

Is intraoperative mapping of music performance mandatory to preserve skills in professional musicians? Awake surgery for lower-grade glioma conducted from a meta-networking perspective

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OBJECTIVE In surgery for lower-grade glioma (LGG) in professional musicians, for whom preserving music ability is essential, a critical question has emerged, namely, is it mandatory to include music performance during awake mapping, as proposed in several reports? In fact, music ability is subserved by a mosaic of interactive cognitive and emotional processes that rest on several networks. Therefore, from a meta-network perspective, the authors investigated whether an integrated multimodal monitoring of these cognitive and emotional functions during stimulation mapping could be efficient in maintaining musical skill. Indeed, it could be difficult for a patient to play a musical instrument in the surgical setting in addition to performing other tasks, such as movement and language.

METHODS An awake mapping-guided resection for LGG without intraoperative music performance was performed in 3 professional musicians. Intraoperative tests were tailored to each patient depending on the critical corticosubcortical circuits surrounding the tumor, including not only sensorimotor or language skills but also higher-order functions with a constant multitasking during the resection.

RESULTS Although music skills were not mapped during surgery, all patients resumed their professional activities, preserving the ability to play music and to perform concerts, to teach and to compose music, or to start learning a new instrument.

CONCLUSIONS A connectome-based resection without intraoperative music performance seems effective in achieving maximal glioma removal while preserving crucial networks subserving musical skills, creativity, and music learning. Neurosurgery should evolve toward a meta-networking approach to better understand higher-order functions mediating complex behavior, such as being a professional musician.

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KEYWORDS awake surgery; connectome; lower-grade glioma; meta-networking theory; musicians

Music ... can name the unnamable and communicate the unknowable.

— Leonard Bernstein

Is music the most important thing we ever did?

— Ian Cross, in Yi SW, ed. *Music Mind and Science*, Seoul National University Press; 1999

Why does our neural reward system get fired because of listening to music?¹ Why is our connectome able to feel pleasure because of an abstract pattern of sound that appears instantly?²⁻⁴ These questions about music, one of the most complex human abilities, have represented for many decades a challenge for neuroscientists, trying to disentangle music's neurobiological, philosophical, and

ABBREVIATIONS DES = direct electrical stimulation; LBT = line bisection task; LGG = lower-grade glioma; PPTT = Pyramids and Palm Trees Test; QOL = quality of life; RME = Read the Mind in the Eyes; SLF = superior longitudinal fasciculus; vPMC = ventral premotor cortex.

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sociological underpinnings.^{3,5,6} Beyond being a perfectly designed vehicle to evoke emotions, the ability to create music necessitates, in addition to sensorimotor and auditory skills, an optimum interaction between several higher-order functions mediating perception,^{5,7,8} attention,⁹ self-awareness^{10,11} and metacognition,¹² creativity,¹³ emotional processing,^{5,6} and social cognition.^{14,15}

Despite this large framework involved in musical skills, previous case series in the literature reported the results of awake surgeries for brain tumors in musicians focusing mainly on music performance by means of singing, humming, melody recognition, score reading, or instrument performance,^{16–19} as if this complex ability could be reduced to a modular function that would be subserved by a specific network acting in isolation. In fact, because music ability is subserved by a mosaic of interactive cognitive and emotional processes that rest on several networks, our main goal was to carry out an intraoperative complex cognitive assessment individualized to each patient from a meta-networking standpoint,^{20,21} namely, by taking into consideration coordination between sensorimotor function and language as well as higher-order functions such as semantics and mentalizing.^{22–24} Indeed, recent advances in connectomics, especially based on neuroimaging and computational neuroscience, have shown that the constant changes in interactions between neural connections^{20,25,26} subserving conation, cognition, and emotion²¹ allow the production of context-sensitive, adapted, complex behaviors.²⁷ This implies that neurosurgery needs to go beyond the classic glioma topography approach to maximize the onofunctional equilibrium between the extent of resection and quality of life (QOL), that is, to evolve toward a modern connectome-oncological neurosurgery,^{28–31} especially in patients with specific professional activities that require complex abilities, such as musicians.

