Temporal summation of repetitive mechanical stimulation in patients with painful temporomandibular joints and healthy controls

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Abstract

Aim: This study was conducted to test segmental and extra-segmental temporal summation (TS) effects of repetitive mechanical stimulation in patients with painful temporomandibular joints (TMJ) and healthy individuals.

Methods: Twenty patients with unilateral pain in the TMJ and 20 gender- and age-matched healthy controls were included. A modified Quantitative Sensory Testing (QST) protocol was performed including pressure pain thresholds (PPT), mechanical pain thresholds (MPT), and numerical rating scale (NRS) scores of TS effects of 10 repeated 0.5 kg, 1.0 kg pressure stimuli and pinprick stimuli were determined as wind-up ratios (WUR) on the glabrous skin of the dominant hand (extra-segmental) and bilaterally in the TMJ region. Kruskal-Wallis test was used for data analysis.

Results: The PPT and MPT were significantly lower on painful TMJs compared to non-painful TMJs (P=0.001) and control TMJs (P=0.001). WUR of repetitive mechanical stimulation on painful TMJs was higher compared to control TMJs ($P \leq 0.012$). Non-painful TMJs also had significantly higher WUR of pinprick stimuli compared to control TMJs (P=0.008). Except the WUR of repetitive mechanical stimulation (P=0.030) no significant differences were detected at the hand for any of the test parameters between the two groups ($P \geq 0.05$).

Conclusion: Patients with unilateral TMJ pain have segmentally, but not extra-segmentally, increased sensitivity to mechanical stimuli including facilitated temporal summation mechanisms at segmental as well at extra-segmental sites.

1. Introduction

Articular disorders in the temporomandibular joints (TMJs) include a group of conditions associated with pain (arthralgia) in the TMJ region, internal derangements of the disc-condyle complex as well as degenerative joint diseases[1]. TMJ pain is often related to function and jaw movements during chewing, talking, and yawning. The diagnosis is based on a main complaint of pain in the TMJ region and pain evoked by palpation of the TMJ and during functional movements i.e., jaw opening, lateral, and protrusive jaw movements[2, 3]. Manual palpation of the TMJ region is used in the clinic to confirm the location and extent of pain and is, indeed, essential for the diagnosis according to the Diagnostic Criteria for TMDs (DC/TMD)[2, 4]. However, standardization of pressure during manual palpation is difficult [4–6] and palpometers (Sunstar Suisse) have been suggested to decrease variability of the test procedure[7, 8].

Temporal summation (TS) of painful stimuli is a substitute measure of wind-up in humans as the repetitive, low frequency stimulus will lead to increased ratings of pain [9]. The temporal and spatial integration of postsynaptic potentials generated by these nociceptive afferent fibers leads to the temporal recruitment of second order central neurons and the following processing and modulation of nociceptive activity within the cortex in order to finally be expressed as pain by the individual [10]. Temporal integration of nociceptive activity is characteristic of the nociceptive system and moderate temporal summation of deep painful stimuli can, indeed, be observed under normal conditions[11]. TS in other joints and regions have been discussed extensively[12–15]. However, mechanical TS effects to exogenous stimuli applied to the painful area (segmental effects) in patients with painful TMJs have not been not sufficiently studied using contemporary techniques and guidelines while some studies have tested mechanical stimuli TS effects on patients with osteoarthritis in other parts of the body. [16, 17].

The purpose of present study was to describe the effect of TS of repetitive mechanical stimulation in patients with painful TMJs and matched controls with the hypothesis that TS would be increased on painful TMJs but not on an extra-segmental control site (hand).

2. Materials And Methods

2.1. Participants

Twenty patients (5 men and 15 women, mean age 38.3 years old) with unilateral TMJ pain were chosen from patients referred to the TMD Clinic, Stomatology Hospital of Jiangsu Province, P.R.C. All patients included in the study presented with a major complaint of a strictly unilateral painful TMJ. The inclusion criteria for the patient group were: (a) complaints of spontaneous pain or pain on movements in the TMJ (b) pain on the same side initiated by palpation of the lateral pole or posterior attachment of the TMJ. Exclusion criteria: (a) history of treatment of TMD during three months, such as medication, splint therapy, intra-articular hyaluronic acid injection; (b) use of current medication such as analgesics or central nervous system affecting drugs;(c) with coarse crepitation (osteoarthritis). No patients fulfilled the criteria for myalgia or myofascial pain according to the DC/TMD. A total of 103 patients were screened before 20 unilateral TMJ pain patients could be recruited.

