New insights into neurocognition provided by brain mapping: visuospatial cognition

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The last century has shown a tremendous amount of progress in neurosurgery going from blind and frequently lethal brain surgery to intraoperative electrical stimulations (IES) for a functional living (in vivo) brain mapping. IES combined with good neuropsychological assessments allows a much better mapping of brain functions, resulting in a clear definition of the borders of a brain resection. Thus, the risks of definitive postoperative neurological deficits can be significantly decreased. Nevertheless, the difficulty to assess nonlanguage cognitive functions during the operations has led to an underestimation of the functional importance of the right hemisphere.

An overview of the historical context of brain stimulations, with a special focus on recent advancements in visuospatial mapping, constitutes the subject matter of this chapter. We first describe the invention of brain stimulation and its application to the neurosurgical practice. We then survey the importance of the right hemisphere for spatial processing. Finally, we review the new insights into visuospatial cognition provided by IES and lesion-based brain mapping. Hopefully, the ideas expressed in this chapter will encourage the practice of awake brain surgery of the right hemisphere and emphasize the importance to assess visuospatial functions with IES.

Intraoperative stimulations of the "dominant" hemisphere

In 1922, Wilder Penfield concluded one of his letters to his mother, "Brain surgery is a terrible profession. If I did not feel it will become very different in my lifetime I should hate it." [47, p. 93]. At that time no method was able to discriminate a functional from a nonfunctional area during the operation, and neurosurgery on brain tumors was frequently unsuccessful. Thus, when the brain excision was too large, patients came out from the operation permanently disabled. Conscientious neurosurgeons chose then to leave a significant portion of the tumor in place, which improved the patient outcome, but that tumor grew and killed patients months or years later [63].

Penfield's prediction had come true, and neurosurgery made giant steps ahead during his lifetime, beginning with the improvement of surgical and antiseptic techniques that dropped the rates of mortality significantly. But the tipping point that changed the neurosurgical practice was the clinical introduction of intraoperative electrical stimulation (IES). IES consists in the temporary perturbation of restricted regions (5 mm) around the tumor by electrical stimuli applied directly on the brain surface. At the moment of the IES, if the patient reports a peripheral sensation or an involuntary movement, the brain area is labeled as functional and will be spared during the operation. Thus, this approach is useful to delimit the functional areas of the brain so that neurosurgeons may be accurately informed about the functional borders of brain tumor excisions [61]. However, Penfield was not the first to apply IES on the human brain. As he acknowledges in one of his papers [64], the credit has to go to Roberts Bartholow. Following previous reports of faradizations (i.e., applications of faradic current to stimulate nerves) of the brains of living animals, such as those by Fritsch and Hitzig in 1870 [32], Bartholow, an American surgeon, described the first application of electrical stimulations to the living human brain: "Mary's health has always been good until thirteen months ago, when a small ulcer appeared on the scalp (...) when she was an infant, she had fallen into the fire, her scalp was badly burned, and the hair was never reproduced (...) The skull is eroded and has disappeared over a space of two inches in diameter, where the pulsations of the brain are plainly seen (...) as the brain has been deeply penetrated by incisions made for the escape of pus, it was supposed that fine needles could be introduced without material injury to the cerebral matter (...). Observation 1. (...) when the needle points were engaged in the dura mater, Mary declared, in answer to repeated questions, that she felt no pain (...) Mechanical irritation of the cerebral matter produced no results on motility or sensibility of the extremities. Observation 2. *To test faradic reaction of the surface of the dura mater.* Two needles insulated were introduced into left side until their points were well engaged in the dura mater. When the circuit was closed, distinct muscular contractions occurred in the right arm and leg. The arm was thrown out, the finger extended, and the leg was projected forward (...) Observation 3. *To test faradic reaction of the posterior lobes.* (...) Mary complained of a very strong and unpleasant feeling of tingling in both right extremities, especially in the right arm, which she seized with the opposite hand and rubbed vigorously." [3, p. 310-311 (Fig. 1)

Fig. 1. Original drawing of the head of Mary (viewed from the top), patient of Roberts Bartholow, who described for the first time electrical stimulations on the human living brain [3]

Fifty years later in Breslau, Foerster and Penfield applied electrical stimulation to the clinical practice of neurosurgery, in order to map functions on the surface of the living brain [31]. This approach, when applied to brain surgery, provided two benefits. It significantly reduced the amount of critical functional brain area removed, minimizing definitive postoperative neurological deficits. And it was the first direct scientific approach to localize the functions of regions in the human living brain.

A few years later, at his newly built Montreal Neurological Institute, Penfield used IES on the cerebral cortex to pinpoint the localization of motor and somatic representation (Fig. 2) [64]. He also induced speech arrest [66] and, most impressively, elicited vivid memories in stimulated patients [65].

Arthur Ward, after his training in neurosurgery with Wilder Penfield at the Montreal Neurological Institute, introduced the practice of IES on awake epilepsy patients to the study of neurophysiology at the University of Washington [79].

In the United States, the next generation of neurosurgeons followed this approach, combining the knowledge from early neuroanatomists – [11], [18], [49] –, neurologists [41], and later from neuropsychologists [57] to map out the different functions of the living brain.

By means of IES on awake patients, the following phenomena were elicited: anomia (impaired object naming) [60], alteration of verbal working memory [56], and different brain localizations for language in bilingual patients [59].