In this paper, we present a case series of professional musicians who underwent an awake surgery for a lower-grade glioma (LGG) based on the meta-networking theory of brain functioning.²⁰ In other words, we considered that music skills were mediated by integrated cognitive systems, and thus, we asked patients to carry out personalized multithread monitoring throughout the resection. This online cognitive monitoring consisted of a tailor-made constant multimodal parallel tasking with periodic changes of cognitive tasks based on the circuits surrounding the tumor and adapted to the professional and personal life of each patient; in this series, they all are professional musicians. Our results show that assessment of musical performance during surgery, which could be difficult to achieve with a high level of reliability in the surgical setting, is not mandatory for musicians to resume a normal professional and creative life.

Methods

We retrospectively analyzed the database of patients who underwent awake surgery for LGG at the Department of Neurosurgery at Montpellier University Medical Center from 2009 to 2022. Only those patients who were professional musicians and for whom musical skills were crucial not only to maintain their professional activities, but also

their personal QOLs were selected. This research was approved by the French College of Neurosurgery.

In the present study, we thoroughly describe 3 cases from the onset and surgical decision to the direct electrical stimulation (DES) mapping in an awake condition and the postoperative period where a regular neuropsychological assessment was performed until the patients returned to their professional musical activities. Within the description of each case, emphasis is placed on 1) the tailored selection of intraoperative tasks to be performed during the functional mapping,³⁰ 2) personalized constant multitasking throughout the resection,³² and 3) the preservation of white matter pathways surrounding the tumor (which have been demonstrated as essential to preserve QOL) describing the connectome-stop points for each of the tracts.^{33,34} In other words, we identified *in vivo* the behavioral impairment elicited by DES that allows us to identify where to interrupt the resection beyond glioma topography, based on a meta-networking approach to optimize the onofunctional balance.

Results

Case 1

A 35-year-old right-handed female professional piano teacher, mother of a 3-month-old child, and polyglot (speaking four languages with a high level of proficiency) presented with a first seizure with speech arrest. A hyperintense lesion was observed on T2-weighted/FLAIR imaging within the junction between the left middle temporal gyrus and the angular gyrus suggestive of an LGG (Fig. 1A). Awake surgery was proposed to carry out corticosubcortical mapping and monitoring of her three main languages (French, English, and Russian), visual function (given the infiltration of optic radiations), and attention and executive functions. After performing a craniotomy that allowed us to expose the ventral premotor cortex (vPMC), the tumor boundaries were identified with ultrasonography and marked with letter tags (Fig. 1B). A speech arrest was elicited during DES of the vPMC (tags 1 and 3) at 3 mA (by using a 60-Hz biphasic current). Dysarthria was also evoked by stimulating the retrocentral portion of the Rolandic operculum (tag 2). A naming task was performed by switching regularly between all languages, highlighting a reproducible critical region within the supramarginal gyrus (tag 5) and within the posterior part of the middle temporal gyrus in which anomia was generated in all languages (tags 4, 6, and 7). While the patient continued to perform multitasking combining right upper-limb movement with the naming task, itself with a switch between the three languages, without any rest (to increase the cognitive demand by recruiting executive control^{32,35}), a corticectomy was performed on both sides of the superior temporal sulcus through a subpial dissection. At the bottom of the sulci, the posterior part of the arcuate fascicle was identified on both the temporal (tag 46) and parietal (tag 40) sides (see Fig. 3B lower), by inducing highly reproducible phonemic paraphasias. A subtotal resection was performed, leaving a 4-cm³ residual tumor within the superior longitudinal fasciculus (SLF) to preserve the subcortical connectivity (Fig. 1C). Pathological examina-

