

Psychotic manifestations in the Context of Brain Neoplasm: a literature review

Paula Serpa¹, Second author name and surname ^b, etc.

¹ São Leopoldo Mandic Medical School in Campinas, São Paulo, Brazil, paulahserpa@berkeley.edu

Abstract. In certain cases, brain neoplasms are preceded or accompanied by psychiatric manifestations, including depression, anxiety, mood disorders, irritability, mania, hallucinations, among others. These symptoms can be caused by the biological activity of the tumor, the physical impact of the tumor, such as increased intracranial pressure, or could simply be a consequence of detection bias. Regardless of the etiology, some cases have reported a delay in tumor diagnosis due to the presence of such psychiatric manifestations. Therefore, this literature review aims to highlight key points from articles in the databases: Google Scholar, Scopus and PubMed, from the last five completed years (2018-2022), in order to synthesize the information published recently regarding the matter at hand. The studies remain inconclusive, however indicate that there might be an association between the psychiatric manifestations and brain neoplasms. Therefore, there is a strong need to further investigate these phenomena and invest in research that present improved diagnostic methods for early detection of brain tumors given psychiatric symptomatology.

Keywords. Brain neoplasm, psychiatric manifestations.

1. Introduction

Brain neoplasms are divided into two main groups: primary and metastatic tumors. The primary tumors are generally benign or malignant and have a large difference in progression in terms of invasion, as well as growth characteristics. Recent studies report an incidence of 12.8/100 000 people for primary tumor compared to 51.4/100 000 people for metastatic tumors [1,2]. Additionally, primary and benign brain tumors are more common in women compared to men. The most common primary brain tumors are the gliomas which include astrocytomas, oligodendromas and ependymomas, and which are usually diagnosed with MRI and, at times, biopsy [2].

Despite discrepancy among studies, recent literature suggests that brain neoplasms may cause a variety of psychological symptoms. Although these manifestations are rare, they are commonly reported along with neurological symptoms due to brain tumors [1,2]. The etiology of such psychiatric manifestations is not entirely known and appears to be potentially multifactorial [1]. Some studies suggest that these symptoms are consequences of biological behavior of the tumors, increased intracranial pressure, or possibly even a result of detection bias, which is the increased likelihood of a disease due to a greater medical surveillance of a

different medical condition [3]. Studies have shown that 50-78% of patients with primary brain tumor may exhibit psychiatric symptoms prior to the tumor diagnosis [3]. The literature also shows that, in certain cases, the brain tumor diagnosis may be delayed due to psychiatric symptoms that mislead the physician into diagnosing a psychiatric illness, while not investigating alternative disorders and conditions that might be leading to the manifested symptoms [4,5,6]. That is especially considering that, at times, psychiatric symptoms may be the only manifestations of brain tumors [2,7].

Literature has shown that brain tumors that affect certain areas of the brain are associated with specific psychiatric symptoms. For instance: depression is commonly found in frontal lobe tumors, apathy in frontal lobe and paralimbic areas; mood disorders, such as mania, are associated with lesions to the right hemisphere, hallucinations and mood swings associated with cerebral cortex, pituitary and pineal regions; personality changes related to lesions in the ventricular cysts or frontal lobe lesions; schizophrenia-like illness associated with lesions to the temporal lobe [1,7,5,8].

There is great variety in what the current literature discusses about the topic at hand, psychiatric manifestations in the context of brain neoplasms.

However, certain foundations have been created and associations have been strengthened, despite the grand variability.

2. Methods

The literature review was generated based on searches on databases Google Scholar, Scopus and PubMed, using the key words: “brain neoplasms” and “psychiatric manifestations”. The word “tumor” was considered as an alternative research key word, however it was discarded as a search term considering that it is a word that is used in a variety of contexts and could have a different meaning such as an increase in tissue volume, however not as specific as neoplasm, which involves the increase in tissue size due to uncontrolled cellular proliferation, which is more aligned with this review’s research question. Only articles in English and published within the years 2018 to 2022, to obtain the most recent information of completed years, were included. Review articles were excluded.

