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Original article

Effects of a manual therapy technique in experimental lateral epicondylalgia

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Abstract

In patients with lateral epicondylalgia, mobilization-with-movement (MWM) is used as an intervention aimed at achieving analgesia and enhancing grip force, although the mechanisms underlying these effects are unclear. The present study investigated the acute sensory and motor effects of an MWM intervention in healthy controls with experimentally induced lateral epicondylalgia. Twenty-four subjects were randomly allocated to either a MWM or a placebo group ($n = 12$). In both groups, to generate the model of lateral epicondylalgia, delayed onset muscle soreness (DOMS) was provoked in one arm 24 h prior (Day 0) to hypertonic saline-induced pain in the extensor carpi radialis brevis muscle (Day 1). Either a MWM or placebo intervention was applied during the saline-induced pain period. Saline-induced pain intensity (visual analogue scale: VAS), pain distribution and pain quality were assessed quantitatively. Pressure pain thresholds (PPTs) were recorded at the common extensor origin and the extensor carpi radialis brevis muscle. Maximal measures of grip and wrist extension force were recorded. In both groups (pooled data), DOMS was efficiently induced as demonstrated by a significant decrease in pre-exercise to pre-injection PPT at the common extensor origin ($-45 \pm 19\%$) and at the extensor carpi radialis brevis ($-61 \pm 23\%$; $P < 0.05$), and a significant decrease in maximal grip force ($-25 \pm 6\%$) and maximal wrist extension force ($-40 \pm 12\%$; $P < 0.001$). Moreover, both groups experienced a significant increase in muscle soreness (3.9 ± 0.2; $P < 0.0001$) at Day 1 compared to pre-exercise. During saline-induced pain and in response to intervention, there were no significant between-group differences in VAS profiles, pain distributions, induced deep tissue hyperalgesia or force attenuation. These data suggest that the lateral glide-MWM does not activate mechanisms associated with analgesia or force augmentation in subjects with experimentally induced features simulating lateral epicondylalgia.

Keywords: Manipulation; Mobilization; Lateral epicondylalgia; Tennis elbow; Experimental muscle pain; Movement

1. Introduction

Mobilization-with-movement (MWM) is a manual therapy intervention commonly used in the management of patients with lateral epicondylalgia. A specific form of MWM—a lateral glide at the elbow—has been reported to exert rapid pain-relieving effects and to enhance grip strength in patients with clinical lateral epicondylalgia (Vicenzino and Wright, 1995; Mulligan, 1999; Abbott et al., 2001; Vicenzino et al., 2001; Paungmali et al., 2003a). Vicenzino et al. (2001) investigated the effects of the lateral glide-MWM in a group of 24 patients with clinical unilateral lateral epicondylalgia using a randomized, double-blind, placebo-controlled design. In the affected arm, the lateral glide-MWM produced significant and substantial increases in pain-free grip force immediately post-application compared with pre-application (58%), and a modest but significant increase (10%) in pressure pain threshold (PPT) (Vicenzino et al., 2001). Abbott et al. (2001) demonstrated similar effects showing a significant increase in maximal grip strength (magnitude of change: 5%) and pain-free grip

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strength (magnitude of change of 17%) following a lateral glide-MWM in 23 patients with lateral epicondylalgia.

While specific physiological effects of the lateral glide-MWM have been documented, the mechanisms underlying the effects of this physical intervention have yet to be elucidated. What has been demonstrated experimentally is that the analgesic effect in response to the lateral glide-MWM in patients with clinical lateral epicondylalgia appears to be rapid in nature, is associated with sympathoexcitation (Vicenzino et al., 1998; Vicenzino et al., 2000) and does not demonstrate decay over repeated administrations (Paungmali et al., 2003b). Wright (1995) proposed that the apparent concurrency of hypoalgesic and autonomic responses might suggest activation of descending inhibitory pathways in the central nervous system.

It is unclear if the treatment effects of the lateral glide-MWM that have been demonstrated in a clinical lateral epicondylalgia patient population can be replicated in subjects with experimentally induced features simulating lateral epicondylalgia. Slater et al. (2003) have previously demonstrated that the pain-inducing effects of injecting hypertonic saline into the extensor carpi radialis brevis muscle, combined with known deep tissue sensitizing effects of delayed onset muscle soreness (DOMS), generated similar sensori-motor characteristics to those seen in patients with clinical lateral epicondylalgia; that is, pain and mechanical hyperalgesia extending along the myotendinous unit from the common extensor origin to the extensor carpi radialis brevis muscle (Slater et al., 2005); pain radiating into the dorsal forearm (Leffler et al., 2000) and attenuation of grip force (Haker, 1993; Stratford et al., 1993; Vicenzino et al., 1996; Vicenzino et al., 1998; Pienimaki et al., 2002a, b). One advantage of using an in vivo model simulating lateral epicondylalgia is that the origin of myotendinous pain and hyperalgesia and the cause of associated motor attenuation are known, and the associated sensory manifestations and motor effects are quantifiable. In contrast, clinical studies are unlikely to provide such insights as the diagnosis of lateral epicondylalgia is still sign and symptom based, and a cause–effect relationship is not clear. While clinical studies of interventions in patients with lateral epicondylalgia have provided important insights into the effects of physical treatments, the mechanisms underlying these effects have not yet been proven. Furthermore, the experimental model simulating lateral epicondylalgia provides a potential vehicle for better insight into the pain mechanisms that may mediate the clinical effects associated with the lateral glide-MWM.