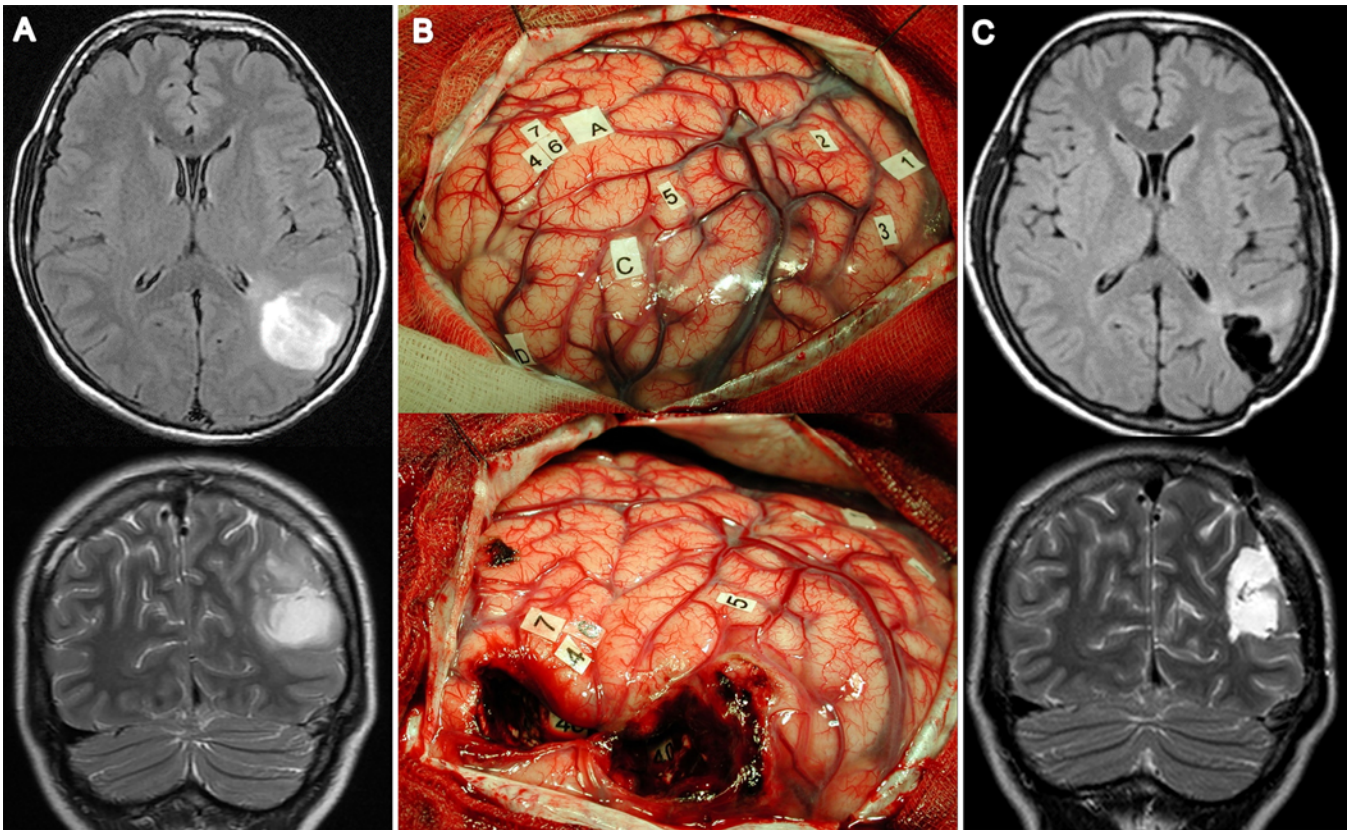


FIG. 1. Case 1. Awake resection of a WHO grade 3 oligodendroglioma involving the left parietotemporal junction in a piano teacher. **A:** Preoperative axial FLAIR (*upper*) and coronal T2-weighted (*lower*) MR images showing a left glioma. **B:** Intraoperative photographs obtained before (*upper*) and after (*lower*) connectome-based resection. **C:** Postoperative axial FLAIR (*upper*) and coronal T2-weighted (*lower*) MR images showing a subtotal resection.

tion revealed a WHO grade 3 oligodendroglioma (IDH mutated), and adjuvant temozolomide was administered. The patient was able to return to her job as a piano teacher 3 months later, with a normal social and family life and without feeling any differences between the preoperative and the postoperative periods in her ability to play and teach piano.

Case 2

A 36-year-old right-handed female professional singer, guitarist, and composer experienced a partial left brachiofacial somatosensory seizure leading to an imaging discovery typical for a diffuse LGG involving the right angular gyrus (Fig. 2A). Awake surgery with DES was proposed to perform a connectome-based resection while monitoring sensorimotor functions, visuospatial cognition, multimodal semantic cognition, and social cognition (mentalizing). The tumor boundaries were detected by ultrasonography and marked with letter tags (Fig. 2B). At the level of the vPMC, DES induced both a speech arrest and a left upper-limb movement arrest at 2 mA (tags 1 and 2). More medially, the primary motor area of the face was identified (tag 4). Dysesthesias were evoked at the level of primary somatosensory cortex of the face (tag 3) and of the left upper limb (tags 5, 6, and 7). Hereafter, the pa-

