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Cerebral Cortical Dysfunction in Patients with Temporomandibular Disorders in Association with Jaw Movement Observation

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RUNNING HEAD: Cortical Dysfunction in TMD patients
Abstract
Temporomandibular disorders (TMD) represent a group of chronic painful conditions in the masticatory musculature and temporomandibular joint. To examine possible changes in cortical machinery in TMD patients, we compared neuromagnetic signals evoked by cortical neurons between healthy subjects and TMD patients while they were carefully observing the video frames of jaw-opening movements performed by another person. During the movement observation task in the healthy subjects, we found cortical activation in the following sequence with left hemisphere dominance: 1) the occipitotemporal region near the inferior temporal sulcus (human homologue of MT/V5 in monkeys), 2) the inferior parietal cortex (IPC), and 3) the anterior part of the inferior-lateral precentral gyrus (PrCG). In the TMD patients, however, we found deficit or marked attenuation of the neuromagnetic responses in the PrCG and IPC, while the activity of the MT/V5 showed no differences from that in the healthy subjects. In addition, we could not find any differences in cortical magnetic responses between healthy subjects and TMD patients when they were observing palm-opening movements, indicating that cortical dysfunction associated with jaw-movement observation is specific phenomena in the patients of TMD. Thus the present study provides new neuropathological evidence that TMD patients exhibit dysfunction of recognition mechanisms in cerebral cortex during motor observation, and suggests that disturbance of cortical functions regulating visuomotor integration would play a crucial role in development as well as aggravation of TMD. **Keywords:** Human/Magnetoencephalography/Motor Cortex/Temporomandibular Disorder / Visual Cortex
Introduction

“Temporomandibular disorder” (TMD) is a collective term including a number of chronic pain related problems that involve the masticatory musculature and/or the temporomandibular joint (Okeson, 1996). Up to 6% of the whole population suffers from TMD-related chronic orofacial pain (Lipton et al., 1993; Matsuka et al., 1996).

Though the etiology and pathological mechanisms underlying TMD have remained poorly understood, recently obtained evidence has convergently suggested that the development of TMD could result from pathological changes in neuronal functions in the central nervous system (Maixner et al., 1995; Okeson, 1996; Svensson and Arendt-Nielson, 2000; Tenenbaum et al., 2001; Romaniello et al., 2003). An electroencephalographic (EEG) study has suggested that orofacial pain in TMD patients is associated with dysfunction of brain regions where trigeminal nociceptive inputs project (Romaniello et al., 2003). It was also indicated that orofacial pain of TMD modulated sensory-motor integration in the central nervous system (Svensson and Graven-Nielsen, 2001). Transcranial magnetic stimulation (TMS) in TMD patients demonstrated that TMD was not caused by the “hyper”-excitability in neurons of the motor cortex inducing hyperactivity in masticatory muscles (Cruccu et al., 1997). In addition, it was reported that TMD-related orofacial pain modified motor performance by reducing motor neuron activities (Lund et al., 1991).

Recent neurophysiological and neuroimaging studies in humans and monkeys have shown that the motor and premotor cortex have not only motor
executive, but also cognitive functions including action organization, space perception, motor imagery, and understanding and imitation of action (Tanji et al., 1996; Rizzolatti and Luppino, 2001; Gallese et al., 1996; Rizzolatti et al., 2001).

Accordingly we assumed that TMD patients might exhibit dysfunction of the motor-related cortical regions that controlled orofacial motor behavior and the masticatory neuromuscular system.

In the present study, with the aim to get a better understanding of the possible modification of the cortical machinery for the orofacial motor functions in TMD patients, we compared using magnetoencephalography (MEG) the temporal/spatial activation patterns of the cortical areas involved in jaw movement observation between healthy subjects and TMD patients to examine our hypothesis that TMD patients might show cortical dysfunction in relation to motor recognition.
Methods

Subjects

Subjects consisted of eight healthy adults (four males and four females; 30.0 years old on the average) and nine patients suffering from TMD (four male and five females; 32.4 years old on the average). The subjects were all right-handed. They gave written informed consent to participate in the present study, which was approved by the Ethics Committee of Tokyo Dental College in accordance with the Declaration of Helsinki. All the TMD patients suffered from masticatory muscle pain (myofascial pain) and joint sounds (disc displacement with reduction). Three out of nine TMD patients had temporomandibular joint pain (arthralgia in one or both joint sites). None of the TMD patients showed symptoms of limited mandibular opening, disc displacement without reduction and pathological conditions in the temporomandibular joint itself including inflammatory/degenerative disorders (Dworkin and LeResche, 1992).

