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Neuroplasticity of edentulous patients with implant-supported full dentures

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Edentulous patients with implant-supported prostheses report improved tactile discriminative capabilities and motor function compared with when they wore complete dentures. 'Osseoperception' is defined as the ability to identify kinesthetic sensation without the input from periodontal mechanoreceptors. This sensation is generated from the temporomandibular joint, masticatory muscle, mucosa, and periosteum, and provides sensory and motor information related to mandible movements and occlusion. The aim of this study was to analyze the cortical plasticity occurring in patients with implant-supported prostheses. Twenty edentulous patients with implant-supported full dentures or traditional complete dentures were recruited for a clenching task. They were scanned by functional magnetic resonance imaging (fMRI), and the data were analyzed using the SPM99 software package to generate activation brain maps. Increased blood oxygen level dependent signals in the primary sensorimotor cortex were found in patients with implant-supported fixed dentures. Other activated areas included prefrontal cortex, Broca's area, premotor cortex, supplementary motor area, superior temporal gyrus, insular, basal ganglion, and hippocampus. We suggest that sensory and motor feedback to the central nervous system can be restored by implant-supported full dentures. Activation of the primary sensorimotor cortex in patients with implant-supported dentures might explain the improved tactile, stereognostic ability, and mastication functions, which are more similar to the natural dentition.

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Many studies in humans, monkeys, and subprimates have addressed the tissue reaction, biomechanics, and functional benefits of implant-supported dentures. These studies showed that, when compared with the edentulous state, patients with implant-supported prostheses displayed improved tactile capabilities and masticatory function (1), approaching or reaching the natural situation over the years. This type of bone-anchored prosthesis helps the patients regain a better quality of life and becomes part of the patient's mind (2). This special sensory awareness, referred to as 'osseoperception', implies that a feedback pathway to the central nervous system is restored with a hypothetical representation in the sensory cortex, allowing a more appropriate modulation of the motor neurons that leads to more natural function and thus avoids overloading (3).

KLINEBERG & MURRAY (4) in 1999 reviewed the concept of osseoperception, and in 2005 a consensus statement on osseoperception was published (5). Osseoperception was defined as the sensation arising from mechanical stimulation of a bone-anchored prosthesis, transduced by mechanoreceptors that may include those located in muscle, joints, and mucosal and periosteal tissues, together with a change in central neural processing in maintaining sensorimotor function (5).

The sensory signals underlying this phenomenon are qualitatively different from the signals evoked when placing a load on a natural tooth. Periodontal mechanoreceptors (PDMs) play a major role in the tactile function of natural teeth, and this information can be used in the continuous modulation of the masticatory motor programs (6). The absence of sensory input from PDMs in edentulous patients results in reduced masticatory forces and distorted spatial control of jaw movements during chewing (7). Patients with dental implants have dynamic detection thresholds that are similar to those of dentate patients (8). Inferior alveolar nerve responses were recorded following vibratory stimulation from both implants and teeth at 2× and 3× threshold, which provided evidence that force application to implants did elicit a proprioceptive response (9).

As a widely observed phenomenon, the underlying mechanisms of osseoperception remain an issue of debate. A hypothesis associates these responses with muscle spindle and joint receptors that substitute for the periodontal ligament of natural teeth (4). Another theory, with accumulating laboratory and clinical evidence, is that the bone in the peri-implant regions contains nerve fibers, which may serve as a source of sensory response (9, 10). Bone strain from occlusal loads, either compression or elongation, may change the cytostructure of osteocytes and serve to activate free nerve endings in the peri-implant regions (9). BRÅNEMARK (2) described

the interaction between the brain and the outer world that was detected through implants. Nevertheless, little is known about the potential use of osseoperception to optimize the psychophysical integration of implants in patients (11).

