Title: Highlighting the lack of neuropsychologists and speech therapists in healthcare services towards an accurate (pre- and postoperative) cognitive assessment in low-grade glioma patients.

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Key-points

- Due to the slow growth of low-grade gliomas, cognitive impairments can be quite difficult to detect at early stages.
- There is a lack of staff specialized on the cognitive and emotional assessment of patients, such as neuropsychologists and speech therapists.
- Brain tumor patients are often misclassified as asymptomatic at the moment of diagnosis.
- An accurate and individually-designed assessment of their cognitive status can significantly improve the treatment strategy for each patient, allowing long-term planning and substantial differences in post-operative outcomes.
- Healthcare facilities treating low-grade glioma patients should give high priority to the formal inclusion of trained professionals capable of designing and implementing adequate pre- and post-operative strategies. By addressing this challenge, it is possible to guide clinical interventions and close the gap between surgery and rehabilitation therapy.

Introduction

Low-grade gliomas (LGGs) are a slow-growth type of brain tumor usually located in the vicinity of areas that are essential for a wide range of cognitive processes including language, memory, or movement, causing disruptions on the patient's daily activities. With all due risks considered, resection is the usual treatment for these cases. Advances in cortical stimulation mapping during awake surgery have achieved outstanding improvements in avoiding postoperative functional deficits in comparison to general anesthesia surgeries**.** However, tumor resection can still hinder postoperative cognitive outcomes. There is extensive literature detailing the cognitive impairments caused by resection, epileptic seizure, or even anti-epileptic drugs usage.

On the other hand, less attention has been drawn to difficulties stemming from the tumor itself which are present at the time of diagnosis. LGGs can infiltrate or displace essential areas, impairing cognitive functions. Even if an epileptic seizure is usually the first indicator for diagnosis, in a huge percentage of cases, LGGs change how patients handle ordinary daily issues. In fact, the majority of them complain about alterations in the execution of common activities or even report changes in their usual mood, decreased empathy, or difficulties in their social relationships (1). Patients' awareness of starting to have limitations to their abilities and capacities, even at early stages of the tumor, contradicts healthcare services often classifying LGG patients as asymptomatic prior to surgery**.** This can be explained by the fact that preoperative assessment is usually done by neurosurgeons or neurologists who carry on just a neurological exploration searching for focal deficits, not paying

attention to cognitive or emotional complaints. In fact, there is evidence of LGG patients performing poorly on objective measures for several domains(1).

For a long time, the priority was to ensure survival, and only severe deficits such as hemiplegia or aphasia were considered relevant. Cognitive abilities and emotional aspects were not included as part of the treatment planning (1), as they were not seen as important indicators of the quality of life after surgery. In this day and age, the considerable improvement in these patients' life expectancy from 6-7 years (2) to 14-16 years (3) has highlighted the importance of accounting for subtle or mild decline and the inclusion of all possible affected domains with the aim of matching former abilities. According to evidence, language assessment has played a major role in cognitive preoperative evaluations for LGGs affecting eloquent areas over the last decades. Consequently, picture naming and verbal fluency tasks have effectively been used to detect word retrieval deficits. Executive functions have also been one of the most commonly studied impairments with assessment of specific functions (i.e., working memory or mental flexibility. Nevertheless, language- and executive functions-related difficulties have not been the only affected domains. Symptoms of clinically significant anxiety and depression have been found in 46% and 13% of patients respectively (4). Other studies show self-reported complaints of tiredness in 40% of patients and emotional disorders in 30% of them (5). Interestingly, personality changes have also been described recently for the first time.

Overall, the reported prevalence of cognitive impairments in LGG patients with no treatment and in preoperative stages of the diagnosis showing cognitive deficits has increased from 10.4%-36.4% of patients in 2008 at an individual level (6) to 62.2% at an individual level and 92.2% when compared to a reference group in 2017 (7). Heterogeneity in clinical and personal characteristics (i.e., number of patients, tumor location, tumor recurrence or personal history) set aside, it seems like one of the reasons could be that the variety and sensitivity of neurocognitive tests is increasing. Even high order cognitive assessments, including mentalizing or types of consciousness, are also starting to be considered (1).

