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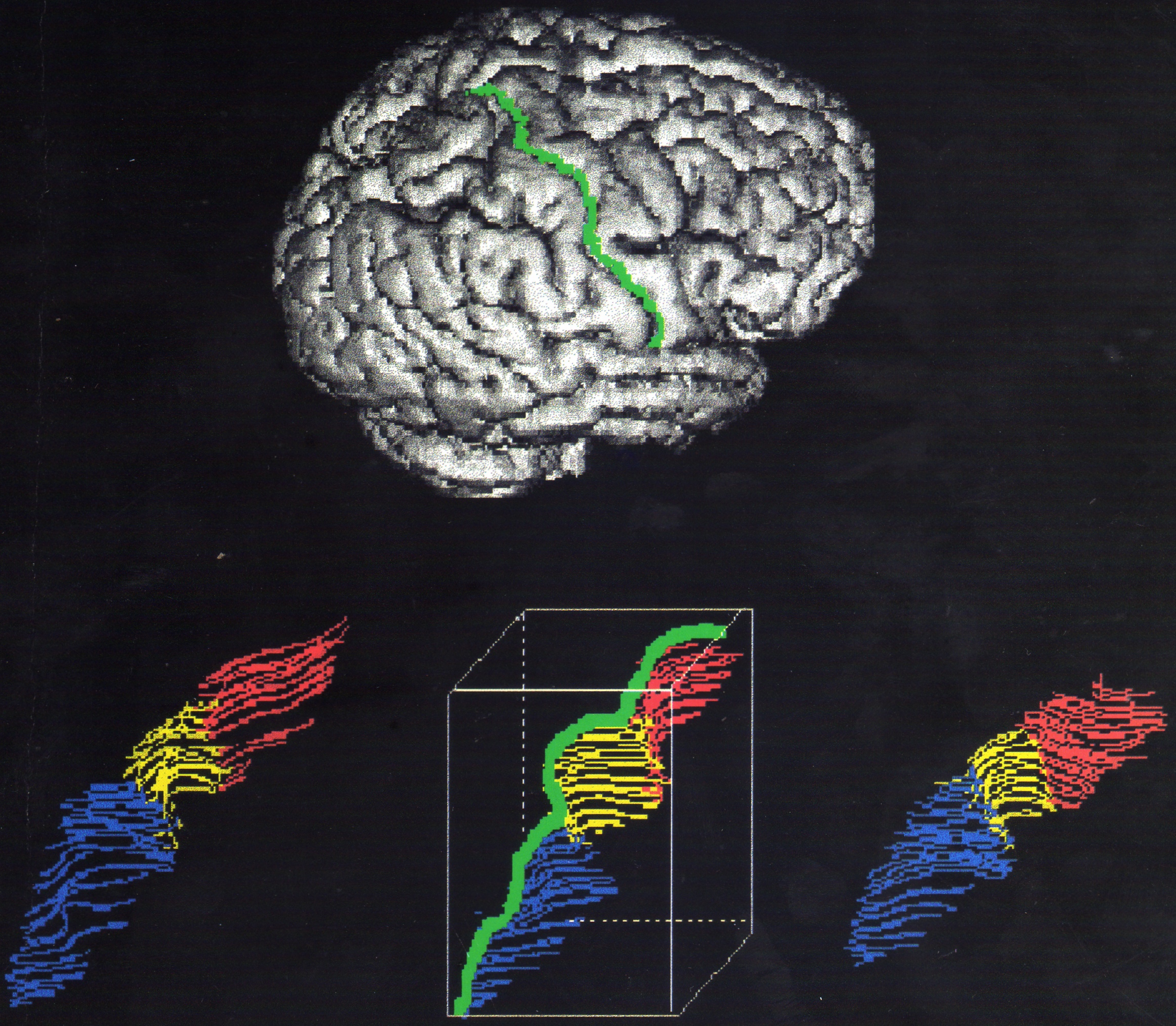

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Cover Picture: The human central sulcus. The classical view of the central sulcus at the surface of the brain is shown in green, in a right lateral view, on the top of the image. The three-dimensional structure of the right central sulcus, isolated from the rest of the brain, in an oblique-anterior view is on the bottom. The three-dimensional morphology of the central sulcus shows three different regions: the upper region is in red, the middle region is in yellow and the lower region is in blue. The middle region corresponds to the hand area, proved by superimposing positon emission tomographic (PET) scans during somatosensory activation studies. See Sastre-Janer *et al.*, pp. 641–647.

Instructions for Authors appear at the end of each issue. Submissions (original manuscript plus three copies) should be sent to P.S. Goldman-Rakic or P. Rakic, Co-Editors, *Cerebral Cortex,* Section of Neurobiology, Yale University School of Medicine, P.O. Box 208001, New Haven, CT 06520-8001.

