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Citation for published version (APA):
van der Linden, S., Gehring, K., Rutten, G-J., Kop, W. J., & Sitskoorn, M. (2020). Prevalence and correlates of fatigue in patients with meningioma before and after surgery. *Neuro-Oncology Practice*, *7*(1), 77-85. https://doi.org/10.1093/nop/npz023

Prevalence and correlates of fatigue in patients with meningioma before and after surgery

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Abstract

Background. Fatigue is a common symptom in patients with brain tumors, but comprehensive studies on fatigue in patients with meningioma specifically are lacking. This study examined the prevalence and correlates of fatigue in meningioma patients.

Methods. Patients with grade I meningioma completed the Multidimensional Fatigue Inventory (MFI-20) before and 1 year after neurosurgery. The MFI consists of 5 subscales: General Fatigue, Physical Fatigue, Mental Fatigue, Reduced Motivation, and Reduced Activity. Patients' scores were compared with normative data. Preoperative fatigue was compared with postoperative fatigue. Correlations with sex, age, education, tumor hemisphere, preoperative tumor volume, antiepileptic drugs (AEDs), symptoms of anxiety/depression, and self-reported cognitive complaints were explored.

Results. Questionnaires were completed by 65 patients preoperatively, and 53 patients postoperatively. Of 34 patients, data from both time points were available. Patients had significantly higher fatigue levels on all subscales compared to normative values at both time points. Mean scores on General Fatigue, Physical Fatigue, and Mental Fatigue remained stable over time and improvements were observed on Reduced Motivation and Reduced Activity. Preoperatively, the prevalence of high fatigue (Z-score $\geq$ 1.3) varied between 34% for Reduced Motivation and 43% for General Fatigue/Mental Fatigue. The postoperative prevalence ranged from 19% for Reduced Activity to 49% on Mental Fatigue. Fatigue was associated with cognitive complaints, anxiety and depression, but not with education, tumor lateralization, tumor volume, or AEDs.

Conclusion. Fatigue is a common and persistent symptom in patients with meningioma undergoing neurosurgery. Findings emphasize the need for more research and appropriate care targeting fatigue for meningioma patients.

Keywords

brain neoplasms | fatigue | meningioma | neurosurgery | patient-reported outcome measures.

Meningiomas are for the most part slow-growing tumors that compress the surrounding, healthy brain and eventually may cause symptoms. They account for approximately one-third of all diagnosed primary CNS tumors.[1] Most meningiomas will remain asymptomatic and undetected during a person's lifetime, but a subset receives medical attention because of related symptoms (eg, seizures or neurological deficits) or because they are coincidentally detected on a brain scan.[2] Observation (wait-and-scan), neurosurgical resection, and (stereotactic) radiation therapy are the most common treatment options. The majority of meningiomas are benign (ie, >90% WHO

grade I) and have a favorable long-term prognosis.[1,3] A distinctly worse prognosis is generally observed in patients with atypical (WHO grade II) or anaplastic (WHO grade III) meningiomas. These tumors grow faster, are more likely to recur, and may invade the brain.[3] It is a common clinical presumption that patients with grade I meningioma have the most favorable recovery in terms of quality of life and return to normal socioprofessional life. However, accumulating evidence indicates that a significant number of these patients experience cognitive deficits and lower quality of life, even long after treatment has ended.[4,5]

Fatigue is a very common symptom in patients with primary brain tumors, with prevalence estimates varying between 39% and 96%.[6–8] Fatigue is described as a subjective feeling of tiredness and a lack of energy.[9] It is a multidimensional construct, wherein a distinction can be made between physical and mental fatigue.[10,11] In healthy individuals, fatigue is a normal and adaptive response to physical or mental activities that can be alleviated by periods of sleep or rest. However, in neurological and oncological patients, fatigue can be a persisting and/or relapsing symptom, which is not in proportion to recent activities and not adequately alleviated by rest.[10,11] Importantly, fatigue can substantially interfere with patients' personal and professional activities, and it can significantly lower patients' quality of life.[6,12]

