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Cognition in Meningioma: Effects of Tumor Location and Tumor Removal

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BACKGROUND: **Meningiomas are the most common type of primary intracranial tumor, yet very few studies have assessed the effects of tumor removal.**

METHODS: **Here we report analysis of patients with meningiomas who underwent routine neuropsychological assessment and surgery at a National Health Service (NHS) hospital in the North East of England over a 6-year period.**

RESULTS: **Surgical removal of tumors significantly improved both phonemic and semantic verbal fluency and some measures of working memory and declarative memory. There were no signs of deleterious effects of surgery. Postoperative improvements in cognition did not appear to rely upon changes in anxiety and mood.**

CONCLUSIONS: **In summary, we conclude that tumor removal in meningioma can be associated with some benefits in cognition.**

INTRODUCTION

Meningiomas are the most common type of primary intracranial tumor.[1,2] US statistics indicate an estimated prevalence rate of 50.4 per 100,000 individuals. Females are more commonly affected than males, by a ratio of 3:1.[3] The majority of meningiomas are slow growing, benign tumors (World Health Organisation grade I),[4] with surgery generally the frontline treatment for grade I meningiomas.[5] Here we focus upon the cognitive consequences of meningiomas, and meningioma surgery, while taking potential effects on emotionality into account. Since emotionality may adversely affect performance in cognitive tests, we first briefly summarize this literature.

Meningiomas: Depression and Anxiety

Higher-than-normal levels of depression in preoperative meningioma patients have been reported by some studies,[6-8] but not all studies,[9] with frontal meningiomas linked to higher levels of depression.[6,10] Postsurgery effects upon depression are unclear (e.g., some studies show increases[11]; some show decreases).[12] Higher-than-normal levels of anxiety in preoperative meningioma patients have been reported by some studies.[10,13,14] Postoperative reductions in anxiety after meningioma resection have been reported in several,[10,13,14,15] but not all studies.[11,12,16]

Meningiomas: Cognition

Studies have reported that meningiomas result in impairments in cognitive domains including working memory, declarative memory, processing speed, and verbal fluency.[14,17-19] Hemispheric location of tumor has received comparatively little attention, but some evidence suggests left more than right hemisphere meningiomas impair verbal tasks.[20] As such, there is scope to further

Key words
- Declarative memory
- Frontal
- Meningioma
- Phonemic fluency
- Resection
- Semantic fluency
- Working memory

Abbreviations and Acronyms
Anti-MS: Anti-multiple sclerosis
BMIPB: Birt Memory and Information Processing Battery
CAT: Categorical fluency test
FAS: The F-A-S test of phonemic fluency
HADS: Hospital Anxiety and Depression Scale
LH: Left hemisphere
NHS: National Health Service
RBANS: Repeatable Battery for the Assessment of Neuropsychological Status
RH: Right hemisphere
SEM: Standard error of the mean
TMT-B: Trail-Making Test B

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characterize the effect of tumor laterality upon cognitive function in preoperative patients.

A major motivation for the present study is that, rather surprisingly, the effects of surgical removal upon cognition are greatly understudied. We estimate that the total global sample size across all preoperative vs postoperative published studies up until 2024 of the effects of meningioma removal upon cognition is less than 700 patients.[9,14,17,18,21-32] Given that surgery is a frontline treatment for meningiomas, there is a clear rationale for developing a thorough understanding of any postoperative effects on cognition. It is far from clear which cognitive domains are most affected by meningiomas, and most likely to improve postoperatively. Some studies indicate postoperative improvements in working and declarative memory,[14,18] and others in verbal fluency.[17,18] However, perhaps due to relatively small sample sizes and task differences, some studies fail to show improvements in these domains (e.g., memory measures[17] and verbal fluency).[26] Thus, there is a clear rationale for further study of the effects of surgical removal upon cognition, which can then be meta-analyzed.

While previous studies often include measures of cognition and emotionality, there has been comparatively little exploration of their inter-relationship in meningiomas. Since, for instance, depression can dampen cognitive performance,[14,33] it is important to understand to what extent, if any, preoperative and postoperative performance on cognitive tests can be attributed to secondary changes in emotionality. With all these considerations in mind, here we present data on cognition and emotionality from a sample of patients undergoing routine neuropsychological assessment and surgery at an National Health Service (NHS) hospital in the North East of England. We compared patients with meningiomas restricted to either the left or right hemisphere on preoperative measures of cognition and emotionality. We also compared preoperative and postoperative cognition and emotionality scores (irrespective of location) to examine whether surgical resection affects either of these domains.

MATERIALS AND METHODS

Participants

Patients underwent neuropsychological assessment and surgery at an NHS hospital in the North East of England between July 2011 and August 2017. Neuropsychological data were collected at preoperative appointments and, for some patients was also collected at postoperative appointments, as a routine part of their care. Data analysis for this study was conducted retrospectively. In total, we had access to data from 142 patients. All identifying information was removed from the dataset by the clinical neuropsychology team thereby ensuring anonymity of the data. Permission to use the data for evaluation and research purposes was granted by the host NHS trust, South Tees Hospitals NHS Foundation Trust. As the analysis presented here is conducted upon different subgroups of patients, demographic data (age and gender) are presented for each of these subgroups (see tables in results section). Patients were excluded from the study if they were unable to complete the test battery. This includes patients with aphasia, visual impairments, and in low and minimally conscious states.

Neurological Details

Neurological details provided by the surgeons are presented for each patient in **Supplementary Table 1**. Tumor location labels were as follows: 1) Hemisphere (left, right, with some tumors involving both hemispheres). Hemispheric analyses compared left-confined and right-confined tumors only, ignoring tumors involving both hemispheres; 2) Lobe (occipital, parietal, temporal, and frontal, with some tumors involving more than one lobe). Lobe-related analyses compared frontal-confined tumors with tumors involving one or more of the occipital, parietal, temporal lobes; and 3) Specific meningeal locations (falcine/parafalcine, lateral sphenoid wing, tentorial, medial sphenoid wing/clinoid, convexity dura, cerebellopontine angle/petrous, sphenoid wing dura, planum sphenoidale, olfactory groove, middle fossa, parasagittal, and sellar/parasellar). **Tables 1—11** detail the patient ID numbers involved in each analysis, thus enabling cross-referencing with **Supplementary Table 1**.

Assessments of Emotionality and Cognition

Patients completed a battery of neuropsychological tests preoperatively and postoperatively. The average time between preoperative and postoperative assessments was 7.3 months. The tests included the Hospital Anxiety and Depression Scale (HADS), for assessment of emotionality, the Controlled Oral Word Association Test to assess phonemic and semantic fluency, Wechsler Adult Intelligence Scale to assess digit span, and Trail-Making Test B (TMT-B) to assess visuomotor processing and set-shifting. Assessment of memory was not standardized across all patients due to a change in the tests used as part of the standard neuropsychological assessment, with patients receiving the memory components of either the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) or the BIRT Memory and Information Processing Battery (BMIPB). Accordingly, patient sample sizes in this study are generally lower for the memory tests than those for the HADS and measures of verbal fluency.

Statistical Analysis

The dataset was comprised of both preoperative and postoperative data, although postoperative data were not available for all patients. We present analysis of a) preoperative assessment data, with a focus on the impact of tumor location on cognition and emotionality, and b) a comparison of preoperative and postoperative data, assessing whether there were any postoperative changes in emotionality or cognition. Preoperative hemisphere data (left hemisphere [LH] versus. right hemisphere [RH]) and preoperative versus postoperative data were analyzed using independent groups and repeated measures *t*-tests, respectively. The preoperative and postoperative TMT-B data were analyzed using Wilcoxon's Z, a method previously employed by other authors.[34] Where equal variances could not confidently be assumed in t-tests, Levene's correction was applied. Where this was the case, it was noted in the main text.

Although the total patient dataset comprised 142 patients, subgroups were necessarily smaller than this (e.g., patients undergoing test X for where both preoperative and postoperative scores were available). In order to reduce the impact of underpowered analyses, data were excluded from analysis whenever patient subgroup sample number was less than 8. This applied to

Table 1. Anxiety and Depression Are Significantly Higher in Preoperative Patients with Meningiomas Restricted to the Left Frontal Lobe Compared to Left Non-Frontal Meningiomas

Test	Hemisphere	Location	N (65)	Age (SD)	Sex†	Handednes‡	Score (SD)	T-Value	*P* Value	Cohen's d
HADS A	Left	Frontal-only	27	58.68 (14.68)	22 F; 5 M	24R; 3 L	7.22 (4.10)	2.37	0.024	0.75
		Non-frontal	9	59.67 (14.39)	5 F; 4 M	7 R; 2 L	4.78 (1.99)			
HADS D	Left	Frontal-only					5.29 (4.11)	2.19	0.037	0.70
		Non-frontal					3.00 (2.06)			
HADS A	Right	Frontal-only	24	59.13 (14.95)*	14 F; 10 M	22 R; 2 L	7.46 (5.23)	0.02	0.988	0.009
		Non-frontal	4	61.75 (10.31)	2 F; 2 M	3 R; 1 L	7.50 (3.87)			
HADS D	Right	Frontal-only					5.58 (4.05)	0.28	0.779	0.13
		Non-frontal					6.25 (6.18)			

Patient ID numbers:
HADS left frontal only (n = 27): 2,4,18,30,44,50,58,59,61,65,66,82,84,86,90,91,93,97,98,109,110,112,115,125,133,135,138
HADS left non-frontal (n = 9): 43,52,77,15,16,33,37,78,132
HADS right frontal only (n = 24): 3,10,12,14,29,34,36,40,53,55,56,60,68,69,73,89,96,99,100,108,114,123,137,141
HADS right non-frontal (n = 4): 27,35,75,85

No significant difference between right frontal and right non-frontal meningioma patients.
HADS, Hospital Anxiety and Depression Scale.
*Age data missing for 1 participant.
†F = female; M = male.
‡R = right-handed; L = left-handed.

