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Exploration of Quantitative Sensory Testing in Latent Trigger Points and Referred Pain Areas

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Abstract

Objective: To investigate somato-sensory nerve fibre function by applying different quantitative sensory testing including thermal, mechanical and vibration thresholds over latent trigger points (TrP) and in its associated referred pain area.

Methods: A total of 20 subjects with unilateral latent TrPs in the extensor carpi radialis brevis were included. Warmth detection threshold (WDT), cold detection threshold CDT) and heat/cold pain thresholds (HPT, CPT), mechanical detection (MDT) and pain (MPT) thresholds, vibration threshold (VT), and pressure pain thresholds (PPT) were blinded assessed over the TrP, in the referred pain area, and in the respective contra-lateral mirror areas. A multilevel mixed-model ANOVA with site (TrP, referred pain area) and side (real or contra-lateral) as within-subjects factors and gender as between-subjects factor was conducted.

Results: No significant differences for thermal detection (WDT, CDT) or thermal pain thresholds (HPT, CPT) were found (all, $P>0.141$). The assessments over the TrP area showed lower PPT and MDT compared to the mirror contra-lateral TrP area ($P<0.05$). MDT were higher ($P=0.001$) but PPT ($P<0.001$) and MPT ($P=0.032$) were lower over the TrP area and contra-lateral mirror point compared to their respectively referred pain areas. Finally, VT was higher over the TrP area than in the referred pain area and over both mirror contra-lateral points.

Discussion: Assessing sensory changes over latent myofascial TrPs reveal mechanical hyperesthesia, pressure pain hyperalgesia, and vibration hypoesthesia compared to a contra-lateral mirror area.

Key words: Trigger point, referred pain, quantitative sensory testing.

Exploration of Quantitative Sensory Testing in Latent Trigger Points and Referred Pain Areas

Introduction

Trigger points (TrPs) are defined as sensitive spots within palpable taut bands of skeletal muscles painful to stimulation and that can give rise to referred pain, referred tenderness, motor dysfunction and autonomic phenomena.[1] TrPs are clinically classified as active or latent. Active TrPs are associated with spontaneous symptoms and, when stimulated, the elicited referred pain is recognized by the patient as a familiar or usual pain.[1] Latent TrPs do not provoke spontaneous symptoms, and the elicited referred pain during stimulation is not recognized as a familiar or usual symptom.[1]

Although the integrated hypothesis continues to be the most accepted model for explaining the formation of a TrP[2]; the exact pathophysiology is still under debate. In the last years, there has been an increasing interest in the association between TrPs with sensitization processes.[3] The presence of active muscle TrPs has been associated with the degree of sensitization in chronic pain conditions such as tension-type headache,[4] post-mastectomy pain,[5] post-meniscectomy pain,[6] or fibromyalgia.[7] In addition, some studies have reported that chemical nociceptive irritation of latent TrPs stimulates both nociceptive (un-myelinated group IV fibres) and non-nociceptive (large-diameter myelinated group III fibres) afferent suggesting that latent TrPs exhibit nociceptive (hyperalgesia) and non-nociceptive (allodynia) mechanical sensitivity.[8,9] In fact, latent TrPs also contribute to occurrence of locally enlarged area of pressure pain hyperalgesia associated with spreading sensitization suggesting that myofascial TrPs may contribute to pain propagation and development of generalized pressure hyperalgesia.[10] Finally, it seems that sensitivity to pressure pain in TrPs also exhibits sympathetic facilitation.[11]

All these studies suggest the involvement of multiple nerve fibres in TrP pain; however, this hypothesis is based on changes observed in just pressure pain sensitivity. The German Research Network on Neuropathic Pain (DFNS) developed a quantitative

sensory testing (QST) battery for testing small and large nerve fibre functions or gain (i.e., hyperalgesia, allodynia) and to assess cutaneous and deep pain sensitivity.[12] This protocol assesses somato-sensory function across the full spectrum of all primary nerve fibre afferents including Aβ fibres (mechanical detection thresholds to von Frey hairs and vibration), Aδ fibres (cold detection threshold and mechanical pain threshold for pinprick stimuli) and C fibres (warm detection and heat pain thresholds).[13] No previous study has investigated somato-sensory nerve fibres function over TrPs. Therefore, the aim of the current study was to investigate somato-sensory function over TrPs and in the associated referred pain area by applying different QST, i.e. pressure, thermal or vibration.