Neurological research during the last 15 yr suggests that the sensory cortex can re-organize itself extensively by training of or losing afferent inputs, even after the critical developmental period of the brain has expired (12). Evidence has been found that after limb amputation or tooth extraction, regions of the cortex deprived of a target acquire new targets. Remodeling takes place at the cortical or subcortical level (13, 14). In recent years there have been several studies on the cortical adaptive changes after hand or thumb replantation, transplantation, or implantation (15–17). However, there has been no detailed investigation of the possible sensorimotor cortical adaptive processes that may be associated with the loss of teeth or with their replacement in humans (1). We postulate that implant-supported full dentures can restore the sensorimotor feedback by a re-organized pattern in the central nervous system and that, based upon the theory of peri-implant nerve endings, fixed restoration with more implants might be the most natural way to facilitate the functional rehabilitation of total edentulous patients.

In this study, we therefore analyzed the adaptive changes in the cerebral cortex by the help of functional magnetic resonance imaging (fMRI). Our findings may offer new perspectives for osseoperception research and may link the anatomical and physiological backgrounds to the clinical observations.

Material and methods

Participants in this study were 20 totally (both upper and lower jaws) edentulous patients from the Department of Implant Dentistry at the Peking University School of Stomatology. Table 1 is an overview of patient characteristics. The average age of the patients in the complete denture (CD), implant-supported over-denture (IOD), and implant-supported fixed denture (IFD) groups was 61.5, 59.1, and 58.0 yr, respectively. There were two types of IODs: one was retained with a telescopic crown, and the other was retained with a milled bar. Implant-supported over-dentures of the maxilla were free of palate coverage. Five patients in the IOD group had IODs in both jaws, the other four patients had IODs only in the mandible but CDs in the maxilla. Complete dentures were made of acrylic resin with no metal reinforcement. Implant-supported fixed dentures consisted of gold alloy porcelain fused to metal (PFM) crowns and three-unit bridges. All the subjects were right-handed and without any history of temporomandibular joint disorders, or neurologic or psychiatric diseases. They were informed in detail before the study about the nature of the experiment and could fully comply with the task sequence during rehearsal. All gave their written informed consent to participate in this study, which was approved by the Medical Ethics Committee of Peking University.

Experimental protocol

Each subject lay comfortably on the scanner table in a supine position with their eyes closed during the experiment. The subject's head was immobilized by a vacuum pad, and earplugs were provided to avoid auditory discomfort. They were asked to practice moderate intercuspal

Table 1

Overview table with patient characteristics

Groups	Gender	Age	Implant system	Retention type	Implant number		Time for loading
					Upper jaw	Lower jaw	
CD (n = 8)	M	72	–	–	–	–	3 yr
	M	59	–	–	–	–	22 months
	F	57	–	–	–	–	3 yr
	M	48	–	–	–	–	11 months
	M	72	–	–	–	–	17 months
	F	64	–	–	–	–	19 months
	M	57	–	–	–	–	2 yr
	F	63	–	–	–	–	5 yr
IOD (n = 9)	M	51	Camlog	TC	6	4	28 months
	F	70	Camlog	MB	0	4	21 months
	F	60	Frialit	MB	0	4	60 months
	M	57	Frialit&IMZ	MB	7	4	62 months
	M	55	Camlog	MB	6	6	10 months
	F	71	Ankylos	MB	0	4	59 months
	M	66	Ankylos	MB	0	4	45 months
	F	48	Frialit&IMZ	TC&MB	8	4	68 months
	M	54	Frialit&IMZ	TC	6	4	60 months
IFD (n = 3)	M	61	Camlog	C&B	12	12	8 months
	M	56	Ankylos	C&B	10	8	48 months
	M	57	Camlog	C&B	12	12	12 months

C&B, crown and bridge; CD, traditional complete denture; IFD, implant-supported fixed denture; IOD, implant-supported over-denture; MB, milled bar; TC, telescopic crown.

