A Functional Magnetic Resonance Imaging Paradigm to Identify Distinct Cortical Areas of Facial Function: A Reliable Localizer

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A Functional Magnetic Resonance Imaging Paradigm to Identify Distinct Cortical Areas of Facial Function: A Reliable Localizer

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Background: Irreversible facial paralysis can be surgically treated by importing both a new neural and a new motor muscle supply. Various donor nerves can be used. If a nerve supply other than the facial nerve is used, the patient has to adapt to generate a smile. If branches of the fifth cranial nerve are used, the patient has to learn to clench teeth and smile. Currently, controversy exists regarding whether a patient develops a spontaneous smile if a nerve other than the facial nerve is used. The authors postulate that brain adaptation in facial palsy patients can occur because of neural plasticity. The authors aimed to determine whether functional magnetic resonance imaging could topographically differentiate activity between the facial nerve– and the trigeminal nerve–related cortical areas.

Methods: A new paradigm of study using functional magnetic resonance imaging based on blood oxygen level–dependent signal activation was tested on 15 voluntary healthy subjects to find a sensitive localizer for teeth clenching and smiling. Subjects smiled to stimulate the facial nerve–related cortex, clenched their jaws to stimulate the trigeminal nerve–related cortex, and tapped their finger as a control condition.

Results: Smiling and teeth clenching showed distinct and consistent areas of cortical activation. Trigeminal and facial motor cortex areas were found to be distinct areas with minimal overlapping.

Conclusions: The authors successfully devised a functional magnetic resonance imaging paradigm effective for activating specific areas corresponding to teeth clenching and smiling. This will allow accurate mapping of cortical plasticity in facial reanimation patients. (*Plast. Reconstr. Surg.* 131: 527e, 2013.)

CLINICAL QUESTION/LEVEL OF EVIDENCE: Diagnostic, IV.

Facial reanimation surgery following irreversible facial paralysis can be achieved with several surgical procedures. Generally speaking, both a strengthened or new nerve supply and a new muscle supply are required to recreate the smile. If the contralateral facial nerve is used as a donor nerve, it is generally accepted that a spontaneous, emotionally driven smile can be achieved. If another nerve, most commonly the trigeminal, is used, however, significant controversy exists as to whether a spontaneous smile can ever be achieved.

The facial nerve is a complex motor/sensitive structure, partially crossed, giving fine movement to a high number of muscles. The choice of surgical reanimation technique is determined mainly by the cause of facial paralysis and by the age and desires of the patient. The techniques most commonly used are the nerve grafts (sixth to seventh, twelfth to seventh, and cross-facial nerve graft),[1,2] dynamic muscle transfers (temporal myoplasty, free muscle transfer),[3–9] and static suspension.[10,11] Some procedures require a two-stage and some a one-stage approach.

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There remains substantial controversy as to whether it is important to use the facial nerve as a nerve supply in facial reanimation or whether an alternative nerve can lead to equivalent results. Using the facial nerve may require a two-stage procedure, especially if a muscle flap is needed. The advantage of using the facial nerve is that the resultant smile will be spontaneous and emotional. In contrast, using a branch of the trigeminal nerve as the motor source (such as the nerve to masseter) along with a free muscle transfer or a temporalis myoplasty simplifies surgery, and results can be achieved in one stage. However, it is still unclear whether using the trigeminal nerve as a motor can lead to a natural, spontaneous smile. At least initially, patients need to learn to clench their teeth to initiate a "smile." It could be, however, that, in time, the smile can become spontaneous, as a consequence of cerebral reorganization.

After central or peripheral injury, molecular and/or structural alterations, also known as brain plasticity,[12–14] lead to a certain degree of functional adaptation. This phenomenon is thought to be particularly important in facial reanimation, where a motor nerve other than the facial nerve is used to create a smile. We have hypothesized that these changes may be mapped using functional magnetic resonance imaging. If this is the case, it could be possible to objectively assess brain plasticity following facial reanimation surgery.

