## **PAPER**

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## Subjective cognitive functioning in patients with a meningioma: Its course and association with objective cognitive functioning and psychological symptoms

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#### **Abstract**

**Objective:** Although meningioma patients show deficits in objective cognitive functioning (OCF) measured with neuropsychological tests, subjective cognitive functioning (SCF) has received little attention. We investigate SCF from pre- to postsurgery and its associations with OCF, psychological, sociodemographic, and clinical characteristics.

**Methods:** SCF was measured using the Cognitive Failures Questionnaire (CFQ) 1 day before (T0) and 3 (T3) and 12 months (T12) after surgery. Patients' scores were compared with normative data and changes over time were assessed. The neuropsychological battery CNS Vital Signs and the Hospital Anxiety and Depression Scale were administered. Correlations of SCF with OCF, psychological, sociodemographic, and clinical characteristics were explored.

**Results:** Patients reported significantly better SCF as compared with controls at TO (N = 54) and T3 (N = 242), but not at T12 (N = 50). A significant decrease in group level SCF was observed from T0 to T12 (n = 24, P < .001). SCF was associated with anxiety at all time points (rs = -0.543 to -0.352) and with depression at T3 and T12 (r = -0.338 and -0.574), but not with OCF, sociodemographic, or clinical characteristics (rs = -0.202 to 0.288).

Conclusions: Meningioma patients experienced better SCF as compared with controls before and 3 months after surgery, which might be the result of phenomena related to disease and recovery. As the findings suggest that cognitive symptoms might increase later on, future studies should further investigate the course of SCF in meningioma patients. In clinical practice, measurements of SCF should be combined with those of OCF and psychological distress in order to determine whether and which interventions are needed.

## KEYWORDS

brain neoplasms, cancer, cognition, meningeal neoplasms, neuropsychological tests, neurosurgery, oncology, patient reported outcome measures

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#### 1 | BACKGROUND

Although meningiomas do not grow from brain tissue but arise from the meninges covering the brain, they are referred to as brain tumors and account for approximately 37% of all primary brain and central nervous system tumors.<sup>1</sup> The far majority of meningiomas are benign tumors<sup>1</sup> that can be treated well and have a favorable long-term prognosis.<sup>2</sup> Current standard of care consists of neurosurgical resection of the tumor, which most likely relieves initial neurological deficits that result from mass effects of the tumor.<sup>3</sup> However, many patients are left with adverse outcomes, such as fatigue,<sup>4</sup> lower quality of life,<sup>5</sup> and/or impairments in objective cognitive functioning (OCF).<sup>6-8</sup>

Although deficits in OCF in meningioma patients, as assessed by neuropsychological tests, have been demonstrated in several studies, 6-8 self-reported or subjective cognitive functioning (SCF) has received little attention. The few studies investigating SCF in heterogeneous, cross-sectional samples of brain tumor patients, also including meningioma patients, found high percentages of patients reporting cognitive problems. 9-11 However, a comparison of patients with normative data was lacking in these studies, except for the study of van der Vossen et al 12 that reported poor SCF in 23% of meningioma patients approximately 32 months after surgery.

Additionally, potential associations between SCF and OCF have not been evaluated in a sample of patients with meningioma only. Prior studies in other neuro-oncological patient groups reported little to no associations between SCF and OCF. 11,13 Instead, poor SCF was more related to anxiety, depression, and fatigue than to OCF. 11,13 Poor SCF can affect many aspects of daily living, such as employment, social functioning, and quality of life. 14

SCF in meningioma patients has not been studied over time including assessments both before and after surgery. The present study examined SCF and changes therein among a sample of meningioma patients before and 3 and 12 months after surgery. Additionally, we examined associations of SCF with OCF, anxiety, and depression for each time point, and with sociodemographic and clinical characteristics for the 3-month follow-up. We hypothesized that meningioma patients would report lower SCF when compared with normative controls. Also, we expected an improvement of SCF in meningioma patients over time as well as SCF to be more related to anxiety and depression than to OCF.

