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Phenomenology of glioma resection in the dorsal medial frontal cortex

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Background: During the latest decades, the hypothesis that the subjective experience of free will is determined by preconscious activity in the dominant dorsal medial frontal cortex (dmFC) has repeatedly challenged our commonly held concepts of moral responsibility.

Aims of the study: To investigate whether dmFC activity determines the sense of free will and to investigate the effects of resections in this area on quality of life (QoL).

Methods: A cohort of nine patients affected by transient declines in speech and movement skills after surgery involving the left dmFC answered questions about their post-operative, subjective experiences of volition in relation to symptoms. In eight cases, resections were performed as part of glioma surgery, and in the ninth case, a meningioma adjacent to the dmFC was resected. In addition, a QoL questionnaire was administered before and after surgery.

Results: None of the patients perceived the transient disabilities related to surgery as associated with a loss or absence of volition. No declines in QoL were detected after surgery. Two QoL domains showed improved function (motor dysfunction and future uncertainty).

Conclusions: The subjective sense of volition is not contingent on dmFC activity. Surgical resections of this area are not typically associated with declines in QoL.

KEYWORDS

higher cortical functions, neurooncology, quality of life

1 | BACKGROUND

In the early 1980s, a series of experiments¹ initiated a debate as to what extent preconscious activity in the dorsal medial frontal cortex (dmFC) is the proximal cause of the subjective experience of conscious free will.^{2,3} Subsequent studies have confirmed that this area of the brain is involved in self-reflection and action monitoring,^{4,5} and direct cortical stimulation of the dmFC in awake patients often

creates an urge or intention to move contralateral parts of the body.⁶ If this means that the feeling of making a conscious decision is actually determined by preconscious dmFC activity, one fascinating implication could be that conscious free will and personal responsibility might be nothing but illusions.⁷

Surgical resections of the dmFC typically cause transient disturbances of the ability to speak and/or to perform non-stimulus-driven motor actions in the contralateral part of the body, a phenomenon

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known as the supplementary motor area (SMA) syndrome.⁸ In the present study, we addressed the role of the dMFC in the subjective perceptions of volition by questioning patients who experienced post-operative SMA syndromes about their experiences. In addition, we also evaluated the effects of surgery among these patients with pre- and post-operative measures of patient-reported quality of life.

2 | METHODS

2.1 | Patients

Eight patients consecutively operated for gliomas in the left dMFC by the last author (RLS) during 2015-2018 (Figure 1) were included. Two of the patients had previous resections done (in 2009 and 2013). These patients as well as another three of the included patients underwent a second extended resection during the study period. The mean age of patients at first surgery was 48.3 years (SD = 13.6). Six patients had one or several preoperative epileptic seizures. None of the patients experienced post-operative seizures that we are aware of. One of the patients had a preoperative right arm paresis that improved after surgery. Pathological anatomical diagnosis was glioblastoma WHO IV in one case, oligodendroglioma WHO II in five cases, and astrocytoma WHO II in two cases. All patients experienced various symptoms related to the SMA syndrome: One of the patients had a 3-hour period of akinetic mutism. Two patients had paresis of the right leg and arm combined with dysphasia, two had a mild paresis of the right hand and dysphasia, one had mild paresis of the right hand with no dysphasia, and two patients had subclinical levels of paresis and dysphasia. All except one recovered from all clinically significant symptoms (one patient had a severe right arm paresis and

a minor paresis of the right leg at 3 months post-op). Extents of resections for the glioma patients are described in Figure 1.

In addition, we included a ninth patient (female, 64 years), operated on at our clinic in 2019. This patient experienced an unexpected SMA syndrome after resection of a meningioma over the left dMFC.

2.2 | Quality of life

The quality-of-life questionnaire (QLQ) C30⁹ and EORTC-BN20¹⁰ were administered to the patients 1-2 days before the first surgery and between 4 weeks and approximately 2 years after the last surgery. For one patient who had her first surgery before 2015, pre-operative QoL data obtained before the re-operation were used. Wilcoxon signed-rank test was used to study changes in pre- and post-operative scores.

2.3 | Questionnaire regarding sense of volition during the SMA syndrome

For four patients, the following questions were asked in the immediate post-operative period (1-2 days after surgery) during the SMA syndrome. For four patients, the questions were asked retrospectively (2-24 month after surgery) after the SMA syndrome was resolved. For the last patient, the questions were asked 1 month after surgery while discrete symptoms remained.

