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Impact of resection location on depressive symptoms following glioma surgery

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Abstract

Background. Glioma surgery aims to maximize tumor removal while preserving functional integrity. Functional outcome usually focuses on neurological and neurocognitive functions, but surgery may also affect mood regulation. We determined the occurrence of depressive symptoms after surgery and investigated associated factors, including preoperative depressive symptoms and the location of the resection.

Methods. We included a single-center retrospective cohort of patients with supratentorial diffuse glioma (WHO grade 2–4) who underwent first-time surgical resection between 2009 and 2021 and who completed the Center for Epidemiologic Studies Depression Scale (CES-D) before and one year after surgery. Resection cavities were segmented on postoperative MRI scans. White matter disconnections were computed, the so-called disconnectome, to examine distant effects. Multivariable regression analysis was used to relate patient, tumor, and treatment characteristics to postoperative depression scores and changes after surgery. Lesion-symptom mapping was used to relate resection and disconnectome locations to these scores and changes.

Results. The study included 83 patients. Before surgery, 25% of patients had depressive symptoms and one year after surgery 34%, which was not statistically different. Resections of gliomas in the right hemisphere were significantly associated with increased depression scores after surgery. A resection involving the left anterior temporal region was significantly associated with low postoperative depression scores. Disconnectome locations were not associated with either postoperative or change in depression scores.

Conclusions. Resection locations affect depressive symptoms in glioma patients. This information may be useful for patient counseling.

Key Points

- Resection location affects depressive symptoms in patients with diffuse glioma.
- Resections in the right hemisphere are linked to increased depression post-surgery.
- Resections of the left anterior temporal area relate to low depression post-surgery.

Diffuse gliomas can cause various physical, psychological, and neurocognitive symptoms.[1,2] Surgical resection is typically the initial treatment for these tumors and aims to maximize tumor removal while preserving functional brain tissue.[2,3] However, surgery could potentially alleviate or worsen existing symptoms and introduce new symptoms. Awake resections can yield better functional outcomes by intraoperatively testing functions such as motor or language functioning.[3] Similarly, increased or decreased depressive symptoms could not only be related to the psychological

Importance of the Study

Glioma surgery aims to remove the tumor while preserving functional brain tissue. Functionalities such as motor function and speech may be measured during surgery. However, mood regulation may also be affected by surgical location, which has not previously been researched. In this study, we therefore aimed to unravel the relationship between resection location and depressive symptoms. We used voxel-wise and disconnectome-based lesion-symptom mapping and incorporated relevant clinical characteristics to provide a comprehensive analysis. Our findings identified regions where resections significantly affect depressive symptoms, offering valuable insights for patient counseling.

impact of the dismal prognosis but also to the reduction of mass effect or disruption of functional brain networks. Depressive symptoms are frequent after treatment and diminish the quality of life and functioning and possibly also survival.[4–7] While several studies with small cohorts linked resection locations to changes in cognitive functioning,[8,9] the link between resection cavities and changes in depressive symptoms after surgery is unknown. Understanding this relationship could enhance awareness among medical professionals.

Lesion-symptom mapping is a method to relate focal brain lesions, such as those caused by a tumor or resection, to symptoms, such as depressive symptoms. Evidence of an association between brain tumor locations and depressive symptoms is limited. Emotional dysregulation has been linked to the cortico-thalamo-limbic circuit being infiltrated by diffuse glioma in patients before treatment.[8] Furthermore, a case study by Manouri et al. suggests a causal relationship between glioma resection in the cingulate gyrus and major depressive disorder.[9] Moreover, in a study including 11.8% of patients after tumor (primarily meningioma) resections, depressive symptoms were correlated with bilateral lesions in the anterior insula and dorsolateral prefrontal cortex and in the left dorsomedial prefrontal cortex.[10]

Traditional voxel-wise lesion-symptom mapping can be useful for localizing symptoms but does not consider spatial relations between brain regions. Voxels are unlikely to represent functional brain units but can be considered as parts of larger functional anatomical brain systems.[11] For instance, white matter tract disconnections have been linked to cognitive impairment, for which disconnectome analysis can be a useful approach to identify brain regions connected with removed tumor-infiltrated brain by white matter pathways.[12] Disconnectome-based lesion-symptom mapping might better reflect a lesion's direct and indirect distant effects.

In this study, we explore whether postoperative depressive symptoms and changes in depressive symptoms following glioma surgery are associated with the location of resections or their disconnected brain regions.