Functional magnetic resonance imaging has become the most useful tool with which to relate functional activity to specific anatomical locations in the brain. In contrast to structural magnetic resonance imaging, functional magnetic resonance imaging detects changes in blood oxygenation (i.e., blood oxygen level–dependent signal)[15,16] because of small distortions in the magnetic field as a consequence of unbound iron to oxygen deoxyhemoglobin. Given that whenever a part of the brain becomes active oxygenated blood flow increases, blood oxygen level–dependent signal changes can be related directly to brain activation.

High spatial resolution of magnetic resonance imaging coupled with blood oxygen level–dependent signal changes make quantitative and qualitative cortical activity imaging possible.[17] Functional magnetic resonance imaging findings on brain plasticity illustrate augmentation of blood flow on the contralateral side[18] and self-tuning of inhibition or stimulation signals of the motor cortex[19,20] with expansion of the cortical representation near the injured area. Brain reorganization occurs throughout life during learning processes, novel experiences, and in response to injury[12,21,22] or even after surgery.[13]

This study aimed to localize cortical activation during smiling (seventh cranial nerve), teeth clenching (fifth cranial nerve), and finger tapping (control) by using a specific functional magnetic resonance imaging paradigm to determine whether the spatial resolution provided by functional magnetic resonance imaging is accurate enough to consistently and reliably distinguish areas of cortical activation between smiling and teeth clenching. These areas of the brain should correlate with activity relating to smile using the facial nerve (represented as smiling in the paradigm) and brain activity relating to a smile created using the trigeminal nerve (represented as teeth clenching in the paradigm). An effective protocol to measure brain plasticity could provide better understanding of the consequences and effectiveness of various surgical procedures in facial reanimation. By comparing groups of patients undergoing different surgical procedures, we will be able to measure any variation in brain plasticity. In turn, this should help clarify the controversy that exists as to whether reanimation techniques using a trigeminal donor (either nerve to masseter or temporalis transfer) truly can lead to a spontaneous smile without conscious teeth clenching. We therefore devised a paradigm to measure cortical activity in healthy subjects while stimulating smiling and teeth clenching, to mimic activity of both the trigeminal and facial nerves, such as would occur in subjects after facial reanimation surgery using either the facial or trigeminal nerve motor nerve supply.

PATIENTS AND METHODS

Fifteen participants (mean ± SD age, 31 ± 12.5 years; eight male and 14 right-handed participants) with normal or corrected-to-normal vision were included in the study. All participants provided written informed consent in accordance with procedures and protocols approved by the local ethics committee of the Centre for Cognitive Neuroimaging, Department of Psychology of the University of Glasgow and NHS Ethical Committee.

Design and Motor Tasks

In a block design, participants were required to perform three motor tasks: smiling, jaw clenching, and finger tapping. Before the beginning of the experiment, all subjects practiced each task for approximately 15 minutes under the experimenter's supervision. The smiling action consisted of a voluntary smile characterized by contraction of the zygomatic major only, movement marked as Ac-

tion Unit 12 in the Facial Action Coding System.[23] Teeth clenching was performed by asking for simple mandible elevation, whereas for finger tapping, participants used their thumb to tap the remaining fingertips.

In the scanner, participants were instructed to perform the motor tasks on visual cue (i.e., the word corresponding to the task of interest). Subjects viewed the screen through binocular visual display goggles (Nordic NeuroLab, Milwaukee, Wis.). The experiment consisted of three 6-minute runs, interleaved with a T1-weighted high-resolution anatomical scan. Each run began with a white central fixation cross for 8000 msec, followed by a word cue (smile, clench, or tap) presented for 1800 msec, indicating the required motor response. A blinking central fixation was then flashed for 500 msec (16 times), dictating the tempo of muscle contraction. Another fixation was subsequently presented for 11,200 msec, preceding the onset of the next cue. Each task was repeated four times per run, with movement sequences lasting approximately 16 seconds. Trial order was randomized, and eye fixation was centrally locked throughout runs; participants were asked to minimize other movements while performing the task.

