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Longitudinal association of subjective prospective and retrospective memory and depression among patients with glioma

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ABSTRACT

Purpose: This study investigated the levels of depression, subjective prospective memory (PM), and subjective retrospective memory (RM) among Chinese glioma patients and explored the bi-directional relationships between depression and memory impairment, including subjective PM and RM.
Methods: Seventy-one participants with glioma were assessed for depression, PM, and RM at two time points (Time 1: within 48 h of being hospitalized; Time 2: two weeks after surgery). A cross-lagged path analysis was conducted to examine the bi-directional relationships between depression and memory.
Main results: Depression at T1 predicted memory impairment total scores ($\beta = 0.22$, $P = 0.011$) and RM ($\beta = 0.29$, $P < 0.001$) at T2. However, depression at TI could not predict PM at T2 ($\beta = 0.15$, $P = 0.090$). Memory, whether PM or RM, at T1 could not predict depression at T2 ($\beta = 0.07$, $P = 0.497$; $\beta = 0.00$, $P = 0.978$; $\beta = 0.06$, $P = 0.321$).
Conclusions: Depression can affect RM memory impairment among glioma patients. Oncology nurses should preoperatively screen for depression in glioma patients to identify high-risk groups, for whom emotional interventions and memory training should be carried out to reduce postoperative RM memory impairment.

1. Introduction

Gliomas are the most common type of brain tumor, accounting for 81% of malignant brain tumors (Ostrom et al., 2014). Malignant or high-grade gliomas are dismal diseases while low-grade tumors can be cured following gross total tumor resection (Bunevicius, 2018). Nevertheless, cognitive status impairments of glioma patients are as high as 91%, and they are not often recognized (Barzilai et al., 2019; Tucha et al., 2000). Moreover, these impairments are associated with a poorer prognosis and quality of life, and shorter survival (Daniels et al., 2011; Johnson et al., 2012; Liu et al., 2018).

Of the cognitive dysfunctions that follow gliomas, memory impairment is probably the most common (Carlesimo, 2012). Memory can be measured subjectively (self-report) or objectively (neuropsychological battery) and it includes many different processes, such as short-term and long-term memory (Paquet et al., 2018; Pranckeviciene et al., 2017; Talacchi et al., 2011). It is necessary, therefore, to focus on how cancer patients describe their memory problems (Paquet et al., 2018). Qualitative studies (Shilling and Jenkins, 2007; Myers, 2012) have documented that cancer survivors often complain about their difficulties remembering to ask their doctors for a new prescription or to buy something when they go shopping. These are examples of prospective memory (PM) impairment that affect memory for activities and events in the future (Mayes, 1997). In addition, cancer patients complain about having difficulties remembering past activities and events, such as forgetting names. These are instances of retrospective memory (RM) impairment (Mayes, 1997; Myers, 2012). A quantitative study of breast cancer patients also confirmed that they reported more PM and RM problems than the control group and that PM and RM problems have a negative impact on their quality of life after surgery (Paquet et al., 2018).

Compared with objective measures, such self-report memory measures take into account the environment in which a person is situated and that they interact with, which reflects the individual's ability or inability to complete tasks specific to his or her own life. These measures help clinical staff gain insights into the impact of such cognitive impairment on the patients' quality of life and daily functioning (Munir et al., 2010; Hansen et al., 2008).Thus, researchers suggest that subjective measures of cognitive functioning should be considered the primary indicator of cognitive impairments in cancer patients (Savard

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and Ganz, 2016).

However, to date, most previous studies have focused only on performance-based memory measures among glioma patients (Campanella et al., 2018; Heitzer et al., 2019; Loaiza et al., 2018; Tymowski et al., 2018). To the best of the authors' knowledge, only one published quantitative study has reported that brain tumor patients have various subjective memory problems (Pranckeviciene et al., 2017). Unfortunately, the study had some limitations. First, the scale for measuring subjective memory was self-developed, and it did not report the validity. Second, it regarded memory problems as dichotomous variables and only reported the percentage of patients with memory problems. The severity of the patients' memory impairment was not studied. Therefore, it was necessary for the current study to quantitatively evaluate the self-reported memory impairment of glioma patients using a well-accepted scale that has good reliability and validity.