Methods

Patients

This study included patients diagnosed with diffuse glioma who had their first resection between 2009 and 2021. Patients were included from several observational studies at Amsterdam UMC location VUmc, which have been reported on before.[8,13] The studies were approved by the Medical Ethical Committee of Amsterdam UMC (2008.52; 2009.189; 2010.126; 2014.297) and conducted in accordance with the Declaration of Helsinki. All patients signed informed consent.

Patients were included if they were (1) at least 18 years old, (2) underwent a first-time resection for (3) a confirmed or revised histopathological diagnosis of supratentorial diffuse glioma WHO 2016 grade 2–4 after surgery, (4) had an MRI scan after surgery, and (5) completed the Center for Epidemiologic Studies Depression scale (CES-D) within a year before surgery and after surgery at approximately one year, at most within two years. MRI included at least a 3D T1-weighted sequence without (T1w) and with gadolinium contrast medium (T1c). T2-weighted (T2w) and Fluid Attenuated Fluid-attenuated inversion recovery (FLAIR) sequences were used when available.

Depressive Symptoms as Outcome

Depressive symptoms were assessed using the CES-D, which has good validity and reliability in cancer patients.[14,15] The CES-D consists of 20 questions about behavior and feelings in the past week. Each question is answered on a scale from zero to three, ranging from never or rarely (less than 1 day), to experiencing the feelings all the time (5–7 days). Hence, a maximum total score of 60 can be acquired, with higher scores representing patients having more and more frequent depressive symptoms. The CES-D can be binarized to no risk of depression (<16) and risk of depression (≥16).[16]

This study used two continuous outcome variables; the cross-sectional postoperative depression score, and the longitudinal change in depressive symptoms after surgery measured by the difference between postoperative and preoperative depression scores. A positive difference represents an increase on the CES-D scale and thus worsening of depressive symptoms.

Patient, Tumor, and Treatment Characteristics

We collected patient, tumor, and treatment characteristics including age, sex, educational level (low, middle, or high, as classified according to the Verhage scale),[17] preoperative Karnofsky Performance Status (KPS),[18] whether or not patients had radiological progression or were in the stable

phase at follow-up, whether or not patients suffering from epilepsy, tumor grade, and type according to the WHO classification, and whether patients received adjuvant therapy (radiotherapy and/or chemotherapy).[19]

Resection Locations

Surgical cavities were segmented to define resection locations and transformed to standard space as described before for tumors.[8] In short, automatic segmentations were generated using an adapted nn-Unet segmentation algorithm.[20] Segmentations were manually verified and edited where necessary (MC, PWH) under the supervision of an experienced neuroradiologist (FB) using 3D slicer v.5.0.2.[21,22] Patients' T1c scans were skull stripped using HD-BET followed by a non-linear registration with cost-function masking to Montreal Neurological Institute 152 (MNI152) standard space and resampled to 2 × 2 × 2 mm spatial resolution using ANTSpy v0.3.2 for Python v3.8.0.[23,24] These transformations were then applied to the segmentation and surgery characteristic, the resection cavity volume and laterality in standard space was extracted. Cavity distribution maps were constructed by summing cavity segmentations over all patients.

Disconnectome

A disconnectome was made for each patient using BCBtoolkit.[25] Within the toolkit, each patient's scan and associated cavity segmentation in standard space was registered to the brain space of 178 healthy subjects from the 7T Human Connectome Project.[26,27] The segmentation of the resection cavity was then used as the seed for tractography in Trackvis based on diffusion-weighted imaging data from these healthy subjects.[28] The tractographies were thresholded to create binary visitation maps, showing for each voxel whether it was intersected by a tract. These binary visitation maps were transformed back to standard space and averaged for each patient over all created visitation maps. The resulting patient-specific disconnectome thus accounts for interindividual variability of tract reconstructions from healthy subjects, with each voxel representing a probability of involvement ranging from 0 to 100%. We binarized these disconnectomes for probabilities over 50% and summarized over patients to create a disconnectome distribution map.[11]

Statistical Analysis

Continuous characteristics were reported with mean and standard deviation for normally distributed variables and with median and interquartile range otherwise. Categorical variables were reported as counts and percentages of the entire population. In further analysis, the following reference categories were used for variables: female for sex, high for educational level, KPS 90–100 for preoperative KPS, astrocytoma for histology, present for IDH mutation status, progression for disease phase, and left for resection side.

