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REVIEW

Prevalence, risk factors, and impacts of sleep disturbances in patients with primary brain tumors: a systematic review

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Abstract

Sleep disturbances are common in patients with primary brain tumors (PBT), significantly affecting their health-related quality of life (QoL), emotional well-being, cognitive function, and clinical outcomes. These disturbances not only impact the patients themselves but also place a burden on their families and caregivers. Despite growing recognition of these problems, a comprehensive understanding of their prevalence, severity, and risk factors remains limited. This systematic review aimed to update the evidence on sleep disturbances in PBT patients, focusing on prevalence, risk factors, and management strategies. Following PRISMA 2020 guidelines, we searched PubMed, EMBASE, Scopus, PsycINFO, and CINAHL for studies published from September 2015 to June 2024. Eligible studies assessed sleep disturbances in adult PBT patients using validated methods. Studies with mixed-cancer samples, pediatric patients, or lacking validated sleep assessments were excluded. A total of 11 studies were included, revealing high rates of sleep disturbances, ranging from 9.2% to over 60%, varying by tumor type and treatment stage. Key risk factors included older age, female gender, certain tumor types (e.g., pituitary), perioperative sleep quality, and psychological distress. Sleep disturbances were linked to worse clinical outcomes, including higher mortality and burden. Addressing sleep disturbances through routine assessment and targeted interventions is essential for improving outcomes in this population.

Keywords Sleep · Brain · Tumor

Introduction

The connection between disrupted sleep and cancer has gained increasing recognition due to its significant impact on patients'well-being and potential effects on treatment outcomes and survival rates [1, 2]. Individuals with both malignant and benign primary brain tumors often experience sleep-related issues across various phases of their treatment, including post-surgery, during chemotherapy and radiation therapy, and even during follow-up care [3, 4]. Sleep disturbances encompass interruptions in sleep quality, quantity, movement, or breathing patterns, which may lead to discomfort and reduced daytime functionality [5, 6].

These sleep disruptions may occur independently or in conjunction with other cancer-related symptoms, such as fatigue, anxiety, depression, and pain [7–9]. Studies suggest that anywhere from 30 to 85% of cancer patients suffer from sleep issues, which can persist throughout the course of the disease and negatively impact quality of life, mood, and cognitive abilities [10, 11]. Understanding the changes in sleep patterns in patients with primary brain tumors at different treatment stages can help healthcare providers develop targeted interventions to address these challenges.

In patients with primary nonmalignant brain tumors, however, sleep disturbances often receive less attention compared to other cancer types, despite their widespread occurrence [12].

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Numerous studies have focused on sleep difficulties such as poor sleep quality and daytime insomnia in patients with pituitary tumors, craniopharyngiomas, and pituitary adenomas [13–19].

Various studies documenting the high prevalence of insomnia, poor sleep quality, and circadian rhythm disruption. Routine screening for sleep disturbances in PBT patients is not commonly conducted, and no standardized tool with established reliability and validity for cancer patients is widely used. The Pan-Canadian practice guideline recommends inquiring about sleep issues and their impact on daily functioning. Several brain tumor-specific questionnaires, such as FACT-BR, EORTC QLQ-C30, BN20, and MDASI-BT, include sleep-related items, offering insight into co-occurring symptoms.

In clinical practice, if sleep disturbances are reported, further evaluation may be necessary, with referral to a sleep specialist for unresolved cases. Polysomnography (PSG) remains the gold standard for diagnosing sleep disorders like sleep apnea and restless legs syndrome [20]. Research settings often employ tools such as the Epworth Sleepiness Scale (ESS) for hypersomnia and the Pittsburgh Sleep Quality Index (PSQI) or Insomnia Severity Scale for insomnia, though these were not originally designed for brain tumor patients. Additionally, the STOP-BANG questionnaire is used for suspected sleep apnea, and PROMIS for Sleep Disturbance has recently gained traction in cancer research. Objective measures like actigraphy and PSG can complement subjective assessments, though feasibility concerns, including cost and patient adherence, may limit their use in clinical studies.

Considering the significant prevalence of sleep disturbances among survivors of primary brain tumors and the substantial impact on their health-related quality of life (QoL) [21, 22], there remains a considerable gap in our understanding of the patterns, severity, and risk factors associated with sleep problems in both patients and their caregivers. This review aims to update current evidence regarding the prevalence and risk factors of sleep disturbances in patients with primary brain tumors.

Materials and methods

We carried out a systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines, and it was registered in the PROSPERO international database (CRD42024543578). Our search approach involved thorough database searches along with manual reviews of reference lists to ensure all relevant studies were included.

Search strategy and study selection

We conducted a comprehensive search across multiple electronic databases, including PubMed, EMBASE, Scopus, PsychINFO, and CINAHL. We conducted our search using a combination of keywords such as primary brain tumor, brain tumor, sleep disturbance, insomnia, sleep disorders, sleep quality, neuro-oncology, prevalence, risk factors, patient preferences, and quality of life. Additionally, we incorporated relevant Medical Subject Headings (MeSH) related to sleep disorders and primary brain tumors, adapting the strategy for each database to maximize comprehensive and relevant literature retrieval. We applied filters to limit studies to English-language publications focused on adult populations, covering the period from September 2015 to June 2024, specifically targeting PBT patients to provide updated insights. Manual searches of reference lists in eligible studies were also conducted to identify any overlooked publications, applying the same inclusion criteria as the electronic searches. To optimize accuracy across databases, we used the Polyglot Search Translator from the Bond University Systematic Review (SR) Accelerator to streamline the search strategy for each database.

Inclusion and exclusion criteria

We included studies examining sleep disturbances or interventions for sleep issues in adults (18+ years) diagnosed with PBT during or after treatment, as well as their caregivers. Eligible studies employed validated methods such as self-report sleep assessments, sleep recording devices, or diaries covering at least seven sleep-wake cycles, and QoL assessments, or symptom measures including sleep-related items.

Strict exclusion criteria were applied to ensure quality and relevance. Excluded were abstract-only publications, studies without validated sleep assessments, mixed-cancer samples, research that focused exclusively on symptoms such as fatigue, and those involving pediatric PBT survivors. Duplicate studies were also excluded to maintain dataset integrity.

Our initial database search identified 2,330 records. After removing 489 duplicates and 69 review articles, we screened 1,841 titles and abstracts, excluding 1,658 irrelevant records. Full-text screening further excluded studies for reasons such as abstract-only availability (23), lack of validated sleep assessments (15), mixed-cancer samples (16), pediatric populations (48), and duplicates (4). Ultimately, 8 studies were selected, with an additional 3 found through manual reference checks, yielding a total of 11 studies (Figure 1).

