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Functional architecture of the somatosensory homunculus detected by electrostimulation

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Key points

- We performed a prospective electrostimulation study, based on 50 operated intact patients, to acquire accurate MNI coordinates of the functional areas of the somatosensory homunculus.
- In the contralateral BA1, the hand representation displayed not only medial-to-lateral, little-finger-to-thumb, but also rostral-to-caudal discrete somatotopy, with the tip of each finger located more caudally than the proximal phalanx.
- The analysis of the MNI body coordinates showed rare inter-individual variations in the medial-to-lateral somatotopic organization in these patients with rather different intensity thresholds needed to elicit sensations in different body parts.
- We found some similarities but also substantial differences with the previous, seminal works of Penfield and his colleagues.
- We propose a new drawing of the human somatosensory homunculus according to MNI space.

Abstract In this prospective electrostimulation study, based on 50 operated patients with no sensory deficit and no brain lesion in the postcentral gyrus, we acquired coordinates in the standard MNI space of the functional areas of the somatosensory homunculus. The 3D brain volume of each patient was normalized to that space to obtain the MNI coordinates of the stimulation site locations. For 647 sites stimulated on Brodmann Area 1 (and 1025 in gyri nearby), 258 positive points for somatosensory response (40%) were found in the postcentral gyrus. In the contralateral BA1, the hand representation displayed not only medial-to-lateral and little-finger-to-thumb somatotopy, but also rostral-to-caudal discrete somatotopy, with the tip of each finger located more caudally than the proximal phalanx. We detected a medial-to-lateral, tip-to-base tongue organization but no rostral-to-caudal functional organization. The analysis of the MNI body coordinates showed rare inter-individual variations in the medial-to-lateral somatotopic organization in these patients with intact somatosensory cortex. Positive stimulations were detected through the 'on/off' outbreak effect and discriminative touch sensations were the sensations reported almost exclusively by all patients during stimulation. Mean hand (2.39 mA) and tongue (2.60 mA) positive intensity thresholds were lower ($P < 0.05$) than the intensities required to elicit sensations in the other parts of the body. Unlike the previous, seminal works of Penfield and colleagues, we detected no sensations such as sense of movement or desire to move, no somatosensory responses outside the postcentral gyrus, and no bilateral responses for face/tongue stimulations. We propose a rationalization of the standard drawing of the somatosensory homunculus according to MNI space.

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Introduction

The primary somatosensory cortex can be divided into four distinct cytoarchitectonic areas (Powell & Mountcastle, 1959; Jones *et al.* 1978), named Brodmann areas (BA) 3a, 3b, 1, and 2 (Brodmann 1909; Vogt & Vogt, 1919), areas 3a and 3b being located within the central sulcus, area 1 in the crown of the postcentral gyrus, and area 2 more caudally in the postcentral sulcus (White *et al.* 1997). Animal studies have shown that BA 3a receives inputs from muscles and joints, whereas BA 3b and 1 receive from the skin, and BA 2 can combine skin and proprioceptive information (Kandel *et al.* 2013). This information progresses hierarchically in a rostro-caudal direction (Iwamura *et al.* 1993) with receptive fields increasing in size from area 3b to area 2 (Gardner, 1988). In primates, there is a cortical magnification of certain body parts (hand, mouth) in the postcentral gyrus (Kaas *et al.* 1979; Nelson & Chen, 2008; Merzenich *et al.* 2014) with a sequential, somatotopic organization of each finger in narrow strips (Shoham & Grinvald, 2001). In hand area 3b, there is a rostral-to-caudal arrangement with the fingertip located rostrally (Paul *et al.* 1972; Kaas *et al.* 1979; Merzenich *et al.* 2014). In contrast, in area 1, the organization of the sensitivity of the phalanx is reversed, with the fingertip located more caudally (Paul *et al.* 1972; Kaas *et al.* 1979; Merzenich *et al.* 2014). Such reversal of the maps between 3b and 1 could be a functional criterion of 3b/1 limits (Sanchez-Panchuelo *et al.* 2012).

Penfield and his co-workers (Penfield & Rasmussen, 1950; Penfield & Jasper, 1954) mostly described the functional anatomy of this area in humans, emphasizing the somatotopic organization of the hemibody. More recently, activation studies have also found a somatotopic organization of the somatosensory hemibody with more activation overlapping in areas 1 and 2 (Nelson & Chen, 2008) than in area 3 (Krause *et al.* 2001). Most studies underline the high functional (Sanchez-Panchuelo *et al.* 2012; Martuzzi *et al.* 2014; Kolasinski *et al.* 2016) and anatomical (White *et al.* 1997) variability of primary somatosensory maps.

However, since the seminal works of Penfield *et al.*, no systematic mapping of the human somatosensory cortex has been performed in a large number of subjects. The present study was based on 50 patients with no somatosensory deficit ('intact' patients). The aims of this prospective electrostimulation study were to acquire accurate coordinates of the functional areas of the somatosensory homunculus in the standard MNI space and to study the human hand and tongue cortical somatotopies in particular. Parameters of excitability of human primary somatosensory areas in conscious individuals are also discussed.

Methods

Ethical approval

Patients less than 18 years old were excluded. The National Consultative Committee of INSERM (Institut National de la Santé et de la Recherche Médicale) gave its approval for the storage of patients' data and preservation of their anonymity. To preserve patient privacy, this study was not registered in a publicly accessible database. However, the study conformed to the standards set by the *Declaration of Helsinki*. All the patients and their families gave their informed consent for a study of the functional areas by direct brain mapping and each chart was discussed pre-operatively in a surgical staff meeting with different neurosurgeons. Once 50 brain mappings had been included, the study was closed.

Inclusion criteria

Data from successive brain mappings were prospectively collected by the same team using the same protocol throughout the 8 years of the study (June 2008–June 2016). Two main conditions of inclusion were defined: patients should have *no initial sensory deficit* and *no brain lesion directly located in the postcentral gyrus*. Patients were examined regarding their absence of initial sensory deficit using clinical tests (see Table 1 for preoperative testing details). Before the operation, each patient underwent three tests: the tuning fork test; the warm/cold test; and the two-points discriminative test on the cheek, the hand (index finger) and the foot (hallux).

According to Weinstein (1968), the mean threshold discriminative distance is around 4 mm in the index (both sexes), 7 mm in the cheek (both sexes), and 11 mm for males and 13 mm for females in the hallux, with no differences between the left and right sides. Our criteria for exclusion were: patients with a discrimination threshold double the normal and/or any perturbed tuning fork or warm/cold test results on any of the three tested regions.

Pathology treated

Electrostimulation for brain mappings was performed to help with the removal of recently discovered brain lesions. The mean time between the first clinical sign and operation was 38 days (range 3–150 days; SD 37 days). We found 15 WHO grade I and II gliomas, 25 WHO grade III and IV gliomas, 4 arteriovenous malformations or cavernomas, 5 metastases and 1 grade II meningioma. They were located in 29 right and 21 left hemispheres. The mean age of patients was 49.5 years (range 29–73 years; SD 14 years). Nineteen of the patients were women. Thirty-seven patients had been recently treated with anti-epileptic drugs, always less than 3 months before the operation. None of them had chronic intractable epilepsy.

