The Amount of TMJ Displacement Correlates with Brain Activity


ABSTRACT: The aim of this functional magnetic resonance imaging (fMRI) study was to investigate the correlation between the severity of malocclusion and brain activation. The fMRI was used to measure blood-oxygenation-level-dependent (BOLD) signals of twelve healthy human subjects while they clench in two different ways to simulate two types of malocclusion. In each malocclusion model, a custom-made splint forced the mandible to each of two retrusive positions (0.5 mm, 0.7 mm). A no-modification splint provided the control. We compared the BOLD signals measured at each clenching position with those measured during the corresponding resting conditions. The BOLD signals were significantly stronger in the amygdala and the prefrontal area (PFA) when subjects clenched in the two retrusive positions compared during clenching in the control position. In addition, the BOLD signal in the PFA increased as the simulated malocclusion became more severe. These results indicate that we may be able to objectively assess the severity of malocclusion via focus on the brain activity.

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to investigate how the amount of TMJ-displacement affects brain activation.

**Material and Methods**

The fMRI data were obtained from 12 healthy subjects (6 males and 6 females, aged 22 to 45 years, mean age 33.4) with no history of psychiatric or neurological disease. And according to sagittal skeletal and occlusal features, they are all dentoskeletal Class I relationships without missing teeth. Each subject gave written informed consent after receiving an explanation of the aims and method of the study, which was approved by the Committee for Research Ethics of Medical University Hospital, Bonn, Germany. After clinically examining the subjects and producing electronic condylographic tracings of mandibular/condylar movement using CADIAX (Computer Aided Axis Recording; GAMMA-DENTAL, Klosterneuburg, Austria), plaster models (Type IV stone plaster; Fuji Rock) were mounted, each with an individual hinge axis, on a fully adjustable articulator (SL, GAMMA-DENTAL, Klosterneuburg, Austria) (Figure 1, Upper left). The articulator programming was written using CADIAX Software.

We took impressions and made maxillary and mandibular dental casts for each subject. Splints were fabricated by vacuum-pressing a 0.5 mm thick, polyvinylchloride sheet over the maxillary dental cast (Figure 1a). A control splint and two retrusive-forcing splints were made for each subject. The two retrusive-forcing splints were made by applying a mound of light-curing resin (Tetric, Vivadent Co., Germany), one 0.5 mm thick and the other 0.7 mm thick, in the premolar region of the vacuum-pressed sheet. Another vacuum-pressed sheet was used without modification as a control splint. The splints were checked using a cross-mounting technique in which the casts could be aligned at pre-programmed positions with a Mandibular Position Variator (MPV, GAMMA-DENTAL, Klosterneuburg, Austria), and an analysis using the CADIAX confirmed that the condylar position along the sagittal condylar path was bilaterally shifted by 0.5 mm in the postero-retrusive direction for one experi-

![Articulator (Reference SL)](image1)

![Habitual ICP](image2)

**Figure 1**
Splints were fabricated on the articulator and mounted at habitual intercuspal position (ICP) (far left figure). The “X” symbols show the mean condylar position for all subjects during clenching with each splint (bottoms). Graph origins correspond to the habitual intercuspal position without a splint. The horizontal (X) axis shows the anteroposterior position of the condyle. The vertical (Z) axis shows the superoinferior position of the condyle.
mental splint and by 0.7 mm for the other experimental splint (Figure 1, b and c). We also verified that the condyles did not shift to postero-retrusive direction while the subjects were clenching with the control splint. In order to minimize measurement error, an experienced dentist tested each subject three times.

The clenching task consisted of five cycles of a 30-sec. clenching period followed by a 30-sec. resting period, during which the subject relaxed the jaw-closing muscles and applied only enough force to keep the mandibular teeth in contact with the maxillary teeth. The five clenching cycles lasted a total of five min. Each subject performed the clenching task three times, once with each of the two retrusive splints (0.5 mm, 0.7 mm) and once with the control splint. After completing one of the clenching tasks, subjects waited at least 30 minutes before performing another of the clenching tasks. This waiting interval prevented one task from influencing the next.

Functional (T2* weighted) images and anatomical (T1 weighted) images were acquired with a MAGNETOM Avanto 1.5T MRI system (Siemens, Erlangen, Germany). The functional images consisted of echo-planar image volumes sensitive to BOLD contrast in the axial orientation (TE=45 ms, TR=3000 ms). The volume included the entire brain with a 64 x 64 matrix and 34 slices (voxel size=3.75 mm x 3.75 mm x 4 mm, slice thickness=3 mm, gap=0.3 mm). Images with 108 volumes were acquired for each experimental condition (two mandibular retrusive positions and the control position). Because unstable magnetization routinely degraded the quality of the first eight volumes, the start of the first cycle of clenching was timed to coincide with the beginning of the ninth image volume. Immediately following each fMRI run (five cycles, 108 image volumes), subjects quantified the subjective discomfort they felt during clenching by marking a visual analog rating scale (VAS) ranging from 0 to 5 (0 = no discomfort, 5 = extreme discomfort) and verbally expressed how they felt during clenching to an interviewer.

