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Psychiatric symptoms in gliomas: a systematic review

Francesca Bardi · Leonardo Monacelli · Romina Caso · Gianmarco Stella · Georgios D. Kotzalidis · Silvia Montanari · Delfina Janiri · Florien W. Boele · Gabriele Sani · Alessio Simonetti

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Abstract

Background Psychiatric symptoms are prevalent among adults with gliomas, yet their recognition and characterization remain limited.

Objective This systematic review aimed to synthesize evidence on prevalence, temporal course, and disease-specific correlates of all reported psychiatric symptoms in adults with glioma.

Methods PubMed, CINAHL, and PsycInfo were searched from inception to September 1st, 2025. Eligible studies enrolled adults with glioma and assessed psychiatric symptoms using validated psychometric instruments or structured/semi-structured clinical interviews. Reporting followed PRISMA guidelines and risk of bias was assessed using the ROBINS-E framework.

Results Among 4,327 records, 130 studies met criteria for qualitative synthesis. Depressive (20-55%) and anxiety (20-58%) symptoms emerged as the most frequent and relevant manifestations. Depressive symptoms were more common in high-grade glioma and were associated with poorer survival and functional impairment, whereas anxiety symptoms were mainly linked to reduced quality of life and showed inconsistent prognostic associations, with distinct phase-dependent patterns across the disease course. Beyond affective disorders, a range of non-affective psychiatric manifestations was identified, including psychotic symptoms, personality traits, sleep disturbances, obsessive symptoms and eating disturbances, and post-traumatic stress symptoms. These manifestations were less frequently reported and tended to occur in specific clinical contexts, such as the peri-operative or treatment phases, or in association with involvement of specific neuroanatomical regions.

Conclusions Psychiatric symptoms are integral, phase-dependent features of the glioma trajectory, shaped by tumor-related factors and active treatments. Screening and management should be prioritized at clinically high-risk stages. Future studies should integrate psychiatric assessments with tumor-related variables to refine mechanistic understanding.

Introduction

Gliomas represent the most common and aggressive category of primary malignant tumors of the central nervous system, accounting for more than 80% of all such brain tumors [1] and affecting nearly 100,000 individuals globally each year [2]. According to the World Health Organization (WHO) classification, gliomas are graded from I to IV, with grades I-II traditionally defined as low-grade (LLG) and grades III-IV as high-grade gliomas (HGG) [1]. While tumor grade remains central to prognostic assessment, molecular markers such as Isocitrate dehydrogenase (IDH)

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Table 1 Inclusion and Exclusion Eligibility Criteria.

Inclusion Criteria	Exclusion Criteria
•Original research articles; •Published in any language, any time; •Conducted on adult populations (≥ 18 years of age) •Included participants with a diagnosis of glioma, defined according to the 2021 WHO Classification of CNS Tumours as primary tumors of glial origin, including subtypes such as astrocytomas, oligodendrogliomas, and glioblastomas; •Investigated psychiatric symptoms using validated psychometric instruments or structured/semi-structured clinical interviews according to established psychopathological constructs and formal diagnostic systems (DSM or ICD).	•Duplicate publications across databases (“Duplicate”); •Reviews, meta-analyses, and consensus meetings or guidelines (collectively labeled as “Review”); •Editorials, commentaries, letters to the editor, and opinion papers such as notes or letters lacking original data (all labeled as “Editorial”); •Study protocols (“Protocol”); •Corrigenda, errata, or other correction notices not containing original data (“Corrigendum”); •Retracted publications, regardless of study type (“Retracted”); •Articles not peer-reviewed or with an ongoing peer-review process (“Preprint”); •Studies not involving human subjects, including in vitro or animal research (“In vitro” or “In vivo”); •Post-mortem studies based on autoptic or histopathological examinations not involving living subjects (“Post-mortem”) •Case reports or case series without systematic methodology (“Case”); •Studies involving participants under 18 years of age (“Lumping”); •Studies that did not report glioma-specific outcomes separately, such as those combining gliomas with other brain tumors without stratified analyses, those whose primary focus was inconsistent with the scope of this review, such as those exploring psychological constructs not related to recognized psychiatric symptoms (e.g., distress, quality of life), studies focusing exclusively on sleep disorders, unless investigated in association with other recognized psychiatric conditions, those providing a narrative description of psychiatric symptoms lacking a scientifically grounded methodology for their assessment (collectively labeled as “Unfocused”).

mutation, 1p/19q codeletion, and enzyme O-6-methylguanine-DNA methyltransferase (MGMT) promoter methylation have increasingly refined risk stratification and therapeutic approaches [3]. Depending on histomolecular features of the tumour, median survival ranges from 1-2 years [4] to several decades [5].

Across the disease trajectory, patients with glioma frequently experience a broad spectrum of symptoms, including motor deficits, seizures, severe fatigue, neurocognitive decline, and psychiatric disturbances, which affect up to 80% of patients at various stages of illness [6, 7]. While cognitive and neurological impairments are widely recognized as clinical hallmarks of gliomas, psychiatric symptoms remain comparatively underrecognized, complicated by the use of a diverse range of screening tools in research studies. Yet, they can manifest at any stage of the disease and, in some instances, may even precede overt neurological deficits representing the first warning sign that brings patients to medical attention [8, 9]. Psychiatric symptomatology associated with gliomas, encompasses not only mood and anxiety disorders, but also psychotic episodes, disturbances in behavior and impulse control, as well as profound alterations in personality and emotional regulation [10]. Their clinical expression is heterogeneous, as it is frequently shaped by intrinsic tumor characteristics. Tumor grade and anatomical location are regarded as major determinants, influencing both the emergence and the clinical expression of such manifestations [11, 12].

