Functional outcome after language mapping for insular World Health Organization Grade II gliomas in the dominant hemisphere: experience with 24 patients

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Object. Despite the report of recent experiences of insular surgery in the past decade, there has been no series specifically dedicated to studying functional outcome following resection of insular WHO Grade II gliomas involving the dominant hemisphere, in patients with no or only mild preoperative language deficit. In this article, the authors analyze the contribution of awake mapping for preservation of brain function, especially language, in a homogeneous series of 24 patients who underwent surgery for insular Grade II gliomas within the dominant insular lobe.

Methods. Twenty-four patients underwent surgery for an insular Grade II glioma involving the dominant hemisphere (22 left, 2 right), revealed by seizures in all but 1 case. The preoperative neurological examination result was normal in 17 patients (71%), whereas 7 patients presented with language disorders detected using an accurate language assessment performed by a speech therapist. All surgeries were performed on awake patients utilizing intraoperative language mapping involving cortical and subcortical stimulation.

Results. There were no intrasurgical complications or postsurgical sensorimotor deficits. Despite an immediate postoperative language worsening in 12 cases (50%), all patients recovered to a normal status within 3 months, and 6 cases even improved in comparison with their preoperative examination results. The 24 patients returned to normal social and professional lives. Moreover, the surgery had a favorable impact on epilepsy in all but 4 cases (83%). On control MR imaging, 62.5% of resections were total or subtotal. Three patients underwent a second or third awake surgery, with no additional deficit. All but 2 patients (92%) are alive after a mean follow-up of 3 years (range 3–133 months).

Conclusions. Although insular surgery was long believed to be too risky, the present results show that the rate of permanent deficit, especially dysphasia, following resection of Grade II gliomas involving the dominant insula has been dramatically reduced (none in this patient series), thanks to the systematic use of intraoperative awake mapping, even in cases of repeated operations. Furthermore, patient quality of life may be improved due to a decrease of epilepsy after surgery. Thus, the authors suggest systematically considering resection when an insular Grade II glioma is diagnosed after seizures in a patient with no or mild deficit, even a glioma invading the dominant hemisphere. (DOI: 10.3171/2009.5.FOCUS0938)

Key Words • awake surgery • direct electrical stimulation • insula • intraoperative functional mapping • language • low-grade glioma

A lthough insular surgery was considered too risky for a long time, several studies have recently demonstrated that it is actually possible to remove tumors involving the insular lobe with a lesser degree of complications than initially believed.12,17,23,25,29,33,38,39,47,50,53,54 However, these patient series were essentially focused on motor function, in particular with the use of intraoperative motor tract monitoring,29 whereas possible language disorders have received less attention. No previous studies have accurately assessed language disturbances using objective and longitudinal examination by a specialist before, during, and after surgery (immediately and at 3 months) within the dominant insula.

To our knowledge, this is the first report of a homogeneous series of 24 patients with no or only slight preoperative language deficit, who underwent awake surgery for a WHO Grade II glioma involving the insular lobe within the dominant hemisphere. All the procedures were conducted under intraoperative electrical mapping, involving the use of both cortical and subcortical stimulation to map the eloquent structures throughout the re-

Abbreviations used in this paper: BDAE = Boston Diagnosis Aphasia Examination; IFG = inferior frontal gyrus; KPS = Karnofsky Performance Scale; OFC = orbitofrontal cortex; QOL = quality of life.
section, especially those crucial for language. Clearly, the goal of this study was not to analyze the impact of tumor removal on the natural history of Grade II gliomas, but to better evaluate the actual risk of inducing a permanent dysphasia following resection of a Grade II glioma located in the dominant insular lobe, using an extensive and objective longitudinal language assessment performed by a speech therapist, as well as to study the contribution of intraoperative awake mapping in this specific indication.

Methods

Patient Population

Between October 1997 and October 2008, 68 patients underwent resection for a WHO Grade II glioma located in the insula, performed by the senior author (H.D.). Among these 68 patients was a subgroup of 24 patients, who underwent surgery while awake. This group was specifically analyzed using intraoperative electrical language mapping for a Grade II glioma involving the dominant insular lobe.

The presenting symptoms, handedness assessed by the Edinburgh inventory, neurological examination results, and KPS score, were evaluated for each patient before surgery. Moreover, language function was tested by speech therapists (P.G. and S.M.G.) using the BDAE.