Data extraction

Data extraction targeted key study characteristics such as design, sample size, demographics, objectives, sleep assessment methods, and main findings. This approach facilitated a thorough understanding of sleep disturbances among PBT

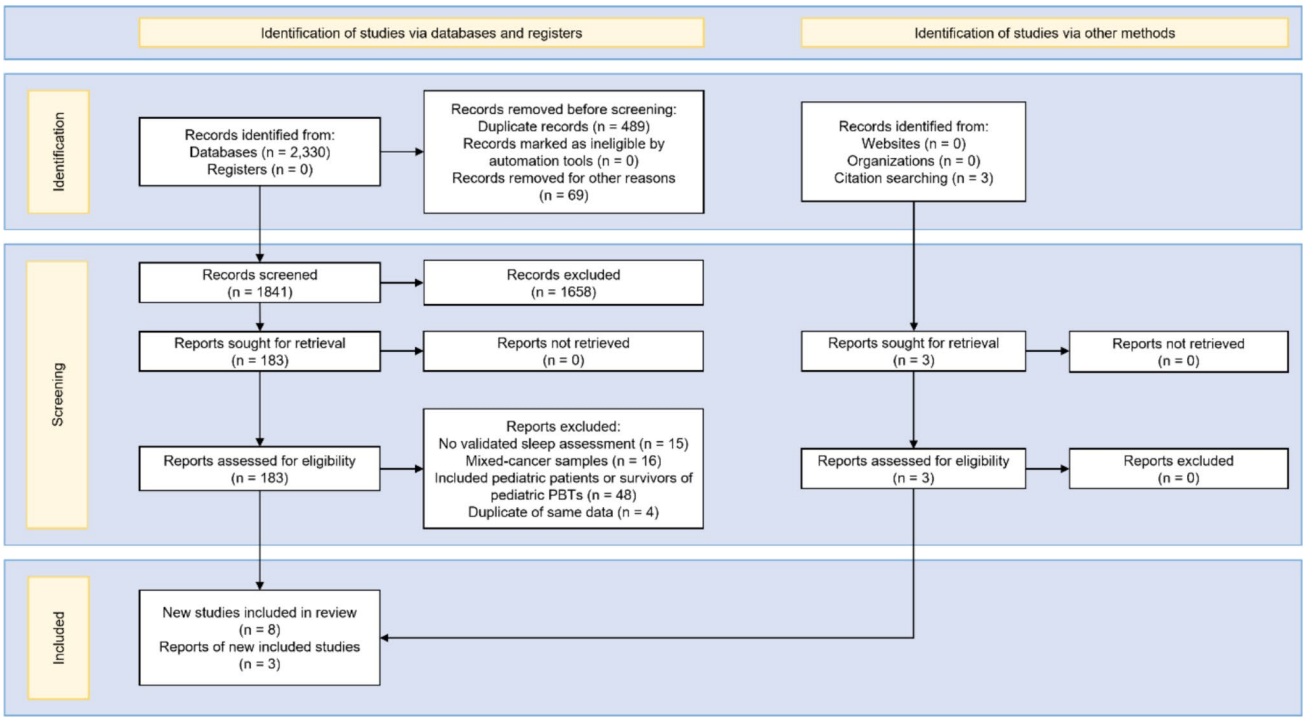

Fig. 1 Flow Diagram of Study Selection. This figure illustrates the flow diagram of the study selection process for this systematic review, adhering to the PRISMA guidelines. The process is divided into three phases: Identification, Screening, and Inclusion. In the Identification phase, a total of 2,330 records were identified through electronic database searches, with no records identified from registers. Duplicate records (489) and other irrelevant records (69) were removed before screening, resulting in 1,841 records. Additionally, 3 records were identified through citation searching. During the Screening phase, 1,841 records were screened, and 1,658 were excluded based on titles and abstracts. Subsequently, 183 reports were sought for retrieval from database searches, and 3 additional reports from other methods. All 183 reports from databases and 3 reports from other methods were assessed for eligibility. Reports were excluded for various reasons, including abstract-only availability (23), lack of validated sleep assessments (15), mixed-cancer samples (16), inclusion of pediatric patients or survivors of pediatric PBTs (48), and duplicates of the same data (4). In the Inclusion phase, 8 studies from database searches and 3 from citation searching were included in the final review, making a total of 11 studies

patients and their caregivers, offering valuable insights into possible interventions and management strategies.

Results

The systematic review encompassed 11 studies with varying designs, including cohort studies, randomized controlled trials (RCTs), cross-sectional, and descriptive studies. Sample sizes ranged widely, from 22 to 4,851 participants. The demographic data revealed a broad age range, primarily focusing on adults, with most participants having mean ages between their late 40 s and early 60 s. Table 1 provides a summary of the key characteristics of the included studies.

The main objectives of these studies were to explore the prevalence, risk factors, and effects of sleep disturbances in patients with primary brain tumors. They aimed to examine the connection between sleep disturbances and clinical outcomes, identify factors influencing sleep quality, and determine effective strategies for managing sleep issues in this population.

The included studies utilized various research designs, including cross-sectional, cohort, randomized controlled trials (RCTs), and observational methodologies, to examine sleep disturbances in patients with primary brain tumors. Sample sizes varied significantly, ranging from 22 patients [23] to 4,851 patients [24], reflecting the diversity of study populations. Most studies focused on adults diagnosed with various types of primary brain tumors, including meningiomas, gliomas, pituitary tumors, and astrocytomas, while some specifically investigated postoperative or untreated brain tumors [25, 26]. The age of participants was generally in the middle to late adulthood range, with mean values spanning from 45.18 years [27] to 57 years [28]. The proportion of male participants also varied, with the lowest being 25% [27] and the highest at 62% [29]. Several studies included caregivers as part of their investigation [29], while others explored the impact of treatment modalities such as radiotherapy [30], craniotomy [24], and hypnotic

Table 1 Study Characteristics and Population Details

Author (Year)	Study design	Population	Main aim/Objective	Sample size (= *n*)	Male (%)	Age (Mean ± SD)
Mei-Ru Lin et al. (2021)	Cross-sectional	Adults with untreated pituitary tumor and meningioma	To explore the prevalence of sleep disturbances and their effects on quality of life in adults with pituitary tumor or meningioma	Total = 77	28.6%	49.16 ± 10.88
				Pituitary tumor = 33	45.5%	48.97 ± 11.68
				Meningioma = 44	15.9%	49.30 ± 10.37
Pei-Ching Lin et al. (2023)	Cross-sectional	Adults with untreated primary brain tumors	Investigate frequency of sleep disturbances and their effects on quality of life in adults with untreated primary brain tumors	Total = 103	42.7%	48.7 ± 11.7
				Benign = 68	29.4%	49.2 ± 11.1
				Malignant = 35	68.6%	47.8 ± 12.5
Amidi et al. (2023)	Cross-sectional	Patients with non-glioblastoma primary brain tumors who received radiotherapy	Investigate associations between radiation dose to sleep-related brain structures and sleep quality	Total = 78	60%	51.53 ± 15.68
				Glioma = 28	N/A	N/A
				Meningioma = 22	N/A	N/A
				Pituitary tumor = 16	N/A	N/A
				Other tumors = 12	N/A	N/A
Choi et al. (2023)	Nationwide cohort study	Patients who underwent craniotomy for brain tumor resection	Assess prevalence and factors of insomnia disorder post-craniotomy, and its impact on 2-year mortality	Total = 4851	53%	N/A
				Unspecified = 3430	N/A	N/A
				Cerebrum, except lobes and ventricles = 387	N/A	N/A
				Frontal lobe = 421	N/A	N/A
				Temporal lobe = 178	N/A	N/A
				Parietal lobe = 96	N/A	N/A
				Cerebral ventricle = 29	N/A	N/A
				Cerebellum = 121	N/A	N/A
				Brain stem = 79	N/A	N/A
				Overlapping site of the brain = 110	N/A	N/A
Jeon et al. (2021)	Prospective Cross-sectional	Adults with primary or metastatic malignant brain tumors and their family caregivers	To determine the prevalence and predictors of sleep disturbance in brain tumor patients and their caregivers and examine the relationship between the patient-caregiver dyad's sleep	Total = 81	62%	51.1 ± 14.3
				Primary malignant = 74	N/A	N/A
				Metastatic = 7	N/A	N/A
				Caregivers = 44	25%	52.7 ± 13.3
Liu et al. (2023)	RCT	Patients with intracranial tumors undergoing elective craniotomy	Investigate associations between perioperative sleep patterns and clinical outcomes	Total = 110	43.6%	Median (IQR) 57 (50–63)
				Meningioma = 43	N/A	N/A
				Glioma = 42	N/A	N/A
				Acoustic Neuroma = 11	N/A	N/A
				Other = 14	N/A	N/A