Magnetic Resonance Imaging Data Acquisition

Magnetic resonance imaging data were collected with a 3-T Siemens Tim Trio System (Siemens Medical, Munich, Germany) with a 12-channel head coil and integrated parallel imaging techniques (integrated parallel acquisition technique factor, 2). Blood oxygen level–dependent signals were measured with an echo-planar imaging sequence (echo time, 30 msec, repetition time, 2000 msec; field of view, 210 mm; flip angle, 62 degrees; 10 percent gap; 36 axial slices; voxel size, $3 \times 3 \times 3$ mm). The slices were positioned to cover the whole brain. A high-resolution three-dimensional anatomical scan (three-dimensional magnetization prepared rapid gradient echo, $1 \times 1 \times$ 1-mm resolution) was obtained during the same session as the functional scans.

Magnetic Resonance Imaging Data Processing

We used BrainVoyager QX software (Brain Innovation, Maastricht, The Netherlands) to analyze blood oxygen level–dependent imaging data. Functional images were preprocessed as follows: first, a slice scan time correction was performed using a sync interpolation algorithm. We then carried out offline three-dimensional motion correction using a trilinear interpolation algorithm: all volumes were spatially aligned to the first volume by rigid body transformations, and the roto-translation information was saved for subsequent elaborations. Spatial smoothing was subsequently implemented using a Gaussian kernel of 4 mm at full width at half maximum. Temporal data were thus filtered using voxelwise linear detrend and high-pass filter at 0.01 Hz. The participant's slice-based functional scan was finally coregistered on their three-dimensional high-resolution structural scan and transformed into Talairach space.[24]

To identify the brain regions responding to different motor movement, we computed a general linear model with separate predictors for smiling, clenching, and tapping. Beta weights were calculated and used in the contrast. Three regions of interest were identified independently per participant in both hemispheres by means of linear contrasts. There were two regions of interest—smiling (smiling versus clenching and tapping) and clenching (clenching versus smiling and tapping)—and a control [tapping (tapping versus smile and clenching)]. For all contrasts, a t map with a maximum threshold of $p < 0.01$ (false discovery rate corrected) was applied. Cluster sizes of greater than 0.27 cm^3 (>10 voxels; voxel size after normalization, $3 \times 3 \times 3$ mm) showing a statistically significant Z score (typically, Z threshold = 3.0) in the comparison were considered.

RESULTS

Comparison between the motor tasks demonstrated no overlap between smiling and teeth clenching regions of interest. The smiling task was significantly associated with increased blood oxygen level–dependent activation in intensive bilateral regions of the primary motor cortex, within the middle precentral gyrus for all of the participants ($p < 0.01$, false discovery rate corrected, 10 voxels minimum) (Table 1 and Figs. 1 and 2). By contrast, a significantly larger activation for clenching compared with smiling plus tapping was identified in a distinct region in the low precentral gyrus of most participants ($n = 13$ of 15 in the left hemisphere, $n = 13$ of 15 in the right hemisphere) (Table 1 and Fig. 2). As shown in Figure 1, the group coordinates for the smile region were 47, −12, 37 (right, $Z = 18.291$, size = 277 voxels) and −50, −14, 36 (left, $Z = 18.113$, size = 302 voxels). Accordingly, the group coordinates for the clenching region were 54, −8, 27 (right, $z = 11.321$, size = 254 voxels) and −60, −8, 31 (left, $Z = 10.913$, size = 66 voxels).

Three participants also showed significantly larger activation for smiling compared with clenching and tapping in the bottom region of the right

Table 1. Mean Coordinate Level of Activation and Size of the Functional Regions Observed in All Participants*