A limited number of reviews addressed psychiatric manifestations in glioma, thereby advancing knowledge on their prevalence and clinical significance [10, 13–16]. Yet, some of the current reviews are narrative in nature rather than systematic [10, 15, 17], others have primarily addressed psychological aspects, defined as non-diagnostic constructs such as emotional distress, quality of life, coping, and subjective well-being, or have combined psychological and psychiatric constructs [18, 19]. Still, others have relied exclusively on case studies [8]. Moreover, available systematic reviews on psychiatric symptomatology have focused mainly on depression and anxiety, in line with their predominance in the glioma literature, while other psychiatric symptoms have been less systematically reviewed [13, 14, 17]. Importantly, no previous systematic review has investigated the broad range of psychiatric

symptoms in relation to tumor-specific features, such as grade and anatomical location, or considered their evolution across the different phases of the disease. Therefore, the aim of this review is to provide a comprehensive systematic synthesis of the literature on the broad spectrum of psychiatric symptomatology reported in adult patients with glioma, extending beyond formally diagnosed psychiatric disorders, with a particular focus on their prevalence, associations with tumor grade and location, and temporal course across the disease trajectory.

Materials and methods

Search strategy

A search strategy on PubMed, CINAHL, and PsycInfo databases was performed of all literature published before September 1st, 2025. The literature search was independently conducted by two physician-researchers using the same databases and search strategy, with results cross-checked to ensure completeness and minimise selection bias. Searches were performed in PubMed, CINAHL, and PsycInfo using key search terms including glioma-related diagnosis combined with neuropsychiatric and behavioural outcomes. The complete search strategies are provided in the Supplementary Material (Table S1-S3).

Study selection

Study selection was performed in two stages. In the first stage, titles and abstracts were independently screened by two physician-researchers according to predefined inclusion and exclusion elegibility criteria (Table 1). In the second stage, full texts of potentially eligible studies were assessed for final inclusion. Disagreements regarding study eligibility were resolved through structured consensus discussions among authors. Consensus was reached through iterative discussion rounds and unanimity was required for inclusion or exclusion. Each screened record was assigned a predefined classification label reflecting the reason for exclusion, as detailed in Table 1. The complete lists of screened records and their assigned labels are provided in the Supplementary Material (Tables S1-S3). Studies meeting all inclusion criteria were assigned the label “Included”. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [20]. The review protocol was registered on the Open Science Framework (OSF; registration ID: 6pnz7).

Data extraction

Data extraction was performed independently by two physician-researchers using a predefined data extraction form. For each included study, the following data were extracted: authors and year of publication; study design; sample characteristics; disease duration (time since glioma diagnosis); glioma subtype; tumour anatomical location; tumour grade according to the WHO classification [21]; psychiatric symptomatology; psychiatric assessment methods (including diagnostic criteria and assessment instruments); evidence tier; study aims; and main psychiatric findings.

Psychiatric domains extracted included mood symptoms, anxiety symptoms, psychotic symptoms, personality traits, obsessive symptoms, eating disturbances, sleep-related comorbidities, and post-traumatic stress symptoms. Given the diagnostically non-specific nature of sleep disturbances, studies focusing exclusively on sleep were included only if sleep-related symptoms were examined in comorbidity with other recognized psychiatric conditions [22].

The evidence tier was assigned to each included study according to the highest level of ascertainment used to assess the specific outcome: level 1 evidence was assigned to clinical evaluation, DSM- or ICD-based diagnoses, or structured or semi-structured diagnostic interviews, such as the Structured Clinical Interview for DSM Disorders (SCID); level 2 evidence was assigned to standardized clinician-administered instruments; level 3 evidence was

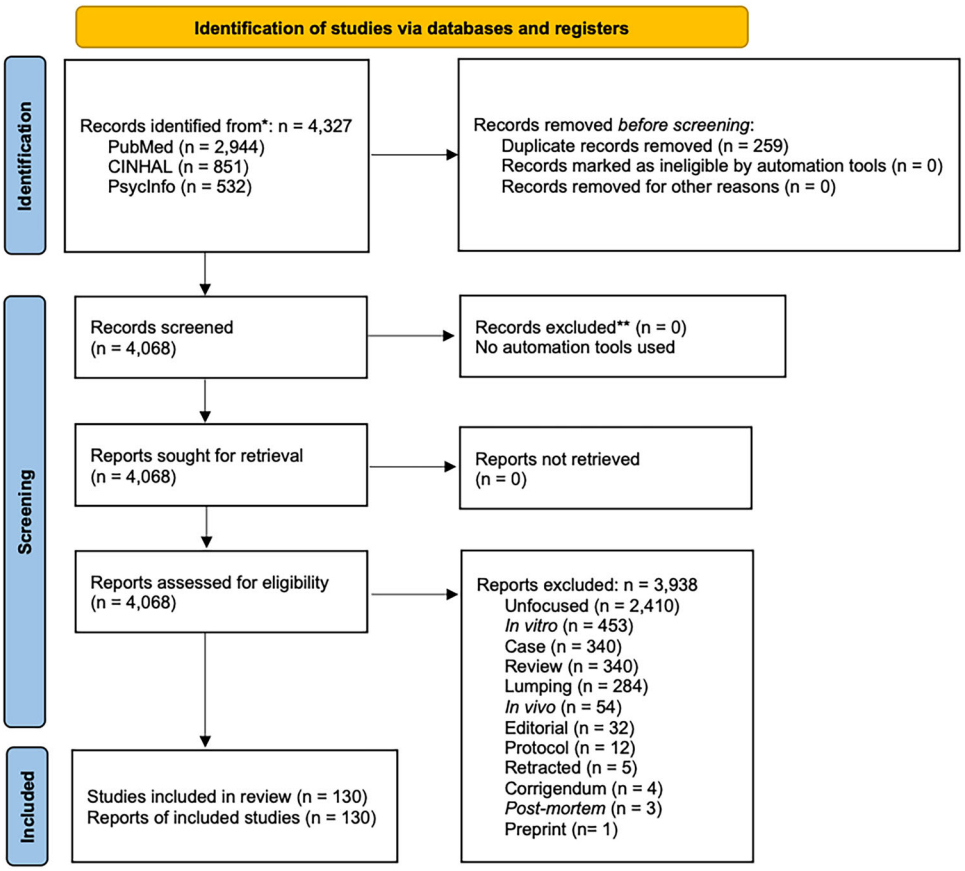


Fig. 1 Flowchart of the systematic literature search according to PRISMA guidelines [20].

assigned to validated self-report questionnaires; finally, level 4 evidence was assigned to studies relying on single items, insufficiently characterized measures, or indirect proxies of psychiatric symptomatology.

