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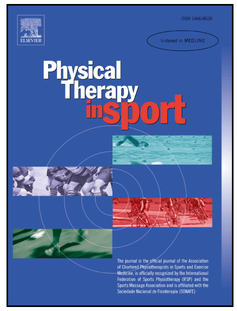

Neural gliding and neural tensioning differently impact flexibility, heat and pressure pain thresholds in asymptomatic subjects: A randomized, parallel and double-blind study

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Neural gliding and neural tensioning differently impact flexibility, heat and pressure pain thresholds in asymptomatic subjects: a randomized, parallel and double-blind study

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Abstract

Objective: To compare the effect of neural gliding and tensioning on hamstring flexibility, nerve function (heat and cold thresholds) and pain sensitivity (pain intensity and pressure pain threshold) of the mobilized and non-mobilized lower limbs at post-intervention and 24 hours follow up.

Design: Randomized, parallel and double blinded trial.

Setting/Participants: Forty-eight asymptomatic participants.

Intervention(s): Participants received neural gliding (n=23) or tensioning (n=25).

Main Outcome Measures – Straight leg raising (SLR; in degrees), heat and cold threshold (ºC), pressure pain threshold (PPT; in Kgf) and pain intensity (visual analogue scale), taken at baseline, post- intervention and at 24 hours follow up.

Results: There was a significant interaction between time, intervention and limb for SLR ($F_{2,45}$= 3.83; p=0.029). A significant interaction between time and intervention for PPT ($F_{2,45}$= 3.59; p=0.036) and heat threshold ($F_{2,45}$= 5.10; p=0.01). A significant effect of time ($F_{2,45}$= 9.42; p<0.001) and of limb ($F_{1,46}$= 4.78; p=0.035) for pain intensity during SLR, and a significant effect of time ($F_{2,45}$= 3.65; p=0.034) for pain intensity during PPT.

Conclusion: Gliding and tensioning had similar and positive effects for flexibility in the mobilized limb, but tensioning was superior for the non-mobilized limb. Gliding was superior to tensioning for pressure pain and heat thresholds.

Key words: neural mobilization; pain; hamstring flexibility; heat threshold

Introduction

The peripheral nervous system is exposed to combinations of tensile, shear and compression forces during body segment movements and postures [1–3]. However, its structural organization allows it to function while tolerating and adapting to these forces in day-to-day activities and sport [4,5]. This is probably due to the peripheral nervous system ability to glide in relation to adjacent structures and of internal fascicules to glide against each other; to the considerable amount of connective tissue that surrounds the nerve protecting it and facilitating movement; to the undulatory course of the nerve fibres that appear suited to accommodate movement and to promote dispersion of forces [6], as well as to the abundant blood vessels with coiled structure to minimize the impact of movement on the peripheral nervous system normal blood supply [7]. However, these mechanisms may be disrupted in some pathologies, such as carpal tunnel syndrome or diabetes [8,9]. Furthermore, both a disrupted response of the sciatic nerve to mechanical forces[10] and impaired function of the sciatic nerve[11] have been identified in individuals with hamstring injuries. This suggest a potential association between the ability of the sciatic nerve to accommodate mechanical stresses and its function, and may also suggest that disrupted mechanical and physiological nerve responses may either be a consequence or a predisposing factor for injury.

Neural mobilization is an intervention used by physiotherapists to restore normal mechanical and physiological responses of the nervous system to movement and posture [12]. It has been suggested that neural mobilization may induce an array of complex neurophysiologic changes that facilitate nerve function and improve symptoms, such as changes in the viscoelastic properties of the nerve, improved nerve mobility, increased intraneural fluid dispersion, activation of the descending pain inhibition, and reduced concentration of inflammatory mediators involved in nerve pain [16–20]. Different combination of joints and movements allow physiotherapists to target different nerves [13] and to modulate the amount of gliding and stress applied to a nerve [14]. In general, two types of neural mobilization are used: gliding and tensioning. Gliding techniques consist of simultaneous movements of at least two joints, so that while the nerve is elongated in one joint it is shortened in the other. In contrast, tensioning techniques elongate the nerve in both joints [5,15]. Neural gliding results in larger amounts of nerve excursion in relation to adjacent tissues while neural tensioning results in higher nerve internal pressure [14]. Conceivably, these different techniques may impact neurophysiological processes differently.

Current systematic reviews suggest that neural mobilization is effective in reducing pain and improving disability, pressure pain thresholds, function and flexibility [21,22]. However, no reference is made on whether the type of mobilization used impacts results. Conceivably, because there are insufficient studies comparing both techniques. A few previous studies compared the effects of gliding and tensioning techniques and reported conflicting results. For example, there are reports that both techniques have positive and equivalent impact on hamstring flexibility [23], hop testing and static postural control [14], that gliding has superior hypoalgesic effects than tensioning [15] or that none of the techniques has a positive impact on postural control [24]. In addition to the reduced number of existing studies comparing gliding and tensioning, studied effects are limited to immediate post-intervention effects on the ipsilateral side of mobilization. The study of the impact of neural gliding and tensioning on other variables, such as heat and cold thresholds, which give an indication on the function of small nerve fibers in peripheral neuropathies [25], is also of relevance. This study aimed to compare the effect of neural gliding techniques against neural tensioning techniques of the dominant lower limb on lower limb flexibility, heat and cold thresholds, pressure pain threshold and perceived pain intensity of the mobilized (dominant lower limb) and non-mobilized (non-dominant) lower limb, immediately after the intervention and at 24 hours follow up. We hypothesized that: i) both techniques will have a positive and similar effect on hamstrings flexibility, ii) that gliding will be superior to tensioning on its impact on heat, cold and pain thresholds and perceived pain intensity, iii) that both techniques will have an impact on the non-mobilized limb, but tensioning will be superior to gliding and that iv) both techniques will have immediate effects that will last 24 hours. The use of an asymptomatic sample decreases sample variability and informs on changes in the absence of pathology providing a pattern against which to compare individuals with pathology. This is particularly relevant as, anecdotally, nervous system mobilization is quite used in sports.

Methods

This was a randomized, controlled and assessor and patient blind trial. Ethical approval was given by the Council of Ethics and Deontology of University of Aveiro and the trial was registered at ClinicalTrials.gov (NCT03029260) prior to participant recruitment.