Table 1. Results of pre-operative testing of the 50 patients

	Tuning fork test			Warm/cold test			Two-point threshold discriminative test		
Patients/sex	Hand	Cheek	Foot	Hand	Cheek	Foot	Hand (index)	Cheek	Foot (hallux)
1/F	1	1	1	1	1	1	3	6	16
2/M	1	1	1	1	1	1	5	12	18
3/F	1	1	1	1	1	1	6	13	22
4/F	1	1	1	1	1	1	4	11	14
5/F	1	1	1	1	1	1	4	13	23
6/M	1	1	1	1	1	1	3	10	20
7/M	1	1	1	1	1	1	2	7	14
8/F	1	1	1	1	1	1	7	9	16
9/M	1	1	1	1	1	1	3	7	19
10/F	1	1	1	1	1	1	2	11	19
11/M	1	1	1	1	1	1	4	5	16
12/F	1	1	1	1	1	1	5	13	23
13/M	1	1	1	1	1	1	7	7	14
14/M	1	1	1	1	1	1	6	8	10
15/M	1	1	1	1	1	1	2	5	13
16/M	1	1	1	1	1	1	2	5	17
17/M	1	1	1	1	1	1	6	10	21
18/M	1	1	1	1	1	1	3	6	18
19/M	1	1	1	1	1	1	4	9	15
20/F	1	1	1	1	1	1	5	12	21
21/M	1	1	1	1	1	1	3	8	17
22/F	1	1	1	1	1	1	5	11	20
23/M	1	1	1	1	1	1	6	12	19
24/F	1	1	1	1	1	1	2	8	18
25/M	1	1	1	1	1	1	4	7	17
26/M	1	1	1	1	1	1	2	5	8
27/M	1	1	1	1	1	1	3	11	18
28/M	1	1	1	1	1	1	4	10	21
29/F	1	1	1	1	1	1	2	10	24
30/F	1	1	1	1	1	1	2	8	21
31/M	1	1	1	1	1	1	2	8	21
32/F	1	1	1	1	1	1	4	11	16
33/F	1	1	1	1	1	1	3	13	20
34/M	1	1	1	1	1	1	5	12	21
35/M	1	1	1	1	1	1	3	10	19
36/M	1	1	1	1	1	1	2	7	17
37/M	1	1	1	1	1	1	3	6	15
38/M	1	1	1	1	1	1	4	8	16
39/F	1	1	1	1	1	1	2	9	18
40/M	1	1	1	1	1	1	2	11	12
41/M	1	1	1	1	1	1	3	9	13
42/F	1	1	1	1	1	1	2	9	10
43/M	1	1	1	1	1	1	2	12	11
44/F	1	1	1	1	1	1	4	8	14
45/M	1	1	1	1	1	1	4	9	15
46/M	1	1	1	1	1	1	2	6	9
47/M	1	1	1	1	1	1	2	6	10
48/F	1	1	1	1	1	1	5	7	8
49/F	1	1	1	1	1	1	4	4	10
50/M	1	1	1	1	1	1	5	4	14

Tuning fork test: Do you feel the tuning fork? Yes: 1; no: 0. Warm/cold test: Do you feel warm/cold? Yes: 1; no: 0. Two-point threshold discriminative test: None of the patients of our study had a discriminative deficit in the tested zones and none failed the tuning fork or warm/cold tests in any of the 3 different regions tested.Discrimination test thresholds:Whole group for index: Mean discriminative test, 3.58 mm. Standard deviation: 1.47.Whole group for cheek: Mean discriminative test, 8.78. Standard deviation: 2.61.Whole group for hallux: Mean discriminative test, 16.42. Standard deviation: 4.16.

Anaesthetic protocol for awake craniotomy

Our awake brain mapping protocol was based on 20 years' experience (Roux *et al.* 2016). Anaesthetic drugs can, in theory, interfere with stimulation thresholds. Our objective during brain mapping was to avoid any anaesthetic drugs. One hour before admission to the operating room, a patch containing a eutectic mixture of prilocaine (2.5 mg g^{-1}) and lidocaine (2.5 mg g^{-1}) (EMLA) was applied in the supraorbital and auriculotemporal regions. Lidocaine (1%) with adrenaline (epinephrine; 1:100,000) was infiltrated to block the supraorbital, auriculotemporal, and occipital nerves. Additionally, the Mayfield head holder (Ohio Medical, Cincinnati, OH, USA) pin site and the surgical skin incision line were infiltrated. Sedation with spontaneous respiration was provided by continuous infusion of Propofol (1–3 mg kg h^{-1}). Fentanyl (1–3 μg kg h^{-1}) or Remifentanil (0.01–0.25 μg kg h^{-1}) was used for analgesia. The depth of procedural sedation was adjusted to keep the patient's vital signs stable. Propofol infusion was stopped during the dural opening (around 10 min before brain mapping) and the patient was fully awakened. Once the cortical mapping procedure was completed, patients were put back to sleep using the same protocol for the rest of the operation.

Cortical procedures

A neuronavigational system was used to guide tumour removal. Anatomical structures (gyri and sulci) were identified according to this neuronavigational data and the visual identification of the shape of gyri and sulci. The cortex was directly stimulated before any surgical approach using the bipolar electrode of the Nimbus cortical stimulator (1 mm electrodes; Innopsys, Toulouse, France) with biphasic square wave pulses of 1 ms duration and 50 Hz trains. The maximum train duration of each stimulation was 5 s. The afterdischarge threshold was determined by electrocorticography using a strip electrode. Although this point remains controversial, the afterdischarge threshold seemed to change little from site to site during one short mapping session (Ojemann, 1993). The level of electrostimulation was always kept 1 mA below that expected to cause electrical diffusion and afterdischarges so as to ensure that the stimulated area remained accurately localized on the area of cortex under study. If any afterdischarge (or epilepsy) was detected, the protocol was adapted to the afterdischarge threshold found.

Only clear brain mapping data were included in this study. Patients' feedback was fundamental: we considered that a response was obtained when the patients acknowledged feeling something. Patients were encouraged to report their sensations during stimulation. The patient's level of alertness in the absence of stimulation was regularly evaluated throughout the testing, as further assurance that changes during stimulation were not random events. Non-reproducible interferences (positive responses to electrostimulation) were not included in this study. The reproducibility criterion was 3/3 (i.e. 3 interferences to validate a cortical site as 'positive'). When a site had a reproducibility of 2/3 we stimulated it at least one more time: reproducibility criteria of 3/4 (or 4/5) were validated but *not* 2/4 or 3/5. At least 3 trials were performed on positive sites.

To evaluate the current amplitude for somatosensory mappings in postcentral gyri, the current amplitude was started at 1 mA and progressively increased by 0.5 mA steps. If allowed by electrocorticography results, the intensity of stimulation was raised to as high as 10 mA if necessary to obtain a response. If patients felt any unpleasant sensation or pain at any time, or any sensation that could evoke seizures, the stimulation was stopped and the intensity reduced.

Because our ability to test the human brain was restrained by clinical requirements, the possibility of delivering stimulations was limited. We tested only what was really useful for the treatment of the patients. Stimulation around and between detected positive areas may not have been tested because such testing was not clinically relevant for the patient. This legitimate constraint limited the ability to find complete somatotopies of the part of the body tested in individual patients.

The presupposition of this study in terms of localization was that, as described in other human anatomical, activation, or receptor-binding studies (Geyer *et al.* 1997; Nelson & Chen, 2008; White *et al.* 1997), BA1 was defined as the crown of the postcentral gyrus from the central sulcus anteriorly to the postcentral sulcus. These divisions are similar to those used for primate studies (Mountcastle, 2005). Because of their localizations deep in the sulci, BA3a, BA3b, and BA2 were not accessible to electrostimulation. Thus, the current functional exploration focused on BA1.

In the 50 patients, 647 sites were stimulated overall on the postcentral gyrus and 1025 in gyri nearby (Table 2). When a functional site was found, it was marked by a sterile ticket of 0.25 mm^2, identified in neuronavigation before moving on to the next test site. It was decided that the minimal spatial resolution of our electrostimulation technique corresponded to the size of the bipolar electrode separated by 3 mm. Once a positive functional area was detected, the cortical areas located 3 mm from it were also tested.

Postsurgical and statistical analysis

Each patient had her/his positive stimulations positioned on the left or right 3D cortical surface reconstructions of

Table 2. Number and localization of cortical sites stimulated in patients

Left and right hemispheric regions stimulated	Number of stimulations ($n = 1672$)
Postcentral gyri	647
Precentral gyri	208
Supramarginal gyri	350
Upper parietal	189
Superior temporal gyri	153
Middle temporal gyri	72
Inferior frontal gyri	53

one of the individual brains (case 12) constituting the PALS atlas (Van Essen *et al.* 2005) provided in the Caret software (Van Essen *et al.* 2001) and normalized in the MNI space. We obtained normalized coordinates of stimulation site locations that were per-operatively visualized and positioned on original 3D images provided by the neuro-navigation software (Brain Lab). For each positive site, MNI space coordinates (X, Y, Z) were obtained and stored year by year in an Excel database, with a detailed account of the type of response obtained.

