

Abstract

Cerebral activity during teeth clenching and fist clenching

Using functional magnetic resonance imaging, we compared the cerebral activity during bilateral light fist-clenching and light teeth clenching to provide more information on the central processing mechanisms underlying awake bruxism. Fourteen subjects participated in our study. Statistical comparisons were used to identify brain regions with significant activation in the subtraction of light fist clenching and light teeth clenching activity minus baseline. Participants also evaluated the perceived effort of clenching for each task, using a visual analogue scale of 0-100, after functional magnetic resonance imaging was performed.

Bilateral light fist clenching significantly activated the bilateral sensorimotor cortex, while light teeth-clenching was significantly associated with activation of the bilateral sensorimotor cortex, supplementary motor area, dorsolateral prefrontal cortex, and posterior parietal cortex. The VAS scores for fist clenching and teeth clenching were not significantly different. As light teeth-clenching activates a more extensive cortical network compared with light fist clenching, we suggest that the teeth clenching may induce a more complex cerebral activity compared with the performance of a hand motor task. The clinical significance of these findings remains unknown but could perhaps be related to the propensity to trigger awake bruxism.

Original publication: Iida T, Kato M, Komiyama O, Suzuki H, Asano T, Kuroki T, Kaneda T, Svensson P, Kawara M. Comparison of cerebral activity during teeth clenching and fist clenching: a functional magnetic resonance imaging study. Eur J Oral Sci 2010; 118: 635-41.

Keywords:
Bruxism;
magnetic resonance imaging;
brain mapping;
cerebral activity;
teeth clenching

Comparison of cerebral activity during teeth clenching and fist clenching: a functional magnetic resonance imaging study

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Bruxism is defined as an awake (non-sleep) or a sleep parafunctional activity that includes clenching, bracing, gnashing, and grinding of the teeth (1). In order to elucidate the central processing mechanisms underlying bruxism in humans, it is important to identify the network of regions in the brain that are active during voluntary activation of the jaw-closing muscles as a proxy of awake bruxism [e.g. unconscious teeth clenching (TC)]. The mechanisms of awake bruxism have been previously investigated. Rao & Glaros (2) proposed that the

aetiology of awake bruxism initially involves a specific muscular response to stress, but is neither a generalized psychological dysfunction nor a generalized autonomic arousal, both of which may develop at some later stage of the disorder. Tahara et al. (3) showed that TC promotes relaxation in people under stress. In addition, Manfredini et al. (4) suggested that awake clenching seems to be associated with psychosocial factors and a number of psychopathological symptoms. However, at present, the mechanism for awake bruxism has not been clarified.

So far, the cortical networks related to various types of voluntary TC have been examined using different methodological approaches, including near-infrared spectroscopy (5), magnetoencephalography (MEG) (6,7), and functional magnetic resonance imaging (fMRI) (8). Shibusawa et al. (5) identified, using near-infrared spectroscopy, the primary motor and sensory cortices as regions related to TC; however, near-infrared spectroscopy was unable to show the brain regional activity over the whole head. Therefore, the level of oxygenated haemoglobin in other regions was not described in this report. In MEG studies, Iida et al. (6,7) reported increased activity in the motor cortex, premotor cortex, somatosensory cortex, and cerebellum, and all areas were involved in the signal pathway immediately before TC.

As MEG measures the weak magnetic fields generated by cerebral electric activity, these MEG studies did not detect the brain regional activity during actual TC as a result of potential artifacts from masticatory muscle activity (6,7). Similarly, MEG studies related to jaw movements have also described the brain regional activity immediately before any actual jaw movements (8,9). In an fMRI study, Tamura et al. (10) reported the brain regional activity evoked by a TC task, in comparison with regional activity when the mandible was kept in a physiological rest position, but they did not describe the Talairach standard coordinates of brain regional activity during teeth clenching in sufficient detail. At present, the cerebral activity underlying TC has not been clarified and remains understudied.

Several fMRI studies have revealed brain regional activity during the performance of a hand motor task (11,12). Jäncke et al. (11) compared the brain regional activity between unimanual and bimanual finger-tapping tasks and showed the detailed pattern of brain regional activity in the sensorimotor cortex (SMC) and in the supplementary motor area (SMA). In contrast, an fMRI study carried out by Luft et al. (12), comparing two body movements, showed motor system activation patterns associated with isolated single-joint movements of corresponding joints in the arm and leg. This report demonstrated that central motor structures contribute differently to isolated elbow and knee movements (12). However, no fMRI studies have directly compared brain regional activity between TC and hand motor task performance in the same subject.