Most of the research on fatigue in brain tumor patients has been conducted in patients with glioma, often malignant tumors that grow from glial or precursor cells in the brain.[1] These studies indicate that symptoms of fatigue are quite common already prior to treatment, and that they can persist several years thereafter.[7,8,13,14] Fatigue in glioma patients has been associated with various factors, including higher age, female sex, left-hemispheric location, radiotherapy, chemotherapy, the use of antiepileptic drugs (AEDs) and opioids, psychological distress, sleep disturbances, and cognitive complaints.[7,15,16]

Little research has been conducted on fatigue in patients with meningioma. Several studies on quality of life in patients with meningioma made use of instruments including a few items on fatigue (eg, Konglund et al[17] and Bunevicius and colleagues[18]). In addition, a handful of studies evaluated the (side) effects of (stereotactic) radiotherapy in which fatigue was one of the outcome measures.[19–22] These studies suggest fatigue is present in patients with meningioma, but firm conclusions cannot be drawn because mostly heterogeneous samples or small samples of meningioma patients were included. Moreover, fatigue has never been included as a primary outcome and, consequently, results regarding fatigue have not always fully been described, have not been described separately for patients with meningioma, or not described at all. Also, a comparison with a control group has often been lacking, which may have distorted findings in patient samples, since fatigue is also a common complaint in the general population. Additionally, all previous studies assessed fatigue with single-item measures (yes/no), or with very brief unidimensional questionnaires or subscales whereas it is a multidimensional construct. As a consequence, there is insufficient understanding of the severity and type of fatigue in patients with meningioma.

This study evaluates fatigue, using a validated multidimensional questionnaire, in a select sample of patients with WHO grade I meningioma, before surgery and 1 year after surgery. Patients' mean levels of fatigue were compared with normative data from a large sample of the general population. Furthermore, proportions of patients with (very) high fatigue scores were examined. Additionally, relationships of fatigue with sociodemographic, clinical, and psychological variables were explored.

Materials and Methods

Participants

Patients with histologically proven intracranial meningioma (WHO grade I), who underwent surgery between June 2014 and July 2017 at the Elisabeth-TweeSteden Hospital, Tilburg, the Netherlands, were included in this study. Patients were excluded if they had multiple meningiomas; a history of intracranial neurosurgery or whole-brain radiation therapy; a history of severe psychiatric or neurological disease; a KPS less than 70; a lack of basic proficiency in Dutch; or severe motor, language, or visual problems, limiting the ability to complete the assessments. Patients with severe surgery-related complications (eg, stroke or meningitis) were excluded from the 12-month postoperative analyses.

Procedure

Data for this study were prospectively collected as part of a larger follow-up study in patients with intracranial tumors who undergo resective surgery at the Elisabeth-TweeSteden Hospital. The study was approved by the Medical Ethics Committee Brabant (project number NL41351.008.12). Informed consent was obtained from all individual patients included in this study.

Neuropsychological assessments are administered 1 day before surgery (T0) and 3 months after surgery (T3; not used in the present analyses). These assessments have been embedded in standard clinical care for patients with intracranial tumors and information from these assessments is also used in the multidisciplinary consultation that takes place every month. Three months after surgery, patients are invited by nurse practitioners to participate in a follow-up assessment (T12) for research purposes. Neuropsychological assessments consist of a standardized interview, questionnaires on anxiety, depression and cognitive complaints, and standardized neuropsychological tests (not included in the present analyses). Questionnaires on work, community integration, and fatigue are administered at T0 and T12, but not at T3. All assessments were conducted in the hospital by well-trained test technicians.

This study focused on self-reported fatigue, which was examined 1 day before surgery (T0) and 1 year after surgery (T12). Because the pre- and postoperative questionnaires on fatigue were added to the existing test protocol simultaneously in June 2015, patients who participated in the 1-year postsurgery measurement between June 2015 and June 2016 (and had their preoperative assessment between June 2014 and June 2015) completed the MFI atT12, but did not fill out the preoperative questionnaire on fatigue.