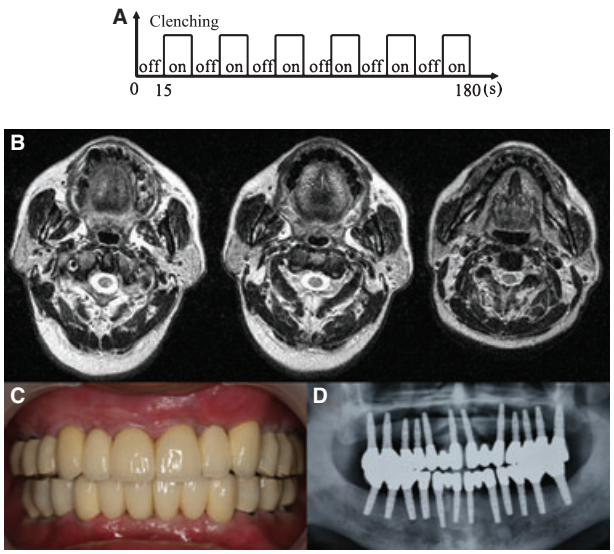

Fig. 1. Task paradigm and images of one patient. (A) Task paradigm; (B) magnetic resonance images of one patient showing few artifacts around the implants; (C) intra-oral frontal view of the patient; (D) panoramic X-ray showing crowns and bridges supported by 24 implants.

clenching tasks. The task paradigm was an alternation between 15 s of clenching (on) and 15 s of rest in the rest position (off). This on–off procedure was repeated six times in each scanning run. Figure 1A shows the clenching task assignment. Before each functional scan, an 8 min whole-brain three-dimensional anatomic image-scanning procedure was performed.

Image acquisition

Magnetic resonance imaging was performed on a 2.0 T Prestige scanner (GE/Elscint, Haifa, Israel). In a single session, 20 contiguous axial slices encompassing the entire brain (each 6 mm thick, with no gaps) were acquired using a single-shot echo-planar image T2*-sensitive sequence [repetition time (TR) = 3,000 ms, echo time (TE) = 45 ms, flip angle (FA) = 90°, field of view = 373 × 212 mm, matrix = 128 × 72]. For display purposes, a high-resolution T1-weighted structural MRI was acquired for each subject using a three-dimensional FLASH sequence (2 mm thick, no gap, TR/TE/FA = 25 ms/6 ms/28°, field of view = 220 × 220 mm, matrix = 220 × 220). Because implants and metals can impose risks on patients during high-field MRI scanning (18), and may cause artifacts in the image (19), we examined all the metal materials from implant dentures under T1-weighted scanning prior to the experiment. No motion, heat, or dislocation were found. Figure 1B shows the anatomical MRI images of one patient with IFD in both jaws supported with 24 implants. Large artifacts threatening the quality of brain image were absent around the implant bodies and upper structures. The frontal images and panoramic X-ray of this patient are shown in Figure 1C,D, respectively.

Statistical analysis and activation determination

Image processing and statistical analysis were based on the SPM99 software package (Wellcome Department of Imaging Neuroscience, University College London, UK). This statistical method was chosen based on its public availability and wide use by the neuroscience community. The first nine volumes were discarded because of instability of magnetization. All images were re-aligned first, corrected for motion artifacts, normalized into the Montreal Neurological Institute space, and smoothed using a 7-mm FWHM Gaussian kernel. Head motion was corrected using SPM99, and it was confirmed that the residual motion did not exceed 1.5 mm in translation and 0.5° in rotation in *x*-, *y*-, and *z*-coordinates (20).

A general linear model was formulated by incorporation of the data from all subjects so that brain activation could be described (21). A *t* statistic was used to determine significance on a voxel-by-voxel basis. Location of the most significant voxels was expressed with their coordinates in the Talairach's space transformed from Montreal Neurological Institute coordinates. TALAIRACH DAEMON CLIENT software (version 1.1; Research Imaging Center, University of Texas Health Science Center, San Antonio, TX, USA) was used for the determination of blood oxygen level dependent signals (22). Individual analysis was performed using the original native data sets and generated an fMRI image of each patient at threshold level cluster volume > 10 voxels and $P < 0.001$; a threshold level at cluster volume > 10 voxels and $P < 0.05$ was set for group analysis to identify the significant activation sites in each patient group.