The aim of this experimental study was to assess the treatment effects of the lateral glide-MWM in healthy subjects with induced sensory changes and motor effects that simulate lateral epicondylalgia (via provoked DOMS and saline-induced pain). The specific hypothesis to be tested was that in healthy subjects with experimentally induced features of lateral epicondylalgia, the lateral glide-MWM would activate mechanisms associated with analgesia and force augmentation in contrast to a placebo intervention.

2. Materials and methods

2.1. Subjects

Two groups each of 12 subjects participated in the study. There were seven males and five females in the MWM group (mean age 23.0 years, range 19–31 years), and six males and six females (mean age 23.1 years, range 19–31 years) in the placebo group. All subjects were right hand dominant with the exception of two, both of whom were in the placebo group. Subjects had no history of upper limb pain, fractures or neurological disorders, were not taking any medications, had not previously received manual therapy for the upper quarter, and nor had they had previous experience of eccentric wrist extensor training. A physical examination was performed to ensure that all subjects had full pain-free range of elbow and wrist motion, and no abnormal tenderness to palpation of the soft tissues in the extensor muscles of the forearm and wrist (Travell and Simons, 1983), or abnormal muscle length. Clinical tests of wrist stability were performed (Taleisnik, 1988) as a precaution against excessive intercarpal motion during the eccentric exercise period. Written informed consent was obtained prior to inclusion in the study. The study was performed in accordance with the National Health and Medical Research Council guidelines and with the Helsinki Declaration. The Human Research Ethics Committee at Curtin University of Technology had approved the study.

2.2. Study design

The study used a randomized, placebo-controlled design. For all subjects, a set of quantitative tests (PPT, muscle soreness, maximal grip force and maximal wrist extension force) was performed, and repeated at each time period (Fig. 1). The effect of combined DOMS and saline-induced pain on deep tissue sensitivity and force inhibition was assessed in the non-dominant arm. Subjects participated in three sessions (Day 0, Day 1 and Day 7). Exercise to induce DOMS was performed at Day 0. There were 23–25 h between Day 0 and Day 1 sessions. For both groups on Day 1, hypertonic saline was injected to evoke pain in the extensor carpi radialis brevis muscle of the DOMS arms. During the saline-induced pain period, either MWM or placebo intervention was administered. The intervention was therefore

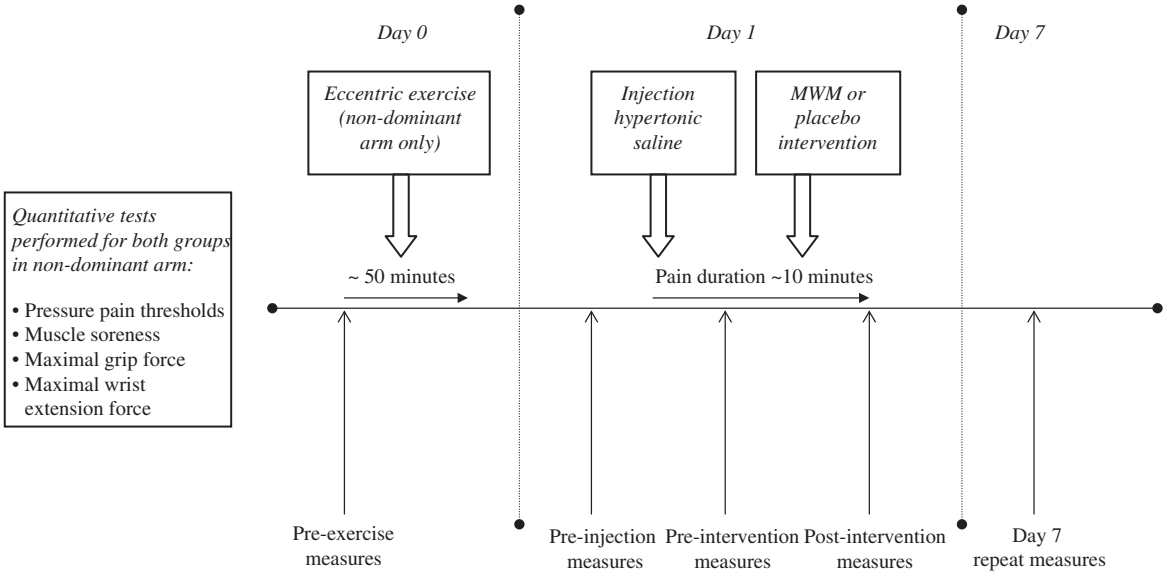

Fig. 1. All subjects performed the eccentric exercise protocol on Day 0. The day following (Day 1), subjects were injected with hypertonic saline into the extensor carpi radialis brevis muscle. During saline-induced pain, subjects received one of two test conditions: a mobilization-with-movement (MWM) or a placebo intervention. A series of quantitative tests were repeated pre exercise Day 0, and at each time point Day 1 and at Day 7.

aimed at alleviating pain associated with the combined effects of DOMS and hypertonic saline. The Day 7 session involved a repeat of pre-exercise measures for all subjects.

2.3. Saline-induced deep pain

Hypertonic saline was infused using a computer-controlled pump (IVAC, model 770, USA), with a 10 ml plastic syringe (Graven-Nielsen et al., 1997a). A tube (IVAC G30303, extension set with polyethylene inner line) was connected from the syringe to the disposable needle (27G, 20 mm). A bolus injection of 1.0 ml of sterile hypertonic (5.8%) saline was injected over 40 s. The needle was removed at the completion of the injection. The site of injection in the extensor carpi radialis brevis muscle belly was identified using a technique described by Riek et al. (2000) and previously used in this model (Slater et al., 2003). Prior to injection, the posterior interosseus nerve was identified by palpation to avoid any direct contact with the nerve. The needle was inserted approximately 10 mm into the muscle belly.

