Motor and language deficits before and after surgical resection of mesial frontal tumour

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ARTICLE INFO

Article history:
Received 11 March 2008
Received in revised form 30 June 2008
Accepted 15 July 2008

Keywords:
Midline frontal region
SMA
Surgery
Motor and language impairment
Low-grade gliomas

ABSTRACT

Objective: The goal of the present study was to better characterize pre- and immediately post-surgical motor and language deficits resulting from the surgery of tumours located in the medial part of the frontal lobe.

Patients and methods: Seven patients treated by surgical resection of low-grade gliomas affecting the medial part of the frontal lobe were studied with neuropsychological tasks investigating motor and language abilities before surgery and at three time points after surgery (first, third and seventh day after surgery). The tasks were constructed in a way that allowed the structured comparison between language and motor functions, and controlled the level of external constraint of the production.

Results: The main results of this study are: (1) globally the patients were impaired in both language and motor production the day after surgery; (2) the performance improved faster for tasks with strongly constrained production; (3) the verbal and semantic fluency were very sensitive and appropriate tasks for examination of the deficits resulting from the resection; and (4) performances were back to normal seven days after the surgery for most of the tasks.

Conclusion: These results confirm that surgery of low-grade gliomas affecting the prefrontal midline areas affects only transiently motor and language functions as tested in this study. They also suggest that verbal and semantic fluency were the most severely affected tests postoperatively. On the basis of these results, the surgical resection of the low-grade gliomas of the prefrontal midline seems a valuable treatment alternative.

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1. Introduction

The midline frontal cortex is constituted of several anatomically and functionally distinct subregions, including supplementary motor (SMA and preSMA) and anterior cingulate areas. These regions are implicated in language and motor processing. The SMA, located on the medial part of Brodmann’s area 6, is especially implicated in motor and speech production, particularly in intentional and internally driven behaviour. Relevant evidence comes from intraoperative electrical stimulation [25], electro-physiological recording [38], neuroimaging [23,7,16,1,3,14,28,29], and neuropsychological data from brain damaged patients [11,15,24,32,39,40]. In contrast, the pre-SMA is considered as an associative prefrontal region. The preSMA is associated with cognitive aspects of tasks such as processing, maintenance or attention to sensorimotor associations [27]. Fewer studies have described patients with cingulate cortex lesion [9]. These studies suggest that the anterior cingulate cortex (ACC) is involved in cognition, especially in...
executive function [35], visuospatial skills [22], attention [30,37], and language [4]. These deficits usually improve or completely resolve within weeks [2,4].

The clinical description of patients with lesion located in the medial wall, particularly in the SMA, show that patients suffered from motor deficits concerning the upper and lower limbs contralateral to the lesion, and had difficulties in speech production [18 for first description]. Usually, there is an initial transient mutism and akinesia that are followed by the recovery phase during which variable speech and motor production deficits are observed. The most characteristic deficits are reduced spontaneous self-initiated speech and motor activity [15,36]. On the contrary, externally driven production (e.g. repetition) is nearly normal. The long-term phase is characterized by normal spontaneous motor activity, deficits in bi-manual alternation tasks, and reduced verbal fluency.

The timing of recovery has also been reported [29]. Recovery of the immediate post-operative mutism started 3–5 days after surgery, and spontaneous speech became fluent 4–12 days later [29]. The severity of motor deficiencies was more variable. On average, the recovery of motor function began 1 week after surgery. Normal, or close to normal, motor function was reached within 4–8 weeks. Other studies of individual cases or small groups of patients suffering from epilepsy and tumours located in the medial frontal lobe and treated surgically, or patients suffering from infarctions in the territory of anterior cerebral arteries [6,8,11,12,16,17,40] reported similar observations. However, there has been no systematic neuropsychological study of the deficits present before and after surgical lesions of the frontal lobe. The present study was conducted in order to characterize immediate post-surgical motor and language deficits, as compared to the pre-surgical motor and speech–related abilities.

The goal of the present study is to better characterize pre- and immediate post-surgical motor and language deficits resulting from the medial frontal lobe lesion. We present a group of patients who have undergone resection of tumours located in this part of the brain. Patients were studied with neuropsychological tasks investigating motor and language abilities before surgery and at three time points after surgery (first, third and seventh day after surgery). Neuropsychological tasks were constructed in a way that allowed the structured comparison between language and motor function.