Sample

Participants were recruited among asymptomatic University students and were randomly allocated into 2 groups: one group received neural gliding and the other neural tensioning, by a researcher not involved in recruitment or intervention. Randomization to treatment was performed using a blocked sequence generated using the Research Randomizer software (https://www.randomizer.org/) and revealed to the researcher performing the intervention immediately before it.

An a priori sample size calculation for each of the two groups was performed using G*Power 3.1.9.2 and the following parameters: ANOVA - repeated measures within-between interaction as the statistical test, an effect size f of 0.25 (medium), an alpha of 5%, and 80% power. It was estimated that 24 participants were required in each group.

To enter the study, participants would have to be 18 years or older, and report no knowledge of nervous system mobilization, no injuries of the lower back and lower limbs in the last 3 months or surgery of the lower back and lower limbs in the last 6 months.

Potential participants were excluded if they reported neurological, cancer or rheumatic pathology. All participants provided their written informed consent.

Procedures

Participants were assessed at baseline, after the intervention and at 24 hours follow up. Measurements were taken for: heat and cold threshold, pressure pain threshold and hamstrings flexibility. Before conducting the full study, a test-retest reliability analysis was performed using 10 participants not included in the full study.

Sociodemographic Data

Participants were asked to provide data regarding age, gender, dominant lower limb (defined as the limb used to kick a ball[26]) and level of education, which were assessed through a questionnaire purposefully developed for this study. Weight and height were also measured.

Heat and cold perception threshold

Heat and cold perception threshold were evaluated using QSense (Medoc Ltd.), a device for quantitative sensory testing, using the limits method in the Medoc Main Station software. To familiarize participants with the procedure, a pre-test was performed in the thenar region. Then, a point corresponding to the region of innervation of the superficial peroneal nerve (the cutaneous branch of the peroneal nerve), defined as a point anterior to the midpoint between the external malleolus and the base of the fifth metatarsus, was marked in both feet. Marking was performed with the participants in supine position and ankle in neutral position. The QSense probe (a cube with about 5 cm) was then fixed to this point (Figure 1A). Participants were told to press a button as soon as they felt a warm (heat threshold) or cold (cold threshold) sensation on a command they hold in their hand and that would stop the temperature from changing. Participants were asked to have his finger next to the button so that the answer was as fast as possible. Four measurements were taken for each threshold and lower limb and its mean used in the statistical analysis.

Pressure Pain Threshold

For the evaluation of the pressure pain threshold (PPT) a pressure algometer (JTECH Medical Industries, Salt Lake City, US) was used. The pressure reading device was attached to a rubber tip of 1 cm^2. Participants were in supine position with knees and hips bent and feet together and fully supported on the bed. PPTs were measured at a point anterior to the midpoint between the external malleolus and the base of the fifth metatarsus. Pressure was applied at a rate of approximately 3 N/s and perpendicularly to the surface (Figure 1B). Participants were instructed to say the word "pain" as soon as the feeling of pressure changed from pressure to pain. A pre-test was performed in the thenar region for participants to get familiar with the procedures. Three measurements were performed at both lower limbs. PPT measurements were found to have acceptable intra and inter-observer reliability (intraclasse correlation coefficient, ICC≥ 0.7) [27] and small measurement error [28].

Flexibility

Lower limb flexibility was assessed using the passive Straight Leg Raising (SLR) test. Each participant was in supine position, in comfortable clothing that did not limit the mobility of the lower limbs. One researcher performed hip flexion with the knee in extension and the ankle dorsiflexed and stopped when participants first reported pain. A second researcher measured the range of hip flexion with a universal goniometer (EZ Read JamarVR Q7 Goniometer). The axis of the goniometer was centered at the greater trochanter, the fixed arm was parallel to the bed (alignment was maintained with the help of a bubble level) and the movable arm was aligned with the mid line of the hip, which was previously marked as the line joining the greater trochanter and the lateral epicondyle of the femur (Figure 1C). Three measurements were taken, and their mean was considered for the purposes of statistical analysis. In previous studies, the passive SLR test showed a test-retest reliability coefficient of 0.87 [29] and an inter-observer reliability coefficient of 0.94-0.96 [30].

All measurements were performed by a researcher that was blind to the type of intervention that each participant received.

Pain intensity

A Visual Analogue Scale (VAS) was used to quantify pain perceived by participants during PPTs and straight leg raising. It consists of a straight line of 10 centimeters, anchored with "0 – no pain" and "10-worst pain imaginable" [31]. Its test–retest reliability has been shown to be high among literate participants (ICC=0.94, P<0.001) [32].

Intervention

Tensioning

Tensioning neural mobilization was performed on the dominant limb using the Straight Leg Raising (SLR) test and a combination of movements to stress the peroneal nerve [5]. Participant were in supine. The investigator placed the ankle in inversion and plantar flexion and the knee in extension and while maintaining these joint positions, took the hip to maximum flexion. As soon as the participant felt pain or discomfort, the investigator decreased hip flexion by 5-10° to a hip position where no pain was felt. The mobilization consisted of taking the hip from this position to mid of available flexion and then again to extension (4 series of 10 repetitions with an approximate rhythm of 6 seconds per cycle, and an interval of 1 minute between series), while maintaining knee extension and ankle plantar flexion and inversion (Figure 2).

Gliding

Gliding was performed with participants in the same position as described for tensioning and movements also targeted the peroneal nerve. From an initial position consisting of ankle dorsiflexion, knee and hip extension the researcher simultaneously performed ankle plantar flexion and inversion, total knee flexion and hip flexion to 90, returning to the initial position (Figure 3). A total of 4 series of 10 repetitions with an approximate rhythm of 6 seconds per cycle, and an interval of 1 minute between series were performed.

