

# Temporal Summation of Repetitive Mechanical Stimulation in Patients with Painful Temporomandibular Joints and Healthy Controls

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**Objective:** The present study aimed to preliminarily explore the temporal summation (TS) response to repetitive mechanical stimulation in patients with temporomandibular joint disorders (TMD).

**Patients and 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 (segmental). Kruskal–Wallis test and Wilcoxon test were used for data analysis.

**Results:** Painful TMJs had significantly lower PPT and MPT compared to controls ( $p \leq 0.002$ ) and non-painful TMJs ( $p \leq 0.001$ ). Their WUR to repetitive mechanical stimulation was higher than control TMJs ( $p \leq 0.033$ ). Non-painful TMJs showed elevated WURs to pinprick stimuli compared to controls ( $p = 0.018$ ). At the hand, only MPT differed ( $p = 0.032$ ).

**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 as extra-segmental sites.

**Significance:** Segmental and extra-segmental temporal summation of repetitive mechanical stimulation were tested in patients with painful TMJ and healthy individuals. The finding suggests that both peripheral and central sensitization processes are involved in patients with unilateral TMJ pain.

**Keywords:** temporomandibular joints, temporal summation of pain, quantitative sensory testing, painful temporomandibular disorders

## 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.<sup>1,2</sup> 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 ie, jaw opening, lateral, and protrusive jaw movements.<sup>2–4</sup> 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).<sup>3,5</sup> However, standardization of pressure during manual palpation is difficult<sup>5–7</sup> and palpometers have been suggested to decrease variability of the test procedure.<sup>8–10</sup>

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.<sup>11</sup> 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.<sup>12</sup> Temporal integration of nociceptive activity is a characteristic of the nociceptive system and moderate temporal summation of deep painful stimuli can, indeed, be observed under normal conditions.<sup>13</sup> TS in other joints and regions have been discussed extensively.<sup>14–17</sup> However, mechanical TS effects to exogenous stimuli applied to the painful area (segmental effects) in patients with painful TMJs have not been 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.<sup>18,19</sup> Yang et al found that 85.3% of Chinese patients exhibited at least one somatosensory abnormality at the painful TMJ, particularly gain-of-function for pressure and punctate pain stimuli, and loss-of-function for mechanical and vibration detection.<sup>20</sup> While previous research had focused mainly on Caucasian populations and reported similar patterns in both trigeminal and extra-trigeminal regions, studies involving Chinese or East Asian populations have been relatively limited. Somatosensory function has been shown to vary significantly across different anatomical regions. For example, Yang et al reported that trigeminal-innervated areas (eg, infraorbital and mental regions) are significantly more sensitive to thermal and mechanical stimuli than distal areas such as the hand, whereas the hand demonstrates higher sensitivity in vibration detection.<sup>21</sup> These findings underscore the importance of site-specific assessment. In our study, the hand was included as an extra-segmental, trigeminal-independent control site to help differentiate localized (segmental) sensitization in the TMJ region from potential widespread (central) sensitization.

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).

## Materials and Methods

### 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. All participants were screened for major psychiatric disorders during clinical interviews. Subjects currently using medications affecting the central nervous system were excluded to minimize psychological confounding factors. All participants signed informed consent. This study was conducted in accordance with the Declaration of Helsinki and was approved by the Human Research Ethics Committee of Nanjing Medical University (No. PJ2016-006-01).

### Procedure

QST parameters, including mechanical pain threshold (MPT) and pressure pain threshold (PPT), were assessed following the protocol of DFNS (German Research Network on Neuropathic Pain).<sup>22</sup> Numerical rating scale (NRS) scores of single and repeated stimuli given by pinprick and palpometers (0.5 kg, 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.

## Quantitative Sensory Testing

### MPT and TS of Pinprick Stimulation

To detect the MPT, nine custom-made pinprick stimulators (Aalborg University, Denmark) were used to deliver pinprick stimulation.<sup>23</sup> Each stimulator had a flat contact surface of 0.2 mm diameter. 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.<sup>24</sup> The pinprick stimulators used in the MPT determinations were also applied for the TS assessment. To measure the TS<sup>25,26</sup> 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.<sup>27</sup> All participants were asked to score pain on an NRS ranging from 0 (no pain) to 100 (worst pain imaginable) after the 1<sup>st</sup> and 10<sup>th</sup> 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.