Table 2. No Significant Postoperative Reductions in Levels of Anxiety or Depression

Measure	N	Age (SD)	Sex*	Handedness†	Preoperative Mean Score (SD)	Postoperative Mean Score (SD)	T-Value	*P* Value	Cohen's *d*
HADS A	23	56.35 (11.71)	17 F; 6 M	19 R; 4 L	8.57 (4.92)	7.96 (4.48)	0.61	0.548	0.13
HADS D	23	56.35 (11.71)	17 F; 6 M	19 R; 4 L	6.48 (4.10)	5.48 (5.70)	1.13	0.270	0.20

Patient ID numbers:
HADS A and D (n=23): 2,10,20,27,30,37,43,55,59,63,67,69,99,104,107,109,112,114,116,123,136,137,140

HADS, Hospital Anxiety and Depression Scale.
*F = female; M = male.
†R = right-handed; L = left-handed.

preoperative and postoperative assessments of performance in BMIPB figure copy, figure immediate recall, and delayed recall tasks. One exception was made for a specific patient subgroup: patients with tumors which were restricted to the RH and in a non-frontal location (n = 4). This was because the other 3 groups in related comparisons (LH frontal, LH non-frontal, RH frontal) had sufficient samples, and there was no obvious sign that a higher subgroup sample number would greatly change the result (see Table 1). Naturally, we advise caution in interpreting the results of this analysis.

Where possible, we compared our data to published normative data, using linear interpolation to calculate predicted normative scores for all participants unless otherwise specified. For the HADS, we used the norms published in Breeman and colleagues,[35] Tables 2 and 3, which stratifies the norms by age and gender. We used linear interpolation to calculate the predicted scores for all participants aged between 25 and 62 years old, and linear regression for those aged 63 and over. For verbal fluency and TMT-B, we used the norms published in Tombaugh et al. (1999) and Tombaugh et al. (2004) respectively,[36,37] adjusting for gender and years of education. We used the published RBANS subtest means, which are stratified by age and form (there are 4 parallel versions of this test), and digit span norms were calculated using Grégoire & Van Der Linden's,[38] which are stratified by age and years of education.

RESULTS

Emotionality and Tumor Location: For Left-Sided Meningiomas, Anxiety was Higher in Patients with Frontal Tumors

Conceivably, changes in emotionality such as increased anxiety or depression could affect cognitive performance. Accordingly, we first present analysis of the emotionality data.

Table 1 and Figure 1 show that preoperative HADS anxiety scores were higher in patients with left frontal meningiomas

Table 3. Preoperatively, Phonemic Fluency Is Significantly More Impaired in the LH-Confined Than RH-Confined Patients

Measure	Hemisphere	N	Age (SD)	Sex‡	Handedness§	Score (SD)	T-Value	*P* Value	Cohen's *d*
FAS	Left	48	60.02 (14.91)	34 F, 14 M	41 R; 7 L	27.92 (14.03)	2.06	0.043	0.47
	Right	34	58.15 (13.49)	31 F; 3 M	31 R; 3 L	33.79 (10.46)			
HADS A	Left*	44	58.55 (14.62)	31 F; 13 M	38 R; 6 L	7.00 (4.13)	0.58	0.564	0.13
	Right†	32	57.93 (13.18)	28 F; 3 M	28 R; 3 L	7.59 (4.77)			
HADS D	Left*	44	58.55 (14.62)	31 F; 13 M	38 R; 6 L	4.93 (3.95)	0.85	0.397	0.20
	Right†	32	57.93 (13.18)	28 F; 3 M	28 R; 3 L	5.71 (4.01)			

Patient ID numbers:
FAS preoperative left hemisphere (n = 48): 2,4,9,15,16,18,20,22,30,32,33,37,43,44,48,50,52,58,61,65,66,67,70,74,77,78,82,87,90,91,93,97,98,109,110, 112,113,115,116,117,119,121,125,132,133,135,136,138 (HADS A and D data unavailable for ppt 9, 22,113,121)
FAS preoperative right hemisphere (n = 34): 3,6,10,12,14,29,34,35,36,40,53,55,56,60,63,64,68,69,73,75,85,89,94,96,99,100,104, 108,114,118, 123, 126, 137,141 (HADS A and D data unavailable for ppt 64 and 126)

HADS scores did not differ between these two groups.
HADS, Hospital Anxiety and Depression Scale; LH, left hemisphere; RH, right hemisphere; FAS, the F-A-S test of phonemic fluency.
*HADS A data unavailable for 4 participants in the left hemisphere group.
†HADS D data unavailable for 3 participants in the right hemisphere group.
‡F = female; M = male.
§R = right-handed; L = left-handed.

Table 4. Preoperatively, Semantic Fluency Performance Is Comparable Between LH-Confined Than RH-Confined Patients

Measure	Hemisphere	N	Age (SD)	Sex	Handedness	Score (SD)	T-Value	*P* Value	Cohen's *d*
CAT	Left	48	60.26 (14.85)	35 F; 13 M	40 R; 8 L	15.61 (5.97)	1.57	0.121	0.36
	Right	33	58.15 (13.49)	18 F; 15 M	30 R; 3 L	17.53 (4.67)			
HADS A	Left	46*	58.84 (14.85)	32 F; 13 M	38 R; 7 L	7.04 (4.10)	0.54	0.590	0.12
	Right	32†	58.68 (13.60)	18 F; 14 M	29 R; 3 L	7.59 (4.77)			
HADS D	Left	46*	58.84 (14.59)	32 F; 13 M	38 R; 7 L	5.04 (3.98)	0.73	0.467	0.17
	Right	32†	58.68 (13.60)	18 F; 14 M	29 R; 3 L	5.72 (4.01)			

Patient ID numbers:
CAT preoperative left hemisphere (n=48): 2,4,9,15,16,18,20,22,30,32,33,37,43,44,48,50,52,58,59,61,65,66,67,70,74,77,78,82,87,90,91,93,97,98, 109,110,112,113, 115,116,117,121,125,132,133,135,136,138 (HADS A and D data unavailable for ppt 22,113 and121)
CAT preoperative right hemisphere (n=33: 3,6,12,14,29,34,35,36,40,53,55,56,60,63,64,68,69,73,75,85,89,94,96,99,100,104,108,114,118,123,126,137,141 (HADS A and D unavailable for 64,126)

HADS scores did not differ between these two groups.
HADS, Hospital Anxiety and Depression Scale; LH, left hemisphere; RH, right hemisphere; CAT, categorical fluency test; F, female; M, male; R, right-handed; L, left-handed.
*HADS A and D data unavailable for 4 participants in the left hemisphere group.
†HADS A and D data unavailable for 2 participants in the right hemisphere group.

(N = 27, M = 7.22 ± 0.79) than those with left other meningiomas (N = 9, M = 4.78 ± 0.66), $t_{37} = 2.37$, P = 0.024. To explore this finding further, we ran a complementary multiple regression examining age, sex, tumor lobe locality (left frontal vs. left other), and tumor size (mm^2). A significant model emerged ($F[4, 25] = 3.059$, P = 0.035, adjusted $R^2 = 0.221$), in which both tumor lobe locality (β = 0.405, P = 0.033, frontal more anxious) and age (β = −0.376, P = 0.040) did predict, but tumor size (β = 0.192, P = 0.278) and sex (β = 0.039, P = 0.839) did not predict, HADS anxiety.

As regards more specific tumor locations within the LH, it was possible to compare convexity dura tumors versus other locations but no difference was observed (convexity dura: N = 16, M = 6.69 ± 0.95; other tumor locations: N = 14, M = 7.36 ± 1.04, $t_{28} = 0.477$, P = 0.637). As regards medication in those with LH-confined tumors, the variety of drugs taken precluded any meaningful drug group analysis. However, we could see no clear effect of drugs upon anxiety (no medication: N = 9, M = 8.67 ± 1.31; medication: N = 19, M = 6.32 ± 1.04, $t_{26} = 1.330$, P = 0.195).