tient was asked to perform a line bisection task (LBT),³⁶ evoking a deviation of 15 mm to the right by stimulating the supramarginal gyrus (tag 8). Finally, the Pyramids and Palm Trees Test (PPTT)³⁷ and the Read the Mind in the Eyes (RME)³⁸ test were used to monitor multimodal semantics and social cognition, respectively. No disturbances in these higher-order cognitive functions were found during cortical stimulation. A corticectomy was carried out according to the functional boundaries, and a resection was performed while the patient was constantly multitasking (left upper-limb movement combined with PPTT and naming alternated with LBT and RME in a nonserial or fixed order).³² The right angular gyrus was completely removed until the posterior aspect of the superior temporal sulcus. In the depth, the fiber bundles were identified to preserve the connectivity as follows. 1) A feeling of dizziness and nausea was induced during DES of the anteroinferior part of the cavity (tag 46), probably due to stimulation of fibers of the vestibular network, since the same phenomenon was induced at the level of the white matter immediately underneath the cortical surface (tag 50). 2) Stimulation of the SLF-II (tags 49 and 45) evoked a significant deviation to the right during the LBT (up to +25 mm). 3) The inferior fronto-occipital fasciculus represented the posterior limit of the cavity (tag 47), stimulation of

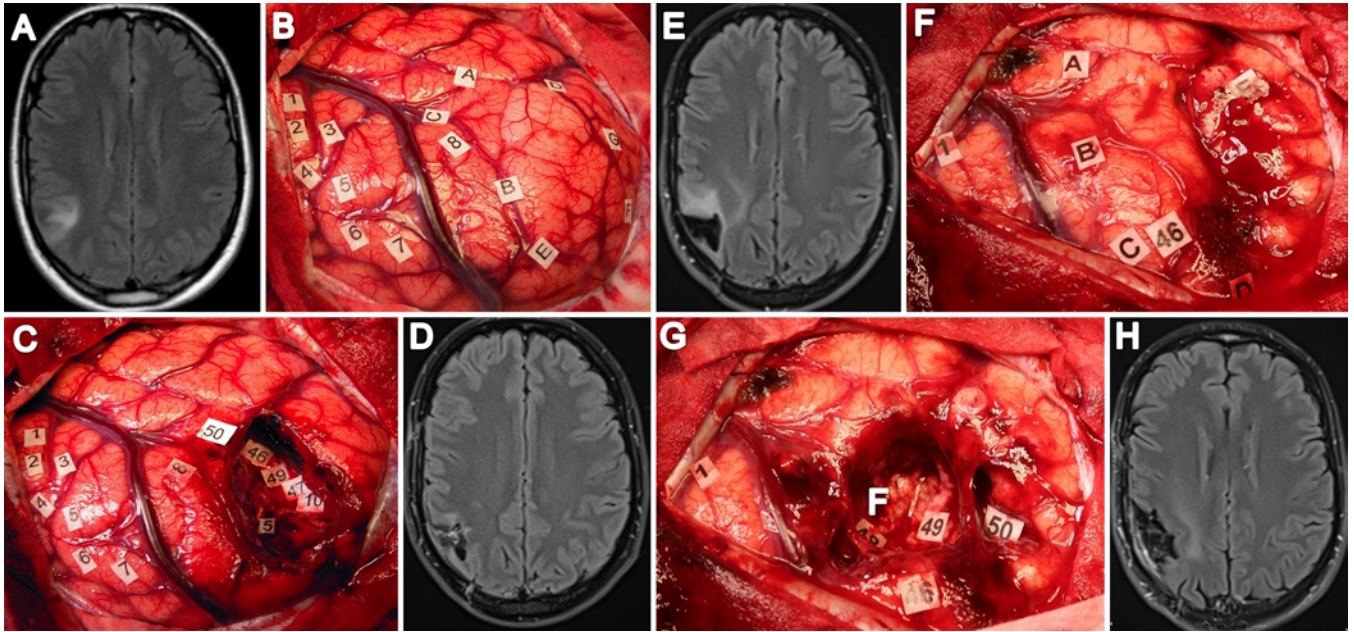


FIG. 2. Case 2. Awake resection of a right parietal WHO grade 2 astrocytoma in a singer, guitarist, and composer. **A:** Preoperative axial FLAIR MR image revealing a right parietal glioma. **B:** Intraoperative photographs obtained before connectome-based resection. **C:** Intraoperative photographs obtained after connectome-based resection. **D:** Postoperative axial FLAIR MR image showing a total resection. **E:** Preoperative axial FLAIR MR image showing a tumor relapse. **F:** Intraoperative photographs obtained before the second resection. **G:** Intraoperative photographs obtained after the second resection. **H:** Postoperative axial FLAIR MR image showing a subtotal resection.