Saline-induced pain intensity was scored continuously on a 10 cm electronic visual analogue scale (VAS) where 0 cm indicated 'no pain' and 10 cm 'most pain imaginable'. The VAS rating was sampled every 5 s by the computer. The saline-induced pain period was divided into two epochs: (1) pre-intervention and; (2) intervention. The duration of the pre-intervention period was approximately 5 min. The intervention epoch incorporated the VAS recorded whilst administering the intervention (approximately 3 min) and the period between completion of the intervention and the termination of the pain period (approximately 2 min). The area under the VAS–time curve (VAS area), time of pain onset and duration of pain were determined from the VAS recordings. Post-intervention, subjects described the pain for the total pain period (that is, both VAS epochs) using the McGill Pain Questionnaire (MPQ) (Melzack, 1975). Words from the MPQ chosen by at least 30% of the subjects were used in data analysis. The saline-induced pain distribution as experienced by each subject was also mapped on a body chart. The circumference was later digitized (ACECAD D9000 Digitiser, Taiwan) and the area calculated in arbitrary units (Sigma-Scan, Jandel Scientific, Canada). Pain areas were also classified from the body charts as local and/or referred. Local pain was defined as a continuous area of pain that may or may not be associated with spread or radiation. Referred pain was defined as a discrete area of pain outside the local pain area (Graven-Nielsen et al., 1997a).

2.4. Delayed onset muscle soreness

Repeated eccentric wrist extension contractions were used to provoke DOMS in the non-dominant arm. The eccentric-exercise protocol used the isokinetic mode of the Kin-Com dynamometer (Chattecx Corp. Hixson, TN). The total exercise period was 25 min, with five bouts each of 5 min duration (60 repetitions per bout), each bout separated by a minute rest interval (Slater et al., 2003). The protocol in this study is identical to that used previously and has been described elsewhere (Slater et al., 2005).

2.5. Assessment of deep tissue sensitivity

PPTs were recorded using an electronic algometer (Somedic AB, Sweden) with a stimulation area of 1.0 cm^2. PPT was calculated as the mean of three trials with a 30 s interval between repetitions. The pressure was increased at a rate of 30 kPa/s until the subject detected the pain threshold. Two sites were assessed: the attachment of the common extensor origin at the lateral epicondyle and the muscle belly of the extensor carpi radialis brevis muscle.

2.6. Assessment of grip force and wrist extension force

Grip force was assessed using an electronic digital dynanometer (MIE Medical Research Ltd., Leeds, UK). The subject's upper limb was positioned in pronation and elbow extension. Peak values determined the maximal grip force, and were found as the mean of three trials. Wrist extension force was recorded via a specifically designed padded hand attachment connected to a force transducer (AFG, range 0–500 N, Mecmesin Ltd., England). The transducer was mounted on a flat platform and placed on a table to the side of the plinth. The height of the hand attachment and force transducer was adjustable to allow for variations in hand sizes. The wrist was positioned in pronation and wrist extension (20°) with the third knuckle abutting the centre of the hand attachment. Subjects were instructed to maximally extend the wrist by pushing the dorsal surface of the hand onto the padded surface of the hand attachment. The height of the device was noted for each subject to ensure reliable measures. Peak values determined the maximal extension force, and were found as the mean of three trials. Subjects were requested to perform maximal contractions for each motor task.

2.7. Mobilization-with-movement intervention

The lateral glide-MWM technique involved the application of a sustained force (glide) produced across the elbow joint with the force being directed against the ulna from medial to lateral, and the humerus being stabilized lateral and proximal to the elbow joint (Fig. 2). This technique is adopted from the description outlined by Mulligan (1999) and previously investigated in clinical studies (Vicenzino and Wright, 1995; Abbott et al., 2001; Vicenzino et al., 2001; Paungmali et al., 2003a). Clinical indications for use of this technique include movement-related pain or stiffness (Mulligan, 1999), features experimentally induced in the current model of lateral epicondylalgia (Slater et al., 2003). The subject lay supine with the upper limb supported on a treatment plinth. The upper limb was positioned in 20° shoulder abduction with elbow extension and forearm pronation. The lateral glide technique was coupled with an isometric gripping action performed actively by the subject. The glide was sustained throughout the 30 s bout of repeated isometric grip. This allowed six repetitions of grip within a 30 s period. The MWM was repeated on three occasions (total 90 s of MWM) with a 30 s rest between the three bouts (Fig. 2A); therefore the total intervention duration was 2.5 min. The placebo technique was the application of a constant, firm manual contact around the medial and lateral aspects of the subject's elbow for an analogous