Results

Figure 2 shows representative fMRI images obtained from subjects in the different groups. Blood oxygen level dependent signals were found in different Brodmann's areas (BA) when the patients with CDs (Fig. 2A), IODs (Fig. 2B) or IFDs (Fig. 2C) performed the clenching task. In a representative CD patient (Fig. 2A), the main activated regions were found in the prefrontal cortex (PFC) (BA11,46,47). The primary somatosensory cortex (SI) and the primary motor cortex (MI) were not activated in this group except in one patient. In an IOD patient (Fig. 2B), activations were bilateral and more symmetric, and signals were found in the precentral gyrus (BA6), Broca's area (BA44,45), and in the basal ganglion (BG). No activation was apparent in the SI or MI. In the IOD group, SI or MI activity was found in two of nine patients. Implant-supported fixed denture patients (Fig. 2C) showed the most extensive brain activity, which included bilateral SI (BA3) and MI (BA4), Broca's area (BA44,45), PFC (BA10,11,47), the middle temporal gyrus (BA21,22), BG, and the insula (BA13). The three patients in the IFD group had nearly the same activation pattern. The difference between individuals was smallest in the IFD group and largest in the CD group. Figure 3 shows a schematic diagram illustrating the activation rate in certain brain regions in the three groups.

Individual differences were also found in the IOD group, but when they were analyzed subject-by-subject, there seemed to be a potential rule of the activation pattern. Figure 4 shows the main typical activation maps from patients wearing an IOD. It was found that one type of brain activity occurred mainly in the superior

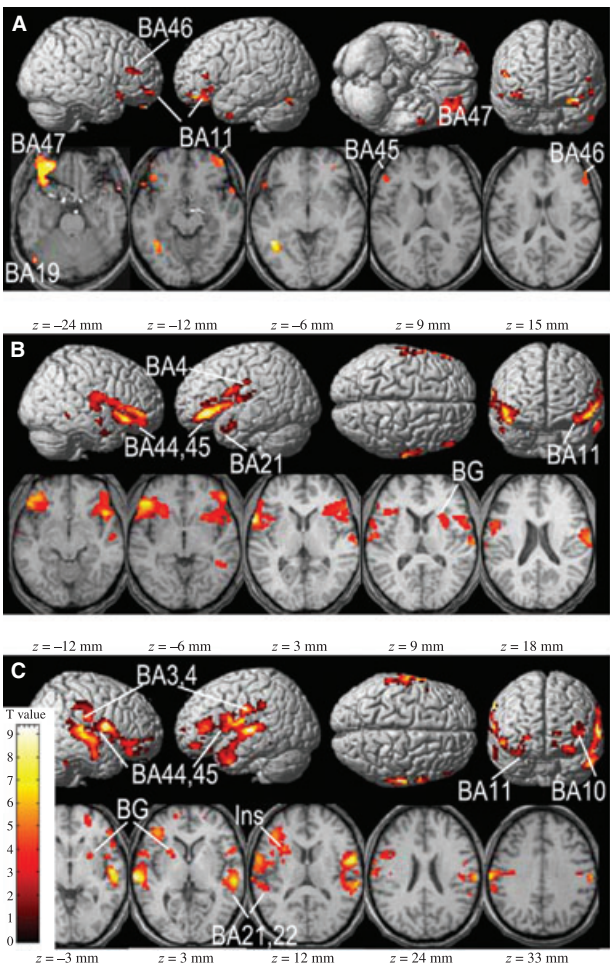

Fig. 2. Activation maps from patients in different groups. (A) Traditional complete denture (CD); (B) implant-supported over-denture (IOD); (C) implant-supported fixed denture (IFD). BA, Brodmann's areas; BG, basal ganglion; Ins, insula.

