline into the latent MTrP. In addition, a small dose of glutamate (0.1 ml, 0.5 M) or isotonic saline (0.1 ml, 0.9%) was chosen to maintain the bolus solutions within the latent MTrP or non-MTrP. After identification the latent MTrP and non-MTrP (usually found at the upper and middle parts of the gastrocnemius medialis) the position of the latent MTrP and non-MTrP was marked with a colored pen. The area of skin around the marked position of a latent MTrP and non-MTrP was then shaved and cleaned with isopropyl alcohol. One pair of bipolar surface EMG

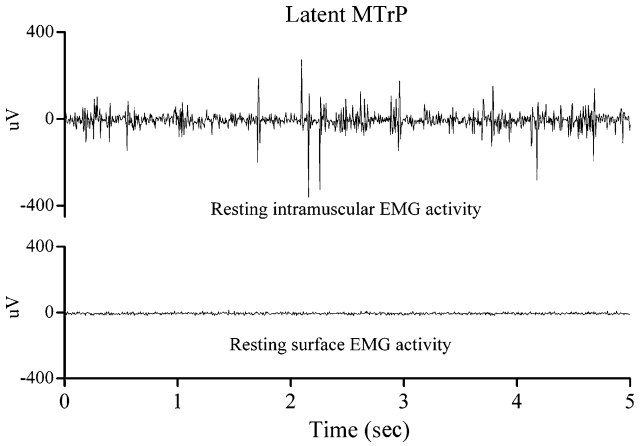

Fig. 1 Resting intramuscular and surface electromyographic (EMG) recordings of a latent myofascial trigger point (MTrP). Note that only intramuscular EMG recording (*upper trace*), but not surface EMG (*lower trace*), shows spontaneous electrical activity

electrodes (Neuroline 720-01-k, Ølstykke, Denmark, intra-electrode distance of 2 cm) was placed 2 cm distal to the marked position. The surface electrodes were used to ensure that gastrocnemius muscle was relaxed prior to injection of glutamate or isotonic saline and to monitor the EMG activity after injection. Before insertion of the EMG-guided injection needle into the marked position a reference surface electrode was placed 2 cm lateral to the marked position. A ground tape electrode was then wrapped around the ankle. The EMG-guided injection electrode (Ambu Neuroline Inoject, 25 × 0.30 mm, Denmark) was first connected to an extension tube (15 cm, filling volume 0.2 ml, IMF GmbH, Germany) and then to a syringe (1 ml in volume). The syringe was pre-filled with 0.3 ml glutamate or isotonic saline, which resulted in 0.2 ml in the extension tube and an injection of 0.1 ml of glutamate or isotonic saline into the latent MTrP or non-MTrP. The extension tube and the syringe were fixed to the skin to prevent displacement of the EMG-guided injection needle during injection. The EMG-guided injection needle was advanced slowly (total injection time 10 ± 1 s), by the experimenter, into the latent MTrP or non-MTrP.

EMG-guided injection needle recordings

The resting spontaneous intramuscular electrical activity of an MTrP or a non-MTrP was recorded for 5 s before injection of glutamate or isotonic saline. After injection of glutamate or isotonic saline, EMG from the EMG-guided intramuscular needle and surface electrodes were recorded for 8 min. EMG from the EMG-guided intramuscular needle and surface electrodes were amplified (Gain of 100 μV/div), filtered (Bandpass 5 Hz–5 kHz for the intramuscular recordings, and 5 Hz–5 kHz for surface recordings), and sampled at 2 kHz and stored for offline analysis.

Muscle cramp as defined by EMG

Muscle cramps were defined as a significant increase in EMG activity, as measured by EMG-guided intramuscular and surface electrodes, when compared to resting EMG activity for at least 5 s. To test for a significant increase in EMG activity, 5 s of EMG-guided intramuscular and surface activity before injection (resting EMG) was compared to 5 s of increased EMG activity (muscle cramp EMG), if present, after injection. In addition, the characteristics of muscle cramps (involuntary, painful, spasmodic contraction of the skeletal muscle) also had to occur in association with the increase in EMG activity.