Any discrepancies in data extraction were resolved through consensus discussion among the authors.

Risk of bias assessment

To assess Risk of Bias (RoB), i.e., the risk of an overestimation or an underestimation of an outcome or effect due to flaws in design, conduct, analyses, and reporting, we followed the Cochrane RoB method as described in the Cochrane Handbook [23, 24]. Risk of bias was assessed using the ROBINS-E framework, which evaluates bias across multiple methodological domains in observational studies [24]. It was applied here as a domain-based framework to capture potential sources of bias across the heterogeneous observational designs included. The following domains were assessed: confounding, selection of participants, measurement of exposure, post-exposure interventions, missing data, measurement of outcomes, and selection of reported results.

Data synthesis

Study characteristics were summarised descriptively using tabulation of sample sizes, sex distribution, and age measures as reported in the original studies. Given the heterogeneity of study designs, psychiatric outcomes, and assessment methods, a quantitative meta-analysis was not feasible; therefore, a qualitative synthesis approach was adopted [25]. Data analysis began during the data extraction phase through immersion and familiarisation with the included studies. Psychiatric outcomes were grouped into clinically meaningful domains based on symptom type,

Table 2 Summary of clinical characteristics of included studies (n = 130).

	Study design	Sample characteristics	Disease duration (time since diagnosis)	Glioma subtype		Tumor anatomical location	Tumor grade (WHO classification)
			Psychiatric symptomatology	Psychiatric assessment		Evidence tier	
Mood							
	Riggs and Rupp, [46]	CS	86 pts	NA	NA	Fronto-parietal	25.6%; temporal 30.6%; parieto-occipital 5.8%; corpus callosum 12.8%; striothalamus 16.3%; hypothalamus 2.3%; diffuse glioblastosis 5%	NA
		Depression; euphoria; hallucinations; delusions	NA	NA				
	Arseni et al., [49]	CS	92 pts	NA	NA		Brainstem	NA
	Racing thoughts; energy; bulimia;	psychomotor activity	NA	NA				
	Taphoorn et al., [6]	CS	60 pts (37♂, 23♀; x̄ age= 44.1 yr ± 20.5 yr)	> 1 yr	Astrocytoma 63.5%; oligodendroglioma 36.5%	NA	I	
		Depression	POMS	3				
	Lovely et al.,1996	Long (BL, post-RT)	73 pts (46♂, 27♀; x̄ age= 56.6 yr ± 11.8 yr)	Post-op	Glioblastoma multiforme		Temporal 19%; frontal 19%; parietal 22%; other 40%. r- 63%; l- 31.5%; bi 5.5%	IV
		Depression	POMS	3				
	Hahn et al., 2003	CS	68 pts (x̄ age= 44 yr)	Newly diagnosed	Glioblastoma multiforme 44%; anaplastic astrocytoma 16.2%; anaplastic oligodendroglioma 4.6%; oligodendroglioma 5.7%; other 13.2%	r-	52.9%; l- 22.1%	NA
		Depression	BDI-II	3				
	Davies et al., [58]	CS	12 pts (12♂; x̄ age= | 44.6 ± 10.9 yr)	2 yr	NA	Corpus callosum 8.3%; parietal 25%; frontal 50%; fronto-parietal 8.3%; parieto-occipital 8.3%. r- 25%; l- 66.7%; central 8.3%	NA
		Depression; anxiety; psychosis	CPRS	2				
	Mainio et al., [36]	Long (BL, 3 mo, 1 yr)	26 pts with glioma (15♂, 11♀) *vs.* 11 pts with	meningioma (3♂, 8♀)	Pre-op	NA	r- 61.5%; l- 38.5%	I–II 48.6%; III–IV 51.4%
Free-floating	anxiety; phobic anxiety; somatic anxiety;	depression; obsessions	CCEI	3				
	Litofsky et al,. [38]	Long (BL, 3, 6 mo)	598 pts (347♂, 251♀; x̄ age= 55 yr)	Pre-op	NA	NA	III-IV	
		Depression	Clinical	evaluation (DSM-IV); SF-36;	1			
	Mainio et al., 2005	CS	31 pts with glioma (18♂, 13♀) *vs.* 44 pts with benign tumors (11♂, 33♀)	Pre-op	NA	NA	I–II 51.6%; III–IV 48.4%	
		Depression	BDI-II; CCEI	3				
	Brown et	CS	194 pts	56.2 ± 20.2 yr)	Newly diagnosed		Glioblastoma	