Three-Dimensional Reconstruction of the Human Central Sulcus Reveals a Morphological Correlate of the Hand Area

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One way to improve our understanding of cortical anatomy is to visualize the three-dimensional (3D) shape of the cerebral sulci which is normally hidden. Here, we reconstructed the 3D morphology of the central sulcus (CS) in 17 normal subjects, using conventional magnetic resonance images and dedicated software. We found that the 3D morphology was remarkably consistent in all central sulci. Our analyses revealed three different regions (upper, middle and lower), which were easily identifiable by morphological criteria and sharply interconnected in the reconstructed CS. These morphological regions appear to have a strong functional significance, since the middle region corresponded precisely to the 'hand area', as verified by hand vibration positron emission tomography activation studies in eight cases. These data suggest that the 3D anatomy of the cerebral cortex may facilitate sulcal recognition, and sulcal subdivision into smaller morphological elements, bearing remarkable relationships with functional cortical maps.

Introduction

The human cerebral cortex has an extraordinarily complex shape (Dejerine, 1895; Ono *et al.*, 1990), and this complexity poses a considerable challenge for the study of precise structure–function relationships with modern human brain mapping techniques. One indirect solution is the use of stereotactic atlases, which describe any cortical region by a set of geometrical coordinates (Talairach and Tournoux, 1988). Despite widespread use, this method does not take into account individual anatomical variability. This variability is demonstrated by cortical surface rendering of the brain which can be obtained from standard magnetic resonance (MR) images, but this is limited by the fact that two-thirds of the cortex is buried within the sulci (Carpenter and Sutin, 1983). Cortical maps of the unfolded cerebral cortex are currently being used in functional studies of cortical anatomy (Carman *et al.*, 1995); however, the shape of the sulci is lost during the unfolding.

We reasoned that three dimensional (3D) sulcal anatomy may reveal characteristic morphological features which might be important for matching anatomy and function in the human brain (Regis, 1994; Regis *et al.*, 1995; Sastre-Janer *et al.*, 1995, 1996). To test this, we focused on the 3D anatomy of the central sulcus (CS) which contains motor and somatosensory maps, somatotopically organized according to the classical 'homunculi' maps of Penfield (Penfield and Boldrey, 1937; Penfield and Rasmussen, 1950). It is interesting to note that Penfield's maps are drawn over the *surface* of the brain, but little is known about their localization *within* the sulcus, although it has been recently suggested that the hand region of the CS may have a specific and easy recognizable shape on conventional two-dimensional (2D) MR images (Rumeau *et al.*, 1994; Yousry *et al.*, 1997).

We studied the 3D shape of the central sulcus reconstructed in 17 normal subjects, using interactive software which isolates the CS from the rest of the brain and reveals its shape. As predicted, we found that CS 3D anatomy had consistent morphological features, and we tested their functional significance in the hand region by superimposing positron emission tomographic (PET) scans during somatosensory activation studies.

Materials and Methods

MR Images

MR images from 17 healthy adult subjects (mean age 29 ± 8 years, range 21–55, 11 men, 6 women) were used in the present study. These images were obtained during the course of functional brain imaging studies in our institution. All subjects had normal general and neurological examinations and a normal MR imaging (MRI) scan.

Horizontal T_1-weighted MR sections parallel to the bicommissural plane (AC–PC), which is tangent to the upper margin of the anterior commissure (AC) and to the lower margin to the posterior commissure (PC) (Talairach and Tournoux, 1988), were obtained using a 0.5 T MR imager (MRMAX, General Electric, Milwaukee, WI) ($n = 9$) or a 1.5 T unit (Signa, General Electric, Milwaukee, WI) ($n = 8$). For the subjects studied on the 1.5 T unit, the MR images were obtained using a classical 3D spoiled gradient acquisition at steady state (SPGR). The imaging parameters used were as follows: repetition time (T_R) = 25 ms, echo time (T_E) = 5 ms, flip angle (FA) = 25°, number of excitations (N_{EX}) = 1, slice thickness = 1.5 mm, field of view (FOV) = 25 cm and matrix size = 256 × 192. The images were reorientated parallel to AC–PC when necessary. The subjects studied on the 0.5 T unit were positioned in the AC–PC plane (Talairach and Tournoux, 1988), and this was verified on a midsagittal image. Contiguous horizontal T_1-weighted 2 mm thick gradient-echo T_1-weighted sections were obtained at T_R = 540 ms, T_E = 14 ms, FA = 90°, N_{EX} = 2, FOV = 25 cm and matrix size = 256 × 256.

