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Glutamate-evoked jaw muscle pain as a model of persistent myofascial TMD pain?

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Abstract

Objective—Compare pain-related measures and psychosocial variables between glutamate-evoked jaw muscle pain in healthy subjects (HS) and patients with persistent myofascial temporomandibular disorder (TMD) pain.

Design—47 female HS and 10 female patients with persistent myofascial TMD pain participated. The HS received an injection of glutamate into the masseter muscle to model persistent myofascial TMD pain. Participants filled out a coping strategies questionnaire (CSQ), the symptom checklist 90 (SCL-90) and McGill Pain Questionnaire (MPQ). Pain intensity was assessed on an electronic visual analog scale (VAS). Pain-drawing areas, Numerical Rating Scale (NRS) scores of unpleasantness, pressure pain thresholds (PPT) and tolerance (PPTOL) were measured. Unpaired t-tests and correlation tests were used for analyses.

Results—The groups were significantly different when comparing the CSQ scores of control, decrease, diverting attention, increase of behavioral activities and somatization. The peak VAS pain, NRS of unpleasantness and MPQ scores were not significantly different between groups, but PPT and PPTOL were significantly lower in the TMD patients. Significant positive correlations were found in the TMD patients between peak VAS pain and CSQ catastrophizing score and SCL-90 somatization. The scores of PPTs and PPTOLs, in patients showed positive correlations with CSQ reinterpreting pain sensations scores and PPTs correlated with CSQ praying/hoping scores.

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Conclusions—Glutamate-evoked pain responses in HS and persistent myofascial TMD pain have similar sensory-discriminative and affective-unpleasantness components but differ in psycho-social features. This study suggests that experimental designs based on glutamate injection into muscle can provide an appropriate model for elucidating persistent myofascial pain conditions.

Keywords

Orofacial pain; temporomandibular disorders; muscle pain; glutamate; trigeminal physiology; coping strategies questionnaire; catastrophizing; experimental muscle pain model

Introduction

The etiology and pathogenesis of persistent myofascial temporomandibular disorders (TMD), characterized by symptoms of localized ongoing and activity-provoked masticatory muscle pain, remains unclear^{1–4}. Previous studies have shown that experimentally increased levels of glutamate in the human masseter muscle produced pain, decreased pressure pain thresholds (PPT) and increased the amplitude of the jaw-stretch reflex which suggest that injection of glutamate into the masseter muscle can produce muscle pain and changes in physiological response similar to those reported for myofascial TMD patients^{5–10}.

Nevertheless, it has to be considered that although human experimental pain models applied to the orofacial area can provide valuable and clinically relevant information, the characteristics of the persistent (months or years) pain experienced by most myofascial TMD patients is more complex than acute (minutes or hours) experimental pain in healthy subjects, for example socio-economic and behavioral factors may differ substantially. Such differences could be related to the natural fluctuation of pain, the chronicity of the pain, psychosocial distress, functional disabilities, and concomitant pain conditions that may all influence the expression of pain¹¹. Pain is, indeed, influenced by a multitude of factors including psychological factors that have been shown to be important determinants of pain experience^{12, 13}. Thus, it has been reported that patients suffering from myofascial pain dysfunction or atypical facial pain are more likely to show elevations in psychometric scales for hypochondriasis and depression¹³. It has also been shown that psychosocial variables, such as coping strategies, may have implications for the underlying physiology of pain, e.g. to predict important clinical outcomes, including pain severity and disability¹⁴. For example, catastrophizing, which has been defined as a negative emotional and cognitive response to pain involving elements of magnification, helplessness and pessimism¹⁵, is considered as the most robust predictor of pain outcomes^{16–18}. Thus, catastrophizers may have a tendency to magnify or exaggerate the threat value or seriousness of the pain sensation¹⁶ and catastrophizing has been significantly associated with patient-reported pain-related activity, interference, and depression¹⁹. Furthermore, it has been suggested that depression and somatization are associated with different measures of experimental pain. Somatization may be related to more attentional and perceptual measures of clinically relevant pain while depression may be related to more behavioral measures of pain²⁰. All these factors suggest awareness and caution when comparing results in experiments involving persistent myofascial TMD pain patients with those obtained from human experimental pain models.