Most importantly, the functional localization of the different aspects of language were shown to be distributed among a large network of cortical areas [58]. As a result an assumption was made that these areas were supported by long-range white-matter pathways connecting the frontal and temporal lobes (arcuate fasciculus) and the frontal and parietal lobes (superior longitudinal fasciculus) [13, 74]. The anatomofunctional correlations between data obtained by IES of the white-matter pathways and post-

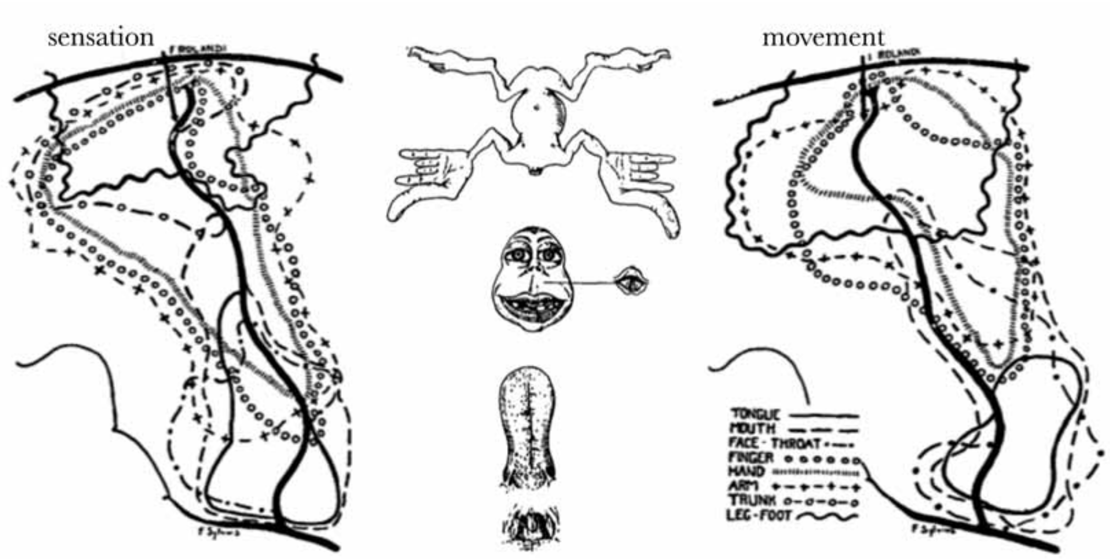

Fig. 2. Wilder Penfield's representation of the areas of stimulations, associated with precise sensory response on the left and motor response on the right hemisphere in 126 patients. Note that motor and sensory areas are not strictly separated by the central (or rolandic) sulcus. The diagram in the middle, which Penfield labeled sensory and motor homunculus [64], is meant as a representation of the comparative size of brain areas associated with different body parts in term of IES results (i.e., a large representation of a body part corresponds to larger area of brain associated with it) (Reproduced with permission from Oxford University Press)

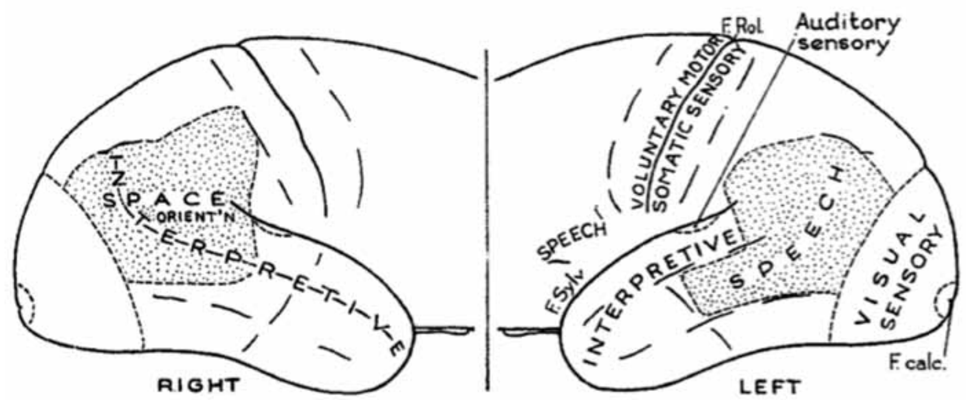

Fig. 3. Wilder Penfield drawing of the areas dedicated to space and speech. "Lateral surfaces of the posterior parts of both hemispheres of a human adult. On the dominant side, local interference-aphasia is produced by a stimulating electrode in the areas marked "speech". Active responses, produced by an electrode on other parts of this interpretive cortex, are of two types – experiential or interpretive. The area marked "space orientation" on the nondominant side (*right*) was outlined by study of the results of cortical excision. Complete removal produces visuospatial orientation impairment (i.e., neglect) in contradistinction to the aphasia produced by destruction of the homologous area on the dominant hemisphere" [62, p 308] (Reproduced with permission from Springer)

operative MRI confirmed in all patients the existence of common pathways that seem essential to language [25]. Even though there was cooperation between neurosurgeons and neuropsychologists, the majority of the studies focused mainly on the mapping of speech functions in the "dominant" left hemisphere.

This focus on the left hemisphere resulted from early fascination and intensive investigation. The attractive simplicity of the Wernicke–Lichteim model [48], combining Broca's hypothesis on the role of the left inferior frontal gyrus in speech [10], Wernicke's hypothesis on the role of the posterior left superior temporal gyrus in the language comprehension, and the white-matter link between these two regions for verbal repetition [80], stimulated the research on language function in the brain. Hence, visuospatial assessment by IES was neglected, overshadowed by the level of interest in the left hemisphere in terms of language functions. Thus, researchers failed to realize the importance of the right hemisphere.