### 2 | Methods

#### 2.1 | Patient population

Data from patients diagnosed with a single histopathologically confirmed meningioma, WHO grade I or II, <sup>15</sup> and treated with intracranial surgery between April 2008 and February 2017 at the Elisabeth-TweeSteden Hospital (Tilburg, The Netherlands) were included. Exclusion criteria included: no available data on SCF at any time point; lack of proficiency in Dutch; age below 18 years; previous craniotomy; history of cranial radiotherapy; neurodegenerative or recent (less than or

equal to 2 years) psychiatric or neurological disorders; other major medical illnesses in the year prior to surgery (eg, myocard infarct); and inability to undergo neuropsychological assessment because of severe motor, visual, or intellectual problems.

### 2.2 | Procedure and measures

Data on SCF, OCF, and psychological variables were collected 1 day before (T0) and 3 (T3) and 12 months (T12) after surgery, as part of the design of a larger longitudinal prospective study on pre- and post-operative functioning in patients with intracranial tumors. Because of expansion of our project over the years, the number of data available differs between time points. Patients who underwent surgery between April 2008 and November 2010 solely filled out the questionnaire on SCF at T3 as part of neurosurgical follow-up care. From upon the clinical implementation of neuropsychological assessments (NPA) in November 2010, patients completed the questionnaire on SCF and the NPA at T0 and T3 as part of clinical care. From upon January 2014, T12 was added for research purposes.

This study followed the Declaration of Helsinki on ethics and was approved by the local Medical Ethics Committee (file number NL41351.008.12). All patients provided written informed consent. There is considerable overlap between the patient sample of this study and four previously published studies. 48.16.17

## 2.3 | Patients' sociodemographic and clinical characteristics

Sociodemographic information was gathered by a checklist and interview. Level of education was self-reported and classified using the Verhage coding system, ranging from 1 (primary school) to 7 (university degree). 18 Clinical information was obtained from the electronic medical charts. Meningioma grades were classified based on the WHO classification into typical (grade I) and atypical (grade II).<sup>15</sup> The neurosurgeon classified tumor location (ie, supratentorial with or without involvement of the frontal lobes, or infratentorial) and the extent of surgical resection (Simpson grade I: macroscopically complete removal of the tumor including resection of underlying bone and associated dura to Simpson grade V: simple decompression with or without biopsy).<sup>19</sup> Tumor volume (in cm<sup>3</sup>) was segmented semiautomatically, followed by manual adjustments, from contrast-enhanced T1-weighted Magnetic Resonance Images with ITK-SNAP software.<sup>20</sup> The American Society of Anesthesiologists (ASA) score, determined pre-operatively by the anesthetist, was considered as a measure of overall health.<sup>21</sup> Psychotropic medication was defined as the use of anti-epileptic drugs, corticosteroids, opioids, benzodiazepines, antidepressants, or a combination of these.

### 2.4 | Subjective cognitive functioning

The Cognitive Failures Questionnaire (CFQ) was used to assess SCF. <sup>22-24</sup> The CFQ is a 25-item questionnaire that measures the

frequency of self-reported everyday cognitive failures over a period of 4 weeks. Response options range from 0 (*never*) to 4 (*very often*). <sup>23,24</sup> Psychometric qualities for the Dutch version of the CFQ were acceptable, with Cronbach's  $\alpha$  of 0.75 and 0.81 and a test-retest reliability of 0.83. <sup>22</sup> The mean (M) and standard deviation (SD) of the total CFQ scores, as reported by Ponds et al <sup>23</sup> (based on 1358 Dutch healthy controls), were used for normative purposes (M = 31.8 and SD = 11.1).