The present fMRI study was designed to detect differences in the brain regional activity during conscious light TC and a hand motor task, namely bilateral light fist clenching (FC). The hypo-

thesis was that there would be distinct cortical-activation patterns because light TC always involves some degree of bilateral commands to the brain stem and motorneurons of the jaw muscles and movement of a single unit (the mandible), whereas light FC can be achieved by deliberate unilateral or bilateral commands to the spinal motorneuron pool and involves the movement of multiple units (6,7,13).

Material and methods

The study included 14 Japanese participants (11 men and three women; mean age \pm SD, 25.6 \pm 1.69 years). None of the participants reported any neurological disorders or abnormalities in stomatognathic function or orofacial pain complaints, based on a medical and dental history that included standard questionnaires and an oral examination. Participants were informed about the experimental procedures, and informed consent was obtained from all study participants. This protocol was approved by the ethics committee of Nihon University School of Dentistry at Matsudo (EC 07-009), based on the guidelines set forth in the Declaration of Helsinki.

Experimental task

The study involved two tasks: a bilateral FC task and a TC task. All

Study design

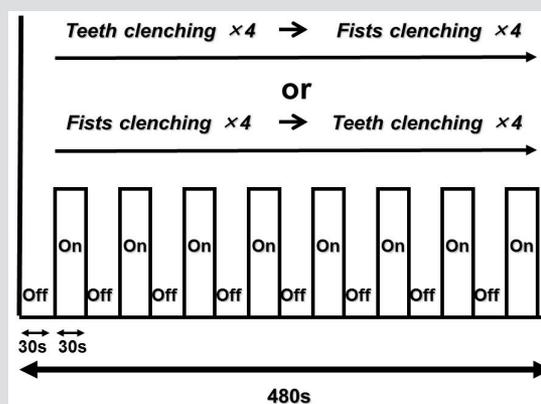


Fig. 1. Experimental task paradigm. Each participant performed fist clenching (FC) and teeth clenching (TC), alternating between a 30-s rest block and a 30-s task block, over a total study time-period of 480 s. Each measurement started with a rest block, followed by a randomly assigned task block (FC or TC).

Fig. 1. Et åbent randomiseret cross-over design af 480 sekunders varighed med 30 sekunders aktivitet (knyttede hænder eller tænderskæren) vekslede med 30 sekunders pause.