Methods

Participants

Volunteers not reporting symptoms in the upper extremity, including shoulder, elbow or wrist, during the previous year were recruited by local advertisement from the general population and invited to participate in the current study. Further, they also were required to exhibit the presence of a latent TrP within the extensor carpi radialis brevis muscle unilaterally. They were excluded if: 1, reported previous trauma or fracture in the upper extremity; 2, had received surgery in the upper extremity, including the neck; 3, cervical radiculopathy diagnosis; 4, previous whiplash injury; 5, reported any medical condition affecting pain sensitivity, e.g., fibromyalgia syndrome; 6, absence of a latent TrP in the extensor carpi radialis brevis; or, 7, presence of bilateral latent TrPs in the wrist extensor muscles. The extensor carpi radialis brevis muscle was chosen as it is the muscle most affected by active TrPs in patients with lateral epicondylalgia.[14]

TrP diagnosis was conducted where there was a hypersensitive spot within a taut band of the extensor carpi radialis brevis muscle that elicited a referred pain pattern to the dorsal aspect of the forearm and/or wrist.[1,14] Since all subjects were asymptomatic,

the elicited referred pain should not reproduce any symptom familiar to the subject; therefore, only latent TrPs were considered in the study.[1] A recent study has observed a 81.7% of agreement on classification (i.e., active or latent) and 85.6% of agreement on location for extensor carpi radialis brevis muscle.[15] All participants read and signed a written consent form prior to their participation in the study. The study was approved by local Ethics Committee of Universidad Rey Juan Carlos, Spain (URJC 23/2016) and it was conducted following the Helsinki declaration.

Procedure

Identification of the latent TrP was conducted by an experienced clinician with more than 15 years of experience in TrP management. The TrP and referred pain areas were marked. Participants were asked to outline on their forearm/wrist the area where they perceived the referred pain sensation. Mirror areas in the contra-lateral side were afterwards marked after the confirmation that no TrP and referred pain were observed in the contra-lateral forearm. A second clinician, blinded to the presence of the real or mirror areas conducted QST assessment as follows: thermal detection threshold, thermal pain thresholds, mechanical detection thresholds, mechanical pain thresholds, vibration detection thresholds, and pressure pain thresholds.[12] This protocol has exhibited good to excellent test-retest and inter-rater reliability.[16] All tests were conducted over the TrP and its referred pain area and their respective mirror areas in a randomized order between areas (**Figure 1**). All tests were first demonstrated over an area that was not tested later during the QST session.

Thermal Detection and Pain Thresholds

All thermal thresholds were tested with a Pathway Model ATS (Medoc, Israel). Cold detection (CDT) and warm detection (WDT) thresholds were firstly determined followed by cold pain (CPT) and heat pain (HPT) thresholds. From a baseline of 32° C, a 5x2.5 cm^2 thermode increased in temperature at a rate of 1°C/s up to a maximum cut-

out of 50° C or decreased temperature at a rate of 1°C/s to a minimum cut-out of 5° C. For WDT and CDT, participants were asked to press the hand switch as soon as they perceived warm or cold sensation. For HPT and CPT they were instructed to press the hand-controlled switch as soon as pain was perceived. The mean of three trials at each point was calculated and used for the main analysis. A pause of 5 seconds was allowed between tests. The reliability of thermal thresholds at the dorsal aspect of the forearm has been found to be excellent in both healthy subjects[17] and patients with elbow pain.[18]

Mechanical Detection Threshold

The mechanical detection threshold (MDT) was measured with a standardized set of modified twenty von Frey hairs that exert forces between 0.25 and 512 mN over a uniform contact area (rounded tip, 0.5 mm in diameter).[19] The final threshold was the geometric mean of five series of ascending and descending stimulus intensities.[12,13]

Mechanical Pain Threshold

Mechanical pain threshold (MPT) was assessed using a set of seven custom-made weighted pinprick stimulators (flat contact area of 0.2 mm diameter) with fixed stimulus intensities from 8, 16, 32, 64, 128, 256, to 512 mN. The pinprick stimulators were applied at an approximately rate of 2sec on, 2 sec off in an ascending order until the first percept of sharpness was reached. The final threshold was the geometric mean of five series of ascending and descending stimuli.[12,13]

