In the era of functional neurooncology, the main goal of modern neurosurgery should be 2-fold: to have a positive impact on the natural history of disease, especially by increasing overall survival, and to preserve or even improve quality of life. To accomplish this goal, neurosurgeons should achieve the best extent of resection while obtaining optimal functional outcome. This implies not only the avoidance of severe disabling neurological deficits (such as aphasia or hemiplegia) but also the preservation of high-order neurocognitive functions, which are crucial for the enjoyment of normal social and professional lives.


To this end, awake mapping has been shown to represent the most reliable method to optimize “onco-functional balance,” which we define as a compromise between achieving maximum tumor resection together with preservation of maximum function. Indeed, a recent meta-
Selection of intraoperative tasks in awake mapping

analysis (Level 2 evidence) comparing outcomes of glioma surgery with or without intraoperative functional mapping (8091 patients) demonstrated that electrical stimulation allowed a significant increase in the extent of resection as well as a significant decrease in permanent severe neurological deficits.24 However, for a long time, awake surgery was only used for the treatment of tumors located within or near language areas in the dominant hemisphere. Nonetheless, when objective neuropsychological assessments have been performed in tumor patients (for a review, see Klein et al.83) visuospatial, memory, attention, planning, learning, emotional, motivational, and behavioral deficits have regularly been observed after brain surgery.3,4,11,12,19,29,55,70,74,75,78,82,87,90,91,101,102,108,111,113,125,137,141,142,149,154

Because these postoperative deficits may have consequences for quality of life, they should lead physicians to change awake surgery paradigms to prevent such permanent cognitive impairments. Indeed, it was recently demonstrated that an increase in reaction time on the picture-naming task, even with normal scores, could prevent patients from returning to normal professional activities.104 As a consequence, such parameters should be clearly explained to the patient and his or her family before surgery in order to define what the patient would consider “tolerable” and to adapt the extent of resection according to this individual “onco-functional balance.”50

This paradigmatic shift implies most importantly an understanding of the individual cerebral anatomo-functional organization, especially in intrinsic brain disease such as glioma. Neurooncological surgeons should change their philosophy by shifting from “tumor surgery” to “brain surgery” and thus perform resections according to functional boundaries and not according to “oncological limits” (which in essence do not exist in glioma). Intraoperative electrical brain mapping (EBM) is actually the gold standard for identifying eloquent structures, both at the cortical and the subcortical levels, and thus for achieving functional mapping–guided resection (that is, resection until eloquent areas have been encountered) to maximize the benefit-to-risk ratio of surgery.41,43–46 In addition, recent evidence provided by EBM has been the basis for moving from a localizationist view of brain processing (that is, cerebral functions as based in modular and segregated regions) to a hodotopical framework (that is, brain functions as the result of integrated, parallel and dynamic large-scale cortico-subcortical networks).14,16

Selecting the adapted intraoperative neuropsychological tasks to map brain functions for each patient is essential. Therefore, it is time to switch from the traditional awake language mapping to a modern tailored and practical characterization of the anatomo-functional connectivity of individual patients with brain tumors.

Tumor and Brain: Dynamic Interactions Within a Hodotopical Framework

Intrinsic cerebral tumors such as gliomas may not only focally interact with the perilesional brain but may also affect the functional connectivity of the whole brain.138 As a consequence, neurological symptoms can be attributable not only to the anatomical region directly involved by the tumor but also to remote areas belonging to the subnetwork disturbed by the lesion—especially with respect to disorders of higher cognitive functions.22 Thus, one should recognize and preserve the integrity of the functional connectivity to avoid permanent deficits. Interestingly, the use of EBM enables surgeons to build a personalized approach for each patient, taking into account interindividual variability and potential functional reshaping due to brain plasticity, especially in cases of a slow-growing tumor such as diffuse low-grade glioma.22

As mentioned, this technique is the gold standard for preservation of brain function,21,128,135 as long as a rigorous methodology is applied. First, regarding stimulation parameters, a bipolar electrode with contacts spaced 5 mm apart is applied to the brain (pulse frequency 60 Hz, single-pulse phase duration 1 msec, amplitude 1–4 mA) under local anesthesia.96 The optimal intensity is identified by inducing complete arrest of articulation during stimulation of the ventral premotor cortex, to benefit from a positive mapping (that is, successful identification of functional areas) in all cases.38,44,45,51,140 The same stimulation parameters are used to perform the subcortical mapping throughout the resection.41,43–46 It is also mandatory to select tasks adapted to each individual patient (related to his or her job, hobby, possible preoperative neurological or neurocognitive disturbances, results of the presurgical functional neuroimaging) and to each lesion (location, nature, volume, kinetics), also taking into account that there is a time limitation for the intraoperative awake mapping procedure.

The goal of the present review is to describe how to develop a personalized, practical, and efficient intraoperative protocol based on relationships between tumor location and functional networks. Such an individualized protocol could help neurosurgeons to perform awake mapping more safely, not only by applying intraoperative language tasks, but also by selecting additional tasks to map high-order functions essential for optimal quality of life.