Study Measures

Fatigue

Symptoms of fatigue were assessed using the Multidimensional Fatigue Inventory (MFI). Participants were asked to report their fatigue experiences over "the last few days." This 20-item questionnaire takes about 5 minutes to administer and covers the following 5 dimensions of fatigue: General Fatigue, Physical Fatigue, Mental Fatigue, Reduced Motivation, and Reduced Activity. These scales are based on ways in which fatigue can be expressed, as indicated in the literature and resulting from patient interviews.[23] Reliability of the 5 different scales are sufficient, with Cronbach α ranging from 0.72 to 0.87.[23] Questionnaires were not included if there were >4 missing answers. In case of 1-4 missing items in less than 5% of the cases (missing at random or missing completely at random), use was made of data imputation (using the mean of a patient's filled-out items on that particular scale). Representative normative data from the general population of Germany (n = 2037) were available for comparison.[24] We used these norms to convert patients' raw scores into sex- and age-corrected Z-scores per subscale for both time points. Higher Z-scores indicate greater fatigue severity. "High" and "very high" fatigue scores were determined by using widely used cut-offs of, respectively, 1.3 (90th percentile) and 2.0 (97.5th percentile).[25,26]

Anxiety and depressive symptoms

The Hospital Anxiety and Depression Scale (HADS),[27] originally developed for somatic outpatients, was used to assess symptoms of anxiety and depression. This widely used screening instrument consists of 14 items, referring to symptoms within the last week, from which an anxiety scale score (HADS-A) and a depression scale score (HADS-D) can be derived. Higher scores indicate more psychological distress. Reliability of the Dutch version of the HADS is satisfactory to good, with test-retest reliability coefficients between 0.86 and 0.90 and Cronbach α ranging from 0.71 to 0.90.[28]

Cognitive complaints

The Cognitive Failures Questionnaire (CFQ)[29] was used to measure subjective cognitive functioning. Frequency of everyday cognitive failures in motor function, perception, and memory was assessed with 25 items, with response options from 0 (never) to 4 (very often). Psychometric properties of the Dutch version of the CFQ were sufficient, with test-retest reliability of 0.83 and Cronbach α of 0.75 and 0.81.[30]

Sociodemographic and clinical variables

Number of years of education and completed level of education were self-reported by the patients during a standardized interview. Education was classified using the Dutch coding system of Verhage,[31] which ranges from 1 (only primary school) to 7 (university degree). Its 7 categories were subdivided into 3 levels, namely low (Verhage 1 to 4), middle (Verhage 5), and high educational level (Verhage 6 and 7). Relevant clinical information was extracted from electronic medical charts. The location of the tumor was classified by the neurosurgeon. Tumor volume was semiautomatically segmented by trained researchers using the software application ITK-SNAP.[32]

Statistical Analysis

Data are presented as means ± SDs or frequencies and percentages. Preoperative and postoperative fatigue scores of the patient sample were compared with the normative sample using 2-tailed 1-sample z-tests. Two-tailed one-sample z-tests are conducted, since the means *and* SDs of the general population (ie, normative sample) are known (M = 0, SD = 1). The standardized mean differences between patients and controls can be interpreted as effect sizes, with 0.20-0.49 indicating small effects, 0.50-0.79 medium effects, and ≥0.80 reflecting large effects.[33] Changes from preoperative to postoperative mean scores were examined using 2-tailed paired-sample t-tests. Effect sizes were calculated by dividing the mean difference by its SD (Cohen $d = M_{diff}/SD_{diff}$), again with 0.20-0.49 small, 0.50-0.79 medium, and ≥0.80 large effects.[34] Automatically, correlation coefficients between preoperative and postoperative levels of fatigue were calculated. Correlation coefficients of 0.10 to 0.29 were considered as small, 0.30 to 0.49 were considered as medium, and 0.50 to 1.0 reflected large correlation coefficients.[34]

The prevalence of high and very high fatigue levels was determined by counting individual patients who scored above the cut-offs of $Z \geq 1.3$ (90th percentile) and $Z \geq 2.0$ (97.5th percentile), respectively,[25,26] for each of the MFI subscales at each time point.