Results

Parameters of stimulation of the somatosensory primary areas in the conscious human

Over 647 sites stimulated in BA1, we found 258 positive areas (40%). Stimulation of somatosensory primary areas had several characteristics (positive intensity threshold; type of outbreak; accuracy; type of patients' feelings). The mean general positive intensity threshold was 2.67 mA (from 0.5 to 7 mA) with a limited standard deviation (SD 0.72 mA). Specific mean finger (2.39 mA) and tongue (2.60 mA) positive thresholds were not statistically different, unlike the intensities required to elicit sensations in the other body parts (legs, shoulder, trunk, arms), which were significantly higher (mean = 3.5 mA; $P < 0.05$ with the Wilcoxon test). No significant difference for positive thresholds was found in patients with or without anti-epileptic drugs ($P = 0.80$; Wilcoxon test). No correlation was detected between the patient's age group (comparing patients over 60 years and younger patients) and the level of the positive thresholds ($P = 0.4576$; Spearman test).

The somatosensory positive areas were located in very small patches of cortex of around 3 mm by 3 mm (Fig. 1). Positive stimulations were detected with a clear-cut 'threshold' effect (for instance, at 1.5 mA, the subject felt nothing and then, at 2 mA, the subject felt something). Tingling (discriminative touch domain) was the main and almost exclusive sensation reported by all patients during stimulation. Pain was felt only once by one patient; another also had a bad taste in the mouth and another reported burning in the hand during some stimulations. No other sensations (from the proprioception domain for instance) were detected. Strictly no other isolated, positive somatosensory sensation was found among the 1025 stimulations performed outside the postcentral gyrus.

The medial-to-lateral sequence of the hand somatotopy

As expected, the ventral parts of the fingers were somatotopically organized from the medial-to-lateral aspects of postcentral gyrus and were symmetrically similar in the right and left hemispheres (Fig. 2*A*–*C*). Finger responses were found in 34 patients and the medial-to-lateral somatotopy was respected with no aberrant localization. Nevertheless, some rare individual variations were noted: two stimulations in two different patients elicited tingling not in individual fingers but in all fingers. They were located in the main postcentral somatotopic representation of the digits. Only one patient reported sensations in the dorsal part of her fingers when one cortical area was stimulated. One stimulation elicited tingling in the little finger and the medial part of the nearby ring finger. More areas were found for the thumb (41 areas) and 2nd finger (31 areas), than for the 3rd finger (25 areas), the 4th finger (19 areas) and the little finger (21 areas). All MNI coordinates of finger positive points are available in Table 3A. We found a certain dispersion of the points between the right and left hemispheres. Dispersions were computed by calculating the Euclidean distance (in mm) between each stimulation point and the barycentre of the corresponding finger. A Student's paired t test across clusters indicated significant differences both in terms of mean distance ($t = 3.2$, $P < 0.05$) and standard deviations ($t = 3.7$, $P < 0.01$) between the left and right hemispheres. This was probably due to the template we used, which was not strictly symmetric. However, there was no significant difference in the distances from the barycentres of each finger between the two hemispheres ($t = 0.4$, $P = 0.68$).

The rostral-to-caudal sequence of the hand somatotopy

In addition to this medial-to-lateral sequence, 10 patients felt either the tip or the base of at least one finger during electrostimulation. Furthermore, four patients displayed both tip and base finger phalange representation, all of them with a caudal discrete representation of the finger tip. Thus, group analysis of these 14 patients who displayed base and/or tip of the finger sensations during stimulation showed a clear rostral-to-caudal finger somatotopy with the tips of the fingers located more caudally than the base, as shown in Fig. 2*D* and *E*.

The tongue somatotopy

Fourteen patients displayed a medial-to-lateral hemispheric tongue somatotopy with the tip of the tongue located more medially than the middle of the tongue or its base (Fig. 3). Patients felt tingling exclusively on the contralateral space of the tongue. Most sensations concerned the middle of the tongue (31 of 44 sites). Tip sensations were rather rare (6 sites), as were sensations of the base of the tongue during stimulation (7 sites). Overall, the medial-to-lateral space devoted to the tongue in BA1 was quite large, around 2.5 cm. Although a rostral-to-caudal somatotopy (for instance different cortical representation for the lateral and the central parts of the tongue) may exist for the human tongue, no such organization was detected. All MNI coordinates of tongue positive points are available in Table 3B.

The medial-to-lateral sequence of the contralateral body

Figure 4 shows the somatotopic sequence of the human body with MNI coordinates. Various contralateral representations of the skin from the feet, knee, abdomen, thorax, eyebrows, gums or jaws were detected in BA1, among other sensations. All MNI coordinates of body positive points are available in Table 3C. As shown in Fig. 5 and in Table 4, the variations in localization were limited. The standard deviations of main regions of interest (thumb, index, middle finger, middle part of the tongue, and lips), calculated from MNI coordinates, were all less than 5 mm.

Discussion

Since the seminal works of Penfield and collaborators (Penfield & Rasmussen, 1950; Penfield & Jasper, 1954), no other work has studied the human somatosensory cortex with so many subjects, whatever the mapping technique. The analysis of MNI coordinates demonstrated that BA1 of the somatosensory cortex in humans was organized somatotopically from the medial to lateral and anterior to posterior parts of the postcentral gyrus. The contralateral cutaneous areas of the body are represented in small patches of cortex and, although almost all cutaneous parts of the contralateral body were found at least once in this series, two main zones were detected: the hand and the face/tongue. Other body zones were found much more rarely. The hand and the face/mouth areas occupied parts of the cortex that were proportionally much larger than their cutaneous surface area, because of their much more marked discriminative properties and small receptive fields. The relatively high number of positive responses found for hand and face/tongue is an indirect sign that the human brain multiplies the cortical representations of small receptive fields to increase its discriminative abilities for these two body regions. More precisely, in the hand