Language and Nonlanguage Mapping in Dominant and Nondominant Hemispheres: Lessons From EBM

Language Mapping

Perisylvian regions in the left dominant hemisphere have been classically described as involved in language.105 Consequently, specific tasks have been applied during surgery for tumors located in these areas in order to avoid permanent postoperative oral or written language disturbances. For example, spontaneous speech; counting; object, action, or face naming; reading; and writing have been used to map the superior and posterior parts of the temporal lobe, the inferior parietal lobule, and the lateral part of the frontal gyrus.8,59,73,128

Thanks to these intraoperative tasks, EBM has made possible anatomo-functional correlations, which have led to a revisiting of language connectivity in general. Indeed, a new model has been proposed, based on parallel and
involved in speech articulation, that is, the left dominant cortico-subcortical regions in the left hemisphere are also SLF underlying the dorsal phonological pathway. Other of identifying language pathway when operating within the authors concluded that “these data emphasize the value superior longitudinal fascicle (SLF), connecting the inferior frontal gyrus and the ventral premotor cortex with the posterior temporal cortex and passing through the inferior parietal lobule, is involved in phonological and articulatory language components—eliciting phonemic paraphasia and articulatory disorders when stimulated. Interestingly, in a recent article studying the morbidity profile following aggressive resection of parietal lobe gliomas without subcortical mapping, 13% of patients experienced postoperative dysphasia. Therefore, the authors concluded that “these data emphasize the value of identifying language pathway when operating within the parietal lobe”—supporting the need to preserve the SLF underlying the dorsal phonological pathway. Other cortico-subcortical regions in the left hemisphere are also involved in speech articulation, that is, the left dominant supplementary motor area, anterior insula, and lentiform nucleus (eliciting dysarthria during stimulation). These circuits converge toward a final common pathway within the primary sensory-motor cortex, which elicits dysarthria or anarthria when stimulated during speech. Moreover, this wide network is modulated by corticostriatal loops, eliciting disturbances of language control when stimulated. In addition, the posterior part of the inferior longitudinal fascicle (ILF) plays a crucial role in visual recognition during picture naming tasks as well as in reading and, unlike the anterior part, cannot be compensated. The uncinate fascicle could also be compensated, even in the left dominant hemisphere. A parallel subnetwork subserving writing was also described, constituted by the left supplementary motor area, the Exner area, and the superior and inferior parietal lobules, as well as the SLF.

Mapping of different languages and mapping of sentence translation processing have been performed in multilingual patients. Furthermore, a language subcircuit dedicated to language switching has also been reported. Language control can be transiently impaired, especially during left caudate nucleus stimulation (which elicits perseverations), showing its role in executive functions such as selection, inhibition, programming, and attention processing. Finally, the right hemisphere, which has been described as having a “mirror” configuration, is more devoted to prosody, semantic processing of words and discourse, and processing of context and pragmatic abilities—in addition to its involvement in executive functions, especially attention and working memory.

Mapping of Other (Nonlanguage) Functions

Regarding sensory-motor function, classical intraoperative neurophysiological monitoring using evoked potentials and/or motor stimulation during asleep surgery enables the mapping of muscle contraction during procedures involving the central region in order to prevent hemiplegia. However, movement is not action. By contrast, EBM in awake patients allows some preservation of high-level visuospatial processing, thanks to mapping of not only motor function but also somatosensory, visual, and vestibular functions, as well as mapping of spatial cognition and even of awareness of intending to act. Performing movements of the contralateral hemibody when the resection comes very close to the pyramidal and thalamocortical pathways adds valuable information for preserving fine motor function essential for a normal quality of life.

In the same vein, a complete hemianopia may have a serious negative impact on a patient’s quality of life, affecting activities of daily living, especially because in most developed countries individuals with this condition are not allowed to drive. Mapping the visual pathways is possible using awake EBM procedures for tumors involving the temporooccipital junction, by eliciting both visual positive responses (for example, phosphenes or hallucinations as metamorphopsias) and negative disturbances such as visual field deficits or blurred vision: thus, avoidance of hemianopia should be more regularly addressed.

In addition, cortical areas (especially the right supramarginal gyrus and/or right superior temporal cortex), as well as the subcortical pathway (right SLF) subserving spatial awareness, can be identified and preserved with a high level of reliability during resection within the right parietooccipital junction by asking the patient to perform a line bisection task. Cerebral structures underlying vestibular function, especially the right superior temporal gyrus and posteroinferior parietoinsular cortex connected by the SLF within the “nondominant” hemisphere for language, can also be mapped and preserved during surgery for temporoparietal lesions using intraoperative corticosubcortical stimulation under awake conditions, eliciting reproducible vertigo. Other high-cognitive functions have received less attention but can nevertheless be tested in awake procedures—for example, calculation tasks during resection within the left parietal lobule, especially in the left angular gyrus.

Stimulation during encoding, storage, or retrieval has also been used to map memory function in awake procedures involving dominant premotor areas, left anterior temporal lobe, or fornix. The frontal eye field, eliciting saccades and related to attention and working memory, has also been mapped. Using a nonverbal semantic association test during intraoperative stimulation, it was possible to map the neural basis underlying multimodal (verbal and nonverbal) semantic processing.