which induced disorders in emotional recognition, naming, and comprehension. 4) Stimulation of the optic radiations in the most posterior and deepest part of the cavity (tag 10) evoked phosphenes in the left visual field (Fig. 2C). MRI showed a total resection (Fig. 2D). Histological examination revealed a WHO grade 2 astrocytoma (IDH mutated), and no adjuvant treatment was administered. Three months after surgery, the patient was able to return to a normal life by singing and guitar playing, releasing an album, and giving concerts.

Four years later, MRI showed a recurrence at the level of the right inferior parietal lobe (Fig. 2E). A reoperation was proposed, following the same procedure. During cortical DES, the primary somatosensory area of the patient's face was identified, causing a speech arrest at 2.75 mA (lateral part of the postcentral gyrus, tag 1) (Fig. 2F). During the LBT, a systematic deviation +15 mm to the right by stimulating the upper part of the supramarginal gyrus was elicited (tag 46). No disturbances were found during PPTT or mentalizing tasks during cortical DES. A corticectomy was carried out while the patient performed continuous multitasking (as described above), allowing us to remove the right supramarginal gyrus while preserving site 46. Subcortical DES was achieved to find the white matters and preserve them, as follows: 1) thalamocortical somatosensory bundle (tag 48) inducing left hemibody dysesthesias; 2) optic radiations (posteromedially in the depth, tag 50), eliciting visual disturbances in the left hemifield; and 3) SLF-II (tag 49) with a rightward deviation (10–15 mm) during the LBT (Fig. 2G). Postoperative MRI demonstrated subtotal removal with a FLAIR hypersignal still

visible (Fig. 2H) because of residual infiltration within the critical white matter tracts. Pathological examination confirmed the diagnosis of WHO grade 2 astrocytoma (IDH mutated). After 3 months, the patient was able to return to a normal social and professional life, composing new songs and again performing concerts.

Case 3

A right-handed 32-year-old male professional singer, guitarist, and composer experienced visual seizures. MRI showed a T2-weighted/FLAIR hypersignal within the left occipital lobe suggestive of a diffuse LGG (Fig. 3A). Given the high risk of homonymous hemianopia, the patient refused surgery at that time, and close clinical and imaging follow-up was performed. After 2 years, the FLAIR hypersignal was substantially larger, and the patient decided to undergo a biopsy. The pathological examination revealed a WHO grade 2 astrocytoma (IDH1 mutated). Because of worsening seizures despite antiepileptic drugs, the patient finally chose to undergo surgery. Awake mapping with DES was proposed to monitor language, verbal and nonverbal semantics, and self-performance.³⁹ The tumor boundaries were identified by ultrasonography and marked with letter tags (Fig. 3B). Anomia was evoked in the posterior part of the left superior temporal gyrus (tag 1) with 2.5 mA. Two critical regions for semantics were found during the PPTT at the level of the posterior superior temporal gyrus (tag 2) and the inferior parietal lobule (tag 3). Resection was achieved while the patient performed continuous multitasking consisting of 1) constant move-