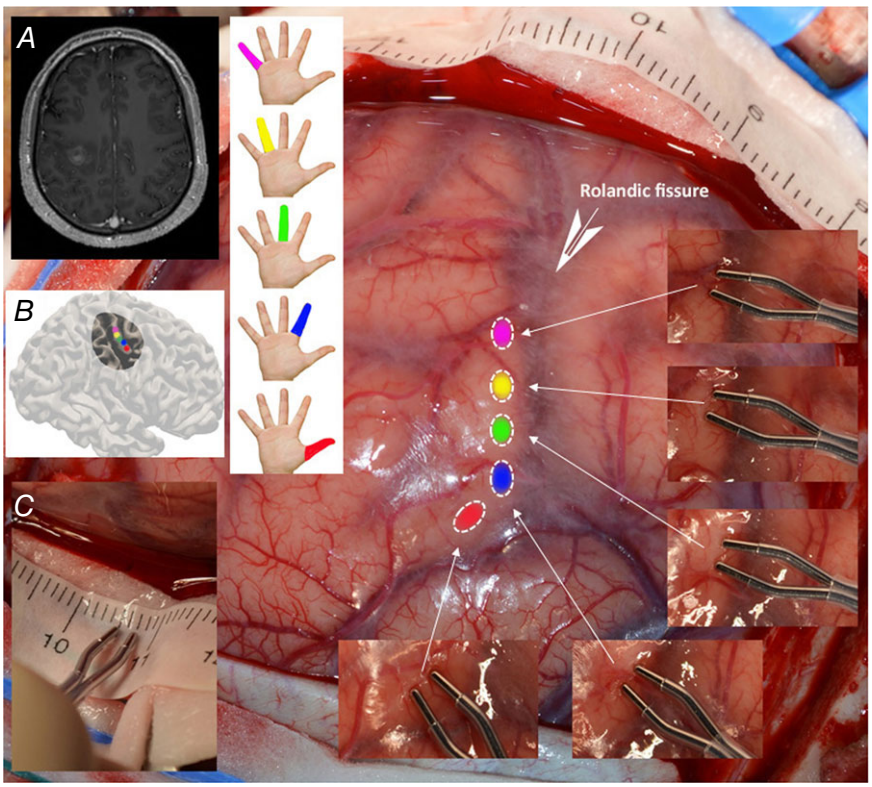

Figure 1. Example of electrostimulation mapping for somatosensory BA1 cortex
A, 38-year-old patient with a right diffuse astrocytoma IDH mutant (WHO 2016) with no sensorimotor deficit. *B*, 3D brain localization of the positive stimulations. In the postcentral gyrus (BA1), electrostimulation showed a clear finger somatotopy, in small (3 mm wide), sharply delimited cortical areas from the little (MNI coordinates: $X = 39.4$, $Y = -31.2$, $Z = 64.2$), ring (42.9, −29.0, 60.4), middle (44.7, −24.8, 59.5), and index (−44.3, −25.8, 59.0) fingers to the thumb (46.0, −25.7, 50.7). We observed that the displacement of the bipolar electrode on the cortex located adjacent to a positive area often induced another interference. *C*, accuracy of the technique with 3 mm distance between the stimulating electrodes. [Colour figure can be viewed at wileyonlinelibrary.com]

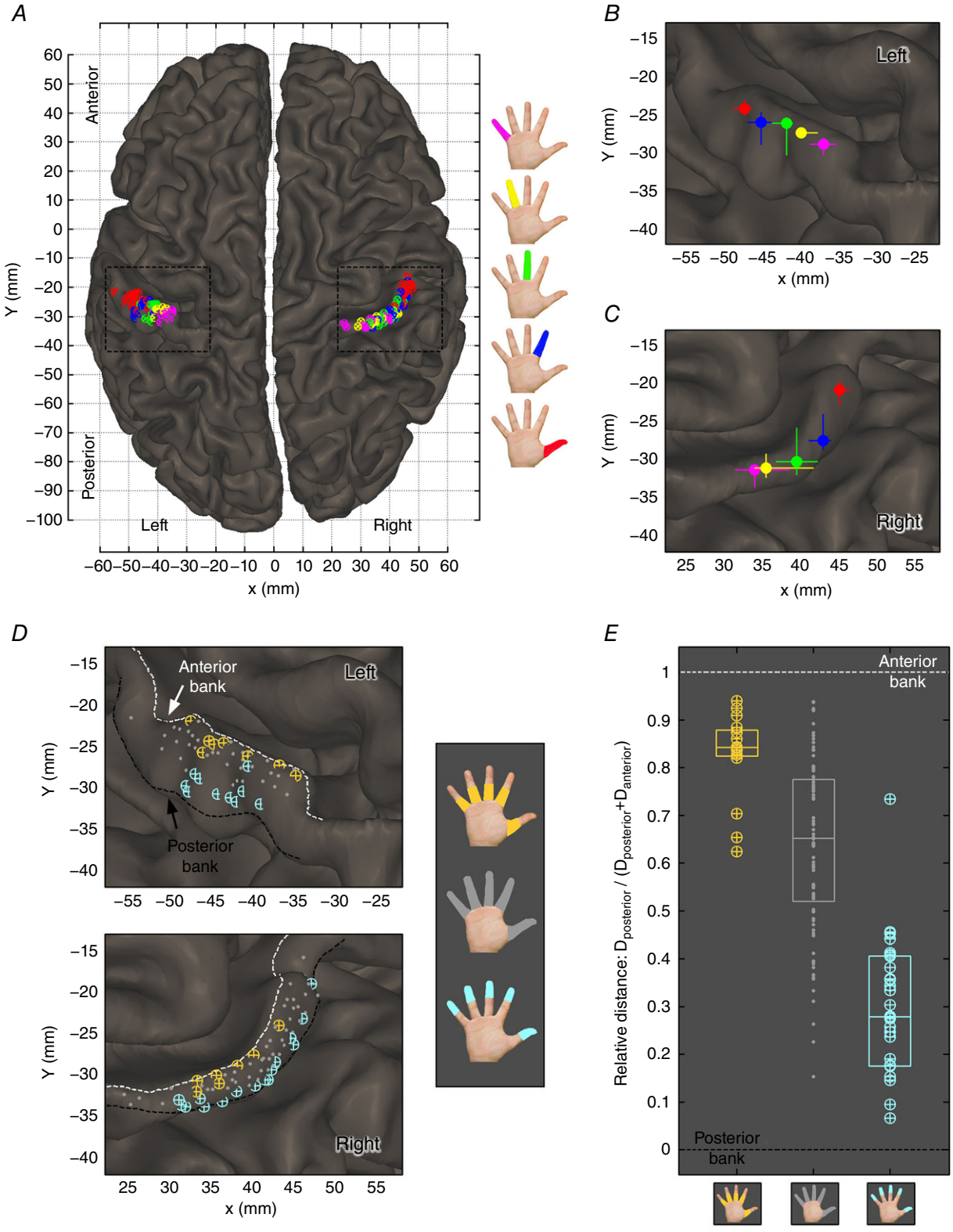

Figure 2. The medial-to-lateral and rostral-to-caudal sequences of the hand somatotopy
A, distribution over the two hemispheres (left and right templates) of the medial-to-lateral somatosensory representation of each finger. *B* and *C*, representation of the barycentre of each finger (coloured dots) in right and left hemispheres with amplitude bars representing the standard variations of each localization (coloured lines). Average right and left MNI barycentres (*X*, *Y*, *Z*) of the thumb (46.2, −22.5, 56.7), index (44, −22.8,

59.9), middle finger (40.6, −28.2, 62.1), ring (37.7, −29.2, 64.8) and little finger (35.4, −30, 66.3). Overall, the medial-to-lateral space (*X* MNI coordinates) devoted to the fingers in BA1 was around 1.5 cm. *D*, right and left hemispheric distribution of the MNI coordinates of the somatosensory base of the fingers (yellow); whole finger sensation (grey); and tips of the fingers (light blue). Individual analysis showed the rostral-to-caudal somatosensory cortical representation of the ventral part of the skin of the fingers. This rostral-to caudal somatotopy was detected at least once in all 5 fingers. *E*, group analysis confirmed this somatotopic representation with average *X*, *Y*, *Z* MNI coordinates for the group of fingertip points located more posteriorly ($X = 41.4$; $Y = -31.1$, $Z = 61.1$) than the whole finger sensations (39.7, −27.3, 62.9) and base of the finger sensations (43.6, −26.1, 60.1). [Colour figure can be viewed at wileyonlinelibrary.com]

area, magnifications of the ventral part of the thumb and index were particularly evident, as described in other studies (Penfield & Rasmussen, 1950; Martuzzi *et al.* 2014; Sanchez-Panchuelo *et al.* 2012).

Finally, activation (Sanchez-Panchuelo *et al.* 2012; Kolasinski *et al.* 2016) or anatomical (White *et al.* 1997) studies argue for the variability of this somatosensory functional organization. The main question concerns what is considered as 'variability' in a functional organization. Our results showed that no aberrant somatotopic organization was detected and the localization of each skin cortical representation within the postcentral gyrus varied little (standard deviations of the barycentre of main cortical representations were less than 5 mm).