Head motion was corrected using SPM5 (University College London, London). A total of 324 functional images (three runs, 108 image volumes per run) obtained from each subject were normalized to the MNI template and spatially smoothed by an 8-mm Gaussian kernel. The data were statistically analyzed by the general linear model approach using SPM5. Proportional scaling removed global changes in the BOLD signals. Statistical contrast images of all subjects for group analysis were used (paired t-test, uncorrected for multiple comparisons) with a random-effects model. A value of p<0.01 is considered statistically significant. For each region of the brain, Tukey’s HSD test was used to compare the BOLD signal changes associated with clenching in the three different positions. BOLD signal changes were also analyzed by ANOVA. Statistical significance was established at p<0.05. In the same way as the BOLD signal changes, the VAS scores were analyzed with Tukey’s HSD test. Statistical significance was established at p<0.05.

Results

A random-effect analysis (n=12) showed that all clenching increased the BOLD signals in the sensory and motor areas of the oral region, cerebellum, and the insula (data not shown). All voxel in an activated area were assigned a value equal to the voxel in that area that had the peak value (statistically significant at p<0.01, Figure 2). Control-position clenching activated the PFA. However, it did not activate the amygdala (Figure 2a). Clenching at the two mandibular retrusive positions (0.5 mm, 0.7 mm) significantly activated both the amygdala and the PFA (Figure 2, b and c). The highest threshold T for statistical significance was 2.76.

In the amygdala, the BOLD signal was greatest when the retrusion distance was 0.5 mm (statistically significant at *p<0.01, **p<0.001, Figure 3a). In the PFA, the BOLD signal was greatest when the retrusion distance was 0.7 mm (statistically significant at *p<0.01, **p<0.001, Figure 3b). The mean VAS score after retrusive-clenching was higher than it was after control-clenching (statistically significant at *p<0.01, **p<0.001, Figure 4). The subjective feeling of discomfort tended to increase as the mandibular position moved backward.

Discussion

A previous study had simply manipulated the mandible to the retrusive position; however, in the present study, the clenching task in two mandibular retrusive positions calculated on the mounted cast activated the amygdala and the PFA. These results corroborate a previous study. However, unlike that previous study, clenching did not activate the anterior cingulate cortex (ACC) in the present study. This discrepancy is due to a difference in the clenching task. In the present experiment, the retrusive splints were produced by adding self-curing dental resin to the posterior regions (from 1st premolar to 2nd molar on both sides) of the maxillary splint. These splints force the mandible to a retrusive position because of contact between upper and lower posterior teeth (from 1st premolar to 2nd molar on both sides). In contrast, the retrusive splint in the previous study was produced by adding self-curing dental resin to the anterior regions (from right
canine to left canine) of the maxillary splint. This splint forced the mandible to a retrusive position because of contact between upper and lower anterior teeth (from right canine to left canine). There is substantial difference between posterior teeth and anterior teeth with regard to the amount of sensory information transmitted.\textsuperscript{12,13} Therefore, the disappearance of activity in the ACC in this study is attributed to the difference of sensory input from different regions of the dental arches. However these two types of mandibular retrusion could be possible in usual dental practice.

The amygdala plays a critical role in determining the response to stress, fear and/or emotion.\textsuperscript{14-16} In the current experiment, the amygdala was significantly activated by clenching at two different values of mandibular retrusion. In contrast, the amygdala was not significantly activated by control-position clenching. In this study, forcing the mandible into a retrusive position promptly caused signals to be transmitted to the amygdala that gave subjects a feeling that they described as unpleasant or fear. These results corroborate a previous study\textsuperscript{5}; however, the activity in the amygdala associated with clenching at the 0.5 mm retrusive position was stronger than that at the 0.7 mm retrusive position. This means that the amygdala activity in the present study probably played a role, not only the unpleasant odor, but also in the transfer area between neuronal networks related to negative emotion. The subject could get used to the situation at the mandibular retrusion and feel a little less fear when clenching at the 0.7 mm retrusive position. At the same time, there was activity in the PFA for all of the clenching conditions in this study. The PFA is closely associated with emotional stress and negative emotional reactions.\textsuperscript{17} The activity in the PFA associated with clenching at the 0.7 mm retrusive position was strongest among all positions. In this study, the PFA activity and the VAS score was
increasing as the malocclusal level worsened. This means that the PFA activity in the present study probably played a role in the scale of unpleasantness.

The PFA is involved with various higher-level cognitive functions, and imaging studies of this brain region are in progress. Hoshi, et al., reported that pleasant or unpleasant emotions can be recognized from cerebral blood flow (CBF), using near-infrared spectroscopy.

Figure 3 (A, B)
Comparison of the percent of increased BOLD signals (%) in the amygdala (A) and the prefrontal area (B) during clenching among the control splint (white), with the 0.5 mm retrusive splint (gray) and with the 0.7 mm retrusive splint (black). Each column represents the mean ± SE. *p<0.05, **p<0.001.

Figure 4
Mean discomfort scores following the clenching series with the control splint (white), the 0.5 mm retrusive splint (gray), and the 0.7 mm retrusive splint (black). Each column represents the mean ± SE. *p<0.01, **p<0.001.
Because the PFA is located in the cerebral cortex, brain-imaging techniques that can produce functional images include functional NIRS, which is a convenient means of imaging the brain. In the future, malocclusion should be assessed, and its treatment should be designed objectively via focus on brain activity in the PFA.

Conclusions

The current study aimed to investigate the correlation between the severity of malocclusion and brain activation. The study’s results were that the PFA activity and unpleasantness increase as malocclusal levels worsen. These results indicate that we may be able to objectively assess the severity of malocclusion by focusing on the brain activity. However, malocclusions range widely and the sample size is not large enough to permit a definitive conclusion. Further research is required.

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References


