# Original article

## Cerebral activation during unilateral clenching in patients with temporomandibular joint synovitis and biting pain: an functional magnetic resonance imaging study

ZHAO Yan-ping, MA Xu-chen, JIN Zhen, LI Ke, LIU Gang and ZENG Ya-wei

***Keywords:*** *functional magnetic resonance imaging; unilateral clenching task; inferior frontal gyrus; precentral gyrus; temporomandibular disorders; synovitis*

**Background** Functional magnetic resonance is a non-invasive method that can examine brain activity and has been widely used in various fields including jaw movement and pain processing. Temporomandibular disorder (TMD) is one of the most frequent facial pain problems. The objective of this study was to investigate the brain activities using functional magnetic resonance imaging (fMRI) during unilateral maximal voluntary clenching tasks in the TMD synovitis patients with biting pain.

**Methods** Fourteen TMD synovitis patients with unilateral biting pain and 14 controls were included in the study. Contralateral biting pain was defined as right molar clenching causing left temporomandibular joint (TMJ) pain. Ipsilateral biting pain was defined as right molar clenching causing right TMJ pain. Symptom Check List-90 (SCL-90) was administered to the patients and controls. Independent sample *t*-test was used to compare the SCL-90 subscales between the two groups. Unilateral clenching tasks were performed by the patients and controls. Imaging data were analyzed using SPM99.

**Results** Patients were divided into contralateral TMD biting pain group ($n$=8) and ipsilateral TMD biting pain group ($n$=6). The SCL-90 subscales were significantly different between the two groups for somatization, depression, anxiety, phobic anxiety, and paranoid ideation. Group analysis of the controls demonstrated brain activations in the inferior frontal gyrus, precentral gyrus, middle frontal gyrus, superior temporal gyrus, and insular. The areas of activation were different between right and left clenching task. In TMJ synovitis patients with contralateral or ipsilateral biting pain, the group analysis showed activations in the inferior frontal gyrus, superior temporal gyrus, medium frontal gyrus, precentral gyrus, and anterior cingulate cortex.

**Conclusions** The inferior frontal gyrus and precentral gyrus play essential roles during the unilateral clenching task. Activation of anterior cingulate cortex in the synovitis patients with biting pain was associated with higher levels of psychological distress.

*Chin Med J 2011;124(14):2136-2143*

Clinical problems involve the masticatory musculature, the temporomandibular joint (TMJ) and its associated structures or both are embraced in the term of temporomandibular disorder (TMD). TMD is one of the most frequent facial pain problems.[1] Patients with TMD pain share characteristics with patients suffering from other chronic pain conditions like headaches and back pain.[2] Stressful life events, anxiety, depression, and somatization are associated with pain intensity and duration.[3]

Recent advances in functional neuroimaging have provided a safe, non-invasive method to measure brain activity during jaw movement and pain processing. Momose et al[4] used positron emission tomography (PET) to examine brain activation during mastication and demonstrated that cerebral blood flow increased in the primary sensorimotor area, supplementary motor area, insula, cingulate, and cerebellum. Functional magnetic resonance imaging (fMRI) results demonstrated changes in brain activity in the sensory, motor, and premotor cortexes of both hemispheres during jaw clenching.[5] The fMRI results indicated that areas in the middle frontal gyrus and inferior frontal gyrus were activated during a gum chewing task, but were not activated during a sham chewing task. These findings indicated that the parieto-frontal network plays an essential role in mastication.[6]

Functional imaging techniques have identified a number

DOI: 10.3760/cma.j.issn.0366-6999.2011.14.011
Department of Oral Radiology and Center for Temporomandibular Disorders, Peking University School and Hospital of Stomatology, Beijing 100081, China (Zhao YP and Ma XC)
Department of Radiology, 306 Hospital of People's Liberation Army, Beijing 100101, China (Jin Z, Li K, Liu G and Zeng YW)
Correspondence to: Prof. MA Xu-chen, Department of Oral Radiology and Center for Temporomandibular Disorders, Peking University School and Hospital of Stomatology, Beijing 100081, China (Tel: 86-10-62179977 ext. 5345. Fax: 86-10-62136628. Email: kqxcma@bjmu.edu.cn)
This study was supported by a grant from the Human Research Ethics Committee at the Peking University Health Science Center (No. IRB00001052-06062).

of brain regions that are activated by painful stimulation.[7] Activations of the thalamus, primary somatosensory cortex, secondary somatosensory cortex and insular cortex appear to be related to the sensory discriminative aspects of pain, while activation of the anterior cingulate cortex (ACC) may be related to the affective and attentional components of pain.[8] Previous study demonstrated that ACC activated in patients with burning mouth disorder, fibromyalgia, and atypical facial pain.[9-11] In the present study, we used fMRI to investigate the difference in location and extent of brain activities during unilateral voluntary clenching task between the TMD patients with biting pain and the controls.

## METHODS

### Enrollment

A total of 30 participants (16 TMD patients with synovitis and 14 controls) were recruited in the study. Sixteen TMD patients with synovitis were 12 females and 4 males, aged 18.0–60.0 years with mean age of (33.7±13.2) years, all right-handed. Clinical TMD diagnosis was made according to the Clinical Diagnostic Criteria published by Truelove et al[12] in 1992. Patients used a visual analog scale (VAS) to subjectively evaluate pain in the joint area. Inclusion criteria for patients were: 1. Signs and symptoms that characterized a diagnosis of unilateral synovitis; 2. Patients with unilateral synovitis rated pain intensity as moderate to severe (VAS ≥5); 3. No history of trauma and systematic arthritis. All patients had unilateral TMJ pain during biting. Contralateral biting pain was defined as right molar clench causing left TMJ pain. Ipsilateral biting pain was defined as right molar clench causing right TMJ pain.