Assessment of local muscle pain intensity

The subjects rated the muscle pain intensity on an electronic visual analogue scale (VAS) beginning immediately after and 8 min following injection of glutamate or isotonic saline. The subjects rated the pain on a 10 cm VAS scale with "no pain" labeled at 0 cm and "most pain imaginable" at 10 cm. The VAS data were sampled (20 Hz) and recorded for 8 min.

Statistical analysis

Two-way repeated measures analysis of variance (Two-way ANOVA) was applied to compare the differences in peak pain intensity (VAS_{peak}) between the glutamate and isotonic saline sessions, and also between the latent MTrPs and non-MTrPs. Chi-square test was used to compare differences in the occurrence of muscle cramps between the glutamate and isotonic saline sessions and also between the latent MTrPs and the non-MTrPs. Student Newman–Keuls Test (SNK) was used as post hoc to compare VAS_{peak} between the latent MTrPs and the non-MTrPs for the glutamate and isotonic saline sessions. Paired *t* test was used to analyse the differences in root mean square (RMS) values of intramuscular and surface EMG before and after glutamate or isotonic saline injections upon the occurrence of a muscle cramp. All the data are expressed as mean ± standard error of the mean (SEM) and the significance level was set to $P < 0.05$.

Results

Pain intensity

Glutamate injections into the latent MTrPs and non-MTrPs resulted in pain duration of 6.5 ± 0.68 min and peaked within 2 min following injection (Fig. 2a). Isotonic saline injection into the MTrPs and non-MTrPs resulted in mild or

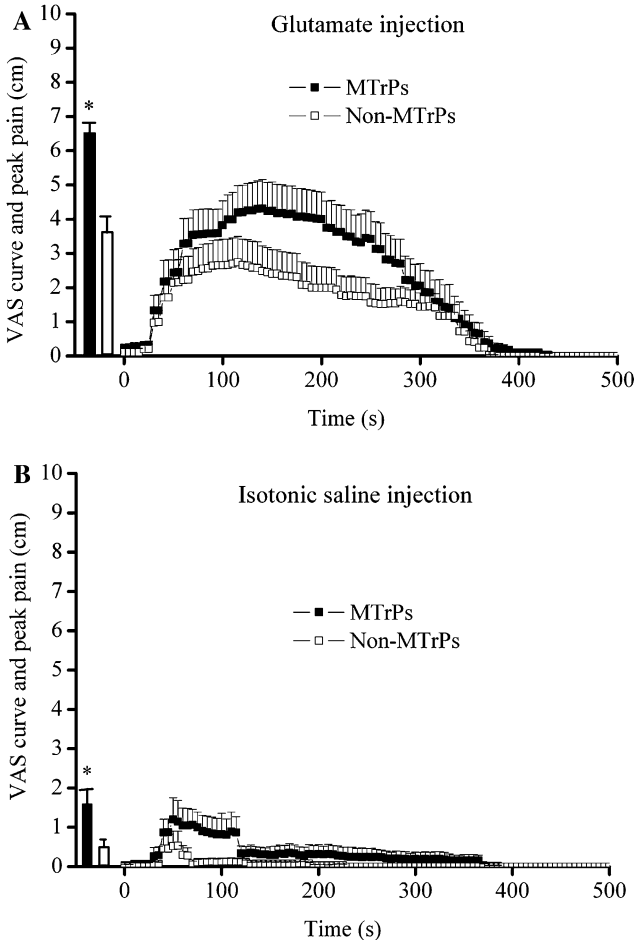

Fig. 2 Visual analogue scale (VAS) curve and peak pain intensity following intramuscular injection of glutamate into a latent myofascial trigger point (MTrP) and a non-MTrP. *Asterisks* indicates higher peak pain intensity (VAS_{peak}) following intramuscular injection of glutamate (**a**) or isotonic saline (**b**) into a latent myofascial trigger point (MTrP) than a non-MTrP

slight pain with the duration of 1.8 ± 0.3 min (Fig. 2b). The peak pain intensity (VAS_{peak}) was higher at latent MTrPs than at non-MTrPs ($F = 7.14$, $P < 0.05$). VAS_{peak} for the glutamate sessions at latent and non-MTrP were significantly higher than the isotonic saline sessions (Fig. 2a; $F = 35.24$, $P < 0.001$). There was no interaction between latent and non-MTrP sites and solutions ($F = 0.693$, $P = 0.420$). VAS_{peak} was higher for the latent MTrP when compared to the non-MTrP during the glutamate (Fig. 2a; SNK, $P < 0.05$) and isotonic saline (Fig. 2b; SNK, $P < 0.05$) sessions.