### 2.5 | Objective cognitive functioning

We assessed OCF with a formal Dutch version of the computerized neuropsychological test battery CNS Vital Signs (CNS VS).<sup>25</sup> CNS VS takes 30 to 45 minutes to administer and consists of seven computerized tests, mostly based on conventional widely-used neuropsychological tests, yielding measures of performance on 11 cognitive domains.<sup>25</sup> Since some domains generated by CNS VS are calculated on the basis of the same test scores, we included a selection of seven cognitive domains in this study.

#### 2.6 | Anxiety and depression

The Hospital Anxiety and Depression Scale (HADS) was used to measure self-reported symptoms of anxiety (7 items) and depression (7 items).  $^{26,27}$  Answer options for each item range from 0 to 3, resulting in a score range of 0 to 21 for each subscale. Higher scores indicate higher symptoms.  $^{26}$  The Dutch version of the HADS has good psychometric qualities, with a test-retest reliability of 0.89 and 0.86, and Cronbach's  $\alpha$  ranging from 0.71 to 0.86.  $^{27}$ 

#### 2.7 | Statistical analyses

#### 2.7.1 | Patients' characteristics

Descriptive and comparative analyses (one-way ANOVA and chisquare tests of independence) of baseline sociodemographic and clinical characteristics of meningioma patients were performed.

#### 2.7.2 | Norms and cutoff levels

Patients with more than 4 missing values on the CFQ were excluded from the analyses. On the basis of the normative data reported by Ponds et al,  $^{23}$  patients' CFQ total scores were converted into z scores (M = 0, SD = 1). For OCF, individual z scores were calculated based on a Dutch normative sample,  $^{28}$  corrected for age, sex, education, and practice effects.  $^{29}$  Higher z scores reflect better SCF/OCF.

The cutoff for low levels of SCF and OCF was set at  $z \le -1.50$ ; for anxiety and depression raw scores, the cutoff was set at 8 for each subscale. The number of patients scoring above each cutoff point was counted.

# 2.7.3 | Comparison of group level SCF with normative data

We performed two-tailed one-sample z tests to examine whether patients differ from normative controls (test values:  $M_{controls} = 0$ ,  $SD_{controls} = 1$ ) in SCF at all time points. We considered patients' mean z scores as effect sizes (ES) of the differences between patients and the normative sample. Note that Glass's delta ES ( $M_{patients} - M_{controls} / SD_{controls}$ ) equals the patients' mean z score,  $^{30}$  with ES less than or equal to 0.49 indicating small effects, 0.50 to 0.79 medium effects, and greater than 0.80 large effects.  $^{31}$ 

## 2.7.4 | Changes in group level SCF

A one-way repeated measures ANOVA was conducted to investigate changes in SCF from pre- to postsurgery in patients who completed all three assessments. Additional post hoc tests were performed.

### 2.7.5 | Individual levels of SCF

To classify individual levels of SCF, individual z scores were categorized as: very low ( $z \le -2.00$ ), low ( $-1.99 \le z \le -1.50$ ), average ( $-1.49 \le z \le 1.49$ ), high ( $1.50 \le z \le 1.99$ ), and very high (greater than or equal to 2.00) SCF. The proportion of patients within each category, as well as their 95% confidence intervals, were calculated for each time point.

# 2.7.6 | Association of SCF with OCF, patient, and psychological characteristics

Pearson's r or Spearman's  $\rho$  correlations in case of categorical or nonlinear/non-normally distributed continuous data, were calculated to explore the association of SCF with OCF, anxiety, and depression at each time point. As only for T3 data from a large sample was available, we explored the associations of SCF at this time point with sociodemographic (ie, sex, age, and education) and clinical variables (ie, tumor hemisphere and localization, WHO grade, tumor volume, ASA score, Simpson grade, and psychotropic medication use) with Spearman's  $\rho$  correlations. In cases of dichotomous variables, Kendall's  $\tau$ -b correlation was used as a nonparametric alternative to the point-biserial correlation. Correlation coefficients of 0.10 to 0.29 were interpreted as small, 0.30 to 0.49 as medium, and 0.50 to 1.0 as large.