Table 1 (continued)

Author (Year)	Study design	Population	Main aim/Objective	Sample size (= *n*)	Male (%)	Age (Mean ± SD)
Chang et al. (2019)	RCT	Patients with brain tumors after resection	Investigate the effect of hypnotics on sleep quality, cognitive function, and depression in brain tumor patients	Total = 22	32%	N/A
				Meningioma = 6	N/A	N/A
				Low grade glioma = 2	N/A	N/A
				Ependymoma = 1	N/A	N/A
				Glioblastoma = 5	N/A	N/A
				CNS lymphoma = 1	N/A	N/A
				Metastatic tumor = 4	N/A	N/A
				Craniopharyngioma = 1	N/A	N/A
				Choroid plexus papilloma = 1	N/A	N/A
				Neuroma = 1	N/A	N/A
Nyholm et al., 2023	Quantitative observational study	1. Severely brain-injured patients (NICU) 2. Brain tumor surgery patients (NIMCU)	Study sleep patterns in severe brain injury patients (NICU) and patients after brain tumor surgery (NIMCU); Identify risk factors for sleep disturbances after surgery	Total patients in NIMCU = 98	42%	53 ± 16
				Glioma grade IV = 49	N/A	N/A
				Glioma grade III = 19	N/A	N/A
				Glioma grade II = 23	N/A	N/A
				Glioma grade I = 1	N/A	N/A
				Other (metastasis, lymphoma, unclassified) = 6	N/A	N/A
Tankumpuan et al. (2015)	Cross-sectional	Postoperative brain tumor patients	To examine the relationships among recovery symptoms, mood state, and physical functioning in postoperative brain tumor patients	Total = 88	25%	45.18 ± 11.49
Willis et al. (2022)	Cross-sectional	Primary Brain Tumor (PBT) patients	To determine prevalence and risk factors of sleep disturbance in PBT patients and assess their treatment preferences	Total = 119	50.4%	52.60 ± 15.39
				Meningioma = 18	N/A	N/A
				Astrocytoma = 27	N/A	N/A
				Oligodendroglioma = 21	N/A	N/A
				Glioblastoma multiforme = 44	N/A	N/A
				Other = 9	N/A	N/A
Koçaşlı et al. (2023)	Cross-sectional	Patients undergoing brain tumor surgery	To examine the effect of postoperative pain on sleep quality in brain tumor patients	Total = 90	50%	47.36 ± 16.17

This table provides an overview of the study designs, sample sizes, demographic information, and tumor types of the included studies in the systematic review

NICU Neuro-Intensive Care Unit, *NIMCU* Neuro-Intermediate Care Unit, *RCT* Randomized Controlled Trial, *SD* Standard Deviation, *IQR* Interquartile Range, *N/A* Not Applicable

medications [23]. Table 1 provides a summary of the key characteristics of the included studies.

A variety of sleep assessment tools were employed across the studies to evaluate sleep disturbances in patients with primary brain tumors. Table 2 provides an overview of the sleep disturbance assessment tools used across the included studies, including indices measured and types of sleep disturbances reported.

- **Pittsburgh Sleep Quality Index (PSQI):** PSQI was widely used to assess overall sleep quality [12, 23, 25, 26, 28–30]. The PSQI is a self-report instrument designed to assess overall sleep quality over the past month. It includes 19 items across seven domains, with higher scores indicating worse sleep quality. It has been shown to have high reliability and validity in various clinical populations, including those with brain tumors [31].
- **Insomnia Severity Index (ISI):** The ISI was utilized to measure insomnia severity. The ISI is a brief self-report tool used to assess the severity of insomnia symptoms. It consists of seven items measuring aspects of sleep disturbances, such as difficulty falling asleep, staying asleep, and daytime functioning. It is widely used and validated in patients with insomnia [32].
- **Actigraphy:** Actigraphy is a method for monitoring activity using a wearable device called an actigraph, which resembles a wristwatch. It tracks movement to assess sleep patterns and detect disorders without directly measuring sleep. By identifying periods of movement and stillness, it helps healthcare providers identify conditions that may disrupt your sleep–wake cycle. Actigraphy is commonly used to evaluate circadian rhythm disruptions and sleep efficiency [25, 26].
- **Richards-Campbell Sleep Questionnaire (RCSQ):** The RCSQ assessed the impact of hospitalization on sleep quality [33]. The RCSQ is a simple 5-item visual analog scale used to assess subjective sleep quality in hospitalized patients. It evaluates sleep depth, latency, awakenings, return to sleep, and overall sleep quality on a 0–100 scale [34].
- **Modified MD Anderson Symptom Inventory for Brain Tumor (MDASI-BT):** The MDASI-BT included disturbed sleep as part of a broader symptom assessment [33]. The MDASI-BT is a patient-reported tool designed to measure symptom severity and interference in brain tumor patients. The MDASI-BT evaluates 13 core symptoms, one of which is disturbed sleep [35].
- **Athens Insomnia Scale (AIS):** The AIS is an 8-item scale designed to assess insomnia based on difficulty with sleep induction, maintenance, and early awakening. It evaluates both nighttime sleep problems and their impact on daytime functioning [36].
- **ICD- 10 Codes (G47.0, F51.0):** Finally, ICD- 10 codes were referenced to identify preoperative and postoperative insomnia disorder diagnoses [24]. The ICD- 10 coding system is widely used for classifying and diagnosing sleep disorders. G47.0 refers to primary insomnia, which is difficulty initiating or maintaining sleep not caused by another condition. F51.0 refers to insomnia that occurs as a symptom of mental health disorders like anxiety or depression [37].

Prevalence and measurement of sleep disturbances in pbt patients

Our review revealed consistently poor sleep quality across studies of primary brain tumor patients, with standardized assessments demonstrating significant sleep disruption in this population. Mean PSQI scores ranged from 11.0 ± 5.5 [26] to 11.53 ± 5.38 [25], substantially exceeding the clinical threshold of 5 that indicates poor sleep quality. Similarly, ISI scores varied from 8.81 ± 6.70 [12] to 12.1 ± 4.1 [23], reflecting moderate to severe insomnia symptoms in many patients.

Interestingly, patterns of sleep disturbance showed some variation across tumor types, though not consistently. Pei-Ching Lin et al. (2023) reported a 59.2% overall prevalence of insomnia, with slightly higher rates in patients with benign tumors (61.8%) compared to those with malignant tumors (54.3%). This counterintuitive finding—that patients with less aggressive pathology might experience more severe sleep disruption—warrants further investigation into potential contributing factors such as differences in treatment approaches, medication regimens, or psychological responses between these patient groups [26].

Postoperative insomnia emerged as a common complication, with Choi et al. (2023) reporting that 9.2% of previously non-insomniac patients developed new-onset insomnia following craniotomy. This finding highlights the direct impact of neurosurgical intervention on sleep regulation and suggests the need for proactive sleep assessment and management in the postoperative period [24].