The Google Scholar search led to 24 articles, Scopus led to 11 articles and PubMed led to 25 articles. Of these, a selection of papers that were most closely aligned to the objectives and research question of this study, were analyzed in greater depth.

3. Results

Table 1, displayed on pages 5 and 6 of this article, presents the articles that underwent closer examination for this review. The table highlights the methods, results and conclusion for each article studied in greater depth.

4. Discussion and Conclusion

The literature review, consisting significantly of case reports, demonstrates that there still remains a great discrepancy among the results presented. Certain articles question the associations that have been consolidated over time, indicating results that show no significance between the brain tumor and psychiatric manifestations of the patients, not even the correlations that have been demonstrated between lesions in given areas of the brain and symptoms presented by the patients. Studies did highlight the possibility of detection bias having an important influence on the associations described [3].

On the other hand, various articles highlight and support the association that has been shown time and again between brain neoplasm and psychiatric manifestations. In fact, one study showed that the association of tumor diagnosis with psychiatric symptoms was about six times stronger for brain cancer than other cancers – a difference too large to be explained solely by detection bias [3].

Despite the differences found and discussed throughout the literature review, there have been efforts towards decreasing the number of misdiagnosis or delayed diagnosis. For instance, a

study discussed a machine learning-based decision-making algorithm that might predict neuropsychiatric problems that are commonly observed in brain tumors [8]. This study demonstrated that, of the models tested, the random forest tree model can be used to predict illnesses linked to brain neoplasm and can aid the physician in pre-diagnosis and these conditions, while assisting in deciding the best therapeutics.

In conclusion, there is a clear need for further investigation, both retrospective and longitudinal studies, to better understand these possible associations between psychiatric symptoms and brain tumors, while continuing to invest in developing improved technology-based, diagnostic methods.

5. References

- [1] Farzaneh R, Malek A, Mirzaei F, Amiri S, Salehpour F, Meshkini A, et al. Evaluation of comorbid psychiatric disorders in patients with primary brain tumors before and after surgery. *Neurol Psychiatry Brain Res* [Internet]. 2020;36:8–13. Available from: <http://dx.doi.org/10.1016/j.npbr.2020.02.003>
- [2] Ali M, Das S. Psychosis as an indicator of recurrent non-Hodgkin’s lymphoma: a rare presentation. *Gen Psychiatr* [Internet]. 2018;31(1):e000005. Available from: <http://dx.doi.org/10.1136/gpsych-2018-000005>
- [3] Bytnar JA, Lin J, Theeler BJ, Scher AI, Shriver CD, Zhu K. The relationship between prior psychiatric diagnosis and brain cancer diagnosis in the U.S. military health system. *Cancer Causes Control* [Internet]. 2022;33(9):1135–44. Available from: <http://dx.doi.org/10.1007/s10552-022-01608-4>
- [4] Gyawali S, Sharma P, Mahapatra A. Meningioma and psychiatric symptoms: An individual patient data analysis. *Asian J Psychiatr* [Internet]. 2019;42:94–103. Available from: <http://dx.doi.org/10.1016/j.ajp.2019.03.029>
- [5] Nazlı ŞB, Sevindik M. Depression as the first symptom of frontal lobe grade 2 malignant glioma. *Turk Psikiyatri Derg* [Internet]. 2021; Available from: <http://dx.doi.org/10.5080/u25957>
- [6] Marku M, Rasmussen BK, Dalton SO, Johansen C, Hamerlik P, Andersen KK, et al. Early indicators of primary brain tumours: a population-based study with 10 years’ follow-up. *Eur J Neurol* [Internet]. 2021;28(1):278–85. Available from: <http://dx.doi.org/10.1111/ene.14527>
- [7] Barnes A, Wang MM, Feltes J, Ko J, Guzman MA. Subependymal giant-cell astrocytoma masquerading as restrictive eating disorder and

depression in an adolescent. *Innov Clin Neurosci* [Internet]. 2020 [cited 2023 Oct 1];17(1-3). Available from: <https://pubmed.ncbi.nlm.nih.gov/32547840/>