Statistical analyses were conducted using SPSS version 24.0. In order to decrease false discovery rate due to multiple testing, we used Benjamini-Hochberg (BH) corrections.<sup>32</sup>

#### 3 | Results

#### 3.1 | Patients' characteristics

Figure 1 presents the flow of patients throughout this study. At TO, SCF data was available for 54 patients, of whom 43 also had SCF data

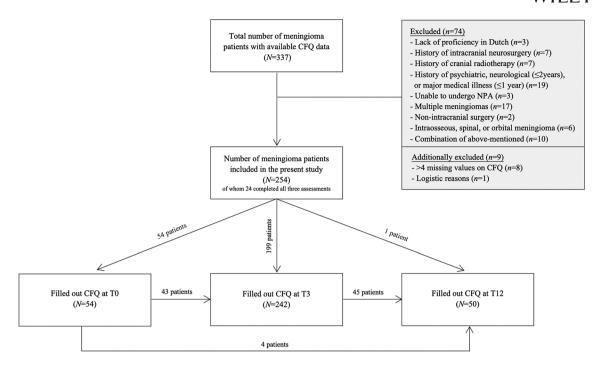


FIGURE 1 Flowchart of patients. Note: CFQ, cognitive failures questionnaire; NPA, neuropsychological assessment

at T3. In total, 242 patients completed the SCF questionnaire at T3, of which the majority did not complete the 12-month follow-up because of the later implementation of the long-term assessment, resulting in 45 patients with a T3 and T12 assessment. Twenty-four patients completed all three assessments. The number of OCF data at T3 is substantially lower (n = 158) as compared with the available SCF data at T3 (N = 242) because of a later implementation of the OCF measurement.

There were no significant differences regarding sociodemographic and clinical characteristics between the samples at different time points (P's > BH-corrected  $\alpha$  of .005) (Table 1).

# 3.2 | Comparison of group level SCF with normative data

Patients reported significantly better SCF as compared with controls at T0 and T3 (Glass's  $\Delta$  respectively 0.57 and 0.46; Table 2). At T12, no significant difference was found between patients and normative controls.

### 3.3 | Changes in group level SCF

For the 24 patients who completed all three assessments, we found a significant effect of time of measurement (F = 8.09, P = .002; Table 2). Post hoc analyses showed a decrease in group level SCF from T0 to T12 (mean difference = -.088, P < BH-corrected  $\alpha$  of .017).

#### 3.4 | Individual levels of SCF

The majority of patients reported average-to-(very)high SCF at all time points. More particularly, 3.7%, 5.4%, and 14.0% of the patients reported very low SCF respectively at T0, T3, and T12 (Table 2).

# 3.5 | Associations of SCF with OCF, patient, and psychological characteristics

Negative z scores for all OCF domains were found at all time points (z scores range = -0.30 to -1.23; Table 3). Mean scores and percentages of patients scoring above the cutoff on measures of OCF and HADS for each time point are shown in Table 3.

SCF was significantly associated with anxiety at all time points, and with depression at T3 and T12, but not with measures of OCF (Table 3), nor with sociodemographic or clinical characteristics at T3 (r's = -0.102 to 0.145, see Table S1; online only).

## 4 | Discussion

The present study investigated SCF and changes therein from pre- to 12 months postsurgery among meningioma patients both at group and individual patient level. Furthermore, associations of SCF with OCF, psychological, sociodemographic, and clinical characteristics were explored.