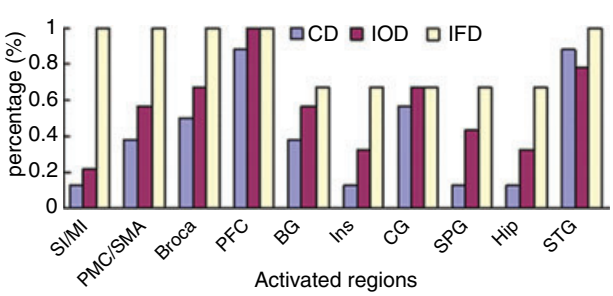

Fig. 3. Schematic diagram illustrating the activation rates in certain brain regions in the three groups. BG, basal ganglion; CD, traditional complete denture; CG, cingulate gyrus; Hip, hippocampus; IFD, implant-supported fixed denture; Ins, insula; IOD, implant-supported over-denture; MI, primary motor cortex; PFC, prefrontal cortex; PMC, premotor cortex; SI, primary somatosensory cortex; SMA, supplementary motor area; SPG, superior parietal gyrus; STG, superior temporal gyrus.

parietal gyrus (BA7,9) and in the dorsal–lateral prefrontal cortex (DLPFC) (BA9,10,46), whereas the other occurred mainly in Broca's area (BA44,45), the middle

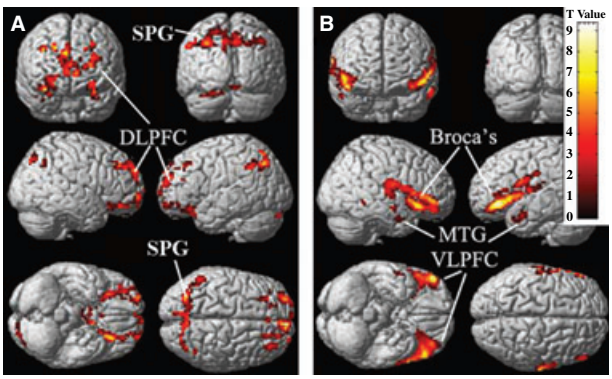

Fig. 4. Two typical activation maps in patients with implant-supported over-dentures. DLPFC, dorsal–lateral prefrontal cortex; MTG, middle temporal gyrus; SPG, superior parietal gyrus; VLPFC, ventral–lateral prefrontal cortex.

temporal gyrus (BA21,22), and the ventral–lateral prefrontal cortex (VLPFC) (BA11,47). A patient's gender, age, retention types, and the time for loading were not correlated with these different activation maps. Whether they had IODs in both jaws or only in the mandible was not an influencing factor.

Group analyses with results from all the patients are listed in Table 2. The broadest and the most consistent brain activation sites were found in the IFD group,

Table 2

Summary of activated regions from group analysis

Subjects	Activated regions	BA
CD (n = 8)	PFC	10, 47
	PMC, precentral gyrus	6
	STG	22, 38
	SPG, precuneus	7
IOD (n = 9)	DLPFC	9, 10, 46
	SPG, precuneus	7
	PMC, SMA	6, 8
	CG	24
	Hippocampus	–
	Thalamus	–
	BG	–
IFD (n = 3)	SI	3
	MI	4
	Broca's area	44, 45
	VLPFC	11, 47
	PMC, SMA	6, 8
	Insula	13
	STG	22, 38
	CG	31
	BG	–
	Hippocampus	–
	Thalamus	–

BA, Brodmann's areas; BG, basal ganglion; CD, traditional complete denture; CG, cingulate gyrus; DLPFC, dorsal–lateral prefrontal cortex; IFD, implant-supported fixed denture; MI, primary motor cortex; PFC, prefrontal cortex; PMC, premotor cortex; SI, primary somatosensory cortex; SMA, supplementary motor area; SPG, superior parietal gyrus; STG, superior temporal gyrus; VLPFC, ventral–lateral prefrontal cortex.

including the SI, MI, Broca's area, PFC, the supplementary motor area (SMA), the insula, and the BG.