The topography of the tumor was accurately analyzed on a preoperative MR image (T1-weighted and spoiled-gradient images obtained before and after Gd enhancement in the 3 orthogonal planes, T2-weighted images, and FLAIR-weighted images). Glioma location was categorized using the classification of Yaşargil. According to this classification system, Type 3 tumors are restricted to the insula or to parts of it (Type 3A) or may include the corresponding opercula (Type 3B). In addition to the insula and the opercula, Type 5 tumors involve one or both of the other paralimbic-orbitofrontal and temporopolar areas, without (Type 5A) or with (Type 5B) parts of the limbic system.

Intraoperative Mapping

All patients underwent awake surgery after administration of local anesthesia so that functional (especially language) cortical and subcortical mapping could be performed using direct electrical stimulation. This method, including the electrical parameters and the intraoperative clinical tasks, was described previously by the authors. Briefly, a bipolar electrode with 5-mm-spaced tips and delivering a biphasic current (pulse frequency of 60 Hz, single pulse phase duration of 1 msec, and amplitude of 2–8 mA) was applied to the brain of the awake patient.

In the first stage, cortical mapping was performed after tumor sulci and gyri identifications were obtained using ultrasonography, and before resection, to avoid any eloquent area damage. Thus, in addition to sensorimotor mapping, the patient was asked to perform counting and picture naming (preceded by a short sentence to read, namely the French translation of “this is a . . .”) to identify the essential cortical language sites known to be inhibited by stimulation. For the naming task, we used the DO (Dénomination d’objet) 80 test, which consists of 80 black-and-white pictures selected according to variables such as frequency, familiarity, age of acquisition, and level of education. The patient was never informed when the brain was stimulated. The duration of each stimulation was 4 seconds. At least 1 picture presentation without stimulation separated each stimulation, and no site was stimulated twice in succession to avoid seizures. Each site of the exposed cortex was tested 3 times. Since the seminal publication of Ojemann et al., it has been accepted that 3 trials are sufficient to ensure that a cortical site is essential for language; for example, generating speech disturbances during 3 stimulations, with normalization of language as soon as the stimulation is stopped. The type of language disturbance was detailed by a speech therapist (P.G. or S.M.G.)—who was always present in the operating room during the functional mapping—by using a classification previously detailed by the authors: speech arrest, anoma, phonetic paraphasia (disorders of the articulatory realization from one to several phonemes), semantic paraphasia (disorders of the meaning of the word), slowness with initiation disturbances, and perseverations (repetition of the previous item while the next item is presented to the patient). Each eloquent site was marked using a sterile number tag on the brain surface, and its location was correlated with the anatomical landmarks (sulci/gyri/tumor boundaries) previously identified on ultrasonography studies. A photograph of the cortical map was systematically made before resection.

Next, taking into account these individual landmarks, the resection began by (operculo- and/or orbito-) frontal and/or (operculo- and/or polar) temporal tumor removal, which provides a better exposure of the insular surface without opercular retraction. This is the reason why, in cases of tumor involving the insula only (Type 3A), although opening of the Sylvian fissure alone can be performed (in only 2 patients in the present series), a part of the overlying opercular cortex not invaded by the tumor was also voluntarily removed. The goal is to gain exposure to the insular lobe, obligatorily after electrostimulation confirmation that the opercula were not essential for the function tested, especially for language.

Another stimulation mapping was then performed on the insular cortex to check for the possible involvement of the dominant insular lobe in language. According to the results of this functional mapping, a subpial resection (to avoid the middle cerebral artery and its branches) of the insular part of the glioma was performed. The awake patient had to continue naming tasks throughout the tumor removal, regularly alternated with stimulation eliciting disruption of speech when performed over crucial language areas. Deeply, using repetitive subcortical stimulation, the motor descending pathways in the internal capsule and centrum semiovale as well as the language tracts were identified in all patients. As at the cortical level, subcortical language structures were also identified by language inhibition during stimulation. Again, the type of language disturbance was detailed online by a speech therapist throughout the resection. To obtain the best possible tumor removal with preservation of the functional language, the patient was particularly stimulated, and the DO (Dénomination d’objet) 80 test was performed immediately after each resection stage.
areas, all resections were continued until eloquent pathways were encountered around the surgical cavity, then followed according to functional boundaries. Thus, there was no tumor margin left around the cortical-subcortical eloquent structures, except deeply to the bifurcation of the sylvian artery, where the removal of the limen insulae leads to the anterior perforating substance. At this level run the lenticulostriate arteries, and this region represents an anatomical limit for resection.