Several studies employed objective measurement techniques to complement subjective assessments. Actigraphy data from multiple studies revealed circadian rhythm disruption in approximately 60% of patients, as indicated by I<O values ≤97.5%. Malignant tumor patients demonstrated lower sleep efficiency (91.2% ± 5.7%) compared to benign tumor patients (93.0% ± 3.3%), suggesting that tumor aggressiveness may influence sleep-wake cycle regulation despite the somewhat contradictory findings regarding subjective insomnia prevalence [25, 26].

Table 2 Sleep disturbance assessment and prevalence data

Author (Year)	Assessment tool used	Indices measured (Mean ± SD)		Type of sleep disturbance	Prevalence of sleep disturbances	
Mei-Ru Lin et al. (2021)	CAIS	Total	8.00 ± 4.48	Insomnia	Total	46.8%
		Pituitary tumor	7.97 ± 4.88		Pituitary tumor	45.5%
		Meningioma	8.02 ± 4.21		Meningioma	47.7%
	CPSQI	Total	11.53 ± 5.38	Poor Sleep Quality	Total	81.8%
		Pituitary tumor	11.52 ± 5.14		Pituitary tumor	87.9%
		Meningioma	11.55 ± 5.61		Meningioma	77.3%
	Actigraphy (Sleep Efficiency	Total	94.59 ± 4.09	Circadian Rhythm Disruption (I < O ≤ 97.5)	Total	59.3%
		Pituitary tumor	94.60 ± 3.96		Pituitary tumor	58.3%
		Meningioma	94.58 ± 4.24		Meningioma	60.0%
Pei-Ching Lin et al. (2023)	CAIS	Total	7.8 ± 4.7	Insomnia	Total	59.2%
		Benign	7.5 ± 4.1		Benign	61.8%
		Malignant	8.3 ± 5.7		Malignant	54.3%
	CPSQI	Total	11.0 ± 5.5	Poor Sleep Quality	Total	77.7%
		Benign	11.1 ± 5.3		Benign	80.9%
		Malignant	10.8 ± 6.1		Malignant	71.4%
	Actigraphy (Sleep Efficiency	Total	92.5%	Circadian Rhythm Disruption (I < O ≤ 97.5)	Total	61.1%
		Benign	93.0% ± 3.3%		Benign	57.7%
		Malignant	91.2% ± 5.7%		Malignant	70.0%
Amidi et al. (2023)	PSQI	Total	5.13 ± 3.13	Sleep Disturbance (PSQI > 5)	Total	37.2%
					Glioma	35.7%
					Meningioma	40.9%
					Pituitary tumor	50%
					Other tumors	16.7%
Choi et al. (2023)	ICD- 10 Codes (G47.0, F51.0)	N/A		Preoperative insomnia disorder	Total	18.8%
				Postoperative insomnia disorder	Total	9.2%
Jeon et al. (2021)	PSQI	Patients	9.51 ± 2.95	Sleep Disturbance (PSQI > 5)	Patients	53%
		Caregivers	10.46 ± 2.83		Caregivers	55%
	ISI	Patients	11.32 ± 4.77	Insomnia (ISI ≥ 15)	Patients	15%
		Caregivers	11.83 ± 4.65		Caregivers	13%
Liu et al. (2023)	PSQI	All patients on the day of admission	Median: 6 (IQR: 3–10)	N/A	N/A	
	PSG	All patients 3 days before and 3 days after surgery	N/A			
Chang et al. (2019)	PSQI	Insomnia group	10.4 ± 2.8	Insomnia (Total sleep time ≤ 360 min, latency > 30 min, or ≥ 4 awakenings per night)	Total	45% (10 out of 22 patients)
		Control group	3.3 ± 1.7			
	ISI	Insomnia group	12.1 ± 4.1			
		Control group	3.1 ± 2.2			
Nyholm et al., 2023	Continuous EEG monitoring	Sleep patterns identified (Stage N1, N2), presence of sleep spindles	N/A	No sleep recorded	Total	26%
				Had sleep patterns (N1 identified)	Total	74%
				Had sleep spindles (N2 sleep spindles)	Total	60%
Tankumpuan et al. (2015)	MDASI-BT	Disturbed Sleep	3.1 ± 3.0	N/A	N/A	
Willis et al. (2022)	PSQI	Total	7.19 ± 4.27	Poor Sleep Quality (PSQI > 5)	Total	61.5%
	ISI	Total	8.81 ± 6.70	Insomnia (ISI ≥ 15)	Total	21.5%

Table 2 (continued)

Author (Year)	Assessment tool used	Indices measured (Mean ± SD)		Type of sleep disturbance	Prevalence of sleep disturbances	
Koçaşlı et al. (2023)	RCSQ	First measurement	38.00 ± 31.23	Sleep affected by hospitalization	Total	90.0%
		Second measurement	59.42 ± 25.97			
		Third measurement	71.04 ± 23.61			

This table summarizes the sleep disturbance assessment tools used across studies, including indices measured and the prevalence of sleep disturbances in patients with primary brain tumors

CAIS Chinese Athens Insomnia Scale, *CPSQI* Chinese Pittsburgh Sleep Quality Index, *PSQI* Pittsburgh Sleep Quality Index, *ICD- 10* International Classification of Diseases, Tenth Revision, *ISI* Insomnia Severity Index, *EEG* Electroencephalography, *MDASI-BT* Modified MD Anderson Symptom Inventory for Brain Tumors, *RCSQ* Richards-Campbell Sleep Questionnaire, *N/A* Not Applicable

More sophisticated neurophysiological assessment through continuous EEG monitoring, as reported by Nyholm et al. (2023), provided deeper insights into postoperative sleep architecture. Their findings that 26% of brain tumor patients exhibited no identifiable sleep stages postoperatively, while 74% had discernible N1 sleep patterns and 60% demonstrated sleep spindles characteristic of N2 stage, reveal significant disruption of normal sleep architecture following neurosurgical intervention [25, 26]. These findings suggest significant disruption to normal sleep architecture following brain tumor surgery.

The hospital environment itself emerged as a significant contributor to sleep disruption. Koçaşlı et al. (2023) documented poor initial sleep quality during hospitalization (RCSQ score 38.00 ± 31.23), with gradual improvement over subsequent days (rising to 71.04 ± 23.61). Notably, 90% of patients reported that hospitalization adversely affected their sleep, highlighting the need for sleep-promoting modifications to inpatient care protocols [33].

Liu et al. (2023) made a unique contribution by conducting correlation analyses between perioperative sleep patterns and clinical outcomes in brain tumor patients using dedicated sleep monitoring technology. This study represents an important methodological advance beyond the subjective assessments or single-parameter analyses that characterize most research in this area, though more such investigations are needed to establish robust relationships between sleep quality and clinical outcomes [28].

While other studies have assessed perioperative sleep, they primarily relied on subjective questionnaires and examined prognostic factors based on single composite scores rather than comprehensive sleep parameters. Furthermore, these investigations typically included mixed neurosurgical populations rather than focusing specifically on primary brain tumor patients.

Caregiver sleep health, though critically important, remains severely understudied. Only one study in our review examined sleep disturbances among caregivers, finding that 55% reported poor sleep quality (PSQI > 5) and 13% met criteria for clinical insomnia (ISI ≥ 15). These sleep disturbances were significantly associated with increased anxiety and emotional distress, suggesting that caregiver sleep represents a crucial but neglected dimension of comprehensive brain tumor care [29].

