Brain hodotopy: new insights provided by intrasurgical mapping

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Introduction

The dilemma of cerebral surgery is to optimize the extent of resection while preserving brain function [18]. This is particularly challenging when the lesion is located within eloquent areas, which is quite frequently the case, for example, for low-grade gliomas [19]. Since anatomical landmarks are crucial but definitely not sufficient to understand the individual anatomo-functional organization, brain mapping methods should now be used in a systematic manner in both the perioperative and the intraoperative period. Functional cortical mapping is the first step, as regularly reported in the recent literature. However, although detection and preserveration of the axonal connectivity are also essential, the subcortical structures have yet received little attention.

The study of both cortical and subcortical organization is mandatory to avoid postsurgical permanent deficit. Indeed, lessons from stoke studies have thought that a damage of the white-matter pathways generated a more severe neurological worsening than lesions of the cortex. By combining cortical function and axonal connectivity, an updated model of cerebral processing has recently been proposed, moving from a classical "localizationist" view to a "hodotopical" framework [4]. In pathology, according to this new concept, a topological mechanism (from Greek *topos*, place) refers to a dysfunction of the cortex (deficit, hyperfunction of a combination of the two), whereas a hodological mechanism (from Greek *hodos*, road or path) refers to a dysfunction related to connecting pathways (disconnection, hyperconnection, or a combination of the two) [5]. In other words, it is mandatory to take into account the complex functioning of a large-scale distributed cortico-subcortical network to understand both the physiology and the functional consequences of a lesion of this circuit, with possibly different deficits depending on the location and the extent of the damage (e.g., purely cortical or purely subcortical or both).

In contrast to extraoperative electrical mapping, intraoperative direct brain stimulation enables to map not only the cortex before any surgical resection but also the white-matter bundles. Such data are very important to tailor the resection according to functional boundaries and thus to optimize the benefit-to-risk ratio of the surgery. In addition, they provide new insights into brain's processing, with fundamental implications in the field of cognitive neurosciences. The aim is to review the new findings brought by intrasurgical cortical and subcortical electrical mapping, which, in combination with functional neuroimaging, open the door to a "connectionist" view of cerebral functioning [13, 15].

H. Duffau (ed.), *Brain Mapping*

Intraoperative electrostimulation: new insights into the anatomo-functional cortical organization (topos)

Anatomo-functional organization of the supplementary motor area

The supplementary motor area (SMA) – the frontomesial area located in front of the primary motor area of the inferior limb – is involved in the planning of movement. Its resection induces the classical SMA syndrome. This syndrome is characterized by a complete akinesia and even mutism in cases of lesions of the left dominant SMA and occurs approximately thirty minutes after the end of the resection as observed in awake patients [22]. It suddenly and spontaneously resolves around the tenth day after surgery, even if some rehabilitation for 1 to 3 months is often needed in order to allow a better recovery. By preoperative fMRI, it has been shown that the occurrence of this syndrome was not related to the volume of the frontal resection but was directly related to the removal of a specific structure called the SMA proper, detectable on the preoperative imaging. Thus, on the basis of the presurgical fMRI, it is now possible to predict before surgery if an SMA syndrome will or will not occur postoperatively and to inform the patient and his family [41, 42]. Moreover, by coupling preoperative fMRI, the pattern of clinical deficit after surgery, and the extent of resection on the postoperative MRI, the existence of a somatotopy within the SMA proper has been demonstrated, namely (from anterior to posterior), the representation of language (at least in the dominant hemisphere), of the face, then the superior limb, and then the inferior limb (immediately in front of the paracentral lobule) [37]. As a consequence, it is also possible to predict before SMA resection the severity and the pattern of the postoperative transient deficit (e.g., only mutism, mutism and akinesia of the superior limb, or akinesia of the entire hemibody). This has an important impact on the planning of a specific rehabilitation.

Role of the insular lobe in language and swallowing

Although tumors, particularly low-grade gliomas, frequently involve the insular lobe, this structure has long been poorly studied for technical reasons. The insula is an anatomical, cytoarchitectonic, and functional interface between the allocortex and neocortex. Recent studies have enabled to better understand the implication of this multimodal lobe in many functions (for a recent review, see [7]), particularly for language. Indeed, preoperative fMRI has regularly showed an activation of the anterior insular cortex in the dominant hemisphere during language tasks as reported for healthy volunteers. Moreover, these results were confirmed by intraoperative electrical mapping (IEM), which induced language disorders and, more specifically, articulatory disturbances when applied on the insular cortex, supporting a role of this structure in the complex planning of speech [16,20, 21, 36] as previously suggested in stroke studies [9]. These data have important implications for the neurosurgeon, since for a left dominant (fronto-temporo-)insular lesion, resection carries a high risk to be incomplete. Moreover, following resection of gliomas involving the right nondominant insulo-opercular structures, the induction of a transient Foix-Chavany-Marie syndrome can be observed, that is, a bilateral facio-linguo-pharyngo-laryngal palsy with a reversible inability of the patient to speak and swallow [25].