Emotionality and Tumor Location: For Left-Sided Meningiomas, Depression was Higher in Patients with Frontal Tumors and Convexity Tumors

As for anxiety, preoperative HADS depression scores were higher in patients with left frontal (N = 27, M = 5.29 ± 0.79) than left non-frontal (N = 9, M = 3.00 ± 0.67) meningiomas $t_{35} = 2.19$, P = 0.037. Within the LH, depression scores were higher in those with convexity dura tumors (N = 16, M = 6.06 ± 0.96) than those in other locations (N = 14, M = 3.43 ± 0.69: $t_{28} = 2.162$, P = 0.035, Levene's correction). Within the LH, we could see no clear sign of drug effects on HADS depression scores (no medication: N = 9, M = 4.56 ± 1.31; medication: N = 19, M = 5.53 ± 0.91, $t_{26} = 0.608$, P = 0.550). Predicting variance in HADS depression was less straightforward than with anxiety: the equivalent regression

Table 5. Significant Postoperative Improvement in Phonemic Fluency (without Significant Changes in Emotionality), with No Postoperative Change in HADS Scores

Measure	N	Age (SD)	Sex†	Handedness‡	Preoperative Mean Score (SD)	Postoperative Mean Score (SD)	T-Value	*P* Value	Cohen's *d*
FAS	21	56.24 (11.68)	14 F; 7 M	18 R; 3 L	31.71 (11.36)	38.19 (11.00)	2.77	0.012	0.58
HADS A	20*	55.90 (11.88)	14 F; 6 M	17 R; 3 L	8.05 (5.01)	7.25 (4.98)	0.74	0.466	0.16
HADS D	20*	55.90 (11.88)	14 F; 6 M	17 R; 3 L	5.95 (4.03)	5.50 (5.62)	0.51	0.617	0.29

Patient ID numbers:
FAS prepost (n=21): 2,10,20,30,35,37,43,55,63,67,69,99,104,109,112,114,116,123,136,137,140 (HADS A and D data unavailable for ppt 35)

HADS, Hospital Anxiety and Depression Scale; FAS, the F-A-S test of phonemic fluency.
*HADS A and D data unavailable for 2 participants.
†F = female; M = male.
‡R = right-handed; L = left-handed.

Table 6. Significant Postoperative Improvement in Semantic Fluency (without Significant Changes in Emotionality), with No Postoperative Change in HADS Scores

Measure	N	Age (SD)	Sex†	Handedness‡	Preoperative Mean Score (SD)	Postoperative Mean Score (SD)	T-Value	*P* Value	Cohen's *d*
CAT	20	58.30 (11.22)	14 F; 6 M	17 R; 3 L	15.60 (4.11)	17.60 (5.30)	2.13	0.046	0.42
HADS A	19*	58.05 (11.47)	14 F; 5 M	16 R; 3 L	7.11 (3.93)	6.89 (4.61)	0.22	0.827	0.05
HADS D	19*	58.05 (11.47)	14 F; 5 M	16 R; 3 L	5.74 (3.90)	4.74 (4.99)	1.03	0.316	0.22

Patient ID numbers:
CAT prepost (n=20): 2,20,30,35,37,43,55,59,63,67,69,99,104,109,112,116,123,136,137,140 (HADS A and D data unavailable for ppt 35)

HADS, Hospital Anxiety and Depression Scale; CAT, categorical fluency test.
*HADS A and D data unavailable for 1 participant.
†F = female; M = male.
‡R = right-handed; L = left-handed.

model to that above for anxiety was not significant ($F(4, 25) = 1.276$, $P = 0.306$): tumor lobe locality ($\beta = 0.277$, $P = 0.178$); age ($\beta = 0.013$, $P = 0.946$); sex ($\beta = 0.177$, $P = 0.405$); tumor size ($\beta = 0.198$, $P = 0.315$), with age being unpredictive, unlike in anxiety.

There were no differences between patients with right frontal and right non-frontal meningiomas (though this latter group was very small), and no effects of laterality for frontal meningiomas (both P values > 0.87).

Emotionality: Effects of Surgery

Average preoperative anxiety scores were above, and average preoperative depression scores were below, the clinical threshold[14]; modest reductions in both anxiety and depression following surgery were not statistically significant (Table 2).

Effects of Meningioma Upon Cognition

Verbal Fluency. Phonemic and semantic fluency were measured using two well-established tasks (the F-A-S test, where patients are asked to name as many words beginning with F, A, and S (FAS), and categorical fluency test (CAT), respectively). To help consider if cognitive effects are secondary to those of emotionality, for each cognitive comparison in a given patient subset, we present the HADS anxiety and depression data from those same patients. As we shall see, there was no specific evidence for cognitive effects being secondary to those of emotionality.

Lower Phonemic Verbal Fluency in Patients with: a) Left-Sided than Right-Sided Tumors; b) Convexity Dura than Falcine/Parafalcine Tumors. Preoperatively, patients with LH-confined meningiomas had lower phonemic fluency (FAS) ($N = 48$, $M = 27.94 \pm 2.03$) than those with RH-confined meningiomas ($N = 34$, $M = 33.79 \pm 1.79$, $t_{80} = 2.06$, $P = 0.043$, Cohen's $d = 0.47$, Table 3 top row, and Figure 2A). Importantly, this left-side lower phonemic fluency is particularly unlikely to be due to higher performance anxiety or reduced motivation since HADS A and HADS D scores are, if anything, lower in the LH-confined

Table 7. Significant Postoperative Improvement on Digit Span Backward, with No Postoperative Change in HADS Scores

Measure	N	Age (SD)	Sex†	Handedness‡	Preoperative Mean Score (SD)	Postoperative Mean Score (SD)	T-Value	*P* Value	Cohen's *d*
Digit span forward	10	57.10 (11.62)	8 F; 2 M	9 R; 1 L	9.10 (2.12)	9.20 (2.10)	0.18	0.864	0.05
Digit span backward	10	57.10 (11.62)	8 F; 2 M	9 R; 1 L	6.80 (1.40)	8.40 (1.90)	2.67	0.026	0.96
Digit span sequencing	10	57.10 (11.62)	8 F; 2 M	9 R; 1 L	7.30 (1.16)	8.00 (1.83)	1.56	0.153	0.46
HADS A	8*	57.63 (10.38)	6 F; 2 M	7 R; 1 L	6.63 (4.60)	7.88 (4.55)	0.72	0.493	0.27
HADS D	8*	57.63 (10.38)	6 F; 2 M	7 R; 1 L	5.88 (4.45)	5.00 (4.31)	0.60	0.567	0.20

Patient ID numbers:
Digit span (n=10): 30,43,57,63,67,69,104,116,132,136 (HADS missing for 57 & 132)

HADS, Hospital Anxiety and Depression Scale.
*HADS A and D data unavailable for 2 participants.
†F = female; M = male.
‡R = right-handed; L = left-handed.

Table 8. Significant Postoperative Improvement on TMT Part B, with No Postoperative Change in HADS Scores

Measure	N	Age (SD)	Sex*	Handedness†	Preoperative Mean Score (SD)	Postoperative Mean Score (SD)	T-Value	*P* Value	Effect Size
TRAILS B	13	56.62 (11.56)	9 F; 4 M	11 R; 2 L	131.00 (86.50)	86.00 (55.05)	1.99	0.046	0.55
HADS A	13	56.62 (11.56)	9 F; 4 M	11 R; 2 L	8.85 (5.87)	6.92 (5.19)	1.39	0.189	0.35
HADS D	13	52.62 (11.56)	9 F; 4 M	11 R; 2 L	6.31 (3.79)	5.69 (6.29)	0.52	0.616	0.12

Patient ID numbers:
TRAILS B, HADS A and B (n=13): 2,10,37,55,63,69,99,107,109,114,123,137,140

HADS, Hospital Anxiety and Depression Scale; TMT-B, Trail-Making Test B.
*F = female; M = male.
†R = right-handed; L = left-handed.

meningiomas group (Table 3 bottom rows). Which hemisphere is language dominant is, of course, modulated by handedness.[39] Accordingly, we reran analysis to exclude left-handed patients, i.e., to exclude some patients who would be expected to be RH language dominant. If anything, the results were even clearer that LH tumors were associated with lower phonemic fluency (LH FAS scores N = 41, M = 25.95 ± 2.01; RH N = 31, M = 34.90 ± 2.08, $t_{70} = 3.043$, P = 0.003, Cohen's d = 0.72). Removing left-handers also did not change the fact that HADS anxiety and depression scores were not significantly different in those with left versus right tumors. As regards specific locations, those with convexity dura tumors (N = 37, M = 28.84 ± 2.04) had lower FAS scores than those with falcine/parafalcine tumors (N = 17, M = 37.71 ± 3.69: $t_{52} = 2.268$, P = 0.027), likely because some convexity meningiomas will include locations nearer to areas important for language such as the perisylvian fissure, whereas falcine/parafalcine tumors are located nearer the midline in the brain. The sample sizes for other specific tumor locations were too low to compare. To further examine the issue of lower phonemic fluency in left-sided meningiomas and to consider tumor size, a multiple regressions analysis was conducted examining hemisphere locality (left vs. right) sex, age, education, and tumor size (mm²). Analysis continued to point to the importance of hemispheric locality (β = 0.250, P = 0.049, left = lower FAS scores), though the overall model was not statistically significant (F(5,63) = 1.620, P = 0.168), alongside weakly/nonpredictive covariables: tumor size (β = - 0.032, P = 0.805), age (β = -0.078, P = 0.534) sex, (β = -0.116, P = 0.385, and education (β = 0.151, P = 0.242).