- [8] Shahid S, Iftikhar S. Machine learning models to predict neuropsychiatric disorders in various brain tumors. *Curr Med Res Opin* [Internet]. 2022;38(5):687-96. Available from: <http://dx.doi.org/10.1080/03007995.2022.2043654>

Title	Author(s)/Year	Objectives	Methods	Results	Conclusion
Evaluation of comorbid psychiatric disorders in patients with primary brain tumors before and after surgery	Farzaneh et al, 2020	Assess the frequency of psychiatric disorders in adult patients with primary brain tumors before and after surgery.	120 patients with primary brain tumors were observed, starting with a diagnostic interview using the DSM-IV criteria before as well as one month after surgery.	Pre-operatively, 26.66% of patients had psychiatric symptoms, which reduced to 22.5% post-operatively, without significance. Findings suggested that tumor location and pathology was not associated with incidence and type of psychiatric disorder.	The most common psychiatric disorder within the group studied was depressive disorder.
Psychosis as an indicator of recurrent non-Hodgkin's lymphoma: A rare presentation	Ali and Das, 2018	Report a case where recurrence of lymphoma was linked to psychotic manifestations without neurological deficit.	Case was reported in great detail.	Relapse associated with only psychiatric manifestation without neurological deficit.	Psychotic behavior is usually secondary to brain tumor, however this case reports the presence of psychotic manifestations as a sign of tumor relapse.
The relationship between prior psychiatric diagnosis and brain cancer diagnosis in the U.S. military health system	Bytnar et al, 2022	Investigate whether psychiatric illness may be an early manifestation of brain cancer, considering potential detection bias effect.	Case-control study, groups compared likelihood of having pre-existing psychiatric diagnosis using conditional logistic regression.	Results demonstrated significant association of psychiatric illnesses with brain cancer, compared to non-cancer controls, especially three months before cancer.	Findings suggest association between diagnosed psychiatric illnesses and subsequent brain cancer diagnosis, not explained solely by detection bias.
Early indicators of primary brain tumours: a population-based study with 10 years' follow-up	Marku et al, 2020	Conduct a population-based case-control study in Denmark to increase knowledge about early indicators	Population-based case-control study including all persons with primary brain tumor between 2005	Increased odds for primary brain tumor after neuropsychiatric manifestations up to	Sub-group of patients diagnosed with or being prescribed medications that target neuropsychiatric

		of brain tumor and improve diagnosis.	and 2014 in Denmark	10 years before brain tumor diagnosis were found.	disorders may be at greater risk of being diagnosed with primary brain tumor.
Subependymal Giant-cell Astrocytoma Masquerading as Restrictive Eating Disorder and Depression in an Adolescent	Barnes et al, 2020	Describe subependymal giant-cell astrocytoma (SEGA) and lateral ventriculomegaly with initial presentation of a restrictive eating disorder and depression.	Case reported in detail.	Diagnosis of SEGA was delayed by an initial psychiatric illness diagnosis and lack of neurologic work-up.	Clinical presentations of brain tumors can be subtle and may be misinterpreted due to a psychiatric condition.
Letter to the Editor: Depression As The First Symptom of Frontal Lobe Grade 2 Malignant Glioma	Nazli and Sevindik, 2022	Present a clinical case where patient with primary brain tumor was initially diagnosed with major depressive disorder	Case reported in detail.	There is a possibility of psychiatric symptoms being the clinical clue for brain cancer and the neuroimaging tests are essential in cases of recent-onset psychosis or mood disorder symptoms.	Emphasize importance of brain imaging and detailed investigation of atypical symptoms for diagnostic approaches to psychiatric disorders