Furthermore, judgment tasks of cross-modal (visual–verbal) association have been performed in awake patients undergoing resection of tumors located within the left dorsolateral dominant prefrontal cortex and the posterior temporal cortex, which are connected by the inferior occipitofrontal fascicle. Emotional aspects of facial emotion recognition (“mirror of the soul”) have also been described during awake EBM in patients harboring posterior perisylvian tumors. Finally, the report of an
Selection of intraoperative tasks in awake mapping

experience using a singing task in 5 patients who were singers, described dissociations between speech and singing outside primary sensorimotor areas.121

The Necessity of Adapting Tasks to Each Awake Patient: Development of a Personalized Protocol

Neurosurgeons should keep in mind that functional eloquence cannot be accurately predicted based on anatomical features alone.33,115 Anatomical knowledge is necessary but not sufficient in order to operate on the brain with a high level of reliability, especially in “functional neurooncology.”126 Thus, neurosurgeons have to take advantage of EBM techniques to delineate individualized planning for each patient, dealing with functional boundaries rather than with tumor boundaries when resecting gliomas.118 Indeed, a major interindividual anatomofunctional variability has already been demonstrated, using functional neuroimaging in healthy volunteers151 as well as using EBM in epilepsy patients.105 In a recent report, Ius et al.79 proposed an atlas of functional resectability in patients harboring a WHO Grade II glioma and identified a core of connectivity, the “minimal common brain,” essentially represented by the main association pathways, which should not be resected if permanent deficits are to be avoided. Conversely, the authors found eloquent areas that could be functionally compensated for, especially at the cortical level. The authors concluded that the resectability of a given area cannot be accurately predicted before surgery due to brain plasticity mechanisms, a finding that highlights the crucial role of EBM as the gold standard for on-line anatomofunctional correlations and preservation of eloquent areas during awake surgery in patients with glioma.

Moreover, EBM is not only an intraoperative tool, but is also an input gate into brain functional networks,96 that allows us to better understand the neural foundations underlying cerebral processing. However, physicians have to bear in mind the ethical aspects of this invasive technique and not forget that the first goal of surgery is benefit for the patient, namely to achieve maximal resection while preserving function. As a consequence, it is essential to select the number of tasks strictly necessary to preserve the patient’s quality of life and not to apply too many tests, which could be time-consuming during awake surgery and inefficient or possibly dangerous.

A multidisciplinary approach, involving neurosurgeons, neurologists, neuropsychologists, and speech therapists, is crucial to the building of a tailored and practical intraoperative protocol for each individual patient—with, if possible, selection of sensitive tests able to evaluate more than one cerebral function. For example, the classical “naming task” allows an integrated testing of visual recognition, semantic processing, lexical access, phonological encoding, and speech production at the same time. A real-time accurate analysis of possible functional disturbances elicited by the electrical mapping or resection itself should be performed by a specialist throughout the tumor removal.45

Toward a Tailored and Practical Characterization of the Individual Anatomo-Functional Profile

Selection of intraoperative tasks should be based on both patient and lesion characteristics. Regarding the patient, the physician must first assess hemispheric dominance. To this end, identifying patient handedness is not enough because crossed aphasia has been reported.148 Thus, the most important factor in evaluating cerebral dominance is the existence of a preoperative language deficit, even a subtle one, revealed by an extensive neuropsychological examination. Preoperative neurofunctional imaging may also help to assess hemispheric dominance. Nonetheless, even a low percentage of activation in the right “nondominant” hemisphere during language functional neuroimaging does not mean that this activation is not critical: resection of the area may generate a permanent aphasia. This is the reason why functional MRI cannot be considered as an alternative to EBM, but only as a valuable adjunct to the presurgical cognitive assessment.87

Furthermore, patients’ life characteristics (job, hobby, habits) should play a fundamental role in the selection of intraoperative tasks. In addition to a common protocol, specific tests should be used to measure the particular needs of each patient. For example, a calculation task could be necessary for a mathematics teacher, especially when he or she has a lesion within the left parietal lobe; a judgment task is important in a lawyer; a task of spatial cognition is crucial in a dancer.

Lesion characteristics (location, volume, natural history) must also be considered. As previously seen, intrinsic lesions not only affect a specific anatomical location, but also involve the whole brain functional connectivity. According to this revisited model of “hodotopy” (that is, brain organization in multiple, parallel, and interconnected large-scale cortico-subcortical networks),22 “lobe-specific symptoms” can be generated either by glioma or by electrostimulation within the tumoral lobe and also by stimulation of cortical and subcortical structures (white matter pathways/deep gray nuclei) outside of the “affect ed lobe.” As a consequence, in this review, in an effort to increase reproducibility among neurooncological centers, we will first focus on lesion location to guide intraoperative task selection. However, we will also discuss task selection based on the relationships between the tumor and the functional networks, especially subcortical white matter connectivity.