Vibration Threshold

The vibration threshold (VT) was tested with a vibrometre (Somedic AB®, Sweden). A constant frequency of 120 Hz was used with a tissue displacement of 1cm. The range of amplitude for the stimulus was 0.1-130 μm, and the rate of change was 0.5 μm/s. Subjects, with their eyes closed, indicated when the vibration sensation first appeared (vibration perception threshold-VPT) and when it disappeared (vibration disappearance

threshold-VDT). Triplicate recordings were taken at each site and the mean values were used for the main analysis. The VT was the mean score of VPT and VDT value.[12,13]

Pressure Pain Threshold

An electronic pressure algometer (Somedic AB®, Sweden) with a 1-cm^2 rubber was used to determine the pressure pain threshold (PPT), that is, the minimal amount of pressure where a sense of pressure first changes to pain. Participants were instructed to push a button to stop the pressure when the sensation first changed from pressure to pain. Pressure was applied at a rate of approximately 30 kPa/cm^2/second. Three trials, with 30sec interval between each, were obtained and the mean was used for the main analysis.[12,13]

Sample Size Calculation

The sample size determination was conducted with the software Tamaño de la Muestra1.1©, Barcelona, Spain. The determinations were based on detecting significant differences of 20% on PPT[20] between the latent TrP and its contra-lateral mirror point with an alpha level of 0.05, and a desired power of 80%. This generated a sample size of at least 16 participants.

Statistical Analysis

Data were analyzed with SPSS 22.0 (SPSS Inc, Chicago, Illinois, USA). Data are presented as means with their 95% confidence intervals (95%CI). A multilevel mixed-model analysis of variance (ANOVA) with site (TrP or referred pain area) and side (real or contra-lateral mirror) as within-subjects factors and gender as between-subjects factor was conducted to determine differences in QST. Tests of simple effects for the pairwise comparisons of interest were undertaken with the experiment alpha rate of 0.05 Bonferonni adjusted. The standardized mean differences (SMD) were calculated by dividing the between-group difference by the pooled standard deviation to enable comparison of effect sizes. Values were considered as trivial when range from 0.0 to

0.2, small from 0.2 to 0.49, moderate from 0.5 to 0.79, and large when greater than 0.8.[21]

Results

Participants

A total 25 of volunteers were recruited and examined for eligibility criteria. Five (20%) were excluded because no latent TrP was found within the extensor carpi radialis brevis muscle on either left/right forearm. Finally, 20 participants (50% women, mean age: 37±7 years) satisfied all criteria and agreed to participate in the study. All subjects were right-handed. Twelve subjects (60%) showed the latent TrP in the right (dominant) extensor carpi radialis brevis muscle whereas the remaining eight (40%) in the left (non-dominant) extensor carpi radialis brevis muscle. All participants perceived the referred pain distally to the dorso-lateral aspect of the forearm (80%) and the wrist (90%).

Thermal Thresholds

No significant differences were observed in CDT (site: F=0.848, P=0.364; side: F=1.032, P=0.447; site*side: F=1.400, P=0.447), WDT (site: F=1.979, P=0.232; side: F=0.483, P=0.613; site*side: F=0.738, P=0.548), CPT (site: F=1.071, P=0.309; side: F=0.129, P=0.780; site*side: F=0.051, P=0.940) and HPT (site: F=1.518, P=0.335; side: F=0.325, P=0.670; site*side: F=1.381, P=0.384) between the TrP and referred pain area and their respective contra-lateral mirror areas. Further, no significant effect of gender was either observed (CDT: F=0.110, P=0.743; WDT: F=0.584, P=0.450; CPT: F=0.04, P=0.953; HPT: F=0.650, P=0.426).