We could see no sign whatsoever of any effects of anticonvulsant and anti-multiple sclerosis drugs upon FAS scores

Table 9. Preoperatively, No Significant Difference Between Hemisphere-Confined Groups on BMIPB Immediate or Delayed Story Recall, HADS Scores Did Not Differ Between These Two Groups

Measure	Hemisphere	N	Age (SD)	Sex‡	Handedness§	Score (SD)	T-Value	*P* Value	Cohen's *d*
BMIPB immediate story recall	Left	21	59.71 (16.54)	16 F; 5 M	18 R; 3 L	23.95 (11.36)	0.33	0.741	0.11
	Right	15	62.50 (14.19)	8 F; 7 M	14 R; 1 L	25.33 (13.46)			
BMIPB-delayed story recall	Left	21	59.71 (16.54)	16 F; 5 M	18 R; 3 L	22.10 (12.19)	0.80	0.428	0.27
	Right	15	62.50 (14.19)	8 F; 7 M	14 R; 1 L	25.67 (14.44)			
HADS A	Left*	20	58.85 (16.48)	15 F; 5 M	18 R; 2 L	6.65 (3.69)	0.090	0.930	0.30
	Right†	13	66.58 (13.90)	7 F; 6 M	12 R; 1 L	7.77 (3.90)			
HADS D	Left*	20	58.85 (16.48)	15 F; 5 M	18 R; 2 L	4.55 (3.97)	0.42	0.680	0.15
	Right†	13	66.58 (13.90)	7 F; 6 M	12 R; 1 L	5.15 (4.24)			

Patient ID numbers:
BMIPB left hemisphere (n=21): 4,15,16,22,30,33,43,44,48,50,61,67,77,78,82,90,115,116,125,132,136. HADS data missing for 22.
BMIPB right hemisphere (N=15): 6,12,29,34,35,40,63,64,69,75,100,104,118,126,141. HADS data missing for 64 and 126.

BMIPB, Birt Memory and Information Processing Battery; HADS, Hospital Anxiety and Depression Scale.
*HADS A and D data unavailable for 1 participant in the left hemisphere group.
†HADS A and D data unavailable for 4 participants in the left hemisphere group.
‡F = female; M = male.
§R = right-handed; L = left-handed.

Table 10. Significant Postoperative Improvement in BMIPB Immediate Story Recall, with No Postoperative Change in HADS Scores

Measure	N	Age (SD)	Sex†	Handedness‡	Preoperative Mean Score (SD)	Postoperative Mean Score (SD)	T-Value	*P* Value	Cohen's *d*
BMIPB immediate story recall	12	59.08 (11.77)	9 F; 3 M	11 R; 1 L	23.08 (9.99)	32.17 (10.85)	3.80	0.003	0.87
BMIPB delayed story recall	12	59.08 (11.77)	9F, 3M	11 R; 1 L	26.83 (20.24)	28.75 (11.64)	0.34	0.737	0.12
HADS A	8*	57.63 (10.38)	6 F; 2 M	7 R; 1 L	6.88 (4.49).	7.63 (4.72)	0.42	0.685	0.16
HADS D	8*	57.63 (10.38)	6 F; 2 M	7 R; 1 L	5.88 (4.45)	5.00 (4.31)	0.60	0.557	0.20

Patient ID numbers:
BMIPB (n=12): 30,35,43,49,57,63,67,69,104,116,132,136. HADS data missing for ppt 35,49,57,132

BMIPB, Birt Memory and Information Processing Battery; HADS, Hospital Anxiety and Depression Scale.
*HADS A and D data unavailable for 4 participants.
†F = female; M = male.
‡R = right-handed; L = left-handed.

([anticonvulsant [N = 12, M = 31.00 ± 3.44] versus. no-medication [N = 16, M = 30.56 ± 3.79, t_{26} = 0.083, P = .935]; anti-multiple sclerosis (anti-MS) [N = 21, M = 30.43 ± 2.68] versus. no-medication: t_{35} = 0.03, P = .976; anticonvulsant vs. anti-MS: t_{31} = 0.130, P = 0.897]). This suggests that drugs were unlikely to be a major confound in attributing fluency impairments to tumor hemisphere or location. In all, we conclude that lower verbal fluency in left-sided meningiomas appeared to be a real, if modest, effect, that convexity dura tumors worsened fluency, and that tumor size played little role in modulating fluency.

The tendency of left-sided meningiomas to reduce fluency was not statistically significant in the domain of semantic fluency (t_{79} = 1.57, P = 0.12, Cohen's *d* = 0.36; see Table 4 and Figure 2B). Removing left-handers from the analysis (see above for rationale) strengthened this tendency but the result did not quite reach statistical significance (LH-confined tumors (N = 41, M = 15.05 ± 0.92); RH-confined tumors (N = 31, M = 17.55 ± 0.84), t_{70} = 1.94, P = 0.057, Cohen's *d* = 0.46). To check for any effect of tumor size, we ran 2 analyses. Firstly, a multiple regression examining hemisphere locality (left vs. right) and tumor size (mm^2). Again, analysis suggested a weak but nonsignificant trend effect of hemispheric locality (β = 0.225, P = 0.083, left = lower CAT scores), with no sign at all of a tumor size effect (β = −0.039, P = 0.760), within an overall model that was not statistically significant (F(2,63) = 1.907, P = 0.157). Secondly, within the LH-confined, right-handed only, subset of the patients, we could see no sign of a correlation between tumor size and CAT scores (r = −0.134, P = 0.424).

Surgery Improved Phonemic Fluency

Surgery improved phonemic fluency: FAS scores were significantly higher postoperatively (N = 21, M = 38.19 ± 2.40) than preoperatively (M = 31.71 ± 2.48; paired t_{20} = 2.77, P = 0.012, Cohen's *d* = 0.58). See Table 5 and Figure 3A. Again, this result seemed clearer when removing left-handers from the sample

Table 11. Significant Improvement in RBANS List Recall, with No Postoperative Change in HADS Scores

Measure	N	Age (SD)	Sex†	Handedness‡	Preoperative Mean Score (SD)	Postoperative Mean Score (SD)	T-Value	*P* Value	Cohen's *d*
RBANS story memory	13	55.54 (13.30)	10 F; 3 M	10 R; 3 L	14.62 (3.33)	13.62 (5.85)	0.80	0.441	0.21
RBANS list recognition	13	55.54 (13.30)	10 F; 3 M	10 R; 3 L	17.77 (2.92)	18.62 (1.71)	1.53	0.152	0.36
RBANS list recall	13	55.54 (13.30)	10 F; 3 M	10 R; 3 L	3.62 (3.10)	4.85 (2.91)	2.62	0.022	0.41
RBANS story recall	13	55.54 (13.30)	10 F; 3 M	10 R; 3 L	6.77 (2.39)	7.00 (3.34)	0.27	0.792	0.08
HADS A	12*	54.50 (13.33)	9 F; 3 M	9 R; 3 L	9.25 (5.22)	7.00 (4.41)	1.65	0.126	0.47
HADS D	12*	54.50 (13.33)	9 F; 3 M	9 R; 3 L	6.42 (3.73)	5.42 (5.98)	0.87	0.405	0.20

Patient ID numbers:
RBANS (n=13): 2,9,10,20,27,37,55,107,109,112,123,137,140. HADS data missing for ppt 9.

HADS, Hospital Anxiety and Depression Scale; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status.
*HADS A and D data unavailable for 1 participant.
†F = female; M = male.
‡R = right-handed; L = left-handed.

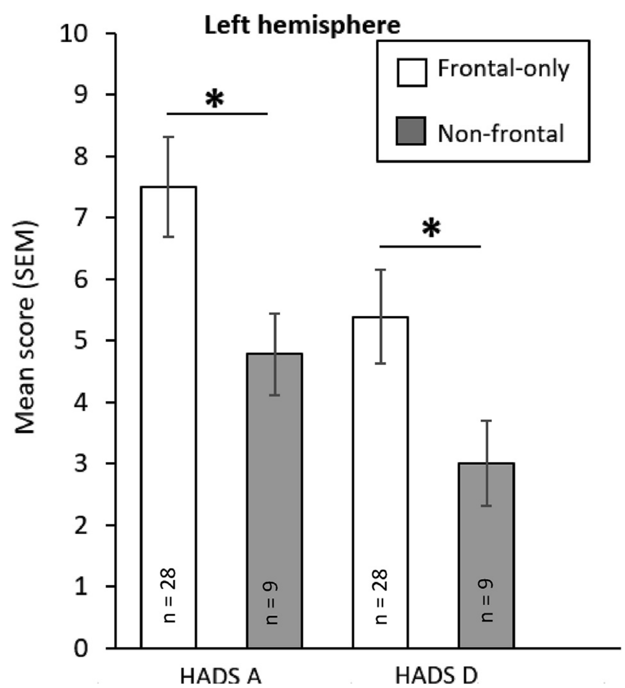

Figure 1. Anxiety and depression are significantly higher in patients with left frontal compared to left non-frontal meningiomas (* = $P < 0.05$; bars show mean score, error bars SEM (standard error of the mean)). HADS, Hospital Anxiety and Depression Scale.