2. Materials and methods

2.1. Patients

We studied seven patients suffering from low-grade gliomas affecting the medial frontal cortex (four women and three men). Patients were treated by surgical resection of the tumour. The mean age of the patients was 33.6 (age range: 24–55 years). Six were native French speakers and 1 was bilingual (English/French). Handedness was assessed using a short questionnaire derived from the Edinburgh inventory [21]. Two patients were left-handed and had tumours in their right hemisphere and five patients were right-handed and had tumours in their left hemisphere (see Table 1). Patients gave their written informed consent for participation in this study. Before surgery patients also underwent bedside assessment of executive functioning (mean = 16.85/18; S.D. = 2.04) [10]. This assessment included for example production of motor sequences, verbal fluency and Go-NoGo task.

2.2. Language and motor tasks

The tasks were created in order to examine different aspects of language production and comprehension, as well as motor output. They were designed so that patients would be able to perform them before and shortly after surgery. For both language and gesture, we studied the impact of task-related external constraint or guidance on performance level. For example, tasks with little external constraint included picture description or free generation of actions; tasks with a strong external constraint included the repetition of words and sentences, or the imitation of hand gestures (see Table 2). Note that tasks did not differ exclusively in their degree of external constraint. Thus, image description and the generation of words from a specified category are both partially constrained language tasks, although the type of relevant constraint is different. It is possible, for example, that the processes of search for words involved in these two tasks are different [20]. The first one is more similar to the natural language production than the second, where searching is dependent on the pre-specified criterion. It may turn out that both the degree and the type of constraint modulates the performance of patients.

There were five tasks examining language and four examining motor functions.

2.3. Language tasks

Two versions of each task were constructed, in order to prevent learning effects.

1. The image description task assessed the spontaneous production of speech. Patients were presented with a picture and were asked to describe as exhaustively as possible the event represented on the picture. We used the Cookie Theft picture (BDAE) or the Bank Robbery picture depending on the test version.

2. The verbal and semantic fluency tasks provided an assessment of internally driven lexical search and self-initiated word production. The patients were asked to produce as many items as possible from a given category. The categories were either orthographic (e.g. nouns that start with the letter “m”) or semantic (e.g. animals). Responses were recorded for 90 s, and scored in three 30 s epochs.

3. The picture naming task assessed language production in a mildly constrained context where word search is externally initiated by the presence of the picture but the production is internally driven. Patients were presented with ten pictures of simple objects corresponding to mono-, bi-, or tri-syllabic names [34]. They were asked to name each picture.

4. The word and sentence repetition tasks were constructed to assess the deficit in externally-driven language production. We selected eight words and six sentences of different lengths (words: 1–6 syllables; sentences: 3–6 words). The word or the sentence was read aloud by the examiner and the patient was asked to repeat it.

5. The word–picture matching task examined word comprehension performance. We created eight displays, each comprising four pictures from Snodgrass and Vanderwart [34]. The patient was presented with one display at a time. The name of one of the pictures was given orally and the patient was asked to point to the corresponding picture on the display (e.g. saw). The three distractors included: a semantic distractor (e.g. hammer), a phonological distractor (e.g. nest) and an unrelated distractor (e.g. accordion).

2.4. Motor tasks

The tasks were completed by the patients with the hand contralateral to the tumour. As for the language tasks, two parallel versions of each task were constructed in order to prevent the
effects of learning. The order of the two versions was counterbalanced across patients.

(1) The free generation of gesture task allowed the examination of the production of self-initiated gestures. Patients were asked to perform any meaningful gesture. They were instructed to perform a gesture that the examiner could recognize without any oral comment or explanation.

(2) The gesture miming on verbal command task assessed the production of verbally triggered but internally driven simple gestures. Five of them were transitive (e.g. show me how to use a hammer), five were symbolic (show me how to say goodbye with your hand) and five were meaningless gestures (e.g. point to your nose).

(3) The gesture imitation task examined the production of visually triggered and externally driven gestures. Patients were asked to imitate as accurately as possible gestures produced by the examiner. The gestures were identical to those of the gesture miming task.

(4) The gesture recognition task assessed possible deficits in the semantic knowledge of gestures. Patients were asked to recognize (name) the transitive and symbolic gestures performed by the examiner. The gestures were different from those used previously (see Appendix A).