The control group included 14 healthy, right-handed subjects (7 males and 7 females with mean age of (23.7±0.9) years). Inclusion criteria for control subjects were: 1. No history of neurological, psychiatric disorders, and systematic arthritis; 2. No history of orofacial pain and TMD. All participants gave written informed consent prior to the study.

### Psychological assessment

Patients and controls completed a psychometric questionnaire using the Symptoms Check List-90 (SCL-90).

### Functional imaging acquisition and analysis

The fMRI data were obtained with a GE Elscint 2.0 T whole-body MRI scanner. T2-weighted functional images of the whole head were acquired with an echo planar sequence using the following parameters: TR=3000 ms, TE=45 ms, 90˚ flip angle, and 20 contiguous axial slices. The field-of-view was 373 mm × 210 mm with a 128 × 72 image matrix. Anatomical images were acquired with a 3D gradient echo sequence with TR=25 ms, TE=6 ms, and a 90˚ flip angle. The field of view was 220 mm × 220 mm with a 220 × 220 image matrix.

In the unilateral clenching task, TMJ synovitis patients bite a cotton roll with their right molars using maximal biting force, while the left molars were without contact. For controls, two unilateral maximal clenching tasks were performed. Task 1 was biting a cotton roll with the right molars, and task 2 was biting a cotton roll with the left molars, while the contralateral molars were without contact. Each task included 5 repetitions of 30 seconds of unilateral maximal clenching and 30 seconds of rest. The total scanning time was 5 minutes for each TMD patient and 10 minutes for each control subject.

### Temporomandibular joint magnetic resonance imaging

All the 16 TMD synovitis patients with unilateral biting pain underwent bilateral TMJ MR scanning with a GE Elscint 2.0 T whole-body MRI scanner. MRI protocols consisted of a parasagittal T1, T2, and proton weighted sequence for both the closed and open mouth positions and a coronal T1, T2, and proton weighted sequence for the closed mouth position. Mouth-close and mouth-open images were selected for analysis of the disc-condyle relationship and assessment of joint effusion.[13,14]

### Statistical analysis

Functional imaging data were analyzed off-line using SPM99 software which was affinitive to MATLAB version 6.5 (*http://www.fil.ion.ucl.ac.uk/spm/*). The functional images for each subject were corrected for head movements. Then the images were spatially smoothed with a 7 mm Gaussian kernel and normalized to the Montreal Neurological Institute (MNI) template.[15] The brain volumes collected during unilateral clenching task (on) were compared with the brain volumes collected during off conditions by Student's $t$ test. Results for fMRI were presented as $t$ values, anatomic regions were identified by 1. inspected of individual functional imagines superimposed on an individual structural image; 2. conversions of the MNI coordinates to the coordinate system of the Talairach-Tournoux atlas and localization using this atlas and automated software. The significance levels were set at $P$ <0.001 with a 20-voxel cluster threshold for individual data analysis and $P$ <0.01 with a 10-voxel cluster threshold for group analysis. Independent sample $t$ test was used to compare the SCL-90 subscales between the patients and the controls. The significance was set at $P$ <0.05.

## RESULTS

### Demographics and psychophysical tests

Two out of sixteen patients were excluded finally because of head movement during MR scanning in one patient and not performing unilateral clenching task according to the requirement in another patient, respectively. The final patient group consisted of 14 patients for data analysis and all of them did not have head movement during MR scanning. Of the 14 TMD synovitis patients, eight cases had contralateral TMJ biting pain and six cases had ipsilateral TMJ biting pain (Table 1). Psychometric tests demonstrated significant differences between the TMD synovitis patients and the controls with regard to the SCL-90 subscales for somatization, depression, anxiety, phobic anxiety, and paranoid ideation (Table 2).

**Table 1.** Clinical and MRI descriptions of the patients with synovitis

| Patients | Sex | Age (years) | Pain side | MRI diagnosis |
|---|---|---|---|---|
| 1 | F | 18 | L | ADDwoR with effusion |
| 2 | F | 27 | L | ADDwoR with effusion |
| 3 | F | 23 | L | ADDwoR with effusion |
| 4 | F | 56 | L | ADDwoR with effusion |
| 5 | F | 27 | L | ADDwoR with effusion |
| 6 | F | 44 | L | ADDwoR |
| 7 | M | 21 | L | ADDwoR |
| 8 | M | 23 | L | Normal |
| 9 | F | 30 | R | Normal |
| 10 | F | 28 | R | ADDwoR with effusion |
| 11 | M | 46 | R | Normal with effusion |
| 12 | F | 50 | R | Normal with effusion |
| 13 | F | 34 | R | Normal with effusion |
| 14 | F | 22 | R | ADDwoR with effusion |

F: female. M: male. L: left. R: right. ADDwoR: anterior disc displacement without reduction. Normal: normal disc position.