EMG activity before and after glutamate and isotonic saline injections

An increase in root mean square (RMS) of intramuscular and surface EMG activity occurred for the glutamate but not for the isotonic saline sessions. RMS of surface (139.39 ± 34.07 μV) and intramuscular (289.62 ± 121.23 μV) EMG activity increased following injection of glutamate at latent MTrP when compared to resting surface (33.22 ± 10.22 μV) and intramuscular (78.54 ± 10.59 μV) EMG activity (Paired *t* test; both $P < 0.001$). Following glutamate injection into the latent MTrPs, "painful muscle contractions" were reported by 13 of the 14 subjects, whereas no "painful muscle contractions" were reported by any subjects after glutamate injection into the non-MTrPs.

Occurrence of muscle cramps

Following glutamate injection into the latent MTrPs the occurrence of muscle cramps (92.86%, 13/14; Fig. 3a, b) was higher when compared to glutamate injection into the non-MTrPs (0/14, Fig. 3c) (Chi-square = 20.68, $P < 0.001$). No muscle cramps was occurred following isotonic saline injection either into the MTrPs (0/14, Fig. 4a) or into the non-MTrPs (0/14, Fig. 4b). Furthermore, multiple episodes of muscle cramps were observed in five subjects, refer to Table 1. The duration of all muscle cramps of all subjects ranged from 16 to 130 s (52.47 ± 8.85 s). The onset of the first muscle cramp following glutamate injection was observed 3.31 ± 0.51 s before the end of the glutamate injection in eight subjects and 14.6 ± 11.12 s after the end of the glutamate injection in five subjects, refer to Table 1.

Discussion

The main finding of this present study was that glutamate injection into a latent MTrP resulted in significant increases in EMG activity, as measured by EMG-guided intramuscular and surface electrodes, when compared to isotonic saline injections. These findings suggest that the occurrence of muscle cramps may increase after noxious stimulation of a latent MTrP. Furthermore, this finding confirms an association between MTrPs and muscle cramps.

Association of muscle cramps with MTrPs

In this study glutamate injection into a latent MTrPs resulted in significant increases in EMG activity and higher pain intensity when compared to glutamate injection into non-MTrPs. These results reproduced similar characteristics of muscle cramps. Previously, it has been shown that injection of a local anesthetic (lidocaine) into active MTrPs can reduce the occurrence of nocturnal calf cramps (Prateepavanich et al. 1999). In this present study, injection of a nociceptive substance (glutamate) into a latent MTrP increased the occurrence of muscle cramps. Therefore, a causal relationship between MTrPs and muscle cramps may