Scoring of the gesture production was conducted according to the following rule using a 0–2 scale: 2 = gestures executed correctly, 1 = gestures executed incorrectly but recognizable and related to the item, and 0 = unrecognizable gestures or absence of gesture. In order to simplify the statistical analyses this scale was reduced to 2 points, 1 for correctly executed gesture and 0 for the incorrectly executed gesture or the absence of gesture.

2.5. Timing of examination

All patients were tested four times: before surgery (D0), the day immediately following surgery (D1), three days after surgery (D3), and 7–10 days after surgery (D7). On D0, D3 and D7, the patients were examined in a separate quiet room. On D1 the testing were performed at bedside.

2.6. Anatomical imaging

All images were acquired using a 1.5 T MR unit. For each patient, axial inversion recovery three dimensional (3D) T1-weighted images covering the whole brain were acquired before (mean delay = 5.13 ± 4.85 days) and after surgery (mean delay = 23 ± 4.7 days) as well as axial fast FLAIR images. Fig. 1 shows the location of the lesions and extent of surgical removal, collected before and after surgery.

3. Results

All patients experienced an immediate postoperative language and motor deficit contralateral to the resection. In all patients, the motor deficit predominated in the upper limb. Muscular strength and reflexes was normal in all patients when movements were possible.

3.1. Language

3.1.1. The image description task

For each testing session, we computed the mean number of words and sentences in the patients' responses. On average patients produced fewer words on D1 (mean = 11.72) than on D0 (mean = 59.4), D3 (mean = 27.6) and D7 (mean = 49.3). They also produced fewer sentences on D1 (mean = 1.4) than on D0 (mean = 6.9), D3 (mean = 4.2) and D7 (mean = 7.1). All patients but one (Patient 2) presented a similar clinical presentation. On D1, patients behave as if they were mute. Speech deficits progressively disappeared from D1 to D3. The left-handed Patient 2 did not present any impairment in speech production between D0 and D1 and D7 (unfortunately we were not able to test this patient on D3). Unexpectedly, her performance on D1 was better than on D0 and D7.

There were individual differences in the number of produced words and sentences with some patients (e.g. Patient 1) performing better than others (e.g. Patient 5). However, these differences were not significant $F(6,28) = 0.27, p = 0.95$.

The patients made very few errors on the different examinations. However, the percentage of errors was slightly higher on D1

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age/sex</th>
<th>Tumour location</th>
<th>Handedness</th>
<th>vol_tum</th>
<th>vol_exe</th>
<th>Brain lesions</th>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SMA PreSMA PCC ACC MFG IFG</td>
</tr>
<tr>
<td>1</td>
<td>25/M</td>
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<td>Right</td>
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<td>22.10</td>
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<tr>
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<td>R</td>
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<td>26.50</td>
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<tr>
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<tr>
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<td>23.00</td>
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<tr>
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<td>Right</td>
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<td>16.9</td>
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Table 2

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</thead>
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<td>Mildly constrained</td>
</tr>
<tr>
<td>Language</td>
<td>Image description</td>
</tr>
<tr>
<td>Motor</td>
<td>Free generation of action</td>
</tr>
</tbody>
</table>
Fig. 1. Pre- and post-operative sagittal T1-weighted MR images in all patients. The preoperative sections were chosen as to show the largest diameter of the tumour. Thus for some patients (2, 5) the mid-sagittal plane could not be respected. The postoperative sections were chosen as to show the cortical resection of the medial aspect of the frontal lobe. Thus, for some patients the view may be several millimetres medial to the preoperative view. Additionally, the pre- and postoperative sections may not be exactly the same because of significant brain displacement due to large surgical resections.

(5%) than on D0 (1%), D3 (4%) and D7 (1%). The errors made were (1) omissions of articles or nouns, for example “director” instead of “the director” and “one … who” instead of “one gangster who” (2) incorrect tense. Besides, the sentences were frequently unfinished, the words were wrongly ordered and patients filled up the sentences with meaningless speech, for example “how do you call it?” “what’s-it”.