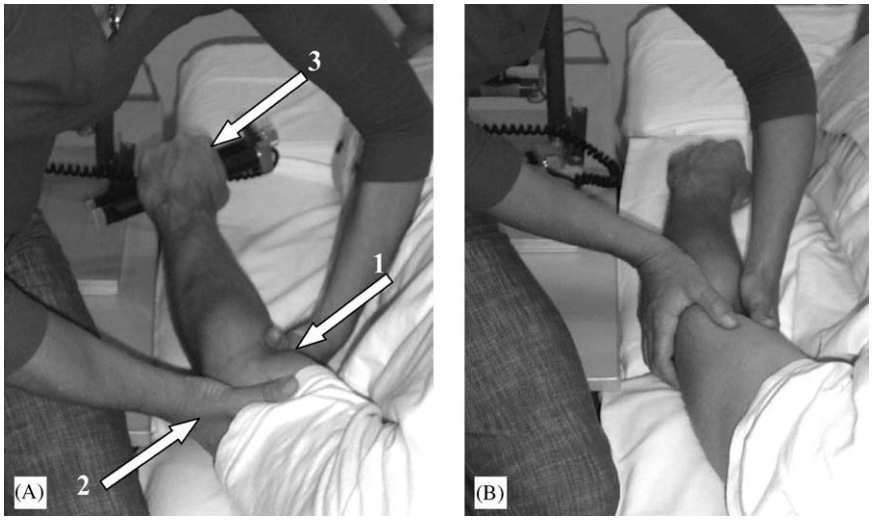

Fig. 2. During saline-induced pain, subjects received either a mobilization-with-movement (A), or a placebo (B) intervention. The white arrows in photograph A indicate the lateral glide force applied to the proximal ulna (1), and the stabilizing counter-force on the lateral aspect of the distal humerus (2). The technique was sustained while the subject maintained an isometric gripping action (3). The placebo condition (B), involved the application of light manual contact to the medial and lateral aspects of the subject's elbow joint while the subject maintained a relaxed grip. For both conditions the contact was sustained for 30 s, with a 30 s interval of rest. Three bouts of each intervention were applied.

time and number of bouts as the MWM intervention (Fig. 2B). Subjects maintained a relaxed grip position throughout the placebo technique. An experienced manipulative physiotherapist performed the interventions.

2.8. Statistical analysis

Based on the results of previous studies on the effects of the lateral glide-MWM in clinical lateral epicondylalgia patients (Abbott et al., 2001; Vicenzino et al., 2001; Paungmali et al., 2003a), a difference of 15% for PPT and motor force parameters was set as a conservative level to detect a significant intervention effect. Between-group differences in means and standard deviations were drawn from a previous study of clinical lateral epicondylalgia patients and matched controls using this experimental pain model (Slater et al., 2005). To achieve power of 0.80 with alpha at 0.05 required a sample size of 12 per group.

Mean and standard error (SE) values are given in the text, tables and figures. A majority of measurements associated with the VAS data failed to meet the requirements of a normal distribution as determined by the Shapiro–Wilk normality test. Consequently, the non-parametric Mann–Whitney-*U* Test was used to compare VAS data between groups. Post-intervention VAS data (pain area and pain peak) was normalized to pre-intervention. PPT, maximal grip force and maximal wrist extension force data were normalized (100%) to pre-injection values. For analysis of PPT, maximal grip force and maximal wrist extension force, two-way repeated measures ANOVA were used, with factors 'time' (repeated, with two levels for pre-exercise and pre-injection; and five levels for pre-exercise-Day 7 times) and 'group' (between group with two levels: 'mobilization-with-movement' and 'placebo'). When significant this was followed by the post hoc Student–Newman–Keuls (SNK) test. Significance was accepted at $P<0.05$.

3. Results

3.1. Effects of eccentric exercise in mobilization-with-movement and placebo groups

3.1.1. Effects of exercise on deep tissue sensitivity

PPT at the common extensor origin and the extensor carpi radialis brevis changed in both groups following eccentric exercise (Table 1; ANOVA: $F_{1,22}=5.1$, $P<0.03$). Post hoc tests demonstrated hyperalgesia to pressure at the common extensor origin and extensor carpi radialis brevis for both groups at pre-injection compared with pre-exercise (Day 0; SNK: $P<0.03$). Muscle soreness changed pre-injection in both groups (Table 1; ANOVA: $F_{1,22}=927.8$, $P<0.0001$). Post hoc tests revealed an increase in muscle soreness in the exercised arm at pre-injection (Day 1) compared with pre-exercise (Day 0; SNK: $P<0.0001$). No subjects reported pain at rest.

Table 1
Effects of an acute bout of eccentric exercise on mean (SE, $n=12$) pressure pain thresholds, muscle soreness, maximal grip force and maximal wrist extension force for the mobilization-with-movement and placebo groups

Deep tissue soreness	Day 0 Pre-exercise	Day 1 Pre-injection
PPT-CEO (kPa)		
MWM group	332 (52)	277 (54)*
Placebo group	362 (45)	251 (34)*
PPT-ECRB (kPa)		
MWM group	236 (41)	206 (56)*
Placebo group	283 (33)	191 (30)*
Muscle soreness (AU)		
MWM group	0.00 (0.00)	4.00 (0.17)*
Placebo group	0.00 (0.00)	3.92 (0.18)*
Maximal grip force (N)		
MWM group	313 (17)	267 (12)*
Placebo group	316 (23)	256 (18)*
Maximal wrist extension force (N)		
MWM group	128 (12)	105 (11)*
Placebo group	145 (15)	110 (13)*

PPT: pressure pain threshold; CEO: Common extensor origin; ECRB: Extensor carpi radialis brevis; RH: Radial head; AU: arbitrary units. *$P<0.05$ (SNK) significantly different compared with pre-exercise.

3.1.2. Effect of exercise on maximal grip force and maximal wrist extension force

Following exercise, maximal grip force and maximal wrist extension force changed in both groups (Table 1; ANOVA: $F_{1,22}=35.8$, $P<0.0001$) with significant decreases at pre-injection compared with pre-exercise (SNK: $P<0.001$).