Questions were adjusted to the specific symptoms exhibited by the different patients. If several symptoms were prevalent, the questions were asked about each symptom:

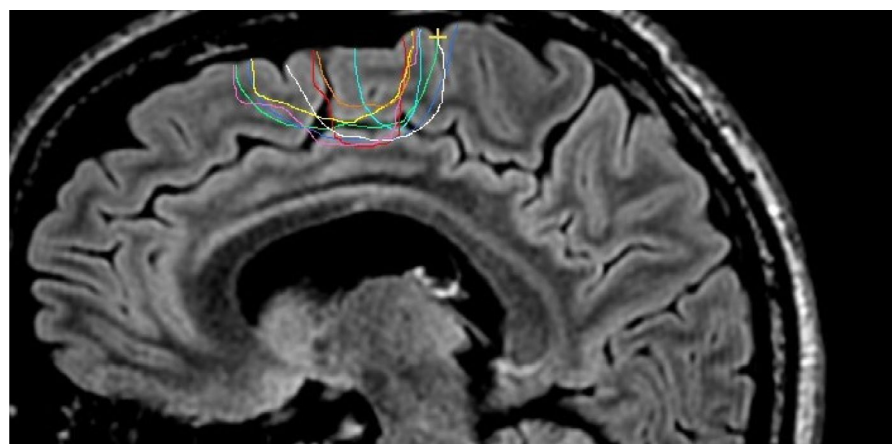


FIGURE 1 Size of resection in the eight glioma patients. *Yellow cross indicates the precentral sulcus, **Precentral sulcus, ¹Interrater reliability $r = .71$, ²Interrater reliability $r = .996$, ³Interrater reliability $r = 1$, ⁴Interrater reliability $r = .93$, ⁵Interrater reliability $r = .81$

Anatomical distance (mm) of resection cavity's

Patient ID	Pat 1	Pat 2	Pat 3	Pat 4	Pat 5	Pat 6	Pat 7	Pat 8	M	Std.
Colour										
Posterior border to PCS** ¹	0	4	6	5	6	-4	8	0	3,13	4,05
Anterior border to PCS** ²	49	19	44	48	28	44	33	36	37,63	10,57
Medial border to midline ³	0	0	0	0	0	0	0	0	0,00	0,00
Lateral border to midline ⁴	28	11	26	25	11	44	29	20	24,25	10,69
Inferior border to cingulum ⁵	1	-1	1,0	-4	6	-3	-3	-2	-0,63	3,25

*Yellow cross indicates the precentral sulcus, **Precentral sulcus, ¹Interrater reliability $r = .71$, ²Interrater reliability $r = .996$, ³Interrater reliability $r = 1$, ⁴Interrater reliability $r = .93$, ⁵Interrater reliability $r = .81$

	Pre-op median	Post-op median	Z-value
Functional scales ^a			
Physical function	93.33	90	0.00
Role function	41.67	66.67	-1.05
Emotional function	50	83.33	-1.56
Cognitive function	83.33	91.67	-0.41
Social function	41.67	83.33	-1.38
Symptom scales ^b			
Fatigue	16.67	27.78	-1.09
Pain	0	0	-0.45
Nausea and vomiting	0	0	0.00
Global health status ^a	54.17	66.67	-0.77
Domains ^b			
Future uncertainty	45.83	4.17	-2.53*
Visual disorder	0	0	-1.73
Communication deficit	11.11	0	-0.95
Motor dysfunction	27.78	0	-2.02*

^aA higher score = higher function. Score range: 0-100.

^bHigher score = higher dysfunction. Score range: 0-100.

* $P < .05$.

TABLE 1 Self-reported quality of life before and after surgery

1. During neurological exams as your impaired [speech/right arm motor function/right leg motor function, etc] was observed, did you feel that your difficulties were caused by a lack of volition? (Yes/No).
2. Please grade your effort to comply with the demands to [speak/move your right arm/leg, etc] during neurological exams on a scale between 1 and 10, where 1 is no effort and 10 is a 100% maximal effort.
3. Please use the same method to grade your effort to move your healthy [arm/leg] during the neurological exam.

All patients answered all questions. However, one of the patients, who was asked questions retrospectively, remembered her motor dysfunction following surgery but not her dysphasia. Because of this, questions about her dysphasia were neither answered nor included in further analyses.

2.4 | Ethical considerations

All surgeries were performed on clinical neuro-oncological grounds, and patients gave informed consent for surgery according to standard clinical procedure. The publication of behavioral data and QoL data on patients was approved by the regional ethics committee at Umeå, Sweden (Dnr: 2016/479-3; Dnr: 2018-402-32M; and Dnr: 2016/200-31). In addition, all patients gave informed written consent to participate in the study.

3 | RESULTS

3.1 | Sense of volition

All questions about volition were answered the same way by all patients. None of the nine patients reported a subjective experience of a lack of volition as influencing their impairments in motor and speech actions during the SMA syndrome. All patients reported maximal efforts (Mdn = 10) to comply with the demands of the physician during post-operative neurological examinations. The same results were found for questions about movement on the non-affected side (Mdn = 10).