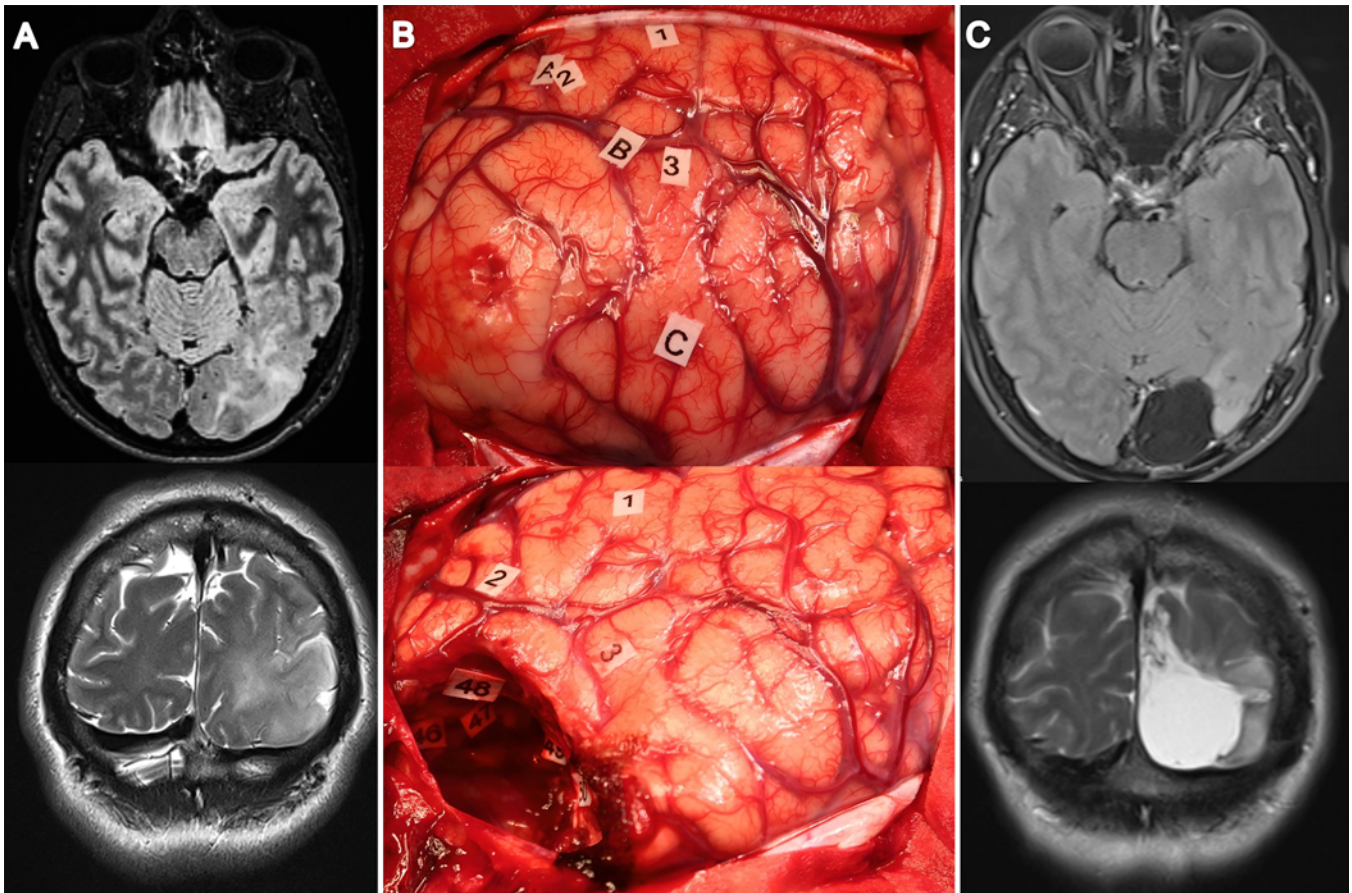


FIG. 3. Case 3. Awake resection of a left occipital WHO grade 2 astrocytoma in a singer, guitarist, and composer. **A:** Preoperative axial FLAIR (*upper*) and coronal T2-weighted (*lower*) MR images showing a left occipital glioma. **B:** Intraoperative photographs obtained before (*upper*) and after (*lower*) connectome-based resection. **C:** Postoperative axial FLAIR-weighted (*upper*) and coronal T2-weighted (*lower*) MR images showing a subtotal resection.

ment of the right upper limb; 2) picture naming combined with PPTT; and 3) a self-performance evaluation. This allowed us to perform a left occipital lobectomy from the posterior part to its anterior aspect, removing completely the occipital lobe basally, up to its junction with the posterior temporal lobe. At this point, subcortical stimulations were carried out to identify the white matter tracts (beyond the optic tracts because the patient accepted that hemianopia could be induced, knowing that he was still able to perform both the reading and naming tests with PPTT properly until the end of the operation despite right visual field deficit) as follows: 1) arcuate fasciculus anteriorly and laterally (tag 48), eliciting phonological disorders; 2) junction between the inferior longitudinal fasciculus and arcuate fasciculus more basally (tag 46) within the fusiform gyrus and its fibers, inducing reading difficulties; 3) inferior fronto-occipital fasciculus more deeply (tag 47), eliciting semantic paraphasias; and 4) more anteriorly and medially, the junction between the posterior part of parahippocampal gyrus and the posterior cingulate (tags 49 and 50), inducing behavioral disturbances (the patient started to cry, described himself as “confused” but still able to evaluate himself since he said that he “wished to