	Right Smile Area Talairach					Left Smile Area Talairach				
	x	*y*	*z*	Z-Score	No. of Voxels	*x*	*y*	*z*	Z-Score	No. of Voxels
S1	38.91	−14.86	44.87	9.084	166	−48.73	−16.96	37.8	9.365	316
S2	51.92	−12.01	40.83	6.521	140	−58.3	−13.39	36.64	6.83	246
S3	51.74	−6.14	35.63	9.287	276	−59.96	−10.74	36.2	7.974	46
	41.45	*−11.31*	*33.85*	*7.863*	*71*	*−50.8*	*−14.03*	*36.23*	*7.883*	*30*
S4	45.28	−9.21	38.49	8.33	224	−50.7	−13.8	36.4	7.785	10
S5	49.29	−11.9	36.43	9.431	198	−50.44	−16.44	38.61	9.51	156
	37.78	*−13.57*	*34.78*	*9.466*	*89*	*−45.31*	*−17.64*	*36.19*	*9.872*	*200*
S6	43.69	−12.03	37.71	8.105	211	−51.69	−12.9	38.37	8.495	218
S7	40.42	−13.39	33.54	6.882	103	−46.12	−13.65	37.81	9.315	301
S8	44.29	−9.67	36.6	8.146	135	−43.25	−17.16	35.67	8.123	83
S9	49.53	−11.15	37.12	13.829	146	−53.03	−18.95	34.19	15.14	370
S10	49.05	−12.43	38.12	5.334	189	−43.52	−10.21	37.09	5.673	163
S11	55.53	−10.35	40.31	5.018	49	−47.73	−15.35	32.6	5.911	204
	41.4	*−15.61*	*37.03*	*5.018*	*90*	*−54.81*	*−13.26*	*35.94*	*5.532*	*362*
S12	52.13	−6.49	40.06	4.534	107	−55.53	−7.87	37.39	4.464	112
S13	42.66	−14.79	34.17	8.512	110	−49	−13.88	37.21	7.534	24
S14	41.83	−16.09	35.56	6.721	75	−47.96	−14.35	36.34	6.822	150
S15	48.25	−21.54	35.66	10.796	158	−53.53	−23.18	29.56	10.832	45
Mean ± SE	46.97 ± 4.91	−12.14 ± 3.84	37.76 ± 2.93	15/15 subjects		−50.63 ± 4.87	−14.59 ± 3.73	36.13 ± 2.39	15/15 subjects	

	Right Clench Area Talairach					Left Clench Area Talairach				
	x	*y*	*z*	Z-Score	No. of Voxels	*x*	*y*	*z*	Z-Score	No. of Voxels
S1	54.33	−7.31	35.53	6.895	205	−57.86	−6.4	26.88	6.385	148
S2	54.28	−11.14	48.19	3.191	72					
S3	46.44	−7.32	29.47	6.32	168	−59.29	−7.28	29.26	6.005	381
S4	61.32	0.5	28.75	5.945	28	−60.76	−4.75	29.97	6.309	89
S5	52.15	−5.19	23.64	7.57	196	−56.17	−7.57	32.3	8.262	345
S6	55.64	−8.15	24.44	4.916	165	−59.83	−5.97	35.72	5.307	174
S7	48.57	−8.91	28.02	4.202	46	−44.4	−10.06	29.83	4.299	52
S8	57.36	−5.91	29.98	7.427	159	−60.23	−5.43	29.62	7.409	145
S9	45.21	−15.55	21.22	7.335	216	−46.71	−14.54	2.03	8.333	266
S10	57.32	−6.53	24.17	6.343	257	−58.21	−6.59	24.53	6.147	99
S11	57	−5.07	37.81	6.983	247	−55.28	−24.19	33.02	6.851	146
S12										
S13	55.79	−12.44	34.06	6.786	102	−63.36	−15.49	28.4	7.552	258
S14	57.98	−5.89	26.18	7.21	194	−59.68	−8.1	23.41	6.844	134
S15	57.59	−18.38	15.14	8.386	29	−61.92	−19.98	12.77	8.978	194
Mean ± SE	54.36 ± 4.68	−8.38 ± 4.75	29.04 ± 8.08	14/15 subjects		−57.21 ± 5.62	−10.49 ± 6.16	25.98 ± 9.14	13/15 subjects	

*A significant smile–clench difference was clearly observed in 15 participants in the right and left middle precentral gyrus. Three participants also showed significant differences in the bottom region of right and left precentral gyrus (S3, S5, and S11, shown as *italic*). Fourteen participants presented significant differences in the lower region of the precentral gyrus in right hemispheres for clench–smile contraction. In the left hemisphere, 13 participants showed a similar significant pattern over the lower region of the precentral gyrus.

