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Localization of the Motor Tongue Area to the Inferior Central Sulcus

A Combined fMRI—Anatomical Study

Dissertation
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INHALTSVERZEICHNIS

1. KURZZUSAMMENFASSUNG

1.1. Ziel

Ziel der Arbeit ist die exakte Lokalisation des primären motorischen Zungenareals mittels funktioneller Magnetresonanztomographie. Dabei soll das motorische Zungenareal in Bezug zu den anatomischen Strukturen der inferioren Zentralregion gesetzt werden.

1.2. Methoden

Die Anatomie der unteren Zentralregion wurde anhand von 24 Probanden und 19 Leichenhemisphären (insgesamt 67 Hemisphären) untersucht. Mit Hilfe von MPRAGE Sequenzen wurden der Sulcus centralis und die benachbarten Gyri und Sulci in einem Abschnitt dargestellt, der vom Genu medius des Sulcus centralis bis zur sylvischen Fissur reicht.
Das motorische Zungenareal wurde bei 11 Probanden (22 Hemisphären) mit Hilfe der funktionellen Magnetresonanztomographie lokalisiert. Das Paradigma hierfür war eine horizontale Zungenbewegung. Die lokalen Maxima wurden dazu sowohl auf axialen Schichten als auch auf einer dreidimensionalen Rekonstruktion der jeweiligen Hirnoberfläche dargestellt. Anschließend wurden die Strukturen, auf denen die lokalen Maxima lokalisiert sind, erfasst und beschrieben.

1.3. Ergebnisse

Das inferolaterale Segment des Sulcus centralis unterhalb des Genu inferior besteht aus zwei Kurven in 46 der 67 (69%) Hemisphären, drei Kurven in 9% und vier Kurven in 19% der untersuchten Hemisphären. Bei zwei Hemisphären (3%) war das inferolaterale Segment des Sulcus centralis eine gerade Strecke.
Signifikante Aktivierungen hervorgerufen durch die Zungenbewegung fanden sich in allen mittels fMRT untersuchten Hemisphären. Daraus wurden 89 lokale Maxima bestimmt, wovon wiederum 84 (94%) der Zentralregion zugeordnet wurden.

Insgesamt lagen 59 lokale Maxima (66%) im Gyrus praecentralis, 25 (28%) im Gyrus postcentralis und 24 (27%) in der Tiefe des Sulcus centralis. Siebenundsechzig (80%) der 84 lokalen Maxima im Bereich des Sulcus centralis wurden entlang der beiden Kurven des Sulcus centralis, die der sylvischen Fissur am nächsten sind, lokalisiert.
Sechsundachtzig Prozent der lokalen Maxima auf der Vorderbank des mittleren und tiefen Abschnitts des Sulcus centralis waren auf drei axialen Schichten lokalisiert, wovon die mittlere der drei Schichten durch die Cella media des Ventrikelsystems führt.

1.4. Zusammenfassung

Der inferiore Abschnitt des Sulcus centralis kaudal des Genu medius ist sehr variabel. Daher ließ sich keine spezifische anatomische Struktur der Hirnoberfläche dem primär motorischen Zungenareal zuordnen.
Bei allen Probanden konnten die axialen Schichten, auf denen das motorische Zungenareal lokalisiert ist, charakterisiert werden. Diese Schichten sind definiert durch die Cella media der Seitenventrikel.

2. ABSTRACT

2.1. Purpose

To define the position of the primary motor tongue area (MTA) by using functional magnetic resonance imaging (fMRI) to display the MTA in relation to the inferolateral segment of the central sulcus (CS).

2.2. Methods

The anatomy of the inferolateral segment of the CS was analyzed in 24 healthy subjects and 19 anatomic specimens (a total of 67 hemispheres), using the MPRAGE sequence to display the contours of the CS, the adjacent gyri, and the adjacent sulci along the low convexity of the cerebral hemispheres. The position of the MTA was defined in 11 subjects (22 hemispheres) by using fMRI and a tongue movement paradigm to identify the sites of maximal activation for each subject in relation to that subject's own CS. The MTA was then displayed (i) in serial MR sections in the three orthogonal planes oriented along and perpendicular to the bicommissural plane, (ii) in lateral surface reformations, and (iii) in the axial sections through the cellae mediae of the lateral ventricles.

2.3. Results

The inferolateral segment of the CS situated inferior to the inferior genu displayed two distinct curves in 46 of 67 (69%) hemispheres, three curves in 9%, and four curves in 19%. In 2 hemispheres (3%), the inferolateral segment of the CS was straight (no curves). Significant paradigm correlated activations were found in every hemisphere. Thereof 89 local maxima were determined. 84 (94%) were located in the region of the central sulcus. A total of 59 (66%) were located in the precentral gyrus, 25 (28%) in the postcentral gyrus, and 24 (27%) in the depth of the CS. Sixty-seven (80%) of the 84 central sulcus activations lay along the two lowest curves of the CS. In 86% of cases, the motor tongue activation points situated on the middle and deep

part of the anterior bank of the CS were encompassed within the 3 axial sections centered on the cella media of the lateral ventricles.

2.4. Conclusion

The inferior portion of the CS shows great anatomic variability. No specific anatomic configuration defines the site of the primary motor tongue area. However, in all of the subjects studied with our paradigm, the position of the MTA could be approximated by the intersection between the CS and the 3 axial planes through, just above and just below the cella media of the lateral ventricles.

3. INTRODUCTION

The primary somatomotor and somatosensory cortices of the brain form a pericentral region composed of the precentral gyrus (preCG), postcentral gyrus (postCG), subcentral gyrus (subCG) and paracentral lobule, arrayed around the central sulcus (CS) (Yousry, 1998). Classically, the CS is divided into three genua (knees) (Broca, 1878, Déjérine, 1895, Yousry, 1998). The superior genu lies along the medial segment of the central sulcus, and has its convexity directed anteriorly. The middle genu lies lateral to the superior genu, has its convexity directed posteriorly, and corresponds to the motor hand knob (Yousry, 1998, Yousry *et al.*, 1997). The inferior genu of the CS is the next curve found along the lateral surface, and has its convexity directed anteriorly. The segment of the CS situated inferolateral to the inferior genu has been stated to be nearly straight and devoid of curves (Sastre Janer *et al.*, 1998), but its precise course has not yet been analyzed in detail.

Functionally, the primary motor and primary somatosensory areas exhibit somatotopic organization, which is classically summarized as the motor and sensory homunculi (Boling *et al.*, 2002, Foerster, 1936, Penfield and Rasmussen, 1950). Recent work using electrical microstimulation of primary motor and premotor cortex in monkeys (Graziano *et al.*, 2002) however indicates, that these regions have a further, more complex organization that directs muscle groups to assume complex body postures, and that the motor homunculus is actually a map of the positions in space at which movements terminate, not a map of which body part is moved.

The locations of the somatotopic regions have been well demonstrated with respect to each other (relative position), but poorly defined in absolute position. Thus far, only the hand motor area has been shown to map to a characteristic protuberance of the posterior face of the precentral gyrus (the motor hand knob at the middle genu of the CS) (Yousry *et al.*, 1997). The motor tongue area (MTA) is known to lie close to the sylvian fissure, but cortical mapping studies have shown that the MTA may be situated either near to (Corfield *et al.*, 1999, Woolsey *et al.*, 1979) or up to 4 cm superior to (Urasaki *et al.*, 1994) the sylvian fissure.