Meningioma patients reported better SCF as compared with normative controls both before and 3 months after surgery. The majority of patients reported average-to-(very)high SCF at all time points. This is remarkable given the high percentages of brain tumor patients with cognitive complaints found in previous studies. <sup>9-11</sup> Moreover, we found lower performance for all OCF domains at all time points, which is in line with several studies clearly demonstrating deficits in OCF among meningioma patients. <sup>6-8</sup>

Methodological differences and limitations may underlie differences in findings between our study and previous research evaluating SCF, including heterogeneous cross-sectional samples of brain tumor

**TABLE 1** Baseline characteristics of meningioma patients at all time points

	T0(N = 54)	T3(N = 242)	T12(N = 50)	F/x <sup>2</sup>	Р
Female, n(%)	41(75.9)	168(69.4)	36(72.0)	0.944	.624
Age (mean;range)	55.4;32-76	57.2;23-82	55.3;33-75	0.918	.400
Education (mode;range) <sup>a</sup>	5;1-7	5;1-7	5;1-7	8.445	.749
Localization of tumor, n(%)				2.686	.612
Supratentorial with frontal involvement	30(55.6)	142(58.7)	25(50.0)		
Supratentorial without frontal involvement	19(35.2)	88(36.4)	21(42.0)		
Infratentorial	5(9.3)	12(5.0)	4(8.0)		
Hemisphere, n(%)				1.167	.884
Left	23(42.6)	101(41.7)	20(40.0)		
Right	22(40.7)	113(46.7)	24(48.0)		
Bilateral	9(16.7)	28(11.6)	6(12.0)		
WHO grade, n(%)				0.386	.824
T	48(88.9)	221(91.3)	46(92.0)		
II	6(11.1)	21(8.7)	4(8.0)		
Tumor volume (mean in cm³)b	43.46	39.10	41.47	0.494	.611
ASA score, n(%) <sup>c</sup>				1.835	.399
ASA I + II	47(87.0)	221(92.1)	44(88.0)		
ASA III + IV	7(13.0)	19(7.9)	6(12.0)		
Simpson grade, n(%) <sup>d</sup>				1.878	.931
Simpson I	10(19.6)	51(23.5)	9(20.9)		
Simpson II	29(56.9)	119(54.8)	22(51.2)		
Simpson III	6(11.8)	19(8.8)	4(9.3)		
Simpson IV	6(11.8)	28(12.9)	8(18.6)		
Psychotropic drug use, n(%) <sup>e</sup>	32(59.3)	137(62.0)	28(57.1)	0.460	.794
Corticosteroids	22(40.7)	83(39.2)	18(36.7)		

Abbreviations: ASA, American Society of Anesthesiologists; WHO, World Health Organization.

patients<sup>9-11</sup> and lack of validated questionnaires.<sup>9,11</sup> More importantly, most studies did not compare patients' scores to normative data,<sup>9-11</sup> which may result in an overestimation of cognitive complaints in these patients, as healthy controls generally also report complaints to some extent. Alternatively, the CFQ, as a generic instrument, might not be suitable in differentiating SCF between meningioma patients and controls. Van Rijsbergen et al<sup>33</sup> showed that a stroke-specific questionnaire on SCF (ie, CLCE-24) was able to differentiate in SCF between stroke patients and controls, whereas the CFQ was not.

Our findings may be explained by some clinical phenomena related to the disease and its recovery. Initially, the disease and its treatment require adjustments of the patient's personal, social, and professional life, for example, passing along domestic chores and/or discontinuing work. During recovery from surgery, patients are (partly) disburdened from their daily roles and responsibilities.<sup>34</sup> This support may result in limited experience of cognitive complaints, as patients have not encountered possible problems (yet).<sup>35</sup> Moreover, when faced with changes in health status, patients might alter their internal standards and values, a phenomenon known as response shift.<sup>36</sup> Initial beliefs about (poor) SCF might be reconsidered and evaluated differently given changes in health status (ie, diagnosis) and/or current functioning. Furthermore, patients' main concerns may be with issues other than SCF, resulting in little attention for and recognition of possible cognitive complaints. Lack of awareness of one's own cognitive functioning could also play a role, resulting from for instance psychological factors, such as denying cognitive deficits and/or from frontal lobe dysfunction.<sup>37</sup> In about half of the included patients in this study,