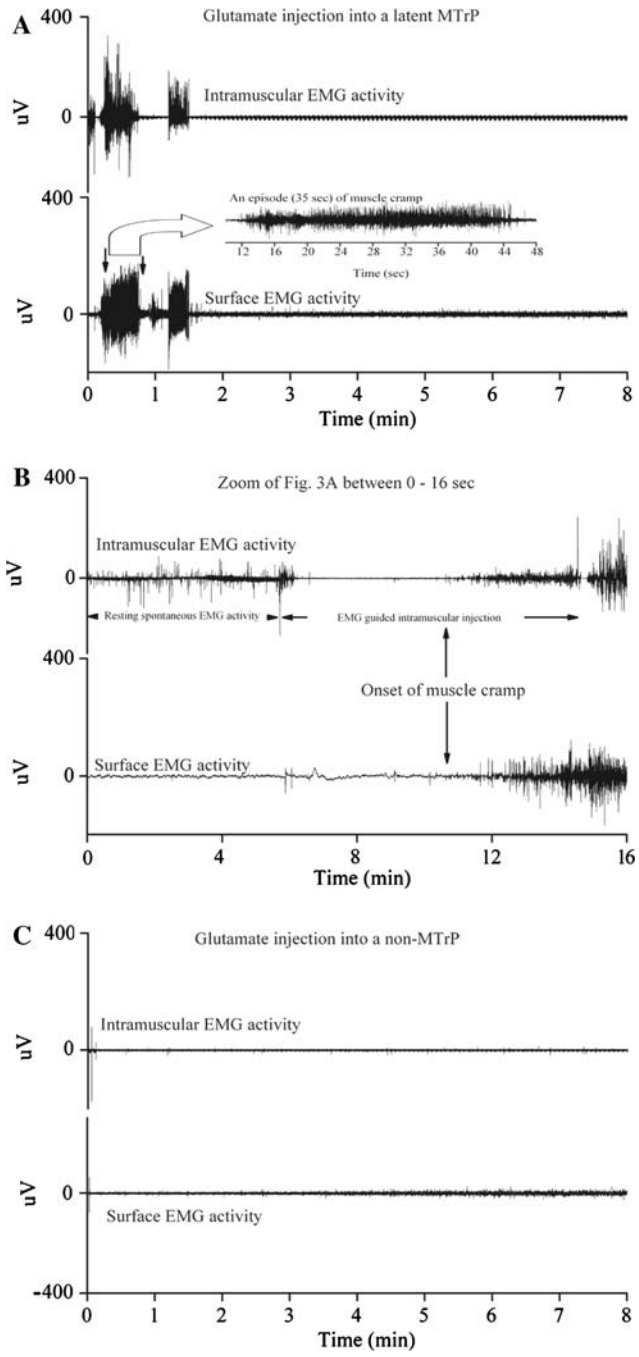

Fig. 3 On both intramuscular and surface electromyographic (EMG) recordings, muscle cramps are observed following glutamate injection into a latent myofascial trigger point (MTrP, **a**), but not into a non-MTrP (**c**). **b** is a zoom-in picture of **a** to show the first episode of muscle cramps happened before the end of the intramuscular injection process

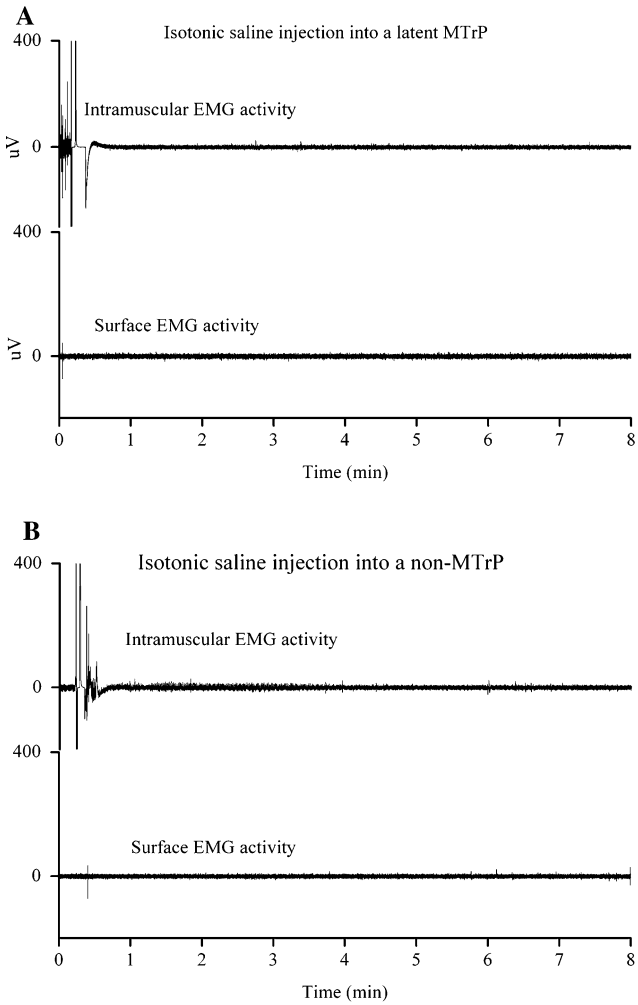

Fig. 4 Intramuscular injection into a latent myofascial trigger point (MTrP, **a**) and a non-MTrP (**b**). Note that injection of isotonic saline into a latent MTrP induces no occurrence of muscle cramps on both intramuscular and surface electromyographic (EMG) recordings

be established, although the mechanism underlying this association is not clear.