Selection of Tasks Based on Tumor Location

A schematic diagram showing the various brain regions and preferred testing paradigms is shown in Fig. 1.

Frontal Lobe. Motor function assessment is of paramount importance when dealing with lesions located in frontal cortico-subcortical regions. An intraoperative motor task is mandatory to minimize the risk of permanent contralateral hemiparesis or hemiplegia during resection near or within the primary motor cortex and/or the corticospinal tract at the level of the corona radiata (posterior limit of resection in patients with a frontal precentral
glioma) as well as at the level of the internal capsule and the superior part of the mesencephalic peduncles (which represent the depth of resection in patients with frontoin- sular glioma).\textsuperscript{79}

The frontal premotor cortex (PMC) (medial: supplementary motor area [SMA] and lateral PMC) is devoted to preparation, initiation, and monitoring of complex motor function. Thus, speech articulation and movement disturbances have been reported during awake procedures using EBM, not only at the cortical level but also at the subcortical level. Indeed, these premotor regions are linked through white matter fiber connections to other frontal areas (fronto-frontal short connections),\textsuperscript{15} parietal lobe (articulatory loop),\textsuperscript{43} tempororooccipital areas (IFOF),\textsuperscript{97} and basal ganglia (cortico-striatal control system).\textsuperscript{41} The motor tasks applied to test these functions vary during electrical stimulation, whether the patient is at rest (by provoking nonvoluntary movement in the contralateral hemibody), is moving the contralateral upper/lower limbs, or is performing bimanual complex motor tasks (by disrupting the movement).\textsuperscript{59,98} In addition, language-specific tasks, such as counting, naming, or reading, have been applied to test these premotor areas, because the left dominant PMC plays a major role in language. Indeed, the left SMA may induce slowness of speech or even mutism when stimulated, especially in its anterior part;\textsuperscript{59} the ventrolateral PMC is involved in complex planning of articulation (eliciting anarthria when stimulated), while the dorsolateral PMC is involved in the naming network (eliciting anomia when stimulated).\textsuperscript{44} Indeed, in our protocol, to avoid negative mapping (that is, mapping without successfully identifying functional areas) and thus to increase the reliability of electrostimulation, we systematically begin the cortical mapping by asking the patient to count and by inducing complete arrest of articulation when we stimulate the ventral premotor cortex—allowing identification of the optimal parameters (especially the intensity of stimulation).\textsuperscript{38,44,45,51} In addition, we have recently confirmed the role of the ventral premotor cortex in “complex planning of articulation.”\textsuperscript{146} It is nonetheless worth noting that premotor areas might be resectable in some patients, even in the left dominant hemisphere, thanks to mechanisms of cerebral reorganization; an exception is the left ventral premotor cortex, which appears to be nonresectable due to a limitation of brain plasticity.\textsuperscript{79,146}

Counting, naming, and reading tasks have been widely applied in frontal cortico-subcortical lesions, while stimulating 1) the SLF or its cortical projections, including inferior frontal cortex, inferior parietal lobe, and temporal lobe (eliciting speech production disorders, syntactic disturbances, involuntary language switching, working memory impairment, or phonemic paraphasia [arcuate fascicule]);\textsuperscript{41,43,103,150} 2) the subcallosal fasciculus, connecting frontomesial structures to the striatum (language control disturbances, transcortical motor aphasia);\textsuperscript{41} 3) the anterior part of the IFOF, connecting orbitofrontal/dorsolateral prefrontal cortex with tempororooccipital regions (semantic paraphasia, cross-modal judgment deficit);\textsuperscript{45} or 4) beneath the mouth motor/sensory cortex (dys- or anarthria) as part of a final common pathway allowing final speech production.\textsuperscript{30} Of note, while these findings have been reported mainly for the left dominant hemisphere in right-handed patients, stimulation of the right frontal lobe can also elicit “mirror symptoms” in left-handed and ambidextrous patients, as well as in a subgroup of right-handed patients.\textsuperscript{48,148}

These perisylvian networks, including the anterior part of the IFOF, both on the right and left sides, appear to be non-

\textbf{Fig. 1.} Schematic diagram showing the various brain regions discussed and the preferred testing paradigms for each site.
Selection of intraoperative tasks in awake mapping

resectable—that is, resection should be avoided in order to prevent permanent postoperative deficits. The anterior part of the IFOF represents the deep limit of resection in patients with intrinsic tumors involving the pars orbitalis of the left inferior frontal gyrus or the dorsolateral prefrontal area.

Cortical stimulation of the dominant inferior and middle frontal gyri has also been reported to produce writing disorders, eliciting variable patterns of writing dysfunction, such as writing arrest, illegible script, letter omissions, and paragraphia. Finally, lesions of the cortico-subcortical perisylvian and other prefrontal regions have been reported not only to have language or writing implications but also to produce executive function impairments (in particular, affecting working memory, attention, control, planning, and decision making) and behavioral changes (notably concerning emotional, social, and metacognitive processes). Such findings raise the question whether it is necessary to add complementary intraoperative tasks such as translation, cross-modal visual-verbal judgment tasks, spontaneous speech, social cognition tasks, or even memory-specific tasks to map and preserve these functions. The answer is probably to adapt the selection to the definition of the quality of life at the individual level, on the basis of the patient characteristics discussed above.