Risk factors for sleep disturbances in PBT patients

A constellation of demographic, clinical, and treatment-related factors contribute to sleep disturbances in patients with PBTs. The most consistently identified risk factors include older age, fatigue, psychological distress, pain, corticosteroid use, and perioperative complications. Table 3 summarizes the risk factors, impacts of sleep disturbances, and treatment effects across the studies included in this review.

Older age emerged as a significant predictor of postoperative sleep disruption. Nyholm et al. (2023) observed that patients experiencing inability to sleep following surgery were significantly older than those who maintained normal sleep patterns. This age-related vulnerability may reflect diminished neurological reserve and reduced adaptability to the physiological stresses of brain surgery [38].

Fatigue stood out as one of the strongest predictors of both insomnia and poor sleep quality. Willis et al. (2022) demonstrated a robust dose-response relationship, with higher fatigue severity substantially increasing the likelihood of insomnia and poor sleep quality. This relationship appears bidirectional, with fatigue both contributing to and resulting from sleep disturbances [12].

Psychological factors—particularly depression, anxiety, and neurocognitive symptoms—showed significant correlations with sleep disturbances across multiple studies. These associations highlight the complex interplay between emotional well-being and sleep regulation in brain tumor patients, who face extraordinary psychological challenges throughout their disease trajectory [29].

Contrary to expectations, several studies found that tumor characteristics (type, size, and location) did not significantly impact sleep disturbances. Both Mei-Ru Lin et al. (2021)

Table 3 Risk factors, impacts of sleep disturbances, and treatment effects

Author (Year)	Risk factors associated with sleep disturbances	Impact of sleep disturbances	Impact of treatment on sleep disturbances
Mei-Ru Lin et al. (2021)	Tumor type and location (no significant effect on sleep disturbances)	Poor sleep quality independently correlated with lower QoL ($B = 0.80$, $p = 0.02$)	No direct treatment effects assessed (untreated brain tumors)
Pei-Ching Lin et al. (2023)	No significant impact of tumor type or location on sleep disturbances	Insomnia significantly correlated with lower QoL ($B = 0.54$, $p = 0.03$, adjusted $R^2 = 0.60$)	No direct treatment effects assessed (untreated brain tumors)
Amidi et al. (2023)	No significant correlation with time since diagnosis or age	No direct effects assessed	Higher radiation doses to the brainstem, hypothalamus, thalamus, and pituitary gland associated with poor sleep quality (PSQI > 5); Increased daytime dysfunction linked to higher radiation doses to multiple brain structures; Unexpected: Poor subjective sleep quality was linked to lower radiation doses to the thalamus
Choi et al. (2023)	Older age (OR 1.02, $p < 0.001$) Reoperation within 1 year (OR 2.12, $p < 0.001$); Newly acquired brain disability (OR 1.32, $p = 0.043$)	Preoperative insomnia: 1.17-fold increased risk of 2-year all-cause mortality (HR 1.17, $p = 0.021$); Postoperative insomnia: 1.85-fold increased risk of 2-year all-cause mortality (HR 1.85, $p < 0.001$)	No direct treatment effects assessed (postoperative insomnia studied)
Jeon et al. (2021)	Patients: Fatigue, lower KPS, depression, anxiety, pain, neurocognitive symptoms (e.g., memory issues); Caregivers: Anxiety, stress, sadness, caregiver burden, comorbid illnesses, longer caregiving hours	Patients with SD reported higher fatigue and neurocognitive deficits (memory, speech); SD significantly correlated with lower KPS, increased daytime drowsiness (27%); Caregivers with SD reported higher anxiety and stress, longer caregiving hours; No significant link between patient and caregiver SD	No direct treatment effects assessed
Liu et al. (2023)	Higher preoperative blood glucose associated with increased frequency of awakenings ($\beta = 0.125$, $p = 0.011$) Reduced preoperative deep sleep time (DST) correlated with anxiety, depression, postoperative complications, and longer hospital stay	Poor sleep patterns correlated with increased postoperative complications (higher CCI, $\beta = 3.075$, $p = 0.003$); Shorter DST linked to higher postoperative anxiety and depression ($\beta = -0.048$, $p = 0.020$); Longer hospital stays associated with shorter DST ($\beta = -0.067$, $p = 0.005$); Long-term sleep quality (PSQI) worsened by poor perioperative sleep (SOL $\beta = 0.097$, $p < 0.001$, DST $\beta = -0.079$, $p < 0.001$)	No direct treatment effects assessed (focus on perioperative sleep patterns)
Nyholm et al., 2023	Older age was significantly associated with inability to sleep post-surgery (mean age 59 vs. 51 years, $p = 0.03$); No correlation with sex, tumor volume, grade of resection, or operated hemisphere	No direct effects assessed	No direct treatment effects assessed
Tankumpuan et al. (2015)	No direct risk factors assessed	Recovery symptoms, including sleep disturbances, correlated with poorer physical functioning ($r = 0.406$, $p < 0.01$) and mood disturbances, especially fatigue and confusion ($r = 0.716$, $p < 0.01$)	No direct treatment effects assessed
Willis et al. (2022)	Patients on corticosteroids were more likely to experience insomnia (OR = 5.97, $p < 0.05$); Higher fatigue levels significantly increased the likelihood of insomnia (OR = 1.66, $p < 0.01$) and predicted poor sleep quality severity (OR = 1.29, $p < 0.05$)	No direct effects assessed	No direct treatment effects assessed

Table 3 (continued)

Author (Year)	Risk factors associated with sleep disturbances	Impact of sleep disturbances	Impact of treatment on sleep disturbances
Koçaşlı et al. (2023)	Postoperative pain significantly worsened sleep quality in a dose-dependent manner; Female patients experienced significantly more pain and worse sleep quality; Preoperative sleep problems increased postoperative pain and worsened sleep quality; Hospital environmental factors (pain, noise, nighttime disturbances) worsened sleep quality	No direct effects assessed	No direct treatment effects assessed

This table provides a summary of the risk factors associated with sleep disturbances, the impacts of sleep disturbances on patient outcomes, and the effects of treatments on sleep quality across the included studies

QoL Quality of Life, *KPS* Karnofsky Performance Status, *SD* Sleep Disturbance, *CCI* Charlson Comorbidity Index, *DST* Deep Sleep Time, *SOL* Sleep Onset Latency, *PSQI* Pittsburgh Sleep Quality Index, *ISI* Insomnia Severity Index, *ESS* Epworth Sleepiness Scale, *VCPT* Visual Continuous Performance Test, *ACPT* Auditory Continuous Performance Test, *BDI* Beck Depression Inventory, *SOL* Sleep Onset Latency, *EEG* Electroencephalography, *RCSQ* Richards-Campbell Sleep Questionnaire, *N/A* Not Applicable, *IQR* Interquartile Range, *NIMCU* Neuro Intensive Monitoring Care Unit, *B* Regression coefficient, *OR* Odds Ratio, *HR* Hazard Ratio

and Pei-Ching Lin et al. (2023) reported no significant differences in sleep quality based on tumor type (benign versus malignant) or anatomical location. This surprising finding suggests that treatment-related factors and psychological responses may exert stronger influences on sleep than the tumor itself [25, 26].

Treatment-related factors emerged as particularly important determinants of sleep quality. Choi et al. (2023) identified reoperation within one year and newly acquired brain disability as independent predictors of postoperative insomnia. However, a significant limitation was the lack of detailed characterization of these disabilities—the authors did not specify their nature, severity, or neuroanatomical correlates, creating a critical gap in our understanding [24].