Statistical analysis

All data analyses were performed using SPSS 24.0 for Windows (SPSS Inc, Chicago, IL). Mean and standard deviation and count and proportion were used to describe continuous and categorical variables, respectively. Data was assessed for outliers, normality and homogeneity of variance. Between group differences for baseline characteristics were explored using a Student's t test (continuous variables). An intraclass correlation coefficient (ICC; two way random, absolute agreement) and respective 95% confidence interval were used for relative reliability analysis and interpret as poor (ICC<0.50), moderate (ICC=0.50-0.75), good (ICC=0.75-0.90) and excellent (ICC≥0.90) [33]. In addition, the standard error of measurement (SEM) was calculated as $SEM = SD * \sqrt{1 - \mathrm{ICC}}$ [34]. A general linear model of repeated measures using time (T0, T1 and T2), intervention (sliding vs. tensioning) and limb (dominant vs. non-dominant) as the factors was used to compare the effects of the interventions. Post hoc comparisons (Bonferroni) were used when a significant main effect was found for time. A significant level was set at p<0.05. Partial eta square was used as an indicator of effect size and interpreted as small (0.01), medium (0.0.06), and large (0.14) effect size [35]. Significance was set at $p<0.05$.

Results

Reliability

Before conducting the full study, a reliability analysis was performed using the same measurements procedures as for the full study with 10 participants not included in the full study. ICC values were moderate to excellent (Table 1).

Sample characteristics

Fifty asymptomatic volunteers were recruited but for technical reasons (i.e. an error occurred when saving data into an excel file), data from 2 participants could not be included (Figure 4). A total of 48 participants (35 females and 13 males) were included in the analysis. There were no significant differences between groups at baseline (Table 2).

Effect of the interventions

A significant interaction between time, intervention and limb was found for lower limb flexibility ($F_{2,45}$= 3.83; $p=0.029$; partial eta^2=0.15). Pairwise comparisons revealed a significant increase from T0 to T1 ($p<0.001$) and from T0 to T2 ($p=0.01$), but not from T1 to T2 ($p>0.05$). Data (Figure 5; Supplementary material) suggests similar effects between techniques for the dominant limb, but higher increases in the tensioning group for the non-dominant limb. A significant effect of time ($F_{2,45}$= 9.42; $p<0.001$; partial eta^2=0.30) and a significant effect of limb ($F_{1,46}$= 4.78; $p=0.035$; partial eta^2=0.09) were found for pain intensity during SLR, but no significant interaction ($p>0.05$). Pairwise comparisons revealed a decrease in pain intensity between T0 and T1 ($p=0.001$) and between T0 and T2 ($p<0.001$), but not from T1 to T2 ($p>0.05$).

A significant interaction between time and intervention was found for PPT ($F_{2,45}= 3.59$; $p=0.036$; partial $eta^2=0.14$). Pairwise comparisons revealed a significant increase from T0 to T2 ($p=0.007$), and from T1 to T2 ($p=0.021$), but not from T0 to T1 ($p>0.05$). Data (Figure 5; Supplementary material) suggests that this increase was higher in the gliding group. There was a significant effect of time ($F_{2,45}= 3.65$; $p=0.034$; partial $eta^2=0.14$) for pain intensity during PPT, but no significant interaction ($p<0.05$). Pairwise comparisons revealed a significant decrease from T0 to T1 ($p=0.013$) and from T0 to T2 ($p=0.011$), but not from T1 to T2.

A significant interaction between time and intervention was found for heat threshold ($F_{2,45}= 5.10$; $p=0.01$; partial $eta^2=0.19$). Data analysis (Figure 5; Supplementary material) suggests a higher increase in the gliding group compared to the tensioning group. Pairwise comparisons revealed a significant increase from T0 to T1 ($p=0.001$), and from T0 to T2 ($p=0.002$), but not from T1 to T2 ($p>0.05$).

No significant main effects were found for cold threshold ($p>0.05$).

Discussion

This study compared the effects of two neural techniques, gliding and tensioning, both at post-intervention and at 24 hours follow up and results partially support our hypothesis. Findings suggest that i) both techniques have similar and positive effects for flexibility in the mobilized limb, but tensioning is superior to gliding for flexibility in the non-mobilized limb; ii) gliding is superior to tensioning for pressure pain thresholds and heat thresholds with similar effects on the mobilized and non-mobilized limb; iv) both techniques have positive and similar effect for perceived pain intensity during SLR and PPT and v) that these effects are of large magnitude and maintained at 24 hours follow up. None of the techniques had an impact on cold thresholds.

Flexibility

The finding that both gliding and tensioning neural mobilization have an impact on hamstring flexibility is in line with a previous study [23]. The current study adds to previous research by showing that improvements are still present at 24 hours follow up and that tensioning neural mobilization is superior for the non-mobilized limb. Furthermore, the decrease in perceived pain intensity at the end of the SLR, supports previous claims that neural mobilization contributes to increase flexibility by means of decreased mechanosensitivity. However, and considering that there was a decrease in perceived pain intensity in both limbs and no significant effect of the intervention, this is unlikely to be the only mechanism and one that does not seem to explain the different impact of gliding and tensioning on the non-mobilized limb. Tensioning is performed near the end of available range of motion and it is possible that this position has a greater impact on the mechanical characteristics of the nerve and that its effects, physiological or mechanical, reach farther. The nerves have been shown to exhibit a time-dependent viscoelastic behavior, including its gradual elongation with time in response to tension [36]. Furthermore, Andrade et al. [36] have shown that increased ankle range of motion was correlated with decreased stiffness of the ipsilateral sciatic nerve after 6 minutes of stretching of the ipsilateral sciatic nerve. It has also been suggested that contralateral tensioning mobilization might reduce electromyographic activity for patients with stroke [36]. Conceivably, the different effects of gliding and tensioning on the non-mobilized limb may be due to a greater impact of tensioning on contralateral nerve stiffness and electromyographic activity. These hypotheses require further investigation in future studies. However, the contribution of non-neural structures to the increased flexibility cannot be completely discarded, particularly for tensioning neural mobilization, as the maintenance of the lower limb at end range positions can stretch muscles and other continuous structures such as fascia. Nevertheless, both gliding and tensioning have been shown to be superior to muscle stretching for hamstring flexibility [23] and fascia seems to require particularly high forces before deformation as a previous study showed that daily stretching for 1 month did not affect shear strain of the fascia [36]. The impact of neural tensioning on the contralateral lower limb flexibility may be of clinical relevance in acute sports injuries or immediate post-surgical rehabilitation when the mobilization of the affected limb may be contra-indicated.