Due to the direct action of the tumor mass or the consequences of surgical, chemotherapy, and radiotherapy treatments, memory impairment in glioma patients seems hard to avoid, despite its importance for the patients' everyday quality of life (Bergo et al., 2019; Campanella et al., 2018). Therefore, it is important for the clinical staff to identify the risk factors of memory impairment that can be eliminated or mitigated.

Depression is considered a risk factor for mild cognitive impairment and is a high and hidden morbidity among glioma patients (Gao et al., 2013; Rooney et al., 2014). A review of 42 observational studies of depression in glioma patients revealed that the suprathreshold median prevalence rate was 27% (Rooney et al., 2014). Very few studies have explored the association of depression and memory among glioma patients. In general, these studies found that positive associations of depression with memory impairment have been assessed via correlations in cross-sectional studies (Grant et al., 1994; Pranckeviciene et al., 2017). There is no study examining the association of depression with subjective PM and PM among glioma patients using longitudinal data. Moreover, some studies suggest that the associations of depression with cognitive function may be bi-directional (Goebel et al., 2013), however, there is no study examining bi-directional relationships between depression and PM and RM memory.

Thus, to explore the bi-directional relationships between PM and RM memory and depression, we used the cross-lagged path model (CLPM). In the CLPM, the stability of the constructs is controlled by including autoregressive relationship, and it is therefore considered that the cross-lagged regression parameters of this model are appropriate measures to study the bi-directional relationship in longitudinal correlation data (Bentler and Speckart, 1981). Thus, this was the first prospective study to explore the bi-directional relationships between depression and subjective PM and RM impairment among glioma patients. In summary, our study's objectives were as follows: (1) to investigate the levels of depression and subjective PM and RM memory impairment among patients with glioma and (2) to examine the bi-directional relationships between depression and subjective PM and RM impairment.

2. Methods

2.1. Participants and procedure

In this prospective study, participants were recruited from neurosurgery wards of a comprehensive hospital in Jinan, Shandong Province, China. The recruitment of participants and collection of data were administered by a well-trained research nurse and a postgraduate nursing candidate. All eligible patients were verbally informed of the purpose and process of this study and asked whether they were willing to participate. Willing participants were invited to complete a paper questionnaire survey at two different time points between January 2016 and June 2017: Time 1 (T1), which was within 48 h of being hospitalized for glioma, and Time 2 (T2), which was approximately two weeks after surgery. The inclusion criteria were that the participants were 1) 18 years of age or older and 2) intending to undergo a glioma resection. The exclusion criteria were patients with 1) recurrent glioma; 2) a history of severe brain injury or mental illness, such as schizophrenia and bipolar disorder; and 3) other serious underlying diseases or complications.

The number of required samples was calculated using G-Power 3.1. The correlation coefficient of depression and memory was 0.44 (Pranckeviciene et al., 2017).We used a significance level of 0.05 (two-tailed), meaning that at least 35 participants were needed if a medium-sized difference was found with 80% power.

Of the 127 patients who agreed to participate in the study, eight did not complete the initial assessment, while 48 did not complete the assessment at T2 (5 patients were transferred to Intensive Care Unit postoperatively; 7 patients were discharged; and 36 were unable to fill out questionnaires because of poor physical conditions and cognition states). In all, 71 patients were treated with surgery and included in the study. The study, which conformed to the Declaration of Helsinki, was approved by the ethics committee of the school of Nursing, Shandong university (ethical approval no. 2016-R-26). All participants verbally provided informed consent.

2.2. Measures

2.2.1. Demographic and clinical information

Demographic information, including age, gender, education, and residence, was self-reported by the participants. The clinical characteristics, which were acquired from the hospital registry databases, consisted of the World Health Organization (WHO) grade, tumor hemisphere, and tumor location.

2.2.2. Memory

The Prospective and Retrospective Memory Questionnaire that assesses PM and RM failures in daily life is a self-rating scale consisting of 16 items rated in terms of frequency from 1 (never) to 5 (very often). Eight items evaluate PM, like, “Do you decide to do something in a few minutes' time and then forget to do it?” Eight items assess RM, such as “Do you fail to recall things that have happened to you in the last few days?” (Crawford et al., 2003). Higher scores represent more PM and RM impairment. The Chinese version has demonstrated good reliability and validity (Wu, 2013). In this study, at T1, the Cronbach's α of the PM, RM, and total scores were 0.890, 0.874, and 0.855, respectively.