To investigate clinical and demographic factors associated with dimensions of fatigue, correlation coefficients were calculated between the subscales of the MFI and sex, age, level of education, tumor hemisphere, preoperative tumor volume, use of AEDs, self-reported symptoms of anxiety/depression, and self-reported cognitive complaints. Selected variables were mainly based on previous studies in neuro-oncological patients.[7,15] Sex- and age-corrected fatigue scores were used,[24] but these variables were included in the correlation analysis as well to check whether there was any additional effect of sex and age in this patient sample. Pearson product-moment correlations (*r*) were calculated for the continuous variables, Spearman rank-order correlations (ρ) were applied to the ordinal variable (ie, level of education), and point-biserial correlations (r_{pb}) were used for the dichotomous variables. Interpretation of the correlation coefficients is described above.

Statistical analyses were conducted using SPSS Statistics (version 24.0), with an α level of 0.05.

Results

Patient Characteristics

Data from preoperative assessments of 65 patients were included in this study (Table 1). Their mean age was 56.2 ± 12.1 years and 74% were female. The majority of tumors were located in the frontal lobe (63%) and mean tumor volume was 42.7 ± 26.0 cm³. At 1-year post surgery,

data were available from 53 patients, of whom 34 also participated in the preoperative assessment. Data imputation was used in 4 cases with single missing values. Table 1 presents sociodemographic and clinical characteristics of the different groups.

Mean Levels of Fatigue in Patients With Meningioma

Results of the group-level analyses are listed in Table 2. Patients' mean scores were significantly higher on each subscale of the MFI, both pre- and postoperatively, compared with norms from the general population (all *P* values < .01). The largest effects were observed on the subscales of General Fatigue and Mental Fatigue, with effect sizes ranging from 0.89 to 1.07.

In the subset of patients who underwent both assessments (n = 34), improvements over time were observed for Reduced Activity and Reduced Motivation. No significant differences were observed between pre- and postoperative mean levels of General Fatigue, Physical Fatigue, and Mental Fatigue (Table 3).

Table 1 Sociodemographic, Clinical and Psychological Characteristics of the Different Groups

Characteristic	Patients at T0	Patients at T12	Subgroup With Both Assessments	
Sample size (n)	65	53	34	
Age at T0 (mean; SD)	56.2; 12.1	54.8; 11.3	54.2; 11.4	
Sex (n female; %)	48; 74%	40; 76%	25; 74%	
Years of education (mean; SD)	14.4; 3.8	14.9; 3.5	14.9; 3.5	
Level of education (n; %)[a]				
Low	17; 26%	12; 23%	8; 24%	
Middle	24; 37%	10; 38%	15; 44%	
High	24; 37%	21; 40%	11; 32%	
Tumor hemisphere (n; %)				
Right	29; 45%	25; 47%	14; 41%	
Left	26; 40%	20; 38%	15; 44%	
Bilateral	10; 15%	8; 15%	5; 15%	
Tumor location (n; %)				
Frontal	41; 63%	28; 53%	19; 56%	
Nonfrontal	16; 25%	18; 34%	10; 29%	
Posterior fossa	8; 12%	7; 13%	5; 15%	
Presenting neurological symptom (n; %)[a]				
Visual deficit	16; 25%	12; 23%	9; 26%	
Headache, dizziness	14; 22%	11; 21%	8; 24%	
Cognitive or language deficits	12; 18%	9; 17%	4; 12%	
Seizure	11; 17%	9; 17%	6; 18%	
Focal weakness	6; 9%	7; 13%	3; 9%	
Accidental finding	3; 5%	2; 4%	2; 6%	
Other	3; 5%	3; 6%	2; 6%	
Preoperative tumor volume (cm^3; mean; SD)[b]	42.7; 26.0	41.7; 27.0	42.4; 25.7	
Use of antiepileptic drugs (n; %)	10; 15%	8; 15%	5; 15%	
Symptoms of anxiety (mean; SD)	7.1; 4.5	4.0; 3.2	6.5; 4.0[c]	3.6; 3.0[d]
Symptoms of depression (mean; SD)	6.1; 4.3	3.7; 3.6	5.3; 4.0[c]	3.4; 3.7[d]
Cognitive complaints (mean; SD)	27.7; 13.0	33.3; 16.0	25.3; 12.5[c]	32.4; 16.4[d]

[a]Percentages may not add up because of rounding.
[b]Data were available for 58 patients at T0 and 49 patients at T12.
[c]At T0.
[d]At T12.