Although the medial-to-lateral organization was described long ago, the anterior-to-posterior organization of the postcentral gyrus in the human is less well known (Nelson & Chen, 2008). This study showed that the finger topography is organized with the tip of the fingers located more posteriorly than their base, in both group and single subject analysis. This finding matches previous studies in primates that suggested such a rostral-to-caudal finger organization in BA1 (Darian-Smith *et al.* 1984; Mountcastle 2005). It is also in line with previous

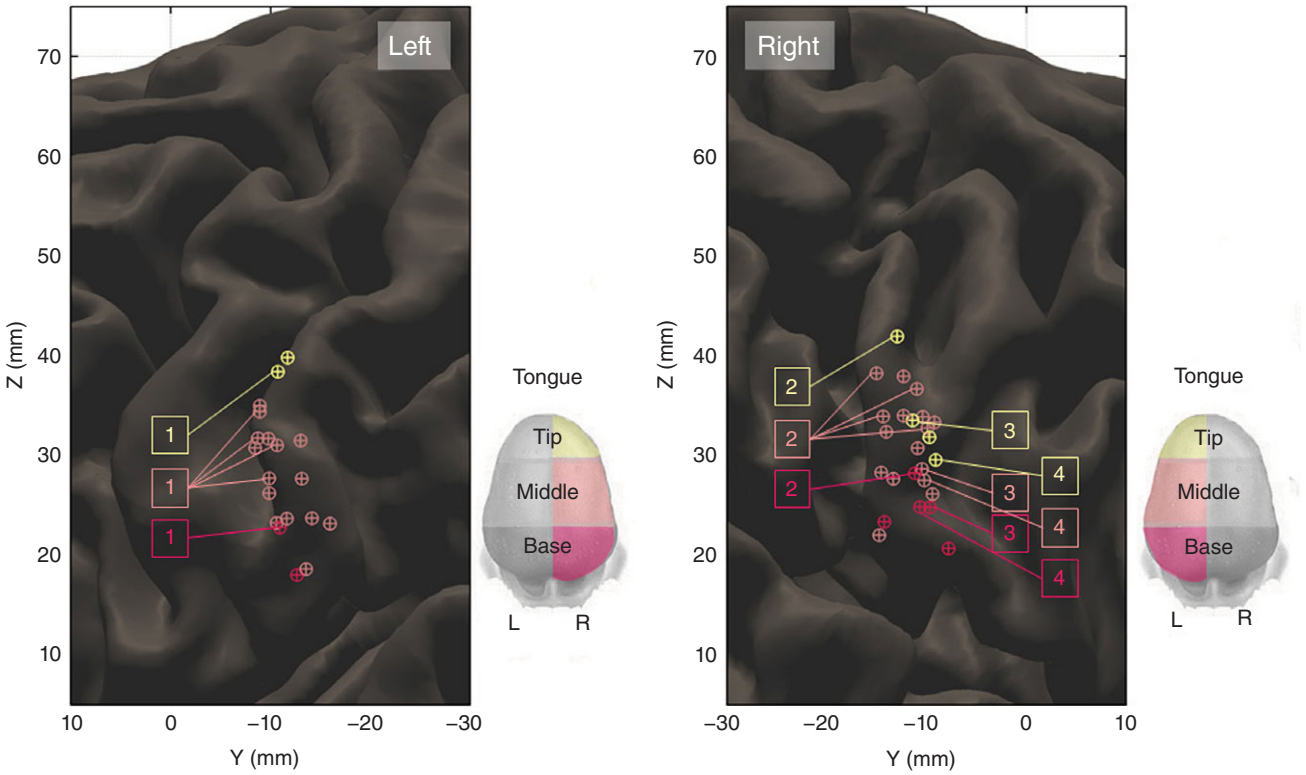

Figure 3. The somatotopic sequence of the tongue
The contralateral somatotopic representations displayed the following somatotopy: base of the tongue (red dots) close to the Sylvian fissure, and middle (pink dots) and tip of the tongue (yellow dots) more medial. The representation of the tongue occupied a large portion of the postcentral gyrus (2.5 cm for the mouth). This figure is composed of isolated points found punctually in some patients and of multiple points found in four individual patients (marked 1, 2, 3 and 4 in square boxes). Although a certain degree of variation may exist within this part of the postcentral gyri in the exact location of the tip, middle, and base of the tongue somatosensory cortical localizations, individual somatotopy respects the tip/medial–base/lateral tongue somatotopy. [Colour figure can be viewed at wileyonlinelibrary.com]

Table 3. MNI coordinates, barycentres (bold) and standard deviations (italics) of main region of interest for all 258 positive points (specific cutaneous sensation reported by patients)

A. Fingers (1)											
Thumb				Index finger				Middle finger			
X	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.
−44	−25	59	1	−45	−26	58	4	−46	−26	58	1
−47	−28	56	1	−41	−29	62	8	−44	−31	57	1
45	−22	59	2	40	−29	64	9	37	−30	66	9
−48	−25	55	4	−48	−28	54	10	−42	−29	60	10
−49	−26	53	7	43	−26	61	11	41	−28	63	11
−47	−26	57	8	41	−29	64	12	37	−32	66	12
−43	−27	59	8	46	−23	58	13	44	−26	60	13
45	−21	59	9	−45	−24	58	14	−42	−26	60	14
42	−27	63	9	−47	−28	56	14	−47	−26	57	15
−51	−25	51	10	44	−22	60	16	42	−26	62	16
44	−23	60	11	42	−28	62	17	43	−24	62	17
46	−22	58	12	42	−28	62	19	−41	−27	62	21
47	−19	56	13	46	−23	58	20	−40	−26	62	22
−48	−23	54	14	−46	−26	58	21	−41	−26	63	23
−50	−23	51	14	−48	−30	56	21	−43	−31	58	26
−47	−25	56	15	−43	−24	60	22	45	−25	59	27
44	−19	58	16	−45	−25	58	23	−41	−26	62	28
47	−19	55	16	43	−27	61	24	−42	−32	60	28
45	−21	59	17	−47	−29	57	26	40	−30	64	34
44	−25	61	17	44	−26	59	27	42	−31	61	34
46	−20	57	20	−46	−18	54	28	38	−29	65	40
−48	−23	54	21	−48	−30	55	28	38	−32	65	40
−47	−22	55	22	43	−24	61	34	34	−34	66	41
−47	−24	56	22	42	−27	62	34	33	−32	68	41
−51	−24	51	23	45	−26	59	34	36	−33	65	50
−49	−23	53	23	40	−28	63	40				
45	−22	59	24	41	−31	62	40				
−49	−24	53	26	34	−34	66	41				
46	−26	51	27	36	−31	67	41				
−47	−24	56	28	−44	−25	59	44				
48	−20	55	30	43	−27	61	48				
−47	−24	55	32								
44	−16	60	33								
47	−19	57	34								
45	−22	59	34								
44	−21	59	40								
−45	−24	58	44								
−48	−22	53	44								
−55	−22	46	46								
45	−21	59	48								
44	−25	61	48								
46.6	**−22.8**	**56.2**		**43.4**	**−26.8**	**59.9**		**40.8**	**−28.6**	**62.0**	
2.49	*2.58*	*3.44*		*3.25*	*3.14*	*3.23*		*3.51*	*2.93*	*3.06*	

(*Continued*)

Table 3. Continued

A. Fingers (2)

Ring finger				Little finger			
X	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.
−41	−26	63	1	−39	−29	65	1
−41	−27	63	4	−37	−30	66	4
30	−32	68	9	24	−32	71	9
37	−31	66	11	34	−31	67	11
29	−33	69	12	25	−34	71	12
43	−28	62	13	40	−31	63	13
−40	−27	63	14	−37	−29	66	14
41	−28	63	16	−42	−28	62	15
42	−29	62	17	38	−30	66	16
−38	−27	64	22	38	−31	65	17
−37	−27	65	23	−35	−28	65	22
35	−32	67	24	−35	−29	66	23
−41	−30	62	26	−39	−32	65	26
43	−29	60	27	39	−31	64	27
−38	−28	65	28	−36	−31	66	28
34	−32	67	34	39	−30	64	30
35	−30	67	40	33	−31	67	40
33	−33	67	40	31	−34	69	40
34	−34	66	41	34	−34	66	41
				31	−33	69	41
				32	−34	68	50
37.5	**−29.7**	**64.8**		**35.2**	**−30.9**	**66.3**	
4.23	*2.47*	*2.47*		*4.65*	*1.93*	*2.34*	