Based on the available literature we decided to complement our previous results¹⁰ with a post-hoc analysis in order to compare different pain-related measures and psycho-social variables between glutamate-evoked jaw muscle pain in healthy subjects and patients with persistent myofascial temporomandibular disorder (TMD) pain.

Materials and methods

To perform this post-hoc analysis, a portion of the data obtained from two previous studies was used^{10, 11}.

TMD patients

Data from a sample of 10 female patients (mean age 29.1 years)¹¹ with persistent myofascial TMD pain was used. All patients fulfilled the inclusion criteria for myofascial TMD pain 1a or 1b in accordance with the Research Diagnostic Criteria for TMD (RDC/TMD)²¹. In addition, all patients had a history of characteristic pain intensity from the masseter muscle region of more than 2 out of 10 on a visual analogue scale (VAS) over a 2-month period.

Healthy subjects

Healthy female subjects (n = 47, mean age 24.2 years) that were mainly university students from our previous reported study were included¹⁰. The specific exclusion criteria for this group were no signs or symptoms of painful TMD²¹, myositis, contracture or spasms.

General exclusion criteria for both groups were presence of systemic musculoskeletal pain disorders such as fibromyalgia, inflammatory joint disease e.g. rheumatoid arthritis²², serious systemic diseases including current malignancies, chronic administration of psychiatric, analgesic or other medications that might influence their response to pain, pregnancy, and high blood pressure. Additionally, all participants confirmed that they had not taken any kind of analgesics 24 hours prior to the experiment.

This study was performed at the Department of Clinical Oral Physiology in the School of Dentistry at the University of Aarhus, Denmark. The study was approved by the local Ethics Committee at Aarhus University and conducted in accordance with the Helsinki Declaration. All the patients read and signed the informed consent forms prior to participating in the study.

Experimental protocol

Experimental pain was induced in healthy subjects by injections of 0.2 ml of a sterile solution of mono-sodium glutamate (1.0 M, ~pH 7.2, Ajinomoto Co. Inc., Japan) prepared by the pharmacy at Aalborg Hospital into the deep masseter muscle. The point of injection was midway between the upper and lower border of the masseter muscle and 1 cm posterior to its anterior border. Injections were performed over a 10 s period with a 27-gauge hypodermic needle and disposable syringe. The most painful side was examined in the TMD pain patient group or if there was bilateral pain of equal pain intensity, the side to be studied was randomized. Fig. 1 shows a schematic diagram of the experimental protocol.

Pain-related measures

Coping Strategies Questionnaire (CSQ)

Prior to the experiment, all participants filled out a Danish version of CSQ²³. From the CSQ eight scores were obtained: pain control ability, pain decrease ability, diverting attention, reinterpreting pain sensations, coping safe statements, ignoring sensations, praying and hoping, increase behavioral activities, and catastrophizing.

Symptom Check List 90 (SCL-90)

Before starting the experiment, the volunteers filled out a Danish version of the RDC/TMD questionnaire²¹. One of the parts of this instrument is the Axis II that is used to assess pain-related disability and psychological status. Axis II of the RDC/TMD includes the SCL-90 that provides 3 scores: depression, non-physical symptoms pain excluded and non-physical

symptoms pain included. Because of the characteristics of the present study only the non-physical symptoms of pain included were used.

VAS pain and unpleasantness

During the experiment, the healthy subjects continuously scored their glutamate-evoked pain intensity on a 10 cm electronic VAS for 15 min. The myofascial TMD pain patients were also asked to score their spontaneous pain on the same 10 cm electronic VAS for 15 min. The lower extreme of the VAS was marked “no pain” and the upper extreme was marked “most pain imaginable”. The peak pain (the highest VAS score) was calculated from the recorded VAS data. The procedure was done in accordance with previously detailed methods^{5, 7–9, 24}.

The healthy subjects were also asked to rate the unpleasantness of the glutamate-evoked pain sensation on a 0–10 numerical rating scale (NRS) where 0 represented “no unpleasantness at all” and 10 “the most unpleasantness imaginable”. The TMD patients were asked to score the unpleasantness of their spontaneous pain on the same 0–10 NRS.