Differences in preoperative versus postoperative depression scores were tested using the Wilcoxon signed-rank test. Linear regression analysis was performed with the postoperative depression score and change scores as dependent variables separately. First, univariate regression was performed to select patient and tumor characteristics ($P < .05$) for multivariable regression in which surgery characteristics resected volume, and resection lateralization were added for coarse resection analysis. For more detailed localization analysis, significant variables from multivariable regression were included in lesion-symptom mapping analysis as confounders. P-values ≤ .05 were considered significant. Analyses were performed in R v4.2.1 and Python v3.8.0.

Resection Cavity Symptom Mapping

We employed voxel-wise lesion-symptom mapping to link the resection cavities and disconnectomes to the postoperative depression scores and score changes.[29] For all analyses we used the randomize function from FMRIB's Software Library (FSL). Randomized performed nonparametric permutation tests with family wise error correction (FWE) and threshold-free cluster enhancement.[30–33] 1000 permutations were used and voxels were masked for ≥3 cavities.[34] Voxels were considered statistically significantly related to the symptom if FWE $P < .05$.

Results

Patient Population

The cohort consisted of 83 patients with a mean age of 41 years (SD 12). Almost two-thirds of patients were male, most patients had received higher education (45.8%), two-thirds of patients were in good condition (KPS 90–100), and 59% of patients had a left-sided resection cavity. See Table 1 for details. For 23 patients we were unable to retrieve IDH mutation status. Therefore, this variable had 3 categories; mutated, wildtype, and unknown.

Depressive Symptoms After Surgery

Before surgery, 25% of patients had depressive symptoms, and after surgery 34% (Table 1, Figure 1A). Depressive symptoms did not change significantly after surgery ($V = 1520.5$, $p = 0.238$). Both increasing and decreasing depressive symptoms were observed with extremes in depression score changes ranging from −25 to + 30 (Figure 1B and C). Effectively, this meant that 19% of patients switched from no risk of depression to risk of depression, and 11% of patients switched from risk of depression to having no depressive symptoms.

IDH Mutation Status and Resection Side Are Associated With Change in Depressive Symptoms Following Surgery

From univariable regression, preoperative depression scores and KPS were associated with postoperative depression scores (Supplementary Table 1). In multivariable

Table 1. Patient Characteristics

	Overall (*N* = 83)
Age, mean (SD)	41.3 (12.0)
Sex male, *n*(%)	51 (61.4%)
Education (Verhage), *n*(%)	
High (6–7)	38 (45.8%)
Middle (5)	29 (34.9%)
Low (1–4)	16 (19.3%)
Preoperative KPS, *n*(%)	
70–80	13 (15.7%)
90–100	70 (84.3%)
Epilepsy, *n*(%)	71 (85.5%)
Progression on follow-up measurement, n(%)	13 (15.7%)
Resection side left, *n*(%)	49 (59.0%)
Resection volume (ml), median [IQR]	22.3 [30.4]
Histology, *n*(%)	
Oligodendroglioma	35 (42.2%)
Astrocytoma	34 (41.0%)
Glioblastoma	10 (12.0%)
Oligoastrocytoma*	4 (4.8%)
IDH-status, *n*(%)	
Mutated	50 (60.2%)
Wildtype	10 (12.0%)
Unknown	23 (27.7%)
Grade, *n*(%)	
2	51 (61.4%)
3	22 (26.5%)
4	10 (12.0%)
Time between baseline depression score and surgery (weeks preoperative), median [IQR]	4.71 [8.29]
Preoperative baseline depression scores (CES-D), median [IQR]	9.00 [10.5]
Time between surgery and follow-up depression score (weeks postoperative), mean (SD)	57.2 (16.2)
Has received chemotherapy, *n*(%)	27 (32.5%)
Has received radiotherapy, *n*(%)	36 (43.4%)

CES-D, Center for Epidemiological Studies-Depression Scale; IQR, Interquartile range; KPS, Karnofsky Performance Scale.
*As defined by the WHO 2007 classification.[19]

regression with the addition of surgery characteristics, high preoperative depression scores were related to high postoperative depression scores (coef = 0.75, CI = 0.51 to 0.99, standardized coef = 0.57; $P < .001$; Table 2). None of the other patient or cavity-related variables were related to postoperative depression score.

IDH mutation status was associated with a change in depression scores in univariable regression (Supplementary Table 2). This association was maintained after stratifying for patients with known IDH mutation status. In multivariable regression of surgery characteristics including all patients, IDH wildtype was associated with a decrease in depression scores (coef = –6.76, CI = –12.41 to –1.19, standardized coef = –0.26; $P = .019$) and having a right-sided resection was significantly associated with an increase of depression scores following surgery (coef = 3.86, CI = 0.19 to 7.53, standardized coef = 0.22; $P = .039$; Table 3).