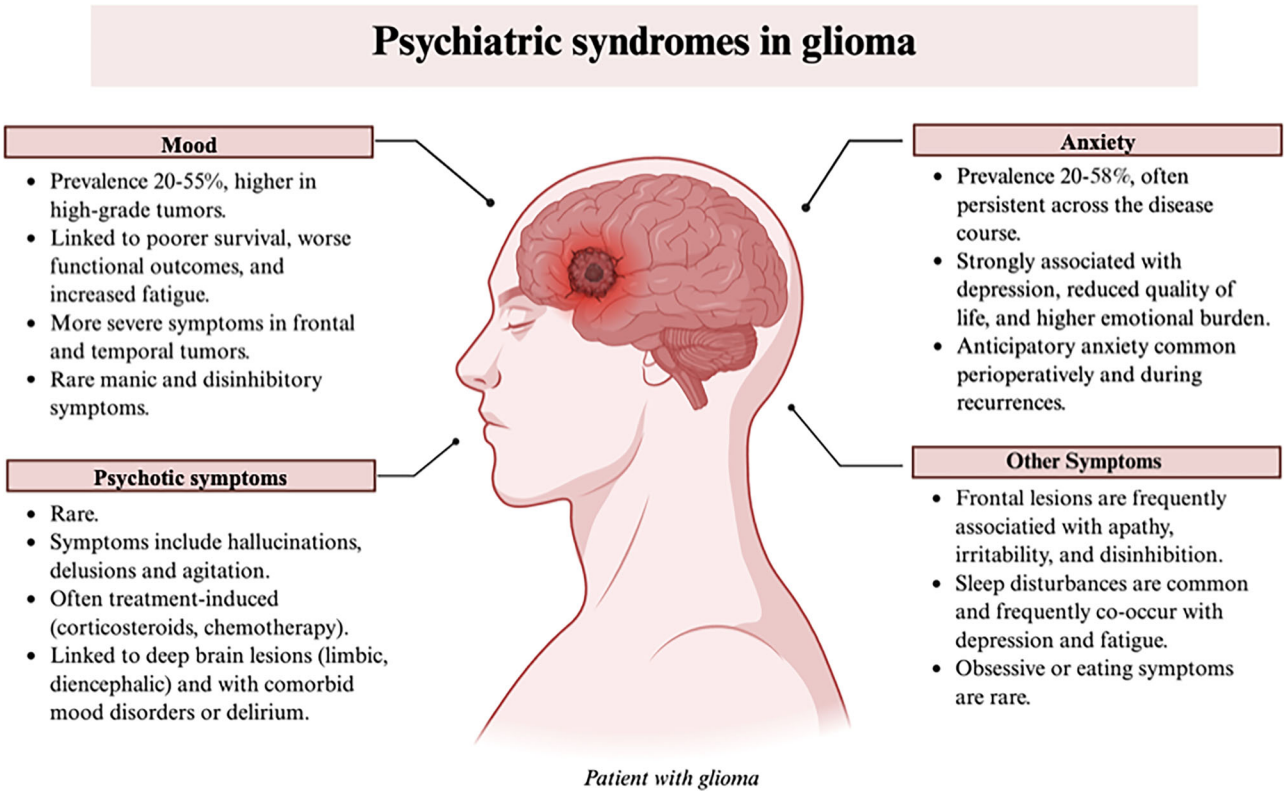


Fig. 2 Psychiatric symptoms in glioma. Schematic representation of the principal psychiatric domains affected in patients with glioma, including mood and anxiety disorders, psychotic manifestations, and other neuropsychiatric symptoms such as apathy, irritability, disinhibition, and sleep disturbances. Created in BioRender. Bardi, F. (2026) https://BioRender.com/cc48aeq.

diagnostic framework, assessment modality, and evidence tier. Patterns and recurring themes across studies were identified, reviewed, and refined through iterative comparison.

To enhance analytic rigor, two researchers jointly conducted the synthesis, allowing for triangulation of perspectives. Disagreements were resolved through discussion and, when necessary, consultation with a third senior physician-researcher with expertise in psychiatric manifestations of brain tumours. Preliminary findings were discussed within the full author team, and feedback was incorporated to refine the final synthesis.

Results

The systematic search yielded a total of 4,327 records, comprising 2,944 from PubMed, 851 from CINAHL, and 532 from PsycInfo. After removing 259 duplicates, 4,068 records were included in a two-stage screening process, consisting of title and abstract screening followed by full-text assessment for eligibility. Application of the exclusion criteria led to the exclusion of 3,938 records, resulting in 130 studies meeting the inclusion criteria. The PRISMA flow diagram is presented in Fig. 1. The PRISMA checklist and detailed results of the database searches with overall judgments for each rated study are provided in Supplementary Material (Table S1-S4). Included studies were retained for qualitative synthesis (Table 2 and Table 3). The full list of references for all included studies is available in the Supplementary Material (References S1). Included studies were published between 1958 and 2025. Among the 130 included studies, 60 (46.15%) were cross-sectional and 70 (53.85%) were longitudinal. All studies adopted quantitative methodologies and involved adult patient populations, with sample sizes ranging from 5 to 20,432 participants.

The results are organized into distinct thematic sections reflecting each of the major psychiatric domains identified across the included studies. Each section explores findings in relation to both tumor severity and related features, such as glioma grade and anatomical location, as well as disease phase, including time since diagnosis and treatment stage. A graphical overview of the main psychiatric domains observed in patients with glioma is provided in Fig. 2.

Mood

Mood-related symptoms were the most extensively explored psychiatric domain across the included studies. Depressive symptoms were investigated in 113 studies [26–31], whereas manic symptoms were addressed in 3 studies [32, 98]. Depression was by far the most frequently assessed condition, with reported prevalence rates ranging from 20% [33] to 55% [34] across studies. Depressive symptoms were evaluated using clinical interviews based on DSM or ICD criteria (n = 13) [27, 35], clinician-administered tools including the Hamilton Depression Rating Scale (HAM-D) (n = 7) [98], validated self-report questionnaires including the Beck Depression Inventory-II (BDI-II), Profile of Mood States (POMS), Center for Epidemiologic Studies Depression Scale (CES-D), Patient Health Questionnaire-9 (PHQ-9), and Hospital Anxiety and Depression Scale (HADS) (n = 89) [26, 28–31, 34], and single-item or indirect measures, such as the EuroQol 5-Dimension questionnaire (EQ-5D) (n = 4) [36].