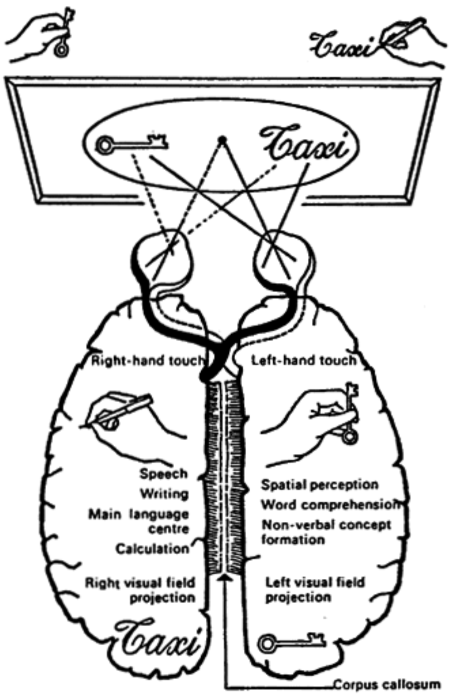

Fig. 4. Roger W. Sperry's illustration of the functional specialization of both cerebral hemispheres. The right hemisphere is shown as dominant for spatial perception, word comprehension, and non-verbal concept formation [17] (Illustration from the Nobel Committee for Physiology or Medicine, based on "Impact of Science on Society" published by UNESCO. © the Nobel Committee)

Interestingly, at the end of his career, Penfield outlined the results of cortical excision of a crucial area in the right hemisphere that, when damaged, led to visuospatial orientation impairment (Fig. 3) (i.e., neglect) [62].

The neglected hemisphere

Whilst it is clear that the left hemisphere has an essential role for language, studies on split-brain patients indicated the right hemisphere networks are crucial for visuospatial processes [35] (Fig. 4).

Visuospatial processing is a broad label referring to a heterogeneous family of processes concerned with the visual interactions with the environment. As with language, several anatomo-functional dissociations have been observed in the visuospatial domain.

For example, response time paradigms and functional magnetic resonance imaging (fMRI) helped dissect distinct forms of visuospatial attention [30, 68, 69].

When attention is dragged by surprise automatically to an unexpected location, fMRI shows increased BOLD (blood oxygen level-dependent; depending on increased oxygen extraction, which should reflect increased neural functioning) response in a ventral attentional network, including the inferior parietal cortex and the inferior and middle frontal gyri, especially in the right hemisphere [15].

When, on the other hand, attention is strategically and voluntarily oriented towards visual targets, more dorsal and bilateral fronto-parietal networks (including the intraparietal sulcus and the frontal eye field) show increased BOLD response [15, 55].

Finally, the general level of arousal or alertness is correlated with more medial cortical regions, principally centered on the cingular gyrus [52].

Damage to these networks in the right hemisphere leads to severe deficits of attentional selection and perceptual consciousness.

For example, patients with vascular strokes in the right hemisphere frequently show signs of left hemispatial neglect [1, 9, 39, 42, 67], "a fairly clear-cut syndrome of inattention directed toward the controlesional visual field" [36]. Neglect patients seem to live in a halved world: they do not eat from the left part of their dish or bump their body into obstacles situated on their left. When copying a linear drawing, they fail to copy the left part of the whole scene or of objects therein. The patients' gaze tends to be captured by right-sided, ipsilesional objects, as if they exerted a sort of "magnetic" attraction due to an imbalance of the attentional distribution between the left and the right hemifield [34].

A quick way to assess the severity of left hemispatial neglect is to ask patients to mark with a pencil the center of a horizontal line [2, 70]. Typically the bisection mark made by neglect patients deviates toward the right extremity of the line as if the left side of the line was underestimated in comparison to the right side. In contrast, patients with visual field defects (left homonymous hemianopia) but without neglect tend to produce bisection errors in the opposite direction (i.e., toward the left) [22], as if they were trying to compensate their sensory deficit by directing their gaze towards the left extremity.

Thus, left hemispatial neglect can be clearly dissociated from hemianopia with a simple line bisection test. Finally, patients with an association of left hemianopia and left hemispatial neglect display rightward deviations even greater than those by patients with "pure" left hemispatial neglect, probably because neglect prevents them from establishing a compensatory strategy for hemianopia [21] (Fig. 5).