2.2.3. Depression

The Patient Health Questionnaire (PHQ-9) is a nine-item screening tool for the presence of depression that is based on the Diagnostic and Statistical Manual of Mental Disorders (fourth edition) criteria. Participants rated each item using a four-point Likert scale ranging from 0 (not at all) to 3 (nearly every day). A validated cutoff PHQ-9 score of ≥ 10 was used to diagnose the presence of depression (Kroenke et al., 2001; Kroenke and Spitzer, 2002; Chen et al., 2013). The Chinese version has shown good reliability and validity (Yeung et al., 2008; Wang et al., 2014). In this study, at T1, the Cronbach' s α was 0.937.

2.3. Data analysis

The one-way analysis of variance (ANOVA), and Pearson correlation analysis were conducted using IBM SPSS 21.0 (IBM Corp., Armonk, NY, USA). ANOVA was conducted to test for differences in depression and memory at T2 in terms of the categorical sociodemographic and clinical information. Pearson correlation analysis was used to evaluate the associations among depression and memory at T1 and T2.

A CLPM, which is from the structural equation modeling approach, was conducted using IBM SPSS AMOS 21.0 (IBM Corp., Armonk, NY, USA) to explore the bi-directional effects between depression and memory. There are three types of relationships regarding the temporal precedence of the variables: 1) a within-time correlation, which refers to the relationship between the two variables when they are assessed at the same time; 2) a stable path, which refers to the variables at T2 being predicted by the same variables as at T1; and 3) a cross-lagged path, which refers to the variables at T2 being predicted by another variable than at T1. The following fit indexes for an acceptable fit of the cross-lagged model were used: the root mean square error of approximation (RMSEA) with associated 90% confidence intervals less than 0.08, the comparative fit index (CFI), the goodness of fit index (GFI), and the Tucker-Lewis index (TLI), which should be more than 0.90 (Daire et al., 2008). Three models were estimated regarding the temporal relationships between (a) depression and memory, (b) depression and PM, and (c) depression and RM. Variables with a P-value below 0.2 in the bivariate analyses were included in the cross-lagged path analysis. An alpha level of $P < 0.05$ (two-tailed) was used as the significance level.

3. Results

3.1. Demographic and clinical characteristics

The participants in the study (mean: 46.27 years old) were younger than the 48 patients (mean: 55.31 years old) who did not complete the T2 assessment ($t = 2.369$, $P = 0.02$). No differences in any other sociodemographic and clinical characteristics were found.

As shown in Table 1, 53.5% of the patients were female, 83.1% of the patients were less than 60 years old, 62% had a junior high school-level of education or less, 50.7% had a WHO grade II tumor, 59.2% had frontal lobe tumors, and 43.7% had tumors located in the left hemisphere. All participants received standardized treatment and had no surgical complications.

3.2. Depression and memory impairment at T1 and T2

Of the patients with glioma, 21.1% reported depression at T1 and 39.4% reported depression at T2 (T1: 6.36 ± 5.00; T2: 8.14 ± 5.59).

Table 2
Scores of Memory and depression at Time 1 and Time 2(n = 71).

	Memory, *M* ± *SD*	PM, *M* ± *SD*	RM, *M* ± *SD*	Depression, *M* ± *SD*
T1	40.55 ± 14.91	20.46 ± 7.77	19.75 ± 8.01	6.36 ± 5.00
T2	42.21 ± 15.94	21.48 ± 8.35	20.73 ± 7.95	8.14 ± 5.59

Abbreviations: *M* ± *SD*, mean ± standard deviation; T1, Time 1; T2, Time 2. PM, prospective memory; RM, retrospective memory.

As presented in Table 2, participants reported worse PM than RM impairment (T1: 20.46 ± 7.77 vs 19.75 ± 8.01; T2: 21.48 ± 8.35 vs 20.73 ± 7.95).

3.3. Bivariate analyses of memory impairment total scores and depression at T2

As shown in Table 1, more memory impairment at T2 was significantly associated with older age ($F = 3.490$, $P = 0.036$). Post-hoc analysis showed that the participants who were over 60 years of age reported higher memory impairment scores than those aged between 18 and 44 years ($P = 0.016$) and between 44 and 59 years ($P = 0.019$). In addition, glioma patients with tumors located in the left hemisphere reported more memory impairment than glioma patients with tumors located in the right hemisphere ($F = 4.265$, $P = 0.043$).