3D Extraction of the Central Sulcus

All MR images were transferred to a Sun SPARCstation-II and treated with interactive Volumetric Image Display and Analysis software (VIDA, University of Pensylvania, USA 1991; SHFJ-CEA, Orsay, France, 1993). First, we identified both CS (left and right) on each section, with the help of detailed neuroanatomical atlases (Dejerine, 1895; Duvernoy, 1992) and if necessary with brain surface rendering software (Voxtool, General Electric, Buc, France). We drew the sulcus boundaries on each section, as a line starting at the surface of the brain, on the precentral gyrus, outlining the anterior wall of the CS, its fundus and its posterior wall up to the surface of the brain, on the postcentral gyrus. For each of these drawings, the level of the corresponding horizontal section was recorded and normalized along the vertical z axis of the Talairach's space, for further analysis.

As shown in Figure 1, the structure of the CS (central sulcus wire-frames) was extracted from the rest of the brain and visualized in three dimensions using dedicated software. The 'extracted' CS could then be rotated on the computer screen in order to detect common features of CS shape in the different subjects.

MRI–PET Correlation

In eight of the subjects, the morphological results were compared with $H_2{}^{15}O$ regional cerebral blood flow (rCBF) activation PET studies. The activation was unilateral vibration of the right hand in four subjects and

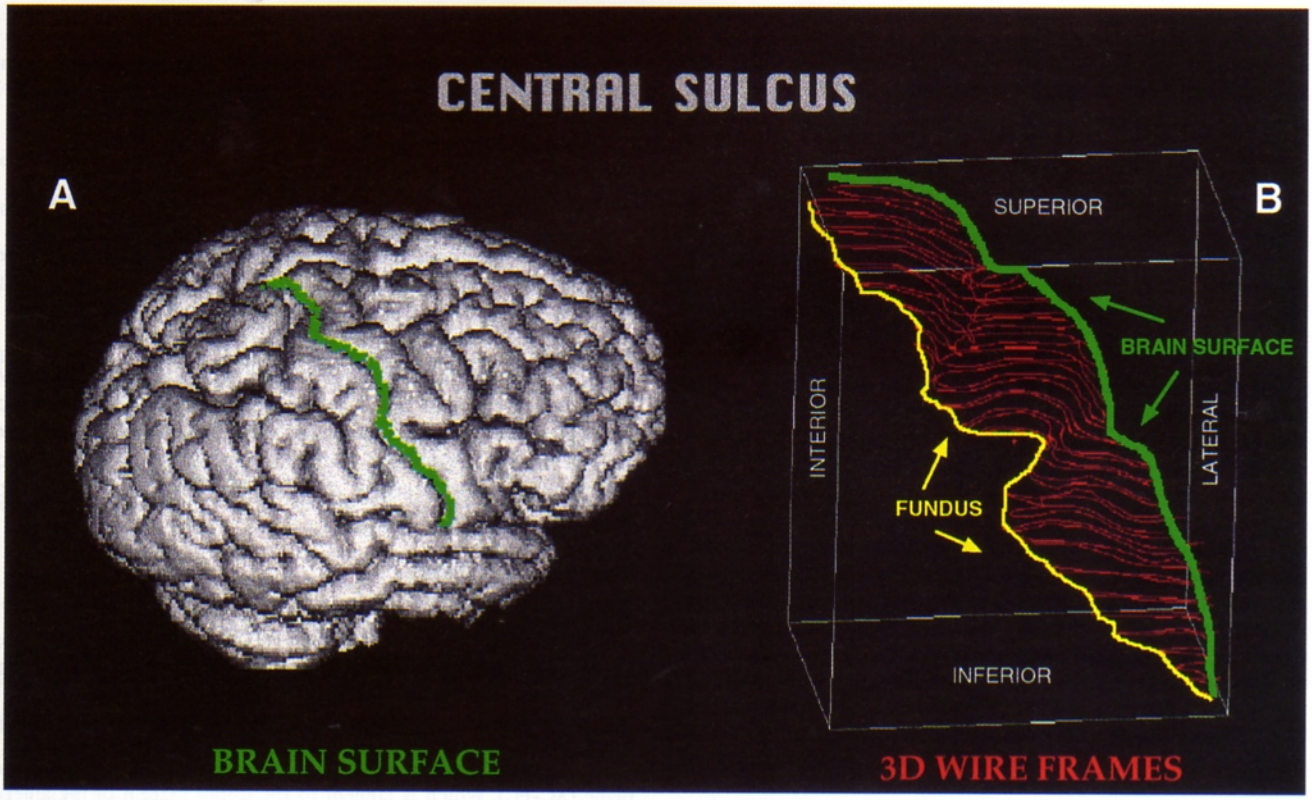


Figure 1. The central sulcus. (*A*) The classical view of the central sulcus at the surface of the brain is shown in green. (*B*) The 3D morphology of the central sulcus isolated from the rest of the brain. The green line represents the surface of the brain, and the yellow line the fundus of the sulcus. The red lines are the drawings of the central sulcus on the horizontal MRI images. Note the marked reduction in the depth of the central sulcus at its mid-level.

Figure 2. The 3D morphology of the central sulcus in three different subjects. Both oblique (*A*) and inferior (*B*) views of the right central sulci show a very similar morphology in the three subjects, with three different regions shown in different colours. The upper region is in red, the middle region in yellow and the lower region in blue.