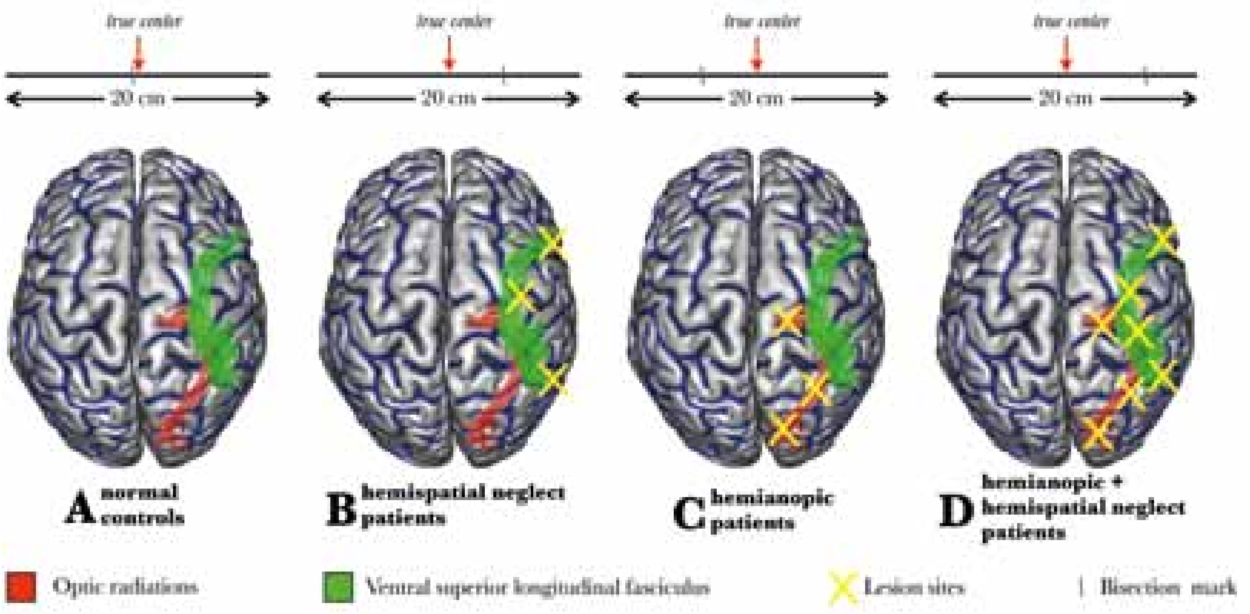

Fig. 5. Pattern of performance in line bisection. **(A)** Normal controls slightly deviate toward the left of the true center of the line (2 mm), a phenomenon reported as pseudoneglect effect and considered as the consequence of the right hemisphere dominance for spatial processing [43]. **(B)** Hemispatial neglect patients show a strong deviation toward the right of the true center of the line [2, 70]. **(C)** Hemianopic patients deviate toward the left side of the line [22]. **(D)** Patients combining neglect with hemianopia demonstrate the greatest deviations toward the right of the true center of the line [21]

Intraoperative assessment of visuospatial functions

IES of visuospatial functions began when a French neurosurgeon trained to use IES on awake patients and a research team dedicated to the study of visuospatial functions met in the historical hospital of the Pitié-Salpêtrière in Paris. Together, they set up a procedure to reduce the probability of a removal of brain areas crucial for visuospatial processing and consequently to preserve patients from developing signs of postoperative hemispatial neglect [72]. Additionally, the use of this protocol allowed them to gather direct evidence on the localization and the functional organization of visuospatial processing in the living human brain.

Two patients were assessed during brain surgery, by asking them to bisect 20 cm long horizontal lines. Patients deviated rightward, upon electrical perturbations of the right supramarginal gyrus (the rostral subdivision of the inferior parietal lobule) and of the caudal part of the right superior temporal gyrus, but performed accurately when more rostral portions of the right superior temporal gyrus or the right frontal eye field were perturbed. More importantly, the strongest deviations occurred in one patient upon perturbations of a white-matter region in the depth of the right inferior parietal lobule, after most of the tumor had been removed. Diffusion tensor tractography on postoperative MRI showed that the tract whose perturbations had brought about the maximal rightward deviation likely corresponds to a branch of the right superior longitudinal fasciculus, the most important frontoparietal pathway. Thus, in this study, functional frontoparietal perturbations dramatically disrupted the distribution of visuospatial attention in the right hemisphere, consistent with previous findings obtained with nonhuman primates [33] and with human patients who had experienced a stroke [4, 20, 46]. Clinically, the neurosurgeon was careful not to remove the regions in which perturbations had pro-

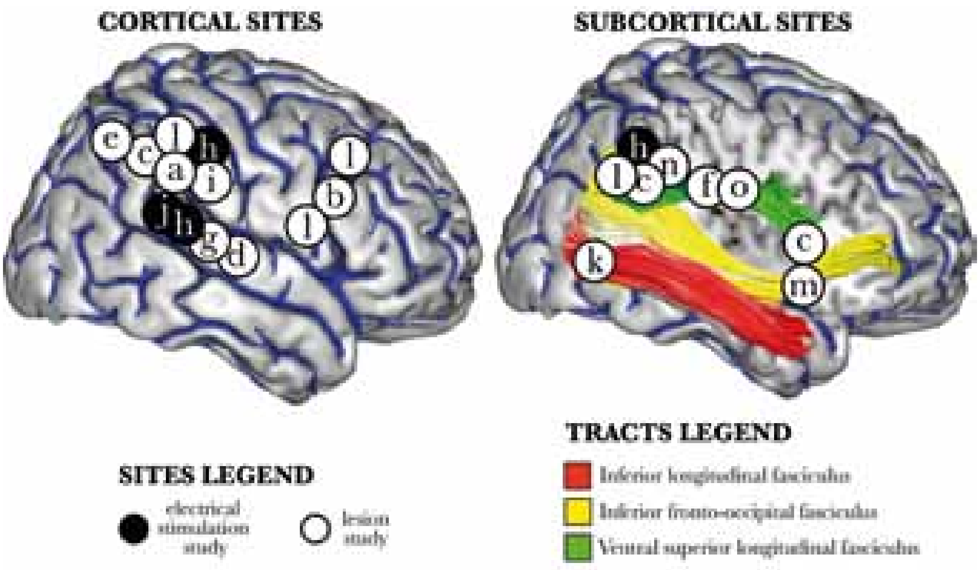

Fig. 6. The mapping of visuospatial functions in the human brain has been driven by group studies of the anatomy of the lesion or IES causing signs of neglect. Meta-analysis of the lesion sites reported in several published papers. Most of the cortical regions reported are parietal (label, reference: *a*, 77; *c*, 46; *e*, 53; *i*, 16; *h*, 72; *l*, 14) or frontal (*b*, 40; *c*, 46; *l*, 14). Other critical areas are also described in the posterior part of the superior temporal gyrus (*d*, 44; *g*, 45; *h*, 72; *j*, 37). Most of the white-matter areas reported belong to the frontoparietal white matter (*c*, 46; *f*, 20; *h*, 72; *l*, 14; *n*, 71; *o*, 78). The frontotemporal inferior longitudinal fasciculus (*k*, 8) and the inferior fronto-occipital fasciculus (*m*, 76) have also been reported as critical white matter pathways leading to hemispatial neglect when disconnected

voked rightward shifts of the subjective line center. As a consequence, a few days after surgery patients showed no signs of hemispatial neglect.

More recently, a study reported the cases of two patients with a right-hemisphere low-grade glioma who underwent neurosurgery [71]. Unfortunately, IES for visuospatial processing was not performed. Both patients showed severe signs of postoperative left hemispatial neglect. In both these cases, postoperative diffusion tensor imaging tractography revealed a disconnection of the frontoparietal pathway.