3.2. Effect of intervention on saline-induced deep tissue pain in DOMS arms

The injection of hypertonic saline into the extensor carpi radialis brevis muscle of the DOMS arms on Day 1 induced similar pain intensity and temporal characteristics between groups (Table 2 and 3; Fig. 3). In response to hypertonic saline subjects reported a localized pain response around the muscle belly with radiation of pain into the dorsolateral forearm (MWM, $n=12$; placebo, $n=10$). Pain was reported to spread proximally into the distal upper arm but only in the MWM group ($n=2$). Subjects reported pain referral to the distal forearm and hand ($n=5$ each for MWM and placebo groups; Fig. 3). The pain descriptors most commonly used were "intense", "aching" and "pressing". There was no

Table 2
Mean (SE, $n = 12$) pre-intervention and intervention (% pre-intervention) pain intensity and peak pain following saline-induced pain in the extensor carpi radialis brevis muscle of the mobilization-with-movement and placebo groups

	Pre-intervention (0–300 s)		Intervention (% of pre-intervention)	
VAS data	MWM group	Placebo group	MWM group	Placebo group
VAS_{area} (cm s)	1352.7 (166.0)	1427.2 (142.9)	41.5 (6.9)	40.7 (9.1)
VAS_{peak} (cm)	5.8 (0.6)	6.1 (0.5)	66.7 (5.2)	72.4 (5.8)

AUC: area under curve; MWM: mobilization-with-movement.

Table 3
Mean (SE, $n = 12$) VAS parameters and pain areas in response to saline-induced pain in the extensor carpi radialis brevis muscle and following intervention for the mobilization-with-movement group and placebo group

VAS parameters	MWM group	Placebo group
VAS_{onset} (s)	25.8 (3.1)	21.3 (2.8)
$VAS_{duration\ of\ pre-intervention}$ (s)	274.2 (3.1)	278.8 (2.8)
$VAS_{duration\ of\ post-intervention}$ (s)	251.7 (38.0)	242.9 (43.3)
Pain area (AU)	5.5 (1.1)	7.6 (2.0)
Pain descriptors (% of subjects)		
Intense	58	50
Aching	50	33
Radiating	50	—
Boring	—	50
Pressing	33	33

MWM: mobilization-with-movement. AU: arbitrary unit.

apparent analgesic effect from the intervention as the spread of pain and referred pain areas were similar between groups (Table 3).

3.3. Effect of intervention on deep tissue sensitivity

Intervention did not influence deep tissue sensitivity in either group. Both groups demonstrated a significant main effect for time on PPT at the common extensor origin (Fig. 4; ANOVA: $F_{4,88} = 8.9$, $P < 0.0001$), consistent with a pressure hyperalgesia at all Day 1 times compared with Day 0 (pre-exercise) and Day 7 (SNK: $P < 0.05$). Additionally, in response to saline-induced pain (but at pre-intervention) there was a significant hypoalgesic effect at the common extensor origin in both groups compared with pre-injection values (SNK: $P < 0.02$). The PPT at the extensor carpi radialis brevis demonstrated a main effect for time (ANOVA: $F_{4,88} = 14.4$, $P < 0.0001$), revealing pressure hyperalgesia at all Day 1 times compared with Day 0 (pre-exercise) and Day 7 (SNK: $P < 0.002$). Muscle soreness changed at Day 1 in both groups (Fig. 5; ANOVA: $F_{4,88} = 611.9$, $P < 0.0001$), with a significant increase in muscle soreness at all times Day 1 compared with Day 0 (pre-exercise) and Day 7 (SNK: $P < 0.0001$).

3.4. Effect of intervention on maximal grip force and maximal wrist extension force

There was no significant force augmentation following intervention in either group. For both groups maximal grip force changed Day 1 (Fig. 6; ANOVA: $F_{4,88} = 28.6$, $P < 0.0001$), with a significant decrease at all Day 1 times compared with Day 0 (pre-exercise) and Day 7 (SNK: $P < 0.001$). Maximal wrist extension force demonstrated a similar change in both groups Day 1 (ANOVA: $F_{4,88} = 30.6$; $P < 0.0001$) with a significant decrease at all Day 1 times compared with Day 0 (pre-exercise) and Day 7 (SNK: $P < 0.001$). Both groups experienced a further attenuation of maximal wrist extension force on Day 1 at pre-intervention (during saline-induced pain) and at post-intervention compared with pre-injection (SNK: $P < 0.05$).

3.5. Post hoc power analysis

A post hoc power analysis of this study showed that a change of 15% would have been detected with the following probabilities: 89% for PPT; 100% for muscle soreness; for the majority of VAS parameters >83%; 97% for force parameters.

4. Discussion

In the current study, the application of a lateral glide-MWM intervention in healthy subjects with experimentally induced features of lateral epicondylalgia failed to elicit significant analgesia or to augment force. This is in contrast to the beneficial effects of the MWM that have been reported in patients with clinical lateral epicondylalgia. The MWM intervention may activate mechanisms that influence central sensitization as suggested to occur in clinical lateral epicondylalgia.

4.1. Sensory manifestations

The current study demonstrated no significant short-term analgesic effects in response to the lateral glide-MWM intervention in subjects with experimentally