This study was undertaken to evaluate the topography of the inferior portion of the CS in greater detail, to evaluate the position of the MTA on fMRI, and to correlate the two to determine whether any specific anatomic feature along the CS could serve as a surrogate landmark for the MTA.

4. METHODS

4.1. Study material

This study was conducted in accordance with the Declaration of Helsinki. All subjects who participated in this study gave written informed consent prior to the beginning of the study.

The anatomy of the central sulcus was evaluated both *in vivo* in 24 healthy subjects (12 men and 12 women ranging in age from 24 to 36 years, mean age: 28 years) and *in vitro* in 19 specimen hemispheres obtained postmortem. The site(s) of the motor tongue area were evaluated by fMRI in 11 healthy subjects (5 men and 6 women ranging in age from 24 to 30 years, mean age: 27 years). All 11 of these subjects were determined to be right handed by the Edinburgh handedness inventory (Oldfield, 1971).

4.2. Data acquisition

The magnetic resonance imaging studies were performed on a 1.5 Tesla magnet (Siemens, Vision), equipped with a gradient booster system and a head volume radio-frequency coil. Head movements were minimized using head pads and a forehead strap.

The images utilized for anatomic analysis, correlation, and three-dimensional (3D) reconstruction, were obtained as magnetization prepared rapid acquisition gradient echo (MPRAGE) sequences, using the following parameters: TR/TE = 11.4/4.4 ms; flip angle = 15°; field of view (FoV) = 256*256 mm; slab thickness = 160 mm; matrix = 256*256; number of 3D partitions = 160; number of slabs = 1; pixel size = 1.00*1.00 mm; effective slice thickness = 1.00 mm; number of acquisitions (acq) = 1; scan time = 14 min 13 sec. The 19 anatomic specimens were also photographed, and the digitized photographs compared to the 3D reconstructions of the same hemispheres, to confirm that the 3D images displayed the sulcal anatomy accurately.

The fMRI was performed as a block design experiment using a BOLD (blood oxygenation level dependent)-sensitive echo planar imaging (EPI) sequence (Ogawa and Lee, 1990, Ogawa *et al.*, 1990, Thulborn *et al.*, 1982) with the following parameters: TR = 6 s, TE = 60 ms, matrix size: 128 *128, Field of view (FOV): 256

mm (rectangular); SL = 5 mm, no gap; voxel size: 2*2*5 mm; number of slices: 26. The axial imaging slices were specifically oriented along and parallel to the bicommissural plane (Talairach and Tournoux, 1988) and centered to cover the entire brain. The sagittal and coronal planes were oriented perpendicular to the bicommissural line.

All subjects were instructed to the performance of the study before they began the study, including the repetitions of sequential periods of tongue activity (the task) and rest positions (control). For the active periods, they were trained to move the tongue from side to side at a frequency of approximately 1 /s, to keep a steady pace of motion, to avoid swallowing, to keep the mouth slightly open, and to minimize mouth movements. For the control condition, they were trained to keep the tongue relaxed in the same position. The functional series consisted of 14 blocks of 5 measurements per block. Each block lasted 30 s. In each block the brain was completely imaged 5 times. The first block of measurements was discarded from analysis to avoid T1-related relaxation effects. The subsequent blocks of measurements were divided into 6 active blocks alternating with 7 control "resting" blocks.

4.3. Data analysis

4.3.1. Anatomy

The MPRAGE sequences of each volunteer and of each specimen were manipulated to generate an individual 3D surface reconstruction using 3D-Tool (Max-Planck-Institut für neurologische Forschung, Köln)(Von Stockhausen *et al.*, 1998). All of the original specimen images and all of the reconstructed surfaces were exported from a Sun Workstation to an Apple Macintosh computer for further analysis. To determine the reliability of the 3D-Tool program, two neuroradiologists (TAY and GF) worked collaboratively to evaluate the course of the CS on the 19 specimen hemispheres, on the scanned photographs of those hemispheres, and on the 3D surface reconstructions of those hemispheres, in random order.

On all of these MR images, the course, contour, anteroposterior deflections, and terminations of the inferior portion of the CS were determined as follows: The motor hand knob was identified first (Yousry *et al.*, 1997). This was taken to be the middle genu. The anterior convex curve of the CS inferolateral to the middle genu was defined as the inferior genu, and the segment of the CS situated inferolateral to the inferior genu was defined as the inferolateral segment of the CS. An "inferolateral CS-segment line" was then drawn along the CS from the posteriormost point (apex) of the motor hand knob to the inferior-lateral termination of the central sulcus at (or near to) the sylvian fissure (Adobe Photoshop + Illustrator). The course of the sylvian fissure just inferior to the inferolateral end of the CS was marked by a second line. The low CS was then scored for continuity into the sylvian fissure, termination short of the sylvian fissure, straight or Y-shaped configuration of the inferior end of any discontinuous CS, and the directions and sequence of any curves of the low CS anterior and/or posterior to the inferolateral CS-segment line. Variations in the shape of the CS were assessed and named according to their form. When curves occurred, the first anteriorly-concave was designated the superior concave curve. The second anteriorly-concave curve was designated the inferior concave curve. The first anteriorly-convex curve of the infero-lateral segment was designated the superior convex curve, and the second anteriorly-convex curve was designated the inferior convex curve. When no curves occurred the inferolateral CS-segment line was described as a straight line.

In all of the volunteers and specimens, the CS lateral to the hand knob was also assessed in relation of the constant junction of the posterior end of the middle frontal gyrus (MFG) with the anterior face of the precentral gyrus (preCG) (Naidich *et al.*, 1995). Using a previously published system (Naidich *et al.*, 1995), we first identified the horizontal and ascending anterior rami of the sylvian fissure, used the two rami to identify the precentral sulcus and the inferior frontal sulcus, and then used the union of these two sulci to delineate the inferior border of the junction of the MFG with the anterior face of the preCG. The junction thus identified was then related to the previously defined curves of the CS. In addition we also measured the straight-line distance between the middle of the motor hand knob and the middle of this junction at the level of the CS.

4.3.2. fMRI

Functional data were analyzed using SPM96 software (Wellcome Department of Cognitive Neurology, Institute of Neurology, London, http://www.fil.ion.ucl.ac.uk/spm) implemented in Matlab 4.2 (Mathworks Inc., Sherborne, Ma, USA). After discarding the first 5 scans of each series, the remaining

EPI scans of each series (65 scans) were realigned to the first functional scan to reduce head movement artifacts. For single subject analysis, the realigned data sets were smoothed spatially with a Gaussian kernel of 6 mm. For group analysis the realigned data were normalized into a standard stereotactic space and spatially smoothed with a gaussian kernel of 8 mm (Friston *et al.*, 1995, Poline *et al.*, 1995). Statistical analysis was performed using the principles of the general linear model (Friston *et al.*, 1995). Low frequency effects such as temporal drift and some cardiac and respiratory influences were filtered out with an implemented high pass filter utilizing a cut off period of 120 s (Holmes *et al.*, 1997). The subsequent scans were globally normalized and temporally smoothed with a 2.8 s. Gaussian kernel. A delayed box car function was used to model the expected response function of the fMRI signal over time (Friston *et al.*, 1994). The condition effect was estimated voxelwise. This ANCOVA analysis was computed as a statistical parametric map of the t-statistic (SPM(t)). The SPM(t) was transformed to the unit normal distribution SPM(z) and thresholded at $Z = 3.09$ and $P < 0.05$ for the extent of activation. The result is a set of spatially distributed significantly activated voxels, which represent areas of the brain activated during the performance of the paradigm (Friston *et al.*, 1995). The group results are reported as significantly activated clusters with their corrected significant local maxima. In the single subject analyses, the results are reported as points of activation corresponding to the local maxima within the cluster of activation (maximum of 5 points for each hemisphere). These local maxima were used in the subsequent anatomic-functional correlation.