Resection Locations are Significantly Associated With Depressive Symptoms After Surgery

The distribution of all patients' resection locations can be seen in Figure 2A. As expected, most resections were located in the frontal and temporal regions. In comparing patients without and with a risk of depression after surgery (Figure 2B), resections are more often located in the left anterior temporal lobe in those without a risk of depression. In voxel-wise lesion-symptom mapping, cavities of the left anterior temporal lobe were associated with lower postoperative depression scores (lowest FWE $P = .046$, Figure 2C), while adjusting for preoperative depression score.

In comparing patients with a decrease in depressive symptoms, ie, a negative difference, and those with an increase in depressive symptoms, ie, a positive difference, we found a similar voxel cluster in the left temporal area to be significantly associated with a larger decrease in depressive symptoms (lowest FWE $P = .037$, Figure 2E), while adjusting for IDH mutation status.

The intersection of these significant voxel clusters can be seen in Figure 3A. There were three voxels, in the same area, only significantly associated with a larger decrease in depressive symptoms. Figure 3B compares the depression scores of patients with and without resection cavity overlap with this specific region, further highlighting that patients after a resection including this region, had lower postoperative depression scores compared to those with a resection cavity outside this region.

Disconnectome Locations Are Not Significantly Associated With Depressive Symptoms After Surgery

Disconnectome locations were not significantly associated with postoperative depression scores (lowest FWE $P = .181$) or change in depression scores (lowest FWE $P = .251$). Disconnectome distributions and statistics can be observed in Supplementary Figure 1.

Preoperative CES-D Scores Do Not Differ Between Left- and Right-Sided Gliomas

We observed that right-sided resection cavities were associated with an increase in depressive symptoms but not with the prevalence of postoperative depressive symptoms. This led us to hypothesize a potential temporal disparity in the onset of depressive symptoms based on cavity lateralization: patients with a left-sided glioma might get depressive symptoms sooner in the trajectory, possibly before surgery, whereas patients with resection for a right-sided glioma develop depressive symptoms at a later stage. To explore this, we did