Postoperative Course

Postoperative functional outcome, especially language status, was assessed postoperatively by the same team using the same tasks as before surgery, both during the immediate postoperative stage at 3 months and then every 6 months. A control MR imaging session was performed in all cases immediately, 3 months, and then every 6 months after surgery. This imaging allowed an objective evaluation of the extent of glioma removal according to the classification method reported on by Berger et al.,3 that is, total resection when absolutely no postoperative signal abnormality was detected, subtotal resection when the volume of residual tumor was < 10 cm³, and partial removal when this volume was ≥ 10 cm³.

Results

Patient Population

This series included 24 patients, 16 men and 8 women, ranging in age from 23 to 61 years (mean age 35 years; Table 1). Twenty-two patients were right-handed and 2...
left-handed, as assessed by the Edinburgh inventory. Presenting symptoms included seizures in 23 cases; 16 of these patients experienced partial seizures (with transient language disturbances in 13), and 7 experienced generalized seizures. Intracranial hypertension was the presenting symptom in 1 case. Pharmacologically resistant epilepsy was present in 11 patients (46%).

Results of the initial neurological examination were normal in 17 cases (71%). There were no motor or somatosensory deficits. However, 7 patients presented with mild language disorders on the BDAE, that is, a slight reduction in verbal fluency and slight naming disorders. Seven patients had a KPS score of 80, 7 patients a score of 90, and 10 a score of 100.

The preoperative MR imaging showed a T1-weighted hypointense and T2-weighted hyperintense lesion in all cases, without enhancement after Gd injection (Fig. 1). Lesion locations were distributed as follows: 22 gliomas were situated in the left insula and 2 in the right insula (in the 2 left-handed patients). According to the Yasargil classification system,6 6 gliomas were Type 3A, 2 were Type 3B, 13 were Type 5A, and 3 were Type 5B. The median volume of the tumor was 59 cm³ (range 20–210 cm³). Neither chemotherapy nor radiation therapy was administered before surgery.

Operative Findings

At the cortical opercular level (frontal or temporal), the functional mapping under local anesthesia allowed the detection of language sites in the 24 cases. As a consequence, even if the sylvian fissure was opened in 2 cases (Type 3A tumors) in the beginning of our experience, the opercula were first removed in all other cases according to the results of the surface language mapping in the dominant side: the IFG/OFC was removed in 15 cases, and the temporal pole/anterior-mid part of the superior temporal gyrus was removed in 11 cases, even in 4 Type 3A tumors without glioma invasion of the opercula (Table 2; Fig. 2). Additional language sites, which induced anarthria or anomia when stimulated, were also detected on the cortex of the dominant insula in 5 patients with a Type 5 tumor, leading to a partial resection.

In addition, the electrical subcortical mapping enabled the identification and preservation of the language pathways in the 24 patients, representing the deep limit of the resection. The arcuate fasciculus, eliciting phonemic paraphasia when stimulated,18 was detected in 18 patients. More anteriorly and inferiorly, the inferior frontooccipital fasciculus, inducing semantic paraphasia during stimulation,21 was identified in 11 patients. Moreover, stimulation of the lateral part of the lentiform nucleus elicited articulatory disturbances in 10 patients, and stimulation of the head of the caudate nucleus generated perseverations in 5 cases. It is worth noting that in 6 patients, sensory and motor responses have also been induced by direct stimulation of the thalamocortical and pyramidal pathways, respectively. In all cases, these subcortical eloquent structures were preserved. Thus, in the 24 patients, the resection was stopped according to functional boundaries.

The awake procedure was well tolerated in all cases, despite transient pain induced during subpial resection immediately during the contact of the sylvian fissure in 4 patients, but without the necessity to stop the procedure. There were no intraoperative seizures in this series. The median length of the awake period was approximately 2 hours.