Parietal Lobe. It is possible to resect the primary somatosensory area involved in superficial somesthesia, situated immediately posterior to the primary motor cortex, in cases of tumor infiltration without inducing a permanent neurological deficit. This is due to brain plasticity mechanisms and to the learning of new compensatory strategies after an immediate postoperative sensory deficit. However, most of the time, sites involved in protopathic function should be preserved, and this makes awake mapping important. In the same vein, the thalamocortical pathways appear to be nonresectable, marking the anterior and deep boundary of resection in patients with a parietal tumor. Indeed, subcortical stimulation while the patient is at rest may induce paresthesia, dysthesia, or proprioceptive responses in the contralateral hemibody.

In the “dominant” hemisphere, the frontal and parietal lobes represent a subcortical continuum for language network, as the complex combining the SLF and the arcuate fascicle connects the inferior frontal cortex (the so-called Broca area) with the posterior temporal cortex (the so-called Wernicke area) through the inferior parietal lobules (the so-called Geschwind territory). Cortico-subcortical stimulation during a picture-naming task in a patient undergoing tumor resection in this parietal region may generate anomia, phonemic paraphasia, speech production disorders, and even involuntary language switching. Interestingly, verbal working memory impairments have also been observed, especially on postoperative extensive neuropsychological examination after resection of left parietal glioma. Thus, the simultaneous addition of a motor task to a naming task when performing cortico-subcortical resection in perisylvian regions may permit testing of working memory, by applying a double task—as ideational apraxia (disorders in production of learned skilled movements; ability to sequence the movement spontaneously but inability to do so when requested) has been reported after SLF lesions. Interestingly, both (left and right) inferior parietal lobules (supramarginal and angular gyri) have been reported to be essential hubs because lesions in these locations may cause major changes in the network topology. In this light, it is necessary to apply specific tasks to test both language function in the dominant hemisphere and spatial awareness in the right side to avoid a left hemineglect. Toward this end, a line bisection task was found to be a reliable method for minimizing spatial neglect caused by brain tumor surgery in this region. Moreover, cerebral structures underlying vestibular function, which is part of a high-order multisensory system that controls body position, especially the postero-inferior parietoinsular cortex and the SLF within the “nondominant” hemisphere, can also be mapped and preserved using intraoperative stimulation under awake conditions (generating reproducible vertigo). Finally, a finger-recognition task has also been applied, in addition to writing and calculation tasks, during surgical procedures involving the left angular gyrus in order to avoid postoperative Gerstmann syndrome. Indeed, the left parietal lobe is involved in multiplication and subtraction processing using numerical processing tasks, which is why we recommend performing calculation mapping with the aim of preventing anararithmia.

Temporal Lobe. Since the seminal work of Ojemann and colleagues, the picture-naming test has widely been applied to test language function while dealing with temporal tumors, especially in the dominant hemisphere. Temporal stimulation may generate language disturbances at both cortical and subcortical levels. Phonemic paraphasia is elicited by stimulation of the temporal part of the arcuate fascicle, determining the posterior limit of temporal lobectomy. Furthermore, stimulation of the IFOF coursing in the roof of the sphenoid and passing through the temporal stem generates semantic paraphasia. A semantic task of association has been used, as a test of nonverbal comprehension, in addition to the usual naming test in mapping the ventral semantic pathway.

Moreover, the temporocingulate cortical areas and ILF seem to play a role in language and visual recognition tasks. Stimulation of these cortico-subcortical structures may induce a transient deficit impeding access to specific semantic information from the visual modality. Thus, reading and picture naming tasks can help to prevent permanent postoperative deficits in the recognition of written words and in high-order object perception, respectively. On the other hand, the anterior part of the ILF has been shown to be nonessential for language. As a consequence, disconnection or resection of the ILF, as for the uncinate fascicle, can be performed, even in the dominant hemisphere, with no functional consequences on the quality of life. Even though it has been reported to participate in the retrieval of word forms for proper names, the uncinate fascicle is nonetheless part of an indirect semantic pathway that is not essential because it...
can be compensated for by the direct semantic pathway represented by the IFOF.66 Visual function should also be considered in patients with temporal lobe tumors, as the majority of optic radiations run over the lateral wall of the sphenoid horn. Although a single quadrantanopia is typically generated by anterior temporal lobectomy, with no consequences on the quality of life, EBM is necessary to prevent a true visual hemianopsia during resection of postero temporal tumor.54 Recently, a modified naming task using 2 pictures presented in opposite quadrants in a computer screen has been proposed, to map not only language but also visual field.72

Finally, memory function has been tested while performing awake surgery for epilepsy and temporal tumors by applying stimulation during the acquisition, consolidation, and retrieval stages of a verbal short-term memory task: such stimulation elicited recall errors.106,112 The authors of a recent case report described the use of memory testing in an awake patient while performing white matter stimulation to isolate the fornix tracts involved in memory function.10