Table 2 Preoperative and Postoperative Mean Patients' Levels of Fatigue Compared With Normative Values

MFI Subscale	N	Mean[a]	SD	z Value	P Value	Effect Size[b]
Preoperative Fatigue (T0)						
General Fatigue	65	1.07	1.46	8.59	<.001[c]	1.07
Physical Fatigue	65	0.76	1.40	6.13	<.001[c]	0.76
Mental Fatigue	65	1.02	1.46	8.20	<.001[c]	1.02
Reduced Activity	65	0.88	1.24	7.12	<.001[c]	0.88
Reduced Motivation	65	0.77	1.40	6.18	<.001[c]	0.77
Postoperative Fatigue (T12)						
General Fatigue	53	0.89	1.34	6.47	<.001[c]	0.89
Physical Fatigue	53	0.44	1.03	3.17	.002[c]	0.44
Mental Fatigue	53	1.07	1.38	7.82	<.001[c]	1.07
Reduced Activity	53	0.38	1.11	2.74	.006[c]	0.38
Reduced Motivation	53	0.36	1.16	2.64	.008[c]	0.36

Abbreviation: MFI, Multidimensional Fatigue Inventory.
[a]Higher scores indicate higher levels of fatigue. Test values (based on norms of Schwarz et al,[24]): $\mu = 0$; $\sigma = 1$.
[b]Standardized mean differences can be interpreted as effect sizes, with 0.20-0.49 indicating small effects, 0.50-0.79 medium effects, and ≥0.80 reflecting large effects.[33]
[c]$P < .05$.

Prevalence and Severity of Fatigue in Patients With Meningioma

Figure 1 illustrates the proportions of patients scoring normal, high, and very high per subscale of the MFI. Preoperatively, the prevalence of high fatigue (Z-score ≥ 1.3) varied between 34% for Reduced Motivation and 43% for General Fatigue and Mental Fatigue. Postoperative prevalence of high fatigue ranged from 19% for Reduced Activity to 49% for Mental Fatigue.

In total, 44/65 patients (68%) scored high (Z-score ≥ 1.3) on 1 or more subscales of the MFI before surgery. Of these 44 patients, 35 scored very high (Z-score ≥ 2.0) on 1 or more subscales. Postoperatively, 30/53 patients (57%) scored high on 1 or more subscales and 21 of these patients scored very high on 1 or more subscales.

Correlates of Fatigue in Patients With Meningioma

As shown in Table 3, the preoperative fatigue scores were weakly to moderately correlated with fatigue scores at T12 (rs between 0.25 and 0.48). Furthermore, correlation analyses showed medium to large associations between fatigue and self-reported symptoms of depression and cognitive complaints pre- and postsurgery, and with anxiety postsurgery (Table 4). We found no clear correlations between standardized scores on the subscales of the MFI and sex, age, education, tumor hemisphere, preoperative tumor volume, and use of AEDs.

Discussion

In this study we comprehensively examined pre- and postsurgical prevalence, severity, and correlates of fatigue in patients with meningioma using a multidimensional fatigue instrument. Symptoms of fatigue were assessed in patients with WHO grade I meningioma prior to surgery (n = 65) and 1 year after surgery (n = 53). On all subscales of the MFI, patients reported more fatigue compared with norms of the general population, both before and 1 year after surgery. In total, 68% and 57% of the patients scored (very) high on 1 or more subscales of the MFI before and after surgery, respectively. In general, proportions of patients scoring very high were larger than proportions of patients scoring high, indicating that the reported symptoms were rather severe than mild. Furthermore, mean levels of General Fatigue, Physical Fatigue, and Mental Fatigue did not decrease significantly over the 1-year follow-up period in a subgroup of patients (n = 34). These findings indicate that fatigue is a substantial and persistent clinical problem in meningioma patients up to 1 year after surgery.