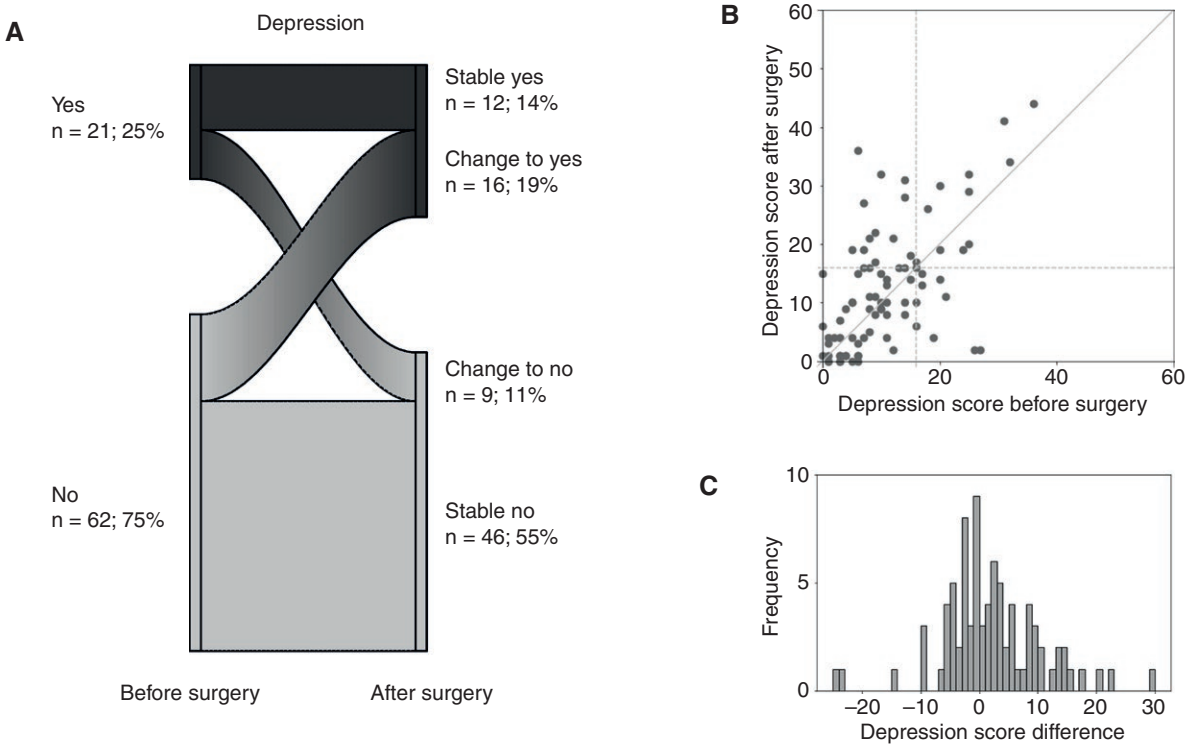

Figure 1. Depressive symptoms scores. (A) Depressive symptoms before and after surgery and the flow of changes in depressive symptoms. (B) Depression scores before and after surgery. (C) Histogram of depression scores after surgery minus depression scores before surgery.

Table 2. Predictors of Postoperative Depression Scores in Multivariable Regression

	Coef	95% CI	Std err	Standardized coef	z	*P* > |z|
Intercept	3.64	−0.60 to 7.88	2.16	−7.63e-17	1.68	.093
Preoperative depression scores *	0.75	0.51 to 0.99	0.12	0.57	6.21	<.001
KPS (70–80)	2.53	−2.74 to 7.80	2.69	0.09	0.94	.347
Cavity volume (ml)	−0.04	−0.10 to 0.02	0.03	−0.11	−1.22	.221
Hemisphere (Right)	3.32	−0.05 to 7.11	1.93	0.16	1.72	.086

CI, Confidence Interval.
*$P < .05$.

Table 3 Predictors of Depression Score Change in Multivariable Regression

	Coef	95% CI	Std err	Standardized coef	z	*P* > |z|
Intercept	2.06	−1.24 to 5.36	1.68	−2.43e-17	1.23	.220
Cavity volume (ml)	−0.03	−0.10 to 0.03	0.03	−0.10	−0.96	.336
Hemisphere (Right) *	3.86	0.19 to 7.53	1.87	0.22	−2.35	.039
IDH Wildtype *	−6.76	−12.41 to −1.19	2.88	−0.26	−2.35	.019
IDH Unknown	−1.52	−5.70 to 2.66	2.13	−0.08	−0.72	.476

CI, Confidence Interval.
*$P < .05$.

a post hoc analysis to compare preoperative depressive symptoms between patients with right- and left-sided gliomas. The results showed no significant difference (Mann–Whitney U = 2052, $P = .959$), indicating that preoperative depressive symptoms did not differ between tumor sides.