<sup>&</sup>lt;sup>a</sup>Data was available for 171 patients at T3;

<sup>&</sup>lt;sup>b</sup>Data was available for 51/163/45 patients at respectively T0/T3/T12;

<sup>&</sup>lt;sup>c</sup>Data was available for 240 patients at T3. Patients within ASA categories I + II were considered (relatively) healthy, patients within categories III + IV as having substantial comorbidities<sup>21</sup>;

<sup>&</sup>lt;sup>d</sup>Data was available for 51/217/43 patients at respectively T0/T3/T12;

<sup>&</sup>lt;sup>e</sup>Data was available for 221 (212 for corticosteroids)/49 patients at respectively T3/T12.

	N	Mean z(SD) <sup>a</sup>	Mean Difference	z Test	Р	ES <sup>b</sup>
Normative comparison of group SCF						
TO(N = 54)	54	0.57(1.17)	0.57	4.17	<.001*	0.57
T3(N = 242)	242	0.46(1.34)	0.46	7.12	<.001*	0.46
T12(N = 50)	50	-0.04(1.39)	-0.04	-0.25	.799	-0.04
	n	Mean z(SD) <sup>a</sup>	Mean Difference	F	Р	ESc
Change in group SCF over time						
Effect for time	24			8.09	.002	.424
Pair 1	24		-0.53		.037	
ТО		0.88(0.85)				
Т3		0.35(1.15)				
Pair 2	24		-0.35		.086	
Т3		0.35(1.15)				
T12		-0.00(1.35)				
Pair 3	24		-0.88		<.001**	
ТО		0.88(0.85)				
T12		-0.00(1.35)				
	T0(N = 5 n(%)(95%		T3(N = 242) n(%)(95% CI)		T12(N = 50) n(%)(95% CI)	
SCF at the individual patient level						
Average-to-(very)high SCF						
Very high	5(9.3)(1.6	5-17.0)	30(12.4)(8.2-16.6	)	2(4.0)(-1.4-9.4)	
High	8(14.8)(5	.3-24.3)	28(11.6)(7.6-15.6	<b>b</b> )	5(10.0)(1.7-18.3)	
Average	39(72.2)(	60.3-84.1)	162(66.9)(61.0-72	.8)	36(72.0)(59.6-84.4)	
(Very)low SCF						
Low	0(0.0)(0.0	0-0.0)	9(3.7)(1.3-6.1)		0(0.0)(0.0-0.0)	

Abbreviations: CI, confidence intervals for proportions; ES, effect size; SCF, subjective cognitive functioning.

2(3.7)(-1.3-8.7)

Very low

13(5.4)(2.6-8.2)

the meningioma was located frontally; however, we did not find an association between frontal localization and SCF. It should be noted that most of the phenomena described may also apply to other neurological patients, which should be investigated in future studies.

On the longer-term, there was a significant decrease in SCF from baseline to 1 year after surgery in a subsample of patients. At that time-point, SCF was at a level comparable with normative controls. One-year postsurgery, 14% of patients reported very low SCF as opposed to 3.7% and 9.1% before and 3 months after surgery. These long-term results appear to be in line with the findings of van der Vossen et al<sup>12</sup> who found that 23% of the meningioma patients

reported cognitive complaints, as measured with the CFQ, approximately 32 months post surgery. These researchers set a slightly higher population mean for normative purposes (32.5) but used a less stringent cutoff (1SD) for determining complaints, which might have resulted in a higher percentage of patients reporting complaints. However, studies among other neuro(onco)logical patient groups using the CFQ, 14,38 solely including a long-term assessment, reported high levels of complaints years after diagnosis, suggesting the possibility that complaints, regardless of type of diagnosis, may manifest later on because of the (inability of) full resumption of daily activities at that time. As the follow-up period in the current study did not exceed