B. Tongue

Base				Middle				Tip			
X	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.
60	−10	25	3	61	−10	29	3	61	−11	34	3
−62	−13	18	18	61	−12	34	6	−57	−11	38	15
62	−14	23	31	−58	−9	34	15	61	−9	30	36
61	−11	25	38	−60	−8	31	18	61	−10	32	38
61	−11	28	43	−60	−10	26	18	58	−13	42	43
−62	−11	23	46	−61	−11	23	18	−57	−12	40	46
62	−8	21	49	−61	−11	31	18				
				−62	−13	28	18				
				−63	−14	24	18				
				59	−9	26	31				
				62	−13	28	31				
				62	−14	32	31				
				61	−9	33	31				
				61	−10	34	36				
				59	−12	38	36				
				60	−10	28	37				
				61	−11	31	37				
				61	−10	29	38				
				−61	−10	32	42				
				−58	−9	34	42				
				−57	−12	40	42				
				61	−10	32	43				

(*Continued*)

Table 3. Continued

B. Tongue

Base				Middle				Tip			
X	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.
				58	−11	37	43				
				62	−14	34	43				
				61	−15	38	43				
				−62	−14	19	45				
				−62	−12	24	45				
				−63	−16	23	45				
				−61	−13	31	46				
				−61	−10	28	46				
				−60	−9	32	46				
				−58	−9	35	46				
				−62	−12	24	47				
				60	−10	25	49				
				61	−10	33	49				
				62	−15	28	49				
				62	−15	22	49				
61.4	**−11.1**	**23.3**		**60.7**	**−11.4**	**30.0**		**59.2**	**−11.0**	**36.0**	
0.78	*1.95*	*1.41*		*1.47*	*2.12*	*4.97*		*2.04*	*1.41*	*4.73*	

C. Body (standard deviation for the palm and lips only)

Feet				Leg				Knee			
X	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.
−4	−41	64	1	−5	−44	67	1	8	−41	78	50
				3	−42	76	50				
4	**−41**	**64**		**4**	**−43**	**71.5**		**8**	**−41**	**78**	

Thigh				Hip				Abdomen			
X	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.
−9	−42	73	1	−19	−37	76	14	−22	−37	72	26
−17	−38	76	26								
11	−41	77	50								
12.3	**−40.3**	**75.3**		**19**	**−37**	**76**		**22**	**−37**	**72**	

Thorax				Shoulder				Elbow			
X	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.
−13	−41	75	1	−33	−35	69	5	26	−32	70	13
16	−40	75	9	−31	−36	70	26	−31	−35	70	14
16	−40	75	50	−25	−35	71	32	19	−33	72	19
								−27	−35	71	28
15	**−40.3**	**75**		**29.7**	**−35.3**	**70**		**25.7**	**−33.7**	**70.7**	

Forearm				Wrist				Palm			
X	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.
36	−32	66	13	−32	−34	69	1	43	−26	62	2
28	−32	69	16	−35	−34	68	14	44	−21	59	12
27	−34	70	24	25	−32	71	19	43	−24	62	13

(*Continued*)

Table 3. Continued

Forearm				Wrist				Palm			
X	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.
30	−34	69	25	−35	−34	68	28	42	−25	62	16
25	−35	70	41	27	−34	70	29	−39	−28	65	21
				33	−32	68	30	−48	−27	54	22
				−29	−36	70	32	−42	−25	61	23
								44	−23	60	25
								44	−23	60	29
								44	−28	60	40
								37	−29	66	41
								38	−30	65	50
29.2	**−33.4**	**68.8**		**30.9**	**−33.7**	**69.1**		**42.3**	**−25.7**	**61.3**	
								3.05	*2.73*	*3.22*	

Eyebrows				Eyes				Nose			
X	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.
−53	−23	48	10	−56	−21	46	8	−56	−19	45	10
53	**−23**	**48**		**56**	**−21**	**46**		**56**	**−19**	**45**	

Face				Lips				Teeth			
X	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.
−55	−15	44	22	55	−13	47	13	62	−8	21	43
				−57	−13	42	15	60	−10	28	43
				52	−13	51	34				
				60	−14	40	37				
				59	−13	40	38				
				57	−13	44	38				
				60	−13	38	39				
				57	−12	44	40				
				59	−13	40	40				
				57	−13	44	42				
				−62	−10	28	45				
				57	−17	43	46				
				−56	−16	43	46				
				−57	−13	42	46				
55	**−15**	**44**		**57.5**	**−13.3**	**41.9**		**61**	**−9**	**24.5**	
				2.44	*1.63*	*4.88*					

Gums				Jaw				Pharynx			
X	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.	*X*	*Y*	*Z*	Pat.
58	−10	37	6	59	−14	42	13	−62	−14	14	18
				61	−14	38	13				
				61	−12	34	37				
				61	−12	36	37				
58	**−10**	**37**		**60.5**	**−13**	**37.5**		**62**	**−14**	**14**	

Larynx			
X	*Y*	*Z*	Pat.
62	−7	19	35
−62	−13	18	46
62	**−10**	**18.5**	

Pat. = patients.

findings of some activation studies performed in humans (Blankenburg *et al.* 2003; Sanchez-Panchuelo *et al.* 2012). The coordinate of the caudal discrete representations of fingertips in area 1 found in group analysis ($X = -47$; $Y = -31$; $Z = 53$) by Blankenburg *et al.* (2003) are extremely close to our coordinates ($X = 41.4$; $Y = -31.1$, $Z = 61.1$). The human cortical representation of the tongue occupies a territory at least as large as that of the hand between, medially, the lips and, more laterally, the pharynx, but its organization is radically different for the tongue, with the tip of the tongue localized more medially than its base.

Human somatosensory cortex positive thresholds

In those patients with intact postcentral gyrus, somatosensory responses were obtained with mean thresholds around 2.5 mA in the tongue and hand areas and with slight individual variations. The positive threshold levels needed to obtain thoracic or lower limb sensations were higher, and levels were different for other parts of the human brain (Roux *et al.* 2016). We found that the age of the patients and the presence of antiepileptic drugs had no effect on these thresholds. Nevertheless, other factors that we did not test could also intervene. For instance, patients who had had previous chemotherapy could have different thresholds.

Human somatosensory positive thresholds could be modified by other confounding factors (Haglund *et al.* 1993) such as current frequencies and monopolar *versus* bipolar stimulation devices, the type of anaesthesia used, stimulations during the refractory period, patients' sensory skills or the presence of a sensory deficit. These possibilities need to be investigated by a subsequent study. Many patches of cortex were observed to be unresponsive to stimulation. In our opinion, the reason may have been that the neurons under the electrostimulation probe did not respond in a way visible to us during the operation.

Lastly, in somatosensory mapping, the responses we obtained depended only on the ability of the patient to be conscious of his/her sensation and to report it. Nothing is known about the possible diffusion of this stimulation in deep brain structures. The stimulation could be located on a functional area without the sensation reaching the patient's consciousness, a phenomenon described in language mappings (Roux *et al.* 2015). Clinical information (and further scientific data) could thus have been missed.

Differences with the previous works of Penfield *et al.*

Although our study matches many findings by Penfield and co-workers, four main differences can be noted.