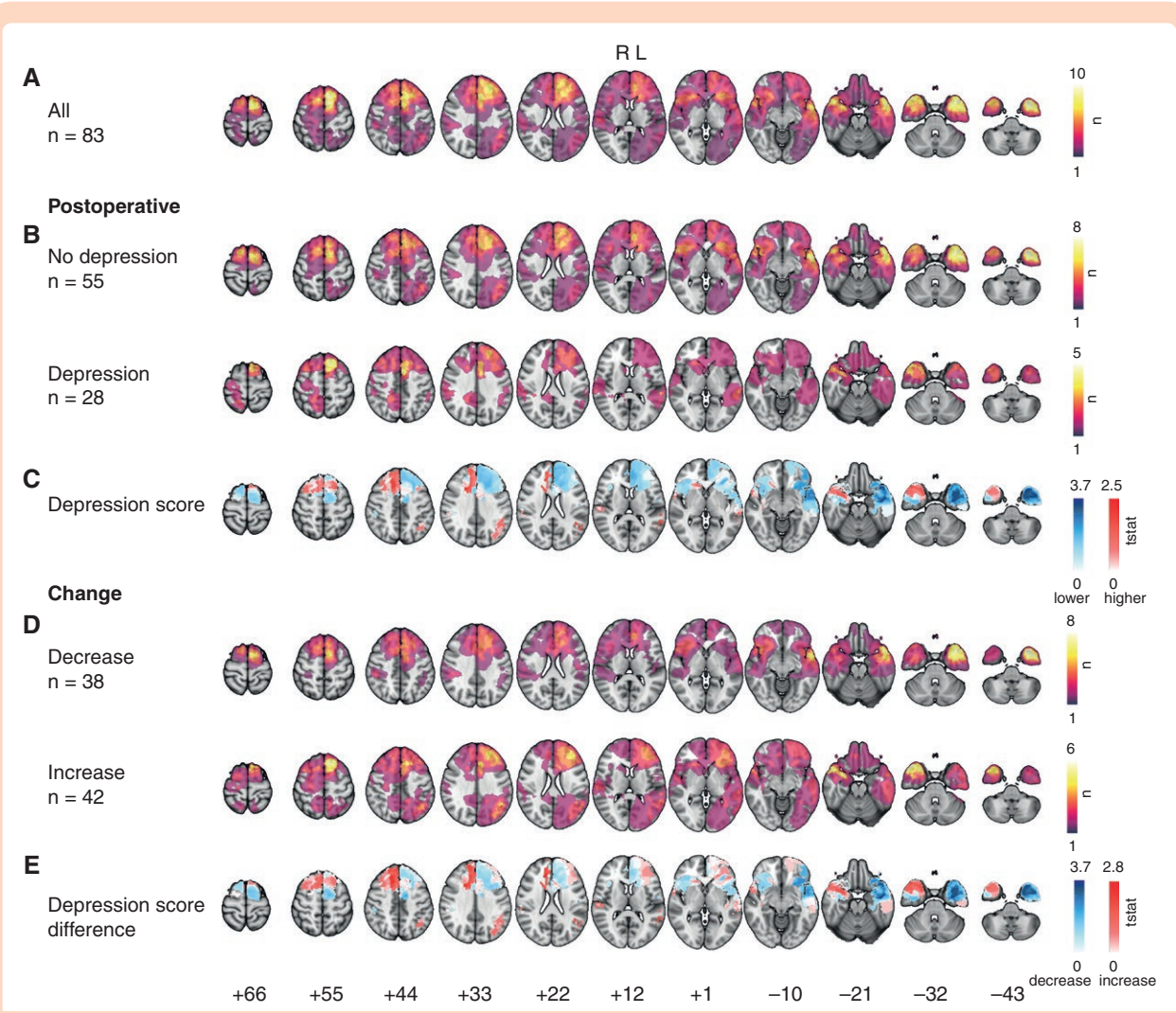

Figure 2. Resection location maps. (A) Distribution map of resection locations for all patients (B) Resection location distributions for patients without and with risk of depression after surgery. (C) T-statistic map of the relation between cavity location and postoperative depression score. Blue colors indicate voxels where a cavity is more likely to be related to low postoperative depression scores and red colors indicate voxels where a cavity is more likely to be related to high depression scores. Color intensity shows relationship strength. The lowest FWE *P* is .046 (significant). (D) Resection location distributions for patients with a decrease and increase in depression score change. For three patients, the depression scores did not change and were omitted from visualization. (E) T-statistic of the relation between cavity location and change in depression scores. Blue colors indicate voxels where a cavity is more likely to be related to a decrease in depression score and red colors indicate voxels where a cavity is more likely to be related to an increase in depression score. Color intensity shows relationship strength. The lowest FWE *P* is .037 (significant). The plotted numbers below represent z-axis slices in standard space.

Discussion

In this study, 34% of patients had depressive symptoms a year after surgery, compared to 25% before surgery, and 19% of patients switched from no risk of depression before surgery to risk of depression after surgery. IDH mutation status related to a decrease in depressive symptoms following surgery and right-sided resections related to an increase in depressive symptoms following surgery. Patients with resection cavities in the left anterior temporal lobe had lower depression scores postoperatively and a larger decrease in depressive symptoms following surgery, compared to scores of patients with resections in other regions.

The percentage of patients with depressive symptoms after surgery corroborated the literature, reporting a depression incidence of 39% across studies.[5] Although a recent systematic review suggests depressive symptoms are more prevalent before than after surgery,[35] another review shows varied findings with some patients experiencing a decrease in depressive symptoms after surgery, while others report an increase.[5] Our findings align with this variability between patients, as we observed a wide range of changes in depressive symptoms, but no significant overall change in depressive symptoms at the group level.