Anatomo-functional organization of the left inferior frontal gyrus

IEM showed that the classical "Broca area" was not basically involved in speech production, but in high-level language processing (such as language switching [51, 52]), with its posterior part (pars opercularis) being more involved in phonological processing, its superior part (pars triangularis) implied in syntatic processing [60], and its anterior part (pars orbitaris) more involved in a large semantic network underlain by the inferior fronto-occipital fascicle [31] (see below). Interestingly, these data provided by IEM are in agreement with those obtained by fMRI, as shown in a recent meta-analysis of the literature [61].

Role of the left premotor cortex in language

Although many studies have allowed a better clarification of the implication of this structure in motor function, its participation in language remains poorly understood. Interestingly, it has demonstrated by IEM that stimulation of the dominant dorsal premotor area (namely, the structure lateral to the SMA, in front of the primary motor area of the hand) induced anomia. On the other hand, stimulation of the dominant ventral premotor cortex regularly elicited anarthria [27]. These results give strong arguments in favor of (i) the involvement of the dorsal premotor cortex in the naming network, in accordance with fMRI studies which have suggested that this region could participate to lexical retrieval and that its engagement might be related to conceptual category, and (ii) the involvement of the ventral premotor cortex in the planification of articulation, explaining why lesion studies have reported that damage of the "lower motor cortex" induced speech apraxia (i.e., aphemia).

Role of the left supramarginalis gyrus in speech and language

In epilepsy surgery, IEM showed that the left supramarinal gyrus was involved in picture naming [53]. More recently, it was demonstrated that stimulation of this structure can also induce speech apraxia [26]. These findings are in agreement with tractography studies which propose that the supramarginal gyrus is a relay between frontal and temporal language sites – the so-called Geschwind territory within the "indirect pathway" [5, 6]. Interestingly, in his model of working memory, Baddeley [1] described an articulatory loop consisting of two parts: a short-term phonological store and an articulatory rehearsal component that can revitalize memorized information. Functional neuroimaging studies suggest that the phonological store involved the left supramarginal cortex, while the subvocal rehearsal system was associated to the left inferior frontal cortex and the ventral premotor cortex [54]. Such knowledge is important during surgery within the supramarginal gyrus and the fronto-parietal loop, in order to avoid postoperative verbal working memory disorders which are still very frequent [10, 57].

Anatomo-functional organization of Wernicke'sar ea

For lesions located in the dominant temporal posterior areas, tasks adapted to test comprehension during IEM have been developped. For instance, a triad of pictures is shown and the patient is asked to pair them by naming two pictures with conceptual links, e.g., a pyramid-and-palm tree test. Interestingly, during stimulation, several sites within the posterior part of the superior temporal gyrus specifically elicited an anomia without comprehension disorders, although other sites within the same gyrus elicited only comprehension disorders with preservation of the ability to name, and other areas generated only phonological disturbances [38]. These results support the complexity of the functional organization of Wernicke's area (in accordance with fMRI results), with its participation, but also with possible dissociation, between comprehension, naming, and phonological processing [61]. In addition, it was recently shown by IEM that the posterior part of the middle temporal gyrus in the left dominant hemisphere was involved in syntactic processing, by eliciting errors of grammatical gender [60]. Furthermore, the posterior part of the superior temporal gyrus seems also to participate in language switching [51, 52].

Role of the right hemisphere in language

This point is extensively discussed in the chapter "Indications of awake mapping and selection of intraoperative tasks".

Role of angular gyrus in calculation

The angular gyrus in the left dominant hemisphere is known to participate in complex cognitive functions, such as calculation. In patients with a left posterior parietal lesion, both multiplication and subtraction can be tested by IEM. Interestingly, functional epicenters more involved in arithmetic facts such as rote multiplication, with tables learned by heart, were found to be located immediately above the posterior end of the sylvian fissure, thus very close to the language sites. On the other hand, actual calculation such as subtraction recruited functional sites located in the superior part of the angular gyrus immediately below the intraparietal sulcus, namely, close to the areas involved in working memory. These results support the existence of a "calculotopy" within the angular gyrus. There was a transient dyscalculia following surgery, but the patients recovered. In addition, these results helped corroborate the "triple code theory" [24].