Discussion

Many studies have reported plasticity of the sensorimotor cortex in task training, peripheral nerve damage, or after limb amputation. Representative SI areas of the dentition in mammals re-organize significantly after the loss of sensory inputs with tooth extraction in naked mole-rats (14). Functional magnetic resonance imaging techniques make it possible to explore, non-invasively, the neuroplasticity in humans. SVENSSON *et al*. (23) found that after 1 wk of daily training in a tongue protrusion task, human subjects showed a significant increase in the MI tongue representation, suggesting that face SI/MI is important in orofacial motor skill acquisition and adaptation to an altered occlusion caused by missing teeth (24). BJÖRKMAN *et al*. (15) used fMRI to study a patient with immediate hand replantation and another with an osseointegrated thumb prosthesis. They found that the primary motor cortex rapidly returned to a normal activation pattern after replantation or implantation, while the SI changed from an initial ipsilateral to a bilateral activation pattern in both patients. This bilateral activation pattern might represent a compensatory mechanism for the inferior tactile function in the replanted hand and the osseointegrated prosthesis.

Edentulous patients with implant-supported prostheses are thought to be the most suitable models for the study of neuroplasticity related to dental implant restoration. It has been shown that the active absolute threshold level is increased in implant-supported dentures when compared with a natural dentition, but remains below the threshold noted in CD wearers (6). Power spectrum analysis revealed a downward shift of the mean power frequency during sustained clenching in patients with CDs and IODs, but not in patients with IFDs (25). Although there is evidence indicating that IODs appear to be no less efficient than IFDs during clenching and chewing performance (26), GEERTMAN *et al*. (27) suggest that an improvement in masticatory performance does not imply the same improvement in chewing experience, and vice versa. It has also been proved that the combination of mandibular IOD and maxillary CD provides significant improvement in masticatory performance compared with CDs in both jaws (28).

Previous studies with fMRI demonstrated that chewing or mandibular movement significantly activated SI/MI, SMA, Broca's area, the thalamus, and the cerebellum in healthy volunteers with natural dentition (29, 30). Studies have revealed that PMC and insular in some subjects were also active during clenching (31). The SI/MI is considered to be responsible for jaw movement in natural dentition. In this study, in agreement with those previous findings, clenching activated the SI/MI, Broca's area, SMA, and the PMC in all the patients with IFDs, whereas SI/MI signals were found only in two of nine patients with IODs and in one of eight patients with CD. We confer that SI/MI may not be essential or not as important as other cortical areas in clenching for those edentulous patients rehabilitated with CDs or IODs. Sensory and motor feedback of the central nervous system in patients with IFDs is closer to that of the natural dentition. Activation of oral facial representative areas in SI/MI may explain the improved tactile, stereognostic ability, and mastication function, which might be the underlying physiologic mechanism of osseoperception.

The fMRI activity of SI/MI was also observed in a hand-grafted patient with early clinical sensorimotor recovery (32). Whether SI/MI activity could be the indicator for regained sensory and motor function in mastication has not been reported. ONOZUKA *et al*. (33) studied the age-related brain activity during chewing using fMRI and found that blood oxygen level dependent (BOLD) signals in SI/MI were always present, but attenuated with aging. However, subjects in their study had a reduced number of remaining teeth from young adults to aged subjects. Is it possible that the decreased SI/MI activity in the aged group is actually related to missing teeth, which leads to reduced periodontal afferent input? Reduction of brain map size, receptive field of sensorimotor representation, and reduced response strength have been described in aged rats, which are best explained by plastic phenomena arising from reduced sensory inputs (34). Laboratory and clinical evidence suggests that bone in the peri-implant regions contain nerve fibers which may serve as a source of sensory feedback instead of the periodontal ligament (9, 10). It is speculated that an increase in the number of implants may improve the patient's sensory and motor functions because of more bone–implant contacts and more nerve endings. This speculation is consistent with our clinical findings concerning the sensorimotor function of the prosthesis. Implant-supported crowns and short bridges can help the patients restore more natural chewing experiences to the greatest extent. We believe that sensory and motor functions of the masticatory system impaired by missing teeth can be restored because of the re-acquired sensory inputs from dental implants as a result of regained SI/MI representations. Those findings suggest that osseoperception may be based on true activation of the primary sensorimotor cortex in the brain, illustrating the capacity of the brain for compensatory gaining mechanisms by recruiting cortical areas to the extent that may be required.