Twenty healthy age- and gender-matched volunteers (5 men and 15 women, mean age 30.3 years old) were recruited from staff and students at Nanjing Medical University as the control group. The exclusion criteria were: (a) with history of trauma, surgery, peripheral neuropathy, and pain involving the TMJ; (b) use of current medications.

All patients and participants were investigated and diagnosed using the DC/TMD by the same calibrated examiner. The study was approved by the Human Research Ethics Committee of Nanjing Medical University (No: PJ2016-006-01).

2.2. Procedure

QST parameters including mechanical pain threshold (MPT), pressure pain threshold (PPT) were assessed following the protocol of DFNS (German Research Network on Neuropathic Pain) [18]. Numerical rating scale (NRS) scores of single and repeated stimulation given by pinprick and palpometers (0.5 kg and 1.0 kg) were measured on the glabrous skin of the right hand and bilaterally in the TMJ region in all participants. NRS score from 0 = no pain to 100 = worst pain imaginable was utilized for assessment of the magnitude of painful sensations produced by the different types of mechanical stimulation. Experiments were carried out in a quiet laboratory with participants sitting on a chair as required per the protocol.

2.3. Quantitative sensory testing

2.3.1. MPT and TS of pinprick stimulation

To detect the MPT, nine custom-made pinprick stimulators (Aalborg University, Denmark) were used to deliver pinprick stimulation [19]. Each stimulator had a flat contact surface of 0.2 mm. To conduct the pinprick tests, the stimulator was applied perpendicular to the examination site with a contact time of approximately 1 s. The instrument, which delivered a force, which the participant reported as “just barely painful”, was chosen. The “method of limits” technique was used to measure the MPT [20]. The pinprick stimulators used in the MPT determinations were also applied for the TS assessment. To measure the TS [21, 22] of repetitive pinprick stimulation, the perceived magnitude of a series of 10 pinprick stimulations was divided by a single pinprick stimulus with the same force, repeated at a rate of 1 Hz [23]. All participants were asked to score pain on an NRS ranging from 0 (no pain) to 100 (worst pain imaginable) after the 1st and 10th stimuli, and the NRS scores were recorded as NRS1 and NRS10, respectively. Three sessions were conducted at each site, with an interval of 5 minutes between sessions. The average value of three measurements was recorded. WUR compared the NRS10 within the NRS1 as the ratio. The WUR scores (NRS10/NRS1) and delta NRS scores (NRS10 minus the NRS1) at each site were calculated for later analysis [24]. The value “10” was added to each NRS score to avoid the loss of “0” NRS values [25].

2.3.2. PPT and TS of pressure stimulation

The PPT was used to test deep pain sensitivity [26]. It was assessed by a handheld pressure algometer (Algometer, MEDOC, Israel) to test the deep pain sensitivity applied to the lateral pole of the bilateral TMJs and hand. The PPT was defined as the amount of pressure (kPa) and determined with a constant application rate of 30 kPa/s and a probe diameter of 10 mm [27], which the participant first perceived to be just barely painful [28]. To determine the TS of pressure stimulation and simulate the finger palpation, two standardized palpometers (0.5 and 1.0 kg) were used to control the pressure[22, 29, 30]. The parameters described above were measured on the glabrous skin of the right hand and bilaterally in the TMJ region for single and 10 repeated stimuli to determine the TS of the pressure stimulation. NRS scores and WUR were recorded and calculated in the same way as described above.

2.4. Data processing

Descriptive statistics were used first to summarize all measurements with median and interquartile ranges (IQR). Parameters included PPT, MPT, NRS scores and WURs were used to compare the TMJ pain patients to the healthy controls. All calculations were performed with the SPSS software version 20.0 (IBM, USA). As data were non-normally distributed, Kruskal-Wallis tests were used for data analysis. The significance level was set at 0.05.