3.4. Correlations between depression and memory impairment at T1 and T2

The correlations among the variables revealed that the higher the level of depression or memory impairment the patients had at T1, whether in PM or RM, the greater the depression or memory impairment they reported at T2 ($r = 0.287$ to 0.581, $P < 0.05$; see Table 3).

Table 1
Bivariate analyses of memory impairment total scores and depression at T2 (n = 71).

	n	%	Depression			Memory		
			M ± *SD*	*F*	*p*-value	*M* ± *SD*	*F*	*p*-value
Sex								
Male	33	46.5	7.97 ± 4.90	0.057	0.812	42.24 ± 15.31	0.000	0.988
Female	38	53.5	8.29 ± 6.18			42.18 ± 16.47		
Age (years)								
18–44	32	45.1	8.78 ± 5.45	0.436	0.648	40.00 ± 13.59	3.490	0.036
44–59	27	38.0	7.41 ± 5.63			40.07 ± 15.15		
≥ 60	12	16.9	8.08 ± 6.13			52.92 ± 20.07		
Education [a]								
Junior high or lower	44	62.0	8.41 ± 5.89	0.860	0.428	40.75 ± 15.00	1.550	0.220
Higher general	13	18.3	5.08 ± 5.96			49.31 ± 15.77		
Graduate/postgraduate	13	18.3	6.38 ± 4.19			40.54 ± 18.39		
Residence								
Urban	25	35.2	6.84 ± 4.83	2.126	0.149	44.72 ± 16.21	0.956	0.332
Rural	46	64.8	8.85 ± 5.89			40.85 ± 15.80		
WHO grade								
I	6	8.5	10.67 ± 5.75	1.111	0.351	49.33 ± 21.57	2.103	0.108
II	36	50.7	8.08 ± 5.06			40.11 ± 13.99		
III	8	11.3	5.38 ± 5.76			53.00 ± 14.04		
IV	21	29.5	8.57 ± 6.27			39.67 ± 16.87		
Hemisphere								
Left	31	43.7	8.48 ± 5.61	0.205	0.652	46.55 ± 19.48	4.265	0.043
Right	40	56.3	7.87 ± 5.63			38.85 ± 11.72		
Location								
Frontal	42	59.2	8.33 ± 5.61	0.106	0.899	43.98 ± 14.64	0.716	0.492
Temporal	11	15.5	8.27 ± 3.52			41.27 ± 10.86		
Other	18	25.4	7.61 ± 6.71			38.67 ± 20.92		

Abbreviations: *M* ± *SD*, mean ± standard deviation; WHO, World Health Organization.
[a] Missing value. *F*, *F*-test statistic.

Table 3
Correlations between depression and memory impairment at time 1 and time 2 (n = 71).

	T1memory	T1PM	T1RM	T2memory	T2PM	T2RM	T1depression
T1memory	1						
T1PM	0.966***	1					
T1RM	0.908***	0.820***	1				
T2memory	0.756***	0.746***	0.718***	1			
T2PM	0.717***	0.722***	0.673***	0.979***	1		
T2RM	0.762***	0.738***	0.733***	0.977***	0.913***	1	
T1depression	0.511***	0.487***	0.491***	0.536***	0.470***	0.581***	1
T2depression	0.311**	0.295*	0.287*	0.434***	0.432***	0.415***	0.485***

Abbreviations: T1depression, depression at Time 1; T1memory, memory at Time 1; T1PM, prospective memory at Time 1; T1RM, retrospective memory at Time 1; T2depression, depression at Time 2; T2memory, memory at Time 2; T2PM, prospective memory at Time 2; T2RM, retrospective memory at Time 2. *P < .05, **P < .01, **P < .001.