Depressive symptoms were frequently found both pre-operatively [30, 31] and during the post-operative or treatment phases [37, 38], including chemotherapy [39], radiotherapy [40], and corticosteroid administration [41].

While several longitudinal studies revealed a worsening course of symptoms over time [28], especially when psychiatric support was lacking [36, 38], others found a persistence of symptoms but not a changing prevalence longitudinally [42, 43]. However, disease recurrence was frequently associated with a resurgence or worsening of depressive symptoms, which manifest with greater intensity than that of initial diagnosis [29, 37].

Depressive symptoms were significantly more prevalent in patients with high-grade gliomas than in those with lower-grade tumors [28, 29], and were consistently associated with poorer survival outcomes across glioma grades. Patients with clinically significant depressive symptoms showed markedly reduced postoperative survival compared with their non-depressed counterparts at 12 months (15% vs 41%) [44] and 20 months (0% vs 21%) [45]. In addition, the severity of depressive symptoms is significantly correlated with reduced functional status and increased overall glioma symptom burden [30, 40].

A small subset of the literature highlights a neuroanatomical gradient. Diffuse gliomas and tumors affecting the left hemisphere and frontal lobe correlate with more severe depressive symptoms [12, 30], whereas right-hemisphere lesions are associated with symptoms like euphoria or mania [35, 46]. Nevertheless, other studies have failed to identify consistent correlations between tumor location or lateralization and specific psychiatric outcomes [26]. Biological biomarkers associated with depressive symptoms in patients with glioma have also been investigated. Changes in the levels of interleukins (such as IL-6, IL-8, IL-17, and TNF-α) and insulin-like growth factors (such as IGF-1 and IGFBP-3) have been linked to the severity of symptoms, supporting the idea that inflammation and neuroendocrine factors play a role in mood dysregulation in gliomas [31, 47].

Collectively, the aforementioned evidences highlight that depressive symptoms can influence disease course and quality of life, and may vary according to disease stage. Nevertheless, several studies have identified a discrepancy between clinician-assessed and self-reported depressive symptoms, with clinicians identifying substantially fewer cases than those captured by patient-reported measures [38, 41, 48].

Alongside depressive symptomatology, 3 cross-sectional studies and 2 longitudinal studies described a broader spectrum of mood-related symptoms [32, 46, 48, 49, 98]. Non-depressive affective manifestations were mainly assessed using tools to capture frontal lobe-related behavioral syndromes, such as the Neuropsychiatric Inventory (NPI-12) [98] and the Frontal Systems Behavioral Scale (FrSBe) [32]. Early case series highlighted the presence of euphoria, racing thoughts, psychomotor agitation, and exaltation [32, 46, 49]. More recent studies reported neurobehavioral symptoms including irritability, agitation, and disinhibition, with prevalence estimates ranging from approximately 3% [48] to 20% or higher [32, 98], particularly in patients with tumors involving the frontal lobes or midline structures.

Anxiety

Anxiety symptoms were investigated in 72 studies, being the second most frequently investigated psychiatric domain in patients with glioma. Reported prevalence rates ranged across studies from approximately 20% [39] to 58% [50]. Anxiety symptoms were assessed through clinical interviews based on DSM or ICD criteria (n = 7) [35, 50], standardized clinician-administered instruments, such as the Hamilton Anxiety Rating Scale (HAM-A) (n = 5) [98], validated self-report measures, including the Hospital Anxiety and Depression Scale (HADS), State-Trait Anxiety Inventory (STAI), Crown-Crisp Experiential Index (CCEI), Generalized Anxiety Disorder-7 (GAD-7), and Beck Anxiety Inventory (BAI) (n = 58) [39, 40, 43, 44, 50, 51], and single-item or indirect measures (n = 2) [41].

Anxiety symptoms frequently manifest at cancer diagnosis, typically associated with the burden of receiving a life-threatening prognosis [44]. Longitudinal studies demonstrated that clinically significant anxiety symptoms tend to persist throughout the disease trajectory, with stable symptom levels observed for months or even years following surgery or radiotherapy [40, 43, 52]. Most longitudinal studies conducted over extended follow-up periods did not report significant changes in anxiety symptom severity between baseline and distal time points [17,51,52]. Furthermore, anxiety symptoms were found to co-occur with depressive symptoms. Owing to more nuanced and overlapping clinical presentations, this comorbidity complicated timely diagnosis and the appropriate management of both conditions [53, 54].

The prognostic relevance of anxiety in glioma is unclear. While some studies found a negative correlation between anxiety symptoms and overall survival [29, 52], others found no significant prognostic effect [55, 56]. Nonetheless, anxiety symptoms were consistently linked to reduced quality of life, heightened cognitive complaints, and increased emotional burden [57].

Anxiety symptoms were significantly influenced by disease course-related factors, including treatment anticipation and the emotional burden of disease recurrence [44, 55]. Anticipatory symptoms were commonly observed during the perioperative and radiotherapy phases [50], and patients with tumor recurrence showed higher anxiety symptoms compared to those who were newly diagnosed [29].

The potential influence of tumor localization on anxiety symptoms remains inconclusive. While some studies have reported a higher prevalence of pre-operative symptoms in patients with right-hemisphere tumors, suggesting a possible lateralization effect [35], other investigations have failed to confirm this association, finding no consistent correlation between tumor location and anxiety symptoms [26].

Psychotic symptoms

Psychotic symptoms were reported in 4 studies across the included literature and were generally confined to isolated case series or observational cohorts. Specifically, 3 cross-sectional studies and one longitudinal study described evident psychotic symptoms, including hallucinations and delusions [46, 48, 58, 98].

Psychotic symptoms were identified trough clinical evaluation based on ICD-10 criteria (n = 1) or standardized clinician-rated instruments, including the Comprehensive Psychopathological Rating Scale (CPRS) and the NPI-12 (n = 2) [58, 98].