Further, Z-scores of WURs, MPTs and PPTs of the patient group were calculated with the data from the healthy control group as the reference data. The formula is: Z-score = $(\text{Mean}_{\text{single patient}} - \text{Value}_{\text{controls}})/\text{SD}_{\text{controls}}$[31, 32]. The 95% confidence interval (CI) of a normal distribution is defined by the expression: $95\%\text{CI} = \text{Mean}_{\text{controls}} \pm 1.96\text{SD}_{\text{controls}}$. A patient with Z-score > 1.96 or <-1.96 is considered pathological [33]. If the Z-score of MPT, PPT is > 1.96 or the Z-score of WUR is < -1.96, the patient is more sensitive to stimuli than the control group (hyperalgesia, paresthesia, and allodynia), and then the function is improved, while Z-score of MPT, PPT is < -1.96 or the Z-score of WUR is > 1.96 indicates decreased sensitivity (hypoalgesia and hypoesthesia low hyperalgesia)[34].

3. Results

All the 20 patients and 20 healthy participants completed the study (Fig. 1). The comparison of all variables including MPT, PPT, WUR and NRS scores of palpation test and pinprick test was performed between the two groups and the three sites; bilateral TMJs and the glabrous skin of the right hand. The median values and interquartile ranges of MPT, PPT on different sites, comparisons between and within groups are presented in Table 1. The median values and interquartile ranges of NRS1 scores, NRS10 scores and WURs (pinprick, 0.5 kg, 1.0 kg) on different sites, inter-/intra-group comparisons are presented in Table 2. Figure 1 presents the flow chart of the study. Figure 2 presents the Z-scores of MPT, PPT and WUR data at different sites. Figure 3 presents the NRS1 and NRS10 scores at bilateral TMJs of the two groups.

Table 1
MPT and PPT on TMJs and hands of each participant and P values of inter-/intra-group comparisons.

Parameters	**MPT (kPa)**	**PPT (kPa)**
Patients (n = 20)		
P-TMJ	90.5 (0)	198.7 (23.8)
NP-TMJ	101.6 (66.4)	260.7 (107.9)
Hand	204.6 (98.6)	398.4 (116)
P-TMJ vs NP-TMJ	0.06	0.007#
Controls (n = 20)		
L-TMJ	90.5 (37.5)	218.5 (37.5)
R-TMJ	101.6 (62.5)	253.4 (172.5)
Hand	143.7 (54)	436.05 (211.1)
L-TMJ vs R-TMJ	0.982	0.289
Comparisons between groups		
Hand	0.118	0.513
C-TMJ vs NP-TMJ	0.715	0.593
C-TMJ vs P-TMJ	0.005#	< 0.001#

Table 2
NRS data (NRS1, NRS and WUR) of mechanical stimulation on bilateral TMJs and hands of each participant and P values of inter-/intra- group comparisons

Parameters	Pinprick			0.5 kg			1.0 kg		
	NRS1	NRS10	WUR	NRS1	NRS10	WUR	NRS1	NRS10	WUR
Patients									
P-TMJ	20 (20)	55 (40)	2.8 (1.4)	5 (10)	17.5 (25)	2.4 (1.9)	12.5 (10)	40 (32.5)	2.4 (1.31)
NP-TMJ	10 (22.5)	30 (37.5)	7.5 (15)	5 (5)	5 (10)	1 (0.4)	10 (5)	12.5 (10)	1.8 (1.5)
Hand	10 (15)	17.5 (30)	1.87 (0.1)	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)	1 (0)
P-TMJ vs NP-TMJ	0.272	< 0.001#	0.002#	0.099	0.001#	0.012#	0.018#	0.001#	0.001#
Controls									
L-TMJ	5 (5)	20 (10)	1.9 (0.9)	0 (0)	0 (0)	1 (0)	0 (5)	5 (5)	3.9 (5)
R-TMJ	5 (5)	12.5 (18.8)	2.6 (1.3)	0 (0)	0 (0)	1 (0)	5 (5)	7.5 (5)	1.8 (5)
Hand	10 (18.8)	22.5 (38.8)	1.9 (1.9)	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)	1 (0.6)
L-TMJ vs R-TMJ	0.988	0.908	0.605	0.39	1	1	0.302	0.626	0.333
Comparisons between groups									
Hand	0.802	0.561	0.030#	0.324	1.000	0.324	0.520	0.350	0.731
C-TMJ vs NP-TMJ	0.033#	0.354	0.602	0.001#	0.005#	0.880	0.000#	0.022#	0.013#
C-TMJ vs P-TMJ	0.001#	< 0.001#	0.789	< 0.001#	< 0.001#	0.295	< 0.001#	< 0.001#	0.684

3.1. MPT

The MPTs at the painful TMJs were significantly lower (more sensitive) than the control TMJs (P = 0.005, Table 1). The MPTs at the non-painful TMJs were similar to the control TMJs (P = 0.715, Table 1).