The prevalence rates found in this study roughly correspond with those found in patients with glioma.[7,8,14] This may seem remarkable given the differences in etiology and oncological prognosis between meningioma and glioma. Gliomas infiltrate the brain and are the leading cause of death in patients because of disease progression. Meningiomas, on the other hand, grow extraaxially and are mostly benign.[1] However, previous studies have also demonstrated long-term impairments
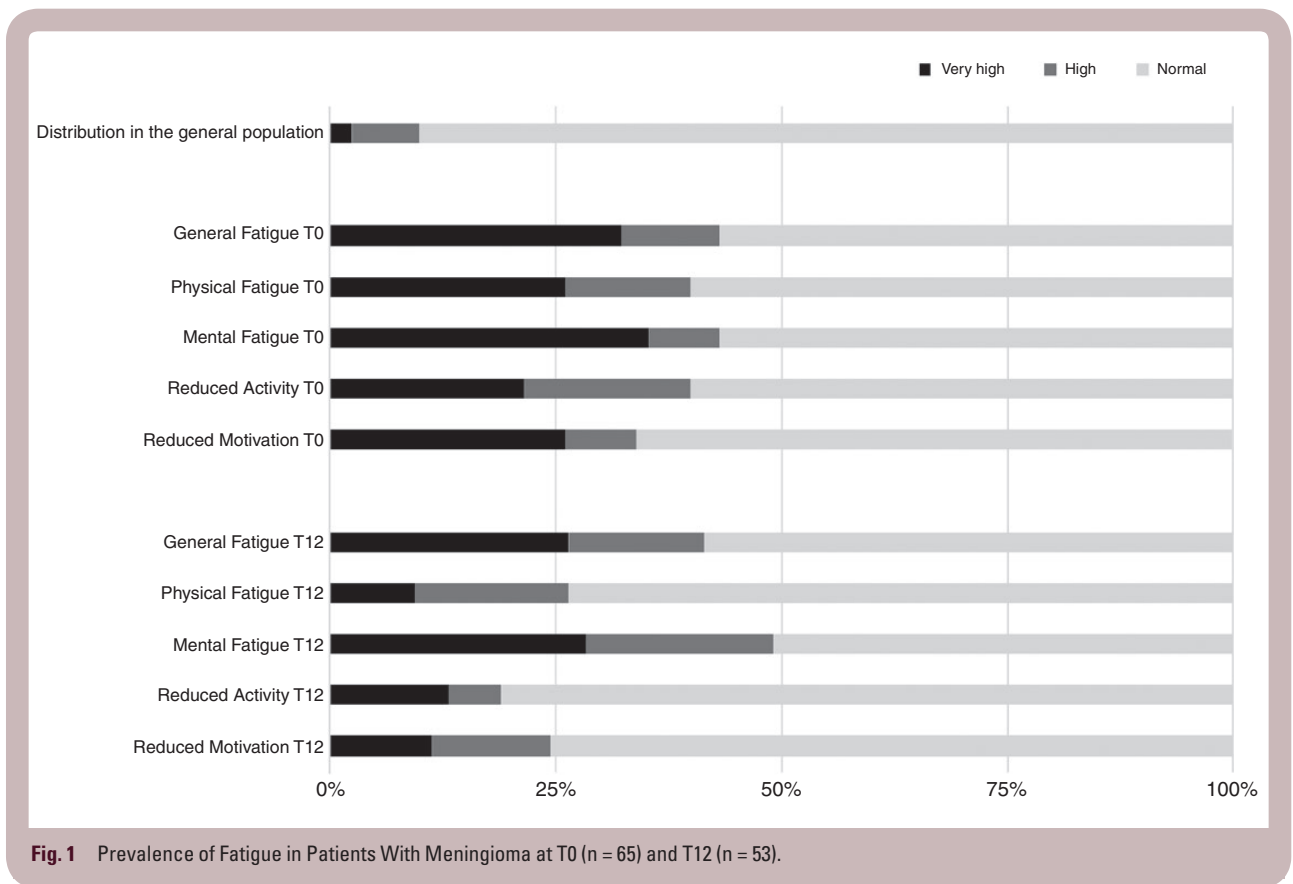
Fig. 1 Prevalence of Fatigue in Patients With Meningioma at T0 (n = 65) and T12 (n = 53).