PPT

Results suggest that gliding is superior to tensioning in promoting hypoalgesia at 24 hours follow up and for body sites located in both the mobilized and non-mobilized limb. The effects distant to the mobilized limb suggest that hypoalgesia is mediated by central mechanisms such as the descending inhibition [15] and opioids [37]. Santos et al [37] found that neural mobilization of injured rats increased the expression of opioid receptors in the Periaqueductal Grey (PAG) region, suggesting that these effects may occur through activation of endogenous opioid-mediated pain modulatory systems. Santos et al [20] reported a decrease of the nerve growth factor and glial fibrillary acidic protein, which are involved in hyperalgesia, in dorsal root ganglion after treating injured rats with neural mobilization. Inhibition of temporal summation has also been reported in asymptomatic persons [38] and in persons with carpal tunnel syndrome [39] after neural mobilization. Temporal summation reflects facilitator mechanisms at the dorsal horn and is mediated by C-fibers.

It has been suggested that the amount of mechanical stimulus may impact hypoalgesia [40], raising the question as to whether the greater movement excursion occurring at a higher number of joints may account for the higher hypoalgesic effects of gliding. This is likely to result in greater stimulation of the large non-nociceptive afferent fibers, increasing the mechanical afferent input from muscles and joints arriving at the dorsal horn. It is also possible that the larger excursion of the nerve in gliding techniques has a greater mechanical impact on the intrinsic innervation of nerve sheaths, the nervi nervorum, which has been shown to have fibers that function as nociceptors but also as mechanoreceptors [41], potentiating hypoalgesic effects. In contrast, the higher elongation of nerves during tensioning may have a greater impact on vasa nervorum [42] elongation decreasing nerve vascularization. Beltran-Alacreu and colleagues [15] reported neural gliding to have a wider hypoalgesic effect than neural tensioning and suggested that the increased hypoalgesic effects of neural gliding was due to its smaller impact on nerve elongation and, consequently, on internal nerve pressure. Future studies could further explore the mechanisms behind gliding and tensioning induced hypoalgesia.

Heat and cold threshold

Neural gliding seems to have a larger impact than neural tensioning on increasing heat threshold, suggesting that neural gliding may contribute to desensitize C fibers in the presence of pain, but raising questions as to the significance of this finding for C-fiber nerve function in non-painful conditions where there is a loss of function and increased threshold. The desensitization of C-fibers may be of great relevance in C-fiber mediated pain syndromes and central sensitization as increased C-fiber activity seems to contribute to the appearance and maintenance of central sensitization [40,43] and is associated with increased activation in pain processing areas of the brain[44]. This suggest that neural gliding may be of clinical relevance when aiming to prevent or reverse signs and symptoms of central sensitization, but this requires further investigation in future studies.

Neural mobilization is believed to improve nerve function by improving its viscoelastic properties, its mobility and by increasing intraneural fluid dispersion [19,45]. Conceivably, the impact of neural mobilization on C-fiber function may differ depending on the condition of the individual. Future studies can explore the impact of neural mobilization on conditions that present with C-fiber loss of function.

None of the techniques significantly impacted cold threshold. While heat threshold is mediated by C fibers, cold threshold is mediated by Aδ fibers. Previous research has shown a different behavior of C and Aδ fibers to thermal stimuli [46] as well as an impact of neural tensioning on C but not on Aδ fibers [38]. Taken together, these findings suggest that neural mobilization impacts the function of C and Aδ fibers differently, at least in asymptomatic individuals.

Limitations

First, participants were asymptomatic subjects and, therefore, findings may not apply to patients with pain and pathology. The dose of mobilization was chosen based on our previous experience as it varies greatly among studies [22] and there is no evidence-based recommendation for the amount of neural gliding or tensioning that should be used. We used the SLR to characterize lower limb flexibility, but it has been suggested that contralateral hip flexor length and increased pelvic rotation can confound the results [47]. Future studies could explore whether measurement procedures impact results on flexibility. We measured pain threshold at one body site only, which corresponded to the cutaneous innervation of the peroneal nerve but was close to the cutaneous innervation of the sural nerve. However, this prevented us from charactering the extension of hypoalgesia. This would have been interesting as the neural mobilization used impacted all nerves in the lower limb. Similarly, this could also have been done for cold and heat threshold. Nevertheless, including more measurements would have increased the duration of the protocol with a potential impact on participants concentration and fatigue.

Conclusions

Our results suggest that neural gliding and tensioning impact both the mobilized and the non-mobilized limb and both impact perceived pain intensity to stretch and pressure to a similar extend; both techniques improved flexibility, but tensioning was superior for flexibility of the contra-lateral limb and neural gliding was superior to tensioning for hypoalgesia to mechanical pressure and heat threshold. Furthermore, most effects are maintained at 24 hours follow up and increased PPT was identifiable 24 hours post-intervention only. The fact that neural mobilization impacts both the mobilized and the non-mobilized limb suggests that it could be used for contralateral treatment of limbs that are immobilized or for which mobilization is contra-indicated or could aggravate symptoms. The slightly different effects of neural gliding and neural tensioning suggest that the choice of the techniques may depend on the treatment aim.

References

1. Rydevik B, Lundborg G, Bagge U. Effects of graded compression on intraneural blood flow. An in vivo study on rabbit tibial nerve. *J Hand Surg*. 1981;6(1):3-12.

2. Topp K, Boyd B. Structure and Biomechanics of Peripheral Nerves: Nerve Responses to Physical Stresses and Implications for Physical Therapist Practice. *Phys Ther*. 2006; 86(1):92-109.

3. Wall EJ, Massie JB, Kwan M, Rydevik B, Myers R, Garfin S. Experimental Stretch Neurophaty - Changes in nerve conduction under tension. *Br Editor Soc Bone Jt Surg*. 1992;74-B:126-129.

4. Silva A, Andrade R, Domingues V, et al. Quantitative in vivo longitudinal nerve excursion and strain in responsoe to joint movement: a systematic literature review. *Clin Biomech*. 2014;29(8): 839-47.

5. Shacklock M. *Clinical Neurodynamics: A New System of Musculoskeletal Treatment*. Edingburgh: Elsevier; 2005.

6. Gifford L. Neurodynamics. In: Pitt-Brooke, ed. *Rehabilitation of Movement: Theoretical Bases of Clinical Practice*. London: Saunders; 1997:159-195.

7. Ugrenovic SZ, Jovanovic ID, Kovacevic P, Simic T. Similarities and Dissimilarities of the Blood Supplies of the Human Sciatic , Tibial , and Common Peroneal Nerves. 2013;882:875-882.