3.2 | Quality of life

As can be seen in Table 1 and Figure 2, the eight glioma patients showed a significant improvement of mean quality of life regarding future uncertainty (presurgery Mdn = 45.83, post-surgery Mdn = 4.17, $Z = -2.53$, $P = .011$) and motor dysfunction (presurgery Mdn = 27.78, post-surgery Mdn = 0, $Z = -2.02$, $P = .043$) when pre-surgical scores were compared with post-operative ones.

4 | DISCUSSION

There are two main findings of the present study. The first one is that patients, after removal of the dMFC, unanimously reported an

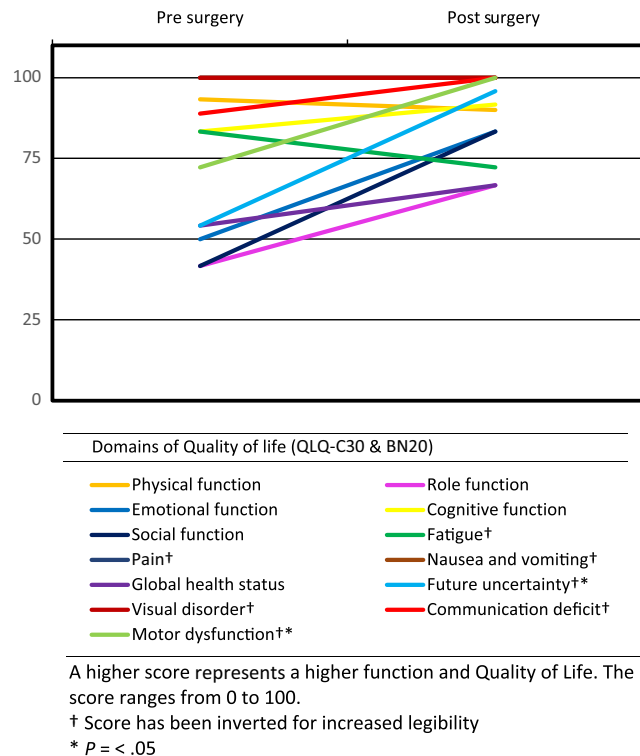


FIGURE 2 Self-reported quality of life before and after surgery. A higher score represents a higher function and quality of life. The score ranges from 0 to 100. †Score has been inverted for increased legibility * $P = < .05$

intact sense of volition and desire to cooperate during neurological examinations even when affected by the SMA syndrome.

The second is that surgery in this area does not seem to impair post-operative quality of life. On the contrary, despite the relatively small sample size, significant improvements between preoperative and post-operative outcome scores were seen for some of the subscales.

The outcome variables of the present study were self-reported data. This was necessary because the variables of interest (sense of volition related to SMA-initiated activity and QoL) are subjective. From this also follows that just like autobiographical memories,^{11,12} these reports can theoretically be subject to influence and manipulation by a host of perceptive cognitive and social factors.^{1,2}

Regarding sense of volition, the self-reports were collected during different circumstances. Five patients gave reports while under the influence of the SMA syndrome, whereas four answered questions retrospectively. Eight of the patients had preoperatively been informed about the risk of an SMA syndrome but the meningioma patient had not.

Even though perceptual phenomena, memory errors, situational demands, or suggestion could all theoretically have influenced these patients' self-reports in different directions, their answers were remarkably consistent. The most parsimonious explanation for this would in our opinion be that the answers convey a subjective experience that is relatively stable across conditions among patients

experiencing the SMA syndrome. This interpretation also fits well with our clinical impression of the patients as cooperative and engaged during examinations, as well as with their willingness to comply with demands during examinations of their unaffected side.

Based on this, we understand our results as incompatible with the idea that the subjective sense of free will can be reduced to a secondary effect of preconscious neural activity in the dmFC. Instead our data would fit better with an understanding of the sense of volition as inferred based on multiple forms of conscious and unconscious sensory input.¹³ One source of such input might be dmFC activity,⁶ since this area appears to harbor a system for cognitive control,¹⁴ that may be routinely utilized in order to achieve long term goals.

Finally, when it comes to the question whether surgery in this sensitive area can be motivated, our results are reassuring. Overall, the only significant changes between pre- and post-operative facets of quality of life in patients were for the better. One possible explanation for the improvements observed might be the reduced burden of epilepsy among these patients.¹⁵ Our sample size was admittedly small and the timing at which post-operative quality-of-life measurements were made varied greatly. Nevertheless, our results seem to clearly support the notion that resections of gliomas in the dominant dmFC should not be hindered by concerns for influencing patient's quality of life.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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