### PPT and TS of Pressure Stimulation

The PPT was used to test deep pain sensitivity.<sup>26,28</sup> 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,<sup>29</sup> which the participant first perceived to be just barely painful.<sup>30</sup> To determine the TS of pressure stimulation and simulate the finger palpation, two standardized palpometers (0.5 kg, 1.0 kg) were used to control the pressure,<sup>10,26,31</sup> which were vertically applied to the glabrous skin of the right hand and bilaterally in the TMJ regions by a single trained operator to deliver precisely controlled single stimuli and series of 10 repeated stimuli at 1 Hz frequency (1-second inter-stimulus intervals), ensuring consistent force vector application throughout all experimental procedures. After each stimulus, participants rated their pain intensity by NRS scores.<sup>32</sup> Each stimulus was followed by a 10-second rest interval, and each condition (single/repeated, 0.5 kg/1.0 kg) was repeated three times, with the average values used for analysis.

### WUR of Pinprick Stimulation and Pressure Stimulation

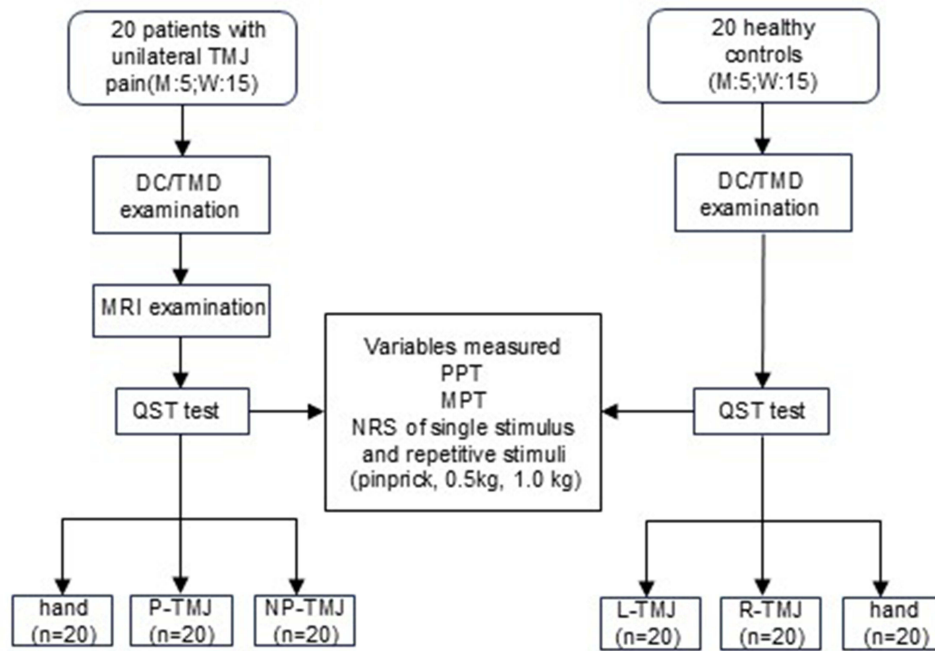
To determine the temporal summation (TS) of pinprick and pressure stimulations, the wind-up ratio (WUR) was calculated as  $WUR = NRS10/NRS1$ . To avoid division errors (eg, if NRS1 = 0), a value of 1 was added to all NRS scores prior to WUR calculation as previously described in QST literature.<sup>32</sup>

## Data Processing

The sample size was calculated with a risk of type I and type II errors of 5% and 20%, respectively, using a conservative estimate of 25% for intra-individual variation. Considering a drop-out rate of 20%, 20 subjects were needed in each group.

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 25.0 (IBM, USA). Due to the non-normal distribution of the data, Kruskal–Wallis tests and Wilcoxon tests were used for intergroup comparisons and intragroup comparisons, respectively. 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:  $Z\text{-score} = (\text{Mean}_{\text{single patient}} - \text{Value}_{\text{controls}}) / \text{SD}_{\text{controls}}$ .<sup>20,33</sup> The 95% confidence interval (CI) of a normal distribution is defined by the expression:  $95\% \text{ CI} = \text{Mean}_{\text{controls}} \pm 1.96\text{SD}_{\text{controls}}$ .