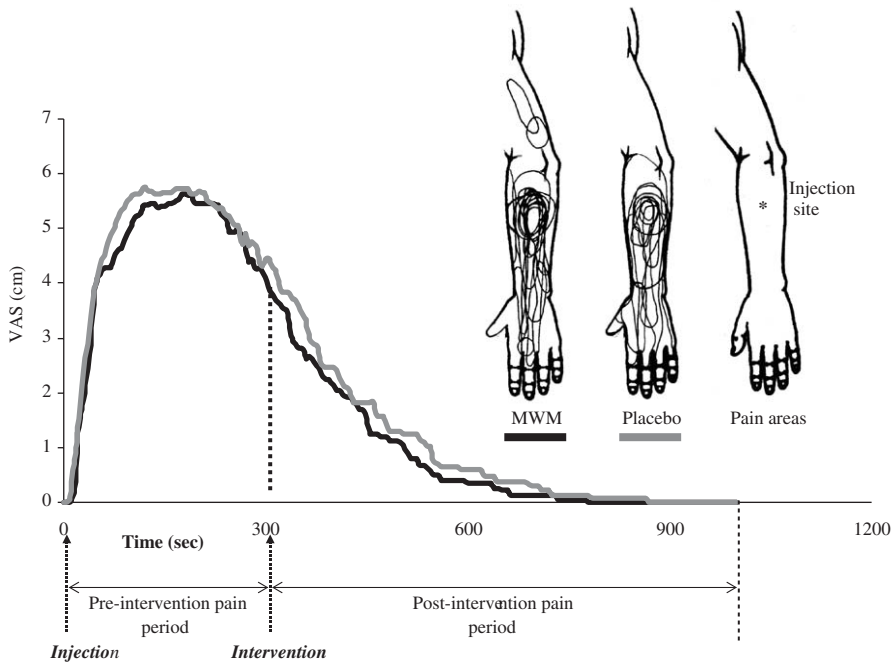

Fig. 3. Mean ($n = 12$) VAS profiles for two pain epochs (pre-intervention and intervention) and the associated mapped areas of pain in response to saline-induced pain in the extensor carpi radialis brevis muscle for mobilization-with-movement (black line) and placebo (grey line) groups. MWM: mobilization-with-movement intervention.

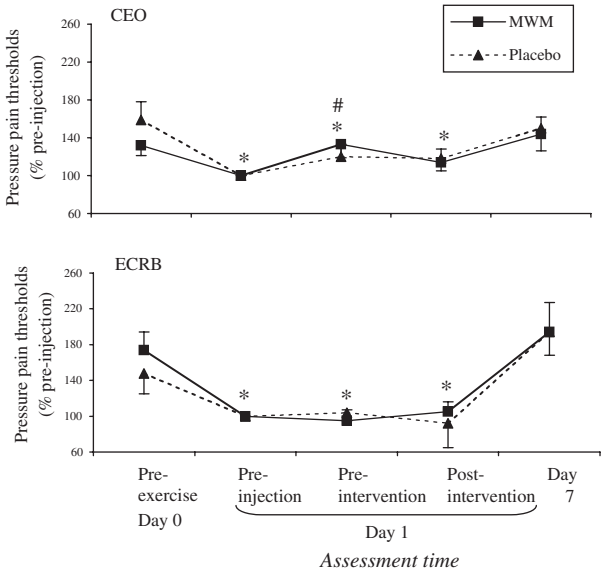

Fig. 4. Mean (±SE, $n = 12$) normalized pressure pain thresholds Day 0 (pre-exercise), Day 1 (pre-injection, pre-intervention, post-intervention) and at Day 7, are shown. At Day 1, hypertonic saline was injected into the extensor carpi radialis brevis muscle in both groups, and subjects received either mobilization-with-movement (MWM) or a placebo intervention during the saline-induced pain period. Pressure pain thresholds were assessed at two sites: the common extensor origin at the lateral epicondyle (CEO) and the extensor carpi radialis brevis muscle belly (ECRB). *A significant decrease in PPT for both groups at Day 1 compared with Day 0 and Day 7 times values (SNK: $P < 0.05$); #A significant increase in PPT in both groups compared with pre-injection Day 1.

induced acute lateral epicondylalgia. Following intervention, there were no significant between-group differences in saline-induced pain intensity parameters (VAS area, peak, onset, offset and pain area). Pain profiles and the mapped areas of pain were similar to those previously demonstrated using this experimental pain model (Slater et al., 2003; Slater et al., 2005). For both groups, the decreased PPT in the myotendinous unit (comprising the extensor carpi radialis brevis and common extensor tendon origin) at pre-injection (Day 1), was consistent with an exercise-induced deep tissue hyperalgesia to pressure as previously demonstrated for this model (Slater et al., 2003). In both groups the persistence of hyperalgesia in the myotendinous unit at post-intervention, and the unchanged muscle soreness levels, indicated that the intervention had no significant analgesic effect on combined DOMS/saline-induced pain. These findings are in contrast with those of Vicenzino et al. (2001) who demonstrated a modest but significant increase in PPT at the common extensor origin in patients with clinical lateral epicondylalgia following application of the lateral glide-MWM at the elbow. If descending pain inhibitory systems are activated by the MWM lateral glide, a generalized analgesic effect may be anticipated; however, Vicenzino et al. (2001) have demonstrated a selective and specific anti-hyperalgesic effect at the affected site (common extensor origin). This difference in effect of the lateral glide-MWM in patients with

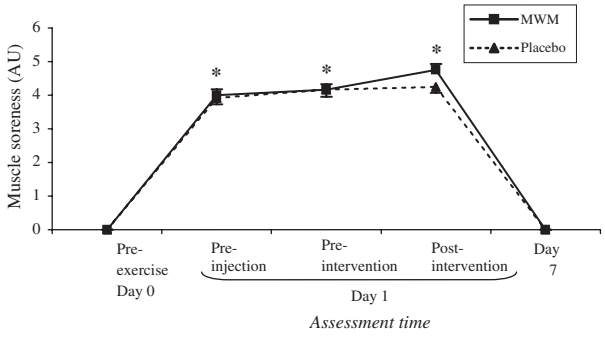

Fig. 5. Mean (±SE, $n = 12$) muscle soreness for all groups in response to eccentric exercise and intervention during saline-induced pain. Muscle soreness was assessed at Day 1, (pre-injection, pre-intervention and at post-intervention), and at Day 7. *A significant increase in muscle soreness compared with Day 0 (pre-exercise) and Day 7 (SNK: $P<0.05$), is shown for both groups. MWM: mobilization-with movement.