in cognitive functioning and quality of life in patients with meningioma.[4,5] Although it is often assumed that meningioma patients recover well after surgery, this research contributes to the finding that a substantial number of patients are left with various problems, even long after medical treatment has ended.

Our results indicate that patients' motivation and activity were significantly increased 1 year after surgery, but serious fatigue remained present in their daily functioning. Persistent symptoms of fatigue can lead to several problems, including difficulties in social participation, mental health issues, or inability to return to (previous) work.[35] Fatigue may affect not only patients' lives, but also the lives of their families.[35] However, results of the within-group analyses must be interpreted with some caution, since only some of the participants completed both the preoperative and postoperative questionnaires (n = 34). Furthermore, although stability is observed at the group level on 3 subscales of the MFI, it is possible that different patterns of change occur at the individual level.[36] An interesting next step would be to look at individual-level change in fatigue scores (compared with change scores of an appropriate control group) and predictors of improvement or decline using a longitudinal study design with more patients.

In the present sample, fatigue was associated with self-reported symptoms of depression, anxiety, and cognitive complaints. These findings correspond with previous observations in patients with glioma,[7,8,17,37] as well as with findings in other patient populations.[38–40] Owing to

interconnectedness and overlap of symptoms, it is difficult to distinguish between, for example, a major depressive disorder and serious fatigue. Depression can cause fatigue and vice versa, and a third factor can cause both depression and fatigue. It is possible that these symptoms are an expression of shared neurobiological mechanisms (eg, inflammation or brain abnormalities), but these mechanisms have not yet been extensively studied in patients with meningioma. Furthermore, sleep-wake disturbances are common in brain tumor patients,[41,42] and often co-occur with symptoms of fatigue, depression, and anxiety, but for this study, we did not collect data on sleep quality. More extensive research is necessary to gain insight into causal relationships between fatigue and its multifactorial determinants in patients with meningioma.

In this study, the highest prevalence rates were found for Mental Fatigue. Short, unidimensional questionnaires or subscales used in previous research often contain floor and ceiling effects due to the narrow range of possible scores and, moreover, tend to measure mainly symptoms of physical fatigue.[43] To prevent problems with (mental) fatigue being underdiagnosed and thus undertreated, we recommend the use of a short, validated, multidimensional screening tool, such as the MFI, for patients with surgically treated meningioma during aftercare. Ideally, for each patient with increased scores, contributing and perpetuating factors should be identified using a comprehensive examination. By addressing these specific factors, treatment can be better tailored to the individual patient.[44] Although only a few intervention studies have been conducted on fatigue

Table 3 Preoperative Levels of Fatigue Compared With Postoperative Levels of Fatigue in Patients With Meningioma

T0-T12 Pairs	N	Mean Difference	SD_{diff}	t Value	P Value	Effect Size[a]	r[b]
General Fatigue	34	0.09	1.67	0.31	.759	0.05	0.37[c]
Physical Fatigue	34	0.40	1.40	1.68	.102	0.29	0.39[c]
Mental Fatigue	34	0.23	1.44	0.94	.355	0.16	0.48[c]
Reduced Activity	34	0.63	1.43	2.57	.015[c]	0.44	0.25
Reduced Motivation	34	0.64	1.29	2.91	.006[c]	0.50	0.45[c]