8. Boyd BS, Gray AT, Dilley A, Wanek L, Topp KS. The pattern of tibial nerve excursion with active ankle dorsiflexion is different in older people with diabetes mellitus. *Clin Biomech*. 2012;27(9):967-971.

9. Hough AD, Moore AP, Jones MP. Reduced Longitudinal Excursion of the Median Nerve in Carpal Tunnel Syndrome. *Arch Phys Med Rehabil*. 2007;88(5):569-576.

10. Turl S, George K. Adverse neural tension: a factor in repetitive hamstring strain? *J Orthop Sport Phys Ther*. 1998;27(1):16-21.

11. Kouzaki K, Nakazato K, Mizuno M, et al. Sciatic nerve conductivity is impaired by hamstring strain injuries. *Int J Sport Med*. 2017;38(11):803-808.

12. Ridehalgh C, Greening J, Petty NJ. Effect of straight leg raise examination and treatment on vibration thresholds in the lower limb : a pilot study in asymptomatic subjects. 2005;10:136-143.

13. Butler D. *The Sensitive Nervous System.* Adelaide: Noigroup Publications; 2000.

14. Silva A, Manso A, Andrade R, Domingues V, Piedade M, Silva AG. Clinical Biomechanics Quantitative in vivo longitudinal nerve excursion and strain in response to joint movement : A systematic literature review. *JCLB*. 2014.

15. Beltran-alacreu H, Jiménez-sanz L, Carnero JF, Touche R La. Comparison of Hypoalgesic Effects of Neural Stretching vs Neural Gliding: A Randomized Controlled Trial. *J Manipulative Physiol Ther*. 2015;38(9):644-652.

16. Calvo-Lobo C, Unda-Solano F, López-López D, et al. Is pharmacologic treatment better than neural mobilization for cervicobrachial pain? A randomized clinical trial. *Int J Med Sci*. 2018;15(5):456-465.

17. Rodríguez-Sanz D, Calvo-Lobo C, Unda-Solano F, Sanz-Corbalán I, Romero-Morales, C López-López D. Cervical Lateral Glide Neural Mobilization Is Effective in Treating Cervicobrachial Pain: A Randomized Waiting List Controlled Clinical Trial. *Pain Med*. 2017;18(12):2492-2503.

18. Efstathiou MA, Stefanakis M, Savva C, Giakas G. ScienceDirect Effectiveness of neural mobilization in patients with spinal radiculopathy : A critical review. *J Bodyw Mov Ther*. 2015;19(2):205-212.

19. Bertolini GRF, Silva TS, Trindade DL, Carvalho AR. Neural mobilization and static stretching in an experimental sciatica model – an experimental study. 2009;13(6):2-7.

20. Santos FM, Silva JT, Giardini AC, et al. Neural mobilization reverses behavioral and cellular changes that characterize neuropathic pain in rats. *Mol Pain*. 2012;8(1):57.

21. Ballestero-Pérez R, Plaza-Manzano G, Urraca-Gesto A, et al. Effectiveness of Nerve Gliding Exercises on Carpal Tunnel Syndrome: A Systematic Review. *J Manipulative Physiol Ther*. 2016;0(0):962746-228.

22. Neto T, Freitas SR, Marques M, Gomes L, Andrade R. Musculoskeletal Science and Practice Effects of lower body quadrant neural mobilization in healthy and low back pain populations : A systematic review and meta-analysis. *Musculoskelet Sci Pract*. 2017;27:14-22.

23. Sharma S, Balthillaya G, Rao R, Mani R. Physical Therapy in Sport Short term effectiveness of neural sliders and neural tensioners as an adjunct to static stretching of hamstrings on knee extension angle in healthy individuals : A randomized controlled trial. *Phys Ther Sport*. 2016;17:30-37.

24. Nunes GS, Uhlig S, do Amaral Ribas LM, Gonçalves FB, Wageck B, de Noronha M. Influence of Neural Mobilization of Lower Limbs on the Functional Performance and Dynamic Balance in Asymptomatic Individuals: A Cross-Over Randomized Controlled Trial. *Hum Mov*. 2017;0(0):13-19.

25. Chéliout-Héraut F, Zrek N, Khemliche H, et al. Exploration of small fibers for testing diabetic neuropathies. *Jt Bone Spine*. 2005;72(5):412-415.

26. van Melick N, Meddeler BM, Hoogeboom TJ, Nijhuis-van der Sanden MWG, van Cingel REH. How to determine leg dominance: The agreement between self-reported and observed performance in healthy adults. *PLoS One*. 2017;12(12):1-9.

27. Fingleton CP, Dempsey L, Smart K, Doody CM. Intraexaminer and interexaminer reliability of manual palpation and pressure algometry of the lower limb nerves in asymptomatic subjects. *J Manipulative Physiol Ther*. 2014;37(2):97-104.

28. Romero-Morales C, Jaén-Crespo G, Rodríguez-Sanz D, Sanz-Corbalán I, López-López D, Calvo-Lobo C. Comparison of Pressure Pain Thresholds in Upper Trapezius and Temporalis Muscles Trigger Points Between Tension Type Headache and Healthy Participants: A Case–Control Study. *J Manipulative Physiol Ther*. 2017;40(8):609-614.

29. Cejudo A, Sainz de Baranda P, Ayala F, Santonja F. Test-retest reliability of seven common clinical tests for assessing lower extremity muscle flexibility in futsal and handball players. *Phys Ther Sport*. 2015;16(2):107-113.

30. Castellote-Caballero Y, Valenza MC, Puentedura EJ, Fernández-de-Las-Peñas C, Alburquerque-Sendín F. Immediate Effects of Neurodynamic Sliding versus Muscle Stretching on Hamstring Flexibility in Subjects with Short Hamstring Syndrome. *J Sport Med (Hindawi Publ Corp*. 2014;2014(April):127471.

31. Kersten P, White PJ, Tennant A. Is the pain visual analogue scale linear and responsive to change? An exploration using rasch analysis. *PLoS One*. 2014;9(6).

32. Hawker GA, Mian S, Kendzerska T, French M. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF. *Arthritis Care Res*. 2011;63(SUPPL. 11):240-252.