Pain drawings and McGill Pain Questionnaire

Fifteen min after the glutamate injection, the healthy subjects were asked to draw their maximum distribution of perceived pain on a lateral view of the face. The pain area was digitized (Sigma Scan Pro 4.01.003) and expressed as arbitrary units²⁵. At the same time point the healthy subjects were asked also to fill out a Danish version of the McGill Pain Questionnaire (MPQ)²⁶. The pain rating indices (PRI) of the sensory-discriminative, affective, evaluative, miscellaneous and total dimension of pain were calculated according to Melzack (1975). TMD patients were also asked to draw their spontaneous pain on a lateral view of the face and to fill out the MPQ.

Pressure pain thresholds and pressure pain tolerance

A pressure algometer (Somedic, Hörby, Sweden) was used to record pressure pain thresholds (PPTs) and pressure pain tolerance levels (PPTOLs) of the masseter muscles bilaterally²⁷. All participants kept their jaw at rest and did not clench their teeth. The pressure was applied to the muscle at a rate of 30 kPa/s, with a 1 cm² diameter probe. All participants were instructed to push a button when they felt that the pressure was just barely painful (PPT) or when pain reached the highest level that they could tolerate (PPTOLs). The PPTs and PPTOLs (kPa) were determined prior to start the electronic VAS recording (baseline) and then every 5 min (PPT) or at 15 min (PPTOLs) after starting the electronic VAS recording (Fig. 1). The PPTs and PPTOLs were determined from a single measurement at each time point, except for the PPT at baseline, which was the average of three repeated measurements

Statistical analyses

Unpaired student t-tests were used to compare the pain-related measures between the two groups and paired t-test were used to compare within groups, as PPT and PPTOL values were normally distributed in healthy subjects and TMD patients. PPT values measured during the most painful time (min 5) in the glutamate-evoked pain group¹⁰ and PPTOLs score values at 15 min after injection were considered for statistical analysis and compared to baseline scores of the myofascial TMD pain patients. To determine correlations between pain-related measures, Pearson's test were used when data was normally distributed, and Spearman's test was used if data were not normally distributed. Chi Square test was used to find significant differences in the most prevalent words chosen in the MPQ. The level of significance was set at $P < 0.05$ and in the specific case of PPT and PPTOL t-test, the level of significance was set at $P < 0.025$ applying the Bonferroni correction.

Results

Baseline clinical characteristics

The baseline clinical characteristics of the two groups are shown in Table 1. The TMD patients showed significantly lower range of jaw movements as well as more painful myofascial or TMJ sites on palpation. Another significant difference was that the age of the TMD pain patients was slightly older than the healthy controls.

CSQ

There were significant differences between healthy controls and myofascial TMD pain patients. The healthy controls had higher scores in sections that assessed ability to control pain decrease pain, divert attention and increase behavioral activities ($P < 0.019$, Table 2).

SCL-90

The myofascial TMD pain patients had significantly higher scores of SCL-90 somatization ($P < 0.001$, Table 2), but not of SCL-90 depression scores ($P = 0.083$) when compared to healthy subjects.

VAS pain and unpleasantness

The injection of glutamate evoked a brief (6.5 ± 0.5 min) period of moderately intense pain. There were no differences between groups in peak VAS clinical pain scores in the TMD patient group and peak VAS glutamate-evoked pain in the healthy group (Table 3) or in NRS scores of unpleasantness between the two groups (Table 3).

Pain drawings and MPQ

The glutamate-evoked pain was felt not only at the site of injection but also spread to include other ipsilateral regions of the face and head (Fig. 2). There were no significant differences between the two groups in terms of pain drawing areas (Fig. 2) or PRI derived from the MPQ (Table 3). Moreover, the most chosen words by the healthy subjects to describe their glutamate-evoked pain in the MPQ questionnaire were: pressing, annoying, taut, spreading, boring, hot, hurting, tender and intense. Even though the myofascial TMD pain patients used similar words to describe their clinical pain: taut, tender, pressing, annoying, tiring, hurting and hot (Table 3), the frequency of use of certain terms (boring, tender, tiring and spreading) were significantly different between groups (Table 3).