3. 2. Ppts

There was no significant difference between groups in PPTs on the hands (P=0.473, Table 1) and non-painful TMJs (P = 0.593, Table 1). Significantly lower PPTs (higher sensitivity) were detected at the painful TMJs compared with the control TMJs (P < 0.001, Table 1) and non-painful TMJs (P = 0.007, Table 1).

3.3. Pinprick stimulation

3.3.1. Single pinprick stimulus

There was no significant difference in NRS1 score of a single pinprick stimulus assessed on the hands (P = 0.802, Table 2) between the two groups. There was no significant intragroup difference in NRS1 scores of a single pinprick stimulus on TMJs within the two groups ($P_{Patients}$=0.272, $P_{Controls}$=0.998, Table 2). However, NRS1 scores of single pinprick stimuli on painful TMJs (P = 0.001, Table 2) and non-painful TMJs (P = 0.033, Table 2) were both higher than control TMJs.

3.3.2 Repetitive pinprick stimuli

TS data (NRS10, WUR) of repetitive pinprick stimulation on the hands were similar between the two groups (P = 0.561, Table 2). TS data on painful TMJs were higher (more sensitive) than non-painful TMJs ($P < 0.001$, Table 2) and control TMJs ($P < 0.001$, Table 2).

3.4. Palpation stimulation

3.4.1. Single pressure stimulus

There was no significant difference in NRS1 scores of single 0.5 kg pressure stimulation (P = 0.099, Table 2). Significant difference was observed in NRS1 scores of single 1.0 kg pressure stimulation (P = 0.001, Table 2) between painful TMJs and non-painful TMJs. A significant difference was observed between the two groups of single pressure stimulation (0.5 kg or 1.0 kg) assessed on both TMJs ($P < 0.001$, Table 2). There was no significant difference between the two groups in NRS scores of single pressure stimulation (0.5 kg or 1.0 kg) on the hand ($P_{0.5\ kg}$=0.317, $P_{1.0\ kg}$=0.917, Table 2).

3.4.2. Repetitive pressure stimuli

There was a significant difference of TS data of repetitive pressure stimulation of 0.5 kg (P_{NRS10}=0.001, P_{WUR}=0.012, Table 2) and 1.0 kg (P_{NRS10}=0.001, P_{WUR}=0.001, Table 2) between painful TMJs and non-painful TMJs. Painful TMJs were more sensitive to repetitive pressure stimuli (0.5 kg and 1.0 kg) than control TMJs. NRS10 scores of repetitive pressure stimuli (0.5 kg and 1.0 kg) on painful TMJs were significantly higher than control TMJs ($P < 0.005$, Table 2). The difference in WUR of repetitive mechanical stimulation (P_{WUR}=0.030, Table 2) was detected at the hand between the two groups.

3.5. Z-score profiles

Z-scores of MPT and PPT > 1.96 or the Z-score of WUR < -1.96 represent a gain-of-function (more sensitive). Z-scores of MPT and PPT < -1.96 or Z-scores on WUR > 1.96 indicates a loss-of-function referring to a lower sensitivity (less sensitive). Figure 2 shows the Z-scores of MPT, PPT and WUR of repetitive mechanical stimulation (pinprick, 0.5 kg, 1.0 kg) calculated for the hands (Fig. 2B) and painful and non-painful TMJs (Fig. 2A). Obvious pathological WUR-pin, WUR-0.5 kg and WUR-1.0 kg on P-TMJ (Fig. 2A) could be detected (Z-score < -1.96), which mean that painful TMJs were more sensitive to TS effect of mechanical stimulus than control TMJs.