Those case reports suggest that the combination of preoperative tractography with perioperative mapping of visuospatial function can significantly improve the functional outcome of the patients.

As with all techniques of brain–behavior analysis, direct brain stimulation has limitations. The sites and the number of stimulations are dictated by clinical needs and are often dismayingly limited for the researcher. Phenomena of cortical plasticity, frequent with low-grade gliomas [19, 24, 54, 75], can complicate the interpretation of the mapping data. However, these limitations are not the same as with other methods, such as the lesion studies with nonhuman primates and humans. In the case of visuospatial functions, evidence from all of these approaches [12, 20, 33] converges in underlining an important role of the frontoparietal pathway. However, the study of distinct, parallel networks should also be considered in the future. In particular, lesions to the inferior longitudinal fasciculus [8] and the inferior fronto-occipital fasciculus [76] have been reported in stroke patients with left hemispatial neglect (Fig. 6).

Patients with damage to the left hemisphere may also show signs of contralateral neglect, albeit rarely [6]. According to some theories [38, 50], each hemisphere processes information coming from the contralateral space, but the right hemisphere can also deal with ipsilateral information, albeit slightly less efficiently [51]. Hence, the right hemisphere can compensate to a certain extent unilateral lesions of the left hemisphere, thus giving left-brain-damaged patients some ability to explore the right hemispace. Such compensation may be more difficult for intraoperative testing, where the patient performs the test during the occurrence of the virtual temporary damage induced by IES.

In order to explore the brain areas dedicated to space in the left hemisphere, we collected preliminary data on two right-handed patients with low-grade gliomas in the left temporoparietal region [73]. Patients marked with a pencil the center of a horizontal line with their right, dominant hand during direct cortical and subcortical electrical stimulation. The stimulation of the caudal left superior temporal gyrus and its subcortical white matter, but not the left supramarginal gyrus, determined leftwards deviations on line bisection (Fig. 7). Further work is needed to confirm these preliminary results, but they seem to suggest that left-hemisphere networks for spatial processing are similar, but not identical, to right-hemisphere ones.

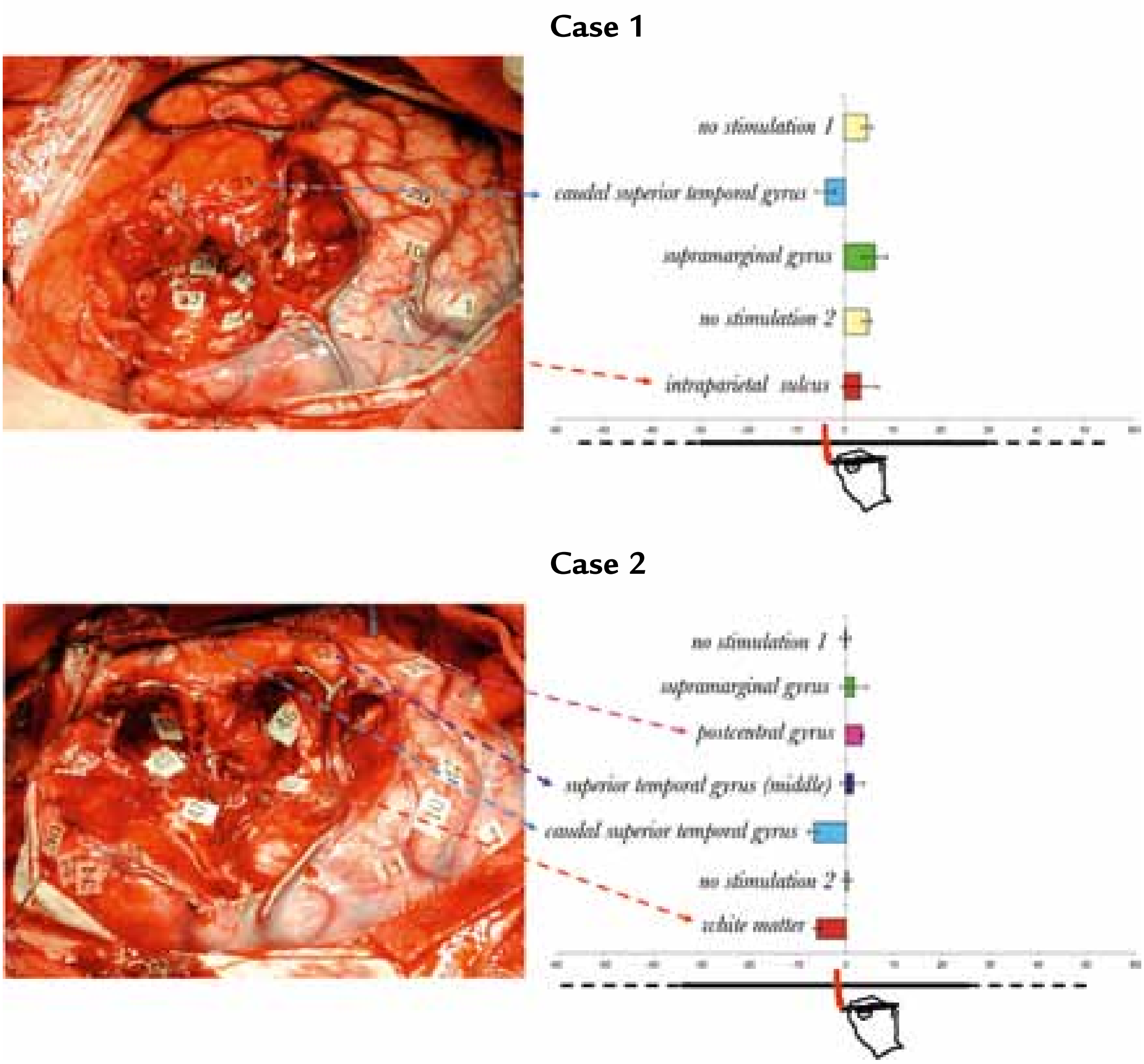

Fig. 7. Performance of two patients in line bisection during IES of the left hemisphere. A picture of the surgical field is shown on the left; mean deviations (in millimeters) with 95% confidence intervals during stimulations are reported on the right