PPTs and PPTOLs

The myofascial TMD pain patients had significantly lower PPTs and PPTOLs compared with the PPTs and PPTOLs baseline scores of the healthy subjects (Fig. 3A and B). Additionally, the same scores of the TMD pain patients were also significantly lower than the PPTs scores obtained in the healthy subjects during the most painful time (min 5)¹⁰ and PPTOLs score values at 15 min after injection of glutamate ($P < 0.001$, Fig. 3C and D). Moreover, healthy subjects showed significantly lower PPT scores on the injected side 5 min after the injection of glutamate compared with the baseline scores ($P < 0.001$, Fig. 3C).

Correlations

In healthy subjects, there were significant inverse correlations between the CSQ scores and some of the PRI scores derived from the MPQ and significant positive correlations between some of the PRI scores of the MPQ and the SCL-90 scores (Fig. 4). Moreover, correlations were observed only in the myofascial TMD pain patient group between VAS peak clinical pain and the CSQ scores for catastrophizing and with somatization scores of the SCL-90 ($R > 0.682$,

$P < 0.030$, Fig. 5A and B). Additionally, the scores of PPTs and PPTOLs in the TMD patients showed positive correlations with CSQ reinterpreting pain sensations scores, PPTs correlated with CSQ praying/hoping scores and PPTOLs scores from one side of face with CSQ coping self statements ($R > 0.650$, $P < 0.042$, Fig. 6). Also in the TMD patient group, NRS scores of unpleasantness correlated with CSQ scores of praying/hoping and SCL-90 scores of depression and somatization ($R > 0.618$, $P < 0.049$, Fig. 5E, F and G). Finally, similar to the healthy group the CSQ increasing behavioral activities was negatively correlated with the evaluative and total scores of MPQ in the TMD pain patients ($R < -0.665$, $P < 0.034$).

Discussion

The present study has shown that glutamate-evoked jaw muscle pain in healthy subjects shares many of the characteristics of persistent pain in the TMD patients (Table 3, Fig. 2) but that in particular the psycho-social scores differ between the two groups (Table 2). Furthermore, significant associations between measures of pain intensity and psycho-social scores were noted predominately in the TMD pain patients. The findings are discussed from the perspective that experimental myofascial pain models can be used to model several features of clinical TMD pain conditions.

The present study supports previous studies that have tried to bring better understanding of the underlying mechanisms of the myofascial TMD pain by using experimental glutamate-evoked pain^{5, 6, 10, 28}. Injection of glutamate into the masseter muscle reliably evokes a brief period of moderate muscle pain followed by a more prolonged period of mechanical sensitization^{6–8, 10, 28}. In addition, healthy female subjects report significantly greater masseter muscle pain after glutamate injection than do healthy male subjects^{5, 8, 7}. These features of glutamate injection into the masseter muscle are reminiscent of certain of the characteristics of myofascial TMD patients, and in fact, in the present study pain intensity produced in healthy subjects after glutamate injection was similar to that reported by myofascial TMD patients. It is tempting to speculate, based on these similarities, that elevated interstitial glutamate levels in the masseter muscle of TMD might be a contributing factor in this disorder. Indeed, there is some evidence that glutamate concentration in the masseter muscle is elevated in myofascial TMD patients (Castrillon et al, unpublished observations). However, the NMDA receptor antagonist ketamine, which has been shown to reduce glutamate-induced masseter muscle pain and mechanical sensitization in healthy men²⁸, is ineffective at the same dose when used against glutamate-evoked pain and mechanical sensitivity in healthy women¹⁰ or against myofascial pain in predominantly female persistent myofascial TMD pain patients¹¹. Recent animal studies suggest that the expression of peripheral NMDA receptors by masseter muscle afferent fibers is higher in females than males, which may partly explain this discrepancy²⁹. Nevertheless, these results demonstrate that while glutamate injection into the masseter muscle is a useful experimental model for some characteristics of TMD-related pain, it remains uncertain what role peripheral glutamate plays in persistent myofascial TMD.