**Table 2.** Comparison between patients with synovitis and the controls with regard to the SCL-90 subscales

| SCL-90 subscales | Patients* | Controls* | *P* values |
|---|---|---|---|
| Somatization | 1.72±0.72 | 1.11±0.11 | 0.013 |
| Obsessive-compulsive | 1.74±0.47 | 1.37±0.47 | 0.065 |
| Interpersonal sensitivity | 1.55±0.55 | 1.33±0.40 | 0.301 |
| Depression | 1.63±0.62 | 1.20±0.27 | 0.040 |
| Anxiety | 1.55±0.53 | 1.18±0.11 | 0.034 |
| Hostility | 1.32±0.40 | 1.15±0.20 | 0.237 |
| Phobic anxiety | 1.30±0.33 | 1.05±0.10 | 0.028 |
| Paranoid ideations | 1.42±0.48 | 1.08±0.14 | 0.034 |
| Pscychoticism | 1.39±0.29 | 1.16±0.37 | 0.077 |
| Additional items | 1.97±0.82 | 1.14±0.21 | 0.003 |

*Data are shown as mean ± standard deviation (SD).

**Activation of brain regions in control subjects performing unilateral maximal clenching tasks**

Of the 14 control subjects, the functional imaging of two male subjects in the bilateral clenching task and one male subject in the right clenching task could not be interpreted because of excessive head motion. Therefore, the final control group consisted of 11 subjects for the right clenching task and 12 subjects for the left clenching task. For the controls' individual data, the brain regions activated during the unilateral clenching task were detected in the inferior frontal gyrus, precentral gyrus, middle frontal gyrus, middle temporal gyrus, superior temporal gyrus, cingulate gyrus, insular, inferior parietal lobule, postcentral gyrus, precuneus, premotor cortex, superior frontal gyrus, angular gyrus, middle occipital gyrus, parahippocampal gyrus, and cerebellum. Group analysis of brain activations for the right clenching task and the left clenching task are showed in Table 3, and Figures 1 and 2. Most of the controls showed activations of inferior frontal gyrus and precentral gyrus. During the right clenching task, the inferior frontal gyrus was activated in all subjects. Most of them were bilateral activation (9/11). Precentral gyrus activation was observed in eight cases, and six out of eight subjects showed bilateral activation. During the left clenching task, six out of 11 subjects showed bilateral activation of the inferior frontal gyrus. Nine cases showed precentral gyrus activation. Individual data demonstrated activation in primary somatosensory cortex in most subjects (7 subjects for right clenching task and 6 subjects for left clenching task).

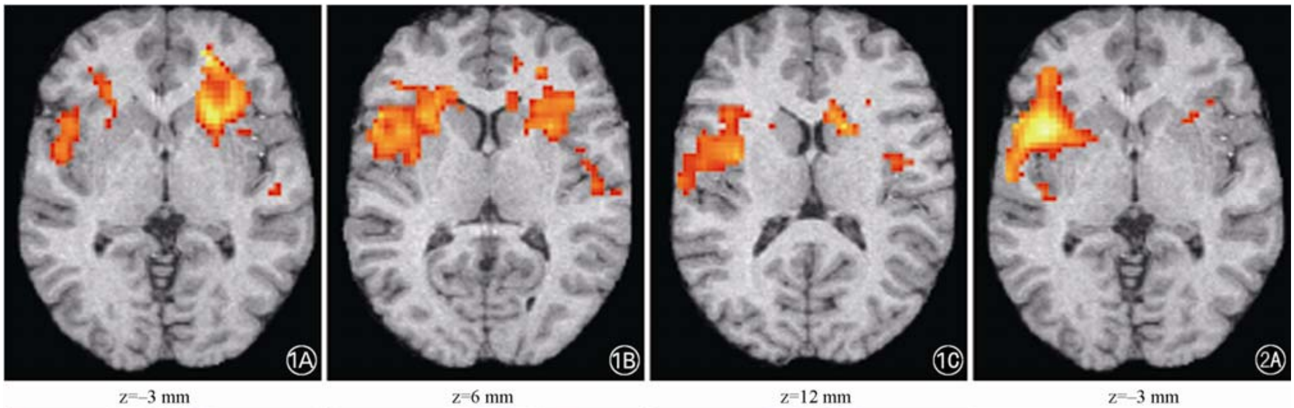
**Table 3.** Group analysis of the control subjects performing unilateral clenching task ( *P* <0.01, voxels >10)

| Activation area | BA | Talairach coordinate | | | *K* values | *t* values |
|---|---|---|---|---|---|---|
| | | X | Y | Z | | |
| Right clenching task for controls (*n*=11) | | | | | | |
| L inferior frontal gyrus | 44, 45 | –53 | 20 | 2 | 817 | 5.09 |
| R inferior frontal gyrus | 44 | 42 | 26 | 1 | 745 | 3.56 |
| L precentral gyrus | 6 | –50 | 1 | 11 | 817 | 3.22 |
| R precentral gyrus | 4, 6 | 42 | –2 | 11 | 71 | 3.16 |
| R middle frontal gyrus | 11 | 30 | 25 | –19 | 745 | 6.08 |
| R superior temporal gyrus | 22,38 | 53 | –14 | 3 | 745 | 5.39 |
| Left clenching task for controls (*n*=12) | | | | | | |
| L inferior frontal gyrus | 45 | –53 | 15 | 2 | 1108 | 6.09 |
| L insular | | –42 | 11 | –3 | 1108 | 6.09 |
| L precentral gyrus | 6 | –50 | 1 | 22 | 125 | 4.26 |
| L superior temporal gyrus | 22 | –48 | 6 | 0 | 1108 | 6.09 |

The brain activation patterns for controls during unilateral clenching were divided into three types: 1. Stronger activation of the right hemispheres (three subjects), showed bilateral inferior frontal gyrus and precentral gyrus activation with stronger activation of right hemispheres or only right inferior frontal gyrus and precentral gyrus activated during right and left clenching task (Figure 3); 2. Stronger activation of the left hemispheres (six subjects), showed bilateral activation of the inferior frontal gyrus and precentral gyrus with stronger activation of the left hemispheres or only the left inferior frontal gyrus and precentral gyrus activated during the unilateral clenching task (Figure 4); 3. Stronger activation of the ipsilateral hemispheres (two subjects), demonstrated bilateral inferior frontal gyrus and precentral gyrus activation, and the activation was stronger on the biting side.