33. Portney LG, Watkins MP. *Foundations of Clinical Research: Applications to Practice*. second. Upper Saddle River, N.J: Prentice Hall Health; 2000.

34. Weir JP. Quantifying test-retest reliability using the intraclass correlation coefficient

and the SEM. *J Strength Cond Res*. 2005;19(1):231-240.

35. Richardson J. Eta squared and partial eta squared as measures of effect size in educational research. *Educ Res Rev*. 2011;6(2):135-147.

36. Kwan MK, Wall EJ, Massie J, Garfin SR. Strain, stress and stretch of peripheral nerve rabbit experiments in vitro and in vivo. *Acta Orthop*. 1992;63(3):267-272.

37. Santos FM, Grecco LH, Pereira MG, et al. The neural mobilization technique modulates the expression of endogenous opioids in the periaqueductal gray and improves muscle strength and mobility in rats with neuropathic pain. *Behav Brain Funct*. 2014;10(1):1-8.

38. Beneciuk J, Bishop M, George S. Effects of upper extremity neural mobilization on thermal pain sensitivity: a sham-controlled study in asymptomatic participants. *J Orthop Sport Phys Ther*. 2009;39(6):428-438.

39. Bialosky JE, Bishop MD, Price DD, Robinson ME, Vincent KR, George SZ. A Randomized Sham-Controlled Trial of a Neurodynamic Technique in the Treatment of Carpal Tunnel Syndrome. *J Orthop Sport Phys Ther*. 2009;39(10):709-723.

40. McLean S, Naish R, Reed L, Urry S, Vicenzino B. A pilot study of the manual force levels required to produce manipulation induced hypoalgesia. *Clin Biomech*. 2002;17(4):304-308.

41. Sauer SK, Bove GM, Averbeck B, Reeh PW. Rat peripheral nerve components release calcitonin gene-related peptide and prostaglandin E2in response to noxious stimuli: Evidence that nervi nervorum are nociceptors. *Neuroscience*. 1999;92(1):319-325.

42. Qureshi A, Saleem M, Ahrar A, Raja F. Imaging of the Vasa Nervorum Using Contrast-Enhanced Ultrasound. *J Neuroimaging*. 2017;27(6):583-588.

43. Hathway G, Vega-Avelaira D, Moss A, Ingram R, Fitzgerald M. Brief, low frequency stimulation of rat peripheral C-fibres evokes prolonged microglial-induced central sensitization in adults but not in neonates. *Pain*. 2009;144(1-2):110-118.

44. Staud R, Craggs J, Perlstein W, Robinson M, Price D. Brain activity associated with slow temporal summation of C-fiber evoked pain in fibromyalgia patients and healthy controls. *Eur J Pain*. 2008;12(8):1078-1089.

45. Brown C, Gilbert K, Brismee J, Sizer P, Roger C, Smith M. The effects of neurodynamic mobilization on fluid dispersion within the tibial nerve at the ankle: an unembalmed cadaveric study. *J Man Manip Ther*. 2011;19(1):9.

46. Palmer S, Martin D, Steedman W, Ravey J. C- and Ad-fibre mediated thermal perception: response to rate of temperature change using method of limits. *Somat Mot Res*. 2000;17(4):325-333.

47. Davis D, Quinn R, Whiteman C, Williams J, Young C. Concurrent validity of four clinical tests used to measure hamstring flexibility. *J Strength Cond Res*. 2008;22(2):583e588.

Tables

Table 1 – Intra-rater reliability analysis (n=10).

Outcome	ICC (95% CI)	SEM
Heat (D)	0.88 (0.74; 0.97)	0.76°C
Heat (ND)	0.90 (0.74; 0.97)	0.71°C
Cold (D)	0.60 (0.30; 0.86)	1.18°C
Cold (ND)	0.59 (0.28; 0.85)	0.50°C
PPT (D)	0.97 (0.89; 0.99)	1.63 Kgf
PPT (ND)	0.95 (0.87; 0.99)	2.14 Kgf
SLR (D)	0.88 (0.69; 0.96)	2.03°
SLR (ND)	0.89 (0.72; 0.97)	1.97°

Legend: D – dominant lower limb; ND – non-dominant lower limb; SEM – standard error of measurement; MDD – minimal detectable difference.

Table 2 – Sample characteristics and baseline measurements.

Outcome		Tensioning (n=25)	Gliding (n=23)	p
Age	years	19.4±1.2	19.6±1.5	0.393
Height	cm	165.1±8.1	169.9±10.1	0.089
Weight	Kg	61.2±11.7	62.5±8.4	0.297
Body mass index	Kg/cm^2	22.5±3.0	21.6±1.7	0.220
Heat Threshold (D)	ºC	35.7±1.8	36.1±2.3	0.195
Heat Threshold (ND)	ºC	35.7±1.5	36.2±1.9	0.152
Cold threshold (D)	ºC	30.1±1.1	30.1±1.4	0.388
Cold threshold (ND)	ºC	30.4±0.7	30.1±1.0	0.329
PPT (D)	Kgf	36.9±22.2	40.2±17.5	0.612
PPT VAS (D)		2.6±2.3	2.9±2.3	0.714
PPT (ND)	Kgf	38.8±20.1	43.7±23.7	0.389
PPT VAS (ND)		2.9±2.6	2.9±2.2	0.117
SLR (D)	º	83.2±21.2	80.7±18.3	0.990
SLR VAS (D)		3.7±2.2	3.4±2.0	0.547
SLR (ND)	º	82.0±23.6	82.5±20.5	0.866
SLR VAS (ND)		4.2±2.4	3.8±2.0	0.538

D – Dominant limb; ND – non-dominant limb; VAS – visual analogue scale; SLR – straight leg raising.

Figure 1 – Measurement procedures: A) heat and cold threshold; B) PPT and C) hip range of motion during SLR.

Figure 2 – Tensioning mobilization: A) participants' maximum hip flexion; B) participants' maximum hip flexion minus 5 to 10º; B to C/C to B) range of hip flexion used in tensioning mobilization maintaining knee extension and ankle dorsiflexion.