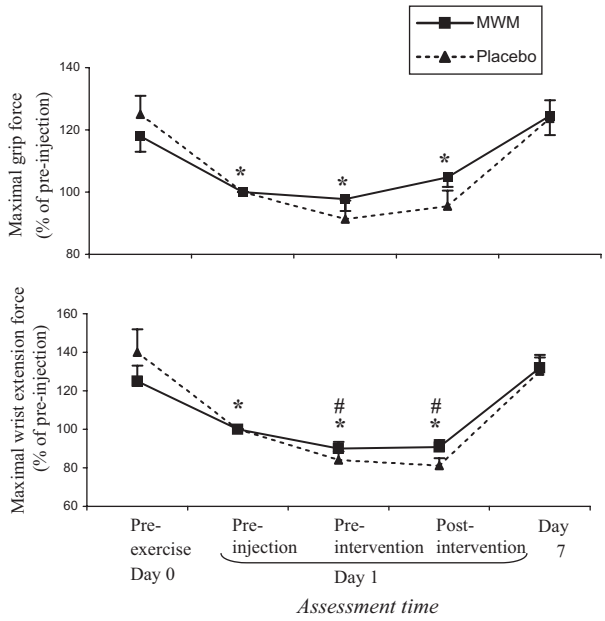

Fig. 6. Mean (±SE; $n = 12$) normalized maximal grip force and maximal wrist extension force at Day 0 (pre-exercise), Day 1 (pre-injection, pre-intervention, post-intervention) and Day 7. *A significant decrease in maximal force, unchanged by intervention, compared with Day 0 (pre-exercise) and Day 7 is shown for both groups (SNK: $P<0.05$). #A significant decrease in maximal force following saline-induced pain compared with pre-injection values (SNK: $P<0.05$), is also demonstrated for both groups. MWM: mobilization-with-movement.

clinical lateral epicondylalgia as opposed to subjects with experimentally induced features of lateral epicondylalgia may indicate that different neural mechanisms are operating to modulate pain associated with prolonged central sensitization, as suggested to occur in patients with clinical lateral epicondylalgia (Slater et al., 2005). The lateral glide-MWM while indicated for use in movement-related pain or stiffness in musculoskeletal disorders (Mulligan, 1999), may be more efficacious in chronic conditions as opposed to acute pain. Alternately, in this study the effect size of the intervention may have been insufficient to effectively modulate the induced deep tissue pain, or an analgesic response may have been slow acting and therefore not demonstrated given the brief post-intervention period.

4.2. Motor effects

For both groups, the substantial decrease in maximal grip force and maximal wrist extension force following DOMS and saline-induced pain was unaltered by the lateral glide-MWM. The absence of force-augmentation may be interpreted as a limited effect for the lateral glide-MWM in musculoskeletal pain conditions associated with partial myotendinous disruption. Given the efficient induction of DOMS in this study, it is reasonable to assume a substantial degree of ultra-structural muscle damage, and given the induced sensitization of the proximal bone–tendon junction, the possibility of additional tissue injury to the common extensor tendon. Furthermore, provoked muscle damage (DOMS) combined with additional force inhibition via saline-induced acute muscle pain will substantially compromise the contractile ability of the extensor carpi radialis brevis muscle. Attenuation of maximal force is consistent with current experimental models of muscle pain demonstrating that muscle pain can reduce maximal voluntary force (Graven-Nielsen et al., 1997b; Svensson et al., 1998; Wang et al., 2000; Slater et al., 2003; Arima et al., 2000). The fact that saline-induced pain in the extensor carpi radialis brevis further decreased the maximal wrist extension force illustrates the parallel effects of compromised peripheral contractile apparatus due to DOMS and the central inhibitory action of saline-induced pain. An intervention operating via mechanisms thought to facilitate the muscle contractile apparatus would conceivably be less effective where there is compromise of contractile elements as in the current study.

4.3. Mechanisms associated with mobilization-with-movement

In this study, failure of the MWM intervention to promote analgesia and improve force capability suggests that: (1) different pain and tissue mechanisms may be involved in experimentally induced and clinical lateral epicondylalgia; (2) the lateral glide-MWM may exert different effects in the patients with clinical lateral epicondylalgia compared with the effects in subjects with experimentally induced lateral epicondylalgia; (3) the effect size of the lateral glide-MWM may be too small to be demonstrated in the experimental model of lateral epicondylalgia used in this study; (4) the post-

intervention time period was too short to measure any potential benefit of the lateral glide-MWM technique.