**Figure 1** Flow-chart illustrating the protocol of the study.

**Abbreviations:** 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 scale score; P-TMJ, patients’ painful TMJs; NP-TMJ, patients’ non-painful TMJs; L-TMJ, left TMJ of controls; R-TMJ, right TMJ of controls.

Somatosensory function in individuals with Z-score > 1.96 or < -1.96 was considered pathological.<sup>34</sup> 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 facilitated, while Z-score of MPT, PPT is < -1.96 or the Z-score of WUR is > 1.96 indicates decreased sensitivity (hypoalgesia and hypoesthesia).<sup>28</sup>

## Results

All the 20 patients and 20 healthy participants completed the study (Figure 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

**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		
P-TMJ	91.3 (13.0)	195.1 (33.1)
NP-TMJ	122.7 (36.2)	262.8 (63.4)
Hand	232.1 (80.6)	428.5 (112.6)
P-TMJ vs NP-TMJ	0.001 <sup>#</sup>	0.000 <sup>#</sup>
Controls (n = 20)		
L-TMJ	249.9 (86.6)	117.8 (46.2)
R-TMJ	285.5(92.5)	117.4 (36.8)
Hand	453.9 (130.88)	190.6 (83.3)
L-TMJ vs R-TMJ	0.733	0.003 <sup>#</sup>

(Continued)

**Table 1** (Continued).

Parameters	MPT (kPa)	PPT (kPa)
Comparisons between groups		
Hand	0.032 <sup>#</sup>	0.473
C-TMJ vs NP-TMJ	0.552	0.850
C-TMJ vs P-TMJ	0.001 <sup>#</sup>	0.002 <sup>#</sup>

**Notes:** MPT and PPT on TMJs and hands of each participant and P values of inter-/intra-group comparisons. Data is described in the manner of median (interquartile range). <sup>#</sup>Indicates P values with significantly difference between groups. C-TMJ = (L-TMJ+ R-TMJ)/2.

**Abbreviations:** MPT, mechanical pain threshold; PPT, Pressure Pain Threshold; NRS1, NRS given after 1 single stimulus; P-TMJ, painful TMJ of patients; NP-TMJ, non-painful TMJ of patients; L-TMJ, left TMJ of controls; R-TMJ, right TMJ of controls; C-TMJ, controls' TMJs.

**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			0.5kg			1.0kg		
	NRS1	NRS10	WUR	NRS1	NRS10	WUR	NRS1	NRS10	WUR
Patients									
P-TMJ	20 (12.5)	52.5 (24.3)	3.0 (1.3)	7.5 (8.2)	20.5 (20.6)	3.2 (2.4)	16 (9.5)	40.3 (20.9)	2.9 (2.0)
NP-TMJ	15.8 (13.0)	26.5 (18.4)	1.9 (1.1)	4.5 (5.4)	6.3(7.2)	1.6 (2.2)	10.3 (8.2)	19.9 (21.0)	2.1(1.4)
Hand	14.6 (10.8)	26 (21.6)	1.7(0.6)	0 (0)	0 (0)	1(0)	1(3.1)	5.5(13.2)	3.2(6.9)
P-TMJ vs NP-TMJ	0.009 <sup>#</sup>	0.000 <sup>#</sup>	0.000 <sup>#</sup>	0.010 <sup>#</sup>	0.000 <sup>#</sup>	0.005 <sup>#</sup>	0.003 <sup>#</sup>	0.000 <sup>#</sup>	0.005 <sup>#</sup>
Controls									
L-TMJ	20 (12.5)	20.9 (19.3)	3.9 (5.9)	0.3 (1.1)	1 (3.1)	1.5 (2.2)	2.5 (3.4)	8 (7.5)	4.4 (3.6)
R-TMJ	8.3 (7.8)	21.7 (20.7)	3.2 (2.9)	0 (0)	1 (4.5)	2 (4.5)	3.5 (3.7)	9.3 (10.5)	3.2 (2.8)
Hand	15.3 (14.1)	30.0 (21.5)	3.3 (3.0)	0.3 (1.1)	0 (0)	1.0 (0.2)	0.5 (1.5)	2.5 (5.3)	2.6 (4.6)
L-TMJ vs R-TMJ	0.713	0.952	0.799	0.317	1	0.655	0.102	0.102	0.244
Comparisons between groups									
Hand	0.989	0.429	0.078	0.317	1.000	0.317	0.917	0.926	0.796
C-TMJ vs NP-TMJ	0.076	0.361	0.018 <sup>#</sup>	0.000 <sup>#</sup>	0.001 <sup>#</sup>	0.270	0.000 <sup>#</sup>	0.004 <sup>#</sup>	0.217
C-TMJ vs P-TMJ	0.001 <sup>#</sup>	0.000 <sup>#</sup>	0.033 <sup>#</sup>	0.000 <sup>#</sup>	0.000 <sup>#</sup>	0.000 <sup>#</sup>	0.000 <sup>#</sup>	0.000 <sup>#</sup>	0.841