The group performance was analysed separately for words and sentences with Friedman repeated measures test with factor being Session (D0, D1, D3, D7). These analyses showed a significant overall effect of Session on the production of words ($\chi^2_2(3) = 15.8$, $p < 0.001$) and of sentences ($\chi^2_2(3) = 14.5$, $p < 0.002$). Patients produced significantly fewer words on D1 than on D0 ($p < 0.03$), D3 ($p < 0.03$) and D7 ($p < 0.05$). Besides, patients produced fewer words on D3 than on D0 ($p < 0.02$). Analyses in terms of number of sentences produced showed a similar profile. Patients produced significantly fewer sentences on D1 than on D0 ($p < 0.03$), D3 ($p < 0.03$) and D7 ($p < 0.05$). In addition, they produced fewer sentences on D3 than on D0 ($p < 0.02$) and D7 ($p < 0.04$).

3.1.2. The verbal and semantic fluency tasks

Deficits were similar across patients with reduced verbal and semantic fluency performances on D1 followed by progressive recovery. Performances improved between successive post-operative sessions. For all patients, the performance was back to pre-operative level on the last examination (D7). For all patients, the most severe reduction in fluency was observed on D1 with six patients not being able to produce any item in both, verbal and semantic fluency. These patients behave as if they were mute. The left-handed Patient 2 produced several items in both semantic and verbal fluency. However, she produced fewer items on D1 examination than on D0 and D7 examinations. Overall, for all patients, the performance on D3 and D7 was characterized by long breaks between the items that were produced. In all but one case (Patient 1 for D0 examination) semantic fluency was better performed than verbal fluency.

The statistical analysis on group performance has shown a post-operative deficit in verbal and semantic fluency, which persisted for several days after surgery. The most pronounced deficit was observed on D1. In addition, there was an improvement in performance between successive post-operative sessions. The two-way repeated measure anova with factors being Session and Fluency Type has shown the main effect of Session $F(3,47) = 30.2$, $p < 0.001$ and Fluency Type $F(1,47) = 20.4$, $p < 0.006$, as well as a significant interaction between these two factors $F(3,47) = 6.9$, $p < 0.004$. The performance was globally better for semantic fluency (mean = 10.5) than for verbal fluency (mean = 5.4). For the verbal fluency condition, all pair-wise comparisons were significant ($p < 0.05$) except the comparison between D3 and D7 examination, which was not statistically significant. For the semantic fluency condition, all pair-wise comparisons were significant ($p < 0.05$) (see Fig. 2A).

3.1.3. The picture naming task

The pattern of performance in the picture naming task was similar to those observed in the previous tasks. On D1 examination, the right-handed patients behave as if they were mute. On the contrary, the two left-handed patients had no naming difficulty. For the right-handed patients, the performance came back to normal quickly, as they reached the pre-operative level on D3 (Fig. 2B).

The statistical analysis, Friedman repeated measure test with factor Session (D0, D1, D3, D7) on the mean performance of all patients showed a significant effect of Session ($\chi^2_2(3) = 173$, $p < 0.0001$). Pair-wise analyses showed that this effect was specifically due to the difference between D0 and D1 ($p < 0.0001$).
3.1.4. The word and sentence repetition tasks

Patients suffered from an immediate post-operative deficit in externally driven language production tasks. This deficit disappeared quite rapidly, as the performance on D3 was back to the pre-operative level.

The performance on word and sentence repetition was similar and data were collapsed. On D1 patients were unable to repeat any stimulus. A Friedman repeated measure test with factor Session (D0, D1, D3, D7) showed significant effect of Session ($\chi^2(3) = 236.7, p < 0.0001$). Pair-wise comparisons showed a significant decrease in performance between D0 and D1 ($p < 0.0001$). The difference was also significant between D1 and both D3 and D7 (both $p < 0.0001$) (see Fig. 2B). Finally, there was no significant difference between D0 and D3 or D7.

3.1.5. The word–picture matching task

The patients were quite accurate in this task and the surgery did not induce any deficit in their capacity to match a written word to the corresponding picture (see Fig. 2B). The statistical analysis did not show any difference between pre- and post-surgery Sessions (Friedman repeated measure test $\chi^2(3) = 3, p = 0.392$). This result suggests that speech comprehension was spared.