**Regional brain activation in synovitis patients with biting pain**

Areas of activation for patients with contralateral or ipsilateral biting pain are shown in Table 4, and Figures 5 and 6. The ACC was distinctly activated in synovitis patients with biting pain, but was not activated in the controls. Decrease in activation magnitude from controls to patients was noted in the inferior frontal gyrus, precentral gyrus, superior temporal gyrus, and middle frontal gyrus. For individual data, four patients with contralateral biting pain demonstrated activation in the left primary somatosensory cortex and two patients with ipsilateral TMJ biting pain demonstrated activation in primary somatosensory cortex (one for left primary somatosensory cortex, the other for right primary somatosensory cortex).



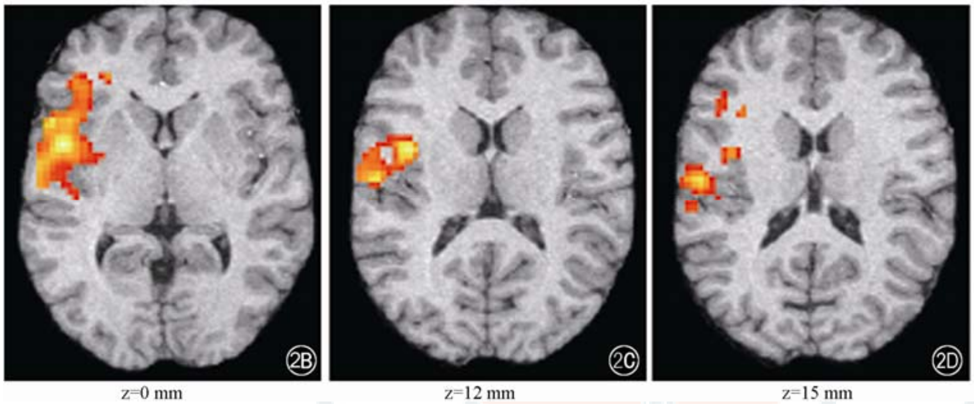
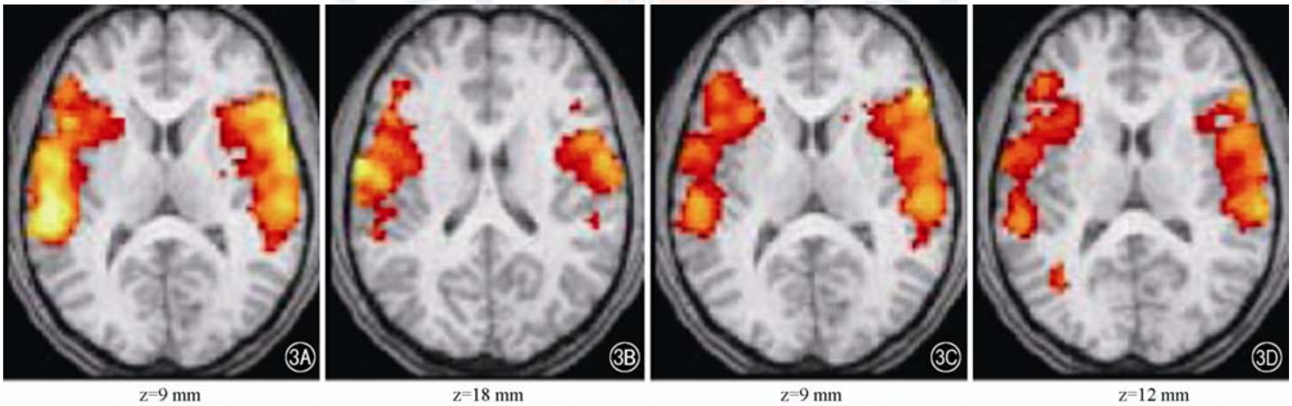




**Figure 1**. Brain activation in healthy subjects performing the right clenching task (*P* <0.01, voxels >10). The right superior temporal gyrus (**A**), bilateral inferior frontal gyrus (**B**), and bilateral precentral gyrus (**C**) were activated.

**Figure 2**. Brain activation in healthy subjects performing the left clenching task (*P* <0.01, voxels >10). The left insular (**A**), left superior temporal gyrus (**B**), left inferior frontal gyrus (**C**), and left precentral gyrus (**D**) were activated.