Evidence indicates that psychotic symptoms appear more frequently in the early post-operative phase and may be influenced by tumor progression or pharmacological factors, particularly corticosteroids, antiseizure drugs, and chemotherapy [46, 48, 58]. Psychotic symptoms, such as delusions and hallucinations, frequently co-occurred with mood disturbances, behavioral changes, disinhibition, and delirium, making it difficult to distinguish their independent clinical trajectory [48, 58]. No studies explicitly examined associations between psychotic symptoms and tumor grade or survival outcomes. However, available evidence suggests that these symptoms are more likely to occur in patients with more advanced or medically complex disease states [48].

In one single study psychotic symptoms exhibited specific neuroanatomical associations. Lesions involving deep limbic, hypothalamic, and diencephalic structures were strongly linked to emotional and behavioral disturbances [46].

Due to their low prevalence and inconsistent characterization, psychotic symptoms in patients with glioma remain poorly defined. Most studies lacked dedicated assessment tools or structured diagnostic frameworks capable of distinguishing organic psychosis, delirium, and frontal lobe behavioral syndromes.

Personality changes

Four studies have examined personality traits and their association with glioma diagnosis and treatment, employing validated self-report instruments such as the Ten Item Personality Inventory (TIPI), Eysenck Personality Questionnaire (EPQ-R), Minnesota Multiphasic Personality Inventory (MMPI), or the Schizotypal Personality Questionnaire (SPQ) (n = 4) [59, 60]. While some studies have noted stable personality traits over time, others identified emotional blunting and irritability, especially in patients with frontal or multifocal lesions [32]. One single study reported increased cognitive-perceptual schizotypal traits in association with left inferior frontal gyrus damage and disconnection of the left uncinate fasciculus [59]. Additionally, elevations in MMPI scales indicative of hypochondriasis, psychasthenia, and schizophrenia-related traits were found to be associated with increased anxiety and depression in the pre-operative phase, indicating a link between trait vulnerability and affective symptoms [60].

Obsessive symptoms

Obsessive symptoms were described in one single study, which investigated their relationship with pre-operative anxiety and depression using the Crown-Crisp Experiential Index (CEI) [35]. The obsessive symptoms, including intrusive thoughts and compulsive checking behaviors, were found to decrease following surgical resection, although no other standardized instruments specifically designed for obsessive-compulsive symptomatology were employed [35].

Eating disturbances

Eating-related symptoms were explored in 2 of the included studies. One study assessed these features using the NPI-12, a standardized informant-rated instrument [98], whereas the other did not specify the assessment method [49]. Changes in appetite, bulimia-like behaviors, or weight fluctuations were associated with hypothalamic dysfunction or comorbid mood disturbances [49, 98]. However, no study systematically assessed eating disorders using DSM-based diagnostic criteria or validated psychometric tools.

Sleep comorbidities

Sleep comorbidities were assessed in 8 studies across the included literature. One study used a standardized informant-rated instrument, namely the NPI-12 (n = 1), whereas the others relied on validated self-report measures, including the Pittsburgh Sleep Quality Index (PSQI), Insomnia Severity Index (ISI), General Sleep Disturbance measures from the Patient-Reported Outcomes Measurement Information System (PROMIS), and the sleep-related component of the General Health Questionnaire-28 (GHQ-28) (n = 7) [32, 57, 61].

Sleep disturbances were often found to co-occur with depression and fatigue [57, 61]. Additionally, patients frequently reported insomnia, fragmented sleep, and diminished sleep efficiency, particularly during post-operative or treatment phases [57, 61].

Post-traumatic stress symptoms

Post-traumatic stress symptoms were examined in 3 studies, including 1 cross-sectional study and 2 longitudinal studies. All studies used structured clinical assessments to evaluate post-traumatic stress disorder (PTSD)-related outcomes (n = 3) [62]. Clinically relevant post-traumatic stress symptoms were reported in approximately half of

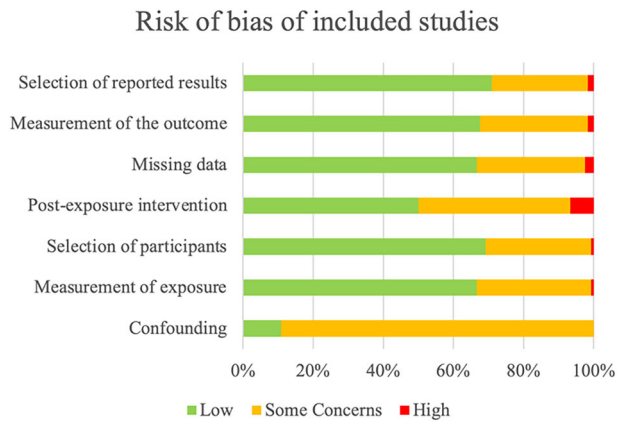


Fig. 3 Summary of risk of bias judgments across included studies [24].

patients following glioma surgery. In addition, frontal lobe involvement was identified as a significant predictor of post-traumatic stress symptomatology, with 16% of patients fulfilling diagnostic criteria for PTSD at 3 months after surgery [62, 63].

Risk of bias

A summary of the risk of bias assessment is presented in Fig. 3, while the evaluations of each included study are reported in the Supplementary Material (Table S5). Overall, the risk of bias across the included studies was considered acceptable for qualitative synthesis, with all domains showing a predominance of studies at low risk of bias.

Discussion

The aim of the present systematic review was to synthesize the available evidence on the broad spectrum of psychiatric symptomatology in adult patients with gliomas. Across the 130 included studies, psychiatric symptomatology results to be a prominent, functionally relevant component of the glioma clinical phenotype. Prevalence estimates consistently indicate depressive symptoms and anxiety symptoms affect approximately 20-55% of adult patients with glioma. These rates appear higher than those reported in the broader oncology population, where depressive symptoms are estimated at 33% and anxiety symptoms at 31% [62], and substantially exceed those observed in the adult general population, where prevalence is estimated at 5.7% for depression [64] and 4.4% for anxiety [65].