Surface projection of brain activity

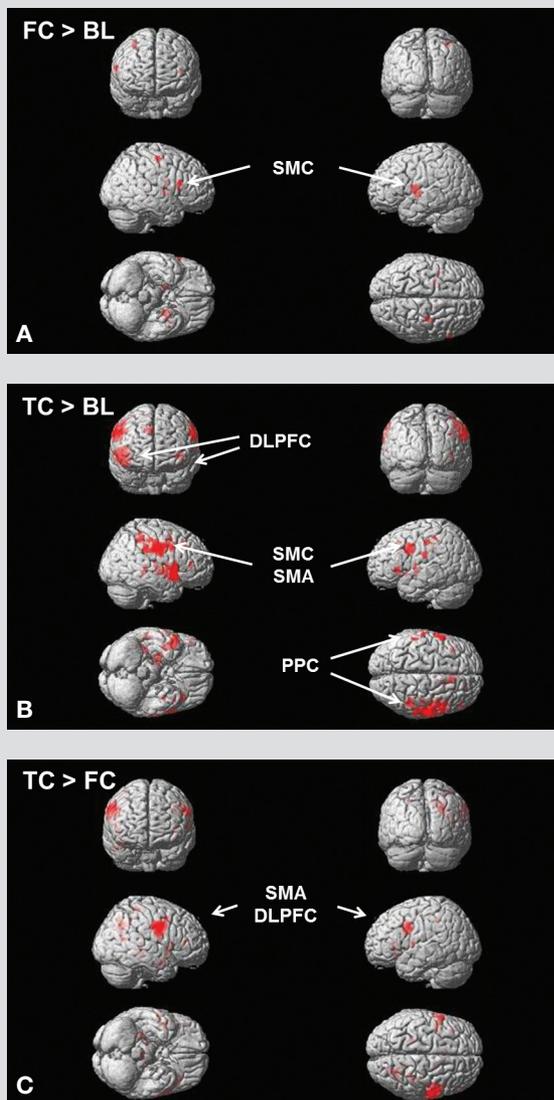


Fig. 2. Surface projection of statistical parametric maps superimposed onto a standard Montreal Neurological Institute (MNI) standard template brain ($P < 0.005$, uncorrected for Multiple comparison). (A) Fist clenching (FC) minus baseline (BL), (B) teeth clenching (TC) minus BL, and (C) TC minus FC. DLPFC, dorsolateral prefrontal cortex; PPC, posterior parietal cortex; SMA, supplementary motor area; SMC, sensorimotor cortex.

Fig. 2. Overfladeprojektion af hjerneområder med signifikant øget iltring af blodet (Statistisk parametriske kortlægningsmetode). (A) Hjernens aktivitet under knyttede hænder minus baseline, (B) hjernens aktivitet under tænderskæren minus baseline og (C) hjernens aktivitet under tænderskæren minus knyttede hænder.

participants were instructed to lightly clench their teeth (lightly was defined as a submaximal jaw muscle contraction that could mimic the level of muscle contraction during unconscious TC). Therefore, TC required the upper and lower teeth to be bitten together continuously in the intercuspal position. Similarly, light FC was defined as a submaximal contraction of the hand muscles that could mimic the level of muscle contraction during unconscious clenching. The FC task required the continuous formation of tight fists bilaterally during the task block. Importantly, the participants were trained in these FC and TC tasks before the fMRI scans. Furthermore, all participants were instructed that during the rest blocks in the scan the lower jaw was to be kept in a natural and relaxed position with the teeth apart and that the fists were to be kept in a natural, unstrained, and relaxed position. Participants alternated between a 30-s rest block and a 30-s task block (continuous contraction) for 480 s, and successively performed each task four times in a single session (Fig. 1). Each measurement series consisted of 160 scans for a total duration of 480 s. As each task block was separated by a 30-s rest period, participants were able to perform the tasks comfortably without muscle fatigue. Each trial began with the rest block and was followed by the task block (FC or TC), allocated randomly, at a given auditory signal. During the rest blocks, participants heard only noise from the scanner. After each scan, participants were asked if they had adhered to the instructions, and if not, or in doubt, the scan and specific task were repeated.

Image acquisition

Functional magnetic resonance imaging was performed using a Philips 1.5 T Achieva system (Philips Medical Systems, Best, the Netherlands). Each participant lay comfortably on the scanner table in a supine position during the experiment. The participants head was immobilized by a forehead strap. During measurements, room lights were dimmed and participants were instructed to keep their eyes closed. Functional images were acquired using a gradient-echo echo-planar imaging sequence with the following parameters: repetition time (TR), 3 s; echo time (TE), 50 ms; flip angle, 90 degrees; field of view (FOV), 23 · 23 cm; pixel matrix, 128 · 128 pixels; and slice thickness, 4 mm. The first three scans were discarded from the analysis because of instability of magnetization. Functional images, followed by anatomical (T1-weighted) images, were acquired for each participant with the following parameters: TR, 20 ms; flip angle, 20 degrees; FOV, 24 cm; and voxel size, 0.98 x 0.98 x 1.02 mm³. No movement artifact analyses were performed at this stage of the study.

Self-reported measures

After the final scan, participants were removed from the scanner and asked to score the perceived effort of clenching for each task on a visual analogue scale (VAS) of 0-100, ranging from 'no clenching' to 'maximum voluntary' clenching'. The VAS scores for each task were therefore based on postscan memory.