Figure 3. The three regions of the central sulcus on horizontal MR images. The four images are obtained 35, 43, 46 and 55 mm above the AC–PC plane. These images demonstrate the horizontal overlap of the three regions of the CS, which are shown in red (upper region), yellow (middle region) and blue (lower region), as in Figure 2. The τ point shows the characteristic junction of the lower and middle regions of the CS, which is always easy to identify on horizontal MR images. The υ point shows the junction of the middle and the upper regions, which may be more difficult to identify without 3D reconstruction.

of the left hand in four subjects. The stimulus was delivered with a vibrator that produces 2 mm amplitude movements at a frequency of 130 Hz (Daito, Higashi, Osaka, Japan) (Fox *et al.*, 1987). The PET camera was an ECAT 953/31B (Siemens/CTI, Knoxville, TN) and rCBF measurements were performed as described in detail elsewhere (Fox *et al.*, 1984; Remy *et al.*, 1994). Measurements were obtained at rest, and during vibration, in order to generate pixel-by-pixel subtraction images. The focus of activation was always visible in the primary sensory-motor hand area on the subtraction images, and its boundaries were automatically determined with a 3D hysteresis thresholding method. The PET scans and MR images were superimposed using a 3D automatic registration procedure described elsewhere (Mangin *et al.*, 1994). Thus, the focus of activation could be superimposed onto the horizontal MR slices, or onto the 3D wire-frame reconstruction of the CS.

Results

3D Structure of the CS

Figure 1 shows an example of the CS at the surface of the brain, and the extracted 3D structure of a CS. At the surface of the brain the CS has the typical genu shape described by Broca. Note that the CS reaches the Sylvian fissure in this subject, a variation found only in 28% of the cases by Damasio (1995). In three dimensions, the CS appears as a large and coherent structure that was always immediately recognizable and could always be unambiguously differentiated from the adjacent sulci. The CS consistently presented an abrupt decrease of its depth localized in Talairach space at $z = +40 \pm 2.4$ mm on the left side and $z = +41 \pm 4$ mm on the right side.

The rotation of the CS 3D shape in different orientations revealed a complex structure, with three distinct regions (Fig. 2). The lower region (Figs 2 and 3; blue) had a nearly planar form, almost orthogonal to the surface of the brain. This region extended vertically in the Talairach space from $z = +17.7 \pm 5$ mm to $z = +49 \pm 3.5$ mm.

The middle region (Figs 2 and 3; yellow) had the shape of a half-cylinder with a posterior convexity. At this level the 2D horizontal sections revealed the 'omega' shape of the 'hand area', recently described on 2D MR images by Yousry *et al.* (1997), and the aspect previously described by Rumau *et al.* (1994) as the 'somatosensory hand area'. This shape was found in 15 of 17 subjects. In the remaining subjects the middle region of the CS had a different shape, which corresponded to the 'epsilon' type of knob described by Yousry *et al.* (1997), with two juxtaposed half-cylinders on 3D reconstruction. In the