**Occipital Lobe.** Visual pathways run from the lateral geniculate nucleus via optic radiations to the primary visual cortex, located in the banks of the calcarine sulcus. As previously mentioned with respect to temporal lobe surgery, stimulation of corticocortical occipital areas may also generate visual disturbances during a modified picture-naming task (2 pictures presented in opposite quadrants). Indeed, stimulation may induce perception of a shadow in a specific visual quadrant (visual suppression, especially due to stimulation of the optic radiation), phosphenes (visual perception, in particular due to stimulation of the visual cortex), or visual hallucination as metamorphopsia (detection of associative structures involved in higher-order visual processing).54,86

In addition, occipital associative extrastriate cortex (located in the convexity surface of the posterior occipital lobe) is the main posterior termination of the IFOF.77 In this region, the IFOF subserves the initial semantic visual processing of pictures, that is, visual object recognition and conceptualization.77,152 Moreover, the posterior part of the ILF plays a critical role in language and visual recognition.78 Therefore, as previously noted for the temporoccipital junction, reading and picture naming tasks could be useful to avoid permanent deficits in the recognition of written words and in high-order object perception, respectively.

**Insular Lobe.** The insular lobe lies in the depth of the sylvian fissure and is covered by the opercula of the frontal, parietal, and temporal lobes. The insula represents a critical node for many cerebral functions, including sensory and motor functions, limbic integration, auditory-vestibular functions, and language and speech planning.5,28,40,56,131 Electrical brain mapping techniques may vary depending on the surgical approach to the insular region. If a transpercolar route is chosen, sensorimotor and language mapping has to be done on the cortical surface before the opercula resection, using sensorimotor, counting and picture naming tasks—as previously described for the frontal and temporal lobes.35,40 Within the insula, intraoperative mapping throughout the resection using a picture naming task is mandatory to assess language function in the “dominant” hemisphere. The deep limit of resection is represented by the language pathways—posteriorly, by the arcuate fascicle eliciting phonemic paraphasia when stimulated and, more anteriorly and inferiorly, under the limen insulae by the IFOF inducing semantic paraphasia during stimulation.31 Moreover, stimulation of the lateral part of the lentiform nucleus may elicit articulatory disturbances.84 A motor task is also necessary, whichever the hemisphere, to stop the resection in the vicinity of the motor descending pathways running within the internal capsule and centrum semi ovale.

Interestingly, despite the multifunctional role of the insula, this associative region is reported to be compensable following resection of insular tumor. Indeed, patients recovered in spite of an immediate postsurgical deficit, thanks to the preservation of the subcortical connectivity.52,79

**Selection of Tasks Based on Relationships Between Tumor and White Matter Connectivity**

Graphic presentations of intraoperative tasks based on relationships between tumor location and projection pathways and relationships between tumor location and association pathways are shown in Figs. 2 and 3, respectively. Although a high degree of cortical plasticity has been described, especially in patients with slow-growing lesions, such as low-grade glioma,25,34 subcortical connectivity has been shown to have much more limited plastic potential.79 Consequently, it is crucial to identify and preserve the anatomo-functional pathways using subcortical EBM, because these bundles will define the deep functional boundaries of the resection for intrinsic brain lesions—especially for diffuse gliomas. Indeed, a recent study showed that subcortical injury was an independent predictor of worsening neurological deficits after awake surgery in which only cortical mapping was performed, underscoring the importance of preserving subcortical fiber tracts.142 Therefore, we will discuss how to determine optimal intraoperative tasks, not on the basis of the location of the tumor, but on the basis of a strong analysis of the relationships between the tumor and the white matter tracts.

**Projection Pathways.** The internal capsule and corona radiata contain descending motor fibers from the frontoparietal cortex to the basal ganglia, brainstem nuclei, cerebellum, and spinal cord, and ascending sensory fibers from the thalamus to the cerebral cortex. These thalamocortical sensory fibers intermingle with motor fibers within the centrum semiovale, which represents the posterior limit of resection in patients with a frontoprecentral tumor and the anterior limit of resection in patients with a parieto-postcentral tumor. More deeply, at the level of the internal capsule, these fibers represent the depth of resection in patients with frontotemporoparietal glioma. This is the reason why awake surgery is recommended for treatment of both superficial and deep tumors in the vicinity of pyramidal and thalamocortical path-
Selection of intraoperative tasks in awake mapping

Optic radiations are part of the posterior thalamic projection system and run to the primary visual cortex—superiorly within the parietal lobe, coursing posteriorly, and inferiorly coursing anteriorly around the temporal horn of the lateral ventricle before turning posteriorly (the Meyer loop). Optic radiations maintain a retinotopic organization along their route, allowing for the application of an intraoperative modified naming task with 2 pictures presented in opposite quadrants in a computer screen (see above). Subcortical stimulation of these fibers will induce...
perception of a shadow or phosphenes or hallucinations in a specific visual quadrant. Thus, resection of parietal tumors, occipital tumors, and/or posterotemporal tumors (in either hemisphere) is stopped according to these visual functional boundaries in order to avoid a complete hemianopia. In addition, these fibers form a compact bundle near the ventricular atrium with the ILF and IFOF called the stratum sagittale, which represents the medial functional boundary during the resection of tumors involving the parietooccipital temporal junction.