Observation Tasks

The subjects were asked to carefully observe two series of video-clips of bilaterally symmetrical jaw-opening movements and unilaterally right hand spreading out the palm movements of another person, which was used as visual stimuli for observation tasks (Fig. 1). One sequence of jaw- and palm-opening movements in the video-clip was presented for 3 s repeatedly with an inter-stimulus interval of 3 s during an experimental session. Each magnetic signal was averaged with reference to the trigger pulse which was generated at
the onset of each movement in the video (Fig. 1). The visual stimulus was presented onto a screen placed 1 m in front of the subject with a video projector.

[Figure 1]

**Recording and analysis**

A 204-channel neuromagnetometer (Vectorview, Neuromag Co., Finland) was used for recording magnetic fields from 102 points with a pair of gradiometers (inset of Fig. 2A). To align the coordinate systems of the MEG and the head magnetic resonance imaging (MRI; 1.5-T Siemens, Germany), the positions of four head position indicator coils and three anatomical landmarks (the bilateral preauricular points and nasion) were measured with a three-dimensional digitizer (Isotrak, Polhemus, Vermont). At the beginning of each recording session, weak currents were led into these coils, and the resulting magnetic fields were measured with the sensor array to find the head location with respect to the sensors.

All the signals were digitized at 1 kHz and bandpass-filtered (0.1-40 Hz for MEG and 0.03-30 Hz for EOG). Vertical electro-oculograms (EOG) were recorded bipolarly to monitor eye movements and blinks. Surface electromyograms (EMGs) were recorded from the left digastric muscle to monitor unconscious jaw muscle activities during the observation task (band pass
filter: 10-2000 Hz). Whenever the records of trials contained any of MEG signals exceeding 1500 fT/cm, EOG deflection exceeding 150 µV and EMG activities reflecting unconscious jaw movements or the subjects appeared to be drowsy, the records of such trials were excluded from analysis and an additional set of data was collected. One experimental session lasted until 100 artefact-free records were obtained.

The magnetic signals were averaged with the trigger pulses generated at the onset of jaw-opening movements or palm-opening movement in the video. The analysis period was set to 1,300 ms, from 500 ms preceding to 800 ms following the trigger pulse (Fig. 1). The mean amplitude of the first 10% of the whole 1,300 ms time window (from -500 ms to -370 ms) served as the baseline for amplitude measurements at each channel. Isocontour maps were constructed from the measured data at selected time points by the method of minimum norm estimates (Hämäläinen and Ilmoniemi, 1994). To identify the sources of magnetic fields, one equivalent current dipole (ECD) was first determined by the least-square search for a subset of channels over the areas where magnetic fields were visually detected. Goodness-of-fit (gof) of the model was also calculated to express in percentage terms how much the dipole model accounted for the measured signal variance. Only ECDs attaining more than 90 % of gof were accepted for analysis, in which the entire time period and all the channels were taken into account for computing the parameters of a time-varying multidipole model (Hämäläinen et al., 1993). The next ECD was identified by removing the effect of the previous sources from the magnetic signal pattern.
(signal space projection method; Uusitalo and Ilmoniemi, 1997) and then searching for additional sources in the response of the residual waveforms. This surveillance was discontinued when the strength of new ECDs could not exceed 5 nAm (Salmelin et al., 1996). Note that the source which could not be detected at a particular brain area was assumed to be 0 nAm in source strength. The ECDs were then superimposed on the subject's MRIs to determine the source locations with respect to the anatomical structures.

The results are expressed as the mean ± SE of mean of \( n \) representing the number of subjects. The difference in the means of the peak latencies and magnitudes of the magnetic fields as well as the strength of ECD between healthy subjects and TMD patients was statistically tested by one-way ANOVA; the significance level was set to \( P = 0.05 \).