(postoperative M = 38.44 ± 2.70: preoperative scores, M = 30.00 ± 2.34, t_{17} = 3.947, P = 0.001, Cohen's *d* = 0.93). Sample size precluded analysis of tumor-location modulation of this effect.

Surgery Improved Semantic Fluency

Surgery also improved semantic fluency (CAT scores, N = 20: postoperative M = 17.60 ± 1.19; preoperative M = 15.60 ± 0.92, t_{19} = 2.13, P = 0.046, Table 6 and Figure 3B). These improvements were accompanied by nonsignificant reductions in both anxiety and depression. We could see no strong sign of specific tumor location affecting the improvement in CAT scores (convexity dura tumors: N = 10, M = +3.30 ± 1.67; other tumors: N = 9, M = +0.78 ± 0.81, t_{17} = 1.36, P = 0.20 [Levene's correction]). When removing the left-handers for this analysis, the surgical improvement in CAT scores was reduced to a not significant trend (preoperative CAT scores N = 17, M = 15.24 ± 1.02; postoperative scores M = 17.29 ± 1.36, t_{16} = 1.872, P = 0.080), perhaps due to underpowered comparison as the effect size was not markedly different between the 2 analyses (left-handers included Cohen's d = 0.47; no left-handers Cohen's d = 0.42).

Surgery Improved Two Measures of Working Memory

Working memory consists of both executive and mnemonic components. Surgery significantly improved 2 of 4 measures of working memory: first, the more difficult digit span backward measure of working memory (N = 10, postoperative M = 8.40 ± 0.60; preoperative M = 6.80 ± 0.44), t_9 = 2.67, P = 0.026, Table 7, Figure 4). This result held when removing left-handers from the analysis (postoperative M = 8.11 ± 0.63, preoperative = M = 6.56

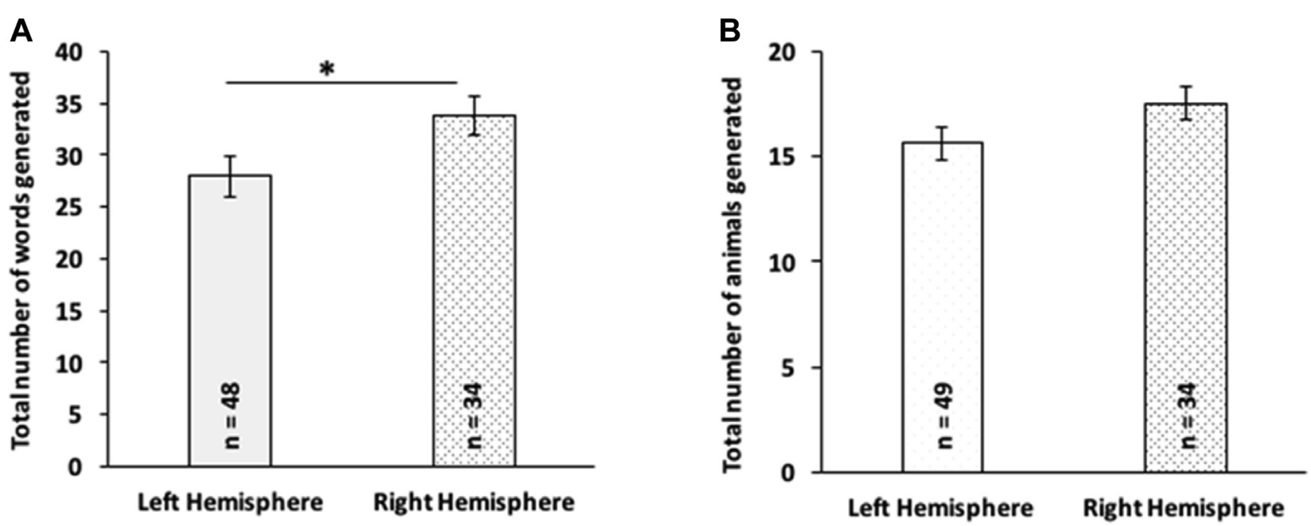

Figure 2. Phonemic (**A**), but not semantic (**B**) fluency is impaired in patients with LH-confined meningiomas compared to patients with RH-confined meningiomas (* = P <0.05; bars show mean score, error bars SEM). LH, left hemisphere; RH, right hemisphere.

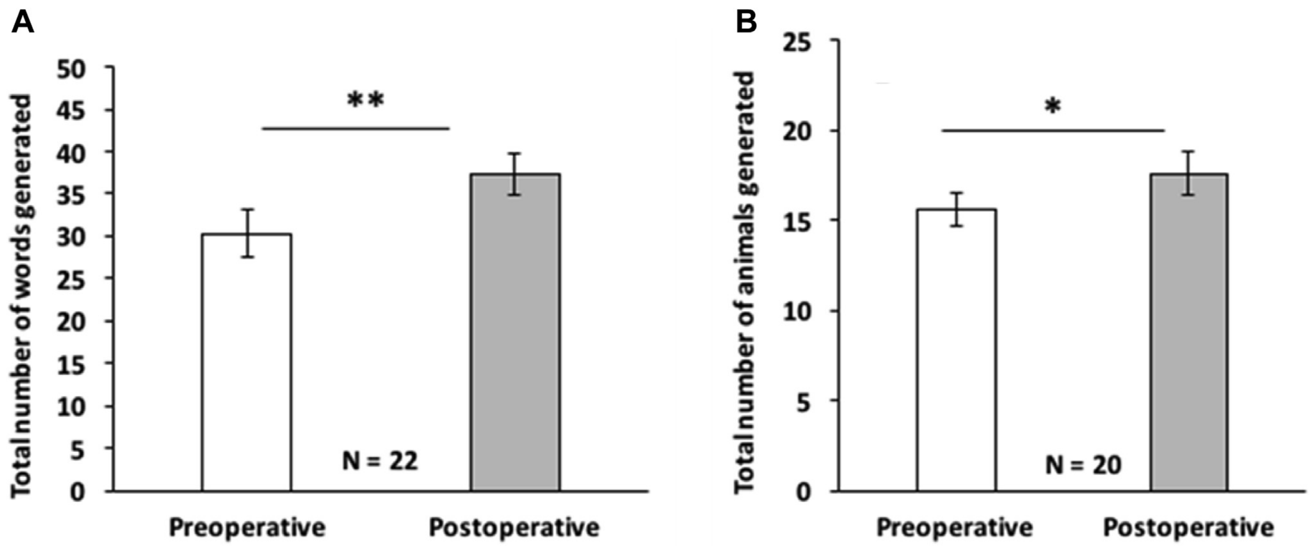

Figure 3. Significant postoperative improvement in phonemic (**A**) and semantic (**B**) fluency (* = P <0.05; ** = P <0.01; bars show mean score, error bars SEM).

± 0.41; t_8 = 1.99, P = 0.041). The easier digit span forward and digit span sequencing measures did not significantly improve (Table 7, Figure 4). TMT part B, an executive-tapping measure of set-shifting and visuomotor processing did also significantly improve (N = 13, postoperative time M = 86.00 ± 15.27 seconds; preoperative M = 131.00 ± 23.99s, t_{12} = 1.99, P = 0.046 (see

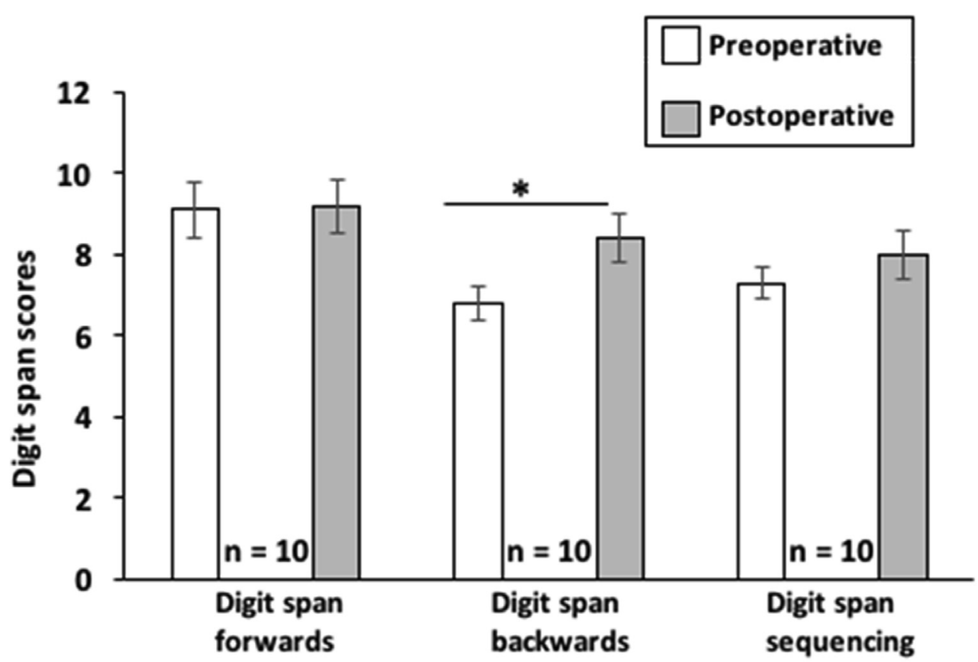

Figure 4. Backward digit span performance, a measure of working memory, improves postoperatively (* = P <0.05; bars show mean score; error bars SEM).