3.2. Motor functions

3.2.1. The free generation of gesture task

Patients were impaired in spontaneous production of simple gestures only immediately after surgery. On D1, patients mostly failed to produce any gesture at all, recognizable or not. There was a significant effect of Session as shown by Friedman repeated measure test ($\chi^2(3) = 21.65, p < 0.0001$). The pair-wise comparisons showed significantly worse performance on D1 as compared to D0 ($p < 0.009$), D3 ($p < 0.01$) and D7 ($p < 0.01$) periods. There was no other significant difference. The recovery was rapid as can be seen from the performances on D3 and D7, which did not differ from D0.

3.2.2. The gesture miming on verbal command task

Patients suffered from a transient impairment in this task, most pronounced on D1. Recovery was rapid. On D7, performances were back to pre-surgery level. The principal difficulty on D1 was to perform any gesture, the patients were simply not able to initiate the gesture and they made no gesture at all. On D3, the principal difficulty was in forming a correct hand’s shape (grasping).

There was a significant global effect of session (Friedman repeated measure test $\chi^2(3) = 161.1, p < 0.0001$). Pair-wise analyses showed a significant deficit on D1 as compared to D0, D3, and D7 (all $ps < 0.0001$). Performances on D0 and D7 were also better than on D3 ($p < 0.0001$ for both) (see Fig. 3A).

Three kinds of gestures were used in this task (transitive, symbolic and meaningless). Separate analyses for each kind of gesture followed the overall evolution pattern.

3.2.3. The gesture imitation task

Following surgery, the patients were impaired in imitation of simple gestures. Their performance did not come back to the normal level even on D7 (see Fig. 3B). The same characteristics of performance were observed in the imitation of gestures as in the miming of gestures. On D1, the patients made no gestures at all and on D3 and D7 the main difficulty concerned grasping aspect of the gesture. A significant effect of Session was observed.
with Friedman repeated measure test ($\chi^2(3)=183$, $p<0.0001$). Performance was significantly impaired on D1, D3 and D7 as compared to D0 (respectively, $p<0.0001$, $p<0.0001$ and $p<0.03$).

As for the gestures miming task, analyses were made separately for the different kinds of gestures. These analyses confirmed the pattern observed for collapsed data, except for the comparison between D0 and D7 for transitive and meaningless gesture, which were not significant. Other comparisons for transitive, symbolic and meaningless gestures were significant (for all kind of gestures $D3 > D1$ and $D7 > D1$, all $p<0.0001$; and $D7 > D3$, $p<0.02$). These results show that externally driven production of simple gestures was impaired after surgery. For transitive and meaningless gestures, the return of performance to a normal level was rapid, as indicated by the absence of a significant difference between D0 and D7. The persistent difficulty on D7 was observed only for the symbolic gestures.

3.2.4. The gesture recognition task

The patients were impaired in gestures recognition on D1 only. Performance was back to pre-surgery level on D3. A significant global effect of Session was observed with Friedman repeated measure test ($\chi^2(2)=76.2$, $p<0.0001$). Different pair-wise comparisons conducted first for all kind of gestures together, and then separately for each kind of gestures showed that the only significant difference was observed between D0 and D1 (all $p<0.0001$ for transitive, symbolic and meaningless gestures). No other comparison was significant.

4. Discussion

In the present study we investigated the immediate post-surgery effects on language and motor abilities of the surgical lesion of the medial part of the frontal lobe, particularly including...
the SMA and the ACC. The main results can be summarized as follows.

Language functions: (1) On the day immediately following surgery (D1), patients were impaired in all tasks examining language production, while the word-picture matching task was spared; (2) 3 days after surgery (D3), performance was back to normal in picture naming and in word or sentence repetition, while it was still impaired in picture description, and verbal and semantic fluency; (3) 7–10 days after surgery (D7), performance was back to pre-surgery level in all tasks except for the verbal and semantic fluency.

Motor functions: (1) On the day immediately after surgery (D1), patients were significantly impaired in all motor tasks; (2) 3 days after surgery (D3), performance was back to the pre-surgery level in the free generation of gestures and the gesture recognition tasks, while performance was still impaired in the gesture miming and the gesture imitation tasks; (4) 7–10 days after surgery (D7), the performance reached the pre-surgery level in the gesture miming task and gesture imitation task (except for the imitation of symbolic gestures).

