Survey on current cognitive practices within the European Low Grade Glioma Network: towards a European assessment protocol

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Abbreviations:
ELGGN = European Low Grade Glioma Network;
DLGG = Diffuse Low Grade Glioma;

Abstract

Background: The European Low Grade Glioma network indicated a need to better understand common practices regarding the managing of Diffuse Low Grade Gliomas. This area has experienced great advances in recent years.

Method: A general survey on the managing of diffuse low grade gliomas was answered by 21 centres in 11 European countries. Here we focused on specific questions regarding perioperative and intraoperative cognitive assessments.

Results: More centres referred the same Speech and Language therapist and/or Neuropsychologist across all assessments; a core of assessment tools was routinely used across centres; fluency tasks were commonly used in the perioperative stages, and Object naming during surgery; tasks that tapped on attention, executive functions, visuospatial awareness, calculation and emotions were sparsely administered; preoperative assessments were performed one month or one week before surgery; timing for postoperative assessments varied; finally, more centres recommended early rehabilitation, whenever needed.

Conclusion: There is an emerging trend towards following similar practices for the management of low grade gliomas in Europe. Our results are descriptive and formalize current discussions in our group. Also, they contribute towards the development of a European assessment protocol.

Keywords: diffuse low-grade-glioma, surgery, cognition, assessment, survey, protocol

Introduction

The European Low Grade Glioma Network (ELGGN) is a discussion group for research and management of primary brain tumours, particularly, diffuse low grade gliomas (DLGG). Access to the collaboration is free and open to professionals working in neurosurgery, anaesthesiology, molecular biology, radiotherapy, oncology, occupational therapy, neurology, neuroimaging, cognitive and language assessment, and related topics[1]. Since 2006, the collaboration has quadrupled its size (currently, 208 registered members). The ELGGN organises an annual meeting that each year takes place in a different European site. The meetings are an excellent opportunity for interdisciplinary and intergenerational discussion and learning. These include talks by relevant keynote speakers; hands-on courses on varied topics such as cadaveric brain dissection, and tractography; and small-group discussions led by leaders in the field.

In this article we summarise the results and follow-up discussions of the cognitive part of a survey on current practices among members of the ELGGN. A review and discussion of the whole survey, which was presented at the 11th meeting of the collaboration (June 2015), can be found in another manuscript [50]. For the first time, we review the common practices of a wide number of European awake surgery teams regarding language and cognition in people with DLGG [for general reviews see 13 and 65]. These areas have experienced great advances in recent years – many of which have been put forward by members of the Network. For example, seminal neurosurgical papers have been revisited and evaluated from a cognitive neuropsychological and neuroscientific perspective, also indicating which tests may be more suitable for intraoperative brain mapping depending on tumour localisation and/or the desired surgical approach [17; 22; 26; 74; 92]; new tests, test batteries and methods for perioperative (i.e., pre- and postoperative) and intraoperative assessments have been developed and standardised in different European languages [24; 29; 31; 32; 36; 48; 49; 53; 59; 70; 75; 76; 77; 83; 86; 94]; the role of cortical and subcortical brain structures has been looked at to scrutinise the types of errors that are more likely to appear during direct brain stimulation in individual subjects [4; 5; 21; 23; 27; 36; 69; 80; 81]; and the behavioural profile of people with

[1]More information and registration can be obtained in the ELGGN website: www.braintumours.eu

DLGG has been comprehensively studied at all stages, including long term follow-up and quality of life assessments [40; 54; 60; 64; 78; 79].

In this article we review the common practices adopted for intraoperative and perioperative assessment by the ELGGN peers. This work contributes to a better understanding of the current state-of-the-art in this field. Its main aim is descriptive, not prescriptive. This implies that frequent answers to one or more of the questions describe current practises, not necessarily recommendations to other centres. Future research may be planned to indicate assessment baselines from which to recommend effective postoperative rehabilitation protocols; to explain and to predict the patient's performance over time; and to report tests that other centres may consider in order to assess, map and monitor the patient while minimising postoperative functional injury. Future discussions within the ELGGN should lead towards the development of a European assessment protocol that could allow comparisons across different centres, languages, and cultures.