Involvement of frontal eye field and cingulate eye field in oculumotor behavior

The functional anatomy of the frontal eye field was studied both by preoperative fMRI and by IEM. This region, located laterally and in front of the primary motor area of the face, is implied in the regulation of the voluntary and unvoluntary ocular saccades. Indeed, IEM over this area evoked contraversive smooth eye movements recorded electro-oculographically. In addition, stimulation of an anterior subregion of this electrically determined frontal eye field both disclosed smooth eye movement and interfered with oculomotor behavior, supressing self-paced saccades in awake patient [49]. It is worth noting that the posterior part of the anterior cingulum, namely, the cingulate eye field, also plays a role in suppression of unwanted saccades (antisaccades), thus in attentional processing [50].

Role of the right supramarginal gyrus and posterior temporal areas in spatial awareness

The use of a line bisection task during awake surgery in patients with a lesion involving the right parieto-temporal junction enables the mapping of the areas involved in spatial awareness. A significant rightward deviation is usually observed during the stimulation of the antero-inferior part of the supramarginal gyrus and the caudal part of the superior temporal gyrus [2]. In other words, a transient and reproducible left neglect is induced by electrical inactivation of cortical sites essential for the visuospatial integration, over the right parieto-temporal junction. If these eloquent areas are preserved, the patients show no signs of neglect a few days after surgery. These findings demonstrate that the supramarginal gyrus and the caudal part of the superior temporal gyrus, at least in the right hemisphere, are critical for the symmetrical processing of the visual scene in humans [58].

Role of the left prefrontal dorsolateral cortex in judgment

For lesions located within the left dominant prefrontal cortex, a task of crossmodal (visual-verbal) congruent and incongruent judgment has been performed in awake patient. Visual and auditory stimuli were presented simultaneously, referring to either the same item (congruence condition) or to different items (semantically or phonologically incongruent condition). It was shown that stimulation of brain areas not involved in naming processing elicited reproducible deficit of incongruent judgment, especially at the level of the left dorsolateral prefrontal region, even though an interindividual variability was observed, as for other functions [55]. Preservation of such executive functions is essential for the daily life, in particular regarding the decision-making and planning of complex strategy.

Interestingly, other anatomo-functional correlations can also be made by IEM in awake patients, in particular with regard to writing, reading, memory, emotional processing, or even control of micturition. Thefore, the neurosurgeon must adapt his strategy, particularly the surgical technique (e.g., the selection of the functional tasks to optimize the reliability of the intrasurgical mapping), so as to apply the better knowledge of the functional anatomy to the individual patient.

Intrasurgical stimulation: a new door to the axonal connectivity (hodos)

Beyond cortical mapping, the study of individual anatomo-functional connectivity underlying the eloquent networks is mandatory in brain surgery, in order to avoid postoperative permanent neurological deficit [3, 12, 14, 17].

Motor pathways

For precentral lesions, after detection and preservation of the primary motor cortical areas by IEM, it is also important to detect by subcortical stimulation the corresponding descending motor pathways and their somatotopy, i.e., the different fibers of the corona radiata, with the pyramidal bundles of the lower limb medially, of the upper limb, and of the face more laterally. As at the cortical level, these subcortical motor fibers constitute the posterior and deep functional limits of the resection, until the opening of the ventricle. The pyramidal pathways may also be identified within the posterior limb of the internal capsule, particularly for (fronto-temporo-)insular tumors, in which the deep boundaries of the resection are given when subcortical stimulation induces motor responses in the inferior part of the corona radiata up to the superior part of the mesencephalic peduncles [11, 16, 28].

Somatosensory thalamo-cortical pathways

In the same way, the thalamo-cortical somatosensory pathways and their somatotopy can be identified by IEM, which induces dysesthesias in awake patients, in cases of retrocentral lesions [19].

Visual pathways

Optic radiations can be mapped in patients who undergo awake surgery for temporo-occipito-parietal lesions by the induction of a transient "shadow" (negative effect) or phosphenes (positive effect) in the controlateral visual field during stimulation of the postero-superior and deep part of the surgical cavity, sometimes also with metamorphopsia (i.e., visual illusion) [30]. Thus, if resection is stopped at this level, patients are left with only a residual quadrantanopsia without consequences on the quality of life, especially for their driving.