Corticosteroid use showed one of the strongest associations with insomnia, with Willis et al. (2022) reporting an odds ratio of 5.97 ($p < 0.05$). This finding highlights an important clinical trade-off: while steroids effectively manage cerebral edema, they significantly disrupt sleep architecture [12]. Pain management also emerged as crucial, with Koçaşlı et al. (2023) demonstrating that postoperative pain worsened sleep quality in a dose-dependent manner. Notably, female patients experienced higher pain levels and consequently worse sleep outcomes compared to males [33].

Impacts of sleep disturbances

Sleep disturbances in PBT patients significantly affect quality of life, cognitive function, fatigue levels, and mental health. Poor sleep quality consistently predicted lower quality of life across studies. Both Mei-Ru Lin et al. (2021) and Pei-Ching Lin et al. (2023) reported strong correlations between sleep disturbances—particularly insomnia—and worse quality of life (B = 0.80, $p = 0.02$ and B = 0.54, $p = 0.03$, respectively) [25, 26].

Cognitive function showed clear impairment with sleep disruption. Chang et al. (2019) found that insomnia was associated with lower attention and memory performance, which improved significantly following hypnotic treatment. This finding suggests that addressing sleep disturbances may represent an underutilized approach to improving cognitive outcomes in brain tumor patients [23].

The relationship between sleep disturbances and fatigue appeared bidirectional and self-reinforcing. Jeon et al. (2021) observed that patients with poor sleep quality experienced higher fatigue levels, lower physical functioning (as measured by Karnofsky Performance Status), and increased daytime drowsiness—creating a potential cycle of deteriorating function [29].

Perhaps most concerning, sleep disturbances showed associations with increased mortality and postoperative complications. Choi et al. (2023) reported that preoperative insomnia increased the risk of 2-year all-cause

mortality by 1.17-fold, while postoperative insomnia had an even stronger impact, increasing mortality risk by 1.85-fold [24]. Additionally, postoperative sleep disturbances correlated with longer hospital stays and higher rates of complications such as nausea and vomiting [28].

Treatment effects on sleep

Various treatments for brain tumors demonstrated differential impacts on sleep quality. Radiation therapy appeared to negatively affect sleep, particularly when higher doses were delivered to sleep-regulating brain structures. Damage to the brainstem, hypothalamus, thalamus, and pituitary gland was linked to poor sleep quality and increased daytime dysfunction [30].

Surgical interventions, particularly craniotomy, contributed significantly to sleep disturbances. Postoperative insomnia developed in 9.2% of previously normal sleepers following craniotomy, with reoperation substantially increasing this risk (OR = 2.12, $p < 0.001$). This postoperative insomnia was not merely a quality-of-life concern but showed associations with increased mortality [24].

Corticosteroid use, while essential for managing cerebral edema, demonstrated one of the strongest associations with insomnia (OR = 5.97, $p < 0.05$). This finding presents a clinical dilemma, as steroids are often necessary for symptom management despite their detrimental effects on sleep architecture [12].

In contrast, targeted sleep interventions showed promising results. Chang et al. (2019) reported that hypnotic medications significantly improved sleep quality, with substantial reductions in ISI and PSQI scores. Moreover, these sleep improvements corresponded with enhanced cognitive function and mood, suggesting potential synergistic benefits beyond sleep itself [23].

Pain management emerged as another critical factor in sleep outcomes. Koçaşlı et al. (2023) identified a dose-dependent relationship between postoperative pain and sleep disturbances, with female patients experiencing more severe pain and consequently worse sleep quality than males [33]. This gender disparity in pain experience and its impact on sleep warrants further investigation and may suggest the need for sex-specific approaches to perioperative pain management.

Collectively, these findings highlight the complex interplay between brain tumors, their treatments, and sleep disturbances. While tumor characteristics themselves may not directly determine sleep quality, the cascade of treatment effects, psychological responses, and physiological changes significantly impacts sleep patterns [25].

Discussion

Sleep disturbances are increasingly recognized as a critical but underexplored issue in individuals with PBTs, with wide-reaching effects on physical, cognitive, emotional, and social functioning. This review highlights that sleep disturbances are highly prevalent in this population, manifesting as insomnia, hypersomnia, circadian rhythm disruption, and poor sleep quality. These disturbances can occur across all stages of the disease trajectory—pre-diagnosis, during treatment, post-operatively, and throughout survivorship—indicating the persistent and multifaceted nature of sleep problems in this clinical context, suggesting that sleep issues are not confined to any one subset of patients. This points to the need for routine screening for sleep disturbances as part of holistic neuro-oncology care.

One of the most consistent findings across the literature is the multifactorial origin of sleep problems in PBT patients. Biological factors include the direct effects of tumors on brain structures involved in sleep regulation. Lesions involving the hypothalamus, thalamus, brainstem, pineal gland, or corpus callosum can disrupt sleep–wake cycles, thermoregulation, hormonal rhythms, and arousal pathways [39].

Beyond direct tumor effects, systemic and iatrogenic factors also play a significant role. Corticosteroids, often prescribed to manage cerebral edema, are known to cause insomnia, mood alterations, and fragmented sleep [12]. Antiepileptic drugs (AEDs), commonly used in this population, have heterogeneous effects on sleep architecture: some may suppress REM sleep, while others exacerbate daytime drowsiness or fatigue. Cranial radiotherapy and chemotherapy can also contribute to long-term fatigue and disrupted sleep through inflammation, neurotoxicity, and hormonal dysregulation [30]. This highlights the need for personalized treatment plans, especially those involving pain management and steroid use, that balance the therapeutic benefits of corticosteroids with their potential negative impact on sleep.

Psychological and behavioral contributors are equally important. High rates of anxiety, depression, existential distress, and anticipatory grief in brain tumor patients significantly affect sleep quality. Sleep disturbance may, in turn, amplify these psychological symptoms, creating a feedback loop. Preoperative anxiety, diagnosis shock, and uncertainty about prognosis can lead to acute sleep loss, which, if not addressed, may persist post-treatment. Moreover, many patients experience reduced physical activity and social engagement, further destabilizing circadian entrainment [23].

Environmental and situational factors—especially during hospitalization—can exacerbate sleep disruption.

Noise, excessive light exposure, frequent nighttime clinical checks, unfamiliar settings, and anxiety related to hospitalization all contribute to poor sleep quality [33]. In neuro-oncology units, where patients may be under close neurological observation, these disruptions are often more frequent and pronounced. These findings underline the importance of addressing hospital-based factors in the management of sleep disturbances. Strategies to improve the hospital environment, such as reducing noise levels, minimizing nighttime disturbances, and optimizing care schedules, could help enhance sleep quality for brain tumor patients.

Assessment and monitoring of sleep

Despite the high prevalence and clinical significance of sleep problems, sleep is rarely assessed systematically in PBT patients [3, 12, 22]. Many studies rely on generic health-related QoL measures or brief, non-specific sleep questions embedded in symptom inventories (e.g., EORTC QLQ-C30, MDASI-BT). These tools may not be sensitive enough to capture nuanced sleep disturbances, such as sleep efficiency, latency, or REM abnormalities.