The fornix is a limbic bundle projection that connects the medial temporal lobe (hippocampus) to the mammary bodies and hypothalamus. Although the fornix is strongly related to memory function, EBM has been successfully used for memory mapping in an awake patient in order to tailor the resection of a tumor impinging on the fornix.

Association Pathways. Association fibers connect cortical centers within the same hemisphere and are subdivided into short (subcortical U-fibers) and long association fibers (deeper in the white matter). The cingulum is a medial long associative bundle, part of the limbic system, that runs all around the corpus callosum from the uncal region in the temporal lobe to the orbitofrontal cortex, connecting the medial temporal, occipital, parietal, and frontal lobes as well as different portions of the cingulate cortex. The anterior cingulum plays a role in attention, volitional control of emotions, and cognitive and motor functions; it is also involved in self-awareness, response selection, and error recognition. Stimulation during the performance of an intraoperative picture naming task may elicit involuntary language control disturbances, such as switching between languages, thus marking the boundary for resection of deep-seated frontal and parietal lobe tumors. Additionally, language control disturbances have also been reported to be elicited during stimulation of the subcallosal fasciculus. This bundle, partially intermingled with the cingulate fascicule, connects the frontomesial structures (cingulate gyrus and SMA) to the striatum. It is involved in initiation and preparation of speech movements.

The SLF is one of the main association bundles; it connects the lateral aspect of the frontal lobe, arching around the insula, with the temporoparietal regions. In the left dominant hemisphere, it is involved in language (deep part, called the arcuate fascicule) and speech articulation (lateral part), while in the right hemisphere, it is involved in visuospatial processing, vestibular function, and some aspects of the superior temporal sulcus. The anterior part of the left MDLF is crucial in the resection of parietal or temporal tumors. Finally, as already discussed, the stratum sagittale, which includes both projection pathways (optic radiation) and association pathways (IFOF and ILF), defines the deep functional boundaries during the resection of parietooccipital and/or temporoooccipital tumors. Electrical stimulation during a picture naming task may elicit semantic paraphasias in this region; stimulation during a semantic task of association may generate impairments of written words, objects, or faces as part of a high-level visual association system. Thus, reading or picture-naming tasks have been used to map this bundle, especially for temporal or occipital tumors. On the other hand, as previously mentioned, the anterior ILF, like the uncinate fascicule, has been demonstrated to be nonessential for language, both structures constituting indirect semantic pathways compensable by the IFOF. The uncinate fascicule connects the anterior temporal lobe with the medial and lateral orbitofrontal cortex, representing a redundant long limbic associative bundle. This bundle has been reported to play a role in emotion, memory, and language processing.

The middle longitudinal fascicule (MdLF) was described for the first time in humans in 2008 using DTI. It is thought to be a white matter fascicule connecting the anterior part of the superior temporal gyrus to the angular gyrus, running between the inferior insular sulcus and the superior temporal sulcus. The anterior part of the left MdLF has been reported not to have an essential role in language, suggesting that the MdLF is part of a redundant and compensatory language network. As a consequence, currently, it has not been shown that its mapping is crucial in the resection of parietal or temporal tumors.

Finally, as already discussed, the stratum sagittale, which includes both projection pathways (optic radiation) and association pathways (IFOF and ILF), defines the deep functional boundaries during the resection of parietooccipital and/or temporoooccipital tumors. Electrical stimulation during a picture naming task may elicit semantic paraphasias in this region; stimulation during a semantic task of association may generate impairments of written words, objects, or faces as part of a high-level visual association system. Thus, reading or picture-naming tasks have been used to map this bundle, especially for temporal or occipital tumors. On the other hand, as previously mentioned, the anterior ILF, like the uncinate fascicule, has been demonstrated to be nonessential for language, both structures constituting indirect semantic pathways compensable by the IFOF. The uncinate fascicule connects the anterior temporal lobe with the medial and lateral orbitofrontal cortex, representing a redundant long limbic associative bundle. This bundle has been reported to play a role in emotion, memory, and language processing.
Selection of intraoperative tasks in awake mapping

in semantic processing, as the deeper component of the IFOF subserves nonverbal semantic processing; and stimulation during a line bisection task may induce spatial perception disturbances in the right hemisphere. In addition, EBM of the optic radiations may elicit visual disturbances (see above). Finally, stimulation of the right ILF may also generate deficits of visual recognition. Of course, confirmatory studies are needed.