Mechanical Thresholds

The ANCOVA revealed significant differences between sites for all mechanical thresholds (MDT: F=14.33, P=0.001; MPT: F=4.99, F=0.032; PPT: F=17.61, P<0.001): MDT were higher, i.e., mechanical hypoesthesia, whereas PPTs and MPT were lower, i.e., pinprick and pressure pain hyperalgesia, over the TrP and over the contra-lateral

mirror point compared to their respectively referred pain areas (**Tables 1-2**). No significant side-to-side differences were observed for any mechanical threshold (MDT: F=0.05, P=0.942; MPT: F=1.256, P=0.371; PPT: F=0.234, P=0.631). In addition, significant side*site interactions were observed for PPT (site * side: F=5.001; P=0.036) and MDT (site * side: F=4.995; P=0.040), but not for or MPT (site * side: F=0.001; P=0.989): the TrP area showed lower PPT, i.e., pressure pain hyperalgesia, and MDT, i.e., mechanical hyperesthesia, than the mirror contra-lateral TrP area. Finally, the effect of gender was significant for PPT (F=5.353; P=0.030), but not for MDT (F=0.145; P=0.805) or MPT (F=0.148; P=0.766): women exhibited lower PPTs in all points than men (P<0.05).

Vibration Threshold

The ANCOVA found significant differences between sites (F=22.914; P<0.001) and sides (F=5.073; P=0.031) and a significant site*side interaction (F=5.445 P=0.027) for VT: 1, VT was higher, i.e., vibratory hypoesthesia, over the TrP and contra-lateral mirror point compared to their respectively referred pain areas; 2, VT was higher, i.e., vibratory hypoesthesia, over the referred pain area compared to the contra-lateral mirror point; 3, the VT was significantly higher over the TrP area than the referred pain area and both mirror contra-lateral points (**Tables 1-2**). Finally, no significant effect of gender (F=1.477; P=0.438) was observed for vibration threshold.

Inter-measure Comparisons of Effect Size

Moderate effects were observed between TrP area and its contra-lateral mirror point comparison for MDT (0.55), VT (0.75) and PPT (0.54) implicating that these QST maybe a characteristic of TrP (**Table 1**). Further, MPT (0.42) and VT (0.55) moderate differences between the referred pain area and its contra-lateral mirror area were also observed (**Table 2**) suggesting that these QST maybe a feature of the referred pain area.

Discussion

In the present study we used, for the first time, a comprehensive QST test platform, measured both locally at the TrP area and at a distant site (referred pain), to provide information that may improve our insight into pain mechanisms underlying TrP pain. We observed that latent TrPs in the extensor carpi radialis brevis muscle showed mechanical hyperesthesia, pressure pain hyperalgesia, and vibration hypoesthesia when compared to a contra-lateral mirror non-TrP area. In addition, the referred pain area showed pinprick and vibration hypoesthesia compared to the contra-lateral mirror non-referred pain area. In general, the TrP and its contra-lateral mirror point exhibited mechanical hypoesthesia, pinprick hyperalgesia, pressure hyperalgesia, and vibration hypoesthesia when compared to their respectively referred pain areas. Finally, thermal pain and detection thresholds were not different between TrP/contra-lateral mirror point and their respectively referred pain areas.

While abnormal thermal QST findings are common in neuropathic pain,[22] they are inconsistently seen in non-neuropathic musculoskeletal conditions.[23,24] Accordingly, thermal QST changes were not observed in the current study over neither the TrP nor its referred pain area. Experimentally-induced muscle pain with hypertonic saline injection induced thermal hyperalgesia throughout the referred pain area.[25,26] However, thermal sensitivity is seldom reported as a symptom associated with myofascial pain syndromes, even though inflammatory cytokines (calcitonin gene related peptide or bradykinin) have been observed in active, but to a lesser extent, over latent TrPs.[27] Our study suggests that thermal hyperalgesia is not associated with latent TrPs. A future study comparing the thermal QST features of latent and active TrPs should be conducted.

Several interesting findings were demonstrated through PPT testing in our study. PPTs were mainly decreased at the latent TrP area, but the corresponding contra-lateral site also exhibited reduced PPTs compared to the referred pain areas. This mirror image

change in nociceptive properties of muscle tissue is thought to occur via crossed-spinal inter-neuronal connections[28] sensitizing contra-lateral tissues likely through neurogenic inflammation,[29] although supraspinal mechanisms may also contribute as well. This is clinically significant and may partially explain the bilateral development of symptoms and sensitivity that is often found in several unilateral musculoskeletal conditions.[30-32] Further, it may also contribute to the spreading sensitivity that occurs with increasing chronicity of a pain condition.[33] Sex differences were observed in PPTs, with females demonstrating lower sensory thresholds as shown in many previous studies. It has been demonstrated that women have an increased number of latent TrPs[34] as well as lower thresholds to pressure[35] but not to other sensory modalities[36] as compared to men.