4.3.3. Anatomic-functional correlation

The local maxima of the motor tongue activation obtained by the functional analysis were overlaid onto the axial, coronal and sagittal MPRAGE images (MPI-Tool, Max-Planck-Institut für neurologische Forschung, Köln)(Pietrzyk *et al.*, 1990) and onto the 3D surface reconstructions (3D-Tool). For each hemisphere of each subject, the exact locations of these maxima were then recorded in relation to the specific anatomical contours of the CS of that hemisphere to discern appropriate landmarks for identifying the position of the MTA on anatomic images.

5. RESULTS

5.1. Anatomy

The courses and contours of the CS identified by use of the specimen hemispheres, the scanned photographs of those hemispheres, and the 3D surface reconstructions of those hemispheres agreed completely with each other. The contour of the CS displayed by all three methods showed complete overlap (Fig 1).

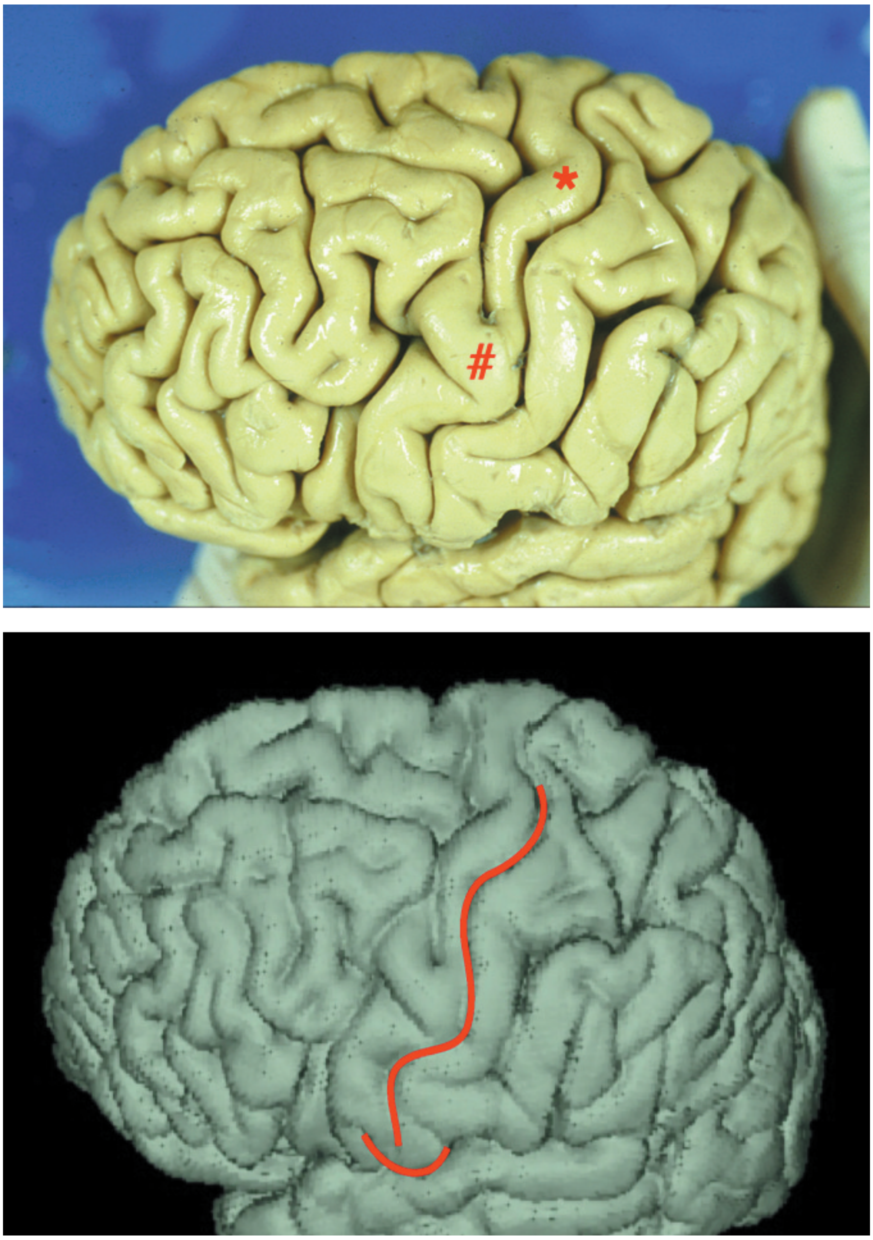

Figure 1

Shape of the central sulcus (CS):

Photograph of a specimen hemisphere (no. 10 left) and the MPRAGE 3D surface reconstruction of that specimen. Their close correspondence demonstrates that the 3D reconstructions can be used to describe the surface anatomy. The coronal red line delineates the central sulcus from the middle genu to the sylvian fissure (middle genu = motor hand knob, # junction between middle frontal gyrus and precentral gyrus). The "horizontal" red line indicates the position of the sylvian fissure inferior to the CS.*

The middle genu was present in all 67 hemispheres, and corresponded to the motor hand knob in each case (100%). The inferior genu was also present in all 67 hemispheres (100%). The contour of the CS inferolateral to the inferior genu was straight with no additional curves in 2 (3%) of hemispheres examined, exhibited 2 additional curves in 46 (69%), 3 curves in 6 (9%), and 4 curves in 13 (19% hemispheres). Because the literature provides names for only the 3 genua of the CS, with no curves defined inferior to the inferior genu (Yousry, 1998), we designated the additional curves encountered, in order from above downward, as the: superior concave, superior convex, inferior concave and inferior convex curves (Figs 2, 3).
The inferiormost end of the CS continued into the sylvian fissure in 20 hemispheres (n=20/67, 30%). In the majority of cases (n=47/67, 70%), the CS terminated short of the sylvian fissure, and ended with a "straight line" configuration (n=37/67, 55%) or with a "Y" configuration (n=10/67, 15%) (Fig 2; Tab 1).