**Notes:** 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. Data is described in the manner of median (interquartile range). <sup>#</sup>Indicates P values with significantly difference between groups. C-TMJ = (L-TMJ+ R-TMJ)/2.

**Abbreviations:** NRS10, NRS scores given after 10 repeated stimuli; NRS1, NRS scores given after one single stimulus; WUR, wind-up ratio; P-TMJ, painful TMJ of patients; NP-TMJ, non-painful TMJ of patients; L-TMJ, left TMJ of controls; R-TMJ, right TMJ of controls.

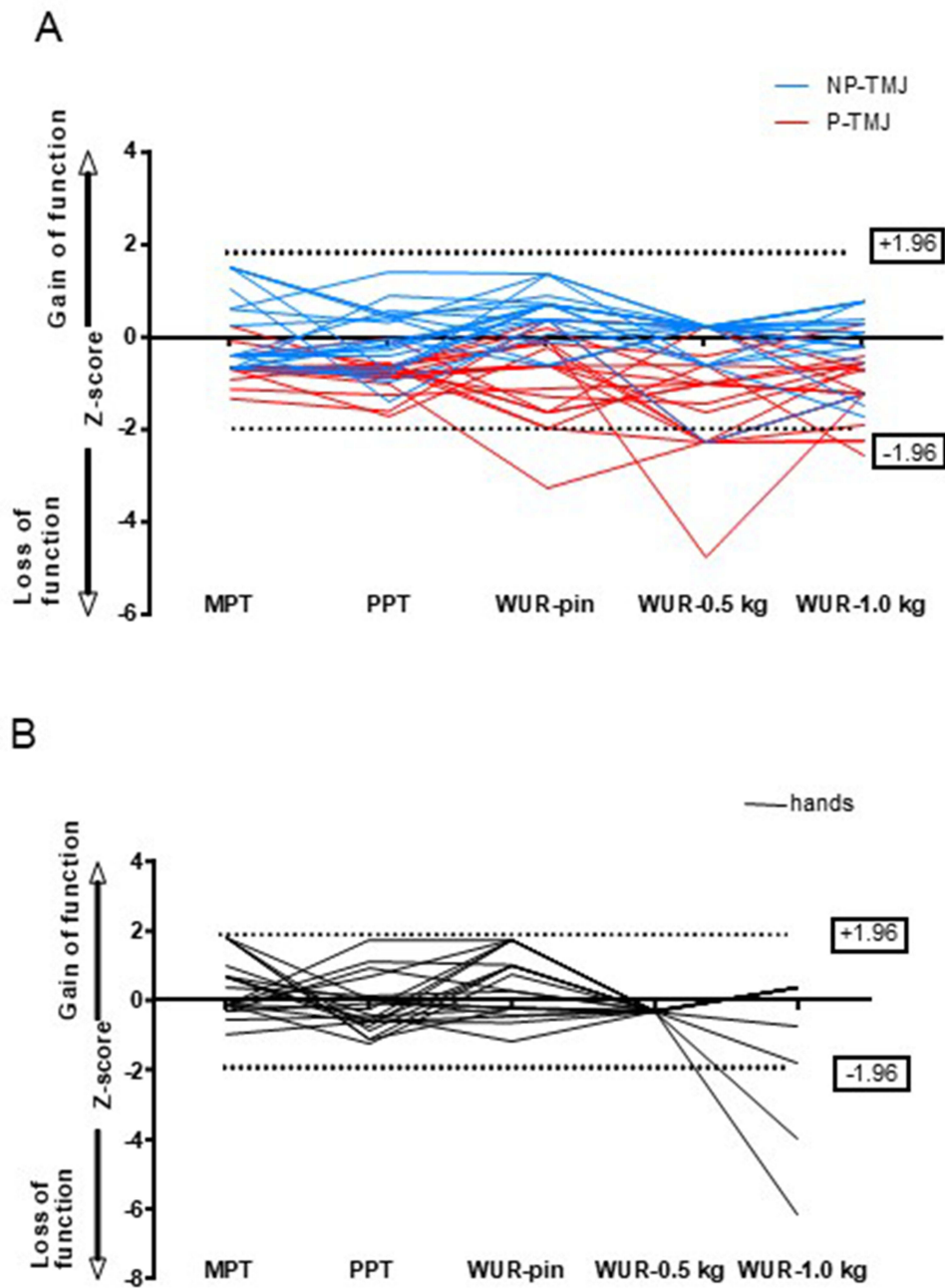
ranges of NRS1 scores, NRS10 scores and WURs (pinprick, 0.5 kg, 1.0 kg) on different sites, inter-/intra-group comparisons are presented in Table 2. Figure 1 presents the flow chart of the study. Figure 2 presents the Z-scores of MPT, PPT and WUR data at different sites. Figure 3 presents the NRS1 and NRS10 scores at bilateral TMJs of the two groups.