Language pathways: the anatomo-functional connectivity of language revisited

For left dominant precentral lesions, after identification of the motor and language cortical sites within the prerolandic and inferior frontal gyri (the so-called Broca area), IEM also enables the detection of the language pathways [34]. Medially, IEM can identify the fasciculus subcallosal medialis (running from the SMA and cingulate gyrus to the head of the caudate nucleus), whose stimulation elicits transient transcortical motor aphasia. This tract is involved in the initiation of language [23]. Posteriorly, the fibers coming from the premotor ventral cortex must be detected by a stimulation inducing anarthria. This pathway is crucial for speech production [27]. More laterally, the operculo-insular connections should also to be detected by generating a complete speech arrest during stimulation. These connections are involved in speech planning [36].

In addition to these loco-regional language pathways, subcortical IEM also detect the long-distance association pathways, with first of all, the deep part of the superior longitudinal fascicle – namely the arcuate fascicle (AF) [34] (Fig. 1). In patients with a lesion involving the left insula or the left inferior frontal gyrus, IEM can identify the anterior part of AF, located

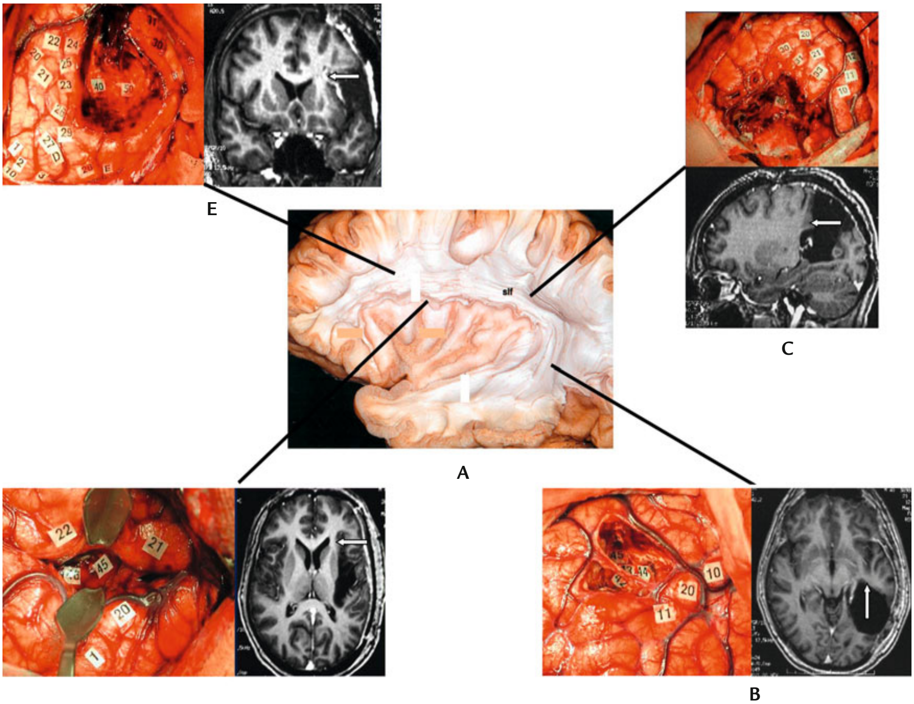

Fig. 1. Arcuate fascicle: dorsal phonological stream. **(A)** Anatomical trajectory of the white matter of the superior longitudinal fascicle (*slf*) studied by dissection. **(B–E)** Surgical field and postsurgical MRI from different patients operated on for a low-grade glioma at various brain locations: temporal **(B)**, parietal **(C)**, insular **(D)**, frontal **(E)**. In all cases, the deep functional boundary of the resection was given by a part of the arcuate fascicle identified by subcortical mapping. Electrostimulation of this tract systematically induced phonemic paraphasia. The precise locations where these language disorders were elicited were marked intraoperatively by number tags in the depth of the cavity. These sites are shown by an arrow on the postoperative anatomical imaging (Reproduced from [34])