Postoperative Course

There were no surgery-related or postoperative deaths. In the immediate postoperative period, a general reduction in language performance was observed on the BDAE in 12 patients (50%; Table 2), with slight naming and articulatory disorders. Moreover, a mild decrease in verbal working memory was noted in the 24 patients. Finally, 1 patient demonstrated an athymhormic syndrome, that is, inertia with loss of interest and affect despite the
Awake surgery for insular gliomas

TABLE 1: Preoperative characteristics of the 24 patients undergoing awake operations for insular WHO Grade II gliomas

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex, Handedness</th>
<th>First Sx (date)</th>
<th>Preop Examination Result (KPS score), Tumor Type, Side</th>
<th>Tumor Vol (cm³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25, M, R</td>
<td>PS (02/1995)</td>
<td>normal (90), PRE, 5A, L</td>
<td>77</td>
</tr>
<tr>
<td>2</td>
<td>46, M, R</td>
<td>PS (05/1998)</td>
<td>normal (90), PRE, 5B, L</td>
<td>114</td>
</tr>
<tr>
<td>3</td>
<td>31, M, R</td>
<td>PS (11/1996)</td>
<td>LD (80), PRE, 3A, L</td>
<td>32</td>
</tr>
<tr>
<td>4</td>
<td>33, M, R</td>
<td>PS (02/2001)</td>
<td>LD (80), PRE, 5A, L</td>
<td>130</td>
</tr>
<tr>
<td>5</td>
<td>38, M, R</td>
<td>GS (02/2002)</td>
<td>normal (100), 3A, L</td>
<td>20</td>
</tr>
<tr>
<td>6</td>
<td>47, M, R</td>
<td>PS (05/1995)</td>
<td>LD (80), 3A, L</td>
<td>40</td>
</tr>
<tr>
<td>7</td>
<td>32, M, R</td>
<td>GS (05/2002)</td>
<td>normal (100), 3A, L</td>
<td>90</td>
</tr>
<tr>
<td>8</td>
<td>30, M, R</td>
<td>PS (08/2003)</td>
<td>LD (80), PRE, 5A, L</td>
<td>140</td>
</tr>
<tr>
<td>9</td>
<td>27, F, L</td>
<td>PS (08/1999)</td>
<td>normal (90), PRE, 3B, R</td>
<td>122</td>
</tr>
<tr>
<td>10</td>
<td>27, M, R</td>
<td>GS (07/2004)</td>
<td>normal (90), 5A, L</td>
<td>75</td>
</tr>
<tr>
<td>11</td>
<td>41, F, R</td>
<td>GS (03/2005)</td>
<td>LD (80), PRE, 5A, L</td>
<td>50</td>
</tr>
<tr>
<td>12</td>
<td>39, M, R</td>
<td>PS (09/2006)</td>
<td>normal (100), 3B, L</td>
<td>45</td>
</tr>
<tr>
<td>13</td>
<td>36, M, L</td>
<td>PS (02/2007)</td>
<td>normal (100), 3A, R</td>
<td>32</td>
</tr>
<tr>
<td>14</td>
<td>38, M, R</td>
<td>GS (03/2007)</td>
<td>normal (100), 5A, L</td>
<td>65</td>
</tr>
<tr>
<td>15</td>
<td>30, F, R</td>
<td>PS (03/2007)</td>
<td>normal (100), 5A, L</td>
<td>53</td>
</tr>
<tr>
<td>16</td>
<td>23, F, R</td>
<td>PS (06/2007)</td>
<td>normal (100), PRE, 5A, L</td>
<td>84</td>
</tr>
<tr>
<td>17</td>
<td>27, M, R</td>
<td>GS (10/2005)</td>
<td>normal (90), PRE, 5B, L</td>
<td>75</td>
</tr>
<tr>
<td>18</td>
<td>26, F, R</td>
<td>PS (11/2007)</td>
<td>LD (80), PRE, 5A, L</td>
<td>100</td>
</tr>
<tr>
<td>19</td>
<td>29, F, R</td>
<td>PS (09/2007)</td>
<td>normal (90), 5A, L</td>
<td>36</td>
</tr>
<tr>
<td>20</td>
<td>38, F, R</td>
<td>ICH (04/2008)</td>
<td>LD (80), 5A, L</td>
<td>210</td>
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<tr>
<td>21</td>
<td>61, F, R</td>
<td>PS (05/2008)</td>
<td>normal (100), 5A, L</td>
<td>45</td>
</tr>
<tr>
<td>22</td>
<td>26, M, R</td>
<td>PS (08/2008)</td>
<td>normal (100), 3A, L</td>
<td>50</td>
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<tr>
<td>23</td>
<td>29, M, R</td>
<td>GS (08/2007)</td>
<td>normal (100), PRE, 5A, L</td>
<td>50</td>
</tr>
<tr>
<td>24</td>
<td>55, M, R</td>
<td>PS (05/2007)</td>
<td>normal (90), 5B, L</td>
<td>32</td>
</tr>
</tbody>
</table>