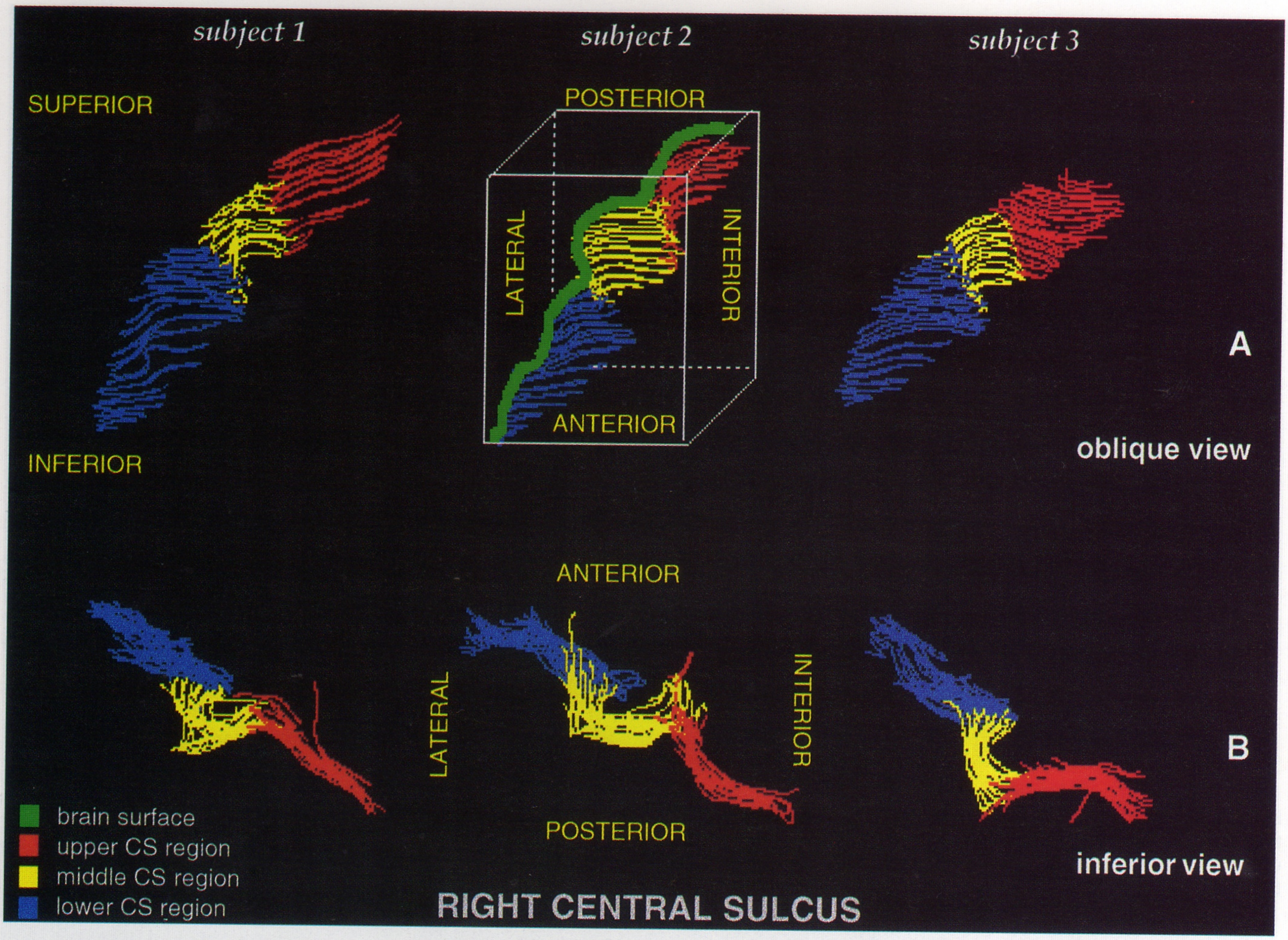


Figure 2

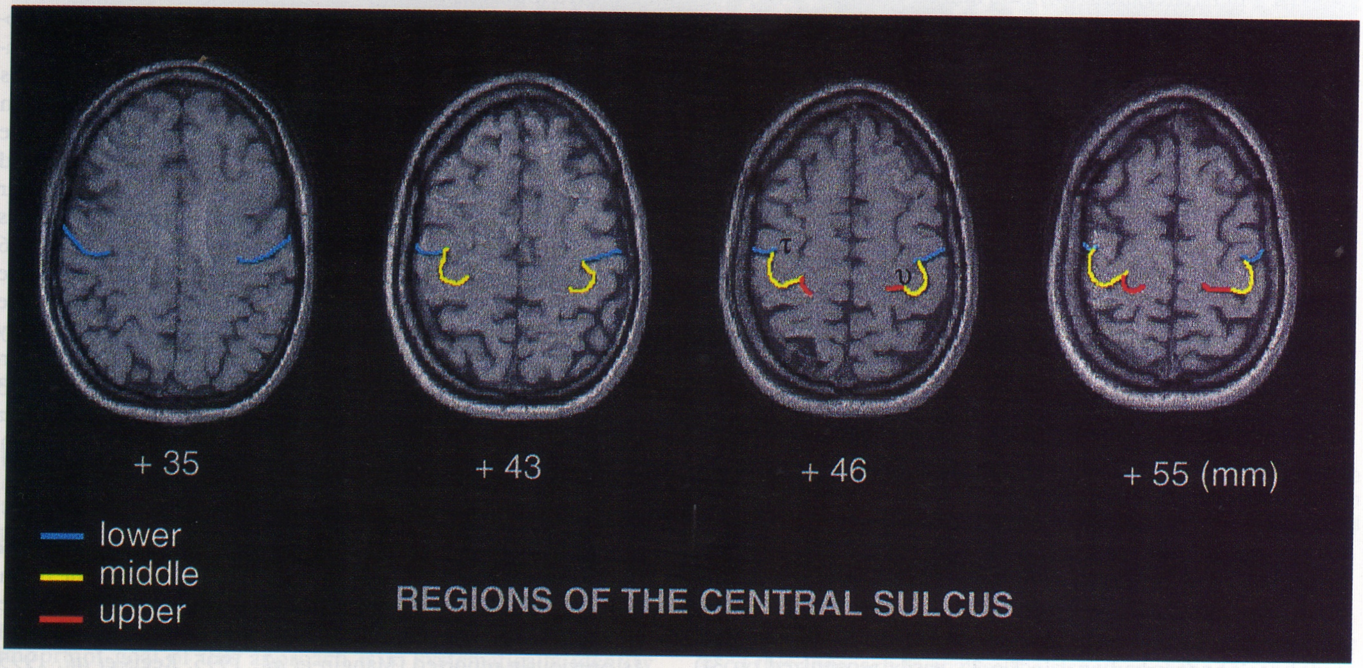


Figure 3

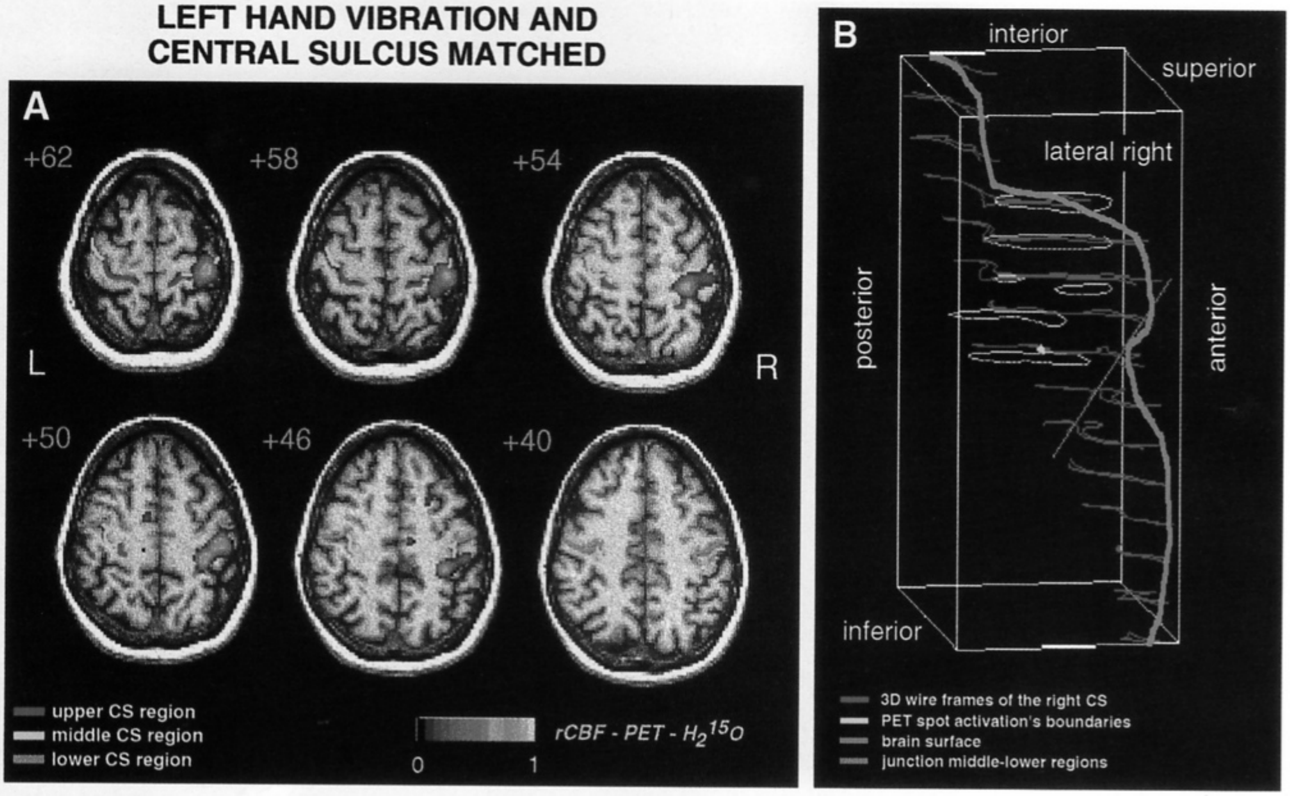


Figure 4. Vibration-induced PET activation of the left hand, and the right central sulcus in the same subject. Following automatic registration of PET and MR data (Mangin *et al.*, 1994), the focus of PET activation is directly superimposed on horizontal MR images (*A*, green-yellow spots) and on the extracted central sulcus (*B*, yellow circles). Note on (*A*) and (*B*) the correspondence between functionally defined hand area, and the morphologically defined middle region of the central sulcus, and their characteristic progressive shift from the lateral part of the brain at high *z* levels to the medial part in the depth of the sulcus at lower levels.

whole group, the middle region extended vertically from z = +37 ± 1 mm to z = +65 ± 2 mm on the left and from z = +40 ± 2 mm to z = +65 ± 2 mm on the right hemisphere. Its center was located at z = +51 ± 2 mm (left) and z = +52 ± 2 mm on the right CS, within millimetres of the z level of the focus of maximal activation described in the literature for the hand vibration, which varies from z = +48 to +55 mm (Meyer *et al.*, 1991; Remy *et al.*, 1994).

The upper region (Figs 2 and 3; red) was almost planar and had a oblique orientation from the middle region (antero-lateral) to the interhemispheric brain surface (postero-medial). This part extended vertically from z = +44 ± 3 mm to z = +70 mm.