Methods

In May 2015, a Google Forms survey was sent to 28 centres where members of the ELGGN are located. Only one survey form could be filled in by each centre, and it was recommended that each centre would complete it in an interdisciplinary consensus meeting. The complete survey contained 69 questions. It was divided in 10 sections following the common pathway of events that a person with a DLGG typically undergoes (i.e., preoperative cognitive assessment; neuroimaging; initial management; intraoperative anaesthetic management; intraoperative cognitive assessment; postoperative cognitive assessment; molecular biology and neuropathology; postoperative strategy; choice and follow-up chemotherapy; and radiation therapy). The full list of the questions can be found in the general manuscript, which has been published elsewhere [49]. In this article, we discuss replies to the 15 questions of the survey that are most relevant to cognitive assessments (see Table 1). Non-parametric statistics were performed to decide whether any response was significantly more frequent than others.

[Please add Table 1 around here]

Results

Complete answers to the survey were obtained from 21 centres in 11 European countries: Austria (Innsbruck); France (Besançon, Montpellier, Nancy, Nice, Paris Lariboisière, Paris Saint-Anne, Poitiers); Germany (Frankfurt); Greece (Thessaloniki); Italy (Brescia, Catania, Udine, Milan); Netherlands (Tilburg); Portugal (Lisbon); Spain (Santander); Sweden (Uppsala); Switzerland (Lausanne); and UK (Cambridge, Leeds). This corresponds to 75% of the centres that we contacted, 23% of which were based in France (7/21). Some questions were not answered by all centres. Therefore, we performed statistical analyses based on the number of total respondents for each question, which we indicated in parenthesis as follows (i.e., number of respondents/total number of respondents).

Personnel involved

In all centres, perioperative assessments were commonly pursued by a Neuropsychologist and/or a Speech and Language Therapist. We encountered no significant differences regarding the type of professional that centres appointed to perform the assessments (Fisher's Exact Test[5]=8.42, p=0.116, two-tailed). The majority of centres appointed only a Neuropsychologist (6/21); a Speech and Language Therapist or a Neuropsychologist (6/21); or both a Speech and Language Therapist and a Neuropsychologist (6/21) to perform these assessments. Less centres appointed only a Speech and Language Therapist (2/21) or a Neuropsychologist alone with the addition of self-computerised testing (1/21). We did not specifically ask about the role of Occupational Therapists and other professionals in this survey. Perioperative assessments were administered more often by the same person who performed the intraoperative assessment, as opposed to a different person (always the same person: 13/21; almost always the same person: 6/21; not so often the same person: 2/21; Fisher's Exact Test =13.12, p=0.002, two tailed).

Core testing battery

Sixteen of twenty-one centres answered to this question. All sixteen centres used phonological and semantic verbal fluency tasks (16/16), which evaluate executive functions and have a strong verbal component [e.g., 14; 55; 88]. Language processing was evaluated with Object Naming (10/16) [e.g., 16; 24; 51; 75] and a semantic association task, particularly, the Pyramids and Palm Trees Test (9/16) [i.e., PPTT, 38]. Attention and working memory were evaluated with the Forward and Backward Digit Span (12/16) [52; 57; 87]; the copy and the long-term reproduction of the Rey-Osterrieth Complex Figure Test (11/16), which are also used to assess planning, problem-solving strategies, organisational skills, as well as motor, perceptual, and episodic memory functions [58; 68]; and the Free and Cued Selective Reminding test (8/16), which also assesses learning [11; 39]. One team indicates that in the follow-up, they change the Rey-Osterrieth Complex Figure Test we use the Modified Taylor complex figure [15]. Other measures of attention and concentration included the D2 Attention test (5/16) [10]; and the Paced Auditory Serial Addition Test (4/16) [34], which also requires calculation. Another task to assess calculation has involved asking participants to do one addition, one subtraction and one multiplication (9/16) [28]. *Executive functions* (i.e., cognitive control, attention, response inhibition) were evaluated with the Trail Making Test (11/16) [20], and the Stroop Test (9/16) [12; 84; 90; 94].

Choice of tests and questionnaires

Most centres tailored the choice of tasks according to tumour location, (yes: 15/21; no: 6/21; chi-square(1)=6.10, p=0.014, two tailed). Centres that chose tasks according to tumour location sometimes included additional perioperative tasks. The most common addition to the perioperative battery was the Bell’s Cancellation Test [30], which was used to assess visual inattention and spatial neglect (8/15). The Reading the Mind in the Eyes test was also frequently added [2], in order to assess low-level emotion recognition/mentalising (7/15). Finally, the number of centres that used quality of life was higher than those that did not use them (yes: 13/19, no:6/19). However, these values fell just short of statistical significance (chi-square[1]=3.79, p=0.052, two tailed).