4. Discussion

Temporal summation (TS) or wind-up is cited as a central spinal (trigeminal) mechanism in which repetitive painful stimulation results in a slow temporal summation that causes increased pain reports [13, 35]. Several pieces of evidence strongly suggest that TS and wind-up share a common central mechanism [36]. It is a widely applicable quantitative sensory test method that invokes neural mechanisms related to the pain-promoting process, which is believed to be the result of C-fiber-induced dorsal horn neuron responses[24]. It can serve as both an amplification and maintenance mechanism for pain and central sensitization[37]. Nevertheless, as wind up is mediated by central mechanisms [38], it can be used in human studies to determine the degree of CNS excitability to nociceptive stimulation[37, 39]. Several studies have found evidence of abnormal wind-up and slower dissipation of painful after-sensations in patients with fibromyalgia, a widespread pain condition that is comorbid with painful temporomandibular disorders (TMDs) [15, 40, 41].

TMDs are common pain problems in the population with uncertain pathophysiology and mechanisms but with good evidence for increased sensitivity to mechanical stimulation[31, 42]. The pressure pain threshold (PPT) was used to test deep pain sensitivity mediated through C- or Aδ-fibers[26]. Mechanical pain threshold (MPT) was used as a test for Aδ-fiber mediated hyper- or hypoalgesia to pinprick stimulation. This study indicated that patients with painful TMJs might be more sensitive to sharp mechanical stimulation with lower MPTs on painful TMJs compared to healthy controls ($P = 0.005$, Table 1).

Significant differences still existed between the TMJs in patients and controls in terms of NRS ratings for repetitive stimulation ($P < 0.05$, Table 2). Indeed, it is commonly reported that somatosensory abnormalities can be detected in patients with painful TMJs both inside and outside the area of primary pain, which strongly indicates disturbances in the central processing of somatosensory stimulation[31]. We hypothesized the patients with TMJ pain would demonstrate abnormal wind-up of second pain as an indication of central sensitization and it was confirmed by the results. Pain catastrophizing could be elicited by repetitive gentle palpation (0.5 kg) stimulation on the non-painful TMJs (increased NRS10 scores), which may indicate that repetitive stimulation should be avoided during a clinical TMJ examination. In addition, the WURs of repetitive pressure stimulation at higher intensities (1.0 kg) at the painful TMJs were similar to the control TMJs ($P = 0.684$, Table 2) while on the non-painful TMJs the WUR were significantly lower than the control TMJs ($P = 0.013$, Table 2). This finding may be related to the high NRS scores for single pressure stimulation, which therefore decreases the ratio, i.e., the WUR has inherent problems when both NRS scores to single and repeated stimuli are increased.

Manual palpation is of great importance in clinical examination of TMD and other musculoskeletal pain conditions in assessment of deep pain sensitivity in muscles and joints [2]. It was suggested that palpation-induced pain in the masticatory muscles might lead to different diagnosis among painful TMDs, primary headaches and bruxism[43]. Previous research showed that manual palpation at light force levels (0.5 kg, 1.0 kg) is related to a tendency to “overshoot” the pressure[30]. In order to get a high level of reliability, two standardized palpometers (0.5,1.0 kg) were used to deliver a more accurate pressure stimulation during palpation. Interestingly, when standardized mechanical stimulation was applied to the non-painful TMJs, the patients were more sensitive to pressure stimulation (0.5 kg and 1.0 kg) and single mechanical stimulation, which might be associated with a sensitization in patients with chronic pain in line with several other studies [44, 45]. In addition, the patients’ painful TMJs were more sensitive to the stimulations described above except the repetitive sharp stimulation and the more intense (1.0 kg) blunt stimulation than the controls, which demonstrated that pressure of 0.5 kg might be appropriate to examine the TMJs in clinical work and repetitive palpations should be avoided during examination of painful TMJs.

Conclusion

The present study found that patients with unilateral TMJ pain have segmentally, but not extra-segmentally, increased sensitivity to mechanical stimuli including facilitated temporal summation mechanisms at segmental as well at extra-segmental sites. Both peripheral and central sensitization processes appear to be ongoing in patients with unilateral TMJ pain.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the guidelines set out in the Declaration of Helsinki II and informed consent was obtained from all participants prior to participation. The study was approved by the Human Research Ethics Committee of Nanjing Medical University (No: PJ2016-006-01).

Consent for publication

All authors read the final manuscript and approved the publication.

Availability of data and material

Data and materials supporting are available from corresponding authors.

Competing interests

The authors state that they have no competing interests.

Authors' contributions

Xiaojing Xi drafted the manuscript and data analysis. Weina Zhou designed the study and prepared the figures and charts. Jinglu Zhang completed the clinical examination and diagnosis of all participants. Linfeng Yu was responsible for laboratory tests and data collection. Kelun Wang and Peter Svensson participated in the design of the study and revised the manuscript. Xiaojing Xi and Weina Zhou contributed equally to this work and

should be considered co-first authors.