Data analysis

Functional image analysis was performed using statistical parametric mapping (SPM2 software from The Wellcome Trust Centre for Neuroimaging, Institute of Neurology, University College London, UK) implemented in MATLAB 2009a (Mathworks, Natick, MA, USA). All functional images were re-aligned to correct for head movement. Images were corrected if the head moved within 1.5 mm (translational) and 1° (rotational) in comparison to the first image in the time series. A T1-weighted anatomical image was co-registered with the mean echo planar imaging (EPI) image and transformed to the standard stereotaxic space [Montreal Neurological Institute (MNI) template]. Functional images were normalized by applying the same transformation parameters. An isotropic Gaussian kernel of 8 mm full-width at half-maximum (FWHM) was applied to spatially smooth the data. A general linear model (GLM) design was used to analyze regional activ-

KLINISK RELEVANS

For at få mere information om hjernens centrale procesmekanismer ved tænderskæren i vågen tilstand anvendes funktionel magnetisk resonansbilleddiagnostik til at måle hjerneaktiviteten ved let tænderskæren og let knyttede hænder. Aktiviteterne sammenlignes med en baseline. Bilateralt knyttede hænder aktiverer den sensomotoriske cortex bilateralt signifikant, mens tænderskæren signifikant aktiverer væsentlig flere foci i hjernen. Eftersom let tænderskæren aktiverer et mere udbredt netværk i hjernen, antages det, at tænderskæren foranlediger en mere kompleks cerebral aktivitet end det at knytte sine hænder. Den kliniske relevans af disse fund er endnu uvis, men kan muligvis relateres til tilbøjeligheden til tænderskæren i vågen tilstand.

Summary of brain activity

Region of activation during fist clenching (FC) and teeth clenching (TC) minus baseline						
Coordinates						
Brain region activated	BA	x	y	z	Cluster size	Maximum t-value
FC minus BL						
SMC	4L	-34	-20	58	151	3.68
SMC	4R	32	-18	54	36	3.32
TC minus BL						
SMC	4L	-42	32	36	461	6.83
SMC	4R	64	-14	34	431	5.54
SMA	6L	-56	8	40	241	6.12
SMA	6R	54	-10	34	212	5.20
DLPFC	9L	-60	8	32	153	6.25
DLPFC	9R	54	8	36	109	6.09
PPC	40L	-66	-16	24	80	4.36
PPC	40R	48	-44	48	74	4.32
TC minus FC						
SMA	6L	-40	8	28	97	6.37
SMA	6R	54	4	34	86	5.62
DLPFC	9L	-60	8	28	51	6.37
DLPFC	9R	54	10	36	41	4.83

Uncorrected $P < 0.005$.

BA, Brodmann's area; BL baseline activity; DLPFC, dorsolateral prefrontal cortex; FC, fist-clenching activity; L, left hemisphere; PPC, posterior parietal cortex; SMA, supplementary motor area, SMC, sensorimotor cortex; R, right hemisphere; TC, teeth clenching activity.

Table 1. Uncorrected $P < 0.005$. BA, Brodmann's area; BL baseline activity; DLPFC, dorsolateral prefrontal cortex; FC, fist-clenching activity; L, left hemisphere; PPC, posterior parietal cortex; SMA, supplementary motor area; SMC, sensorimotor cortex; R, right hemisphere; TC, teeth clenching activity.

Tabel 1. Opsummering af de mest aktive foci i hjernen under tænderskæren og med knyttede hænder.



Activity in sensorimotor cortex

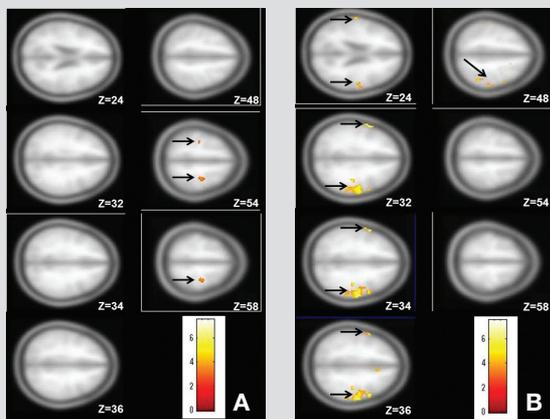


Fig. 3. Activated sensorimotor cortex (SMC) along the axial plane ($z = 24, 32, 34, 36, 48, 54, \text{ and } 58$) on the Montreal Neurological Institute (MNI) standard template brain. Clusters of at least 10 neighbouring voxels are shown ($P < 0.005$, uncorrected for multiple comparisons). Black arrows indicate activation of the sensorimotor cortex region of interest (ROI). (A) Fist clenching (FC) minus baseline (BL), and (B) teeth clenching (TC) minus BL. Colour scale: t -value.