continue to retain his self-assessment abilities” critical for his work). Postoperative MRI showed a subtotal resection preserving the subcortical connectivity, with the exception of the visual system (Fig. 3C). Pathological examination confirmed a diagnosis of WHO grade 2 astrocytoma. Three months after the operation, the patient did not feel any subjective differences between the pre- and postoperative period regarding his musical ability and creativity. He also began to learn to play the piano. After 6 months, the patient was able to give concerts again.

Discussion

The first report of an awake surgery performed on a professional musician comes from 1942,^{40,41} when the famous Romanian pianist Clara Haskil was operated on by Marcel David because of a suprasellar tumor while she was asked to mentally play Mozart’s Piano Concerto No. 9 in E flat major, thus attempting to maintain herself as one of the most important pianists of Mozart’s work. Of note, DES was not applied, because her tumor was an extra-axial tumor, also probably because of the lack of surgical equipment in the middle of World War II,⁴² and because

DES was not regularly used at that time.⁴³ Currently, DES is the gold standard for identifying critical neural networks in vivo^{29,44,45} not only for cortical mapping, but also at a subcortical level to preserve the connectivity, and then maintain the patient's QOL.^{31,34,46–49} Nonetheless, cognitive mapping has been neglected for decades by neurosurgeons who focused mostly on avoiding hemiplegia and aphasia, with no specific considerations concerning higher-order functions,^{21,32,46,50} despite the fact that increasing the number of cognitive processes to be mapped, as well as the cognitive load during awake mapping, is associated with higher rates of return to work, reaching 94%–97% after LGG resection in some series.^{21,32,46,50–52}

For a better understanding of higher-order cognitive functions, new developments in the field of network neuroscience need to be known and introduced into modern oncological neurosurgery. Based on recent theoretical models proposed by Thiebaut de Schotten and Forkel⁵³ and Herbet and Duffau,²⁰ it is important to highlight certain points. 1) In addition to other complex living systems, within the human brain, the interactions of the components must be considered as much as the properties of the isolated components,⁵³ given that 2) brain functions may arise as an emerging property of the interaction between several brain areas⁵⁴ that form networks. 3) Some complex cognitive functions may be supported by a transient meta-network (network of networks) characterized by a specific pattern of large-scale between-system integration.^{54–56} 4) White matter connectivity is critical for this integration through these networks or circuits.^{20,21} Taking all this into account, we proposed to conduct these awake procedures from a meta-networking perspective. These recent advances in connectomics are a unique and necessary opportunity to lay aside the localizationism (a particular brain region is associated with a given function) to face new challenges in awake brain surgery.

In professional musicians, only very few cases of awake surgery have been reported.^{16–19,57,58} In these series, the musical performance or music production was mapped during DES. However, beyond the fact that it may be difficult to play some instruments in a surgical setting (e.g., due to the risk of brain swelling by playing wind instruments such as the saxophone), as well as the difficulty in combining music performance with other tasks (it seems unlikely that one could play drums or the oboe while naming objects), using only a music task as if musical skills were a discrete cognitive function seems reductionist and based on a modular view of brain functioning, as if music ability was subserved by an isolated, specific circuit. In fact, musical ability should be understood as a complex cognitive construct that requires the dynamic coordination of several brain systems, including motor, auditory, cognitive, and emotional. Therefore, understanding music performance as the output of such a complex mosaic of interactive cognitive and emotional processes requires a meta-network understanding of brain functioning, where many higher-order cognitive processes that rest on several networks are interplaying beyond the sensorimotor or language networks.