## MPT

The MPTs at the painful TMJs were significantly lower (more sensitive) than the control TMJs ( $P = 0.001$ , Table 1). The MPTs at the non-painful TMJs were similar to the control TMJs ( $P = 0.552$ , Table 1).

## PPTs

There was no significant difference between groups in PPTs on the hands ( $P = 0.473$ , Table 1) and non-painful TMJs ( $P = 0.850$ , Table 1). Significantly lower PPTs (higher sensitivity) were detected at the painful TMJs compared with the control TMJs ( $P = 0.002$ , Table 1) and non-painful TMJs ( $P < 0.001$ , Table 1).

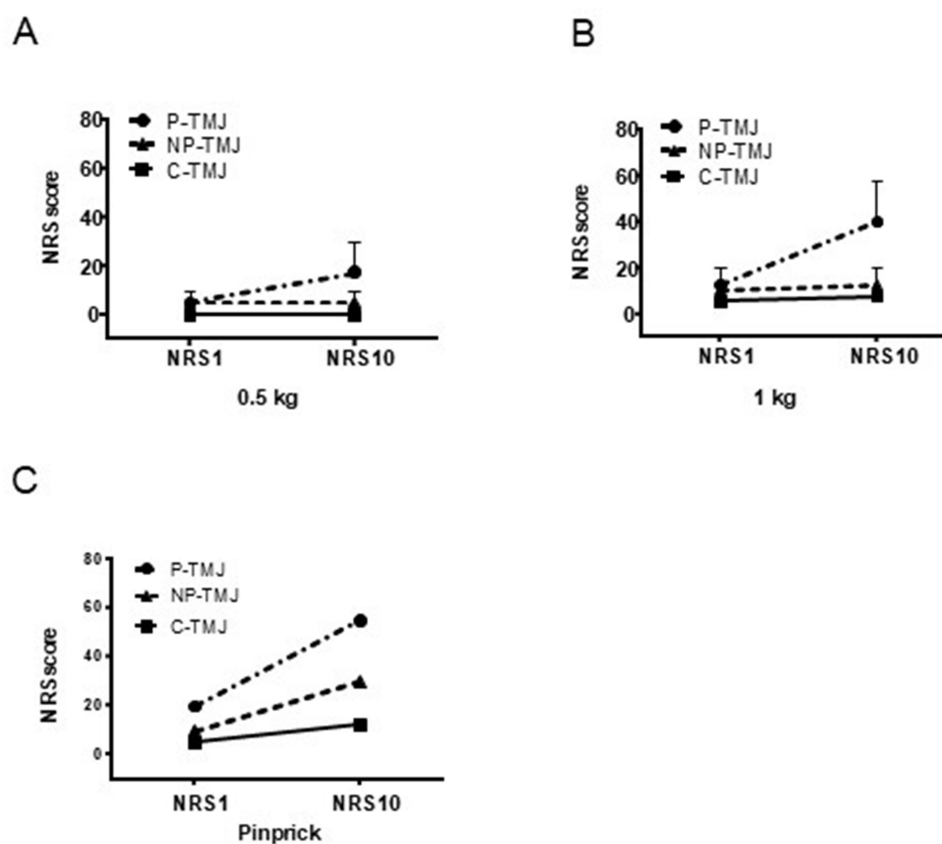


**Figure 2** Somatosensory Z-score profiles of patients with painful TMJs. The zone between the two lines ( $-1.96 < z < 1.96$ ) is the normal range based on the healthy material. The positive Z-values represented a gain of sensory function; negative Z-scores represented a loss of sensory function of 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.

## Pinprick Stimulation

### Single Pinprick Stimulus

There was no significant difference in NRS1 score of a single pinprick stimulus assessed on the hands ( $P = 0.989$ , Table 2). The NRS1 score for the single pinprick stimulus on the painful side was higher than that in the control group ( $P = 0.001$ , Table 2) and the non-painful side of patients ( $P = 0.009$ , Table 2).



**Figure 3** Medians 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.

**Abbreviations:** P-TMJ, patients' painful TMJs; NP-TMJ, patients' non-painful TMJs; C-TMJ, controls' TMJs; NRS1, NRS score of single stimulus; NRS10, NRS score of repetitive stimuli.