Fig. 3. Aktive områder i den sensorimotoriske cortex: En sammenligning mellem aktivitet ved kryttede hænder minus baseline og tænderskæren minus baseline. De sorte pile angiver områder af interesse. (A) Kryttet næve (FC) minus baseline (BL) og (B) tænderskæren (TC) minus BL.

ity differences between FC or TC and baseline (BL) values, with each condition modeled by convolving a box-car function for each participant (14). Statistical parametric maps of the t -statistic were generated on a voxel-by-voxel basis, and these individual data were then analyzed as a group in a random effects model. The statistical threshold level for individual analysis was set to $P < 0.001$ (corrected) at cluster level. The statistical threshold level for group analysis was set to $P < 0.005$ (uncorrected) at voxel level and cluster volume > 10 voxels. Cerebral activation was rendered T1-weighted MRI image and the surface of a standard MNI brain. The locations of brain regional activities were transformed from MNI coordinates into Talairach standard coordinates (15) using TALAIRACH DAEMON CLIENT (version 2.4.2; University of Texas Health Science Center, San Antonio, TX, USA). Finally, the Spearman's rho (s) test was used to analyze the association between VAS scores for each task and the maximum t -value in these specific areas for each task. Maximum t -values for each subject were averaged between both hemispheres in these specific areas. The statistical analyses were conducted at a 95% confidence level, and a P -value of < 0.05 was considered statistically significant.

Results

The VAS scores for FC and TC tasks were (mean \pm SD) 35.8 ± 11.0 and 37.4 ± 11.5 , respectively. There was no significant difference between the FC and the TC VAS scores in paired t -tests ($P = 0.684$; $t_0 = 0.416$; degrees of freedom = 13). In addition, a positive correlation was found between the VAS scores for FC and VAS scores for TC ($r_s = 0.81$; $P = 0.001$). The head movement in the image-correlation analysis was (mean \pm SD) 1.07 ± 0.31 mm. The FC and TC tasks resulted in significantly increased activity (relative to BL measurements) in various brain regions. The TC task activated the bilateral SMC, bilateral SMA, bilateral dorsolateral prefrontal cortex (DLPFC), and bilateral posterior parietal cortex (PPC) in all participants. Statistical maps of brain regions with significant increases in blood oxygenation level-dependent (BOLD) contrast during FC and TC group analysis are shown in Figs. 2A and 2B, respectively. Indirect comparison of brain regional activity between the two tasks revealed that TC activated a more extended area of the brain than FC (compare Fig. 2A with Fig. 2B). Figure 2C directly compares brain regional activities between TC and FC by showing residual activity during TC relative to FC. Direct comparison of brain regional activity between the two tasks also revealed that TC activated a more extended network of brain regions than FC. The locations of the most significant foci of activation (multiple comparisons) for these regions are summarized in Table 1, in which Talairach coordinates of anatomical regions with maximum t -values are shown. Fist clenching significantly activated the bilateral SMC ($P < 0.005$) (FC minus BL in Table 1). Teeth clenching significantly activated the bilateral SMC, bilateral SMA, bilateral DLPFC, and bilateral PPC ($P < 0.005$) (TC minus BL in Table 1). Direct comparison of brain regional activity, with TC minus FC, revealed activation of the bilateral SMA and bilateral DLPFC ($P < 0.005$) (TC minus FC in Table 1). Activated brain areas in the axial planes $z = 24, 32, 34, 36, 48, 54, \text{ and } 58$ during the FC task and the TC task are shown in Figs. 3A and 3B, respectively. In axial planes $z = 24, 32, 34, 36, \text{ and } 48$, a BOLD response was detected during TC but not during FC. In axial planes $z = 54$ and 58 , a BOLD response was detected during FC but not during TC. In addition, positive correlations were found between VAS scores for each task and the SMC during FC (Fig. 4A; $r_s = 0.53$; $P = 0.003$), the SMC during TC (Fig. 4B; $r_s = 0.42$; $P = 0.011$), the SMA during TC (Fig. 4C, $r_s = 0.29$; $P = 0.045$), the DLPFC during TC (Fig. 4D, $r_s = 0.52$; $P = 0.004$), and the PPC during TC (Fig. 4E, $r_s = 0.41$; $P = 0.013$).