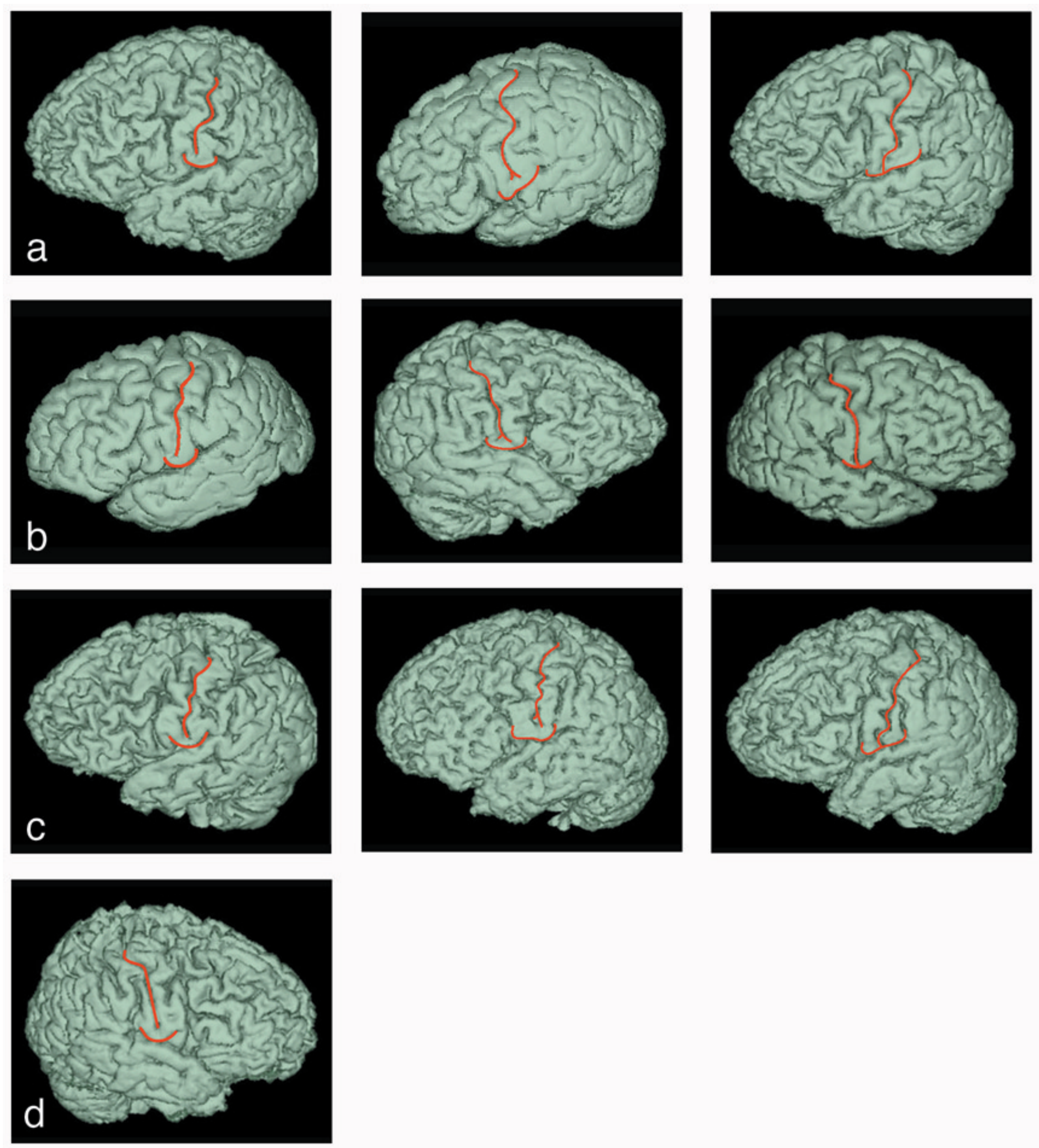

Figure 2

Rows a to d: Variations in the course of the central sulcus (CS): (Row a): The CS shows 2 additional curves below the inferior genu. From left to right, the inferior terminations of the CS are straight or Y-shaped without connection to the sylvian fissure, or connected to the sylvian fissure. (Row b): 3 additional curves below the inferior genu. (Row c): 4 additional curves below the inferior genu with similar relationships with the sylvian fissure as described for row a. (Row d): In 2 cases (one subject and one specimen hemisphere) no additional curve was found below the inferior genu.

Central sulcus	Local maxima n	(%)	Cella media n	(%)	Junction MFG-preCG n	(%)
Middle genu	4	(4,8)				
Inferior genu	5	(5,9)			12	(17,9)
Superior concave	24	(28,6)	3	(6,5)	47	(**70,1**)
Superior convex	43	(**51,2**)	32	(**69,6**)	6	(9,0)
Inferior concave	5	(5,9)	5	(10,9)	2	(3,0)
Inferior convex	3	(3,6)	6	(13,0)		

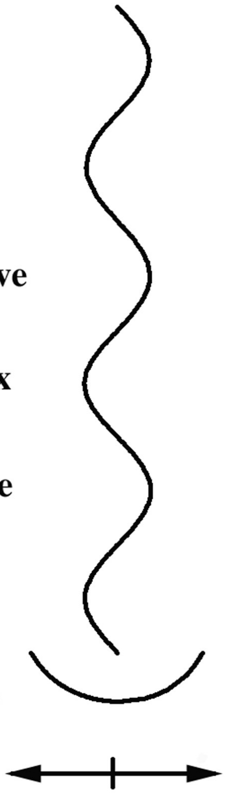

Figure 3

Nomenclature of the curves. Anatomic-functional relationships:

Schematic diagram of the central sulcus (CS) from the middle genu (= motor hand knob) to its inferolateral termination at or near to the sylvian fissure, oriented as in Fig. 1. The nomenclature proposed for the separate curves of the inferolateral segment are: superior concave, superior convex, inferior concave and inferior convex curvatures, in descending order.

Correlation of the curves of the inferolateral segment with the distribution of local maxima of activated areas in the central region (column 1, total 84 points in 22 subject hemispheres), the location of the cella media when projected to the convexity surface (column 2, total 46 hemispheres) and the location of the junction between the middle frontal gyrus (MFG) and the precentral gyrus (preCG) (column 3, total 67 hemispheres: 48 subject hemispheres and 19 specimen hemispheres).

Table 1

Courses of central sulcus found in hemispheres of volunteers and specimens (n=67)

Lower CS endings		CS with additional				Total
		2 curves	3 curves	4 curves	0 curves	
Without connection to the SF	straight	30	2	3	2	37
	"inverted Y"	6	3	1	0	10
With connection to the SF		10	1	9	0	20
Total		46	6	13	2	67

The junction of the posterior MFG with the anterior face of the preCG was identified in all specimen hemispheres and all volunteers (100%). From superior to inferior, this junction lay opposite the inferior genu in 12 hemispheres (18%), opposite the superior concave curve in 47 hemispheres (70%), opposite the superior convex curve in 6 hemispheres (9%), and opposite the inferior concave curve in 2 hemispheres (3%) (Figs 1, 3; Tab 2).

Table 2

Relation of the junction (middle frontal gyrus to precentral gyrus) with the various CS curves (n=67 hemispheres)

Central sulcus curves	Hemispheres left	right	all
Inferior genu	5	7	12
Superior concave	26	21	47
Superior convex	2	4	6
Inferior concave	1	1	2
Inferior convex	0	0	0

CS curve: curve at which the junction was found

A relationship was found between the topographic features of the CS and the axial plane of the cella media (central part of the lateral ventricle) in all 48 hemispheres of volunteers. We excluded the specimen hemispheres from this analysis, because of the deformation of their configuration due to the fixation process. In 29 of the 33 hemispheres with two additional curves inferior to the inferior genu, the plane of the cella media intersected the CS at the level of the lowest curve present, *(i. e.* the superior convex curve) (88%). In the 2 of the 3 hemispheres with 3 curves, the axial plane through the cella media still intersected the CS at the lowest curve present, (*i. e.* the inferior concave curve) (67%). In 6 of the 11 hemispheres with 4 curves, the cella media was also found at the lowest curve *(i. e.* the inferior convex curve) (55%). In one hemisphere the course of the CS inferior to the inferior genu ran straight with no additional curves. The axial plane through the cella media intersected the straight portion of the CS in that patient. In one of the 33 hemispheres with 2 curves, the CS terminated unusually far superiorly, so that the plane of the cella media intersected the subcentral gyrus inferior to the CS.