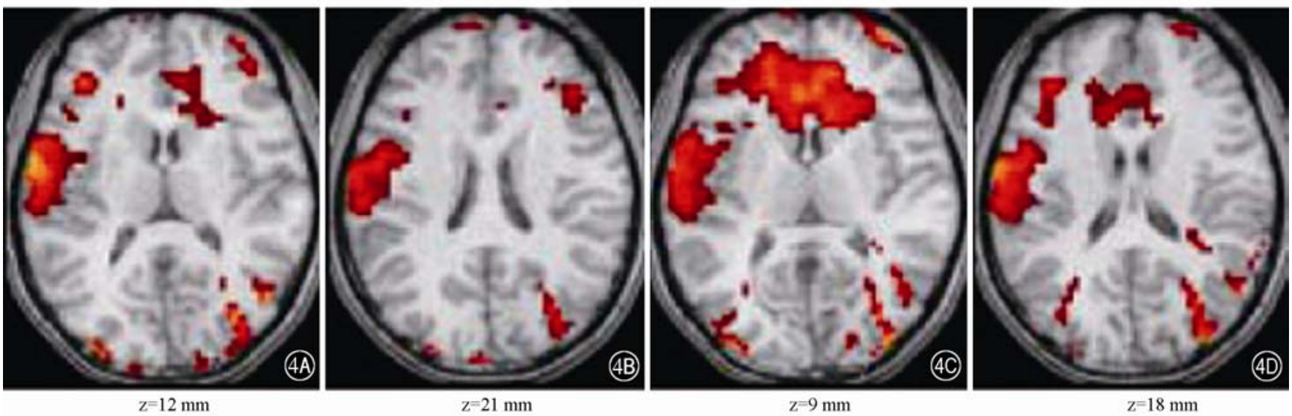




**Figure 3**. Individual data of brain activation in control subject No. 1 performing the unilateral clenching task (*P* <0.001, voxels >20). The bilateral inferior frontal gyrus (**A**) and precentral gyrus (**B**) were activated during the right clenching task, the bilateral inferior frontal gyrus (**C**) and precentral gyrus (**D**) were activated during the left clenching task,

**Figure 4**. Individual data of brain activation in control subject No. 14 performing the unilateral clenching task (*P* <0.001, voxels >20). The left inferior frontal gyrus (**A**) and left precentral gyrus (**B**) were activated during the right clenching task, the left inferior frontal gyrus (**C**) and left precentral gyrus (**D**) were activated during the left clenching task.

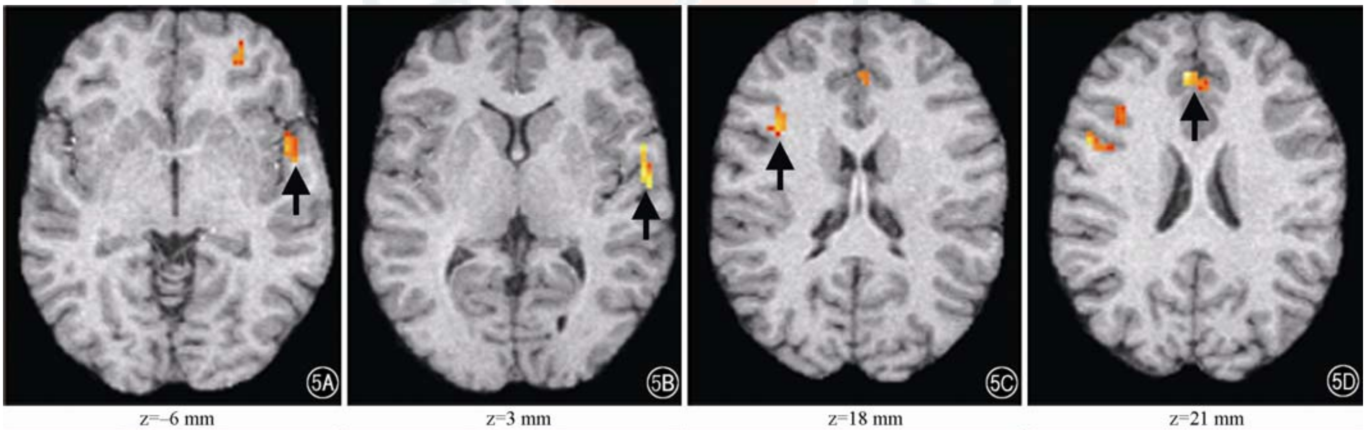
**Table 4.** Activated areas in the TMD synovitis patients with unilateral biting pain performing the right clenching task ($P$ <0.01, voxels >10)

| Activation area | BA | Talairach coordinate | | | *K* values | *t* values |
|---|---|---|---|---|---|---|
| | | X | Y | Z | | |
| Patients with contralateral biting pain (*n*=8) | | | | | | |
| R superior temporal gyrus | 22 | 59 | –6 | 6 | 48 | 5.91 |
| L ACC | 24,32 | 3 | 22 | 27 | 17 | 4.35 |
| R ACC | 24 | 3 | 13 | 30 | 17 | 3.16 |
| R middle frontal gyrus | 11 | 33 | 52 | –10 | 14 | 3.73 |
| L inferior frontal gyrus | 44,45 | –48 | 13 | 19 | 24 | 4.23 |
| Patients with ipsilateral biting pain (*n*=6) | | | | | | |
| R cingulate cortex | 23 | 15 | -25 | 26 | 46 | 5.66 |
| L inferior frontal gyrus | 47 | –56 | 17 | –1 | 115 | 6.09 |
| R inferior frontal gyrus | 44,45 | 48 | 12 | 16 | 23 | 5.08 |
| L inferior frontal gyrus | 44 | –53 | 7 | 19 | 11 | 4.38 |
| L superior temporal gyrus | 21,38 | –39 | 2 | –15 | 15 | 5.89 |
| R inferior frontal gyrus | 47 | 33 | 29 | –12 | 60 | 3.89 |
| L precentral gyrus | 6 | –45 | 4 | 16 | 11 | 5.01 |

## DISCUSSION

In this study, we examined the brain activations during unilateral clenching task in the TMD synovitis patient with contralateral or ipsilateral biting pain and the controls. Significant activations of the inferior frontal gyrus and precentral gyrus were found in both groups. TMD synovitis patients showed distinct activation of the ACC.