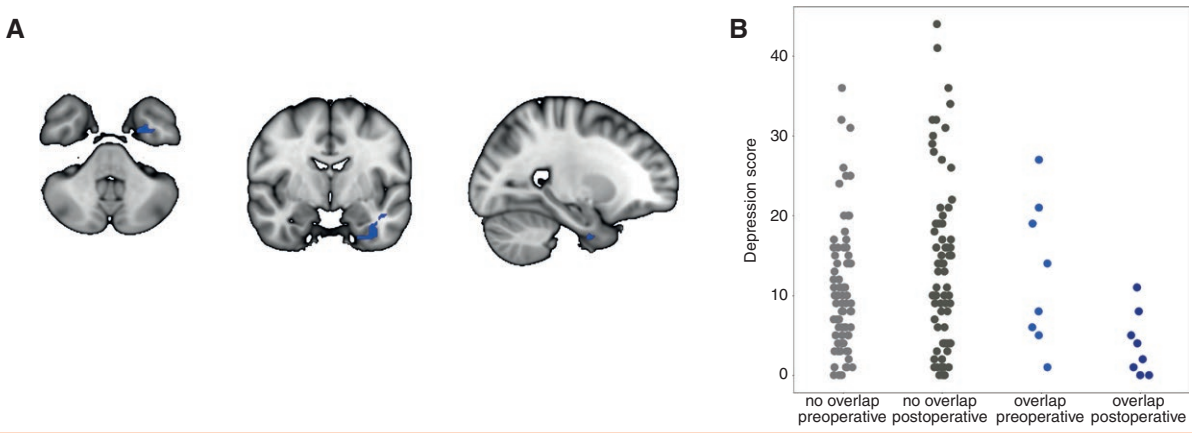

Figure 3. (A) Map of intersecting resection locations significantly associated with lower postoperative depression score and a larger decrease in depression score (FWE $P < .05$). (B) Preoperative and postoperative depression scores of patients with and without resection that overlap with the region depicted in panel A. Lower depression scores reflect less depressive symptoms.

Right-sided resections were related to an increase in depressive symptoms but not to the prevalence of postoperative depressive symptoms. The literature on hemispheric involvement of lesions and their relation to depression presents contradicting findings. A systematic review of brain tumor patients shows no association between tumor side and depressive symptoms in 6 out of 8 studies, with the timing of assessments mostly postoperatively or mixed (both pre and postoperatively).[5] The 2 studies that identified a link between depressive symptoms and the left hemisphere were both in preoperative patients,[36] supporting our speculation that depressive symptoms manifest first in patients with left-sided lesions, followed by those with right-sided lesions. However, we could not confirm an association between tumor side and preoperative depressive symptoms suggesting that the depressive symptoms could originate from the resection itself, or from other postoperative factors, such as functional impairment, still allowing for a temporal disparity in the onset of depressive symptoms postoperatively. This aligns with a theory in post-stroke depression, where it has been hypothesized that left-sided lesions are associated with depressive symptoms in the acute phase and right-sided lesions with depressive symptoms several months after stroke.[37] This may explain the increase in depressive symptoms in patients with right-sided lesions. Depressive symptoms resulting from different functional impairments may also explain a temporal disparity. For example, patients with left-sided tumors may experience communication deficits from the onset whereas patients with right-sided gliomas may encounter cognitive difficulties such as processing problems at a later stage.[38]

Alternatively, surgery on the right side could exacerbate depressive symptoms due to the resection itself, as we found that right-sided resections were associated with increased depressive symptoms. Functions such as language and motor function are generally monitored during surgery when the tumor is located in an area at higher risk for dysfunction, often in the left hemisphere. Mood regulation is typically not monitored as it is unknown which regions are involved. Consequently, these symptoms may be more prone to worsening if the responsible area, potentially on the right side, is resected. Indeed, as we showed before, some right-sided regions are preoperatively associated with severe depressive symptoms, ie, the fornix, the corticospinal tract, and the inferior fronto-occipital fasciculus.[8] Moreover, patients with a right-sided glioma often have problems with processing skills when performing everyday life tasks,[38] and diminished activity in right-sided regions has been related to a cognitive subtype of depression.[39,40] Possibly, the lack of observed differences in preoperative depression scores between tumor sides is attributed to selection bias. In our study where right-sided glioma lesions related to severe depressive symptoms before surgery,[8] 29% had a grade 4 tumor. In contrast, only 12% of our cohort had a grade 4 tumor, likely due to the one-year interval after surgery, during which patients may have been lost to follow-up due to tumor progression. Lower-grade gliomas, which were overrepresented in our study and are characterized by their slower growth, could allow for neuroplasticity that preserves certain functions, whereas faster-growing tumors or the acute effects of surgery could disrupt these processes. This difference could explain why we did not find a preoperative difference in depression scores but we observed that right-sided resection locations were still associated with an increase in depressive symptoms after surgery.

Of note, a resection cavity in the left anterior temporal lobe was related to lower postoperative depression scores and a larger decrease in depression scores following surgery. This region does not overlap with known structures involved in crucial functions like language, motor skills, or mood regulation. This may indicate a region involved in depressive symptoms and resection of this region could potentially alleviate symptoms. Additionally, this region could also be a previously unknown area involved in either resilience or pathological absence of depressive symptoms. These findings highlight the need for further research to clarify the role of the left anterior temporal lobe in depressive symptoms.