Measurement of PPTs within the area of referral provided a means to assess if secondary hyperalgesia occurs in the presence of latent TrPs. PPTs in the referred pain areas were not significantly different between both sides, and fell within ranges similar to those of healthy controls in the same anatomical area.[37] With secondary hyperalgesia, expansion of receptive fields occurs via opening of 'silent synapses' at the spinal cord,[38] which is referred to as heterosynaptic facilitation. Previous research has reported that 'further nociceptive input' into a latent TrP will result in subjective report of expanded distribution of pain and secondary hyperalgesia as measured by sensitivity to pressure pain. [8-10] Our findings support the notion that the referred pain area from latent TrPs is not associated with increased sensitivity; however, considering the findings of Wang et al[10] a propensity exists for TrP to become sensitized to nociceptive stimuli. In fact, Xu et al found that painful stimulation of latent TrPs induced generalized sensitization in healthy subjects, since irritation of latent TrPs increased pressure sensitivity in extra-segmental areas.[39] It is possible that referred pain areas elicited by active painful TrPs show pressure pain hyperalgesia. In fact, the referred pain area elicited by intramuscular

infusion of acidic phosphate buffer into the tibialis anterior muscle showed mechanical hyperalgesia.[40]

This study represents the first investigation on assessment of cutaneous pain thresholds in subjects with latent TrPs. MPT examines the cut-point at which a series of graduated pinprick stimuli, applied to the skin, is perceived as punctate pain rather than pressure. In such an instance, a musculoskeletal input (i.e., TrP) resulted in sensitization of receptors in adjacent cutaneous tissues (the overlying skin), a phenomenon which is likely centrally mediated.[3] Further, MPT measures over the TrP area were similar to the corresponding site on the contra-lateral point; however, thresholds were significantly lower than measures in the area of pain referral, indicating hyperalgesia at the site of insult and the mirror image site, but not in the area of referral.

We found hypoesthesia to VT and MDT over latent TrP and the corresponding contralateral site. While hypoesthesia may occur in instances where receptor damage has occurred, an alternative and perhaps more plausible explanation in our study is that innocuous sensation is inhibited as result of altered pain processing. Apkarian et al[41] observed reduced vibrotactile sensitivity after experimentally inducing pain in healthy volunteers. They referred to this phenomenon as a 'touch gate' suggesting that pain may inhibit sensory input at a supra-spinal level. However, others have suggested that this mechanism of pain induced hypoesthesia may be spinally mediated.[42] Some studies of individuals with chronic musculoskeletal pain conditions, including patellofemoral pain,[22] knee osteoarthritis,[43] or temporomandibular pain[44] have reported hypoesthesia in the symptomatic area. While some researchers have reported that this pain-induced hypoesthesia may be limited to the site of pain,[45] our study also found mirror image hypoesthesia suggesting that TrP pain activity may be able to induce bilateral mirror hyposensitivity. Although less robust, VT was also significantly bilaterally increased

(decreased acuity) in the referred pain area. Potential functional ramifications of pain-related hypoesthesia exist. In a study including 1800 subjects with knee OA, Shakoor et al[43] observed that vibratory acuity and quadriceps muscle strength were important predictors of the incidence and worsening of knee instability. Future studies examining functional sequelae of vibration hypoesthesia due to TrPs would be beneficial.

Although latent muscle TrPs are, by definition, asymptomatic, there is evidence supporting neurophysiological and clinical relevance of latent TrPs.[46] In fact, current and previous[8-10,26,38,46] findings from our study would support that, although latent TrPs are not spontaneously painful, yet, they do provide nociceptive barrage into the dorsal horn and, probably, to the brainstem. Nevertheless, differentiation between active and latent TrPs in relation to QST is needed to further determine the sensory disturbances associated with myofascial pain.

Conclusion

The predominant and salient feature usually associated to latent TrPs has been pressure hyperalgesia. The current study demonstrates that the QST profile over TrPs is more complex. The latent TrP was characterized by mechanical hyperesthesia, pressure pain hyperalgesia, and vibration hypoesthesia whereas the referred pain area exhibited pinprick and vibration hypoesthesia. No aberrant thermal thresholds were observed.