Objective measures, including actigraphy and polysomnography, are infrequently used, largely due to logistical and resource constraints. However, when applied, they reveal significant alterations in sleep-wake patterns, including reduced sleep efficiency, prolonged sleep latency, and excessive nocturnal awakenings. Currently, only one published study has directly examined the occurrence of sleep disturbances in Australian brain cancer patients, including both PBT and metastatic cases, using validated sleep assessment tools [29]. Importantly, even EEG, for monitoring brain activity, which used by one study for sleep assessment, is not routinely provide a comprehensive evaluation of sleep, representing a missed opportunity for integrated neurophysiological assessment [38]. For a thorough analysis, EEG should be interpreted alongside additional physiological measures within a full polysomnography (PSG), which includes electromyography (EMG), electrooculography (EOG), and respiratory monitoring

There is also a lack of validated sleep assessment tools specifically designed for brain tumor populations. Instruments used in insomnia or cancer fatigue research may not adequately account for the unique cognitive, neurological, and functional limitations faced by PBT patients. Developing tailored tools that integrate patient-reported outcomes, neurocognitive data, and physiological measures is a priority

Risk factors for sleep disturbances

Our analysis identifies several key risk factors for sleep disturbances in brain tumor patients, which can be categorized into demographic, clinical factors, tumor-related, treatment-related, and environmental factors.

- **Demographic Factors:** Age emerges as a significant predictor of sleep disturbances in one study, with older patients experiencing significantly more postoperative sleep difficulties. Statistical analysis confirms this relationship, with increased odds of postoperative insomnia associated with advancing age [38]. This age-related vulnerability may reflect decreased neuroplasticity and adaptive capacity in older patients, potentially limiting their ability to compensate for tumor-related and treatment-related disruptions to sleep-regulating neural networks.
- **Clinical Factors:** Surgical history influences sleep outcomes, with reoperation within one year significantly increasing insomnia risk This suggests cumulative effects of multiple surgical interventions on sleep regulation, possibly due to increased inflammation, neuronal damage, or psychological distress. Similarly, newly acquired brain disability independently predicts postoperative insomnia, highlighting how functional impairments may directly or indirectly impact sleep [24]. However, types of this disabilities are not clearly explored and mentioned and requiers more investigation.
- **Tumor-Related Factors:** Interestingly, tumor characteristics (type and location) show inconsistent associations with sleep disturbances across studies. Multiple investigations found no significant relationship between tumor type or location and sleep issues, suggesting that factors beyond the direct physical presence of the tumor may drive sleep disruption [25, 26]. This finding challenges simplistic models of sleep disturbance in brain tumor patients and points to the need for more nuanced understanding of contributing mechanisms.
- **Treatment-Related Factors:** Treatment plans showed significant impact on sleep quality in brain tumor patients. Radiation therapy demonstrates dose-dependent effects on sleep, with higher radiation doses to sleep-regulating brain structures correlating with poorer sleep quality and increased daytime dysfunction [30]. This relationship highlights the importance of considering sleep-regulating neural networks in treatment planning. Additionaly, Pharmacological interventions show complex relationships with sleep. Corticosteroids, commonly used to manage tumor-associated edema, dramatically increase insomnia risk, likely through direct effects on arousal and circadian regulation [12]. Conversely, targeted sleep medications can significantly improve sleep quality, with studies demonstrating reduced insomnia severity and improved sleep quality scores following hypnotic medication use. Postoperative pain emerges as another critical factor worsening sleep quality, particu-

larly in female patients and those with preexisting sleep problems [33]. This relationship underscores the importance of effective pain management as an indirect sleep intervention in the postoperative period.

Impact on patient outcomes

Sleep disturbances significantly affect multiple domains of patient outcomes, including quality of life, cognitive function, survival, and treatment response.

- **Quality of Life and Functional Status:** Poor sleep quality independently predicts reduced QOL in PBT patients, as does insomnia. These statistical relationships remain significant even after controlling for other factors, suggesting a direct causal link between sleep disruption and diminished well-being [25]. The mechanisms likely involve both direct effects of sleep loss on mood, energy, and cognitive function, and indirect effects through exacerbation of other symptoms like pain and fatigue [26]. Patients with sleep disturbances demonstrate higher levels of fatigue, neurocognitive deficits (particularly in memory and speech domains), and lower performance status scores. These functional impairments create a potential negative feedback loop, where decreased activity and engagement further worsen sleep quality.
- **Mortality and Survival:** Perhaps most concerning is the relationship between sleep disturbances and mortality. Both preoperative and postoperative insomnia increase the risk of all-cause mortality, with postoperative insomnia showing a particularly strong effect. This relationship extends to both cancer-specific mortality and non-cancer mortality [24]. These striking mortality associations suggest that sleep disturbances may not merely be symptomatic concerns but could fundamentally influence disease trajectory and treatment response. Potential mechanisms include impaired immune function, altered inflammatory processes, and decreased tolerance for aggressive treatments—all of which are known to be affected by chronic sleep disruption.
- **Postoperative Complications:** Sleep disturbances also predict surgical outcomes, with poor preoperative sleep patterns linked to increased postoperative complications and prolonged hospital stays [28]. This relationship suggests that addressing sleep issues before surgery could potentially improve recovery trajectories and reduce healthcare utilization.
- **Caregivers Impact:** The effects of patient sleep disturbances extend beyond the patients themselves. Caregivers of brain tumor patients with sleep problems report higher anxiety, stress, and longer caregiving hours. This increased caregiver burden may create another negative cycle, where caregiver fatigue and stress further compromise the quality of patient care and potentially worsen patient sleep. Unfortunately, research specifically examining caregiver sleep remains extremely limited, with only one study in our review addressing this critical aspect [29].

Treatment approaches and interventions

Despite the high prevalence and serious consequences of sleep disturbances in brain tumor patients, evidence-based interventions remain limited. The available research suggests several promising approaches but highlights significant gaps in our understanding of optimal management strategies.

- **Radiation Therapy Considerations:** Radiation therapy planning should consider effects on sleep-regulating brain structures. The complex relationship between radiation dose and sleep quality—with higher doses to the hypothalamus, thalamus, pituitary, and brainstem linked to poorer sleep outcomes—suggests the potential benefit of advanced planning techniques that minimize exposure to these critical regions when oncologically feasible [30].
- **Pharmacological Approaches:** Hypnotic medications show promise for improving sleep quality in brain tumor patients, with demonstrated benefits for both subjective sleep measures and daytime functioning. Beyond direct sleep improvements, these medications appear to enhance cognitive function (particularly attention and memory) and reduce depressive symptoms, suggesting broader neuropsychiatric benefits [23]. However, medication selection requires careful consideration of potential interactions with other treatments. The strong association between corticosteroid use and insomnia highlights the need for proactive sleep management when these medications are necessary [12]. Balancing the anti-edema benefits of corticosteroids against their sleep-disrupting effects represents an important clinical challenge that may require individualized approaches.
- **Environmental Modifications:** Hospital environmental factors significantly impact sleep quality, particularly in the postoperative period. Noise, nighttime interruptions, and frequent medical interventions all contribute to sleep disruption [33]. Addressing these modifiable factors through noise reduction strategies, consolidated care activities, and sleep-promoting environments could significantly improve inpatient sleep quality without requiring pharmacological interventions.

Limitations of current evidence and research priorities

Despite valuable insights gained from existing studies on sleep disturbances in brain tumor patients, several significant

limitations constrain our current understanding and clinical approach to this important issue. Below, we outline these key limitations and propose specific future research directions to address each gap.