* GS = generalized seizures; ICH = intracranial hypertension; L = left; LD = language disorders; PRE = pharmaco -logically resistant epilepsy; PS = partial seizures; R = right.

preservation of executive functions. In this patient series, there were no sensory or motor deficits. The median length of hospital stay was 1 week. Each patient underwent language rehabilitation at home, even the 12 patients with no dysphasia immediately after surgery, because of the impairment in verbal working memory.

On examination at 3 months after surgery, all patients had improved and returned to their initial neurological levels, or even exceeded them on the BDAE in 6 of the 7 patients with preoperative language disturbances. Furthermore, of the 23 patients who presented with epilepsy before surgery (11 with pharmaco-logically resistant epilepsy), only 4 patients continued to experience seizures following resection. Thus, surgery had a favorable impact on epilepsy in 83% of cases, although these patients continued to receive antiepileptic drugs.

All patients returned to a normal social and professional life, even if a professional reclassification was necessary in a truck driver whose profession was reclassified due to persistent epilepsy. The KPS score was 80 in 1 patient, 90 in 7 patients, and 100 in 16 patients (Table 2). Therefore, there was neither additional permanent worsening nor any other definitive neurological deficit in the present series.

According to the Berger classification system,³ postoperative MR imaging showed a total resection in 3 cases (12.5%), a subtotal removal in 12 cases (50%; Fig. 3), and a partial resection in 9 cases (37.5%). The median volume of the residual tumor was 9 cm³ (range 0–60 cm³). Results of the pathological examination revealed a WHO Grade II glioma in all cases.

Three patients had a second awake surgery, and 1 patient had a third awake surgery, with no additional permanent deficit, in particular without language worsening on the postoperative BDAE. The resection was subtotal in 2 cases (although partial in 1 case after the first surgery), and partial in 1 case. Results of the pathological examination revealed that the later tumors continued to be WHO Grade II gliomas in the 3 patients.

Of the 24 patients, 10 underwent an adjuvant treatment within the years following the surgery. Chemotherapy alone was administrated in 7 patients, and in 3 patients chemotherapy and radiation therapy were administrated because of anaplastic transformation. Two patients (8%) died during follow-up, due to anaplastic transformation of the tumor. The mean follow-up was 36 months since the first surgery (range 3–133 months) and 53 months since the first symptom (range 4–165 months).