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Figures

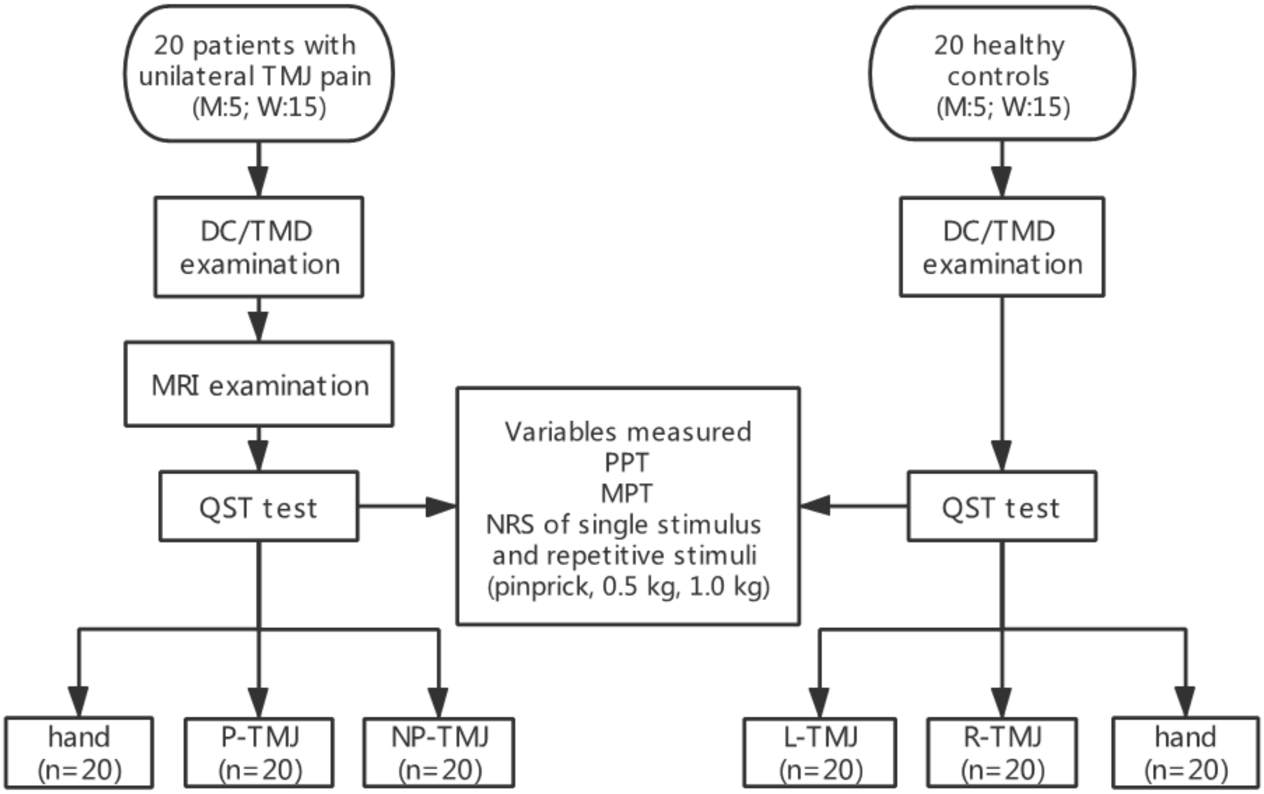

Figure 1

Flow-chart illustrating the protocol of the study. M=man. W=woman. TMJ=temporomandibular joint. DC/TMD Diagnostic Criteria for temporomandibular disorders. MRI=magnetic resonance imaging. QST=quantitative sensory testing. PPT=pressure pain threshold. MPT=mechanical pain threshold. NRS=numerical rating score.