A comprehensive evaluation of neurocognitive and psychological aspects prior to surgery is of crucial importance for designing an accurate treatment, surgical strategy, and effective lesion follow-up; it can facilitate setting rehabilitation goals at the very beginning, even before surgery. Consequently, for establishing a multidisciplinary therapeutical plan, professionals from different backgrounds are needed in healthcare facilities following the idea of establishing a holistic neuro-oncological approach when treating these patients (8). Psychology and language experts, like neuropsychologists and speech therapists, are becoming increasingly common in centers where awake craniotomy (AC) is performed and their presence is advised. The role of these professionals in AC services around the globe may vary and can include the evaluation of language prior to surgery,

identification of preoperative cognitive symptoms, careful selection of intra-operative tasks and the monitorization of possible alterations caused by brain mapping during AC in order to report behavioral errors (e.g., anomia, speech arrest, apraxia) to surgeons as well as performing postoperative evaluation. Although the existence of pre-designed tools for this purpose may suggest testing cognitive functions without these professionals is feasible, evidence shows otherwise. Their direct implication has resulted in more extensive and accurate resections, a drastic drop in surgical time and the differentiation between reversible and irreversible mild cognitive deficits before and after surgery.

Surprisingly enough, considering their undeniable professional value, to our knowledge, there is no clear estimation of the real number of neuropsychology and language experts in AC services around the globe or quantitative measures of their involvement in the service (i.e., number of hours spent with each patient) (9). In a relatively recent attempt to gain a clearer picture of the preoperative and postoperative cognitive assessment of LGG patients, the European Low-Grade Glioma Network (ELGGN) sent a survey to 28 medical centers in Europe. Answers were received from 21 centers (75% of the total) from 11 different countries; however, 7 (23%) of them were based in France (10), so results should not be considered fully representative. All mentioned centers reported neuropsychologists and speech therapists to be in charge of the preoperative assessment but reached no consensus on the tasks administered.

On a similar note, in the UK, (9) sent out a survey for a better understanding of the role of language experts (neuropsychologists and speech therapists) in neurosurgical departments performing AC. They collected 24 responses out of an unknown number of professionals working in the mentioned service, obtaining striking results. Only 7 of them (29%) had funding to be involved in those services or even had a related specification in their job description. Another interesting aspect is that they quantified the number of hours dedicated to patients in each step. The results were 2.9h for the preoperative part as opposed to 4.1 for the intra-operative and 3.4 to the postoperative, being the preoperative assessment the one to which they dedicated the lesser time (see (9) for a full description of direct and indirect times)**.** Preoperatory diagnostic work (i.e., patient case, imaging data, personal interview) is key for establishing the basis for an accurate strategy and improving patient's prognosis to a high cognitive functioning level. In fact, in the survey, only 8 professionals (33%) agreed that they believed the needs of each patient were correctly identified and handled before surgery (9). Moreover, ensuring that the same professionals are in charge of the postoperative assessment would improve the quality of the evaluation, contributing to a better rehabilitation plan and higher full recovery rates.

This is the ideal time to reflect on the imminent need to adopt holistic but also personalized approaches in the diagnosis and subsequent treatment of LGG patients. We want to emphasize the importance of accurate and exhaustive evaluation and diagnosis of subtle or mild cognitive impairments before and after surgery. Considering the diverse personal and clinical characteristics of

each patient, designing a fixed procedure seems unfeasible. Thus, tailored diagnosis and treatment strategies seem to be the future of LGG patients' treatment course of action. The integration of neuropsychologists in the neurosurgical and neurological services is the only way to achieve this goal. Only through a multidisciplinary approach will we be able to maximize positive postoperative outcomes that would ultimately improve patients' quality of life.

Clinical Implications

An accurate and individually-designed assessment of their cognitive status can significantly improve the treatment strategy for each patient, allowing long-term planning and substantial differences in postoperative outcomes.

Study Limitations

This work was intented as an overview of the current situation regarding the assesment of low grade glioma tumor patients in healthcare facilities and therefore it does not include data. Future studies should focus on gathering evidence of the mentioned problems.

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