Effective modulation of DOMS-associated pain is relevant when discussing the lack of efficacy of the lateral glide-MWM intervention in the current study. Very few interventions have demonstrated efficacy in modulating DOMS-associated pain, probably because the mechanisms underlying DOMS-associated pain are still poorly understood. In a placebo-controlled, double-blind study, high or low-intensity transcutaneous electrical nerve stimulation (TENS) demonstrated no convincing evidence of reducing DOMS-associated pain or improving function (Craig et al., 1996b). Additionally, other clinical trials have indicated that post-exercise muscle strength recovery or soreness is not affected by ultrasound treatment (Craig et al., 1999b; Plaskett et al., 1999), by acupuncture (Barlas et al., 2000b) or by combined phototherapy/low-intensity laser therapy at low pulse repetition rates (Craig et al., 1996a; Craig et al., 1999a). A lack of efficacy of selected oral systemic analgesics (aspirin, codeine, paracetamol) compared with placebo has also been demonstrated in experimentally induced muscle soreness (Barlas et al., 2000a). However, application of transdermal ketoprofen appears to be effective in reducing self-reported DOMS after repetitive muscle contraction, particularly after 48 h (Cannavino et al., 2003). Topical application of ibuprofen compared with systemic ibuprofen and placebo, has been shown to increase PPT but not pressure pain tolerance or maximal voluntary force of the masseter muscle with DOMS (Svensson et al., 1997). Similarly, the non-steroidal medications, flurbiprofen (Howell et al., 1998a) and ibuprofen (Howell et al., 1998b), were shown to be ineffective in relieving DOMS-associated pain and stiffness in trained cyclists.

Modulation of deep tissue hyperalgesia and the concurrent excitation of the motor and sympathetic nervous system previously demonstrated in response to the lateral glide-MWM in patients with clinical lateral epicondylalgia has been suggested to involve descending pain inhibitory systems (Vicenzino et al., 1998; Vicenzino et al., 2001; Paungmali et al., 2003b). Additionally, in patients with clinical lateral epicondylalgia, the lateral glide-MWM has been shown to induce rapid onset analgesia that does not decay over repeated applications (Paungmali et al., 2003b), possibly indicating facilitation of non-opioid endogenous pain inhibitory systems. Animal studies have also examined the effects of manipulation-induced antihyperalgesia in an attempt to better understand the involved pain mechanisms. Skyba et al. (2003) using behavioural pharmacology techniques in an animal model of experimental pain found that following injection of capsacin into the ankle joint, rats demonstrated an increase in threshold of the mechanical withdrawal reflex for 45 min post-manipulation of the ipsilateral knee joint. Blockade of various spinal receptors suggested that manipulation-induced antihyperalgesia appeared to involve descending inhibitory mechanisms that utilize both serotonin and noradrenaline as neurotransmitters. In contrast, in the same study spinal blockade of opioid or γ-aminobutyric acid ($GABA_A$) receptors had no effect on manipulation-induced antihyperalgesia. Sluka and Wright (2001) have also shown that in response to knee joint manipulation capsaicin-induced secondary mechanical hyperalgesia in rat paw is reduced. However, despite the findings of these human and animal studies, the specific mechanisms underlying the effects associated with the manual physiotherapy techniques, including the lateral glide-MWM, remain largely putative.

We propose that beneficial effects associated with the lateral glide-MWM in clinical studies of clinical lateral epicondylalgia are likely to be related to multiple and potentially interacting mechanisms. For example, in regard to motor mechanisms, the phenomenon of post-exercise facilitation may be relevant to the improved grip force associated with the lateral glide-MWM. Muscle facilitation is achieved via a voluntary contraction of a target muscle (in the case of the lateral glide-MWM there is synergistic activity of wrist flexors and wrist extensors associated with the active task of sustained gripping). Facilitation has been shown to increase the response rate, shorten latency and enhance the amplitude of motor evoked potentials post-contraction (Nørgaard et al., 2000). Post-exercise facilitation has been demonstrated to be associated with greater potentiation for sustained contraction (Lentz and Nielsen, 2002) and the facilitation persisted beyond the cessation of the contraction (Brasil-Neto et al., 1993). This post-exercise facilitation may imply that for a few seconds following muscular contraction, the excitability of the motor pathways innervating the muscle is increased, thereby facilitating repetitive movements (Nørgaard et al., 2000). In this way, the lateral glide-MWM that involves a sustained gripping action may help to facilitate improved grip function. However, in the present experimental model such an effect is not likely due to the inefficient contractile elements as discussed above.

Furthermore, activation of proprioceptive mechanisms via the lateral glide-MWM may contribute beneficially to joint position sense, to the sensation of force or effort of a required workload, or possibly to the perceived timing of muscle contraction. These are all important aspects of proprioception, a key sensory mechanism for motor control (Gandevia et al., 1992; Gandevia, 1994). To date, there is a lack of research investigating proprioceptive function in patients with lateral epicondylalgia and the implication of alteration of proprioceptive function on motor control strategies. Such a mechanism would be consistent with the lack of response in the current study where DOMS was

generated in the wrist extensors, and the wrist flexor group passively exercised. Altered proprioceptive input from the wrist flexor muscles would be less likely in this situation. Factors such as the role of expectation and selective attention in motor learning also need to be considered. Expectant patients (as opposed to experimentally induced pain in healthy controls) may tend to concentrate their attention on a therapeutic stimulus such as the lateral glide-MWM, thereby potentially suppressing nociceptive input and favouring a different pattern of proprioceptive input (Zusman, 2004).

5. Conclusion

Based on the findings of this study, the mechanisms evoked by DOMS and saline-induced pain and the mechanisms underlying the effects of the lateral glide-MWM do not match. There was no evidence of modulation of combined DOMS and saline-induced myotendinous pain in response to the lateral glide-MWM intervention. It is possible that the effects of the MWM intervention are too weak to be detected or the technique is ineffective or inappropriate in this experimental pain model. Alternately, central sensitization as suggested to occur in clinical lateral epicondylalgia, may be affected by this technique and therefore explain the beneficial responses previously demonstrated. Further investigation is required in order to improve the understanding of pain and tissue mechanisms associated with lateral epicondylalgia and the mechanisms underlying the effects of specific physical therapy interventions in this musculoskeletal condition. This will allow better "matching" of interventions to patients with the potential for better clinical outcomes.

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