An important question in the pathophysiology of muscle cramps is the site of their origin. Several lines of evidence suggest that cramps arise from spontaneous discharges of the motor nerves rather than from within the muscle itself (Miller and Layzer 2005). It has been proposed that muscle cramps may result from hyperexcitability of the terminal branches of motor axons (Bertolasi et al. 1993; Layzer 1994). Alternatively, it has been proposed that muscle cramps may result from hyperexcitability of motoneurones (Norris et al. 1957; Ross and Thomas 1995). However, these proposals for the origin of muscle cramps do not explain (1) why muscle cramps can still be evoked in curarized muscle (Lambert 1969; Layzer and Rowland 1971); (2) why muscle cramps can be elicited by electrical stimulation of the peripheral nerve, even after proximal nerve block (Bertolasi et al. 1993); and (3) the temporal and spatial surface EMG characteristics of muscle cramps (Roeleveld et al. 2000). Roeleveld et al. (2000) proposed that the temporal and spatial surface EMG characteristics of muscle cramps imply that the muscle cramp is initiated close to or even at the muscle fiber level. As a result we know that the origin of muscle cramps may be multifactorial. Muscle pain

Table 1 Muscle cramps following glutamate injection into the latent MTrPs

Subject number	Number of cramp episodes	Duration of each episode (s)	First cramp started before (+) or after (−) the end of injection (s)
1	0	0	
2	1	100	+4
3	1	70	+4.5
4	3	50, 30, and 45	+2
5	1	120	−5
6	2	130, 70	−2
7	2	22, 10	+2
8	1	90	−59
9	1	50	+5
10	2	20, 82	+2
11	1	10	−2
12	1	27	−5
13	2	60, 16	+5
14	1	40	+2

mechanisms may be involved in the initiation of muscle cramps.

Restless legs syndrome and leg cramps are significantly more prevalent in patients with fibromyalgia syndrome and those with rheumatoid arthritis than in normal controls (Yunus and Aldag 1996), and in other generalized and focal muscle pain syndromes (Miller and Layzer 2005). A cross-sectional epidemiologic survey indicates that muscle cramps and fasciculations are more frequent in musculoskeletal pain patients than other pain conditions (Jansen et al. 1992). In healthy subjects the frequency threshold of electrically elicited muscle cramps is decreased when experimental muscle pain is present (Serrao et al. 2007). In this present study we also showed that nociceptive input at latent MTrPs resulted in muscle cramps, thus MTrPs may contribute to the occurrence of muscle cramps. MTrPs, which are presumed to be at and around the motor endplate region (Simons 2004), may be a possible candidate for the origin of muscle cramps.

Increased nociceptive sensitivity at MTrPs mediates the occurrence of muscle cramps

In this present study the algesic chemical glutamate was injected into the latent MTrPs to increase nociceptive sensitivity of the latent MTrPs to the level of active MTrPs. Injection of glutamate, but not isotonic saline, into the latent MTrPs resulted in muscle cramps, and this suggest that increased nociceptive sensitivity at the latent MTrPs may mediate the occurrence of muscle cramps. It has been previously shown that glutamate injected into the latent MTrPs increases nociceptive sensitivity by exciting and sensitizing small diameter muscle afferents through activation of peripheral excitatory amino acid receptors (Cairns et al. 2002). In this present study, injection of glutamate into the latent MTrPs also resulted in higher pain intensities than isotonic saline injection, which suggests that excitation of small diameter muscle afferents occurred. Factors leading to an increase in nociceptive sensitivity at the latent MTrPs may thus increase the risks of developing muscle cramps in both healthy subjects and pain patients.