7(14.0)(4.4-23.6)

<sup>&</sup>lt;sup>a</sup>Positive z-scores indicate better SCF;

<sup>&</sup>lt;sup>b</sup>Glass's  $\Delta$  (M<sub>patients</sub>-M<sub>controls</sub>/SD<sub>controls</sub>) equals the patients' mean z score<sup>30</sup>, with ES: less than or equal to 0.49: small; 0.50 to 0.79: medium; greater than or equal to 0.80: large<sup>31</sup>;

<sup>&</sup>lt;sup>c</sup>Partial eta squared, with ES 0.01: small; 0.06: moderate; 0.14: large<sup>31</sup>;

<sup>\*</sup>P < Benjamini-Hochberg corrected  $\alpha$  of .030;

<sup>\*\*</sup>P < Benjamini-Hochberg corrected  $\alpha$  of .017.

TABLE 3 Mean (z-)scores on measures of OCF, anxiety and depression, and associations of SCF with these measures at all time points

	T0(n range = 50 to 54)				T3(n range = 155 to 159)			T12(n range = 48 to 50)				
	Mean z (SD)	≥Cutoff, n(%)	SCF r/ρ	P	Mean z (SD)	≥Cutoff, n(%)	SCF r/ρ	Р	Mean z (SD)	≥Cutoff, n(%)	SCF r/ ρ	Р
OCF <sup>a</sup>												
Verbal memory	-0.38(1.22)	6(11.1)	0.286 <sup>c</sup>	.036	-0.97(1.27)	50(32.3)	0.056	.490	-0.71(1.24)	13(26.0)	0.259	.069
Visual memory	-0.48(1.19)	10(18.5)	0.050 <sup>c</sup>	.719	-0.30(1.28)	25(16.0)	0.001 <sup>c</sup>	.986	-0.54(1.16)	10(20.0)	0.210	.142
Psychomotor speed	-1.20(1.63)	23(42.6)	0.182	.188	-0.68(1.12)	35(22.2)	0.091 <sup>c</sup>	.258	-0.75(1.22)	10(20.8)	0.262 <sup>c</sup>	.072
Reaction time	-1.20(2.40)	14(25.9)	0.288 <sup>c</sup>	.035	-1.06(1.89)	45(28.2)	0.027 <sup>c</sup>	.741	-0.48(1.65)	10(20.0)	-0.052 <sup>c</sup>	.722
Complex attention	-1.23(2.79)	17(34.0)	0.140 <sup>c</sup>	.332	-1.21(2.26)	50(32.3)	-0.025 <sup>c</sup>	.762	-0.58(1.97)	11(22.4)	-0.010 <sup>c</sup>	.944
Cognitive flexibility	-1.05(2.39)	19(37.3)	0.172 <sup>c</sup>	.226	-1.03(1.66)	47(30.3)	-0.026 <sup>c</sup>	.744	-0.44(1.48)	10(20.4)	0.090 <sup>c</sup>	.540
Processing speed	-1.12(1.28)	19(35.2)	0.095 <sup>c</sup>	.495	-0.69(1.07)	35(22.3)	-0.060 <sup>c</sup>	.459	-0.56(1.06)	10(20.4)	-0.202 <sup>c</sup>	.164
	Mean (SD)	≥Cutoff, n(%)	SCF r/ρ	Р	Mean (SD)	≥Cutoff, n(%)	SCF r/ρ	Р	Mean (SD)	≥Cutoff, n(%)	SCF r/ρ	Р
HADS <sup>b</sup>												
Anxiety	7.25(4.51)	25(47.2)	-0.463	<.001	* 4.55(3.63)	27(17.0)	-0.352 <sup>c</sup>	<.001*	* 4.46(3.12)	10(20.8)	-0.543 <sup>c</sup>	<.001**
Depression	6.34(4.75)	18(34.0)	-0.346 <sup>c</sup>	.011	3.57(3.27)	16(10.1)	-0.338 <sup>c</sup>	<.001*	* 4.31(3.77)	12(25.0)	-0.574 <sup>c</sup>	<.001**