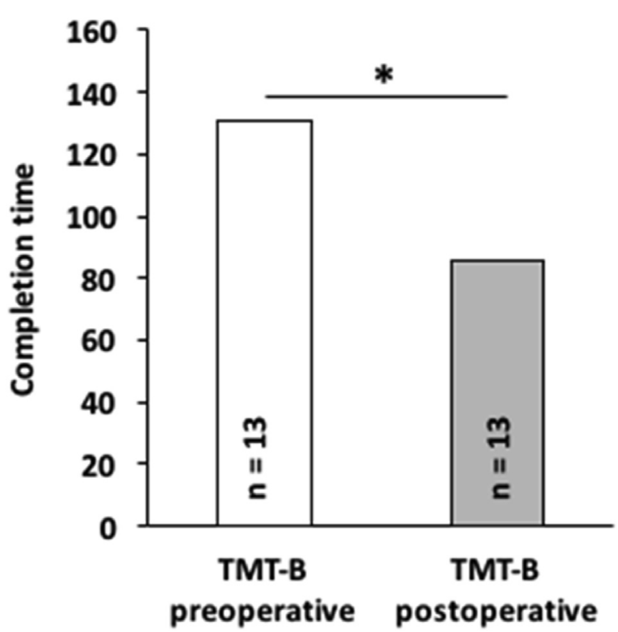

Figure 5. TMT-B, a measure of executive function, completion time reduces postoperatively. TMT-B, Trail-Making Test B.

Table 8, Figure 5). Sample size precluded analysis of tumor-location modulation of these effects.

Declarative Memory and Tumor Location

Comparison of preoperative LH and RH groups did not reveal any effects of laterality on BMIPB immediate and delayed story recall (Table 9).

Surgery Improved Some Measures of Declarative Memory

Clear postoperative improvement was seen on BMIPB immediate story recall (N = 12, postoperative M = 32.17 ± 3.13; preoperative M = 23.08 ± 2.88, t_{11} = 3.80, P = 0.003), a finding that held when removing left-handers from the analysis (postoperative M = 33.82 ± 2.92, preoperative M = 23.82 ± 3.05, t_{10} = 4.13, P = 0.001). Delayed story recall did not significantly improve (Table 10 & Figure 6). Postoperative improvement was also seen on one of four RBANS measures of declarative memory, i.e. list recall, a measure of delayed memory (N = 13, postoperative M = 4.85 ± 0.81; preoperative M = 3.62 ± 0.86, t_{12} = 2.62, P = 0.022, Table 11 & Figure 7). Sample size precluded analysis of tumor-location modulation of these effects.

Comparison with Normative Scores: Emotionality

Preoperatively, patient anxiety scores (N = 23, M = 8.57 ± 1.03) were higher than normative scores (N = 23, M = 6.21 ± 0.12, t_{44} =

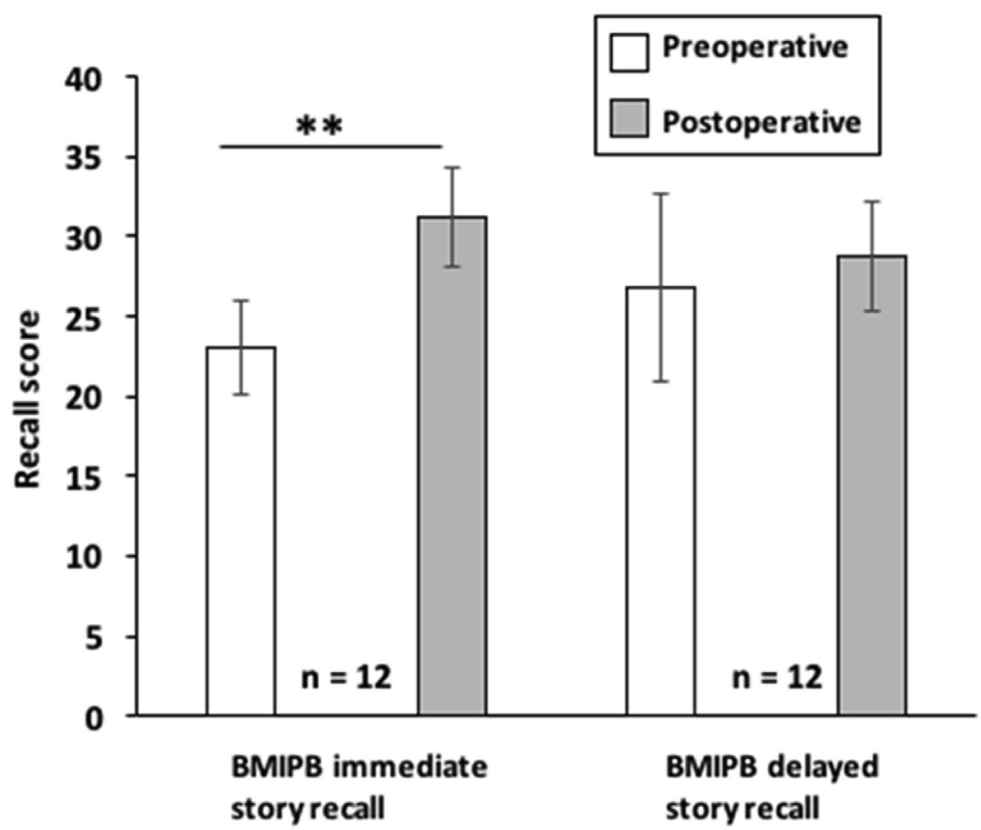

Figure 6. BMIPB immediate recall demonstrates significant postoperative improvements (* = $P < 0.05$; ** = $P < 0.01$; bars show mean score; error bars SEM). BMIPB, Birt Memory and Information Processing Battery.

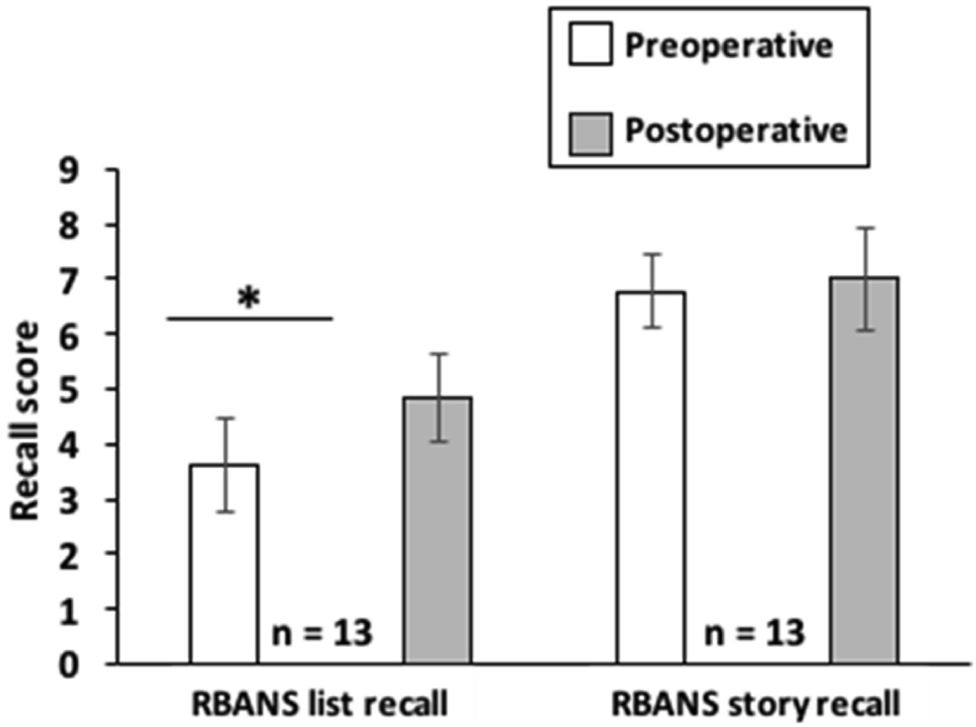

Figure 7. RBANS list recall demonstrates significant postoperative improvements (* = $P < 0.05$; ** = $P < 0.01$; bars show mean score; error bars SEM). RBANS, Repeatable Battery for the Assessment of Neuropsychological Status.

2.85, P = 0.032), and this remained as a nonsignificant trend after surgery (postoperative anxiety N = 23, M = 7.96 ± 093, t_{44} = 1.85, P = 0.08). As regards depression, preoperative patient scores (N = 23, M = 6.48 ± 0.85) were markedly higher than normative scores (N = 23, M = 4.05 ± 1.35), t_{44} = 2.84, P = 0.007, an effect that surgery removed (postoperative depression N = 23, M = 5.48 ± 1.19, t_{46} = 1.20, P = 0.243) (Table 12). Preoperatively, patients with meningiomas restricted to the right frontal lobe scored significantly higher on HADS-depression (N = 24, M = 5.78 ± 0.82) than matched norms (N = 24, M = 3.97 ± 0.04, t_{44} = 2.15, P = 0.042). There were no other significant differences between HADS scores and the normative scores in preoperative patients with LH or RH frontal/non-frontal meningiomas (Table 12). In all, this suggests meningiomas tended to increase aversive emotionality, with surgery reducing depression more than anxiety.