We consider this approach, based on recent advances in connectomics, a conceptual prerequisite to perform a

tailored connectome-based resection in professional musicians. To achieve this goal, we performed corticosubcortical DES mapping in awake patients to preserve neural networks underlying conation, cognition, and emotion as well as between-network coordination due to constant multitasking throughout surgery.³² This cognitive testing applied during tumor resection enabled us to ensure that both multitasking (motor + cognitive) combined with sequential-tasking (PPTT, LBT, and RME) abilities were monitored. Even though it is well known that this set of cognitive processes is crucial to preserve the QOL of patients,^{32,51,59} few solutions have been proposed to monitor higher-order functions during awake brain surgery. This constant nonserial multitasking with time constraint could give online information to the neurosurgeon in agreement with the 3-level model of neural disruption induced by DES proposed recently⁴⁶ to adapt the surgical strategy accordingly. Based on this model, DES might induce not only a disruption of unimodal networks (first level) generating a “positive” response (e.g., an involuntary movement) or distributed specialized circuit eliciting a within-system impairment (e.g., not being able to do mentalizing tasks without any other impairment), but also an intersystem disruption (third level) resulting in a transient incapability to achieve multitasking while the patient is able to complete each task separately.³² Within the framework of a meta-networking processing of brain functioning, multimodal integration might transiently be created to succeed in complex goal-directed behaviors adapted to an ever-changing world. In this line, other authors have put forward possible solutions to monitor online this kind of cognitive function during awake stimulation mapping, such as real-time neuropsychological testing proposed by Tomasino et al.^{59,60} in prefrontal brain tumors. Although real-time neuropsychological testing protocols seem feasible and provide significant data with respect to the patient's postsurgery neuropsychological outcome, it is important to highlight that 1) tasks are applied in a serial order, limiting the cognitive demand; 2) this model of fixed-sequences stimulus presentation could lead to the risk of presenting stimuli that are not relevant to the circuits surrounding the tumor in real time,⁶⁰ decreasing the reliability of the functional mapping;³² and 3) it is limited to right and left frontal and premotor tumors and not based on the circuits surrounding the tumor regardless of its location, even though it is well known according to recent advances in connectomics,^{20,21,53,55} how important it is to preserve deep connectivity in order to maintain the higher-order functions and, consequently, QOL.^{20,21,30,61}

In the 3 patients presented above, a behavioral approach with intraoperative mapping à la carte was performed, from a meta-networking perspective of brain functions^{21,30} rather than mapping directly the music performance from a modular and rigid view of brain processing. In addition to sensorimotor and language functions, we also monitored some aspects of executive control (by asking the patient to perform multitasking continuously and/or to switch from one language to another as in case 1), higher-order cognitive functions (such as multimodal semantics using the PPTT and/or visuospatial awareness using LBT), emotional processing (through RME), and

some aspects of metacognition (self-performance monitoring). Remarkably, preserving these complex functions was enough to give the opportunity to these professional musicians to resume their normal activities, not only as a piano or guitar player or singer, but also concerning their capacity to teach music (the patient in case 1 was a piano teacher), to create music (the patient in case 2 composed music and released a new album), and to learn new skills (the patient in case 3 learned to play the piano). In this vein, we propose that further DES studies in professional musicians would include some specific postoperative testing to strengthen the objectivity of the functional outcome in these patients, for example, 1) playing a previously well-learned piece of music; 2) playing a piece never practiced before, testing auditory-sensorimotor coupling,⁶² as well as music sight-reading; and 3) composing a melody, examining some aspects of creativity¹³ and self-performance evaluation.¹⁰

Based on the results already discussed, musical performance during awake surgery does not seem to be mandatory to preserve professional skills in professional musicians; appropriate tasks can be selected in a more integrated view of brain processing, as previously reported for other employments.³²

Conclusions

In professional musicians with an LGG, awake connectome-based resection from a meta-networking perspective without intraoperative music performance seems safe and reproducible to optimize the onco-functional balance, since all patients were able not only to return to work (e.g., to play music and to perform concerts), but also to teach music, to create and compose music, and even to start learning a new instrument. Further awake DES studies are needed to draw formal conclusions about the real usefulness of testing musical skills in the operating room by means of intraoperative music performance (what has been popularized in social media and news broadcasts), and above all, to better understand the complex neurobiology mediating musical cognition and abilities in professional musicians (from virtuosity to artistic creativity), from a rigid modular view to a multidemanding, delocalized, and constantly-in-motion network processing.

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Disclosures

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

Conception and design: Duffau, Martín-Fernández. Acquisition of data: all authors. Analysis and interpretation of data: Duffau, Martín-Fernández, Herbet. Drafting the article: Martín-Fernández. Critically revising the article: all authors. Reviewed submitted version of manuscript: Duffau. Approved the final version of the manuscript on behalf of all authors: Duffau. Study supervision: Duffau.

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