Discussion

IES has rendered possible the study of the living brain functions while preserving functional areas in patients [28]. It also pinpointed directly the importance of the white-matter networks for specific cognitive functions [25–27, 29, 72]. Despite its potential, IES has long remained limited to few functions such as sensory motor capacities and speech abilities. Furthermore, awake IES is too often performed solely during surgery of the left hemisphere. Such a situation does not render justice to the complexity and importance of the functions which belong to the right hemisphere, such as spatial processing, complex and nonlinguistic perceptual tasks, emotion, affect, and paralinguistic aspects of communication [7, 51]. Other right-hemisphere functions are likely to be discovered in the future. Penfield and Perot [65], in their review of 1.288 cases of focal electrical stimulation of the human cerebral cortex, found that highly organized visual or auditory events, which they labeled as "experiential responses", such as seeing people in the room or hearing a song, were exclusively evoked by stimulations applied to the cortex of the temporal lobe. As Brenda Milner once remarked to one of the present authors, the majority of temporal sites whose stimulation evoked experiential responses seemed localized in the right hemisphere. This intriguing possibility, which suggests a deep involvement of the right hemisphere in conscious experience, has never been formally tested. Thus, whereas IES of language functions has advanced significantly; IES of other "high-level" cognitive functions still needs much investigation to reach a similar level of understanding.

Recent mapping results demonstrated that visuospatial functions are distributed on a large frontoparietal network of cortical areas interconnected by long-range association pathways [4, 20, 23, 46, 72]. Surgery-induced visuospatial deficits can be prevented by preserving the cortical areas and subcortical connections dedicated to these functions [5, 71].

The next steps in visuospatial mapping and cognition will be to understand the behavioral dissociations in neglect according to the different sites of lesion and to explore which anatomical nodes between the sensory input and the motor output are crucial to make the visuospatial cognition possible. IES of the right hemisphere is likely to become a key tool to precisely and directly map these complex cognitive abilities on brain structures and networks.

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References

[1] Anton G (1889) Ueber die Selbstwahrnehmung der Herderkrankungen des Gehirns durch den Kranken bei Rindenblindheit und Rindentaubheit. Arch Psychiatr 32: 86–127

[2] Axenfeld T (1915) Hemianopische Gesichtsfeldstörungen nach Schädelschüssen. Klin Monatsbl Augenheilkd 55: 126–143

[3] Bartholow R (1874) Art. I. – Experimental investigations into the functions of the human brain. Am J Med Sci 66: 305–313

[4] Bartolomeo P, Thiebaut de Schotten M, Doricchi F (2007) Left unilateral neglect as a disconnection syndrome. Cereb Cortex 17: 2479–2490

[5] Bartolomeo P, Thiebaut de Schotten M, Duffau H (2007) Mapping of visuospatial functions during brain surgery: a new tool to prevent unilateral spatial neglect. Neurosurgery 61: E1340. DOI 10.1227/01.neu. 0000306126. 46657.79

[6] Beis JM, Keller C, Morin N, Bartolomeo P, Bernati T, Chokron S, Leclercq M, Louis-Dreyfus A, Marchal F,

Martin Y, Perennou D, Pradat-Diehl P, Prairial C, Rode G, Rousseaux M, Samuel C, Sieroff E, Wiart L, Azouvi P; French Collaborative Study Group on Assessment of Unilateral Neglect (GEREN/GRECO) (2004) Right spatial neglect after left hemisphere stroke: qualitative and quantitative study. Neurology 63: 1600–1605

[7] Benowitz LI, Bear DM, Rosenthal R, Mesulam MM, Zaidel E, Sperry RW (1983) Hemispheric specialization in nonverbal communication. Cortex 19: 5–11

[8] Bird C, Malhotra P, Parton A, Coulthard EJ, Rushworth MFS, Husain M (2006) Visual neglect after right posterior cerebral artery infarction. J Neurol Neurosurg Psychiatry 77: 1008–1012

[9] Brain RW (1941) Visual disorientation with special reference to lesion of the right brain hemisphere. Brain 64: 244–272

[10] Broca P (1863) Localisation des fonctions cérébrales. Siège du langage articulé. Bull Soc Anthropol Paris I Ser 4: 200–208

[11] Burdach KF (1819–1826) Vom Baue und Leben des Gehirns und Rückenmarks. Dyk, Leipzig

[12] Buschman TJ, Miller EK (2007) Top-down versus bottom-up control of attention in the prefrontal and posterior parietal cortices. Science 315: 1860–1862

[13] Catani M, Jones DK, ffytche DH (2005) Perisylvian language networks of the human brain. Ann Neurol 57: 8–16

[14] Committeri G, Pitzalis S, Galati G, Patria F, Pelle G, Sabatini U, Castriota-Scanderbeg A, Piccardi L, Guariglia C, Pizzamiglio L (2007) Neural bases of personal and extrapersonal neglect in humans. Brain 130: 431–441

[15] Corbetta M, Shulman GL (2002) Control of goal-directed and stimulus-driven attention in the brain. Nat Rev Neurosci 3: 201–215

[16] Corbetta M, Kincade M, Lewis C, Snyder A, Sapir A (2005) Neural basis and recovery of spatial attention deficits in spatial neglect. Nat Neurosci 8: 1603–1610

[17] Deglin VL (1976) Our split brain. UNESCO Courier 29(1): 4–14, 16, 31–32

[18] Déjerine J (1895) Anatomie des centres nerveux. Rueff, Paris

[19] Desmurget M, Bonnetblanc F, Duffau H (2007) Contrasting acute and slow-growing lesions: a new door to brain plasticity. Brain 130: 898–914