within the anterior floor of the external capsule (under the superior part of the insula) and also under the posterior part of Broca's area (namely, the pars opercularis and pars triangularis of the inferior frontal gyrus). Stimulation induces transient symptoms observed in conduction aphasia, i.e., phonemic paraphasia and repetition disorders. In the same way, the AF must also be detected at the level of its postero-superior loop, located under the supramarginal gyrus, in patients operated on for a left parietal lesion. The same symptoms associating phonemic paraphasias and repetition disorders are induced by stimulation. Again, the AF is detected for posterior temporal lesions, the posterior part of its posterior funiculus corresponding to the anterior functional limit of the resection. Finally, the anterior part of the anterior funiculus of the AF must also been used as the posterior functional boundary of left dominant anterior and mid-temporal lobectomy [23]. Interestingly, the left AF seems also to subserve a wide network involved in language switching (from a native language to another language or vice versa): IEM can disrupt such function, crucial to detect and to preserve in bilingual patients [51, 52]. More recently, grammatical gender errors were elicited by axonal stimulation of the left AF, supporting the possible role of this pathway (connecting the middle temporal gyrus and the inferior frontal gyrus, structures whose stimulation induced the same grammatical disturbances) in syntactic processing [60].

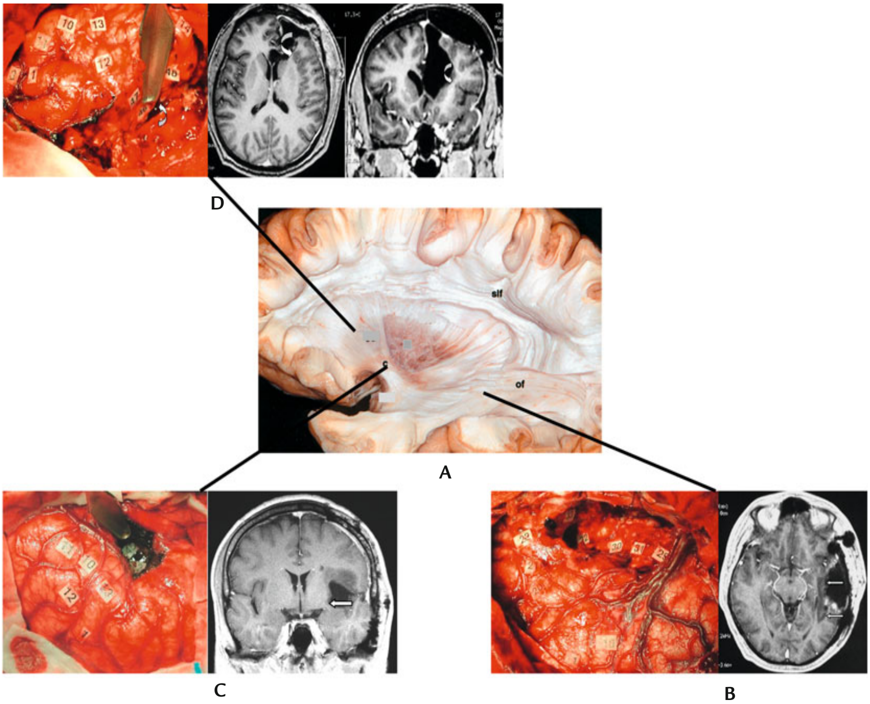

Fig. 2. Inferior fronto-occipital fascicle: ventral semantic stream. **(A)** Anatomical trajectory of the white-matter bundle of the inferior fronto-occipital fascicle (*of*) studied by dissection. **(B–D)** Surgical field and postsurgical MRI from different patients operated on for a low-grade glioma at various brain locations: temporal **(B)**, insular **(C)**, frontal **(D)**. In all cases, the deep functional boundary of the resection was given by a part of the IFOF identified by subcortical mapping. Electrostimulation of this tract systematically induced semantic paraphasia. The precise locations where these language disorders were induced were marked intraoperatively by number tags in the depth of the cavity. These sites are shown by an arrow on the postoperative anatomical imaging (Reproduced from [34])

In addition to the AF, there is a lateral part of the superior longitudinal fascicle. In patients harboring a left retrocentral suprasylvian lesion, IEM detects not only the language cortical sites at the level both of the ventral premotor cortex in front of the tumor and of the supramarginal gyrus and/or angular gyrus behind it but also a fronto-parietal subcortical network whose stimulation induces speech apraxia [26]. This operculo-opercular loop might underly the anatomo-functional connectivity of the working memory circuit. Indeed, this loop corresponds to the anterior segment of an indirect pathway of the classical superior longitudinal fascicle, which runs parallel and lateral to the AF, by connecting Broca's territory with Geschwind's territory in the inferior parietal lobe as recently shown by tractography [6]. This tract might be involved in the vocalization of semantic content. Thefore, this example illustrates well that IEM and diffusion tensor imaging can be combined in order to better understand the anatomo-functional connectivity of the brain [15, 33].