Group analysis in this study also found that bilateral PFC was active in almost all patients. Different BA areas of PFC were activated in different groups. The PFC, especially the DLPFC, is suggested to play a key role in learning and memory. It was proved that the DLPFC may contribute to long-term memory through its role in active processing of relationships during encoding, whereas the VLPFC may have a more general role in promoting successful long-term memory formation (35). The motor circuit (involving the putamen) is associated with motor-skill learning, and the DLPFC circuit (involving the caudate) is associated with cognitive-habit learning (36). Thus, we are under the impression that bilateral PFC might take part in the adaptive changes

occurring as a result of teeth restoration that is related to long-term memory and skill learning.

In this study, we found two typical activation maps from the patients wearing IODs. No correlation was found between these different signals and patients' characteristics, such as gender, age, retention types, and time for loading. Although direct mucosal loading by CDs is different from that of IODs, the activation patterns were not correlated with CDs or IODs on the maxilla. Whether those different activation maps are related to different adaptive ability or chewing experience of the patients was not explored in this study, but it seems that they showed some features in brain mapping that were different from those of the other two groups. The fact that activation maps had the greatest individually dependent diversity in the CD group might indicate that this type of restoration depends more on denture quality, denture mobility, oral condition, and patient's adaptive ability.

Basal ganglion was one of the main activation sites in patients with implant-supported dentures, especially in IFD wearers. SEIDLER *et al*. (37) observed that activation of basal ganglion, along with PFC, SMA, and parietal regions, might support the sensorimotor processes of early phases of sensorimotor adaptation. The hippocampus gyrus was activated in five of 12 patients with implant-supported dentures but in only one of eight patients with CDs. There are reports on the relationship between hippocampus and memory. Reduced mastication leads to impairment of spatial memory and degeneration of hippocampal neurons in aged mice (38). An fMRI study indicated that involvement of chewing in the neuronal circuit to the hippocampus in the elderly plays an important role in preventing age-related deterioration in the hippocampus (39).

This study had a limited number of patients because of variance reasons, a control group of old dentate volunteers should have been added for more convincing results. If possible, a more suitable sensory stimulation of dental implants instead of clenching should be designed in the future, which may simplify the neural transmission without motion output. The combination of fMRI with microstimulation will enable more detailed studies of the representation of the body surface in human somatosensory cortex and further studies of the relationship of that organization to short-term plasticity in the human SI cortical response to natural tactile stimuli (40).

In conclusion, this pilot study suggests that fitting of implant-supported dentures evoked a change in somatosensory and motor inputs to the brain that was markedly different from what occurred with CDs. Sensory and motor feedback to the central nervous system in patients with IFDs was closer to that of the natural dentition. Activation of an oro-facial representative area in the SI/MI in patients with IFDs may explain the improved tactile, stereognostic ability, and mastication functions, which might be the underlying mechanism of osseoperception. Activation maps had the greatest individually dependent diversity in patients with CDs and the lowest individually dependent diversity in IFD wearers. It follows that the closer the final prostheses come to restoring original function, the closer the sensory motor system will come to re-establishing its original characteristics (11).

Further studies are crucial to clarify the cortical neuroplasticity associated with oral environment changes and the adaptive mechanisms associated with these changes. It may be directly related to the individuals' ability to accommodate their new prosthesis and their subjective mastication experience. In the future, the extent of these changes, together with specific outcome differences and individual oral dental characteristics, may explain why some patients experience more difficulty than others in the process of adapting to their prostheses. In this regard, the recent fMRI studies of cochlear implants have presented us with a promising possibility that brain organization assessed immediately before cochlear implantation can efficiently predict subsequent speech outcome (41).

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