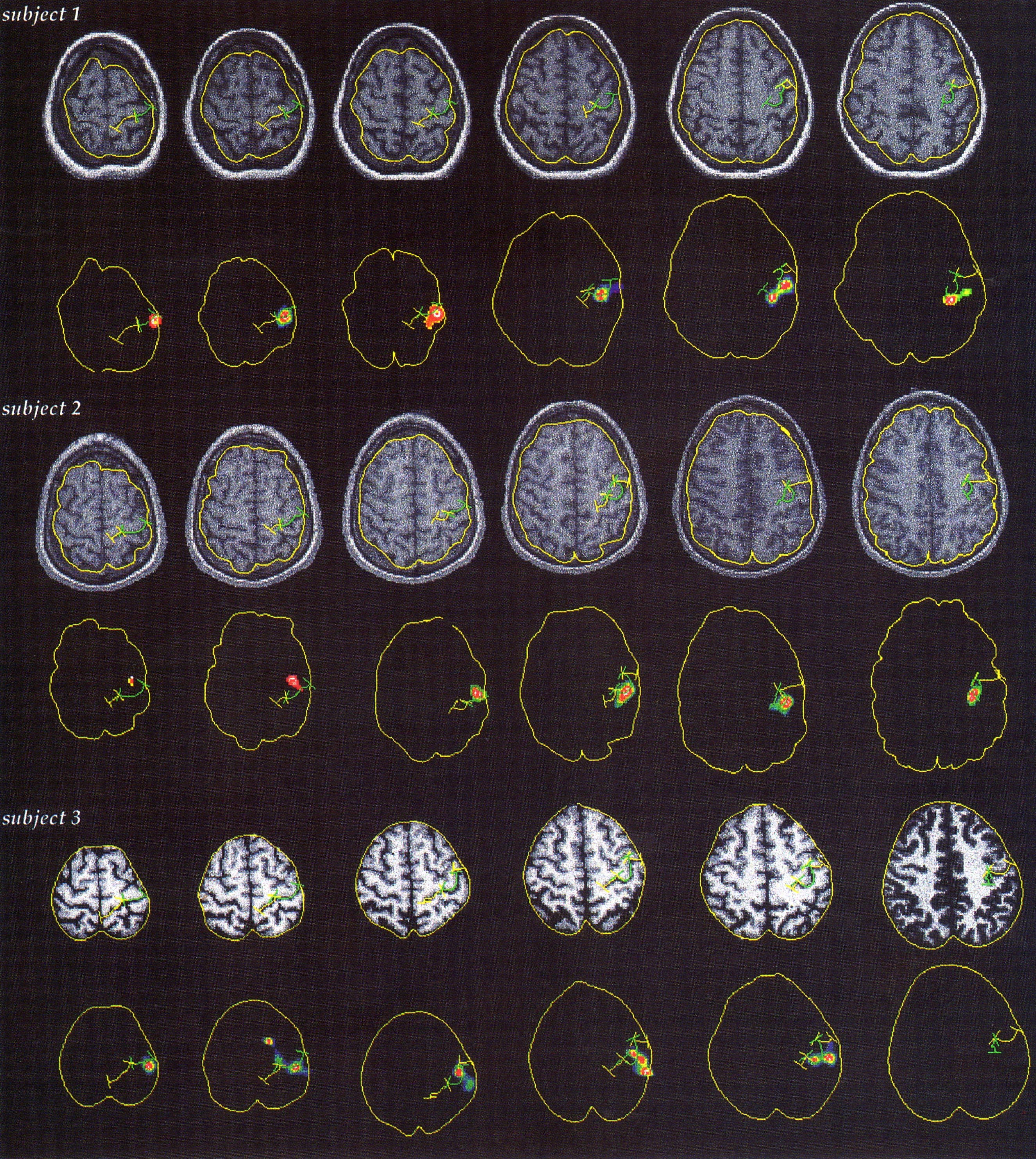
Figures 2*A* and 3 show in more detail the relationship between these three regions, and their orientation with respect to the surface of the brain. The lower region is the only one that reaches the surface of the brain for its entire z extent. Conversely, the middle region is located deep in the sulcus at low z levels (for example +43 and +46 mm of Fig. 3), and progressively reaches the surface of the brain at higher z levels (+55 mm of Fig. 3). Similarly, the upper region of the CS reaches the surface of the brain only at very high z levels. This results in a marked vertical overlap of the three CS regions that are all simultaneously visible on some sections (+46 and +55 mm, Fig. 3). The junction of the lower and the middle CS regions was always very easy to identify on 2D horizontal MR images, as a sharp angle, often τ-shaped, located deep in the CS (Fig. 3, levels +43, +46 mm). Conversely, the junction of the middle and the upper regions (marked as υ in Fig 3), easily recognized on 3D reconstruction (Fig. 2), was occasionally more difficult to detect on 2D horizontal MR images. This was so especially at high z levels, because the two parts were in apparent continuity in some instances (e.g. left CS, +55 mm, Fig. 3).