Parallel to this "dorsal phonological root", IEM supported the likely role of the inferior fronto-occipital fascicle (IFOF) in the semantic system, the "ventral semantic root" [31] (Fig. 2). In patients with a frontal lesion immediately in front and above Broca's area, i.e., within the pars orbitaris of the left inferior frontal gyrus and the dorsolateral prefrontal area, the anterior part of the IFOF has been identified under these regions by eliciting semantic paraphasias by subcortical stimulation. In the same way, the IFOF was detected in surgery for left insular lesions by stimulation in its intermediate part located in the anterior floor of the internal capsule (in front and inferior to the AF and behind and superior to the uncinate fascicle) inducing the same symptoms (semantic paraphasias). Again, the IFOF was detected for left temporal lesions by stimulation eliciting semantic disorders; it constituted the deep limit of the resection (above the roof of the temporal horn of the ventricle) [31].

Interestingly, stimulation of the anterior part of the inferior longitudinal fascicle, in front of the visual word form area (i.e., the basal part of the temporo-occipital junction, involved in high-level visual processing such as reading) [43], as well as stimulation of the uncinate fascicle [35], never generated language disturbances. In the same way, stimulation of the anterior part of the middle longitudinal fascicle (i.e., a pathway connecting the angular gyrus to the temporal pole and running under the superior temporal sulcus) never elicited language disorders [8]. Thus, these fasciculi can be removed without risk of aphasia. It seems that this indirect pathway from the temporo-occipital areas to the prefrontal region, with a relay in the temporal pole (temporo-occipital area, inferior longitudinal fascicle, temporal pole, uncinate fascicle, orbito-frontal and prefrontal areas) might be compensated by the direct pathway constituted by the IFOF [34]. It is nonetheless worth noting that the posterior part of the inferior longitudinal fascicle should be preserved, because it plays a crucial role in reading, as demonstrated by IEM which elicited reproducible visual paraphasia and dyslexia during stimulation [44].

Beyond the stimulation of the white matter, IEM also allows the mapping of the deep gray nuclei, sometimes invaded by tumors such as (low-grade) gliomas. Indeed, stimulation of the head of the dominant caudate in patients with a frontomesial lesion coming in contact with the striatum in the depth generally gener-

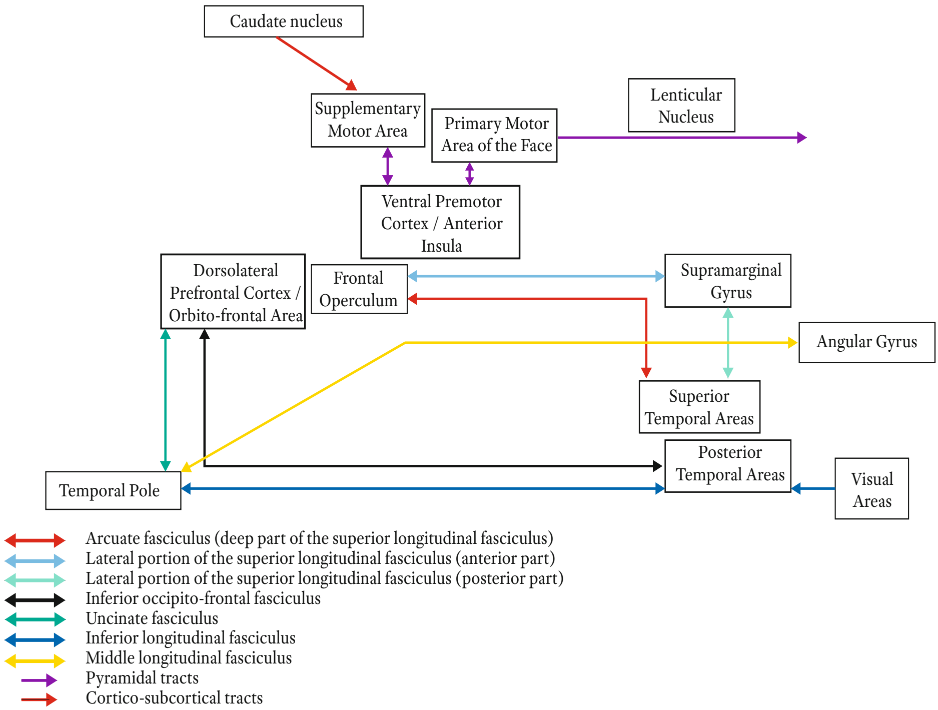

Fig. 3. Scheme of subcortical language pathways

ates perseverations, namely, the repetition of the previous item while the next item is presented to the patient. These results support an inhibitory role of the caudate in the control of cognition [40]. Equally, it is important to map the lateral part of the dominant lentiform nucleus, at the end of the resection of an insular glioma [40]. Lentiform stimulation induces anarthria, supporting the likely role of this structure in the planning of articulation, in association with the insula and ventral premotor cortex [34].