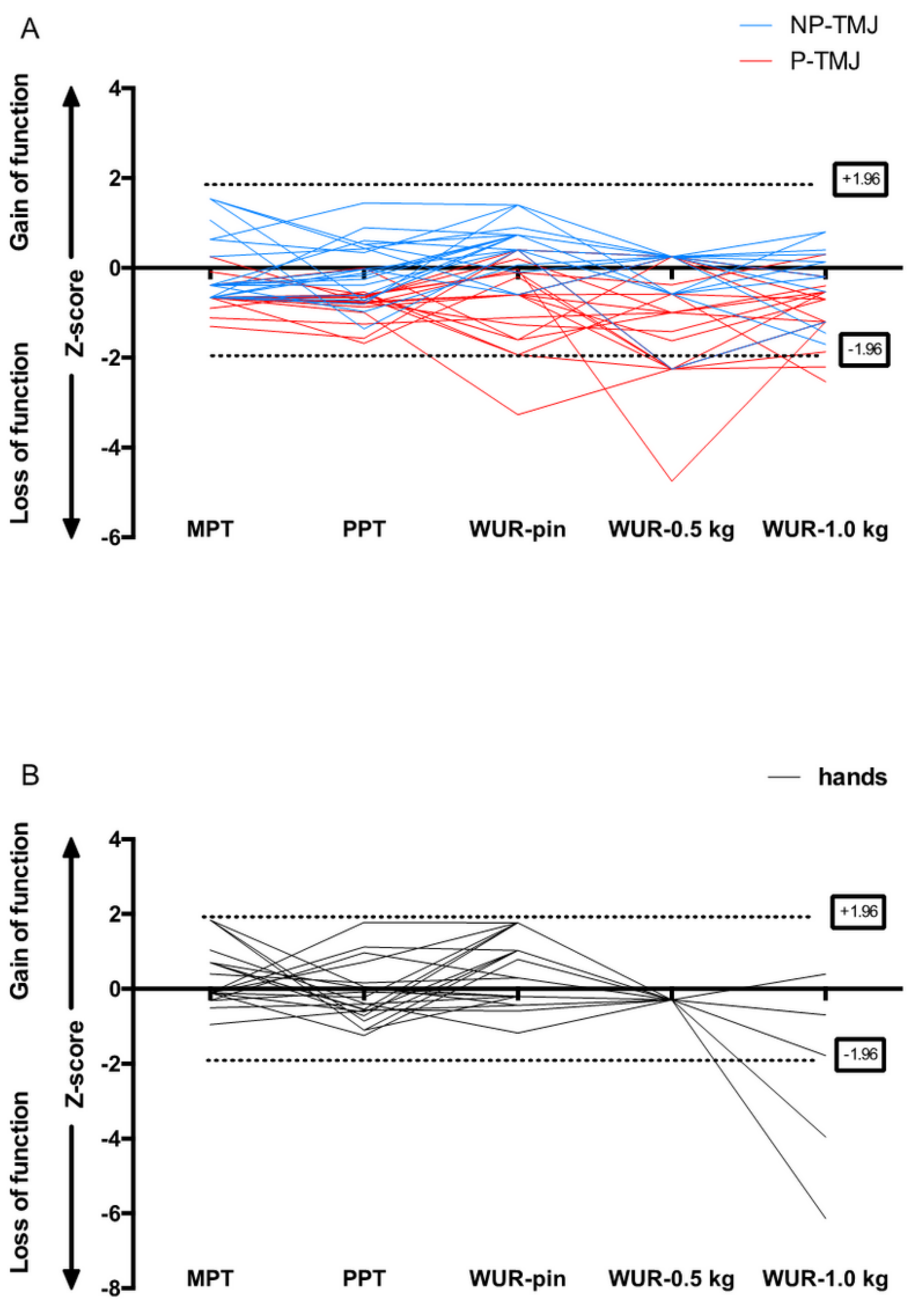

Figure 2

Somatosensory Z-score profiles of patients with painful TMJs. The zone between the two lines (−1.96 < z < 1.96) is the normal range based on the healthy material. The positive Z-values represented a gain of sensory function; negative Z-scores represented a loss of sensory function of mechanical pain threshold (MPT), pressure pain threshold (PPT), wind-up ratio of pinprick stimulation (WUR-pin), wind-up ratio of 0.5 kg palpation (WUR-0.5 kg) and wind-up ratio of 1.0 kg palpation (WUR-1.0 kg). A. Z-score profiles of painful TMJs and non-painful TMJs of patients. The reference data was the somatosensory profiles of controls' TMJs. B. Z-score profiles of patients' hands. The reference data was the somatosensory profiles of controls' hands.