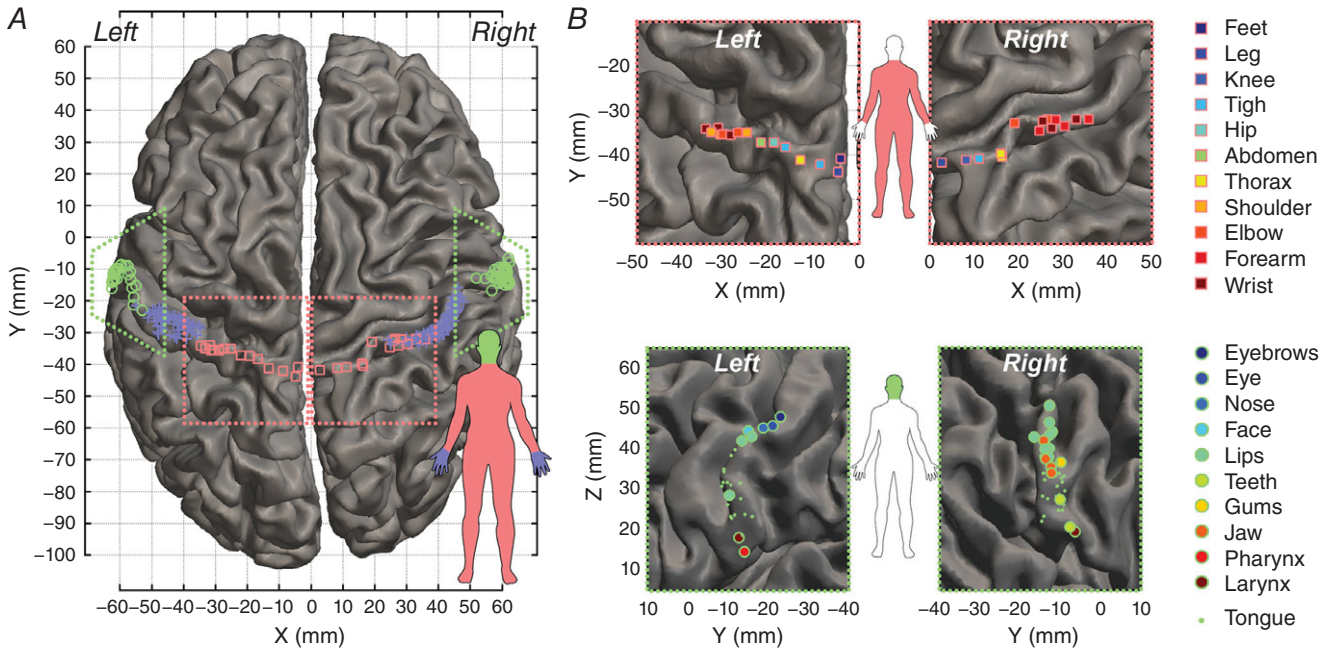

Figure 4. The somatotopic sequence of the body
A, global somatotopic organization of the body (flesh colour), hand (mauve), and head (green). Dotted boxes: regions of interest for body and face somatotopies. *B*, top: somatotopic representation of the limbs with their medial-to-lateral somatotopic sequence. *B*, bottom: somatotopic representation of the face (excluding tongue represented in Fig. 3). The medial-to-lateral somatotopic sequence of the eyebrows, eyes, cheeks, both lips, teeth, gums, jaws, pharynx, and larynx is shown. [Colour figure can be viewed at wileyonlinelibrary.com]

Firstly, they found that 25% of the somatosensory responses were outside the postcentral gyrus, in the precentral gyrus or parietal lobe (Penfield & Rasmussen, 1950; Penfield & Jasper, 1954). They also described a small 'second sensory' area in the superficial bank of the Sylvian fissure of the precentral gyrus (Penfield & Roberts, 1959). We detected no somatosensory responses outside the postcentral gyrus. A second difference is that we recorded no bilateral responses for stimulation in the face and tongue regions, whereas 13% (27 out of 202) of the responses in Penfield and collaborators' works were bilateral (Penfield & Rasmussen, 1950). One hypothesis is that paradoxical responses may not have been uncommon in the epileptic patients treated by Penfield, particularly in those with organic lesions and chronic epilepsy (Urasaki *et al.* 1994). Some of Penfield's patients had huge brain lesions around the central gyri and thus possible cerebral reorganizations. The findings of somatosensory responses outside the postcentral gyri may not have been uncommon.

Thirdly, Penfield's team also described some sensations produced by stimulation, such as a sense of movement and, more rarely, a desire to move (Penfield & Rasmussen, 1950; Penfield & Jasper, 1954), that were never reported by our patients.

Fourthly, we reported rare sensations on the dorsal part of the hand or fingers, a cutaneous territory Penfield & Rasmussen (1950) did not identify in the cortex 'because of its small size'. Seldom studied, the somatotopic representation of the dorsal surface of the digits could be comparable to that of the ventral surface in human area 3b (Druschky *et al.* 2002). This finding is perhaps a question of opportunity. During their career, Penfield and colleagues used different types of stimulators, the frequency of which was not always controlled (Penfield and Roberts, 1959). It is possible that the accuracy of the stimulator we used, in terms of localization (with 3 mm wide electrodes) and stability of the electric frequency, allowed us to detect such rare sensations.

Table 4. Standard deviations (in mm) of MNI coordinates of positive points for main regions of interest calculated

Region of interest	*X*	*Y*	*Z*
Thumb (41 points)	2.49	2.58	3.44
Index (31 points)	3.25	3.14	3.23
Middle finger (25 points)	3.51	3.14	3.06
Middle part of tongue (37 points)	1.47	2.12	4.97
Lips (14 points)	2.44	1.63	4.88

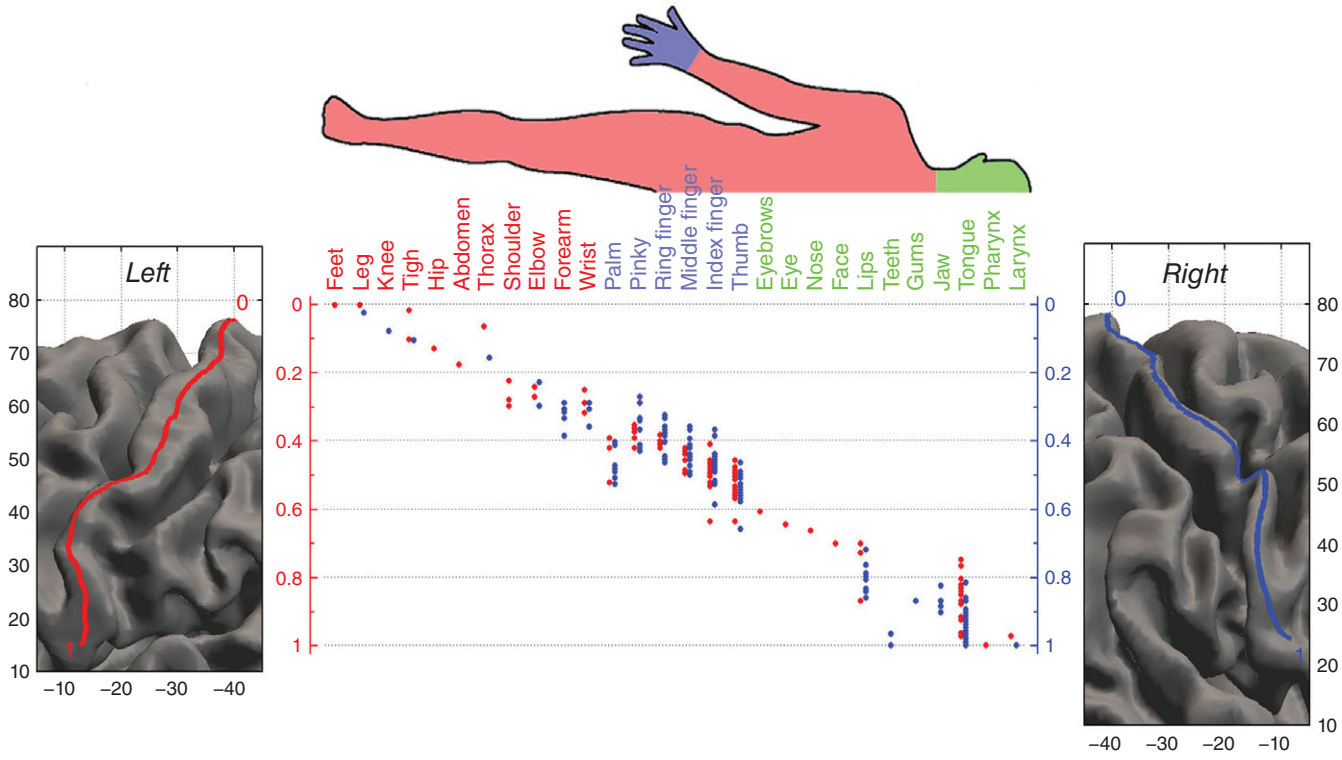

Figure 5. Anatomical relative variations of the human somatosensory cortex
Representation of the relative variations of the human somatosensory cortex on a scale from 0 (medial part) to 1 (lateral part of the postcentral gyrus). [Colour figure can be viewed at wileyonlinelibrary.com]

References

Blankenburg F, Meyer R, Schwiemann J & Villringer A (2003). Evidence for a rostral-to-caudal somatotopic organization in human primary somatosensory cortex with mirror-reversal in areas 3b and 1. *Cereb Cortex* **13**, 987–993.