[20] Doricchi F, Tomaiuolo F (2003) The anatomy of neglect without hemianopia: a key role for parietal-frontal disconnection? Neuroreport 14: 2239–2243; Erratum in Neuroreport 15: 217 (2004)

[21] Doricchi F, Galati G, DeLuca L, Nico D, D'Olimpio F (2002) Horizontal space misrepresentation in unilateral brain damage. I. Visual and proprioceptive-motor influences in left unilateral neglect. Neuropsychologia 40: 1107–1117

[22] Doricchi F, Onida A, Guariglia P (2002) Horizontal space misrepresentation in unilateral brain damage. II. Eye–head centered modulation of visual misrepresentation in hemianopia without neglect. Neuropsychologia 40: 1118–1128

[23] Doricchi F, Thiebaut de Schotten M, Tomaiuolo F, Bartolomeo P (2008) White matter (dis)connections and gray matter (dys)functions in visual neglect: gaining insights into the brain networks of spatial awareness. Cortex 44: 983–995

[24] Duffau H (2008) Brain plasticity and tumors. Adv Tech Stand Neurosurg 33: 3–33

[25] Duffau H, Capelle L, Sichez N, Denvil D, Lopes M, Sichez JP, Bitar A, Fohanno D (2002) Intraoperative mapping of the subcortical language pathways using direct stimulations. An anatomo-functional study. Brain 125: 199–214

[26] Duffau H, Gatignol P, Denvil D, Lopes M, Capelle L (2003) The articulatory loop: study of the subcortical connectivity by electrostimulation. Neuroreport 14: 2005–2008

[27] Duffau H, Gatignol P, Mandonnet E, Peruzzi P, Tzourio-Mazoyer N, Capelle L (2005) New insights into the anatomo-functional connectivity of the semantic system: a study using cortico-subcortical electrostimulations. Brain 128: 797–810

[28] Duffau H, Lopes M, Arthuis F, Bitar A, Sichez JP, Van Effenterre R, Capelle L (2005) Contribution of intraoperative electrical stimulations in surgery of low grade gliomas: a comparative study between two series without (1985–96) and with (1996–2003) functional mapping in the same institution. J Neurol Neurosurg Psychiatry 76: 845-851

[29] Duffau H, Thiebaut de Schotten M, Mandonnet E (2008) White matter functional connectivity as an additional landmark for dominant temporal lobectomy. J Neurol Neurosurg Psychiatry 79: 492–495

[30] Fan J, Wu Y, Fossella JA, Posner MI (2001) Assessing the heritability of attentional networks. BMC Neurosci 2: 14

[31] Foerster O, Penfield W (1930) The structural basis of traumatic epilepsy and result of radical operation. Brain 53: 99–119

[32] Fritsch G, Hitzig E (2009) Electric excitability of the cerebrum (Über die elektrische Erregbarkeit des Grosshirns). Epilepsy Behav 15: 123-130

[33] Gaffan D, Hornak J (1997) Visual neglect in the monkey. Representation and disconnection. Brain 120: 1647–1657

[34] Gainotti G, D'Erme P, Bartolomeo P (1991) Early orientation of attention toward the half space ipsilateral to the lesion in patients with unilateral brain damage. J Neurol Neurosurg Psychiatry 54: 1082–1089

[35] Gazzaniga MS, Bogen JE, Sperry RW (1965) Observations on visual perception after disconnexion of the cerebral hemispheres in man. Brain 88: 221–236

[36] Geschwind N (1965) Disconnexion syndromes in animals and man. II. Brain 88: 585–644

[37] Gharabaghi A, Fruhmann Berger M, Tatagiba M, Karnath HO (2006) The role of the right superior temporal gyrus in visual search – insights from intraoperative electrical stimulation. Neuropsychologia 44: 2578–2581; Erratum in Neuropsychologia 45: 465 (2007)