The magnetic amplitude was measured at the maximum value of the root mean square (RMS) of the magnetic field strength taken over each hemisphere.
Results

Waveforms

Using a whole-head MEG, we obtained magnetic signals produced by neurons in the cortex while the subjects observed videotaped jaw-opening and palm-opening movements of another individual (Fig. 1). During the observation task of jaw-opening movements, we found prominent magnetic fields in subsets of the neuromagnetic sensor array (Fig. 2A, B) located in the occipital region and parietotemporal region bilaterally in both the healthy subjects and the TMD patients. In the TMD patients, however, we consistently found marked attenuation of magnetic signals recorded from the sensors over the parietotemporal regions in both hemispheres compared with those from the same areas in the healthy subjects, while the signals recorded from the occipital sensors on both sides of TMD patients looked nearly equivalent in magnitude to those of healthy subjects (Fig. 2B). During palm-opening movement observation, however, we did not find any difference in the neuromagnetic signals between the healthy subjects and TMD patients (see below).

During observation of jaw-opening movements, in the healthy subjects as well as TMD patients, two peak signal components (termed 1M and 2M) were consistently detected in the magnetic wave forms bilaterally (Fig. 2B). In the healthy subjects, these 1M and 2M components showed dipolar magnetic field patterns (Fig. 2C) expecting multiple current source. Their peak latencies were approximately 140 ms for 1M and 230 ms for 2M in both hemispheres in both the healthy subjects (open columns) and TMD patients (filled columns) (Fig. 3A).
During observation of palm-opening movements, bilateral peak signal components of 1M (ca. 120 ms) and 2M (ca. 230 ms) were also found in both the healthy subjects (open columns) and TMD patients (filled columns) (Fig. 3C). For each observation task, there were no significant differences in peak latencies of 1M and 2M components either between the healthy subjects and TMD patients or between the left and right hemispheres in either group of subjects (i.e., no interhemispheric differences). However, the peak amplitudes of 2M component during jaw-opening movement observation were significantly smaller bilaterally in the TMD patients (filled columns) than those in the healthy subjects (open columns; $P < 0.05$; Fig. 3B), while the peak amplitude of 1M component were equivalent between the healthy subjects and TMD patients. During palm-opening movement observation, no differences in the peak amplitudes of 1M and 2M components could be found between the healthy subjects and TMD patients (Fig. 3D). Note that there were no significant differences in the peak magnetic amplitudes and latencies for 1 and 2M between male and female in either group of subjects ($n = 8$ for healthy subjects and $n = 9$ for TMD patients) accompanying each observation task ($P > 0.05$).

[Figures 2 and 3]

**Source distribution and strength**
To make a model with multi-dipoles generating the magnetic signal distribution over the sensors on the occipital region and the lateral parietotemporal region, and to assess the differences on the cortical response between the TMD patients and healthy subjects (Figs. 2 and 3) during jaw-opening movement observation, we examined the fields by time-varying multi-dipole analysis (see Methods). Modifications in cortical neuromagnetic responses between healthy subjects and TMD patients were observed by viewing jaw-opening movements, thus we evaluated cortical activation patterns during the observation task. The locations of the estimated equivalent current dipoles (ECDs) in each healthy subject and TMD patient were superimposed on the individual MRIs to determine the source locations.

During observation of jaw-opening movements in the healthy subjects, activation of three source areas was detected in: 1) the occipitotemporal area near the inferior temporal sulcus (the human homologue of the monkey MT/V5, hereafter called MT/V5) (Watson et al., 1993), 2) the inferior parietal cortex (IPC), and 3) the anterior part of the inferior-lateral precentral gyrus (i.e., the posterior wall of the inferior precentral sulcus; PrCG) with the left hemisphere dominance (Fig. 4A). The locations of the three sources were consistent across all the healthy subjects. On the other hand, in the TMD patients, we could consistently detect only two main source areas in the MT/V5 and IPC predominantly in the left hemisphere across all the TMD patients. The activation of the PrCG, which was consistently detected in the healthy subjects, was defective in eight of nine TMD patients.
To assess the strength of activation in the three source areas during jaw movement observation, we calculated the values of the strength of ECDs (source strength) as a function of time. Fig. 4B shows source strength waveforms from three different areas in a healthy subject (left traces) and a TMD patient (right traces). 1M component in the magnetic waveform corresponded to the time of the MT/V5 activation, while 2M component coincided with the IPC and PrCG activation (see Figs. 2 and 3) in the healthy subjects. Their magnitudes of the source strength of the main source areas in the healthy subjects (n = 8) and the TMD patients (n = 9) were 13 ± 3 nAm and 12 ± 3 nAm for the MT/V5, 22 ± 5 nAm and 10 ± 2 nAm for the IPC, 16 ± 3 nAm and 1 ± 1 nAm for the PrCG, respectively (bar graphs in Fig. 4C; the source strength in the PrCG that could not be detected in eight of nine patients was assumed to be 0 nAm). Activation of the PrCG and IPC during observation of jaw-opening movements in the TMD patients was significantly smaller than the healthy subjects (P < 0.05 for the IPC and P < 0.0001 for the PrCG in source strength; Fig. 4C), while MT/V5 activation was equivalent between the healthy subjects and the TMD patients (P > 0.05). These results of temporal and spatial analyses of the cortical responses indicated that the TMD patients exhibited abnormal IPC and PrCG responses during observation of jaw-opening movements.
Discussion