The mechanism by which nociceptive stimulation at the latent MTrPs results in muscle cramps is debatable. One of the earliest proposals by which muscle cramps may occur is the activation of nociceptive muscle afferents (Serratrice et al. 1980). In support of this proposal, activation of nociceptive muscle afferents decreases the frequency threshold for electrically induced muscle cramps (Serrao et al. 2007). Furthermore, stimulation of small diameter muscle afferents in leg muscles often produces an increase in the response of group II spindle afferents (Appelberg et al. 1983; Thunberg et al. 2002) and thus increases the afferent input to motoneurones. A positive feedback loop between peripheral afferents and alpha motor neurons is a possible mechanism underlying muscle cramp (Ross and Thomas 1995). In this present study, the greater pain response following isotonic saline injection into the latent MTrPs than non-MTrPs may suggest the increased sensitivity of myelinated muscle afferents at the latent MTrPs. This present result supports the notion that a positive feedback loop between peripheral afferents and alpha motor neurons may be a mechanism for muscle cramps. However, this mechanism cannot adequately explain all the findings associated with muscle cramps. For example, an increased response of group II spindle afferents disappeared after peripheral denervation but muscle cramps could still be induced after proximal nerve block (Bertolasi et al. 1993). These findings further support that muscle cramps may be multifactorial.

Another potential mechanism by which noxious stimulation may induce a muscle cramp is that an intense noxious stimulation of the latent MTrPs would decrease the inhibitory input to motoneurones, thus mediating a muscle cramp. In support of this mechanism, by which noxious stimulation may induce a muscle cramp, intramuscular injection of the algesic chemical ascorbate (which activate group III and IV muscle afferents) decrease spinal inhibitory inputs conveyed by Ib afferents (Rossi and Decchi 1997; Rossi et al. 1999). Further, it is well known that stretching the muscle involved in the muscle cramp terminates the muscle cramp possibly via spinal inhibition by activating Golgi tendon organ (Ib) afferents (Rowland 1985; McGee 1990). Additionally, intramuscular injection of the algesic chemical ascorbate has also been shown to facilitate the H-reflex (an indirect measure of motoneurone

activity) in a relaxed muscle and conversely, inhibit the H-reflex in a contracted muscle (Rossi et al. 2003). In a relaxed muscle the excitability of Renshaw cells involved in recurrent inhibition is not modified by noxious stimulation (Rossi et al. 2003). In this present study, muscle cramps were induced in the relaxed gastrocnemius muscle after glutamate injection into the latent MTrPs, therefore these muscle cramps may not have been mediated by a recurrent inhibition mechanism, possibly by spinal inhibition mediated by Ib afferents. Regardless of the mechanisms by which nociceptive stimulation of latent MTrPs results in muscle cramps, nociceptive stimulation of the latent MTrPs induces a net increase in α-motoneurone excitability.

In conclusion, this is the first study to reveal that increased nociceptive sensitivity at MTrPs may underlie the association between MTrPs and muscle cramps. MTrPs may contribute to muscle cramps in both young and old healthy subjects without other noticeable reasons. Treatments directed at MTrPs may provide therapeutic relief of muscle cramps.

References

Appelberg B, Hulliger M, Johansson H, Sojka P (1983) Actions on gamma-motoneurones elicited by electrical stimulation of group III muscle afferent fibres in the hind limb of the cat. J Physiol 335:275–292

Bertolasi L, De Grandis D, Bongiovanni LG, Zanette GP, Gasperini M (1993) The influence of muscular lengthening on cramps. Ann Neurol 33:176–180

Cairns BE, Gambarota G, Svensson P, Arendt-Nielsen L, Berde CB (2002) Glutamate-induced sensitization of rat masseter muscle fibers. Neuroscience 109:389–399

Cummings M, Baldry P (2007) Regional myofascial pain: diagnosis and management. Best Pract Res Clin Rheumatol 21:367–387

Fernandez-de-Las-Penas C, Ge HY, Arendt-Nielsen L, Cuadrado ML, Pareja JA (2007) Referred pain from trapezius muscle trigger points shares similar characteristics with chronic tension type headache. Eur J Pain 11:475–482

Ge HY, Fernandez-de-las-Penas C, Arendt-Nielsen L (2006) Sympathetic facilitation of hyperalgesia evoked from myofascial tender and trigger points in patients with unilateral shoulder pain. Clin Neurophysiol 117:1545–1550

Gerwin RD, Dommerholt J, Shah JP (2004) An expansion of Simons' integrated hypothesis of trigger point formation. Curr Pain Headache Rep 8:468–475

Jansen PH, Joosten EM, Van Dijck J, Verbeek AL, Durian FW (1991) The incidence of muscle cramp. J Neurol Neurosurg Psychiatry 54:1124–1125