Beyond their high prevalence, depressive and anxiety symptoms show distinct prognostic trajectories in glioma: depressive symptoms correlate with reduced survival, whereas anxiety symptoms mainly impair quality of life. Both appear to result from interacting biological, therapeutic, and existential stressors. The diagnosis of glioma represents a sudden and profound disruption, often occurring within a matter of days or weeks, that rapidly overwhelms coping resources and exceeds adaptive capacity [66, 67]. The confrontation with an incurable and unpredictable disease, together with limited survival expectancy, fear of neurological decline, and perceived stigma, evokes existential distress and perceived loss of control, fostering depressive and anxious symptoms [56]. Hopelessness and demotivation can reduce treatment adherence and indirectly impact survival. Conversely, anxiety symptoms mainly compromise quality of life, with persistent worry about recurrence sustaining hypervigilance and anticipatory arousal that interferes with recovery and cognitive functioning [68, 69].

Findings from the selected articles suggest that psychiatric symptoms fluctuate along the oncological trajectory, peaking at predictable points of vulnerability. Anxiety and depressive symptoms evolve dynamically, intensifying in response to key transitions within the disease course. In contrast, psychotic symptoms, obsessive symptoms, and

comorbid sleep disturbances appear more episodic and lack a consistent temporal pattern [70, 71]. Anxiety symptomatology was most prevalent during early, stimulus-rich phases, such as diagnosis, treatment initiation, and prognostic communication, whereas depressive symptoms predominated in later phases marked by disease progression, neurological decline, and functional impairment. These phases can be conceptualized as active versus progressive periods of illness, with anxiety symptoms clustering around active, anticipatory stages, and depressive symptoms emerging during more functionally impaired or pharmacologically burdened phases [67]. This divergence aligns with neurocircuitry models proposing that anxiety is mediated by hyperactivation of the amygdala and salience networks in response to uncertainty and threat anticipation, whereas depression involves dysregulation within mesolimbic-prefrontal reward circuitry, including reduced ventral striatal dopaminergic signaling, medial prefrontal cortex hypoactivity, and altered functional connectivity between the anterior cingulate and hippocampus, resulting from chronic stress exposure, excitotoxic injury, and neuroinflammatory processes [72, 73]. These circuit-level alterations are increasingly understood as downstream effects of tumor-induced immune and endocrine dysregulation. Inflammatory cytokines (e.g., IL-6, IL-8, IL-17, TNF-α) and disrupted IGF signaling interfere with neural circuits involved in mood regulation [74, 75]. Through activation of indoleamine-2,3-dioxygenase, inflammation shifts tryptophan metabolism toward the kynurenine pathway, reducing serotonin availability and producing neurotoxic metabolites [76, 77]. It also impairs dopaminergic signaling and promotes glucocorticoid resistance, leading to HPA axis overactivation and hippocampal dysfunction [78]. Reduced IGF-1 levels further compromise neurogenesis and synaptic plasticity [79]. These changes, alongside chronic inflammation and impaired immune surveillance, may amplify neuropsychiatric vulnerability and contribute to recurrence in more aggressive gliomas [80, 81]. Together, they support inflammation-based models of mood disorders and help explain the affective burden observed in glioma patients [82].

Among episodic symptoms, obsessive symptoms appeared to attenuate post-surgery. This may reflect a reduction in acute preoperative anxiety, given the well-established relationship between anxiety and obsessive-compulsive phenomena [83]. From a neurobiological standpoint, this improvement may also result from partial restoration of fronto-striato-thalamo-cortical network integrity following surgical decompression or disconnection of hyperactive associative loops [84, 85]. Psychotic symptoms were primarily associated with postoperative periods and corticosteroid or chemotherapy exposure. While corticosteroid- and chemotherapy-induced psychosis likely reflects direct iatrogenic neurotoxicity [86], postoperative psychosis may represent a form of neuroinflammatory delirium triggered by surgical stress and cortical injury. Glioma patients are particularly susceptible, with postoperative delirium reported in over 30% of cases [87], and preoperative anxiety and depression identified as independent risk factors [88]. Sleep disturbances were most prevalent in the postoperative and active treatment phases, likely driven by hospitalization-related stress, neuroinflammatory responses, corticosteroid-induced insomnia [89, 90], and the bidirectional relationship between affective dysregulation and sleep disruption [91].

Although neuroanatomical correlates remain inconclusive, some recurring patterns can be cautiously inferred. Severe depressive symptoms have been associated to left hemisphere lesions, while anxiety and manic symptoms to right-hemispheric involvement. These findings align with models of emotional valence and hemispheric specialization, which propose that right prefrontal regions exert inhibitory control over limbic arousal, whose disruption may facilitate anxiety, irritability, or mania, whereas left-sided lesions may impair approach-related affective processing, contributing to depressive symptoms [92, 93]. Psychotic symptoms have been most commonly linked to deep-seated lesions involving the thalamus and hypothalamus, central structures for salience attribution, emotional integration, and sensory gating. Thalamic dysfunction may disrupt cortico-striato-thalamo-cortical loops that filter and prioritize incoming stimuli, leading to aberrant salience processing and misattribution of significance to neutral percepts, a mechanism implicated in psychosis [94]. Likewise, hypothalamic involvement may alter dopaminergic and neuroendocrine regulation, contributing to affective and perceptual instability [95]. Lesions in fronto-limbic and fronto-striatal networks, including the prefrontal cortex, anterior cingulate, and uncinate fasciculus, may further predispose to schizotypal or manic-like syndromes. These disconnection phenomena impair top-down modulation of limbic and mesolimbic pathways, leading to dysregulated dopaminergic signaling, emotional lability, and impulsivity [96]. Despite these insights, neuroanatomical localization of glioma-related psychiatric symptoms remains an emerging

area, and the observed associations should be interpreted with caution given the heterogeneity of tumor sites and confounders.