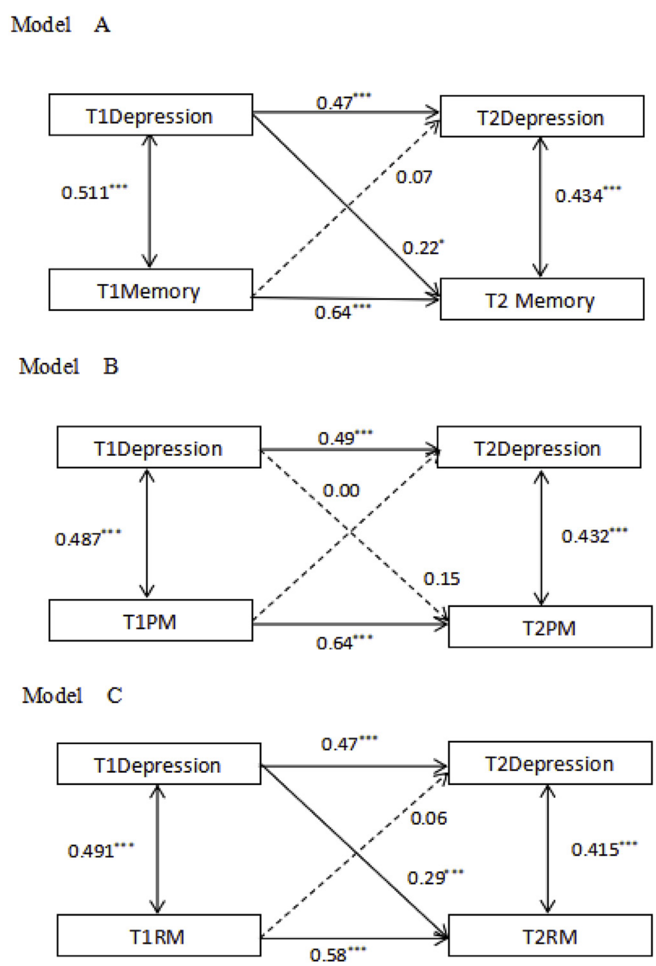

Fig. 1. Cross-lagged association of depression and memory. Model A Cross-lagged association between depression and memory total scores. Model B Cross-lagged association between depression and prospective memory. Model C Cross-lagged association between depression and retrospective memory. Abbreviations: *P < .05, **P < .01, ***P < .001. PM, prospective memory. RM, retrospective memory. T1, Time 1. T2, Time 2. Double-headed arrows denote correlations and single-headed arrows denote direct paths (variables pointed by arrows are dependent variables).Solid lines indicate statistically significant associations and dashed lines indicate insignificant associations.

3.5. Examination of the cross-lagged models

Fig. 1 shows the standardized coefficients and paths for the CLPM after controlling for age, residence, WHO grade, and tumor hemisphere. As shown in Fig. 1, the analysis of Model A revealed that high depression and memory impairment total scores were related to individual differences, as those with high levels of depression and memory impairment total scores at T1 tended to have high levels of depression and memory total scores at T2 ($\beta = 0.47$, $P < 0.001$; $\beta = 0.64$, $P < 0.001$). More importantly, the analysis revealed that higher levels of depression at T1 predicted an increase in the memory impairment total scores from T1 to T2 ($\beta = 0.22$, $P = 0.011$); however, higher memory impairment at T1 was not found to predict higher depression at T2 ($\beta = 0.07$, $P = 0.497$).

Likewise, Model C in Fig. 1 reveals that while depression at T1 could predict RM impairment ($\beta = 0.29$, $P < 0.001$) at T2, RM impairment at T1 could not predict depression at T2 ($\beta = 0.06$, $P = 0.321$). However, as shown in Model B, we did not find that depression at TI could predict PM impairment ($\beta = 0.15$, $P = 0.090$) or that PM impairment at TI could predict depression at T2 ($\beta = 0.00$, $P = 0.978$). As presented in Table 4, the fit indexes of the three theoretical models were all good, suggesting that all three theoretical models were good representations of our data.

4. Discussion

This study assessed the levels of depression and subjective memory impairment of patients with glioma in China and explored the bi-directional effects between depression and subjective memory impairment. The results of the present study suggest that patients with glioma suffer from high levels of depression symptoms and subjective memory impairment. The depression and subjective memory impairment had a positive association; in particular, the presence of depression could predict subjective RM impairment. To the best of our knowledge, this study was the first to examine the subjective memory impairment of patients with glioma using a well-accepted scale and the first to explore the bi-directional relationships between depression and subjective memory impairment using a prospective design.

Patients with glioma in this study had a high level of depression, which is in line with previous studies (Pranckeviciene et al., 2017; Rooney et al., 2014).The diagnosis of the tumor per se and the fear of both the tumor treatment and the risk of recurrence can negatively affect the mental state of patients (D'Angelo et al., 2008). Our sample reported more PM and RM problems (M = 20.46 and 19.75, respectively) than the Swedish (Ronnlund., 2008) normative data (M = 17.90 and M = 14.75, respectively), which consisted of 540 healthy adults

Table 4
Fit indexes of the models (n = 71).