Discussion

In this fMRI study, TC appeared to activate an extended network of brain areas, such as the bilateral SMC, bilateral SMA, bilateral DLPFC, and bilateral PPC. Fist clenching also activated the bilateral SMC. However, the localization of brain regional activity in the SMC differed between FC and TC, in accordance with the known differences of somatotopic organization between jaw muscles and hand muscles (11,16,17). Importantly, a direct

Scatterplots: VAS versus level og activity

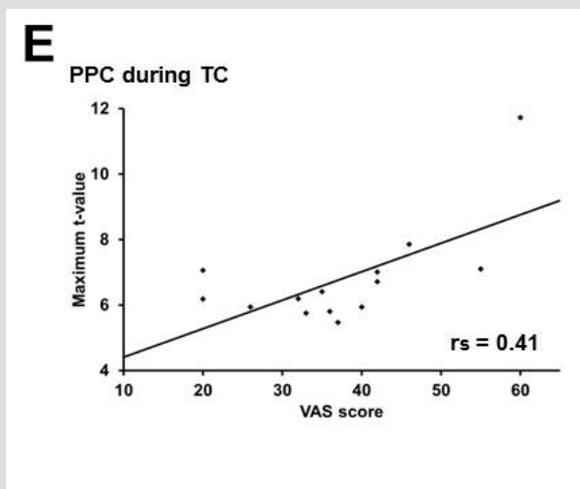
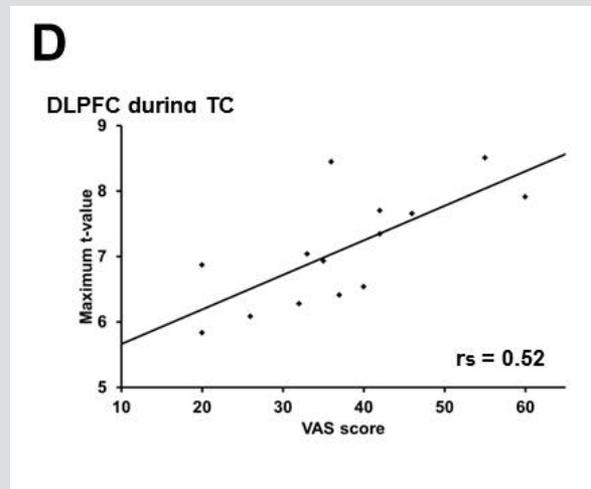
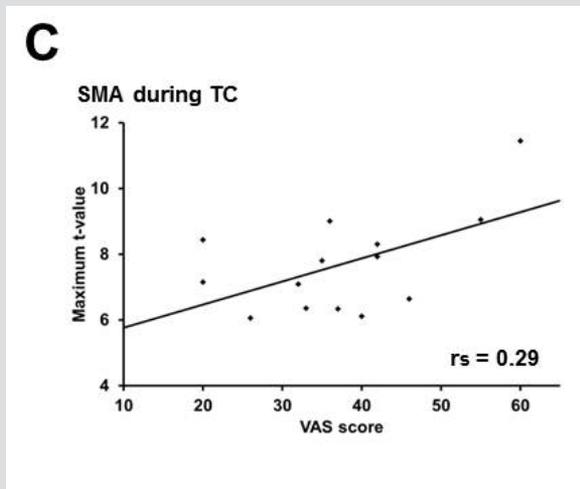
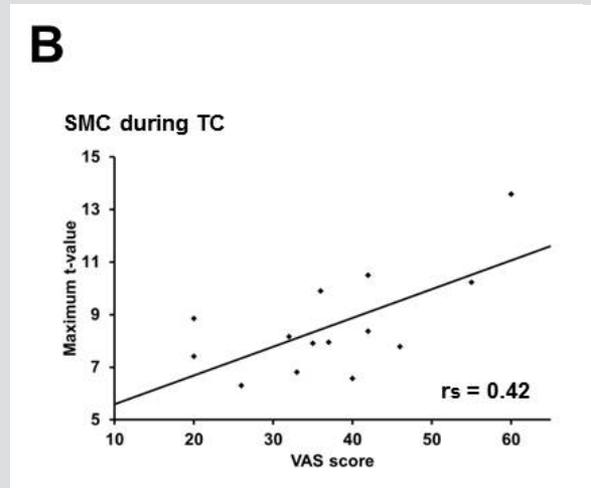
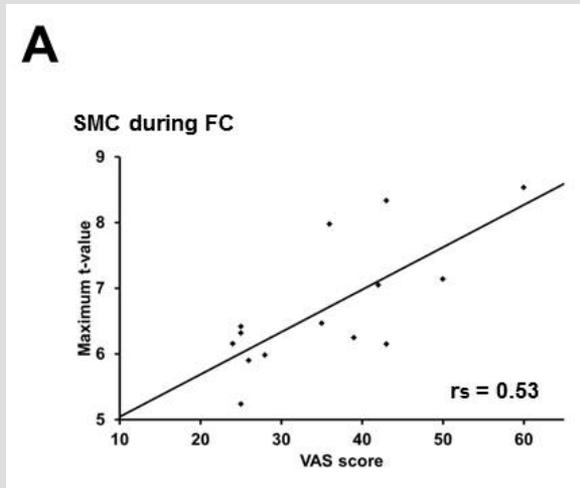