Ultimately, depressive symptoms correlated with higher tumor grade, which nonetheless predicted poorer prognosis. Psychotic symptoms were largely confined to medically complex and heavily treated patients. As a result, the psychiatric burden appears to stem from the cumulative impact of tumor aggressiveness, therapeutic stress, and functional decline rather than isolated neurobiological causes [97]. Patients with high-grade gliomas typically experience a rapid clinical trajectory, repeated hospitalizations, and heavier corticosteroid and chemoradiotherapy regimens, all of which can erode psychological resilience and amplify perceptions of hopelessness and loss of autonomy [17, 18]. These insights underscore the importance of integrating psychosocial and palliative dimensions into neuro-oncological care, recognizing psychiatric symptoms as integral to the overall disease burden of glioma.

Limitations

Several limitations must be acknowledged. As a systematic review, our findings are inherently dependent on the quality and heterogeneity of the included studies, which varied substantially in study design, assessment instruments, outcome definitions, and timing of psychiatric evaluations. This heterogeneity limited direct comparability across studies and, for several outcomes, precluded quantitative synthesis, thereby constraining the generalizability of prevalence estimates and symptom trajectories. By design, case reports and small case series were excluded, which may have resulted in an underrepresentation of rare or atypical psychiatric manifestations. Among these, suicidal ideation was not addressed due to its inconsistent assessment and reporting across the included studies. Given its recognized clinical importance in the existing literature in this population, future research should more systematically investigate suicidality in this population. Data on specific glioma subtypes, molecular profiles, and treatment modalities were inconsistently reported, precluding fine-grained analyses of subtype-specific psychiatric risk. Neuroanatomical correlates should be interpreted cautiously, given the limited and heterogeneous evidence currently available. Lastly, although the overall methodological quality was considered acceptable, a small proportion of studies were rated as having a higher risk of bias across specific methodological domains.

Conclusions

This systematic review highlights that psychiatric symptoms in glioma patients are not secondary complications, but rather integral features of the disease trajectory, arising from the interaction between active treatments, tumor biology, neuroanatomical location, and systemic inflammation. Depressive and anxiety symptoms, the most frequent manifestations, follow a dynamic and phase-dependent course that reflects glioma progression. Psychiatric screening should therefore be incorporated at clinically high-risk stages of the neuro-oncological trajectory, including diagnosis, perioperative period, active oncological treatment, disease progression, and recurrence. Brief validated rating scales assessing multiple psychiatric symptoms, such as the NPI-12, can be used outside psychiatric settings [98] and may provide a feasible first-line screening approach in routine clinical care. Positive screening results should prompt specialist assessment, including a comprehensive clinical evaluation, supported by structured or semi-structured diagnostic interviews, such as the SCID. Clinician-administered symptom-specific scales may further support severity assessment and longitudinal monitoring.

Management should be adapted to symptom profile, clinical urgency, and disease phase. Antidepressants may be considered for the long-term management of depressive and anxiety symptoms, as well as obsessive-compulsive or trauma-related symptoms [99]. However, during acutely stressful phases, such as immediately after diagnosis or prognostic communication, their delayed onset of action may be insufficient for rapid symptom relief. In these settings, benzodiazepines or non-benzodiazepine anxiolytics may be added [100], while anticonvulsants or low-dose antipsychotics may represent alternatives when benzodiazepines are contraindicated, ineffective, or poorly tolerated [101, 102]. Nevertheless, these strategies have not been systematically evaluated in cancer populations, and further

treatment studies are needed. Non-pharmacological interventions should likewise be tailored. Supportive, psychoeducational, and symptom-focused approaches may be most appropriate for acute anxiety following diagnosis or recurrence [100], whereas longer-term depressive, anxiety-related, and post-traumatic symptoms may benefit from more structured interventions incorporating psychoeducation, cognitive-behavioral strategies, cognitive rehabilitation, existential support, and family involvement [103–105].

Future research should integrate detailed psychiatric phenotyping with tumor-related variables, including histology, grade, molecular profile, anatomical location, and biological biomarkers. Translational models are needed to clarify how tumor-related factors contribute to behavioral symptoms and to inform treatments aimed at reducing psychiatric burden. Such an integrated neuro-oncological approach may not only improve quality of life but may also positively influence clinical and oncological outcomes in patients with glioma.

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Authors and Affiliations

Francesca Bardi[1] · Leonardo Monacelli[1] · Romina Caso[1] · Gianmarco Stella[1] · Georgios D. Kotzalidis[2] · Silvia Montanari[1,2] · Delfina Janiri[1,2] · Florien W. Boele[3,4,5] · Gabriele Sani[1,2] · Alessio Simonetti[2,6]

1 Section of Psychiatry, Department of Neuroscience, Università Cattolica del Sacro Cuore, Rome, Italy

2 Section of Psychiatry, Department of Neuroscience, Head-Neck and Chest, Fondazione Policlinico Universitario Agostino Gemelli IRCCS, Rome, Italy

3 Patient-Centred Outcomes Research, Leeds Institute of Medical Research, Faculty of Medicine and Health, University of Leeds, Leeds, UK

4 Academic Unit of Health Economics, Leeds Institute of Health Sciences, Faculty of Medicine and Health, University of Leeds, Leeds, UK

5 Stichting Epilepsie Instellingen Nederland (SEIN), Heemstede, the Netherlands

6 Menninger Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, Houston, TX, USA

These authors contributed equally: Gabriele Sani, Alessio Simonetti.