Discussion

Gliomas, especially Grade II gliomas, were demonstrated to be frequently located in eloquent areas in about 25% of cases in this series, in particular within the in-
### TABLE 2: Intraoperative and postoperative characteristics of the 24 patients*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Date</th>
<th>Surgical Approach</th>
<th>Insula Language Site</th>
<th>Immediate Examination Result</th>
<th>KPS Score†</th>
<th>MRI Vol (cm³)</th>
<th>Treatment &amp; Illness Course</th>
<th>Mos from 1st Op (from 1st Sx)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10/97</td>
<td>resec OFC/IFG &amp; TP</td>
<td>yes</td>
<td>normal</td>
<td>100</td>
<td>partial (35)</td>
<td>2nd AS 01/2001 (partial), chemo 2005</td>
<td>no 133 (165)</td>
</tr>
<tr>
<td>2</td>
<td>05/00</td>
<td>resec TP</td>
<td>yes</td>
<td>trans dysph</td>
<td>90</td>
<td>partial (40)</td>
<td>chemo 2003</td>
<td>yes 104 (128)</td>
</tr>
<tr>
<td>3</td>
<td>02/01</td>
<td>opening Sylvian Fissure</td>
<td>no</td>
<td>trans dysph</td>
<td>100</td>
<td>total</td>
<td>chemo 2003, AT 2005, RT 2005, died 05/2006</td>
<td>no 63 (114)</td>
</tr>
<tr>
<td>5</td>
<td>06/02</td>
<td>opening Sylvian Fissure</td>
<td>no</td>
<td>trans dysph</td>
<td>100</td>
<td>subtotal (1)</td>
<td>2nd op 02/2007 (subtotal), no RT/chemo</td>
<td>no 77 (81)</td>
</tr>
<tr>
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<td>10/02</td>
<td>resec TP</td>
<td>no</td>
<td>trans dysph</td>
<td>100</td>
<td>subtotal (9)</td>
<td>chemo 2004, AT 2005, RT 2005, died 10/2006</td>
<td>no 48 (137)</td>
</tr>
<tr>
<td>7</td>
<td>01/04</td>
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<td>no</td>
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<td>partial (20)</td>
<td>chemo 2007</td>
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<tr>
<td>8</td>
<td>06/04</td>
<td>resec OFC/IFG</td>
<td>yes</td>
<td>trans dysph</td>
<td>80</td>
<td>partial (60)</td>
<td>chemo 2008</td>
<td>yes 53 (63)</td>
</tr>
<tr>
<td>9</td>
<td>01/05</td>
<td>resec OFC/IFG</td>
<td>no</td>
<td>trans dysph</td>
<td>100</td>
<td>partial (27)</td>
<td>chemo 2006, AT 2008, RT 2008</td>
<td>yes 46 (111)</td>
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<tr>
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<td>resec OFC/IFG</td>
<td>no</td>
<td>normal</td>
<td>100</td>
<td>total</td>
<td>no RTIchemo</td>
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<td>06/06</td>
<td>resec OFC/IFG</td>
<td>no</td>
<td>trans dysph</td>
<td>90</td>
<td>partial (16)</td>
<td>no RTIchemo</td>
<td>no 29 (44)</td>
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<tr>
<td>12</td>
<td>01/07</td>
<td>resec IFG</td>
<td>no</td>
<td>normal</td>
<td>90</td>
<td>subtotal (4)</td>
<td>no RTIchemo</td>
<td>no 22 (26)</td>
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<tr>
<td>13</td>
<td>05/07</td>
<td>resec OFC/IFG</td>
<td>no</td>
<td>normal</td>
<td>100</td>
<td>subtotal (5)</td>
<td>no RTIchemo</td>
<td>no 18 (21)</td>
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<tr>
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<td>no</td>
<td>trans dysph</td>
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<td>chemo 2008</td>
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<td>no</td>
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<td>no RTIchemo</td>
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<td>normal</td>
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<td>subtotal (9)</td>
<td>yes 12 (14)</td>
<td>no 9 (46)</td>
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<tr>
<td>17</td>
<td>03/08</td>
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<td>no</td>
<td>trans dysph</td>
<td>100</td>
<td>subtotal (9)</td>
<td>no RTIchemo</td>
<td>no 8 (13)</td>
</tr>
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<td>18</td>
<td>04/08</td>
<td>resec OFC/IFG</td>
<td>no</td>
<td>athymohormia</td>
<td>100</td>
<td>partial (50)</td>
<td>no RTIchemo</td>
<td>no 7 (15)</td>
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<td>19</td>
<td>05/08</td>
<td>resec TP</td>
<td>no</td>
<td>normal</td>
<td>100</td>
<td>total</td>
<td>no RTIchemo</td>
<td>no 7 (15)</td>
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<tr>
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<td>05/08</td>
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<td>yes</td>
<td>normal</td>
<td>100</td>
<td>partial (55)</td>
<td>chemo 2008</td>
<td>no 7 (15)</td>
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<td>21</td>
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<td>trans dysph</td>
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<td>subtotal (3)</td>
<td>no RTIchemo</td>
<td>no 3 (7)</td>
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<td>22</td>
<td>09/08</td>
<td>resec OFC/IFG</td>
<td>no</td>
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<td>100</td>
<td>subtotal (3)</td>
<td>no RTIchemo</td>
<td>no 3 (4)</td>
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<td>23</td>
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<tr>
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* AT = anaplastic transformation; AS = awake surgery; chemo = chemotherapy; resec = resection; RT = radiotherapy; TP = temporal pole; trans dysph = transient dysphasia.
† At 3 months after surgery.
‡ All patients regained a normal QOL.
Awake surgery for insular gliomas

Intraoperative Mapping

Intraoperatively, the use of direct electrostimulation under local anesthesia enabled us to identify language structures bordering the insular lobe in all patients. Such mapping allowed the removal of frontal and/or temporal opercula according to functional boundaries in 22 patients, even in 4 cases with no involvement of the operculum by the tumor (Figs. 1–3). This resection first permitted us to remove the opercular part of the glioma in 18 cases, and in all cases provided a better exposure of the insula with no additional functional risk because the areas crucial for language had been detected using stimulation before any resection.