Jansen PH, van Dijck JA, Verbeek AL, Durian CW, Jeurissen ME (1992) Neuromuscular hyperexcitability features in patients suffering from musculoskeletal pain: a neuroepidemiologic survey. Funct Neurol 7:31–34

Lambert EH (1969) Electromyography in amyotrophic lateral sclerosis. In: Norris FH Jr, Kurland LT (eds) Motor neuron diseases: research on amyotrophic lateral sclerosis and related disorders. Grune and Stratton, New York, pp 135–153

Layzer RB (1994) The origin of muscle fasciculations and cramps. Muscle Nerve 17:1243–1249

Layzer RB, Rowland LP (1971) Cramps. N Engl J Med 285:31–40

Lucas KR, Polus BI, Rich PA (2004) Latent myofascial trigger points: their effects on muscle activation and movement efficiency. J Bodyw Mov Ther 8:160–166

McGee SR (1990) Muscle cramps. Arch Intern Med 150:511–518

Miller TM, Layzer RB (2005) Muscle cramps. Muscle Nerve 32:431–442

Norris FH, Jr., Gasteiger EL, Chatfield PO (1957) An electromyographic study of induced and spontaneous muscle cramps. Electroencephalogr Clin Neurophysiol 9:139–147

Parisi L, Pierelli F, Amabile G, Valente G, Calandriello E, Fattapposta F, Rossi P, Serrao M (2003) Muscular cramps: proposals for a new classification. Acta Neurol Scand 107:176–186

Prateepavanich P, Kupniratsaikul V, Charoensak T (1999) The relationship between myofascial trigger points of gastrocnemius muscle and nocturnal calf cramps. J Med Assoc Thai 82:451–459

Reeves JL, Jaeger B, Graff-Radford SB (1986) Reliability of the pressure algometer as a measure of myofascial trigger point sensitivity. Pain 24:313–321

Roeleveld K, van Engelen BG, Stegeman DF (2000) Possible mechanisms of muscle cramp from temporal and spatial surface EMG characteristics. J Appl Physiol 88:1698–1706

Ross BH, Thomas CK (1995) Human motor unit activity during induced muscle cramp. Brain 118(Pt 4):983–993

Rossi A, Decchi B (1997) Changes in Ib heteronymous inhibition to soleus motoneurones during cutaneous and muscle nociceptive stimulation in humans. Brain Res 774:55–61

Rossi A, Decchi B, Ginanneschi F (1999) Presynaptic excitability changes of group Ia fibres to muscle nociceptive stimulation in humans. Brain Res 818:12–22

Rossi A, Mazzocchio R, Decchi B (2003) Effect of chemically activated fine muscle afferents on spinal recurrent inhibition in humans. Clin Neurophysiol 114:279–287

Rowland LP (1985) Cramps, spasms and muscle stiffness. Rev Neurol (Paris) 141:261–273

Serrao M, Arendt-Nielsen L, Ge HY, Pierelli F, Sandrini G, Farina D (2007) Experimental muscle pain decreases the frequency threshold of electrically elicited muscle cramps. Exp Brain Res 182:301–308

Serratrice G, Mei N, Pellissier JF, Cros D (1980) Cutaneous and muscular unmyelinated afferent fibres. Clinical, histological and experimental study. Possible explanation of muscular cramps (author's transl). Sem Hop 56:1665–1670

Shah JP, Danoff JV, Desai MJ, Parikh S, Nakamura LY, Phillips TM, Gerber LH (2008) Biochemicals associated with pain and inflammation are elevated in sites near to and remote from active myofascial trigger points. Arch Phys Med Rehabil 89:16–23

Simons DG (2004) Review of enigmatic MTrPs as a common cause of enigmatic musculoskeletal pain and dysfunction. J Electromyogr Kinesiol 14:95–107

Thunberg J, Ljubisavljevic M, Djupsjobacka M, Johansson H (2002) Effects on the fusimotor-muscle spindle system induced by intramuscular injections of hypertonic saline. Exp Brain Res 142:319–326

Yunus MB, Aldag JC (1996) Restless legs syndrome and leg cramps in fibromyalgia syndrome: a controlled study. BMJ 312:1339