Abbreviations: HADS, Hospital Anxiety and Depression Scale; OCF, objective cognitive functioning;  $r/\rho$ , Pearson/Spearman correlation (0.10-0.29: small; 0.30-0.49: medium; 0.50-1.0: large<sup>31</sup>); SCF, subjective cognitive functioning.

the first year after surgery, of interest is what happens on the longerterm. We have added a 24-month time point to our project.

In line with previous studies in neuro-oncological patient groups, 11,13 SCF was not related to OCF. Instead, close associations between SCF and anxiety and depression have been described, 11,13 as was also the case in our meningioma sample. The lack of associations between SCF and OCF might be because of different assessment techniques: whereas SCF is often assessed using self-reported questionnaires (reflecting a broader period of time and different situations), OCF is assessed at one point in time using neuropsychological measurements in a clinical setting. Neuropsychological tests can suffer from insufficient ecological validity and might therefore not reflect patients' (experience of) cognitive functioning in daily life. 39

## 4.1 | Study limitations

Some study limitations should be considered. First, the number of data available differs between time points because of expansion of our research project, although we found no differences regarding patient characteristics between time points. Second, we solely included relatively well-functioning patients who were appropriate candidates for

surgery, and who were also capable of filling out the CFQ and performing the NPA. On the other hand, patients with very small (less than 3 cm) meningioma (in absence of symptoms) adopt a wait-and-scan approach or are treated with Gamma Knife radiosurgery in our hospital. Consequently, our results may not be representative for the general population of meningioma patients. In addition, although SCF is known to be related to fatigue, 4.13 we were not able to study this relationship in this sample for the 3-month time-point. However, a former study of our group, that included a partially overlapping sample of patients from the current study, demonstrated that substantial (mental) fatigue was very common prior to as well as 1 year after surgery. 4

In conclusion, although meningioma patients are known to have deficits in OCF, they reported significantly better SCF when compared with a normative sample both before and 3 months after surgery. A significant decrease in group level SCF was observed from baseline to 1 year after surgery in a subsample of patients. At that time point, SCF did not differ from the normative group. Consistent with the literature, SCF was associated with symptoms of anxiety at all time points and with depression at 3- and 12-months postsurgery, but not with OCF nor with sociodemographic or clinical characteristics at 3-months follow-up.

<sup>&</sup>lt;sup>a</sup>Positive z-scores indicate better OCF;

<sup>&</sup>lt;sup>b</sup>Data was available for 53/159/48 patients at respectively T0/T3/T12;

 $<sup>^{\</sup>rm c}$ Non-linear and/or non-normally distributed data, Spearman's  $\rho$  was used;

<sup>\*</sup>P < Benjamini-Hochberg corrected alpha of .005;

<sup>\*\*</sup>P < Benjamini Hochberg corrected alpha of .011.

## 4.2 | Clinical implications

Future studies should evaluate SCF in meningioma patients and other brain tumors longer after surgery as data suggest that cognitive complaints might manifest later on. Moreover, future research may help to compare findings on the CFQ with other measures of SCF in patients with brain tumors.

In clinical practice, to evaluate cognitive function, SCF should be assessed together with OCF, as patients' reports on their SCF does not allow conclusions about their OCF. The patients that do report poor SCF should also be screened for psychological symptoms, as poor SCF might be an indicator of emotional distress. In providing optimal care and in determining whether and which interventions (eg, cognitive rehabilitation or pharmaceutical agents<sup>40</sup>) are needed the patient should be considered as part of a complex environment, taking psychological distress and social support into account.

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#### **CONFLICT OF INTEREST**

The authors declare no potential conflict of interest.

## DATA AVAILABILITY STATEMENT

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

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#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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