Moreover, our study did not identify a significant association between resection locations and higher postoperative depression scores. Interestingly, the variation in depression change scores was high, with some people experiencing a large increase in symptoms. Although we did not find a group effect, surgery or the period thereafter might have a large impact on individual patients. Existing literature does suggest lesion-depression correlations in both brain tumor patients and patients with other lesion types.[8,41,42] This discrepancy with our study might be due to our relatively small sample size of 83 patients, which possibly introduced variability in resection locations too broad for precise analysis. Moreover, the power of our methods could be too low to uncover correlations. Furthermore, depressive symptoms may not arise from dysfunction in isolated brain regions, but rather from disturbances within broader circuits involved in depression, as previously suggested in a study including various lesion etiologies.[43] Future research should explore how specific regions within a resection cavity might converge to a common depression brain circuit.

Strengths and Limitations

This study is the first to investigate the relationship between resection locations and depressive symptoms. Moreover, by performing a multivariable analysis, we aimed to comprehensively analyze potential influences on depressive symptoms. We employed modern imaging and disconnectome analysis techniques. However, this study also has some limitations. The moderate sample size and the varied distribution of resection cavities may have constrained our ability to detect robust associations of specific brain regions involved in depressive symptoms. Due to the sample size, we were unable to stratify the analysis according to tumor type. We did include IDH mutation status as a confounder in our analysis to account for its effects, however, this data was missing for some patients because archival tissue of older samples was unavailable. Additionally, rigorous testing standards, including conservative adjustments for multiple comparisons, were used, which might limit the detection of clinically significant anatomical correlates that could emerge under less stringent criteria or a larger cohort. Furthermore, selection bias may have occurred due to the inclusion of patients suitable for 1-year follow-up assessment, as reflected by the lower representation of patients with glioblastoma in our cohort. Moreover, cavity segmentations are subject to inter and intra-rater variability, and registrations of lesioned brains to standard space are inherently difficult.[44,45] These factors may introduce spatial inconsistencies and misrepresent the resection cavity in standard space. However, we tried to limit these errors by manual verification of segmentations and registrations.

Conclusion

Over a third of patients with glioma experienced depressive symptoms one year after surgery, whereas a quarter of patients had depressive symptoms before surgery. Resections in the right hemisphere related to an increase in depressive symptoms compared to baseline before surgery, but not to the prevalence of depressive symptoms at one year, possibly reflecting a temporal disparity in the onset of depressive symptoms between hemispheric involvement. A resection location involving the left anterior temporal lobe related to a lower depression score one year postoperative. This study is a step towards understanding changes in mood regulation that may occur following surgery.

Supplementary material

Supplementary material is available online at *Neuro-Oncology Advances* (https://academic.oup.com/noa).

Keywords:

brain neoplasms | connectome | depression | Lesion-symptom mapping | mood disorders

Lay Summary

Gliomas are common brain tumors. Surgeons try to remove as much of the tumor as possible while preserving important brain functions. After surgery, some patients experience mood changes or depression, while others do not. The authors of this study wanted to see if the location of tumor removal in the brain could affect whether or not patients develop depressive symptoms after surgery. To do this they studied 83 patients with brain tumors who completed mood questionnaires before surgery one year afterwards. They found that, for most patients, depressive symptoms did not change much after surgery. However, removing tumors from certain areas of the brain, such as the right hemisphere, was linked to more depressive symptoms, while removing tumors from the left anterior temporal region was associated with fewer symptoms.

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Conflict of interest statement

The authors declare no conflicts of interest.

Authorship statement

All authors commented on previous drafts and approved the final manuscript. Conceptualization: V.B., M.N.G.v.G., M.T.d.S., R.S.E., and P.C.d.W.H. Data collection: L.D. and M.K. Segmentation: A.F., M.C., and P.C.d.W.H. Analyses: V.B., M.N.G.v.G., and M.T.d.S. First draft: V.B and M.N.G.v.G.. Review and editing: M.T.d.S., M.C., L.D., A.F., F.B., M.K., J.M.N., R.S.E., and P.C.d.W.H. Supervision: F.B., J.M.N., R.S.E., and P.C.d.W.H.

Data availability

The primary patient dataset including clinical variables and MRI scans are not publicly available due to privacy regulations.

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