The group analysis results in our study showed that the unilateral clenching task activated several brain areas. Significant differences of the activation regions between right and left clenching task were found in inferior frontal gyrus and precentral gyrus. Previous functional neuroimaging studies have revealed that mastication, clenching, and tapping activate several cerebral regions, with the greatest activation in the primary sensorimotor cortex (SI/MI) in both hemispheres, without any significant difference between hemispheres[16] or with stronger activation of right motor cortex.[17] Individual data of this study showed activation in contralateral and/or ipsilateral primary somatosensory cortexes in seven subjects. The heterogeneous results may explain that our results of group analysis failed to reveal the activation in primary somatosensory cortexes. These differences in fMRI findings could reflect the variation in tasks and the stronger activation of the inferior frontal gyrus and precentral gyrus during unilateral clenching task. Further research to investigate the relationship between TMJ biting pain with the activation of the primary



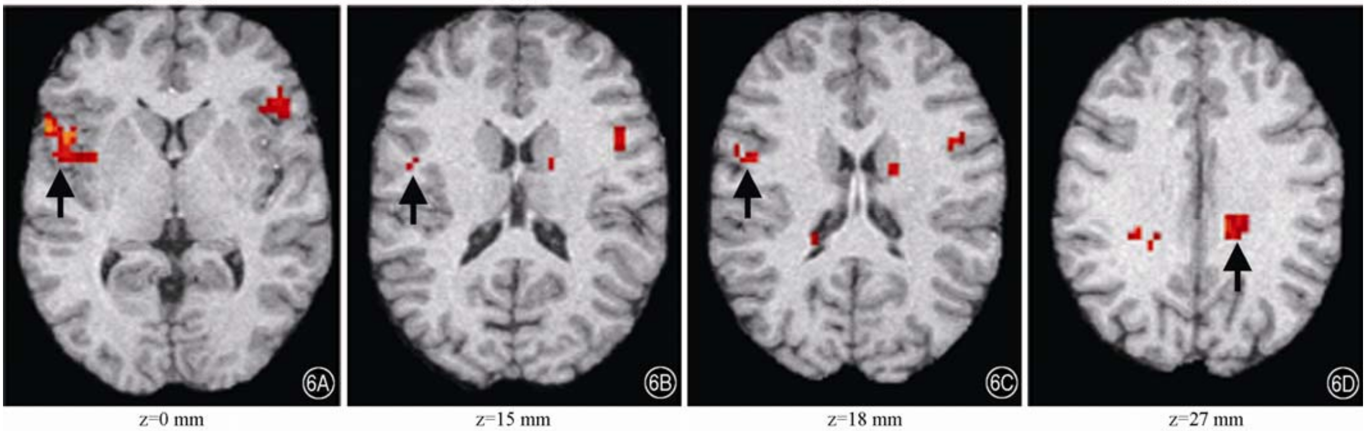




**Figure 5.** Brain activation in eight patients with contralateral TMJ biting pain performing the right clenching task ($P$ <0.01, voxels >10). The right middle frontal gyrus (**A**), right superior temporal gyrus (**B**), left inferior frontal gyrus (**C**), and bilateral anterior cingulate cortex (**D**) were activated when performing the right clenching task.

**Figure 6**. Brain activation in six patients with ipsilateral TMJ biting pain performing the right clenching task ($P$ <0.01, voxels >10). The left superior temporal gyrus (**A**), left precentral gyrus (**B**), left inferior frontal gyrus (**C**), and right cingulate cortex (**D**) were activated when performing the right clenching task.

somatosensory cortexes are needed.

Significant activation of inferior frontal gyrus/Broca's region (BA44, BA45) was obtained in our study when unilateral clenching task was performed. Takada and Miyamoto[6] reported that the gum chewing task significantly activated the several brain regions including the left inferior frontal cortex and the middle frontal cortex. Previous studies have demonstrated that the human ventral premotor cortex overlaps with Broca's region in the dominant cerebral hemisphere; that is known to mediate the production of language and contributes to language comprehension. This region is constituted of Brodmann's areas 44 and 45 in the inferior frontal gyrus.[18] Physiological and neuroimaging evidence indicated that area F5 in the macaque brain and BA 44 in the human brain share anatomical and functional homologies.[19] Stimulation and recording experiments showed that F5 was involved with the movement of both hands and mouth.[20] In humans, it has been found by fMRI studies that the non-language related motor functions of Broca's region comprise complex hand movements.[21] Our results showed that stronger activation was noted in the inferior frontal gyrus, which supported that the inferior frontal gyrus/Broca's area plays an essential role in unilateral clenching tasks.

Our group analysis data demonstrated stronger left cerebral cortex activation during left clenching task. The cerebral cortex controls contralateral body movements. Recent physiological studies have challenged the idea that the control of distal movements is exclusively contralateral.[22] Functional imaging studies revealed that ipsilateral activation was more pronounced when right-handed people used their left hand in movement tasks. Left-handed individuals also tended to preferentially recruit the left hemispheres when performing complex movements.[23] In contrast with contralateral brain control of the body, the motor control of masticatory muscle function is bilateral and guided by both hemispheres. Patients with unilateral cortical brain infarction, which caused marked handicap and serious impairment of upper limb function on the contralateral side, showed some differences in bite force between the healthy and paralyzed sides.[24] Electromyographic data have demonstrated that the bilateral masseter and anterior temporalis muscles are active during unilateral molar biting with an asymmetrical activation.[25] Distribution of TMJ reaction force between working and balancing side was associated with bite force direction.[26] Our findings provide a basis for further electromyographic study of unilateral clenching task.