[a]Cohen d = M_{diff}/SD_{diff}, with 0.20-0.49 indicating small effects, 0.50-0.79 medium effects, and ≥0.80 reflecting large effects[34]
[b]Coefficients for correlations between pre- and postsurgery fatigue; coefficients of 0.10 to 0.29 were considered as small, 0.30 to 0.49 as medium, and 0.50 to 1.0 reflected large correlation coefficients.[34]
[c]P < .05

Table 4 Correlates of Fatigue in Meningioma Patients

	Preoperative Assessment (T0) (n = 65)					Postoperative Assessment (T12) (n = 53)				
	General Fatigue	Physical Fatigue	Mental Fatigue	Reduced Activity	Reduced Motivation	General Fatigue	Physical Fatigue	Mental Fatigue	Reduced Activity	Reduced Motivation
Sex	0.02	0.09	0.04	−0.02	0.03	0.20	0.13	0.07	0.08	−0.05
Age	−0.24	−0.23	−0.15	−0.11	0.14	−0.14	0.08	−0.19	0.06	0.10
Level of education	−0.06	0.03	−0.12	−0.11	−0.15	0.12	0.08	0.06	0.15	0.01
Tumor hemisphere[a]	0.03	−0.08	0.02	0.09	−0.06	−0.14	−0.06	−0.07	−0.16	−0.06
Preoperative tumor volume	0.18	0.20	0.10	0.20	0.11	−0.23	−0.15	0.06	−0.29[b]	−0.14
Use of AEDs	−0.10	−0.10	0.00	0.01	−0.26[b]	0.21	0.27	0.13	0.26	0.04
Anxiety	0.17	0.14	0.16	0.09	**0.36[b]**	**0.39[b]**	**0.37[b]**	**0.49[b]**	**0.31[b]**	**0.44[b]**
Depression	**0.44[b]**	**0.47[b]**	**0.38[b]**	**0.49[b]**	**0.65[b]**	**0.58[b]**	**0.61[b]**	**0.59[b]**	**0.59[b]**	**0.56[b]**
Cognitive complaints	**0.38[b]**	**0.40[b]**	**0.47[b]**	**0.41[b]**	**0.30[b]**	**0.54[b]**	**0.43[b]**	**0.71[b]**	**0.38[b]**	**0.39[b]**

Abbreviation: AEDs: anticonvulsant drugs.
Correlations of 0.10 to 0.29 were considered as small, 0.30 to 0.49 as medium, and 0.50 to 1.0 reflected large correlation coefficients.[34] Correlations >.29 in bold.
[a]Patients with bilateral tumors were not included in these analyses.
[b]P < .05.

in patients with brain tumors, there is some evidence that patients who experience fatigue may benefit from exercise interventions or psychological interventions (eg, cognitive behavioral therapy or educational programs) to help patients manage symptoms of fatigue.[41,45–48] Treatment with psychostimulants have been shown to have insufficient effect on symptoms of fatigue in patients with brain tumors.[49,50]

This study has some limitations that should be addressed in further studies. The sample sizes were relatively small, and only a subset of patients completed both the preoperative questionnaire and the 1-year follow-up assessment. There are other factors that may have affected generalizability. For example, we included participants who underwent surgery and who had relatively favorable clinical characteristics (eg, patients without a history of neurological/psychiatric disorders, with a KPS above

70, and without surgery-related complications). This could have resulted in an underestimation of fatigue in patients with meningioma in general. It is also possible that the timing of the first assessment (ie, 1 day before surgery) may have influenced the results, since psychological distress appeared to be related to self-reported fatigue.

The current study is a necessary first step in investigating fatigue in patients with meningioma, but clearly more work has to be undertaken in this area. The relationship among fatigue, sleep quality, medication use, and objective measures of cognitive functioning should be further clarified. At the same time, research on treatment options for fatigue in patients with brain tumors should be expanded.[45]

The findings of the current study indicate that fatigue is a serious, common, and persistent symptom in patients with meningioma undergoing neurosurgery. Health care providers and researchers should be aware of this,

pay attention to this debilitating symptom, and provide appropriate care.

Conflict of interest statement. None declared.

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