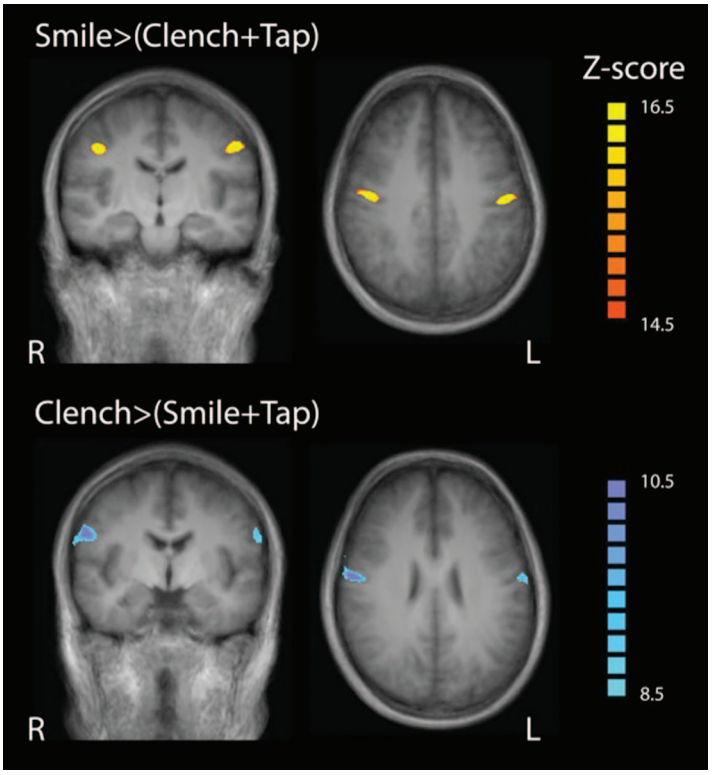

Fig. 1. Group *t* map showing areas in which significant increases in blood oxygen level–dependent activation responded to smile (*upper*) and clench (*lower*). The coordinates of the smile region are 43, −12, 37 (*right*, $Z = 18.291$, size = 277 voxels) and −48, −13, 38 (*left*, $Z = 18.113$, size = 302 voxels). The coordinates of the clench region are 59, −4, 30 (*right*, $Z = 11.321$, size = 254 voxels) and −59, −6, 32 (*left*, $Z = 10.913$, size = 66 voxels).

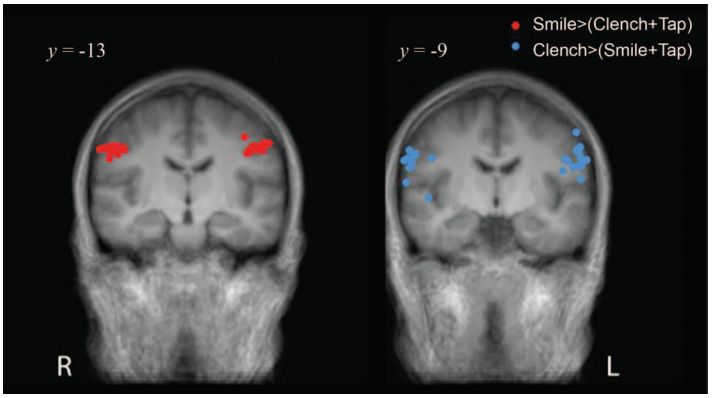

Fig. 2. Schematic representation on two Talairach slices ($y = -9$ and -13) of the areas of activation in the precentral gyrus for smile and clench.

and left precentral gyrus (see Table 1, participants S3, S5, and S11, whose values are shown in *italics*). The mean coordinates for this secondary smile region were 39, –13, 35 (right, mean $Z = 7.449$, mean size = 83 voxels) and –49, 15, 35 (left, mean $Z = 7.762$, size = 197 voxels).

DISCUSSION

The mechanism of cerebral cortical reorganization is not well established in facial reanimation patients. Specifically, whether a truly spontaneous and emotional smile is achievable using neural input from a nonfacial nerve is still open to debate.