Over all of the cases, therefore, the plane of the cella media lay at or below the level of the lowest curve in 38 hemispheres (79%) and correlated with the two lowest curves in 45 hemispheres (94%) (Fig 3; Tab 3).

Table 3

Relation of the cella media with the central sulcus curves (n=47 hemispheres)

Central sulcus curve	Cella Media					
	central sulcus with additional			hemispheres		
	2 curves	3 curves	4 curves	left	right	total
Superior concave (n=47)	3	0	0	0	3	3
Superior convex (n=47)	29	1	2	18	14	32
Inferior concave (n=14)	0	2	3	3	2	5
Inferior convex (n=11)	0	0	6	3	3	6
Subcentral gyrus (n=48)	1	0	0	0	1	1
Total	33	3	11	24	23	47

n: number of hemispheres

5.2. fMRI

5.2.1. Group analysis

After correction for multiple comparisons, significant, paradigm-correlated activation was found in (i) the inferior precentral and postcentral gyri, (ii) the medial and posterior portions of the superior frontal gyrus bilaterally, most probably corresponding to the supplementary motor area (SMA), (iii) the cerebellum bilaterally, and (iv) the brainstem (Fig 4; Tab 4).

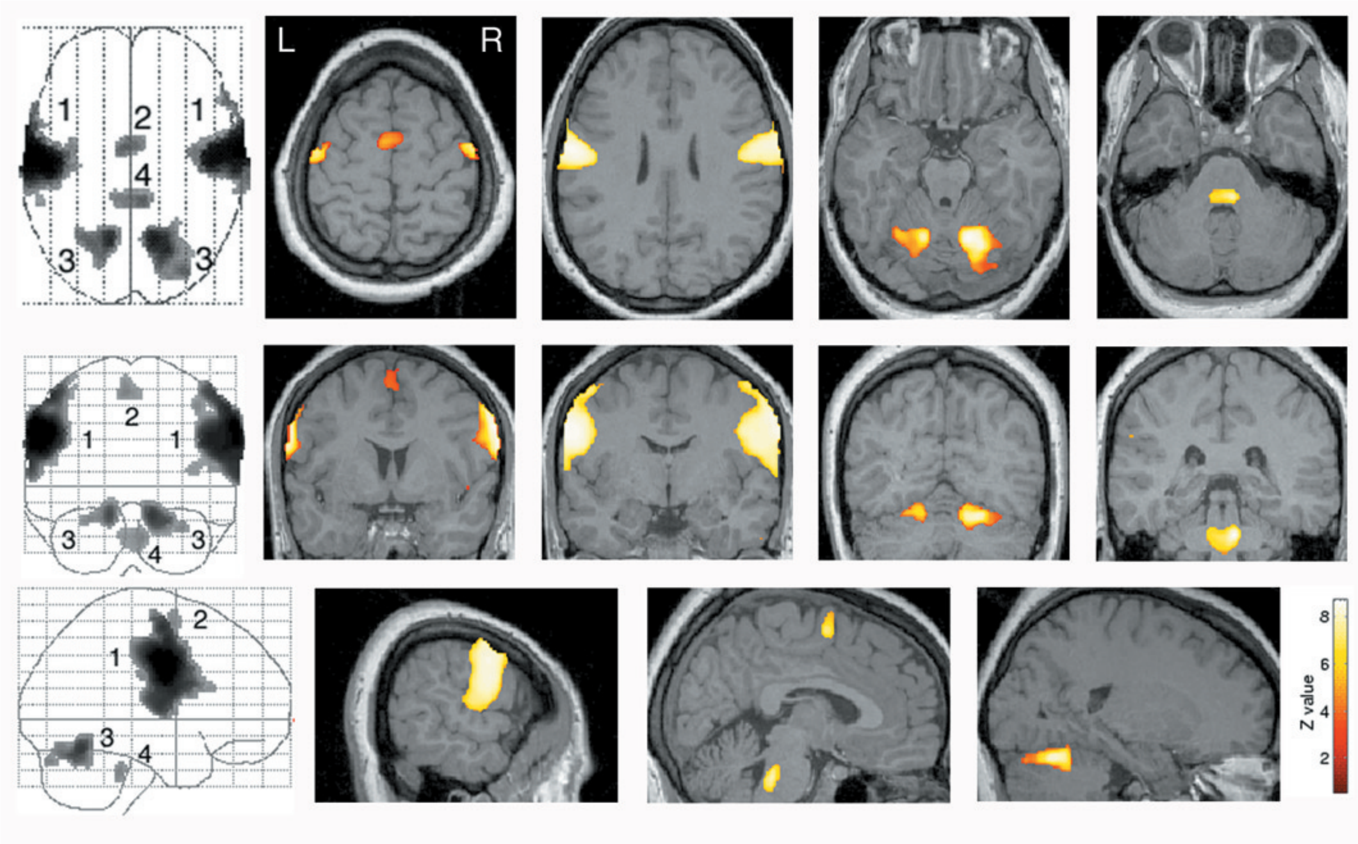

Figure 4

fMRI group analysis:

Group results derived from 11 subjects performing a horizontal tongue movement. Activated regions are displayed in the glass brain view and overlaid on normalized axial, coronal and sagittal T1 weighted anatomical scans. Significant activation is seen in the inferior pre- and postcentral gyri bilaterally (1), in the SMA (2), in the cerebellum bilaterally (3) and in the posterior aspect of the brainstem (4).

Table 4

Results of the group analysis

Area	Anatomical region	Left				Right			
		x	y	z	Z-score	x	y	z	Z-score
1	Primary sensory-motor cortex	-62	-6	34	8.71	66	-6	30	8.58
2	Supplementary motor area	-4	-2	60	5.42	6	2	70	4.80
3	Cerebellum	-14	-60	-18	7.24	14	-60	-18	7.72
4	Medulla	-8	-32	-32	4.91	8	-36	-32	5.46

Area: area in Fig 1; x, y, z: SPM coordinates

5.2.2. Single subject analysis

In every hemisphere significant activated clusters were found. Thereof 89 points maximally activated by the tongue-movement paradigm were assessed and their exact anatomical locations were described. From these 89 local maxima, 84 (94%) lay along the precentral and postcentral gyri, (59 of 89 (66%) at the precentral gyri; 25 of 89 (28%) at the postcentral gyri) (Fig 5). The other 5 of the 89 activation points lay in the adjacent supramarginal gyrus (2 points), in the inferior frontal gyrus (2 points) and in the middle frontal gyrus (1 point). The precentral and postcentral gyri were activated approximately symmetrically (precentral gyrus: right 27, left 32; postcentral gyrus: right 13, left 12). Sixty-two of the 84 precentral and postcentral activation points (74%) lay along the anterior bank (46/62) and posterior bank (16/62) of the CS. Twenty-two of the 46 activation points on the anterior bank lay in the middle and deep part of the CS (Fig 5; Tab 5). Two hemispheres revealed no activation in the anterior bank of the CS.