### Repetitive Pinprick Stimuli

TS data (NRS10, WUR) of repetitive pinprick stimulation on the hands were similar between the two groups ( $P_{\text{NRS10}} = 0.429$ ,  $P_{\text{WUR}} = 0.078$ , Table 2). TS data on painful TMJs were higher (more sensitive) than non-painful TMJs ( $P < 0.001$ , Table 2) and control TMJs ( $P_{\text{NRS10}} < 0.001$ ,  $P_{\text{WUR}} = 0.033$ , Table 2). Moreover, the non-painful side joints of patients were more sensitive to the superimposed effects of pinprick stimuli than healthy controls' ( $P_{\text{WUR}} = 0.018$ , Table 2).

## Palpation Stimulation

### Single Pressure Stimulus

A significant difference was observed in the NRS1 scores for single pressure stimulation at both 0.5 kg ( $P = 0.01$ , Table 2) and 1.0 kg ( $P = 0.003$ , Table 2) between painful and non-painful temporomandibular joints (TMJs). Additionally, a significant difference was noted between the two groups when single pressure stimulation (either 0.5 kg or 1.0 kg) was assessed on both TMJs of patients ( $P < 0.001$ , Table 2). However, no significant difference was found between the two groups in the NRS scores for single pressure stimulation (0.5 kg or 1.0 kg) on the hand ( $P_{0.5\text{kg}} = 0.317$ ,  $P_{1.0\text{kg}} = 0.917$ , Table 2).

### Repetitive Pressure Stimuli

There was a significant difference of TS data of repetitive pressure stimulation of 0.5 kg ( $P_{\text{NRS10}} < 0.001$ ,  $P_{\text{WUR}} = 0.005$ , Table 2) and 1.0 kg ( $P_{\text{NRS10}} < 0.001$ ,  $P_{\text{WUR}} = 0.005$ , 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 patients' non-painful TMJs were significantly higher than control TMJs ( $P_{0.5\text{kg}} =$

0.001,  $P_{1.0\text{kg}} = 0.004$ , Table 2). A difference in WUR of repetitive mechanical stimulation at 0.5 kg ( $P_{\text{WUR}} < 0.001$ , Table 2) was detected at the P-TMJ compared with healthy controls.