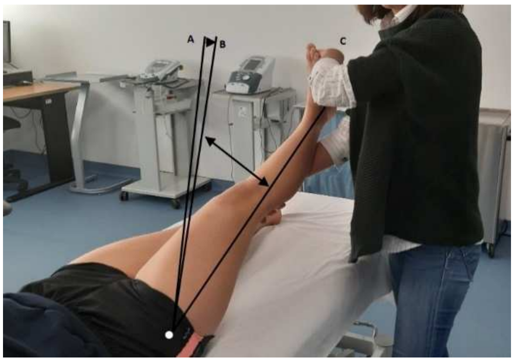

Figure 3 – Initial (left) and final (right) position for gliding mobilization.

Figure 4 – Flowchart of the trial.

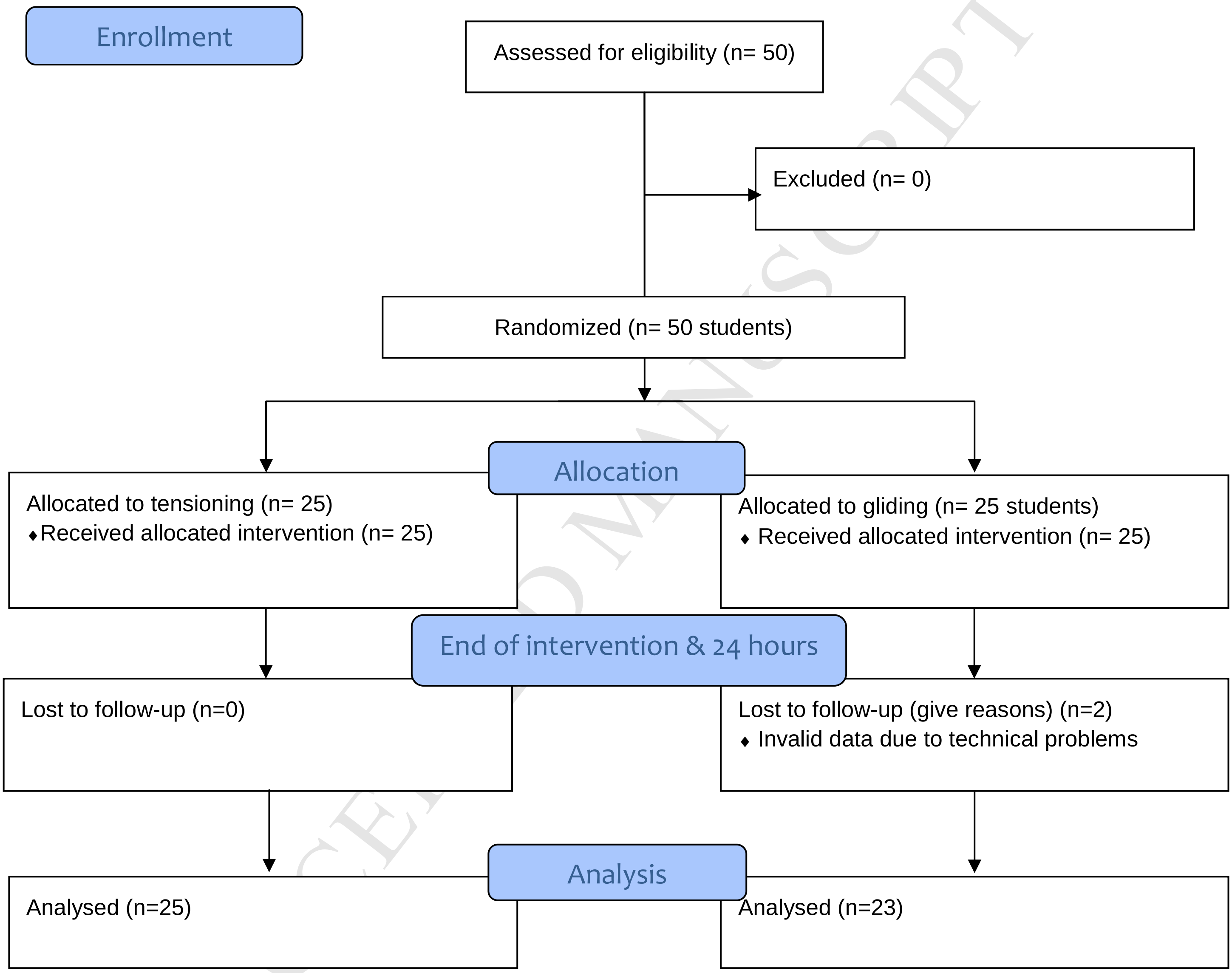

Figure 5 – Mean and 95% confidence interval of the mean for PPT, SLR and VAS at baseline (1), post-intervention (2) and 24 hours follow up (3) for both the dominant (D) and non-dominant (ND) limb.