- **Methodological Heterogeneity:** The heterogeneity across studies presents a fundamental challenge for synthesizing findings and drawing reliable conclusions. Research to date encompasses widely varying tumor types (from benign meningiomas to aggressive glioblastomas), treatment phases (preoperative, postoperative, during adjuvant therapy), and assessment methodologies. This diversity, while reflecting the complex reality of brain tumor care, complicates efforts to identify consistent patterns or develop standardized approaches. The use of different sleep assessment tools—ranging from validated questionnaires like the Pittsburgh Sleep Quality Index and Insomnia Severity Index to actigraphy and self-reported measures—further fragments the evidence base and may partially explain inconsistent findings across studies. Future studies should implement standardized assessment protocols and more carefully defined study populations. Researchers should adopt common measurement tools and reporting standards to facilitate cross-study comparisons and meta-analyses. Collaborative research networks could develop consensus guidelines for sleep assessment in neuro-oncology to ensure greater methodological consistency and enhance the interpretability of findings across different research settings.
- **Predominance of Cross-Sectional Designs:** The predominance of cross-sectional research designs represents another critical limitation. Most studies capture sleep disturbances at isolated timepoints rather than tracking their evolution throughout the disease trajectory. This approach fundamentally limits our ability to establish causal relationships between sleep disturbances and important clinical outcomes such as disease progression, treatment response, cognitive function, and survival. Without longitudinal data, we cannot determine whether sleep problems represent transient reactions to diagnosis and treatment or persistent issues with long-term implications for patient well-being and prognosis. Well-designed longitudinal studies should track sleep patterns from diagnosis through treatment phases and into survivorship or end-of-life care. These studies should capture the temporal evolution of sleep disturbances and examine their relationship to disease trajectory, treatment milestones, and quality of life outcomes. Such research would provide invaluable insights into how sleep problems develop, persist, or resolve over time, and how they interact with disease progression and treatment response.
- **Limited Intervention Research:** Perhaps most concerning is the striking paucity of intervention research. Our review identified only one study directly evaluating pharmacological interventions for sleep disturbances in this population. While this study showed promising results for hypnotic medications, it represents an isolated finding in a field desperately needing evidence-based interventions. The absence of research on non-pharmacological approaches is particularly problematic, as interventions like cognitive-behavioral therapy for insomnia, sleep hygiene programs, and relaxation techniques have demonstrated efficacy in other clinical populations but remain virtually unexplored in neuro-oncology. Randomized controlled trials should evaluate both pharmacological and non-pharmacological sleep interventions specifically tailored to brain tumor patients. These studies should incorporate appropriate control conditions and sufficient sample sizes to detect clinically meaningful effects. Particular attention should be given to adapting evidence-based approaches from other fields—such as cognitive-behavioral therapy for insomnia, mindfulness-based interventions, and structured sleep hygiene programs—to address the unique challenges facing brain tumor patients.
- **Lack of Personalized Approaches**: The literature also lacks personalized approaches to sleep management that account for individual patient characteristics and treatment contexts. Given the heterogeneous nature of brain tumors and their treatments, sleep interventions likely require customization based on tumor type, location, treatment modality, and patient-specific factors. Without research addressing these distinctions, clinicians lack guidance on tailoring sleep interventions to individual patient needs and circumstances. Research should develop and evaluate individualized sleep management strategies based on tumor characteristics, treatment modalities, and patient-specific factors. Studies should identify which interventions work best for specific patient subgroups—such as those with different tumor types, treatment regimens, or comorbidities—to optimize effectiveness and address the heterogeneous nature of sleep disturbances in this population. This precision medicine approach could significantly enhance treatment outcomes compared to one-size-fits-all interventions.
- **Neglect of Caregiver Sleep Health:** The impact on caregivers represents another significant blind spot in current research. Despite the substantial burdens faced by those caring for brain tumor patients, our review identified only one study addressing sleep disturbances

among caregivers. This gap is particularly concerning given the interdependence between caregiver well-being and patient care quality. Sleep-deprived caregivers may struggle to provide optimal support, potentially affecting patient outcomes through reduced attentiveness or diminished emotional resources. Studies should examine sleep patterns among diverse caregiver populations and investigate bidirectional relationships between caregiver sleep quality and patient outcomes. Research should include caregivers with different relationships to patients (spouses, parents, adult children) and from various socioeconomic and cultural backgrounds to capture the full spectrum of caregiving experiences. Longitudinal designs should track how caregiver sleep evolves throughout the patient's disease trajectory and develop interventions that support both patients and caregivers as an integrated care unit.

- **Limited Understanding of Biological Mechanisms:** Current research provides limited insight into the biological mechanisms linking sleep disturbances to tumor progression, treatment response, and survival outcomes. Without this mechanistic understanding, it remains difficult to develop targeted interventions that address the underlying causes rather than merely treating symptoms. Mechanistic investigations should explore the biological pathways connecting sleep disturbances to clinical outcomes in brain tumor patients. Research should examine how sleep disruption affects inflammatory processes, immune function, neuroplasticity, and other biological systems relevant to tumor progression and treatment response. Understanding these mechanisms could reveal novel therapeutic targets and inform more effective interventions that address fundamental pathophysiological processes rather than just symptomatic relief.
- **Inadequate Assessment of Sleep:** Most studies rely heavily or exclusively on subjective sleep measures, with limited use of objective assessment tools that can characterize specific sleep architecture disruptions. This approach may miss important aspects of sleep disturbance that patients cannot self-report, such as changes in sleep stages, microarousals, or subtle breathing disturbances. Research should incorporate comprehensive objective sleep measures—particularly PSG—alongside subjective reports. This multimodal approach would provide more detailed characterization of sleep architecture disruptions and potentially identify specific sleep parameters most affected by brain tumors and their treatment. Such information could guide more targeted interventions addressing the particular aspects of sleep most disrupted in this population.
- **Insufficient Attention to Hospital Environment:** Despite evidence that the hospital environment significantly impacts sleep quality, few studies have systematically evaluated how to optimize inpatient settings for brain tumor patients. Factors such as noise, lighting, care schedules, and monitoring practices may substantially affect sleep during critical recovery periods. Hospital-based interventions should be systematically evaluated for their impact on inpatient sleep quality. Research should examine how simple environmental modifications, care protocol adjustments, and staff education programs might improve sleep during hospitalization. These studies should measure not only sleep outcomes but also potential downstream effects on recovery trajectories, complication rates, and length of stay to demonstrate the clinical importance of sleep-promoting hospital environments.

By addressing these specific limitations through targeted research initiatives, the field can develop more comprehensive and effective approaches to managing sleep disturbances in brain tumor patients. This research agenda would not only advance scientific understanding but also provide clinicians with evidence-based tools to improve quality of life, treatment tolerance, and potentially clinical outcomes in this challenging patient population.

Conclusions

This systematic review highlights the significant prevalence and impact of sleep disturbances in patients with PBT, along with their potential effects on caregivers. The findings reveal significant risk factors and adverse effects on quality of life and clinical outcomes, highlighting the urgent need for targeted interventions. A comprehensive analysis of 11 studies, encompassing various research designs and tumor types, provides valuable insights into the prevalence, contributing factors, and consequences of sleep disturbances in this population. Given the substantial burden of sleep disturbances, integrating sleep management into routine neuro-oncology care is essential. Addressing these issues through tailored clinical strategies and policy measures can significantly enhance patient well-being and support caregivers. Future research should focus on developing evidence-based interventions and longitudinal studies to further understand the long-term impact of sleep disturbances and optimize care for PBT patients and their caregivers.

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