A consistent finding in the present study was the difference in PPT and PPTOLs between the two groups (Fig. 3). A number of studies have shown that TMD pain patients have lower PPTs on their painful muscles as well as on the non-painful side^{30–32}. In the present study, we compared the myofascial PPT values 5 min after the glutamate injection in healthy subjects to the baseline PPT values in myofascial TMD pain patients. Although the PPTs in the healthy subjects were significantly decreased compared to their baseline values¹⁰, the PPTs in the patient group were still lower. This suggests that the magnitude of glutamate-induced mechanical sensitization in healthy controls is smaller than the magnitude of sensitization in TMD pain patients. There is good evidence that glutamate-induced mechanical sensitization is mediated through a peripheral mechanism involving the activation of peripheral NMDA receptors^{28, 33}. Therefore, one possible explanation for this difference could be a central

sensitization component that is present in persistent myofascial TMD pain conditions³⁴, but is not recruited by the acute glutamate-induced masseter muscle pain.

TMD pain patients have been described as having more psycho-social / psychometric distress than matched control subjects^{35–37} and in accordance with this notion, the present results showed that some psychological characteristics of the myofascial TMD pain patients differed from the healthy subjects (Table 2). These disparities between the groups of the present study were specifically on their ability to cope with pain expressed by the differences in their control over the pain, their ability to decrease the pain, the ability to divert their attention, and ability to increase behavioral activities (Table 2).

The CSQ assessment is based on subjects' ability to recall previous pain experiences. One disadvantage of the application of this instrument for measuring healthy subjects in the present study was that they have usually not experienced persistent pain before and therefore they could find some difficulties to use the CSQ. This is not the case for the chronic pain sufferers, because they can immediately identify strategies that they have developed in order to cope with their chronic pain. For that reason, we can not establish if these psychosocial characteristics were consequences of a chronic pain condition or they were pre-existing conditions to the establishment of persistent myofascial TMD pain and it worked as one of the etiological conditions. The possibility that coping strategies may have implications for the underlying physiology of pain, e.g. to predict important clinical outcomes, including pain severity and disability can not be ruled out¹⁴, because the present experiment design was not a longitudinal prospective study that followed the healthy volunteers to see if they developed persistent TMD pain and its associated characteristics. Interestingly, we found that the CSQ catastrophizing scores were positively correlated to the MPQ sensory dimension (Fig. 4D) of the glutamate-evoked muscle pain. This has been reported previously in other studies, for example with catastrophizing that is considered the most robust predictor of pain outcomes^{16–18}. Therefore, another option might be that the inability in some coping strategies could work as facilitators to establish chronic pain. This last rationale is based on evidence that during mild pain there is a relationship between catastrophizing and activity in cortical regions associated with affective, attention, and motor aspects of pain, including dorsolateral prefrontal, insula, rostral anterior cingulate, premotor, and parietal cortical regions³⁸. Additionally, the same study showed that during more intense pain, prefrontal cortical regions implicated in the top-down modulation of pain are negatively correlated with catastrophizing³⁸. This finding supplies a possible physiological explanation for how psychological factors may interfere with pain responses and facilitate their establishment.

Even though we did not find differences in all coping strategies (CSQ) and SCL-90 scores between groups (Table 2), it can be seen that compared to healthy subjects with acute muscle pain, myofascial TMD patients exhibited a decreased ability to cope with their ongoing pain, and an increased somatization that likely influenced the emotional component of this pain. Moreover, several studies have shown that catastrophizing scores may influence the perception of pain^{39–45}. This notion is supported by the results of the present study. The present results have shown that there were significant correlations of peak VAS pain with the catastrophizing CSQ and somatization scores (Fig. 5).

One of the greatest differences between TMD patients and healthy controls in the present study was the finding of a considerable correlation between PPT and PPTOL values and coping scores in TMD patients, but no evidence of similar correlations in healthy subjects injected with glutamate. As mentioned above, injection of glutamate into the masseter muscle of healthy subjects did not achieve the same degree of mechanical sensitization observed in TMD patients. In addition, individual healthy subjects may have experienced significant challenges when

responding to the questions about pain coping strategies. These factors likely explain the absence of correlations between mechanical pain and coping scores in healthy subjects.