Commissural Pathways. Commissural fibers are the cornerstones of functional interhemispheric integration. Among them, the corpus callosum represents not only the largest commissural tract but also the largest fiber bundle of the human brain. It connects the homologous frontal, temporal, parietal, and occipital areas of both hemispheres. Although it was reported to be involved in several motor, perceptual, and cognitive functions, stimulation of this fiber tract does not generate any specific and reproducible clinical response in awake patients. Therefore, it is possible to perform limited callosections when this structure is involved by a tumor to improve the extent of resection, on the condition that the association white matter pathways of the contralateral hemisphere are spared. The anterior commissure crosses the midline just anterior to the columns of the fornices, connecting the anterior and ventral temporal lobes of the 2 hemispheres. The functions of the anterior commissure have been poorly described, and no EBM study to date has reported any specific task to map this bundle in awake patients.

Proposal of a Minimal Common Protocol

In light of these recent data, we propose the elaboration of a minimal common protocol, testing not only language but also other cognitive functions, which could be applied preoperatively, intraoperatively, and postoperatively in awake tumor surgery. The goal would be to facilitate reproducibility among the different neurooncological centers.

We suggest that a minimal standard pre- and postoperative protocol to test language function may include (Table 1): a subjective questionnaire/complaints inventory, assessment of handedness, assessment of fluency/informativity (spontaneous speech), a naming task with calculation of reaction time, a timed semantic association task, and a timed reading task. Of course, it would be possible to add more tasks depending on variables related to the individual patient (for example, his or her job) and the tumor location (especially the relationship to specific pathways). Examples of these specific tasks might include pragmatics of language, repetition, or reading and writing.

A proposal for a pre- and postoperative protocol to test nonlanguage functions may include: a subjective questionnaire/complaints inventory and assessment of information processing speed, working memory, executive functioning (flexibility, inhibition) motor and reflexive praxis, and visuospatial cognition. Again, it could be possible to add more tasks that would assess various aspects of social cognition or emotion as needed for individual patients.

Moreover, in this review, we focused on the selection of intraoperative tasks, on the basis of a better knowledge of dynamic functional anatomy (distinction between compensable areas versus minimal common brain), to help neurosurgeons in clinical practice. To this end, we propose the following minimal common intrasurgical protocol.

For Tumors Involving the (Left) “Dominant” Hemisphere

For tumors in the frontal, parietal, temporal, and insular lobes, at the cortical level, mapping would include a counting task (ventral premotor cortex), sensory-motor mapping (central region), and a picture naming task ( cortical language sites); at the subcortical level, it would include double tasks combining picture naming and continuous movement (subcortical language networks, sensory-motor pathways, and attentional processing/working memory, thanks to double task). Of note, for parietotemporoccipital tumors, naming tasks should include 2 pictures presented in opposite quadrants to map optic radiations.

For tumors restricted to the occipital lobe, only a picture naming task would be included.

For Tumors Involving the (Right) “Nondominant” Hemisphere

For tumors involving the “nondominant” hemisphere, a line bisection task should be used (in addition to the above tasks) throughout the resection to map visuo-spatial cognition.

Additional Tasks

Finally, we should insist on the fact that, in addition to such a common protocol, further tasks should be incorporated according to the specific needs of each patient. Among other tasks, these might include tests of calculation; semantic tasks of association; tasks involving cross-modal visual-verbal judgment; reading; writing; naming in different languages (for multilingual patients); or assessment of facility with syntax facility.

Utility of the Suggested Tasks

Of course, these tasks are only proposed. It is nonetheless worth noting that they have already been validated on the basis of favorable functional outcomes reported in hundreds of glioma patients following extensive resection, performed according to functional boundaries identified thanks to the use of these tasks during cortical and subcortical mapping. Beyond language, we have already demonstrated that intraoperative mapping has also allowed the preservation of high neurocognitive functions, such as working memory, spatial cognition, calculation, language switching, cross-modal judgment, and cognitive control.

Conclusions

The optimization of selection of intraoperative tasks for awake surgery is based on an improved understanding of the individual patient’s functional anatomy and
brain connectivity, as well as their interactions with the natural course of the tumor. The intraoperative protocol may include a minimal common core, which may then be adapted to the individual patient by the incorporation of additional tests chosen on the basis of his or her specific profile, to preserve an optimal quality of life. Only an interactive multidisciplinary collaboration will improve our understanding of the neural basis of cerebral functions and will enable transfer of this knowledge to daily neurooncological practice.

**Disclosure**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**Author contributions to the study and manuscript preparation**

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**References**

Selection of intraoperative tasks in awake mapping


37. Duffau H, Capelle L: [Functional recuperation after resection of gliomas infiltrating primary somatosensory fields. Study of perioperative electric stimulation.] *Neurochirurgie* 47:534–541, 2001 (Fr)


41. Duffau H, Lopes M, Arthuis F, Bitar A, Sichez JP, Van Effen-

A. Fernández Coello et al.


156. Zimmermann P, Fimm B: Test for Attentional Performance (TAP), Herzogenrath, Germany: PsyTest, 1995

__________

Please include this information when citing this paper: published online September 20, 2013; DOI: 10.3171/2013.6.JNS122470. Address correspondence to: Hugues Duffau, M.D., Ph.D., Department of Neurosurgery, Hôpital Gui de Chauliac, CHU Montpellier, 80 Av Augustin Fliche, Montpellier 34295, France. email: h-duffau@chu-montpellier.fr.