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Conflict of interest statement

The authors have no conflicts of interest to declare.

Contributors: All authors contributed to the study concept and design. SAQ and JLAB did the statistical analysis. SAQ and JLAB contributed to analysis and interpretation of data. CFdlP, CC and LAN contributed to draft the report. CFdlP and LAN obtained funding. CFdlP and CC provided administrative, technical, and material support. CFdlP, CC and LAN supervised the study. All authors revised the text for intellectual content and have read and approved the final version of the manuscript.

Legend of Figure

Figure 1: Trigger point (TrP) in the extensor carpi radialis brevis muscle and its referred pain area (RPA) over the dorsal aspect of the wrist and its contra-lateral mirror points.

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Table 1: Mean data and between-sides mean differences (95% confidence interval) for Quantitative Sensory Testing (QST) in the trigger point (TrP) area and its contra-lateral mirror point

	TrP area	**Contra-lateral Mirror Point**	**Mean Difference (95%CI)**	**SMD**
Cold Detection Threshold (ºC)	30.7 (30.3, 31.1)	30.6 (30.2, 31.0)	0.1 (-0.3, 0.5)	0.10
Warm Detection Threshold (ºC)	34.3 (33.8, 34.8)	34.3 (33.7, 34.9)	0.0 (-0.5, 0.5)	0.00
Cold Pain Threshold (ºC)	23.3 (20.8, 25.8)	22.8 (20.2, 25.4)	0.5 (-0.5, 1.5)	0.04
Heat Pain Threshold (ºC)	40.6 (39.1, 42.1)	39.7 (37.5, 41.9),	0.9 (-1.0, 2.8)	0.21
Mechanical Detection Threshold (mN)	2.0 (1.8, 2.2)	2.3 (2.1, 2.5)	-0.3 (-0.5, -0.1)*	0.55 #
Mechanical Pain Threshold (mN)	32.7 (18.9, 46.5)	30.2 (16.7, 43.7)	2.5 (-1.6, 6.6)	0.26
Vibration Threshold (μm)	1.7 (1.0, 2.4)	1.0 (0.4, 1.7)	0.7 (0.4, 1.0)*	0.75 #
Pressure Pain Thresholds (kPa)	227.7 (193.1, 262.3)	251.7 (217.1, 286.3)	-24.0 (-35.3, -12.7)*	0.54 #

Confidence intervals that do not contain 0 are marked with * as they are statistically significant to the $p < 0.05$ level. The SD and standardised mean difference (SMD) for the comparisons are also presented.