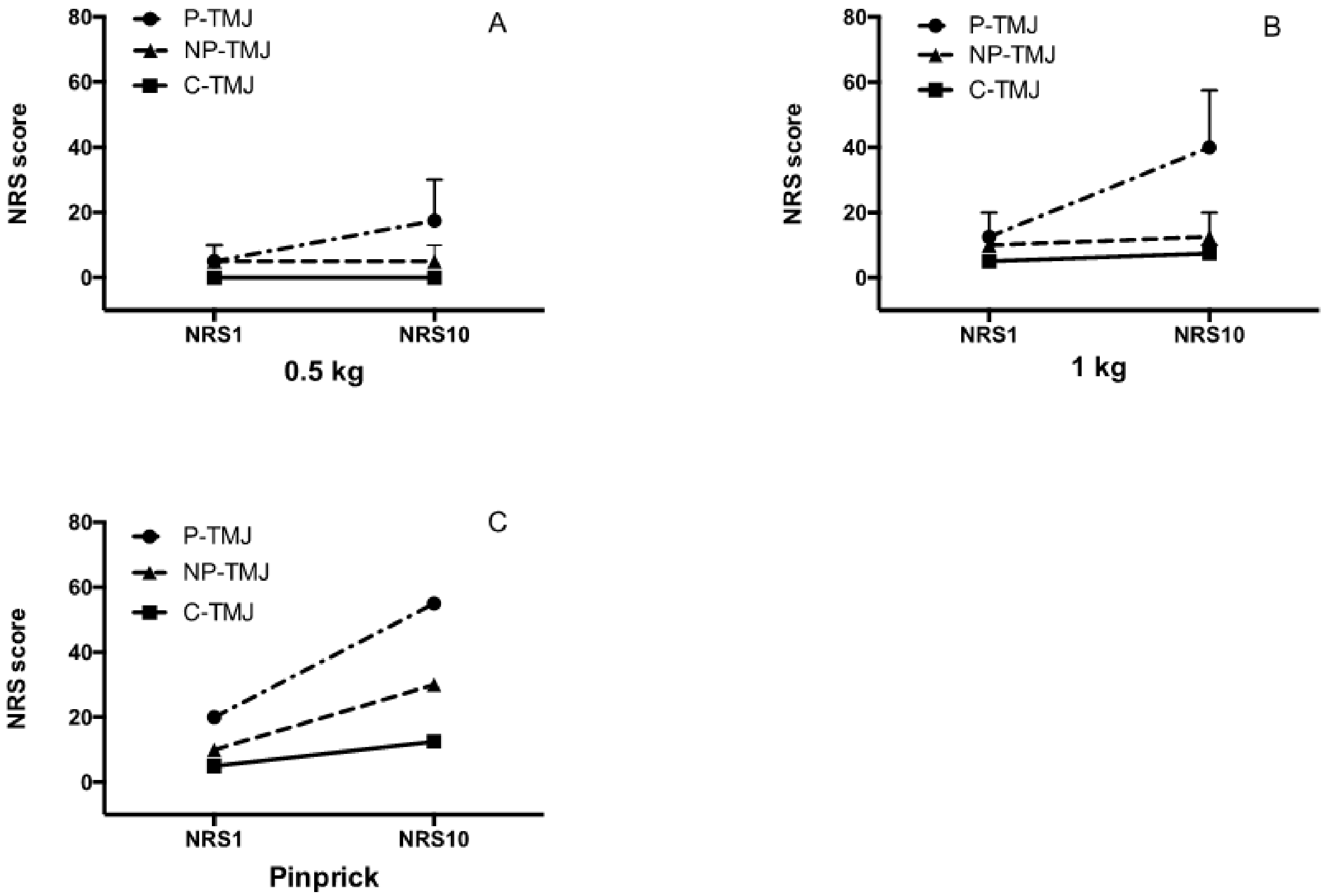

Figure 3

edians and interquartile ranges (IQR) NRS scores in response to single stimulus and repetitive stimuli on TMJs of patients and controls. (A. 0.5 kg pressure palpation; B.1.0 kg pressure palpation; C. pinprick). P-TMJ indicates patients' painful TMJs; NP-TMJ indicates patients' non-painful TMJs; C-TMJ indicates controls' TMJs. NRS1 means NRS score of single stimulus; NRS10 indicates NRS score of repetitive stimuli.