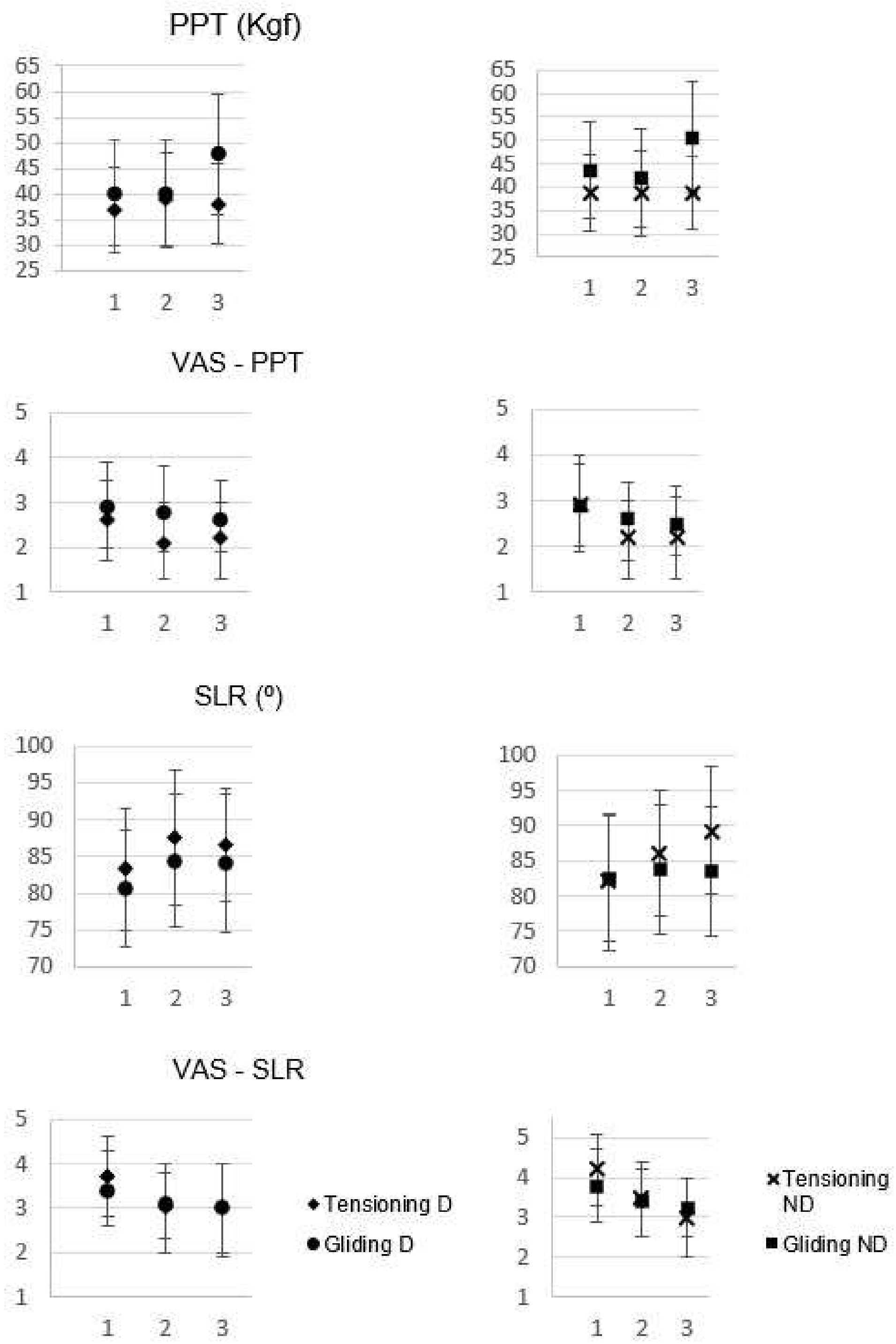

Figure legend: PPT - time x intervention (F2,45= 3.59; p=0.036; partial eta^2 =0.14);

Flexibility – time x intervention x limb ($F_{2,45}$= 3.83; p=0.029; partial eta^2=0.15); Pain intensity at the end of SLR - time ($F_{2,45}$= 9.42; p<0.001; partial eta^2=0.30), limb ($F_{1,46}$= 4.78; p=0.035; partial eta^2=0.09), interaction (p>0.05); Pain intensity during PPT - time ($F_{2,45}$= 3.65; p=0.034; partial eta^2=0.14).

Figure 6 – Mean and 95% confidence interval of the mean for heat and cold thresholds at baseline (1), post-intervention (2) and 24 hours follow up (3) for both the dominant (D) and non-dominant (ND) limb.

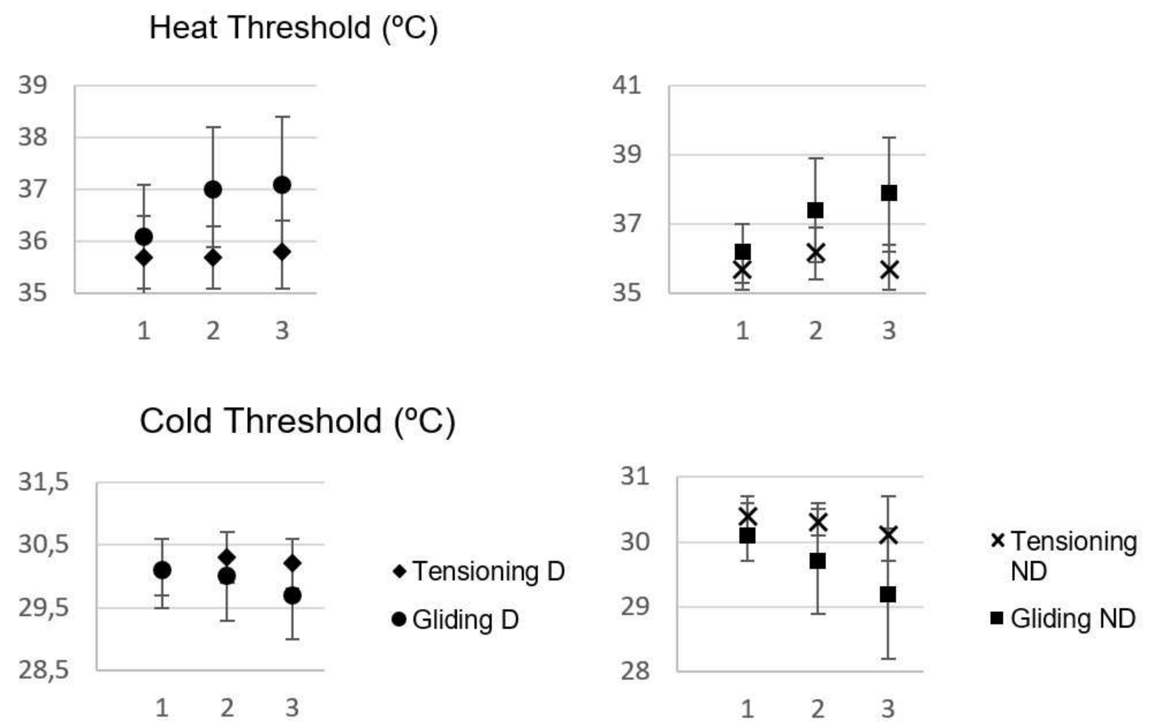

Figure legend: Heat threshold - time x intervention ($F_{2,45}$= 5.10; p=0.01; partial eta^2=0.19); Cold threshold: no significant main effect (p>0.05).

Highlights

- Neural gliding and tensioning impact both the mobilized and the non-mobilized limb
- Neural gliding is superior to tensioning for hypoalgesia to mechanical pressure and heat threshold
- Neural gliding and tensioning impact perceived pain intensity to stretching and pressure
- Neural gliding and tensioning improve flexibility, but tensioning is superior for the contralateral limb.

Ethical statement

(1) Ethical Approval

Ethical approval was given by the Council of Ethics and Deontology of University of Aveiro.

ACCEPTED MANUSCRIPT