Another finding that should be acknowledged is that even though both groups have used similar words of the MPQ to describe their pain experience, the frequency of use of some words differed significantly between TMD patients and healthy subjects (Table 3). The increased frequency of the use of the term “tender” by TMD patients seems likely to be related to their increased mechanical pain sensitivity, which was clearly greater than that which could be produced in healthy subjects after intramuscular injection of glutamate. The increased frequency of use of the term “spreading” by the healthy controls shows the anatomical area of influence of the peripheral glutamate evoked pain condition. On the other hand, the increased frequency of the use of the term “tiring” by TMD patients and “boring” by healthy volunteers suggests that the ongoing pain experienced by patients has a different emotional component than the acute muscle pain experienced by healthy controls receiving intramuscular injections of glutamate. These findings serve to further illustrate that while single intramuscular injections of glutamate can for a short time produce a similar magnitude of muscle pain in healthy controls, this type of acute pain is not able to recruit the degree of emotional response that chronic muscle pain in TMD patients appears to.

Conclusions

Healthy subjects exposed to glutamate-evoked jaw muscle pain and persistent myofascial TMD pain patients have many similarities in terms of the sensory-discriminative and affective-unpleasantness component of pain but clearly differ in terms of psycho-social measures such as e.g. catastrophizing and somatization. This study supports the view that experimental myofascial pain can appropriately model certain characteristics of persistent myofascial pain conditions.

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Figure 1. Schematic illustration of the experimental protocol. PPT: Pressure Pain Thresholds, PPTOL: Pressure Pain Tolerance, MPQ: McGill Pain Questionnaire, TMD: Temporomandibular Disorders, RDC/TMD: Research Diagnostic Criteria for TMD, NRS: Numerical Rating Scale, SCL-90: Symptom Check List 90.

TMD patients

Healthy subjects

Figure 2.

Perceived areas of pain drawn by the persistent myofascial TMD pain patients (n=10) compared with the ones drawn by healthy subjects (n = 47) after the injections of 0.2 ml of sterile solutions of glutamate. The pain areas were not significantly different between groups.

Figure 3.

Pressure pain thresholds (PPTs) and pressure pain tolerance thresholds (PPTOLs) in healthy subjects ($n = 47$) at baseline (A and B) (mean values $\pm$ SEM) and 5 min (PPTs) (C) and 15 min (PPTOLs) (D) (Relative changes compared to baseline) after injection of 0.2 ml glutamate into the masseter muscle (white bars). The control side (grey bars) was not injected in the healthy subjects. For comparison, the PPTs and PPTOLs in myofascial TMD pain patients ($n = 10$) (black bars) are shown on both sides in A and B and in C and D the relative changes were calculated by dividing the mean values of the patients by the mean values of baseline on healthy volunteers. * indicate significant difference within the healthy group (paired t-tests: $P < 0.01$). # indicate significant difference between groups (unpaired t-tests: $P < 0.01$). n.s. = no significant difference.

Figure 4.

The scatter plots show significant correlations between psychometric measures and glutamate-evoked pain responses in healthy subjects obtained with the Spearman tests.

Figure 5.

The scatter plots show significant correlations between psychometric measures and clinical pain characteristic in persistent myofascial TMD pain patients obtained with Pearson (A and B) and Spearman (C – G) correlation tests.

Figure 6.

The scatter plots show significant correlations between psychometric measures and mechanical pain sensitivity in persistent myofascial TMD pain patients obtained with Pearson correlation tests.

Table 1

Baseline clinical characteristics of the patients with persistent myofascial TMD pain (n=10) and the healthy subjects (n=47). Mean values and SEM.