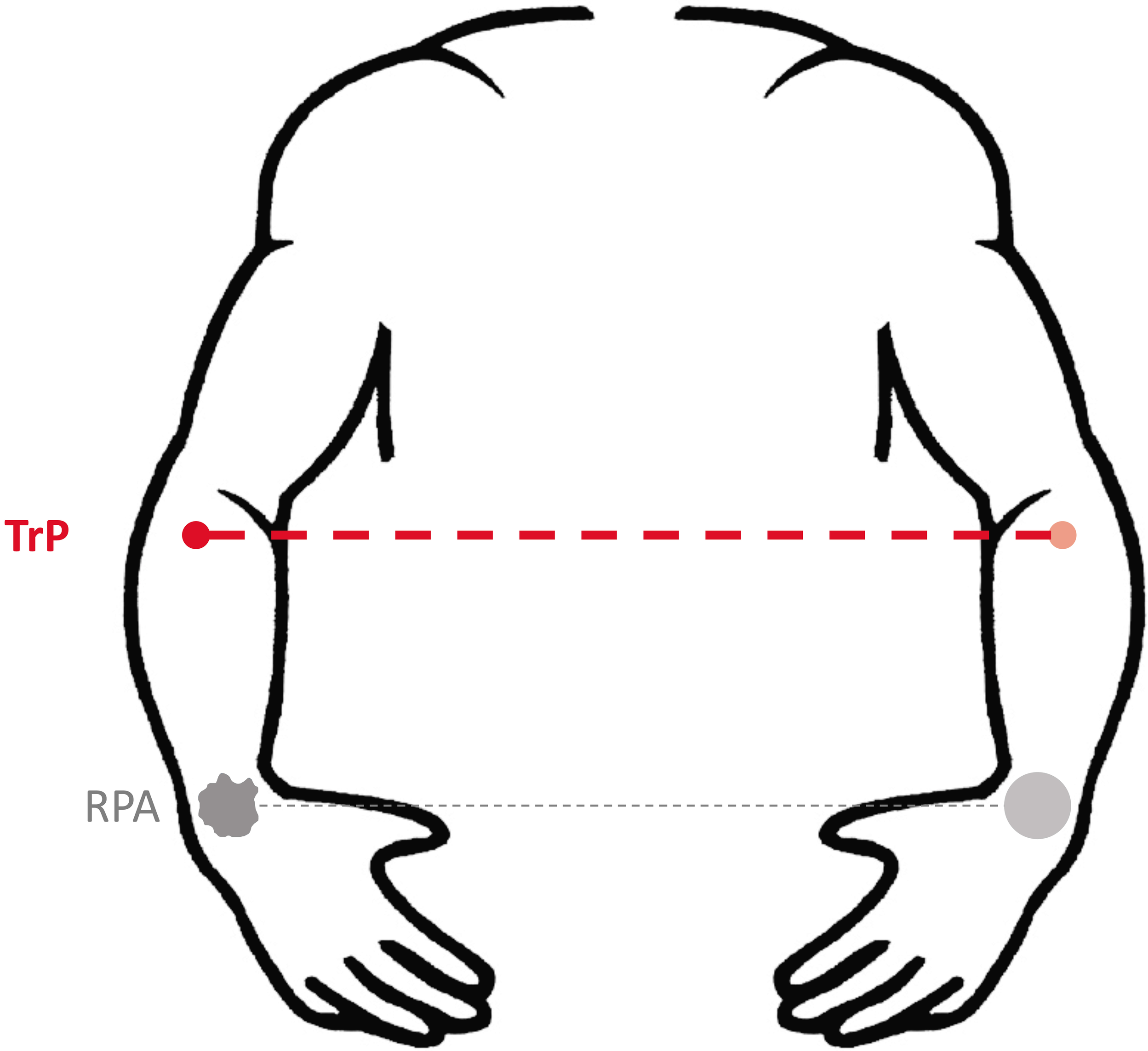
SMD of reasonable magnitude (moderate effect size);

Table 2: Mean data and between-sides mean differences (95% confidence interval) for Quantitative Sensory Testing (QST) in the referred pain area (Ref P) and its contra-lateral mirror area

	Ref P area	**Contra-lateral Mirror Area**	**Mean Difference (95%CI)**	**SMD**
Cold Detection Threshold (ºC)	30.3 (29.8, 30.8)	30.5 (30.2, 30.8)	-0.2 (-0.8. 0.4)	0.19
Warm Detection Threshold (ºC)	35.0 (34.4, 35.6)	34.4 (33.7, 35.1)	0.6 (-0.2, 1.4)	0.27
Cold Pain Threshold (ºC)	24.2 (21.9, 26.5)	23.6 (21.2, 26.0)	0.6 (-2.3, 3.5)	0.08
Heat Pain Threshold (ºC)	42.2 (40.7, 43.7)	40.5 (38.6, 42.4)	1.7 (-0.2, 3.6)	0.35
Mechanical Detection Threshold (mN)	1.8 (1.6, .20)	1.7 (1.5, 1.9)	0.1 (-0.1, 0.3)	0.21
Mechanical Pain Threshold (mN)	44.2 (26.6, 61.8)	36.5 (17.3, 53.8)	7.7 (2.5, 12.9)*	0.42 #
Vibration Threshold (μm)	0.8 (0.5, 1.1)	0.5 (0.3, 0.7)	0.3 (0.05, 0.55)*	0.55 #
Pressure Pain Thresholds (kPa)	295.9 (245.3, 346.5)	286.2 (235.6, 336.8)	9.7 (-18.1, 37.5)	0.15

Confidence intervals that do not contain 0 are marked with * as they are statistically significant to the $p < 0.05$ level. The SD and standardised mean difference (SMD) for the comparisons are also presented.

SMD of reasonable magnitude (moderate effect size);


TrP
RPA