This is the first neuromagnetic study on patients suffering from TMD. The main neurophysiological findings in the present study were twofold. First, the magnetic recordings revealed that the activities of the PrCG and the IPC were modified when the healthy subjects observed jaw movements of another individual. Second, the further analysis of magnetic fields demonstrated the decreased activities in the PrCG and the IPC during jaw movement observation in the TMD patients (i.e., the lack or marked attenuation of the PrCG and IPC responses; see below). On the other hand, the neural activities in the left posterior temporooccipital cortex (MT/V5; Watson et al., 1993; Tootell et al., 1995; Nishitani and Hari, 2000) were equivalent between the healthy subjects and TMD patients. No differences were found in either the peak latencies of magnetic fields or the activation timing of the MT/V5 and IPC. In addition, no differences in the peak amplitudes and latencies of 1M and 2M component in the neuromagnetic signals during palm-opening observation could be found between the healthy subjects and TMD patients (Fig. 3C and D), indicating that lack of brain signals in the PrCG and IPC is specific during jaw-opening movement observation in the TMD patients. Since there were no significant gender differences in the neuromagnetic responses in either group of subjects accompanying each observation task, we exclude gender difference as a factor in the neuromagnetic responses. Therefore, the sequential hypofunction or functional disruption of both the IPC and PrCG is a crucial problem for the pathological changes in the central nervous system of the TMD patients.
We recorded magnetic fields from the sensors located at the bilateral parieto-temporal-occipital region (Figs. 2 and 3). However, we found the remarkable left hemisphere dominance of the brain activities during jaw-movement observation task (Fig. 4A). Bilateral (left and right hemisphere) activation of the face motor area and IPC was reported in association with observation of mouth movements (Buccino et al., 2001; Nishitani and Hari, 2002). In contrast, a recent study (Leslie et al., 2004) has reported that passive viewing of “emotional facial expression” yielded largely right hemispheric activation in the ventral premotor area, whereas active imitation of the observed movements led to bilateral hemispheric activation. Thus, Leslie et al. suggested that the motor area of the left hemisphere would mediate control of the facial musculature, while that of the right hemisphere would play a role in emotional processing (Leslie et al. 2004). In addition, a recent neuroimaging study has suggested that the left inferior parietal lobule computes the sensory-motor associations necessary to imitate motor action (Meltzoff and Decety, 2003). The observation task in our study consisted of showing only the mouth region (see Methods and Fig. 1), to rule out possible contribution of the neural activities involved in empathy by facial expression to the experimental results. Thus, our results suggest that the left hemisphere dominance of neural activation would reflect motor functions, including cognitive and/or sensory-motor association mechanisms of jaw movements by viewing streaming video-clips of the movements.

The most noteworthy result in this study is that activities of the PrCG and IPC are markedly attenuated in the TMD patients while they observed
jaw-opening movements. Alterations in the human higher nervous functions have recently been reported to be associated with pathogenesis of TMD (Maixner et al., 1995; Carlson et al., 1998; Tenenbaum et al., 2001).

Activation of the PrCG and IPC when a subject observes jaw movements is in line with recent neurophysiological and neuroimaging evidence. A recent MEG study has shown activation of the inferior parietal lobe and the oral region of the primary motor cortex (M1) elicited by watching lip posture (Nishitani and Hari, 2002). In addition, neuroimaging studies have shown that observation of mouth and hand action activates the mouth- and hand-area of M1, respectively (MEG studies; Hari et al., 1998; Jarvelainen et al., 2001), as well as the premotor cortex (ventral region of Brodmann's area 6) and the inferior parietal lobe somatotopically (fMRI study; Buccino et al., 2001).