Our data showed that three subjects had stronger activation of right hemispheres and five subjects had stronger activation of left hemispheres, suggesting that the activation of inferior frontal gyrus and precentral gyrus had side-preference during unilateral clenching task. Most subjects do not chew symmetrically, but chew predominantly on one side of the mouth, which is called the chewing-side preference (CSP). Mioche et al[27] performed a video fluorographic study of human intra-oral food management and found that 66% of chewing occurred on one side only. Contralateral dominance during activation of the primary sensorimotor cortex during tongue movement has been shown to be associated with CSP.[28,29] Our findings indicated that the left hemispheres played a prominent role during the unilateral voluntary clenching task, and the brain activation patterns were different between subjects.

Our fMRI results demonstrated that different brain areas were activated in TMJ synovitis patients with contralateral from patients with ipsilateral biting pain while performing the right clenching task. We found that the activated areas in patients with contralateral biting pain were similar to the controls performing the left clenching task. This suggests that the activities of the balancing side (left) masticatory muscles are stronger, and the larger left joint load results in left (contralateral) joint pain. The activated areas in patients with ipsilateral biting pain were similar to controls performing the right clenching task. This suggests that the activities of the working side (right) masticatory muscles are stronger, and the larger right joint load results in right (ipsilateral) joint pain. Previous studies have indicated the complexity of unilateral clenching. Results of mandibular movements study suggested that the ipsilateral joints were less heavily loaded during chewing and chopping than the contralateral joints.[30] Other biomechanical studies indicated that the reaction forces acting on the TMJ during unilateral clenching do not always load the balancing side joint more than the working side joint. Furthermore, we found that patients with contralateral biting pain commonly had disc displacements without reduction (7/8) in the affected side, while the patients with ipsilateral biting pain commonly had normal disc position in the affected side (4/6). These results demonstrated that joint loading of the working and balancing sides were different between the synovitis patients with biting pain and suggested that unilateral TMD biting pain occurring on the contralateral or ipsilateral sides were associated with different cerebral activation patterns and disc displacement types.

In terms of the location, we demonstrated that the biting pain patients had unique ACC activation. And there were significant differences between the patients and the controls on SCL-90 subscales for somatization, depression, anxiety, phobic anxiety, and paranoid ideations. Our results were consistent with the findings of Albuquerque et al[9] who studied burning mouth disorders using fMRI. Patients with TMD pain are similar to patients with other chronic pain conditions and associated with psychosocial factors. Dworkin and LeRerschel[31] proposed a research diagnostic criterion (RDC) for the classification of TMD patients, which includes physical and psychosocial-behavioral axes. Functional neuroimaging studies have shown that pain activates a number of brain regions, and the ACC is related to the affective and cognitive aspects of pain.[9,10,32] Our findings suggested the hypothesis that activation of the ACC in synovitis patients with biting pain associated with higher level of psychological distress.

Intrinsic limitation of this study was caused by the weakness that fMRI analysis is strongly influenced by excessive head motion associated with jaw movements. The data obtained in our study was limited by the sample size. Further investigation should be made to explore the central mechanism of unilateral clenching and TMD-related pain.

In summary, this study showed that the inferior frontal gyrus and precentral gyrus were activated during the unilateral clenching task. Different cerebral regions were activated in the TMJ synovitis patients with contralateral or ipsilateral biting pain during the right clenching task. Synovitis patients with biting pain had unique activation of ACC. The findings demonstrated that the inferior frontal gyrus and precentral gyrus play an essential role in unilateral clenching tasks and the activation of ACC in the synovitis patients with biting pain might be associated with higher levels of psychological distress.