PET–MRI Correlation

We found a remarkable correspondence between the morphologically defined middle region of the CS, and the vibration-induced activation focus in all cases. This correspondence is visible on the example of MRI–PET superimposition shown in Figures 4 and 5. The focus of activation is located near the surface of the brain at high z levels (+54 to +62 mm in Fig. 4 and green boundaries in Fig. 5), and does not involve the CS upper region, which is more medial. Conversely, the activation is shifted within the depth of the sulcus at lower z levels (+50, +46 mm, Fig. 3 and green boundaries in Fig. 5), and did not involve the CS lower region, which is more superficial. Finally, the maximal focus of activation was located at z = +55 ± 6 mm, very close to the centre of the middle region, and using the 3D hysteresis method this focus extended, in the z vertical axis, from +43 ± 3.8 mm to +64 ± 1.3 mm, corresponding remarkably to the z extent of the morphologically defined middle region (see above).

Discussion

Although the cerebral sulci are buried in the brain, they are classically described as lines running on the surface of the brain, and little attention has been paid to their hidden 3D structure, which is lost on anatomical or radiological sections of the brain. As previously reported (Mangin *et al.*, 1995; Regis *et al.*, 1995; Sastre-Janer *et al.*, 1995, 1996) the extraction of cerebral sulci, and their vizualization as 3D objects may lead to a better


subject 1
subject 2
subject 3

three dimensions. The CS shape emerged as a coherent structure, which was always and unambiguously differentiated from the adjacent sulci. This easy identification is a major improvement over current 2D and surface CS identification. For example, Sobel *et al.* (1993) reported that the localization of the Rolandic cortex by anatomical landmarks in MR was unreliable in 16% of healthy subjects, whereas a recent study reported that interobserver reliability was at best 76% (Yousry *et al.*, 1996). It should be outlined that the easy and immediate visual sulcal recognition suggest that 3D sulci extraction is of major interest for the development of automatic sulci identification techniques (Mangin *et al.*, 1995; Regis *et al.*, 1995; Manceau-Demiau *et al.*, 1997).

Second, the 3D structure of the CS could be divided into three different regions based on morphological criteria. Their shapes were so consistent that each of the three CS regions could be recognized in all of the 34 CS analyzed. Thus, the 3D anatomy of the CS appears to be more stable than its trajectory at the surface of the brain, which is quite variable, as outlined by recent anatomical (Ono *et al.*, 1990) or radiological studies (Damasio, 1995). Furthermore, the morphologically defined regions of the CS appear to have a functional significance, since the middle region corresponded exactly to the hand area. Its vertical location corresponded in Talairach's space to that of the primary somatosensory cortex of the hand, as detected by hand vibration during PET activation studies (Meyer *et al.*, 1991; Remy *et al.*, 1994). This correspondence was directly verified by the superimposition of PET and MRI images from eight subjects in this study. Therefore, the analysis of the 3D anatomy of the CS confirms previous studies, which have described a typical aspect of the CS 'hand area' in 2D MR images (Rumeau *et al.*, 1994; Yousry *et al.*, 1997).

Third, our 3D approach allowed a better understanding of the somatotopic spatial representation within the CS, which appears to be organized not only along the classical vertical axis (Penfield *et al.*, 1937; Penfield and Rasmussen 1950), but also along a latero-medial horizontal axis. As a result of the horizontal organization, the three CS regions are simultaneously visible at some levels (Fig. 3, z = +46 and +55 mm), with the hand area located between the 'lateral' lower region and the 'medial' upper region. Finally, the horizontal organization accounts for the shift of the hand area from the lateral part of the CS at high z levels, to its medial part at lower z levels, as also previously noticed in a fMRI study of hand movement (Sanes *et al.*, 1995).

In summary, 3D visualization facilitates the identification of the CS, and allows its division into different 'subsulcal' regions that have consistent morphological features. Furthermore, we found here a striking structure–function relationship at the level of the 'hand area', a finding which extends previous 2D analyses of CS shape (Rumeau *et al.*, 1994; Yousry *et al.*, 1997). Therefore, at the level of the CS, the 3D approach emerges as a useful tool to improve our knowledge of cortical anatomy. It will improve the accuracy of morphometric cortical measurements in normal subjects. This approach will also facilitate multimodality imaging studies of post-lesional reorganization of sensory-motor functions. Developing 3D cortical anatomy may also reveal consistent morphological information in other cortical regions, which are often more variable than the CS at the surface of the brain. This will be greatly facilitated by the current development of fully automatic methods of sulcal extraction (Mangin *et al.*, 1995), which are much less time-consuming than the semi-manual method used here.

Notes

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