In the monkey, neurons in the inferior parietal lobe, namely in area PF (area 7b), responded to observation of action (Gallese et al., 2002). Most PF neurons also discharge during action execution (Gallese et al., 2002). The IPC was reported to be the human homologue of the monkey PF (Nishitani and Hari, 2002). Neuroimaging studies in humans have revealed that activation of the IPC is related to production of imitation for action and to distinguishing one’s own actions from those of others as well as formation of the kinesthetic copy of movements during movement observation (Iacoboni et al., 1999; Decety et al., 2002). This copy (indicating joint positions) is then used during action execution (Iacoboni et al., 1999). In addition, PrCG activation (Fig. 4) in our healthy subjects is in line with recent neurophysiological evidences that clearly indicate
that action observation is related to activation of cortical areas that are involved in motor control in humans (Nishitani and Hari, 2000, 2002; Rizzolatti et al., 2001). As well known, most of the human precentral gyrus is occupied by Brodmann’s area 6, while area 4 is largely confined to the central sulcus (Brodmann, 1903, and see also Preuss et al., 1996). Especially, the ventral precentral gyrus contains area 6 representing the face in the motor homunculus as the face motor area involved in jaw movements (see Preuss et al., 1996), suggesting that activation of the PrCG in our study would correspond to activation of the primary motor cortex along with area 6aa. The lateral part of the precentral gyrus includes Brodmann’s area 6aa representing the orofacial motor function, which was reported to be involved in a visuomotor transformations (Matsumoto et al., 2003). Thus, activation of the PrCG as well as IPC by observation of jaw movements (Figs. 2-4) may play a crucial role in orofacial motor functions including motor behavior and/or cognition (Rizzolatti and Arbib, 1998; Rizzolatti et al., 2001; Matsumoto et al., 2003), by automatically generating an internal replica of the observed jaw movements (Buccino et al., 2001; and see also above). In addition, we observed a sequential cortical activation pattern from occipital region to IPC, from there to PrCG during jaw movement observation, suggesting information processing pathway for motor recognition as previously reported (Nishitani and Hari, 2000, 2002). In the TMD patients, therefore, the lack of PrCG and IPC activation as well as reduced connectivity of cortical activation in association with jaw movement observation (Figs. 2-4) would reflect changes in cortical motor executive/cognitive function, which could result in uncontrolled
orofacial motor behavior.

On the other hand, the parietal cortex including the IPC plays an important role in the sensorimotor integration and the representation of body image. In the monkey, the posterior parietal cortex possesses multimodal representation of the body and the peripersonal space which is used for planning and execution of purposeful movements (Andersen et al., 1997). Neuropsychological studies in humans have demonstrated that the patients with damage to the parietal lobe show the neglect syndrome of their own bodies and the introspective experiences of distortion and extinction of their body images (Holmes, 1918; Triggs et al., 1994; Berlucchi and Aglioti, 1997). Specifically, in the body cognition disorder, the angular gyrus could be a crucial role in a neural network that mediates one’s own body perception (Halligan et al., 1995). The abnormal temporomandibular joint sensation and chronic pain frequently found in TMD patients could result from the disorder of sensorimotor integration and body image, caused by the IPC dysfunction.

In conclusion, we propose that the attenuated activities of the IPC and lack of activities of the PrCG (Figs. 2-4) would induce the disorder of motor cognition and the distorted sensation in masticatory musculature and temporomandibular joint. Although the roles of such disorders of these neural activities as a factor to cause TMD need to be further investigated, these functional disorders in cortical mechanisms in TMD patients could aggravate the symptom of TMD. This in turn would worsen the cortical functional disturbance. Thus, this vicious circle could clinically results in uncontrolled orofacial motor
behavior (e.g., teeth clenching and grinding, jaw thrusting) (Okeson, 1996) and subsequent chronic pain in TMD patients.
Acknowledgements

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References


Figure Legends

Fig. 1: Visual stimuli for observation tasks. Panels (Videotaped stimuli) show the series of the vide-clip representing each one jaw-opening (upper) and palm-opening movement (middle) sequence, moving from the left to right. Each image shows the first frame of every 5 consecutive frames (30 frames/s); the interval between 2 frames corresponds to 1/6 s. Lower panel shows the recording period. The magnetic signals were averaged with reference to the trigger pulse which was generated at the onset of each movement in the video. The white circle at the bottom of a video frame (upper and middle panels; the circles appear at the start of each opening movement) serves as the marker to generate the trigger pulse by a photo sensor which was placed in front of the video projector. The sensor detected a change in luminance elicited by a small white circle which appeared at the start of opening movement at the bottom of the one video frame. The circle was invisible to the subjects. There was no delay time between appearing of white circle on the visual stimulus and generation of the trigger pulse.