Comparison with Normative Scores: Fluency

Phonemic fluency was markedly poorer than normative scores, in patients with meningiomas confined to the left and right hemispheres, with impairment stronger on the left (left: patients N = 48, M = 28.53 ± 1.96; normative N = 48, M = 39.64 ± 0.71; t_{94} = 5.28, P < 0.001: right: patients N = 33, M = 33.52 ± 1.83; normative N = 33, M = 40.50 ± 0.78; t_{64} = 3.51, P = 0.001). In those patients undergoing surgery, preoperative phonemic fluency (N = 21, M = 31.71 ± 2.48) was also markedly lower than normative scores (N = 21, M = 41.38 ± 0.79, t_{40} = 3.71, P = 0.001), a difference that no longer obtained after surgery (postoperative scores N = 21, M = 38.19 ± 2.40, t_{40} = 1.26, P = 0.22, Table 12).

Semantic fluency was poorer in those with meningiomas in the left (normative N = 49, M = 17.91 ± 0.32; sample N = 49, M = 15.61 ± 0.85; t_{96} = 2.51, P = 0.015), but not the RH (Table 12). In those patients undergoing surgery, preoperative semantic fluency was also significantly poorer (N = 20, M = 15.60 ± 0.92) than in the normative sample (M = 18.21 ± 0.51, t_{40} = 2,48, P = 0.018), a difference that no longer obtained after surgery (M = 17.60 ± 1.19; t_{40} = 0.47, P = 0.64). In summary, normative comparisons indicated that meningiomas impaired both phonemic and semantic fluency, with effects stronger for left-sided tumors and that surgery ameliorated fluency impairments.

Comparison with Normative Scores: Declarative Memory and Working Memory

As regards the 4 RBANS memory measures, preoperatively, meningiomas appeared to impair story memory and story recall the most, then list recall, with list recognition the least affected (normative versus. patients [same patient sample throughout]: story memory P = 0.003; story recall P = 0.003; list recall P = 0.019, list recognition P = 0.057, further details Table 12). The effect of surgery on RBANS list recall was that there was no

Table 12. Summary of Comparison to Normative Scores

Measure	Comparison	N	Normative Mean Score (SD)	Actual Mean Score (SD)	T-Value	*P* Value	Cohen's d
	1 = left frontal actual and normative mean scores						
	2 = left non-frontal actual and normative mean scores						
	3 = right frontal actual and normative mean scores						
	4 = right non-frontal actual and normative mean scores						
	5 = preoperative actual and normative mean scores						
	6 = postoperative actual and normative mean scores						
	7 = left hemisphere actual and normative mean scores						
	8 = right hemisphere actual and normative mean scores						
HADS A	1	27, 27	6.25 (0.74)	7.22 (4.10)	1.21	0.232	0.33
	2	9, 9	5.57 (1.17)	4.78 (1.99)	−1.03	0.320	0.67
	3	24, 24*	5.90 (0.81)	7.70 (5.22)	1.63	0.116	0.48
	4	4,4	5.46 (1.26)	7.50 (3.87)	1.00	0.356	0.71
	5	23	6.21 (0.59)	8.57 (4.92)	2.28	0.032	0.67
	6	23		7.96 (4.48)	1.85	0.077	0.55
HADS D	1	27, 27	3.97 (0.26)	5.30 (4.11)	1.66	0.102	0.56
	2	9,9	3.91 (0.23)	3.00 (2.06)	−1.31	0.224	0.62
	3	24, 24*	3.97 (0.21)	5.78 (4.02)	2.15	0.042	0.64
	4	4, 4	4.02 (0.20)	6.25 (6.18)	0.72	0.523	0.51
	5	23	4.05 (6.48)	6.48 (4.10)	2.84	0.007	0.84
	6	23		5.48 (5.70)	1.20	0.243	0.35
FAS	5	21	41.38 (3.64)	31.71 (11.36)	−3.71	0.001	1.15
	6	21		38.19 (11.00)	−1.26	0.219	0.39
	7	47, 47*	39.64 (4.93)	28.53 (13.55)	−5.28	0.000002	1.09
	8	34, 34*	40.50 (4.49)	33.52 (10.50)	−3.51	0.001	0.86
CAT	5	20	18.21 (2.30)	15.60 (4.11)	−2.48	0.018	0.78
	6	20		17.60 (5.30)	−0.47	0.640	0.15
	7	49, 49	17.91 (2.26)	15.61 (5.97)	−2.51	0.015	0.51
	8	34, 34*	18.30 (2.12)	17.64 (4.70)	−0.74	0.463	0.18

Preoperative HADS-D scores for patients with meningiomas restricted to the RH frontal lobe were significantly higher than normative scores. There were no other significant differences between emotionality and tumor location. Preoperative phonemic fluency scores for patients with meningiomas located in either LH or RH were significantly lower than normative scores, as were semantic fluency scores for LH patients. Surgery appeared to improve some aspects of executive function and declarative memory.

HADS, Hospital Anxiety and Depression Scale; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; FAS, the F-A-S test of phonemic fluency; CAT, categorical fluency test.

*Age information missing for 1 participant, precluding estimation of a normative score for this participant. TRAILS B = median scores and IQR reported, HADS = mean and SD reported.

†TRAILS B = Wilcoxon Z reported; HADS = T reported.

‡TRAILS B = Effect size = Z÷square root of N.

Continues

Table 12. Continued

Measure	Comparison	N	Normative Mean Score (SD)	Actual Mean Score (SD)	T-Value	*P* Value	Cohen's d
TRAILS B	5	13	67.08 (17.89)	131.00 (86.50)	−1.93†	0.054	1.37‡
	6			86.00 (55.05)	−0.75†	0.555	0.53‡
RBANS story memory	5	13	17.74 (0.43)	14.62 (3.33) 13.62 (5.85)	−3.63	0.005	1.31
	6				−2.54	0.026	0.99
RBANS list recognition	5	13	19.48 (0.20)	17.77 (2.92) 18.62 (1.71)	−2.11	0.057	0.83
	6				−1.81	0.095	0.71
RBANS list recall	5	13	5.97 (0.62)	3.62 (3.10)	−2.69	0.019	1.05
	6			4.85 (2.91)	−1.36	0.195	0.53
RBANS story recall	5	13	9.18 (0.20)	6.77 (2.39)	−3.63	0.003	1.42
	6			7.00 (3.34)	−2.35	0.037	0.92

Patient ID numbers:

HADS comparison 1 (N = 27):2,4,18,30,44,50,58,59,61,65,66,82,84,86,90,91,93,97,98,109,110,112,115,125,133,135,138

HADS comparison 2 (N = 9): 15,16,33,37,43,52,77,78,132

HADS comparison 3 (N = 24): 3,10,12,14,29,34,36,40,53,55,56,60,68,69,73,89,96,99,100,108,114,123,137,141 (age data missing for ppt 141)

HADS comparison 4 (N = 4): 27,35,75,85

HADS comparison 5 (N = 23): 2,10,20,27,30,37,43,55,59,63,67,69,99,104,107,109,112,114,116,123,136,137,140

HADS comparison 6 (N = 23): 2,10,20,27,30,37,43,55,59,63,67,69,99,104,107,109,112,114,116,123,136,137,140

FAS comparisons 5 and 6 (N = 21): 2,10,20,30,35,37,43,55,63,67,69,99,104,109,112,114,116,123,136,137,140

FAS comparison 7 (N = 47): 2,4,15,16,18,20,22,30,32,33,37,43,44,48,50,52,58,61,65,66,67,70,74,77,78,82,87,90,91,93,97,98,109, 110, 112,113,115,116,117,119,121,125,132,133,135,136,138

FAS comparison 8 (N = 34): 3,6,10,12,14,29,34,35,36,40,53,55,56,60,63,64,68,69,73,75,85,89,94,96,99,100,104,108,114,118,123, 126,137,141 (age data missing for 141).

CAT comparisons 5 and 6 (N = 20): 2,20,30,35,37,43,55,59,63,67,69,99,104,109,112,116,123,136,137,140

CAT comparison 7 (N = 49): 2,4,9,15,16,18,20,22,30,32,33,37,43,44,48,50,52,58,59,61,65,66,67,70,74,77,78,82,87,90,91,93,97,98, 109,110,112,113,115,116,117,119,121,125,132,133,135,136,138

CAT comparison 8 (N = 34): 3,6,10,12,14,29,34,35,36,40,53,55,56,60,63,64,68,69,73,75,85,89,94,96,99,100,104,108,114,118,123, 126,137,141 (age data missing for 141)

TRAILS B comparisons 5 and 6 (N = 13): 2,10,37,55,63,69,99,107,109,114,123,137,140

RBANS comparisons 5 and 6 (N = 13): 2,9,10,20,27,37,55,107,109,112,123,137,140

Preoperative HADS-D scores for patients with meningiomas restricted to the RH frontal lobe were significantly higher than normative scores. There were no other significant differences between emotionality and tumor location. Preoperative phonemic fluency scores for patients with meningiomas located in either LH or RH were significantly lower than normative scores, as were semantic fluency scores for LH patients. Surgery appeared to improve some aspects of executive function and declarative memory.