In addition, a new language mapping at the level of the insular cortex within the dominant hemisphere found language sites in 5 patients (21% of the population). These results are in accordance with previous lesion, functional neuroimaging, and stimulation studies, which provided strong arguments in favor of the role of the dominant insula in language, especially in complex planning of articulation. However, no language disturbances were elicited in 19 patients, allowing a resection of the insular lobe. It could be hypothesized that the slow growth of the Grade II glioma in the dominant insula has induced a functional reorganization, as already demonstrated in other eloquent brain regions such as the Broca area. Previous works using both electrophysiological methods and functional MR imaging in insular Grade II gliomas have supported a recruitment of periinsular structures and/or the contralateral insula to compensate for the involvement of the dominant insula by a slow-growing tumor, thus enabling its resection with no permanent aphasia. However, in light of the present findings, we suggest that this reshaping may have some limitations, explaining why the insula was still implicated in language in 21% of patients despite its invasion by a Grade II glioma (and why we performed only a partial resection in these 5 cases), a result in agreement with the other patient series in the literature that analyzed the rate of brain areas still functional within Grade II gliomas. As a consequence, we advocate the use of awake surgery with intraoperative language mapping for resection of Grade II gliomas located in the dominant insula to minimize the risk of aphasia.

Finally, subcortical stimulation enabled the identification of essential language pathways in these 24 patients; that is, the arcuate fasciculus that runs under the posterosuperior part of the insula (crucial for phonemic processing), and the inferior frontooccipital fasciculus that runs under the anteroinferior part of the insula (crucial for semantic processing). Although the use of anatomical boundaries alone has been suggested to be sufficient during resection within the insula and for the detection of deep gray nuclei, there are no reliable landmarks within the white matter that allow the identification of language tracts. This point is very important, because insular Grade II gliomas were demonstrated to migrate along the main subinsular bundles. Therefore, despite recent advances in diffusion tensor imaging that nevertheless have yet to be validated, we recommend performing the entire removal of the glioma within the dominant insula under local anesthesia to benefit from online language feedback throughout the resection, and to stop the removal when the language pathways are encountered with the aim of optimizing the extent of resection while avoiding a disconnection syndrome. Interestingly, in the dominant hemisphere, these main language pathways run under the insula but laterally to the anterior perforating substance and the lenticulostrate arteries. Thus, they represent a very important deep limit to prevent any damage to perforating arteries, explaining why no stroke occurred in the present selected subset of patients who underwent operations while awake, contrary to the other patient series reported in the literature in which permanent deficits were always observed, mostly due to vascular injury. On the other hand, because most paralimbic Grade II gliomas migrate along the fasciculi and then into the anterior perforating substance, preservation of functional pathways under the insula also explains why only 3 patients underwent a complete resection in this series (Table 2), in addition to the 5 patients with a left insula still involved in language, as mentioned above.
**Postoperative Period**

In the immediate postoperative period, the cost of a maximal resection performed according to functional boundaries (with no margin) was language worsening in 50% of the patients (Table 2). Such a high rate of transient dysphasia after awake mapping, which enables removing a tumor until eloquent cortical and subcortical structures are encountered, has already been described for other cerebral regions. Thus, it is important to inform the patient and his or her family about the surgery and about the fact that language rehabilitation can be performed. Moreover, objective language assessment showed that, even in the 50% of patients with no postsurgical dysphasia, disorders of verbal working memory were detected on the BDAE, as previously reported following Grade II glioma surgery in other brain locations. This result indicates that a standard neurological examination is not sufficient to evaluate cognitive status following cerebral surgery, especially for lesions involving the dominant insula.