Baseline characteristics			
	TMD patients (n = 10)	Healthy controls (n = 47)	P value
Age (years)	29.1 (2.2)	24.2 (0.4)	<0.001*
Duration of myofascial TMD pain (years)	8.0 (2.0)	0.0 (0.0)	<0.001*
Maximum unassisted opening without pain (mm)	47.0 (3.1)	53.0 (0.8)	0.007*
Maximum unassisted opening pain included (mm)	50.3 (3.1)	57.7 (0.7)	<0.001*
Maximum assisted opening pain included (mm)	51.0 (3.1)	59.5 (0.7)	<0.001*
Number of muscle sites with pain on palpation (0 – 20)	12.2 (1.6)	0.7 (0.2)	<0.001*
Number of temporomandibular joint (TMJ) sites with pain on palpation (0–4)	0.8 (0.4)	0.0 (0.0)	0.048*
Number of patients with TMJ sounds	1 (10.0%)	4 (8.5 %)	

* indicate significant difference between groups (unpaired t-test).

Table 2

Baseline CSQ and SCL-90 scores of the patients with persistent myofascial TMD pain (n=10) and the healthy subjects (n=47). Mean values and SEM. The values in the parentheses next to the CSQ categories indicate the possible score range. Low scores = less ability to cope, high scores = greater ability to cope.

CSQ scores			
	TMD patients (n = 10)	Healthy controls (n = 47)	P value
Control (0 – 6)	2.8 (0.7)	4.1 (0.1)	0.002 *
Decrease (0 – 6)	2.2 (0.5)	3.6 (0.2)	<0.001 *
Diverting attention (0 – 36)	7.9 (2.1)	14.8 (1.0)	0.006 *
Reinterpreting sensations (0 – 36)	7.0 (1.8)	9.2 (1.1)	0.395
Coping statements (0 – 36)	18.6 (2.3)	21.2 (0.9)	0.254
Ignoring sensations (0 – 36)	22.1 (2.6)	17.6 (0.9)	0.056
Praying / hoping (0 – 36)	8.8 (2.6)	11.2 (1.1)	0.365
Catastrophizing (0 – 36)	6.6 (2.3)	6.0 (0.7)	0.769
Increase of behavioral activities (0 – 36)	10.9 (2.0)	15.6 (0.8)	0.018 *
SCL – 90			
Depression (0 – 4)	0.5 (0.1)	0.3 (0.1)	0.083
Somatization (0 – 4)	0.7 (0.2)	0.3 (0.1)	<0.001 *

* indicate significant difference between groups (unpaired t-test).

Table 3

Pain-related responses in healthy subjects (n = 47) evoked by injections of 0.2 ml of sterile solutions of glutamate in comparison with persistent myofascial TMD pain (n=10). Mean values and SEM with P values for unpaired t-test. The table also shows the number of subjects (#) using the most chosen words (> 30%, indicated on bold fonts) from the MPQ questionnaire. The P values shown in the most used chosen words are from the Chi Square test.

Pain measures	TMD patients (n = 10)		Healthy controls (n = 47)		P value
	#	%	#	%	
VAS peak pain (0 – 10)	4.3 (0.8)		5.2 (2.3)		0.261
NRS unpleasantness (0 – 10)	4.2 (0.8)		5.6 (0.3)		0.063
MPQ sensory (0 – 42)	8.1 (1.9)		10.5 (0.7)		0.187
MPQ affective (0 – 13)	1.0 (0.3)		0.7 (0.2)		0.501
MPQ evaluative (0 – 5)	1.6 (0.5)		1.8 (0.3)		0.701
MPQ miscellaneous (0 – 17)	2.2 (0.8)		2.8 (0.3)		0.488
MPQ (PRI) total (0 – 77)	12.9 (3.1)		15.8 (1.2)		0.312
MPQ most used words (> 30%)					
Boring	1	10.0	21	44.7	*0.041
Pressing	7	70.0	29	61.7	0.621
Hot	2	20.0	21	44.7	0.149
Hurting	4	40.0	18	38.3	0.920
Tender	7	70.0	17	36.2	*0.049
Taut	8	80.0	23	48.9	0.073
Tiring	5	50.0	5	10.7	*0.003
Annoying	7	70.0	23	48.9	0.226
Intense	1	10.0	15	31.9	0.161
Spreading	1	10.0	22	46.8	*0.031