## REFERENCES

1. Dworkin SF, Huggins KH, LeResche L, Von Korff M, Howard J, Truelove E, et al. Epidemiology of signs and symptoms in temporomandibular disorders: clinical signs in cases and controls. J Am Dent Assoc 1990; 120: 273-281.
2. LeResche L, Mancl LA, Drangsholt MT, Saunders K, Korff MV. Relationship of pain and symptoms to pubertal development in adolescents. Pain 2005; 118: 201-209
3. Turner JA, Holtzman S, Mancl L. Mediators, moderators, and predictors of therapeutic change in cognitive-behavioral therapy for chronic pain. Pain 2007; 127: 276-286.
4. Momose I, Nishikawa J, Watanabe T, Sasaki Y, Senda M, Kubota K, et al. Effect of mastication on regional cerebral blood flow in humans examined by positron-emission tomography with $^{15}$O-labelled water and magnetic resonance imaging. Arch Oral Biol 1997; 42: 57-61.
5. Tamura T, Kanayama T, Yoshida S, Kawasaki T. Analysis of brain activity during clenching by fMRI. J Oral Rehabil 2002; 29: 467-472.
6. Takada T, Miyamoto T. A fronto-parietal network for chewing of gum: a study on human subjects with functional magnetic resonance imaging. Neurosci Lett 2004; 360: 137-140.
7. Casey KL, Morrow TJ, Lorenz J, Minoshima S. Temporal and spatial dynamics of human forebrain activity during heat pain: analysis by positron emission tomography. J Neurophysiol 2001; 85: 951-959.
8. Morgan V, Pickens D, Gautarn S, Kesslr R, Mertz H. Amitriptyline reduces rectal pain related activation of the anterior cingulate cortex in patients with irritable bowel syndrome. Gut 2005; 54: 601-607.
9. Albuquerque RJ, de Leeuw R, Carlson CR, Okeson JP, Miller CS, Andersen AH. Cerebral activation during thermal stimulation of patients who have burning mouth disorder: an fMRI study. Pain 2006; 122: 223-234.
10. Gracely RH, Geisser ME, Giesecke T, Grant MAB, Petzke F, William DA, et al. Pain catastrophizing and neural responses to pain among persons with fibromyalgia. Brain 2004; 127: 835-843.
11. Derbyshire SW, Jones AK, Devani P, Friston KJ, Feinmana C, Harris M, et al. Cerebral responses to pain in patients with atypical facial pain measured by positron emission tomography. J Neurol Neurosurg Psychiatry 1994; 57: 1166-1172.
12. Truelove EL, Sommers EE, LeResche L, Dworkin SF, Von Korff M. Clinical diagnostic criteria for TMD. New classification permits multiple diagnosis. J Am Dent Assoc 1992; 123: 47-54.
13. Tasaki MM, Westesson PL, Isberg AM, Ren YF, Tallents RH. Classification and prevalence of temporomandibular joint disc displacement in patients and symptom-free volunteers. Am J Orthod Dentofac Orthop 1996; 109: 249-262.
14. Emshoff R, Rudisch A. Temporomandibular joint internal derangement and osteoarthrosis: are effusion and bone marrow edema prognostic indicators for arthrocentesis and hydraulic distention? J Oral Maxillofac Surg 2007; 65: 66-73.
15. Talairach J, Tournoux P. Co-planar stereotaxic atlas of the human brain. In: Talairach J, Tournoux P, eds. Three-dimensional proportional system: an approach to cerebral imaging. Stuttgart: Thieme; 1988: 38-90.
16. Tamura T, Kanayama T, Yoshida S, Kawasaki T. Functional magnetic resonance imaging of human jaw movements. J Oral Rehabil 2003; 30: 614-622.
17. Wang YW, Ma XC, Jin Z, Zhang L. Brain activities during maximum voluntary clenching with soft Occlusal pad in healthy adults by functional magnetic resonance imaging. West Chin J Stomatol (Chin) 2005; 23: 57-59.
18. Binkofski F, Amunts K, Stephan KM, Posse S, Schormann T, Freund HJ, et al. Broca's region subserves imagery of motion: a combined cytoarchitectonic and fMRI study. Hum Brain Mapp 2000; 11: 273-285.
19. Koski L, Iacoboni M, Dubeau MC, Woods RP, Mazziotta JC. Modulation of cortical activity during different imitative behaviors. J Neurophysiol 2003; 89: 460-471.
20. Rizzolatti G., Camarda R, Fogassi L, Gentilucci M, Luppino G, Matelli M. Functional organization of inferior area 6 in the macaque monkey. II. Area F5 and the control of distal movements. Exp Brain Res 1988; 71: 491-507.
21. Simon O, Mangin JF, Cohen L, Le Bihan D, Dehaene S. Topographical layout of hand, eye, calculation, and language-related areas in the human parietal lobe. Neuron 2002; 33: 475-487.
22. Rogers BP, Carew JD, Meyerand ME. Hemispheric asymmetry in supplementary motor area connectivity during unilateral finger movements. NeuroImage 2004; 22: 855-859.
23. Verstynen T, Diedrichsen J, Albert N, Aparicio P, Ivry RB. Ipsilateral motor cortex activity during unimanual hand movements relates to task complexity. J Neurophysiol 2005; 93: 1209-1222.
24. Kemppainen P, Waltimo A, Palomaki H, Salonen O, Kononen M, Kaste M. Masticatory force and functon in patients with

hemispheric brain infarction and hemiplegia. J Dent Res 1999; 78: 1810-1814.
25. Iwasaki LR, Petsche PE, McCall WD, Marx D, Nickel JC. Neuromuscular objectives of the human masticatory apparatus during static biting. Arch Oral Biol 2003; 48: 767-777.
26. Mao J, Osborn JW. Direction of a bite force determines the pattern of activity in jaw-closing muscles. J Dent Res 1994; 73: 1112-1120.
27. Mioche L, Hiiemae KM, Palmer JB. A posterio-anterior videoflurographic study of the intra-oral management of food in man. Arch Oral Biol 2002; 47: 267-280.
28. Shinagawa H, Ono T, Honda E, Sasaki T, Taira M, Iriki A, et al. Chewing-side preference is involved in differential cortical activation patterns during tongue movements after bilateral gum-chewing: a functional magnetic resonance imaging study. J Dent Res 2004; 83: 762-766.
29. Shinagawa H, Ono T, Ishiwata Y, Honda E, Sasaki T, Taira M, et al. Hemispheric dominance of tongue control depends on the chewing-side preference, J Dent Res 2003; 82: 278-283.
30. Naeije M, Hofman N. Biomechanics of the human temporomandibular joint during chewing. J Dent Res 2003; 82: 528-531.
31. Dworkin SF, LeReschel L. Research diagnostic criteria for temporomandibular disorders: review, criteria examinations and specifications, critique. J Craniomandib Disord 1992; 6: 301-355.
32. Buffington AL, Hanlon CA, Mckeown MJ. Acute and persistent pain modulation of attention-related anterior cingulate fMRI activations. Pain 2005; 113: 172-184.

*(Received October 19, 2010)*
*Edited by PAN Cheng*