Nevertheless, in our present series, all patients completely recovered. There was no permanent postsurgical morbidity, demonstrating the major role of awake mapping not only to preserve language structures, but also to indirectly avoid any damage to the perforating arteries, as discussed above. Even if dramatically reduced, the rate of permanent functional deficit in Grade II glioma surgery is not zero in the main series reported in the literature: 8.5% in the series of Yaşargil et al., 9% in the series of Vanaclocha et al., 15% in the series of Zentner et al., 9.7% in the entire series of insular gliomas of Neuloh et al. (no details regarding Grade II gliomas specifically), 8% in the entire series of insular gliomas of Moshel et al. (no details regarding Grade II gliomas specifically), and 13% in the series of Simon et al. More specifically concerning language, permanent dysphasia after insular glioma surgery (whatever the grade, because no details were given regarding Grade II gliomas) has been observed in 9% in the series of Vanaclocha et al., 6% in 6% of cases in the series of Zentner et al., 5% of cases in the series of Moshel et al., and in 13% of cases in the series of Simon et al. Interestingly, in the only patient series with no definitive language disorders after resection of Grade II glioma (in 21% of patients in our experience), third, awake mapping is a well-tolerated procedure, which allows a decrease of the mass effect on the periinsular language structures identified intraoperatively (because the median volume of the glioma was big before surgery [59 cm^3]), and might also be explained by the postsurgical language rehabilitation.

In addition, of the 23 patients who presented with epilepsy before surgery (11 with pharmacologically resistant epilepsy), only 4 patients continued to experience intractable epilepsy following tumor resection. Thus, surgery had a favorable impact on epilepsy in 83% of cases (although patients continued to receive antiepileptic drugs). These results confirm the data of previous reports, which suggest the involvement of the insula in pharmacologically resistant seizures, and an improvement in QOL (relief of epilepsy in 84% of cases in the study of Yaşargil et al., in 89% of patients in the series of Zentner et al., and in 76% in the series of Simon et al.).

Finally, despite the small number of patients who underwent reoperations, our findings show that it is possible to perform a second and even a third awake surgery for Grade II gliomas involving the dominant insula with no additional morbidity (Table 2), and even with an improvement of the extent of resection due to mechanisms of brain plasticity, as previously demonstrated for Grade II gliomas located in extrainsular regions. Such an original strategy based on repeated resections under local anesthesia and applied to insular Grade II gliomas in the dominant hemisphere is made possible by the fact that the awake procedure is well tolerated by patients, both in our experience and in the experience of others in the literature.

Although not a main emphasis of this paper, it is worth noting that anaplastic transformation, defined as the occurrence of enhancement during follow-up, was diagnosed in only 3 patients (12.5%), independently of the extent of resection (1 complete, 1 subtotal, and 1 partial resection). Interestingly, these 3 patients had the most significant delays between the first symptoms and the operation (89, 65, and 51 months), although the delay was < 32 months for all other patients. Thus, even if a longer follow-up is still needed to clearly demonstrate the impact of resection on the natural history of insular gliomas, this argument supports earlier surgery after diagnosis of a paralimbic Grade II glioma.

**Conclusions**

This homogeneous patient series provides new insights into surgery for insular Grade II gliomas within the dominant hemisphere. First, an accurate language assessment should be performed by a specialist before and after each operation because it can reveal more deficits than previously believed according to a standard neurological examination. Second, the dominant insula may still be involved in language despite invasion by a Grade II glioma (in 21% of patients in our experience). Third, awake mapping is a well-tolerated procedure, which allows a safe resection of the opercula when invaded by Type 3B or Type 5 gliomas, or even in Type 3A gliomas, to provide a better exposure of the insular surface. This mapping enables one to detect, and thus to preserve, the possible language areas within as well as around the insula, especially white matter language pathways that represent a functional boundary in the dominant hemisphere protecting the lenticulostrate arteries running more medially. Fourth, thanks to improved knowledge and techniques, resection of dominant insular Grade II gliomas...
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can be performed not only with a very low functional risk (none in this series), but also with a possible improvement of the patient’s neurological status and a better control of intractable seizures, and thus an optimization of QOL. And fifth, repeated awake surgeries may be considered with no additional morbidity, even in this particular brain region. Therefore, resection of insular Grade II gliomas should be considered in a more systematic manner, especially taking into account the fact that recent molecular biology studies have suggested that sensitivity of insular Grade II gliomas to adjuvant treatment could be lower in comparison with extrainsular Grade II gliomas.28

The next step is now to better adapt the pre, intra- and postoperative cognitive assessment, in light of the improved understanding of the pathophysiology of the insular lobe; that is, its involvement in interception, self-recognition, risk prediction and anticipation, time perception, attention, perceptual decision making, cognitive control and performance monitoring, as well as emotional awareness.59 Thus, the insular lobe is involved in numerous important daily functions, even if it is often underestimated in the neurosurgical literature.

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

Acknowledgment
The authors would like to thank Mary Catherine Lombard for English editing.

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