## 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  $> 1.96$  indicate 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 (Figure 2B) and painful and non-painful TMJs (Figure 2A). Obvious pathological WUR-pinprick, WUR-0.5 kg and WUR-1.0 kg on the painful TMJ (Figure 2A) could be detected (Z-score  $< -1.96$ ), which means that painful TMJs were more sensitive to TS effect of mechanical stimulus than control TMJs.

## 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.<sup>15,35</sup> Several pieces of evidence strongly suggest that TS and wind-up share a common central mechanism.<sup>36</sup> 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.<sup>37</sup> It can serve as both an amplification and maintenance mechanism for pain and central sensitization. Nevertheless, as wind-up is mediated by central mechanisms,<sup>38</sup> it can be used in human studies to determine the degree of CNS excitability to nociceptive stimulation.<sup>39,40</sup> 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).<sup>17,41,42</sup>

TMDs are common pain problems in the population with uncertain pathophysiology and mechanisms but with good evidence for increased sensitivity to mechanical stimulation.<sup>20,43</sup> The pressure pain threshold (PPT) was used to test deep pain sensitivity mediated through C- or A $\delta$ -fibers. Mechanical pain threshold (MPT) was used as a test for A $\delta$ -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 ( $P = 0.001$ , 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 stimuli.<sup>20</sup> 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. Moreover, despite patients had higher NRS scores for both single and repetitive pressure stimulation on both sides of the joints ( $P \leq 0.004$ , Table 2), the WURs remained similar to those of the control joints. This finding may be related to the high NRS scores for single pressure stimulation, which therefore decreases the ratio, ie, 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 joint. It was suggested that palpation-induced pain in the masticatory muscles might lead to different diagnosis among painful TMDs, primary headaches and bruxism.<sup>44</sup> Previous research showed that manual palpation at lower force levels (0.5 kg, 1.0 kg) is related to a tendency to “overshoot” the pressure.<sup>10</sup> In order to get a high level of reliability, two standardized palpometers (0.5 kg, 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, 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.<sup>45,46</sup> 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.

Clinically, enhanced TS responses may serve as behavioral indicators of central sensitization and could support more individualized pain management strategies in patients with TMD. In particular, the findings suggest that excessive mechanical stimulation—such as repeated palpation during examination—may exacerbate pain in sensitized individuals and should be minimized. Mechanistically, the results may reflect increased excitability of second-order nociceptive neurons within the trigeminal nucleus or spinal dorsal horn, contributing to abnormal pain facilitation in TMJ pain.<sup>47,48</sup> Further studies with larger, more diverse samples are warranted to confirm these findings and explore underlying sex-specific or psychosocial modulators.

This study has certain limitations. Although the control group was matched for age and gender, the psychological status of participants was not evaluated using standardized questionnaires (eg, PCS or HADS). Additionally, due to limited sample size and analytical constraints, p-values in this study were not corrected for multiple comparisons (MCC), and results should be interpreted cautiously considering the exploratory nature of the research. Future studies may incorporate standardized psychological assessments and increase sample size to better control for confounding factors. The concern regarding the limited sample size is acknowledged. This study was intentionally designed as an initial exploratory investigation to assess the feasibility of implementing a standardized mechanical TS protocol in patients with TMJ pain. A larger, adequately powered study is planned in the future. Additionally, there was a gender imbalance in both study groups, with 15 out of 20 participants being female. It reflects the typical clinical demographics of TMD, which are more prevalent among women. Future studies should aim for a more balanced gender distribution and further investigate sex-specific mechanisms in pain processing.

## 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 as extra-segmental sites. Both peripheral and central sensitization processes appear to be ongoing in patients with unilateral TMJ pain. While some extra-segmental alterations (eg, in the hand) were observed, these effects were less consistent and should be interpreted cautiously due to the preliminary nature of the study, small sample size, and inter-individual variability.

## Abbreviations

TS, Temporal summation; TMJ, temporomandibular joints; QST, Quantitative Sensory Testing; PPT, pressure pain thresholds; MPT, mechanical pain thresholds; NRS, numerical rating scale; WUR, wind-up ratios; DC/TMD, Diagnostic Criteria for TMDs; CI, confidence interval.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically

reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

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