Fig. 2: Magnetic wave forms. A, whole-scalp magnetic responses in healthy subject 4 during observation of jaw-opening movements. Traces are plotted on the flattened head as viewed from above with the nose upward. Upper and lower traces of each pair represent the latitudinal and longitudinal derivatives of the radial magnetic fields. The inset shows the locations of 102 sensors and the groups of sensor arrays in the frontal (open circles), parietal (filled circles),
temporal (open squares) and occipital (open triangle) regions on the flattened head. Solid lines divide the sensor arrays into the groups corresponding with the inset. B, enlarged superimposed traces of the magnetic signals in association with observation of jaw-opening movements in healthy subject 2 (left traces) and TMD patient 2 (right traces) from the frontal (red), parietal (purple), temporal (yellow) and occipital (blue) regions on the left (upper traces) and right (lower traces) hemisphere. These regions corresponded with the group of sensor arrays indicated by the inset (shown by each color) and the regions divided by the solid lines in A. The two successive peak signal components were named 1M and 2M. Each trace in A and B starts 500 ms preceding the presentation of the frame showing the start of jaw-opening movements (vertical lines in B) and terminates 800 ms after it. Surface EMGs (bottom trace in B) were recorded from the left digastric muscle showing no jaw muscle activities during the task. C, a typical isocontour maps of 1M (left panel) and 2M (right panel) in the healthy subjects. In this figure, isocontour maps are drawn at 20 fT steps. Solid and dashed lines indicate outgoing and ingoing fluxes, respectively. A image for 1M shows the map of bilateral occipital region, and that for 2M shows left hemisphere.

Fig. 3: Latencies and magnitudes of peak of magnetic signals of 1M and 2M. A to D, summary bar graphs showing the mean peak latencies (A and C) and the mean values (B and D) in magnetic signals calculated by RMS of the left (upper graphs in A to D) and right hemisphere (lower graphs in A to D) obtained from the healthy subjects (open columns) and TMD patients (filled columns) during observation of jaw- (A and B) and palm-opening (C and D) movements. The
amplitudes for 2M component were 154 ± 19 fT/cm in the left and 146 ± 19 fT/cm in the right hemispheres in the healthy subjects (n = 8), and 116 ± 8 fT/cm in the left and 111 ± 9 fT/cm in the right hemisphere in the TMD patients (n = 9). Each column represents the mean ± S.E. of all the healthy subjects and TMD patients. Statistically significant differences between each pair of columns are indicated by asterisks. *P < 0.05.

Fig. 4: Current source analysis. A, locations of ECDs producing the cortical magnetic responses in the healthy subject during observation of jaw-opening movements. By time-varying multi-dipole analysis we found three ECDs during jaw movement observation task in the healthy subjects. The red circles show the locations of ECDs on frontal (left images), sagittal (middle images) and coronal (right images) planes of MRIs (subject 4). These three sources are located in the MT/V5 (upper images), IPC (middle images) and PrCG (lower images) in the left hemisphere. B, the traces show the current source strength of the MT/V5 (top traces), IPC (middle traces) and PrCG (bottom traces) in healthy subject 1 (left column) and TMD patient 6 (right column), as a function of time. C, summary bar graphs showing the mean values of source strength in the MT/V5 (upper pair), IPC (middle pair) and PrCG (lower pair) in the healthy subjects (open columns) and TMD patients (filled columns). Each column represents the mean ± S.E. of all the healthy subjects and TMD patients, respectively. Statistically significant differences between the columns of each pair are indicated by asterisks. *P < 0.05; **P < 0.0001.
**Fig. 3**

**A**
Jaw movement observation

Mean peak latencies

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Mean values

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**B**

**C**
Hand movement observation

Mean peak latencies

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**D**

Healthy subjects

TMD patients