Fig. 4. Scatter plots of relationships between the visual analogue scale (VAS) score for each task and (A) brain activity in the sensorimotor cortex (SMC) during fist clenching (FC), (B) brain activity in the SMC during teeth clenching (TC), (C) brain activity in the supplementary motor area (SMA) during TC (D) brain activity in the dorsolateral prefrontal cortex (DLPFC) during TC, and (E) brain activity in the posterior parietal cortex (PPC) during TC. A positive linear regression line is fitted to the data.

Fig. 4. Scatterplots af forholdet mellem VAS-score for selvurderet styrke af tænderskæren/knyttede hænder og hjerneaktiviteten i aktive foci under udførelse af aktiviteten.

comparison of brain regional activity, subtracting FC from TC, demonstrated significant differences in the bilateral SMA and bilateral DLPFC. It has been demonstrated that the SMA plays an important role in motor planning, motor imaging, and control of movements (18-20), whereas DLPFC plays an important role in the working memory (21-24). In our study, discrete areas of significant brain regional activity associated with TC directly compared with FC were found in the SMA and in the DLPFC. Byrd et al. (25) demonstrated that activation of the SMA during TC in participants with normal function was significantly higher than for participants with bruxism. In our study, TC stimulated significantly greater activity in the SMA than did FC. Furthermore, brain regional activity has been observed in the bilateral SMA during maximum voluntary teeth clenching (MVT) (10). Taken together, these data suggest that SMA activity during TC may be a critical part of the cortical network in normal individuals. Another fMRI study has demonstrated that TC differentially activated the prefrontal cortex in normal individuals and in a patient with an implant-supported prosthesis (26). Additionally, a study that used fMRI to compare brain regional activity during a gum-chewing task and a sham chewing task found greater activity in the prefrontal cortex during gum chewing (27). The results from our study suggest that TC was more likely to activate the DLPFC than FC. However, cerebral blood flow during gum-chewing, revealed by positron emission tomography (PET) and fMRI, showed increased blood flow in the bilateral parietal lobes (27,28). Other fMRI studies indicated that the activation of the inferior parietal lobule is related to tactile object identification (29). Based on the indirect comparison of regional brain activity during FC and TC, we suggest that PPC activation during TC may result from the sensation of contact between teeth (i.e. a mechanosensitive input).

The somatotopic locations of the SMC activity differ between FC and TC, as expected. Penfield et al. (16) reported isolated activation in the dorsal aspect of the SMC and also showed that locations of SMC activity differed between jaw movement and hand movement. Other fMRI studies using normal subjects reported BOLD responses ranging from $z = 40$ to $z = 60$ during hand movements in the axial plane (11) and ranging from $z = 30$ to $z = 38$ during orofacial movements in the axial plane (17). Using a functional neuroimaging technique, our study demonstrated significant activation in similar locations of the SMC for the two tasks. In addition, TC activated a wider area of the brain in the SMC than did FC. The results are consistent with the data for the brain regional activity of the maxilla-orofacial-oral area of the SMC in the original report of Penfield et al. (16).