Finally, it is also important to use IEM for language mapping, at both cortical and subcortical levels, for lesions involving the right hemisphere in left-handed and ambidextrous patients [32], or even in some atypical right-handers [59], due to a possible bilateral distribution of language networks, generally, with a mirror organization of both hemispheres. In all cases, these language bundles should constitute the subcortical functional limits of the resection.

Pathways subserving spatial awareness

Using a task of line bisection during awake surgery for patients harboring a lesion within the right parieto-temporal junction (as previously described at the cortical level), IEM must also detect the white-matter tracts implied in spatial processing, in order to avoid postoperative left neglect. During the stimulation of the part II of the superior longitudinal fascicle, a significant rightward deviation is regularly observed [58]. As a consequence, it seems that this parieto-frontal pathway subserves spatial awareness and that a lesion at its level may generate a permanent left neglect.

Stimulation of the right superior longitudinal facsiculus may also induce vertigo, by disrupting a large network between the parieto-insular vestibular cortex, the visual and the sensory-motor areas [56].

These results suggest that damage to restricted regions of white matter can cause dysfunctioning of large-scale cognitive networks. Also, these data show that it is possible to adapt the intraoperative testing to each patient with the goal to map the subcortical pathway underlying cognitive functions other than language. Interestingly, although IEM of the interhemispheric white-matter pathways has been performed, no functional responses were elicited by the stimulation of the corpus callosum. Such results have allowed resection of lesions involving this structure without any consequence on the quality of life, whatever the location of the "callosectomy" [29].

Conclusions and perspectives

In summary, the vision of the neural basis of cognition begins to shift from the earlier localisationist and later associationist view towards the concept of a "hodotopical" organization (i.e., dynamic parallel large-scale networks able to compensate one another). Indeed, from Lichtheim to Geschwind [39], cognitive functions such as language were conceived in associationist terms of centers and pathways, the general assumption being that visual and auditory linguistic information were processed in localized cortical regions with a serial passage of information between regions through white-matter tracts. Presently, an alternative hodotopical account is proposed, in which language is conceived as resulting from parallel distributed processing performed by distributed groups of connected neurons rather that individual centers [15]. In contrast to the serial model of language, in which one process must be finished before another level of processing can be reached by the information, the new models of "independent networks" state that different processes can be performed simultaneously with interactive feedbacks. Interestingly, the recent methodological advances in tractography and intraoperative cortico-subcortical electrical mapping have enabled to study directly in vivo in humans the anatomo-functional connectivity that underlies cognitive functions, supporting and completing Mesulam's large-scale neural network model of language [48]. In particular, it seems that there are at least two parallel pathways, namely, the dorsal phonological stream and the ventral semantic stream, which converge into a common final tract allowing speech production (Fig. 3). Furthermore, this whole network is modulated by cortico-striato-pallido-thalamo-cortical loops. Of course, it is worth noting that the goal of this new concept is not to substitute the cortical centers (topology) with subcortical pathways (hodology) but rather to envision the common interactive processing of both grey and white matters (hodotopy). The next step to progress in the understanding of the brain connectivity might be a more accurate analysis of the interactions between the language circuit and the networks underlying the other cognitive functions, in particular, the visuospatial component, in which the role of the superior longitudinal fascicle has been emphasized, and the emotional and behavioral aspects. Such a multimodal approach seems to represent a unique opportunity to move towards an integrative model of the various functions. In this way, the