Surgical techniques using either the facial or the trigeminal nerve can lead to fairly symmetrical facial movement with regard to smiling. However, a myriad of techniques are commonly used, and which of these leads to better and more natural results is still currently debated.

The successful use of functional magnetic resonance imaging to differentiate between neural activity of the facial and trigeminal nerves has promising implications in determining the nature of cortical reorganization in facial reanimation. This is important, as it provides an objective measure of brain plasticity between groups of patients who have had reanimation using both facial and trigeminal nerve donors. Moreover, the reliable spatial resolution provided by functional magnetic resonance imaging promises to resolve the controversy surrounding trigeminal donor reanimation (either nerve to masseter or temporalis transfer), namely, whether this technique can truly lead to a spontaneous smile in the absence of teeth clenching.[25]

When Zuker et al. introduced the use of the motor branch to the masseter muscle, a branch of the trigeminal, to activate segmental gracilis muscle transplants in facial reanimation children with Möbius syndrome, they concluded that a fully spontaneous smile was not achievable.[7] However, in 2011, Schaverien et al., performing electromyography of the masseter muscle in patients with free gracilis–to–masseter nerve transfer, showed a natural contraction of the masseter muscle during normal smile occurring in 50 percent of their subjects.[25] The phenomenon of patients achieving a spontaneous smile following free gracilis–to–masseter nerve transfer is another sign of brain plasticity. With practice, patients can develop the ability to smile spontaneously and without jaw movement.[8]

Ziemann et al. showed in study of the modulation of practice-dependent plasticity in human motor cortex that motor practice leads to expansion of trained representations in the motor cortex,[26] probably because of the preexisting but latent horizontal connections in the cortex. One explanation for the development of a spontaneous smile following the use of a trigeminal motor nerve is if, for example, a free gracilis–to–masseter nerve transfer induced change in cortical motor reorganization through the use of preexisting but latent horizontal connections in the cortex. In this scenario, there could be the potential for a spontaneous smile without jaw movement. The successful use of functional magnetic resonance imaging to differentiate between activities in the facial nerve–related cortex activating a smile and the trigeminal cortex activating teeth clenching is able to provide a satisfactory answer to this question.

One previous study has looked at functional magnetic resonance imaging in smile generation and successfully demonstrated a distinct cortical area relating to smile generation.[27] Talairach coordinates found in this study generally correlate well with those seen in our study.

Importantly, we did not aim to isolate the neural differences between voluntary and involuntary smile. This is to date an extremely controversial topic, with some authors[28] arguing for the existence of different pathways of activation for the two types of smile, others[29] reporting no difference between them, and a final strand claiming that cultural and social influence render cortical activations following voluntary or involuntary smile unpredictable.[30] However, based on current knowledge, we can confidently state that the brain regions isolated here account for only the motor component of smiling, which represents the final stage of this process, and it is thus well beyond this dichotomy.[30] Whether a smile is voluntary or involuntary would indeed produce differential neural patterns. This difference, however, would affect only subcortical regions (such as the amygdala) or regions involved in emotional evaluations. Crucially, both types of neural patterns elicited by involuntary and voluntary smile would trigger neural activity in the same motor-cortical area, responsible only for producing the movement of a smile (which is the same regardless of the cause). Therefore, this difference will not impact on the location and the activation for the smile we found here.

CONCLUSIONS

For the first time, we show that there are two distinct cortical areas subserving smiling and teeth clenching. This result allows an objective assessment of cortical reorganization between groups of facial and trigeminal nerve donor reanimation patients. Having successfully and consistently identified these two cortical areas by investigating the variations in blood oxygen level–dependent signal activity among them, we can finally assess the extent and nature of cortical reorganization. The latter has been shown to occur in clinical settings such as Braille reading,[18] limb amputation,[19,20] and nerve injuries[31] and thus is likely to also occur in facial reanimation patients. In the future, it will be possible to follow any changes in cortical activity directly related to brain plasticity as patients recover following facial reanimation surgery using either the facial nerve or trigeminal nerve branches as a motor. This will allow surgeons to advise patients regarding the likelihood of devel-

oping a spontaneous smile using different techniques of facial reanimation.

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