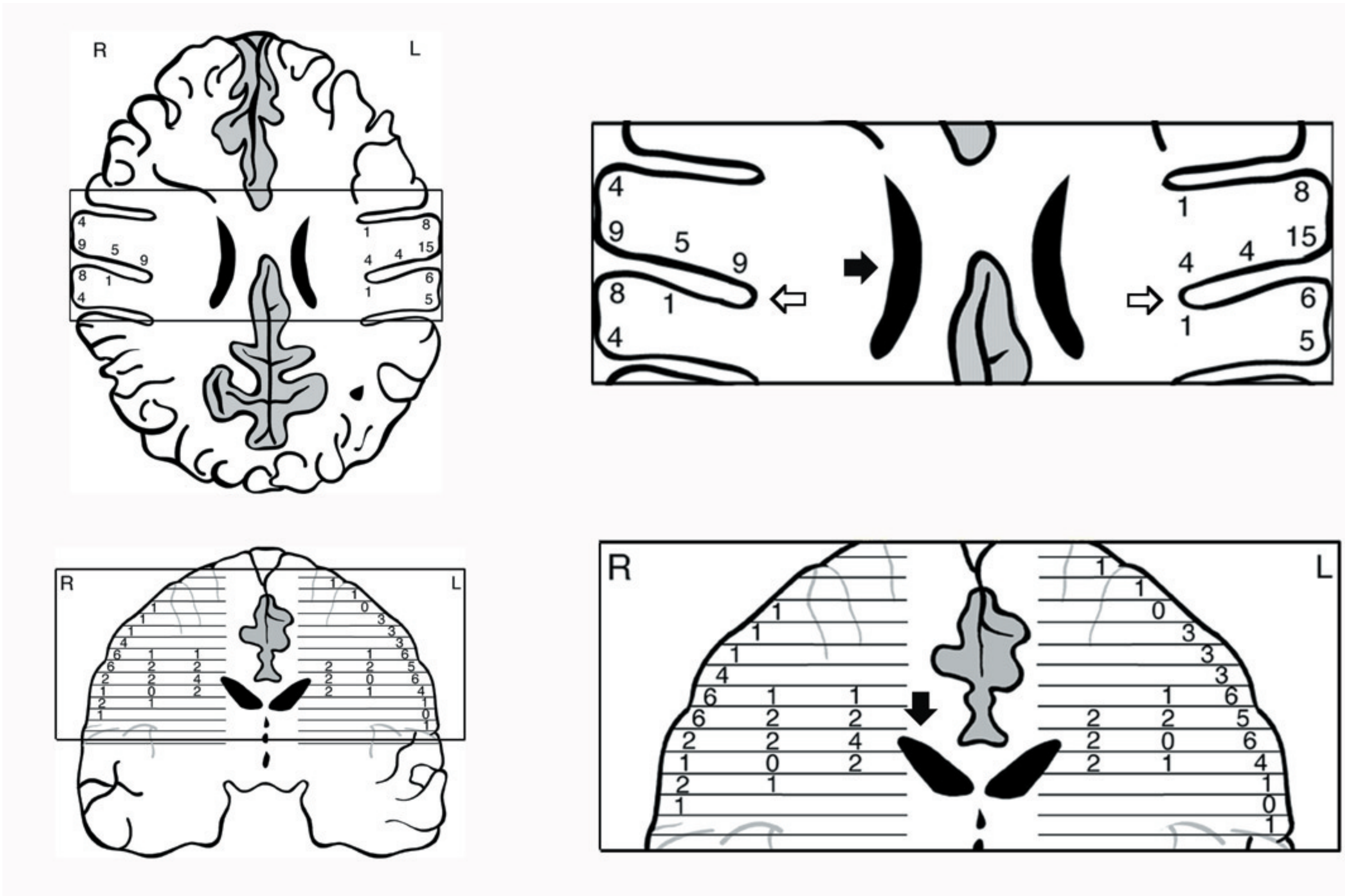

Figure 5

Relationship between the cella media and the location of the local maxima of motor tongue activation:

The local maxima of all volunteers occurring in the central region (n=84) are summarized in a schematic diagram in the axial and coronal plane (open white arrow: central sulcus, solid black arrow: cella media of the ventricular system). A clear concentration of local maxima is visible in the anterior bank of the central sulcus bilaterally. The middle and deep local maxima are less widespread and centered around the level of the cella media.

Table 5

Distribution of the pre- and postcentral local maxima (n=84)

Anatomical region	local maxima					
	Left		Right		Total	
	n	(h)	n	(h)	n	(h)
Precentral gyrus	32	(10)	27	(10)	59	(20)
Postcentral gyrus	12	(8)	13	(8)	25	(16)
Central sulcus anterior bank	23	(10)	23	(10)	46	(20)
Central sulcus posterior bank	7	(6)	9	(7)	16	(13)
Central sulcus middle/deep anterior bank	8	(6)	14	(9)	22	(15)
Central sulcus middle/deep posterior bank	1	(1)	1	(1)	2	(2)
Total	44	(11)	40	(11)	84	(22)

n: number of local maxima; h: number of hemispheres

The highest numbers of MTA activation points were observed on the axial slices through the cella media of the lateral ventricles. We therefore defined this slice as the “0” slice, the slice above as +1, and the slice below as -1. Nineteen of the 22 (86%) middle and deep activations observed on the *anterior* bank of the CS were encompassed within the three slices centered on the 0 slice (0 +/-1 slice). All 22 middle and deep activations observed along the *anterior* bank of the CS were encompassed within the 5 contiguous slices centered on the cella media (0 +/- 2 slices). Further, the 2 middle and deep activation points observed along the *posterior* bank of the CS, and 64 of all 84 activation points located in the pre and postcentral gyri (76%) fell within these five contiguous slices. (Figs 5, 6; Tab 6)