First, the overall evolution profile conforms to the pattern reported in previous studies concerning medial frontal lobe lesions, namely an initially severe deficit in producing speech and limb gestures, followed by the recovery of most symptoms within days [26,29]. The initial deficit affected equally all tasks requiring behavioural output, irrespective of their underlying cognitive components. This is compatible with the hypothesis of an impaired initiation of language and motor output resulting from the resection in the medial part of the frontal lobe, especially including the SMA and pre-SMA. Several studies have pointed out that the SMA and pre-SMA are directly involved in the selection, planning and production of voluntary movements [27,19], and speech [5,13,16,40]. In agreement with this idea, comprehension tasks were spared: patients were not impaired on the word–picture matching task even on D1. The initial impairment in gesture comprehension does not run against this account, as this task required verbal responses.

Second, we hypothesized that tasks with reduced external guidance would be more sensitive to SMA deficit than strongly stimulus-driven tasks, and therefore recovery for these tasks would be slower. Language tasks conformed to this pattern: recovery was faster for word and sentence repetition tasks (strongly constrained) than for verbal and semantic fluency tasks (mildly constrained) and image description task (slightly constrained). The recovery occurred, however, faster for the image description task (performance on D7 was back to normal) than for the verbal and semantic fluency tasks, as performance for these tasks was still impaired on D7. The fact that recovery was faster for the image description task than the verbal and semantic fluency tasks may be due to differences in the search processing that are involved in these two tasks. The verbal fluency task is frequently used to measure executive processing. It was suggested that the ACC plays some role in the executive processing. As the surgical lesions in our patients included the ACC, it is possible that the more important deficit and the slower recovery observed in these tasks are due to the additive effects of the SMA and of the ACC lesion. However, it is important to note that the patients were not impaired on the bedside examination of executive functioning as assessed with the BREF [10].

For motor tasks, the pattern of recovery diverged slightly from what was expected. Performances at the free generation of gestures returned to normal before the gesture imitation and miming tasks. However, the scoring procedure may have been more stringent for the former than for the latter tasks, as somewhat approximate gestures could be scored as correct in the generation but not in the imitation and miming tasks. There was no difference in recovery between the miming and imitation tasks as for both tasks patients' performance was globally back to normal on D7. It is possible that finest way of scoring of gestures production should be used in order to reveal a difference in performance between these two tasks.

The motor tasks in this study were focused on the investigation of upper limb function. However, it would be interesting for the future study to include tasks examining oculomotor functions that depend on the Supplementary Eye Field (SEF), the area of the dorsomedial cortex. Because these functions were not tested in our patients we cannot exclude the presence of some deficits related to the SEF lesion [33].

Third, from a clinical point of view, the fact that recovery was not complete 1 week after the surgery points out the importance of the long term evaluation of the patients with the resection of medial part of the frontal lobe. Previous clinical studies give rather incomplete descriptions of the protocols used to examine language and motor performances. In the present study the same well specified tasks were used for all patients and for different sessions of examination. Interestingly, some of the tasks seemed more adequate to reveal motor and language disturbances resulting from the resection of the medial part of the frontal lobe, especially the SMA. The verbal and semantic fluency for language tasks, and the imitation of gestures for motor tasks appeared very sensitive. Our study did not include detailed explorations of executive functioning, and no firm conclusions can be drawn on this point. However, according to the recent study [2] the ACC does not play a central role in cognitive functioning. These authors suggest that the ACC is rather involved in the generation of bodily arousal during volitional behaviour. In this hypothesis, the disturbances observed in our patients would more likely result from the SMA lesion.

Consequently, verbal fluency and imitation tasks seem suitable for the clinical examination of language and motor performances after SMA resection. Last, the present study confirms that patients recover well from the post-operative deficits and this should facilitate indication of surgical treatment of the low-grade gliomas affecting the SMA. However, as our study did not investigate some other functions dependent on medial frontal cortex such as learning and performance of sequential behaviour [13] and executive functions such as for example decision making, voluntary movement selection based on reward and encoding the serial order of movements in sequences [31] further investigation are necessary in order to better characterized the consequences of the medial frontal lobe resection.

Acknowledgment

This study was supported by grants from PHRC AOR01109.

Appendix A. Stimuli used in motor examination

- Transitive gestures to following objects:
  1. Hammer
  2. Screwdriver
  3. Scissors
  4. Egg bitter
  5. Hairbrush
- Symbolic gestures:
  1. Wave goodbye
  2. Make a “v” for victory
  3. Somebody is mad
  4. Reprimand
References