[38] Heilman KM, Van Den Abell T (1980) Right hemisphere dominance for attention: the mechanism underlying hemispheric asymmetries of inattention (neglect). Neurology 30: 327–330
[39] Holmes G (1918) Disturbances of visual orientation. Br J Ophthalmol 2: 449–468, 516–520
[40] Husain M, Kennard C (1996) Visual neglect associated with frontal lobe infarction. J Neurol 243: 652–657
[41] Jackson H (1915) On the physiology of language. Brain 38: 59–64
[42] Jackson JH (1876) Case of large cerebral tumour without optic neuritis and left hemiplegia and imperception. R Lond Ophthalmic Hosp Rep 8: 434–444
[43] Jewell G, McCourt ME (2000) Pseudoneglect: a review and meta-analysis of performance factors in line bisection tasks. Neuropsychologia 38: 93–110
[44] Karnath HO, Ferber S, Himmelbach M (2001) Spatial awareness is a function of the temporal not the posterior parietal lobe. Nature 411: 950–953
[45] Karnath HO, Fruhmann Berger M, Küker W, Rorden C (2004) The anatomy of spatial neglect based on voxelwise statistical analysis: a study of 140 patients. Cereb Cortex 14: 1164–1172
[46] Leibovitch FS, Black SE, Caldwell CB, Ebert PL, Ehrlich LE, Szalai JP (1998) Brain–behavior correlations in hemispatial neglect using CT and SPECT: the Sunnybrook Stroke Study. Neurology 50: 901–908
[47] Lewis J (1981) Something hidden. Doubleday Canada, Toronto
[48] Lichtheim L (1885) On aphasia. Brain 7: 433–484
[49] Mayo H (1827) Brain and spinal chord in man. Burgess and Hill, London
[50] Mesulam MM (1981) A cortical network for directed attention and unilateral neglect. Ann Neurol 10: 309–325
[51] Mesulam MM (1999) Spatial attention and neglect: parietal, frontal and cingulate contributions to the mental representation and attentional targeting of salient extrapersonal events. Philos Trans R Soc Lond B Biol Sci 354: 1325–1346; Erratum in Philos Trans R Soc Lond B Biol Sci 354: 2083 (1999)
[52] Mesulam MM, Nobre AC, Kim YH, Parrish TB, Gitelman DR (2001) Heterogeneity of cingulate contributions to spatial attention. Neuroimage 13: 1065–1072
[53] Mort DJ, Malhotra P, Mannan SK, Rorden C, Pambakian A, Kennard C, Husain M (2003) The anatomy of visual neglect. Brain 126: 1986–1997
[54] Noble M, Dietrich J (2004) The complex identity of brain tumors: emerging concerns regarding origin, diversity and plasticity. Trends Neurosci 27: 148–154
[55] Nobre AC, Sebestyen GN, Gitelman DR, Mesulam MM, Frackowiak RS, Frith CD (1997) Functional localization of the system for visuospatial attention using positron emission tomography. Brain 120: 515–533
[56] Ojemann GA (1971) Alteration in nonverbal short term memory with stimulation in the region of the mammillothalamic tract in man. Neuropsychologia 9: 195–201
[57] Ojemann GA (1986) Mapping of neuropsychological language parameters at surgery. Int Anesthesiol Clin 24: 115–131
[58] Ojemann GA, Mateer C (1979) Human language cortex: localization of memory, syntax, and sequential motor-phoneme identification systems. Science 205: 1401–1403
[59] Ojemann GA, Whitaker HA (1978) The bilingual brain. Arch Neurol 35: 409–412
[60] Ojemann GA, Fedio P, Van Buren JM (1968) Anomia from pulvinar and subcortical parietal stimulation. Brain 91: 99–116
[61] Penfield W (1936) Epilepsy and surgical therapy. Arch Neurol Psychiatry 36: 449–484
[62] Penfield W (1972) The electrode, the brain and the mind. Z Neurol 201: 297–309
[63] Penfield W (1977) No man alone: a neurosurgeon's life. Little, Brown, Boston
[64] Penfield W, Boldrey E (1937) Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain 60: 389–440
[65] Penfield W, Perot P (1963) The Brain record of auditory and visual experience. A final summary and discusssion. Brain 86: 595–696
[66] Penfield W, Rasmussen T (1949) Vocalization and arrest of speech. Arch Neurol Psychiatry 61: 21–27
[67] Pick A (1898) Über allgemeine Gedächtnisschwäche als unmittelbare Folge cerebraler Herderkrankung. Beiträge zur Pathologie und pathologischen Anatomie des Centralnervensystems mit Bemerkungen zur normalen Anatomie desselben. Karger, Berlin
[68] Posner MI, Cohen Y, Rafal RD (1982) Neural systems control of spatial orienting. Philos Trans R Soc Lond B Biol Sci 298: 187–198
[69] Posner MI, Walker JA, Friedrich FJ, Rafal RD (1984) Effects of parietal injury on covert orienting of attention. J Neurosci 4: 1863–1874
[70] Schenkenberg T, Bradford DC, Ajax ET (1980) Line bisection and unilateral visual neglect in patients with neurologic impairment. Neurology 30: 509–517
[71] Shinoura N, Suzuki Y, Yamada R, Tabei Y, Saito K, Yagi K (2009) Damage to the right superior longitudinal fasciculus in the inferior parietal lobe plays a role in spatial neglect. Neuropsychologia 47: 2600–2603
[72] Thiebaut de Schotten M, Urbanski M, Duffau H, Volle E, Levy R, Dubois B, Bartolomeo P (2005) Direct evidence for a parietal-frontal pathway subserving spatial awareness in humans. Science 309: 2226–2228; Erratum in Science 317: 597 (2007)
[73] Thiebaut de Schotten M, Urbanski M, Duffau H, Volle E, Dubois B, Levy R, Bartolomeo P (2007) Networks for spatial attention in the human left hemisphere: evidence from intraoperative stimulation. In: Cognitive Neuroscience Society Annual Meeting Program 2007. Cognitive Neuroscience Society, Davis, CA poster D22

[74] Thiebaut de Schotten M, Kinkingnehun S, Delmaire C, Lehéricy S, Duffau H, Thivard L, Volle E, Levy R, Dubois B, Bartolomeo P (2008) Visualization of disconnection syndromes in humans. Cortex 44: 1097–1103
[75] Thiel A, Herholz K, Koyuncu A, Ghaemi M, Kracht LW, Habedank B, Heiss WD (2001) Plasticity of language networks in patients with brain tumors: a positron emission tomography activation study. Ann Neurol 50: 620–629
[76] Urbanski M, Thiebaut de Schotten M, Rodrigo S, Catani M, Oppenheim C, Touzé E, Chokron S, Méder JF, Levy R, Dubois B, Bartolomeo P (2008) Brain networks of spatial awareness: evidence from diffusion tensor imaging tractography. J Neurol Neurosurg Psychiatry 79: 598–601
[77] Vallar G, Perani D (1986) The anatomy of unilateral neglect after right-hemisphere stroke lesions. A clinical/CT-scan correlation study in man. Neuropsychologia 24: 609–622
[78] Verdon V, Schwartz S, Lovblad KO, Hauert CA, Vuilleumier P (2010) Neuroanatomy of hemispatial neglect and its functional components: a study using voxel-based lesion–symptom mapping. Brain 133: 880–894
[79] Ward AJ (1961) The epileptic neuron. Epilepsia 2: 70–80
[80] Wernicke C (1874) Der aphasische Symptomencomplex. Eine psychologische Studie auf anatomischer Basis. Cohn und Weigert, Breslau