HADS, Hospital Anxiety and Depression Scale; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; FAS, the F-A-S test of phonemic fluency; CAT, categorical fluency test.

*Age information missing for 1 participant, precluding estimation of a normative score for this participant. TRAILS B = median scores and IQR reported, HADS = mean and SD reported.

†TRAILS B = Wilcoxon Z reported; HADS = T reported.

‡TRAILS B = Effect size = Z÷square root of N.

postoperative impairment relative to norms (pre $P = 0.019$ -> post $P = 0.195$). Notably, this normative comparison RBANS list recall is consistent with the significant within-patient postsurgical improvement effect in list recall shown above (**Figure 7**). For RBANS story memory and RBANS story recall, postoperative scores approached but still fell short of normative scores (normative versus. patients: story memory [$t_{24} = 3.63$, $P = 0.026$]; story recall [$t_{24} = 3.63$, $P = 0.037$, see **Table 12**]). As regards an executive function component of working memory, patients appeared to be impaired on the TMT-B task relative to norms before surgery, which was not the case after surgery (normative vs. patients: pre $P = 0.054$; post $P = 0.555$, see **Table 12**), consistent with the significant within-patient improvement effect in TMT-B shown above (**Figure 5**).

DISCUSSION

Summary and Comparison with Previous Studies

Since the effects of meningioma laterality and surgical removal on emotionality and cognition are understudied, we provide Supplementary Table 2, which presents the results outlined in this article alongside previous studies which have conducted broadly similar assessments of postoperative changes in cognitive function, and/or hemispheric differences. Here, we have reported postoperative increases in verbal fluency, in working memory (TMT-B and backward list span), and in immediate and delayed memory performance, results which are consistent with previous findings.[17,18,24,31] Here, we have reported preoperative hemispheric differences in verbal fluency (left-sided = stronger tendency to impairment), but lacked the sample size to assess any hemispheric differences in immediate or delayed memory as reported by Pranckevičienė and colleagues.[40] While postoperative improvements are not always apparent,[9,26] it is important to note the absence of any results which hint at postoperative reduction in these cognitive functions.

Effects of Tumor Location: Frontal Lobe

We observed here that preoperative patients with LH frontal meningiomas have higher levels of symptoms of depression and anxiety than patients with LH non-frontal meningiomas. This is consistent with previous reports of a relationship between depressive symptoms and frontal meningiomas,[6,10] and generally with associations of frontal cortical areas with anxiety, likely driven by limbic-frontal connectivity.[41-43]

Importantly, current literature cannot rule out the possibility that effects upon emotionality include a causally indirect component. For example, rather than impinging on mood-modulating neural regions directly, frontal tumors may have negative quality-of-life outcomes upon communication and relationships that, subsequently, raise depressive risk.

Effects of Tumor Location: Hemisphere

Preoperatively, patients with meningiomas restricted to LH were significantly more impaired on a measure of phonemic fluency than the RH group. Norm comparison suggested fluency impairment was restricted to phonemic fluency in RH patients, with both phonemic and semantic fluency impaired in LH patients. Other studies have reported similar left-biased impaired performance preoperatively: Liouta et al.'s LH patients performed more poorly on verbal fluency (phonemic and semantic) than their RH group[17]; Goldstein et al.'s LH patients performed significantly worse on semantic fluency than the RH group, with a nonsignificant trend of LH phonemic fluency impairment.[44] These left-sided impairments may be attributed to the dominance of the LH in verbal fluency.[45-47]

Effects of Tumor Location: Convexity Tumors

Interestingly, we found that phonemic verbal fluency was lower in patients with convexity dura tumors than those with falcine/parafalcine tumors. Moreover, within LH tumors, depression scores were higher in patients with convexity dura tumors than those in other locations (an effect that was *not* seen with anxiety scores in the same patient set). It is not inconceivable that these 2 effects have overlapping causes. As noted above, verbal impairments affecting communication and relationships could potentially raise depressive risk.

No Significant Postoperative Reduction in Anxiety and Depression

Although emotionality was not the main focus of this study, we found that the postoperative reductions in anxiety and depression scores were of low effect size, and not statistically significant. We could find no clear postoperative within-subject improvement in anxiety or depression, adding to an already mixed evidence base in relation to the effects of surgery on emotionality. Postoperative reductions in anxiety have been reported previously,[10,13-15] but this is not a consistent finding.[11,12,16] Findings are also mixed in relation to depression, with Williams and colleagues reporting a postoperative decrease while D'Angelo et al. reported a postoperative increase in depression.[11,12] Our normative comparisons suggested a greater tendency toward postoperative reductions in depression than anxiety. Statistically reliable reductions in anxiety and depression might be seen with larger patient samples, and with longer postoperative assessment intervals than the average 7.3 months in this study.

Benefits of Tumor Removal for Verbal Fluency

Performance on both phonemic and semantic fluency improved significantly postoperatively, and moreover postoperative scores were no longer significantly different from normative scores, suggesting that the preoperative impairment was tumor-related. Similarly, Liouta et al. reported improvements in verbal fluency (phonological and semantic), with a 1-year interval between surgery and postoperative assessments.[17] The significant improvements in verbal fluency reported here were observed within a somewhat shorter time frame, with our average preoperative-postoperative assessment interval being 7.3 months. Hendrix et al. did not find significant improvements in fluency, when neuropsychological testing occurred 2 months after surgery.[26] Conceivably, allowing a greater interval between surgery and postoperative assessments may be important in observing beneficial outcomes of surgery.

Benefits of Tumor Removal on Measures of Working Memory and Declarative Memory

We found postoperative improvements in working memory, namely in the digit span backward and TMT-B tasks. These results are consistent with previous research.[9,17,18,24-26] We also found a postoperative improvement on 2 declarative memory measures (BMIPB immediate story recall and RBANS list recall). These findings are consistent with some previous studies which have also reported improvements in immediate and delayed memory.[14,18,26]

We presented anxiety and depression data alongside the analysis of each cognitive domain. Importantly, the absence of clear postoperative changes in anxiety or depression suggests that postoperative changes we report in aspects of cognition were driven by tumor removal rather than due to emotionality-induced test performance changes.

Limitations

In general, our sample sizes did not offer enough statistical power to detect weak but potentially important effects, or to detect potentially complex interactions between the different dimensions of tumor location such as lobe, hemisphere, and meningeal location (e.g., convexity vs. falcine/parafalcine), and between tumor location variables and medication. While low sample sizes precluded most analyses of drug types (except anti-MS and anticonvulsant drugs), we could see no complicating effect of drugs. While acknowledging these sample size limitations, we consider that the paucity of published data on the effects of surgery upon postoperative function merits analysis of smaller samples and enables subsequent meta-analyses. While we did not have a control group, we used normative data to provide some indication of control values of emotionality and cognition. Indeed, normative scores have been used by other authors to assess the effects of surgery upon postoperative function.[14,48]

While preoperative size of the tumor was available to us for analysis, one limitation was that details regarding the degree of resection were not available to us. As it turned out, we could not detect any effect of preoperative tumor size. However, our results should not be taken to infer that tumor size is unimportant in affecting cognition. Rather, the relatively benign nature of meningiomas and the absence of general neuroimaging screening means that the distribution of tumor sizes may tend to be skewed toward later-presented larger sizes (here the mean tumor area was 1193.4 ± 83.0 mm^2), precluding analyses comparing mature with relatively early meningiomas. Similarly, details of surgical factors such as duration of surgery, type of anesthesia used, postoperative edema, and other complications were not available for analysis. Analysis of large patient samples should consider the role of such factors in modulating improvements in cognition.

We acknowledge that there are factors not explored in this study that can modulate levels of anxiety. Studies exploring psychological well-being in meningioma patients have found no association between their HADS anxiety score severity and factors such as socioeconomic status, level of education, marital/family status, or tumor location.[8,49-51] There is an argument that factors such as tumor residue, reduced cognitive function, the need for further radiotherapy, and/or a lack of information can increase anxiety symptoms in brain tumor patients.[52,53] We cannot rule out all potential modulation effects in our findings and there is scope for further exploration of their interplay with anxiety in the context of brain tumors in future studies.

CONCLUSIONS

Regarding tumor location, we found that anxiety and depression are worse in patients with frontal tumors on the left side of the brain and that phonemic fluency is impaired in patients with left-sided tumors. Importantly, our data support the notion that surgical resection can lead to improvements in cognitive functioning; we found postoperative improvements in phonemic and semantic verbal fluency, and in components of working memory and declarative memory. These cognitive improvements would be likely to bring about real-world improvements in quality of life.[54]

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Islay Barne: Data curation, Formal analysis, Investigation, Project administration, Writing – review & editing. **Christine E. Wells:** Conceptualization, Data curation, Formal analysis, Investigation, Project administration, Visualization, Writing – original draft. **Miranda Wheeler:** Data curation, Project administration, Resources. **Helen Bairstow:** Investigation, Writing – review & editing. **Donald Brechin:** Conceptualization, Project administration, Supervision. **Stephen Evans:** Conceptualization, Data curation, Investigation, Project administration, Supervision, Writing – review & editing. **Colin Lever:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Project administration, Supervision, Writing – review & editing.

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