	χ^2/df	RMSEA	CFI	GFI	TLI
Model A	1.224	0.057 (0.000, 0.132)	0.968	0.941	0.940
Model B	1.260	0.061 (0.000, 0.138)	0.963	0.943	0.927
Model C	1.113	0.040 (0.000, 0.123)	0.983	0.946	0.968

Abbreviations: CFI, comparative fit index; GFI, goodness-of-fit index; RMSEA, root mean square error of approximation; TLI, Tucker-Lewis fit index.

($t = 2.78$, $P < 0.001$ and $t = 5.26$, $P < 0.001$). This finding suggests that depression symptoms and subjective memory impairment are present in patients with glioma, which require more attention.

Our results also demonstrated that a higher level of depression could predict an increase in subjective memory impairment. There are two well-known hypotheses for the memory impairment in depression that can account for our findings. One is the resource allocation hypothesis that proposes that depressed people have deficits in some effortful cognitive processes, including remembering, due to a decline in their cognitive capacity (Ellis and Ashbrook, 1988). The other is the affective interference hypothesis that proposes that because depressed people focus on processing emotional material, they perform well on tasks that require them to deal with emotional stimuli, but they are affected on tasks that require them to ignore emotional cues, such as memory (Siegle et al., 2002). In addition, previous studies of other populations have shown that depression can induce higher cortisol levels that are related to worse memory function (Glienke and Piefke, 2017; Herbert, 2013). Therefore, depression may also affect memory through the cortisol levels.

Notably, depression could not predict subjective PM, which might indicate that PM and RM are related to different cognitive processes. RM is largely dependent on the region of the medial temporal lobe, such as the hippocampus (Vargha-Khadem et al., 1997), whereas PM usually requires a higher level of retrieval and is considered to be located primarily in the frontal region (Neulinger et al., 2016). Furthermore, brain-imaging studies have found that in depressed patients, the reduction of the hippocampus is associated with accelerated forgetting, which could explain the relationship between depression and RM (Voss et al., 2017). However, we have not found that subjective memory impairment can predict depression symptoms. Previous studies have reported cross-sectional association between memory and depression (Grant et al., 1994; Pranckeviciene et al., 2017). This study further suggests that memory is more likely a consequence than a cause of depression symptoms. Preoperative depression screening could help nurses give priority to high-risk patients who would benefit from emotional interventions and memory training to reduce their postoperative RM memory impairment.

5. Limitations

Some limitations of this study need to be highlighted. First, different lobes have specific cognition functions (Noll et al., 2016), however, the small sample size limited our examination of the effects of different lobes on relationships between depression symptoms and memory. A larger sample is needed in future studies to explore whether the relationships between memory and depression are dependent on different lobes. Second, this study experienced a high dropout rate between time point 1 and 2. However, the drop-out rate is a general problem in research of brain tumor patients (Jakola et al., 2015; Litofsky et al., 2004; Liu et al., 2018; Wolf et al., 2016; Viereck et al., 2016). The participants who were ultimately analyzed in this study were younger than those who were lost to follow-up, which may limit the generalizability of the findings. However, we controlled for age in the cross-lagged analysis and discovered subjective memory impairment in glioma patients even in younger samples, which further emphasizes that the memory function of glioma patients requires urgent attention.

6. Implications for clinical practice and research

Oncology nurses should pay attention to glioma patients' PM and RM as well as their depression before and after surgery. Preoperative depression screening could help nurses give priority to high-risk patients who would benefit from emotional interventions and memory training to reduce their postoperative RM memory impairment. We assessed patients at approximately two weeks after surgery. It's possible that the depression symptoms that were assessed two weeks after surgery were a normal reaction (Rooney et al., 2014).There may have been different findings if the evaluation was taken a month after surgery. Future research should assess depression symptoms a month after the initial diagnosis to allow initial sadness to subside.

7. Conclusions

Despite these limitations, this study was the first to explore the bidirectional relationship between depression and subjective memory impairment among patients with glioma using cross-validation. These findings highlight the importance of addressing depression in order to improve subjective memory function, and thus improve the quality of life of patients with glioma.

Declarations of interest

No conflict of interest.

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