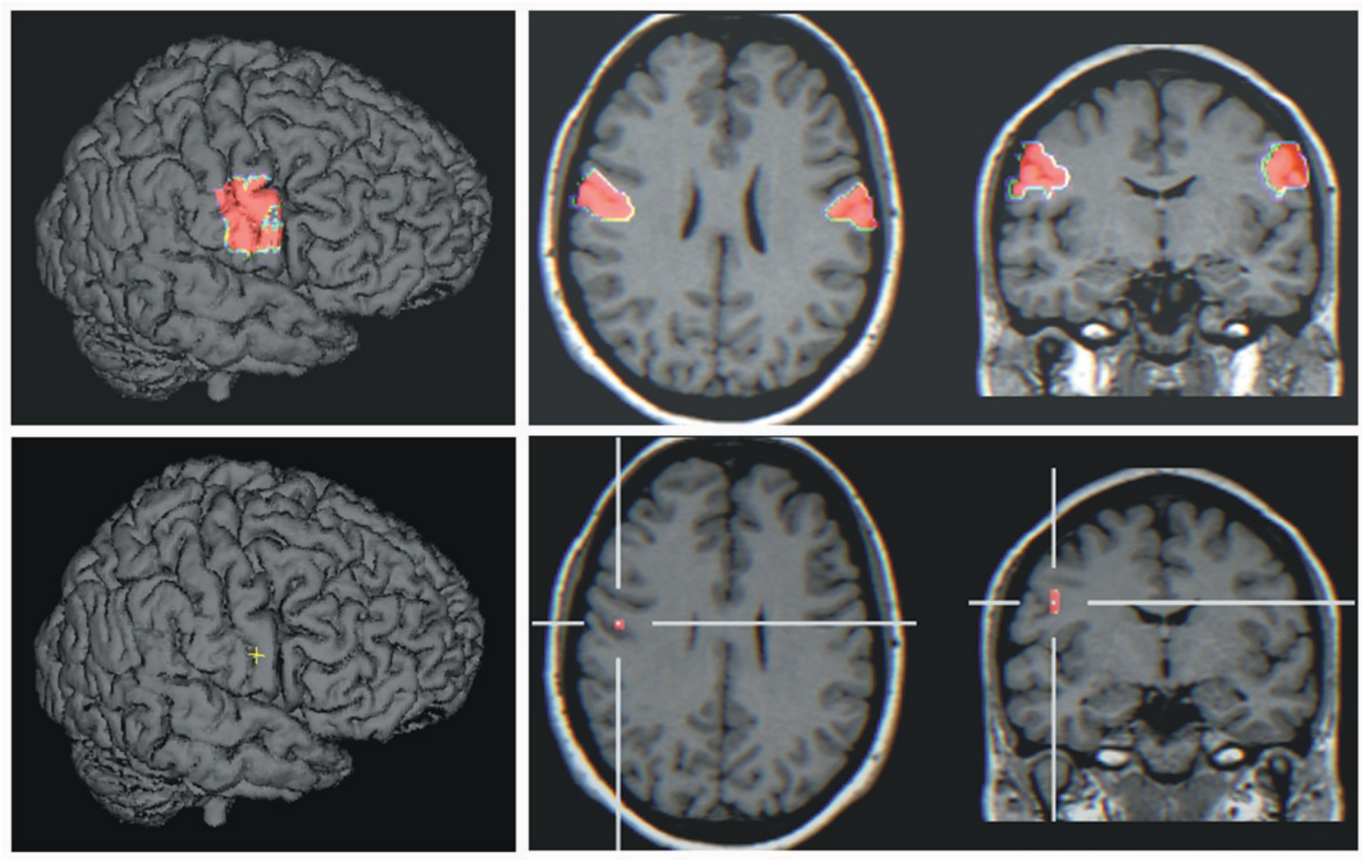

Figure 6

Motor tongue activation:

Single subject analysis (Subject no. 5) displayed on that individual's 3D MPRAGE surface reconstruction and on axial and coronal sections:

Upper row: the primary motor tongue area is shown as a cluster covering a large part of the lower central area on the brain surface. On the axial and coronal MR section the activated area is located at the level of the cella media of the ventricular system.

Lower row: The local maximum is situated deep in the anterior bank of the central sulcus.

Table 6

Relation of middle and deep local maxima with cella media (in 22 hemispheres)

Slice level (0 = cella media)	local maxima: anterior bank of the CS (n=22)		local maxima: pre- and postcentral (n=25)	
0	7	32%	8	32%
0 +/-1	19	86%	21	84%
0 +/-2	22	100%	25	100%

n= number of middle and deep local maxima; slice thickness: 5 mm

5.3. Comparison of fMRI and anatomical data

5.3.1. Relationship of activation points with CS curves

In the 22 hemispheres evaluated by fMRI, 67 (80%) of the 84 activation points found in the precentral and postcentral gyri were concentrated at the lateral superior concave and the lateral superior convex curves. Viewed differently, the motor tongue activations were found in the lowest curve of the inferolateral segment in 43% (36 of 84 activation points) or in the lowest two curves of the inferolateral segment of the CS in 80% (67 of 84 activation points). Specifically, in the 16 hemispheres with just two additional curves, 21 of the 59 activation points were located in the lateral superior concave and 32 were located in the lateral superior convex curve (53 of 59 = 90% of activation points in the individuals with this anatomy). In the 2 hemispheres with three additional curves, one of the 10 activation points was located in the lateral superior concave and 6 were located in the lateral superior convex curve (7 of 10 = 70% of activation points in the individuals with this anatomy). In the 4 hemispheres with four additional curves, 2 of the 15 activation points were located in the lateral superior concave and 5 of the 15 activation points were located in the lateral superior convex curve (7 of 15 = 47% of activation points in those individuals with this anatomy) (Fig 3; Tab 7).

Table 7

Relation of the anatomic location of the activation points to the CS curves (n = 22 hemispheres)

central sulcus curve	Activation points			
	Hemispheres with			
	2 curves (n=16)	3 curves (n=2)	4 curves (n=4)	Total
Middle genu (n=22)	3	0	1	4
Inferior genu (n=22)	3	2	0	5
Superior concave (n=22)	21	1	2	24
Superior convex (n=22)	32	6	5	43
Inferior concave (n=6)	0	1	4	5
Inferior convex (n=4)	0	0	3	3
Total (n=22)	59	10	15	84

n: number of hemispheres

5.3.2. Relationship of activation points to the junction of the MFG with the anterior face of the preCG

Seventy-three of the 84 activation points in the pre- and postcentral gyri (87%) were located inferior to the junction of the MFG with the preCG, while 11 were located superior to the junction (Fig 7; Tab 8).

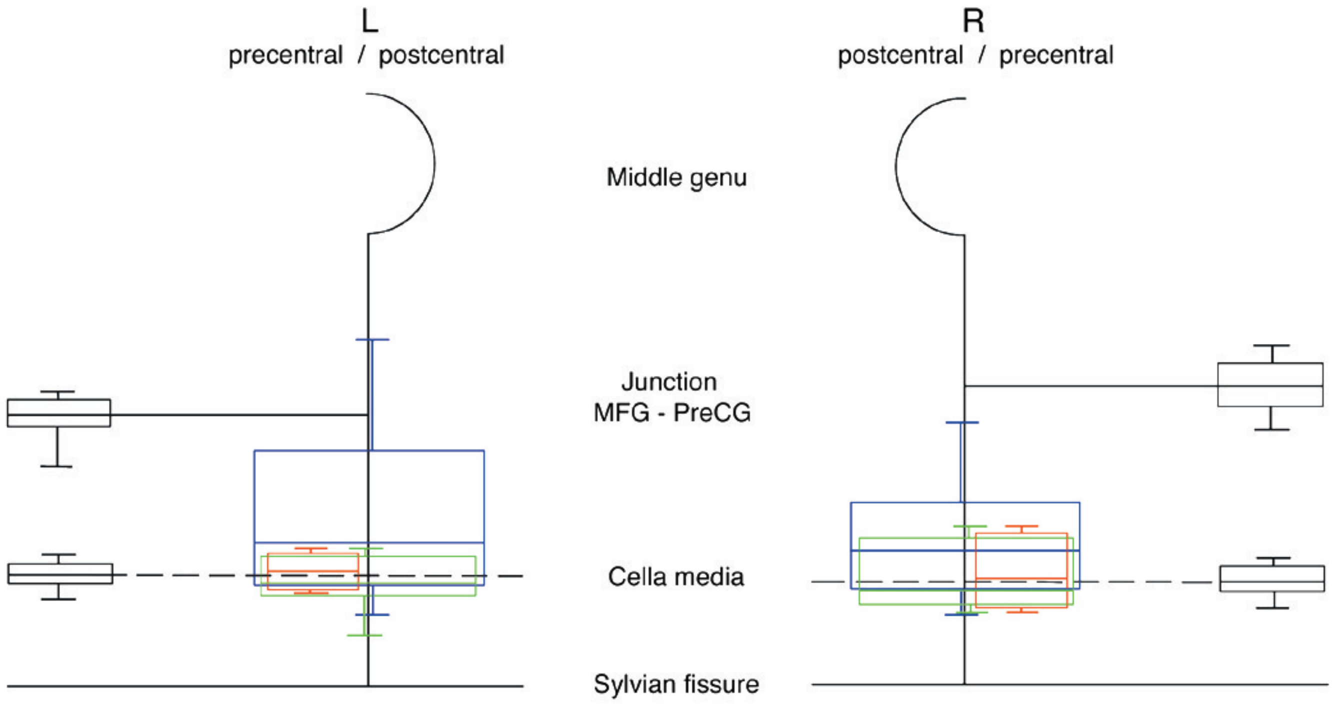

Figure 7

Diagrammatic representation of the position of the MTA with respect to the CS and the cellae mediae:

Schematic central sulcus (left and right) drawn from the middle genu to the sylvian fissure. For simplification the lower central sulcus is displayed as a straight line. Starting from the middle of the motor hand knob (middle genu) we measured the distances to the sylvian fissure in every hemisphere (n=22). Then we measured the distances form the middle of the motor hand knob to the junction between the precentral and middle frontal gyrus, to the surface projection of cella media, and to the surface projection of every local maximum. The variance of these distances are reported relative to the distance from the motor hand area to the sylvian fissure as boxplots discriminating between all local maxima (blue) the middle and deep local maxima (green), and the middle and deep precentral local maxima (red). The results demonstrate, that the middle and deep local maxima as well as the middle and deep precentral local maxima are located around the cella media, and that most of the local maxima are located inferior to the junction between the precentral and the middle frontal gyrus.

Table 8

Variance of distances relative to the distance between motor hand knob and sylvian fissure

	knob - junction mfg / precg		knob - cella media		middle and deep precentral maxima		middle and deep maxima		all maxima	
Percentiles	left	right	left	right	left	right	left	right	left	right
0.1	42.6	34	74.2	75.6	72.3	68.6	72.5	69	32.3	50
0.25	44.25	37.75	76.25	77.25	74	70	75	71.25	54	65.5
0.5	47	42	78	80	77	79.5	79.5	81	71.5	74
0.75	49	46	79.75	82	81	84	82	84	80.5	81
0.9	56.8	50.8	82.8	85.4	81.7	85.2	90.5	86	86.2	86.5

6. DISCUSSION

6.1. Anatomy

Classically, the CS is divided into three curves or genua (Broca, 1878, Cunningham, 1892, Déjérine, 1895, Sastre Janer *et al.*, 1998, Testut, 1911, Yousry, 1998, Yousry *et al.*, 1997). Of these, the middle (posterior convex), and the inferior (anterior convex) genua are constant (Cunningham, 1892, Eberstaller, 1890, Horsley, 1887, Yousry, 1998). The superior (anterior convex) genu (Yousry, 1998) is less constant, probably accounting for those studies that report the existence of only the lower two curves (Cunningham, 1892). Classically, the segment of the CS inferolateral to the inferior genu has been described as a linear structure. In this study, however, only 3% of hemispheres exhibited the "classic" straight course of the CS, with no additional curves inferolateral to the inferior genu (Rademacher *et al.*, 2001, Sastre Janer *et al.*, 1998). Instead, the great majority (97%) of the CS in this study manifested from 2-4 additional curves, most commonly two additional curves (69%). The variability of these curves probably accounts for the fact that they have not been reported previously. The middle and inferior genu and the additional curves described in this study are easily identifiable on the brain surface and on surface reformations (Yousry *et al.*, 1997). However, only the middle genu is also easily seen on axial images and thus far only the middle genu has proven to be a reliable landmark in axial imaging studies (Cunningham, 1892, Naidich and Brightbill, 1996, Yousry *et al.*, 1997).

6.2. Tongue sensory area

Boling et al. (Boling *et al.*, 2002) have recently demonstrated that the tongue sensory area falls within a triangular tongue region situated at the base of the postcentral gyrus, just superior to the sylvian fissure. This region lies immediately posterior to the tongue motor area defined in the present study.

6.3. Tongue motor area

Prior work using cortical mapping localized the MTA (Penfield and Rasmussen, 1950, Woolsey *et al.*, 1979) to a zone 1 cm anterior to the CS with little spread further anterior and posterior to the CS (Foerster, 1936, Foerster, 1936, Libet, 1973, Libet *et al.*, 1964, Penfield and Boldrey, 1937, Penfield and Rasmussen, 1950, Uematsu *et al.*, 1992). Using subdural electrodes, Urasaki et al. documented a "wide" distribution of tongue motor responses on the lateral surface of the brain. In patients with no known organic lesions, the motor tongue responses ranged from the sylvian fissure up to 4 cm superior to the sylvian fissure (5 cm in patients with organic lesions), and from 4.5 cm anterior to 3 cm posterior to the CS. The highest rate of motor responses (41%) was found in an area up to 1.5 cm anterior to the CS and 1-2 cm superior to the sylvian fissure, followed by an area immediately superior to that area (33%), and a third area immediately inferior to that area (27%). The mean location was 0.77 cm ($\pm$ 0.93 cm) anterior to the CS and 1.6 cm ($\pm$ 0.85 cm) superior to the sylvian fissure. Among the motor responses, 81% were located anterior and 19% posterior to the CS (Urasaki *et al.*, 1994). PET studies localized the motor tongue area to a site 2.1 cm ($\pm$ 0.4 cm) superior to the sylvian fissure (Grafton *et al.*, 1991). Using fMRI, the MTA was identified and localized to the inferior primary sensorimotor cortex (Corfield *et al.*, 1999, Lotze *et al.*, 2000, Riecker *et al.*, 2000, Wildgruber *et al.*, 1996). These findings are in good agreement with our findings.

6.4. Anatomic-functional correlation

With the paradigm and the pulse sequences employed in this study, fMRI depicted the cortical representation of the motor tongue area (MTA) in each patient studied. The sites activated extended over a wide area of the inferior central region bilaterally. The activation points in the single subject analysis revealed a distribution that is similar to the results of mapping with the subdural electrodes.

Most of the motor tongue activation points lay inferolateral to the inferior genu. Eighty percent lay at the lateral superior concave or the lateral superior convex curves. However, the variability of the inferolateral segment of the CS precluded assigning the MTA to a specific section of the CS. The inability to identify these curves on axial images precluded their use in standard axial imaging. An anatomical-functional landmark could not be defined along the CS.

A more nearly consistent relationship was found between the MTA activations and the axial sections obtained parallel to the bicommissural line and centered at the level of the cella media. The primary motor tongue area is believed to lie within the cytoarchitectonic area BA4. The anterior border of BA4 shows considerable variation (Amunts and Zilles, 2001). However, BA4 is known to cover the posterior surface of the precentral gyrus medially and exhibit a decreasing gradient from medial to lateral (Rademacher *et al*., 2001). Therefore, a conservative approach would be to restrict the functional localization of the primary MTA to those activation points detected along the anterior bank of the central sulcus, especially those located in the depth of the central sulcus. These activation points are clustered. In this study, 86% of the middle and deep MTA activations found along the anterior bank of the CS lay at the level of the cella media +/- one contiguous slice. Therefore, in axial images obtained parallel to the bicommissural plane, the three axial images centered at the cella media intersect the CS at a level that most frequently marks the site of the MTA. To our knowledge these findings have not been reported before. Until imaging is able to display the cytoarchitecture of the primary motor cortex (BA4) at the depth of the CS, the axial plane through the cella media may serve as an approximation to the MTA and as a surrogate landmark for the MTA. In practical terms, therefore, this study provides a method to identify the primary MTA on axial slices, a finding that can be of use in routine MRI analysis.

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