Brodmann K (1909). *Vergleichende Lokalisationslehre der Grosshirnrinde*. Johann Bart, Leipzig, Germany.

Darian-Smith I, Goodwin A, Sugitani M & Heywood J (1984). The tangible features of textured surfaces: their representation in the monkey's somatosensory cortex. In *Dynamic Aspects of Neocortical Function*, eds Edelman GM, Gall WE & Cowan WM. Wiley & Sons, New York.

Druschky K, Kaltenhäuser M, Hummel C, Druschky A, Pauli E, Huk WJ, Stefan H & Neundörfer B (2002). Somatotopic organization of the ventral and dorsal finger surface representations in human primary sensory cortex evaluated by magnetoencephalography. *Neuroimage* **15**, 182–189.

Gardner EP (1988). Somatosensory cortical mechanisms of feature detection in tactile and kinesthetic discrimination. *Can J Physiol Pharmacol* **66**, 439-454.

Geyer S, Schleider A & Zilles K (1997). The somatosensory cortex of human: cytoarchitecture and regional distributions of receptor-binding sites. *Neuroimage* **6**, 27–45.

Haglund MM, Ojemann GA & Blasdel GG (1993). Optical imaging of bipolar cortical stimulation. *Neurosurg* **78**, 785–793.

Iwamura Y, Tanaka M, & Hikosaka O (1993). Rostrocaudal gradients in the neuronal receptive field complexity in the finger region of the alert monkey's postcentral gyrus. *Exp Brain Res* **92**, 360–368.

Jones EG, Coulter JD & Hendry SH (1978). Intracortical connectivity of architectonic fields in the somatic sensory, motor and parietal cortex of monkeys. *J Comp Neurol* **181**, 291–347.

Kaas JH, Nelson RJ, Sur M, Lin CS & Merzenich MM (1979). Multiple representations of the body within the primary somatosensory cortex of primates. *Science* **204**, 521–3.

Kandel ER, Schwartz JH, Jessell TM, Siegelbaum SA & Hudspeth AJ (2013). *Principles of Neural Science*, Fifth edn. McGraw-Hill, New York.

Kolasinski J, Makin TR, Jbabdi S, Clare S, Stagg CJ & Johansen-Berg H (2016). Investigating the stability of fine-grain digit somatotopy in individual human participants. *J Neurosci* **36**, 1113–1127.

Krause T, Kurth R, Ruben J, Schwiemann J, Villringer K, Deuchert M, Moosmann M, Brandt S, Wolf K, Curio G & Villringer A (2001). Representational overlap of adjacent fingers in multiple areas of human primary somatosensory cortex depends on electrical stimulus intensity: an fMRI study. *Brain Res* **899**, 36–46.

Martuzzi R, van der Zwaag W, Farthouat J, Gruetter R & Blanke O (2014). Human finger somatotopy in areas 3b, 1, and 2: a 7T fMRI study using a natural stimulus. *Hum Brain Mapp* **35**, 213–226.

Merzenich MM, Kaas JH, Sur M & Lin CS (2014). Double representation of the body surface within cytoarchitectonic areas 3b and 1 in "SI" in the owl monkey (*Aotus trivirgatus*). *J Comp Neurol* **181**, 41–73.

Mountcastle VB (2005). *The Sensory Hand: Neural Mechanisms of Somatic Sensation*. Harvard University Press, Cambridge, MA, USA.

Nelson AJ & Chen R (2008). Digit somatotopy within cortical areas of the postcentral gyrus in humans. *Cereb Cortex* **18**, 2341–2351.

Ojemann G (1993). Functional mapping of cortical language areas in adults. In *Electrical and Magnetic Stimulation of the Brain and Spinal Cord*, eds Devinsky O & Beric A. Raven Press, New York.

Paul RL, Merzenich M & Goodman H (1972). Representation of slowly and rapidly adapting cutaneous mechanoreceptors of the hand in Brodmann's areas 3 and 1 of *Macaca mulatta*. *Brain Res* **36**,229–249.

Penfield W & Jasper H (1954). *Epilepsy and the Functional Anatomy of the Human Brain*. Little, Bown and Company, Boston.

Penfield W & Rasmussen T (1950). *The Cerebral Cortex of Man*. Hafner Publishing company, New York.

Penfield W & Roberts L (1959). *Speech and Brain Mechanisms*. Princeton University Press, Princeton, NJ, USA.

Powell TP & Mountcastle VB (1959). The cytoarchitecture of the postcentral gyrus of the monkey *Macaca mulatta*. *Bull Johns Hopkins Hosp* **105**, 108–131.

Roux FE, Durand JB, Djidjeli I, Moyse E & Giussani C (2016). Variability of intraoperative electrostimulation parameters in conscious individuals: language cortex. *J Neurosurg* **15**, 1–12.

Roux FE, Miskin K, Durand JB, Sacko O, Réhault E, Tanova R & Démonet JF (2015). Electrostimulation mapping of comprehension of auditory and visual words. *Cortex* **71**, 398–408.

Sanchez-Panchuelo RM, Besle J, Beckett A, Bowtell R, Schluppeck D & Francis S (2012). Within-digit functional parcellation of Brodmann areas of the human primary somatosensory cortex using functional magnetic resonance imaging at 7 tesla. *J Neurosci* **32**, 15815–15822.

Shoham D & Grinvald A (2001). The cortical representation of the hand in macaque and human area S-I: high resolution optical imaging. *J Neurosci* **21**, 6820–6835.

Urasaki E, Uematsu S, Gordon B & Lesser RP (1994). Cortical tongue area studied by chronically implanted subdural electrodes – with special reference to parietal motor and frontal sensory responses. *Brain* **117**, 117–132.

Van Essen DC (2005). A population-average, landmark- and surface-based (PALS) atlas of human cerebral cortex. *Neuroimage* **28**, 635–662.

Van Essen DC, Dickson J, Harwell J, Hanlon D, Anderson CH & Drury HA (2001). An integrated software system for surface-based analyses of cerebral cortex. *J Am Med Inform Assoc* **8**, 443–459.

Vogt C & Vogt O (1919). Allgemeinere Ergebnisse unserer Hirnforschung. *J Psychol Neurol* **25**, 279–462.

Weinstein S (1968). Intensive and extensive aspects of tactile sensitivity as a function of body part, sex and laterality. In *The Skin Senses*, ed. Kenshalo DR, pp. 195–222. Charles Thomas, Springfield, IL, USA.

White LE, Andrews TJ, Hulette C, Richards A, Groelle M, Paydarfar J & Purves D (1997). Structure of the human sensorimotor system. I: Morphology and cytoarchitecture of the central sulcus. *Cereb Cortex* **7**, 18–30.

Additional information

Competing interests

The authors declare that they have no competing interests.

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Author contributions

Experiments were performed at The University of Toulouse III. F.E.R. was responsible for the study design. F.E.R. and I.D. carried out the experiments. F.E.R., I.D. and J.B.D. analysed and interpreted the data. F.E.R. and J.B.D. drafted the paper. All authors revised the article critically for important intellectual content. All authors have approved the final version of the manuscript and agree to be accountable for all aspects of the work. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.