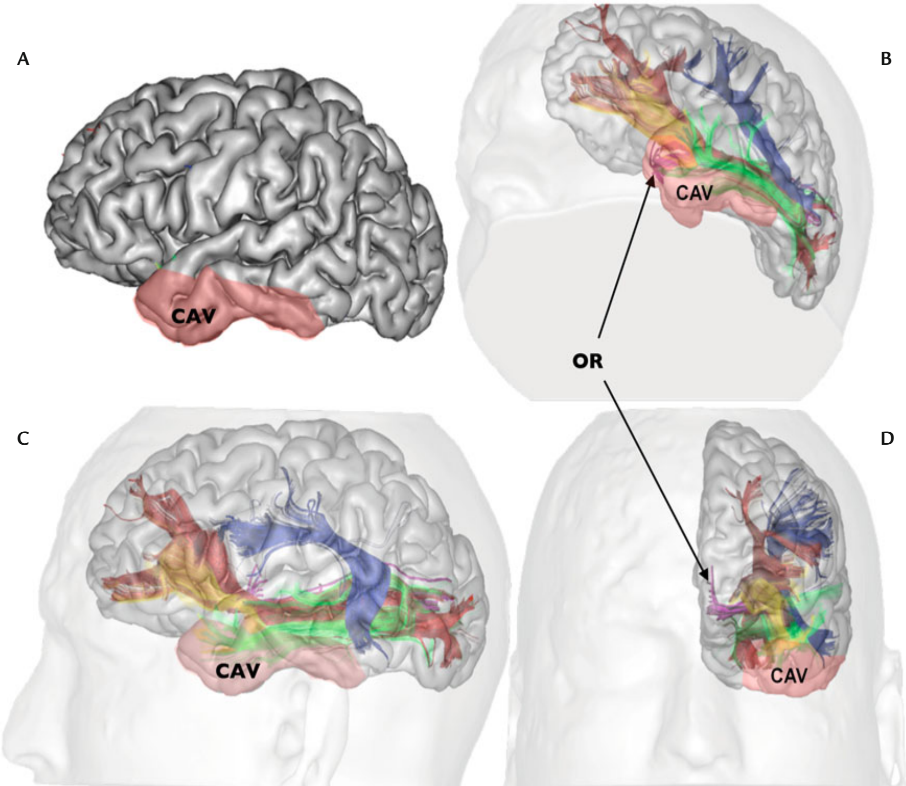

Fig. 4. (A–D). Fiber tracking of the superior longitudinal fascicle (*blue*), inferior longitudinal fascicle (*green*), inferior fronto-occipital fascicle (*red*), uncinate (*yellow*), and optic radiation (*OR*) was performed using regions of interest. A "two-region of interest" approach was used for each fascicle tracking. The procedure consisted in defining a second region of interest at such a distance from the first region of interest that it contained at least a section of the desired fascicle but did not contain any fibers of the undesired fascicle that passed through the first region. Diffusion tensor images and high-resolution three-dimensional anatomical images (**B–D**) were registered by Brainvisa 3.0.2. The derived tracts were displayed by Anatomist 3.0.2 (http://brainvisa.info). We have drawn a virtual resection cavity (*CAV*) according to essential subcortical pathways (IFOF and AF), while removing the "nonessential" tracts (uncinate, inferior longitudinal fascicle and anterior part of the optic radiation). By reporting this cavity on the three-dimensional surface reconstruction **(A)**, we have obtained a resection according to cortical boundaries, similar to those classically reported in the literature (Reproduced from [33])

recent advances in biomathematical modelization of the electrophysiological and hemodynamic signals, which allow a reliable study of the activity time course within the neuronal networks via the analysis of the synchrony (the so-called chronoarchitecture), may open a new door to the effective connectivity, i.e., the influence that one neural system exerts on another.

Consequently, beyond the fundamental interest, it is also crucial for the neurosurgeon to improve her or his knowledge of the anatomo-functional connectivity in order to integrate more easily and more systematically the concept of subcortical mapping in the surgical strategy: first, because gliomas by their nature involve both cortical and subcortical structures and thus they may alter the connectivity; second, because lesions of the white matter may elicit more severe permanent deficits than do cortical damages. To this end, recent insights given by tractography are very useful (Fig. 4). In addition, new anatomic dissections of the white-matter pathways are now to be performed in the light of data provided by axonal mapping, especially with regard to the cortical terminations of the subcortical pathways still poorly known [46, 47]. Indeed, all neurocognitive models should take into account anatomic constraints, an essential point for their validation.

In conclusion, direct electrostimulation of a cerebral region (cortical or subcortical) does not correspond to the stimulation (i.e., a transient virtual lesion) of a "discrete site" but actually corresponds to the stimulation of an input gate to a complex network and thus allows the study of a large-scale distributed circuit in a connectionist framework [45]. In addition, such hodotopical view may explain why some epicenters considered as essential for language in a localisationist model, for instance, Broca's area, in certain conditions can be involved by a tumor (or even surgically removed) with no aphasia, because of a functional compensation within a large distributed network, i.e., the so-called brain plasticity.

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