This study was designed to examine brain activity associated with voluntary TC; however, it is difficult to measure cerebral activity of an unconscious behaviour using fMRI. Furthermore, participants were in a horizontal position on the scanner table during the fMRI scans, which clearly differs from naturally occurring awake bruxism. Further studies on postural influences on jaw

motor control using other neuroimaging techniques are needed. Although recent studies have reported that non-ferrous electromyograph (EMG) methods (carbon fibre EMG) can be used to directly measure and compare muscle activity during fMRI scanning (30,31), this method was not feasible in the present study. Nevertheless, recording and analysis of EMG signals during fMRI scans will obviously allow better control of different motor tasks and should be pursued. In the present study we used VAS scores to quantify the perceived efforts of both tasks, in accordance with another fMRI study (32). In our study, there were no significant differences in VAS scores between FC and TC. Although positive and significant correlations were found between VAS scores and the brain regional activity in specific brain areas, the highest r s value was only 0.53 and it is suggested that VAS scores should be obtained immediately after each task to minimize the variability of postscan recalls. Further studies will, indeed, be needed to demonstrate relationships between brain regional activity and self-reported measures; however, some near infrared spectroscopy studies have also reported positive correlations between bite force and brain regional activity in SMC and SMA (8,33). Taken together, these findings suggest that there is a positive correlation between the intensity of TC and cerebral activity.

Previous fMRI studies have examined motor tasks using a gum-chewing task (17,27,34) and a teethtapping task (35), both of which are rhythmic, repetitive movements (36). Although the tasks of gum-chewing and teeth tapping are classified as repetitive muscle actions (37-39), the TC used in our study is a continuous muscle action (40,41). The present study used FC as a comparison with TC, because this hand motor task can also be classified as a continuous muscle action. Although Luft et al. (12) showed detailed brain regional activity in the SMC and the SMA during bimanual repetitive muscle action in a hand motor task, we detected activation only in the bilateral SMC during FC. In addition, Tamura et al. (35) suggested that there are differences in cerebral activity between TC and the gum-chewing task.

Our results therefore suggest that repetitive muscle action tasks may activate larger areas of the cortex compared with more continuous muscle tasks. In other words, isotonic (same force) muscle actions, such as gum-chewing and teeth tapping (42,43), may activate larger areas of the cortex compared with isometric (same length) muscle actions such as TC (44,45).

Based on these findings, we suggest that there are significant differences in cerebral activity between a TC clenching task and the performance of a bilateral hand motor task. The clinical significance of the present findings remains unknown but might be related to the propensity to trigger awake bruxism.

Acknowledgements – This study was supported by a grant-in-aid for young scientists (B 21791921) from the Ministry of Education, Culture, Sports, Science, and Technology of Japan, and by a grant-in-aid for scientific research (C 20592285 and C 22592164) from the Japanese Society for the Promotion of Science.

Abstract (Dansk)*Tænderskæren stimulerer hjernen mere end knyttede næver*

Under anvendelse af funktionel magnetisk resonansbilleddiagnostik sammenlignedes den cerebrale aktivitet hos 14 forsøgspersoner med let knyttede hænder og under let tænderskæren for at få mere information om de centrale procesmekanismer bag brugsisme (tænderskæren) i vågen tilstand.

Statistiske sammenligninger med subtraktion af baseline anvendes til at identificere hjerneområder med signifikant hjerneaktivering, når forsøgspersonerne henholdsvis knyttede deres hænder og skar tænder. Forsøgspersonerne evaluerede selv på en VAS-skala (1- 100) den kraft, de lagde i at knytte hænder og skære tænder efter funktionel magnetisk resonansbilleddiagnostik.

Bilateralt let knyttede hænder aktiverede bilateralt den sensoriske cortex signifikant, mens let tænderskæren kunne associeres med signifikant aktivering af såvel den sensoriske cortex bilateralt som supplementært motorisk område, den dorsolaterale præfrontale cortex og den posteriore parietale cortex. Forsøgspersonernes VAS-evalueringer af anvendt kraft til at knytte hænderne og til at skære tænder var ikke signifikant forskellige.

Da let tænderskæren aktiverer vidt udbredt kortikalt netværk sammenlignet med let knyttede hænder, antager vi, at tænderskæren foranlediger en mere kompleks cerebral aktivitet end den aktivitet, der forårsages af knyttede hænder. Den kliniske betydning af disse resultater er endnu ukendt, men kunne være relaterede til tilbøjeligheden til at udløse tænderskæren i vågen tilstand.

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