Preoperative assessments

With regards to preoperative assessments, most centres systematically assessed patients one month (7/21) or one week before surgery (7/21), compared to centres that perform assessments one day before surgery (3/21), or on a more varied schedule: between one month or one week before surgery (4/10), one day or one month before surgery (1/10), one day or one week before surgery (1/10), or one day, one week, or one month before surgery (1/10) (Fisher's Exact test[6]=16.76, p=0.004, two tailed). The total time dedicated to the preoperative assessment amounted to more than one hour in all centres (21/21). The majority of centres used timed tasks (i.e., any task where stimulus presentation is 4 seconds and the patient is asked to respond in 4 seconds) in the preoperative assessments, although these differences were not significant (used timed tasks 12/19; did not use timed tasks 7/12, chi-square[1]=1.68, p=0.194, two tailed).

Intraoperative assessments

Regarding tests for intraoperative mapping, Object naming [e.g., 16; 24; 51; 75] was used in all centres (21/21), followed by reading (12/21) [e.g., 31], a semantic association task (11/21) [38], repetition (9/21), and action naming (2/21) [e.g., 46; 72]. Twelve centres asked participants to perform a motor task whilst giving answers to object naming or carrying out another intraoperative task (i.e., a double task [18]). This number was not significantly different from that of centres which did not include a motor task (included a double task: 12/21; did not include a double task: 9/12; chi-square[1]=0.38, p=0.537, two tailed). Depending on tumour location, for example, for temporoparietal lesions in the right hemisphere as well as lesions in the optic radiations, centres added a line bisection task (12/17) where patients are asked to indicate the centre of one or more straight black lines [8; 41]; also, a visual field task (12/17) where patients are instructed to fixate a red cross located in the midpoint of the screen and name (or read the name of) objects located in two or four quadrants of the image [33; 71]. For patients harbouring other lesions, for example, those located in the right frontal lobe, a smaller number of centres included a Reading the Mind in the Eyes test (4/17) [2]. Some centres also indicated the use of a double task depending on tumour location (11/17).

For the awake surgery, the majority of centres did not use hypnosis (no hypnosis: 19/20; yes hypnosis: 1/20, Fisher's Exact test[1]=30.85, p=0.001, two tailed). However, seven centres expressed interest in developing this technique (considers hypnosis interesting for awake surgery: 7/18; does not consider hypnosis interesting for awake surgery: 11/18; chi-square[1]=1.00, p=0.317, two tailed).

Postoperative assessments

Most centres performed immediate postoperative assessments within 3 to 5 days after surgery, although comparable numbers of centres referred patients for postoperative assessments earlier or later than 3 to 5 days (1 to 2 days after: 4/20; 3 to 5 days after: 10/20; more than 5 days after: 6/20; Fisher's Exact test[2]=4.02, p=0.160, two tailed). Regarding the issue of cognitive rehabilitation, significantly more centres recommended to start rehabilitation immediately after surgery, as opposed to centres that recommended commencing 1-3 months after surgery (rehabilitation right after surgery: 15/20; rehabilitation 1-3 months after: 5/20; chi-square[1]=8.10, p=0.004, two tailed). The number of centres that did and did not know about work resumption was not significantly different (knew about work resumption: 8/20; did not know about work resumption: 12/20; chi-square[1]=0.90, p=0.343, two tailed). Among the 8 centres that knew about it, resumption rate was estimated at 80-90% by four, and 50 to 65% by two others. The remaining two centres did not respond to this question.

Discussion

Fifteen questions regarding cognitive aspects of the ELGGN survey were analysed [see 50 for a summary of the whole survey]. Survey compliance was high, as evidence by complete responses from 21/28 centres, spanning 11 European countries. This work regarding commonalties among expert centres in the managing of DLGG in Europe and further discussions within the ELGGN should bring us towards the development of a European assessment protocol.

Personnel involved

Centres typically identified one or two Neuropsychologists or Speech and Language Therapists as responsible for perioperative and intraoperative assessments for a particular patient. Having the same professional assessing the patient at all stages seems relevant to achieve a more accurate picture of the patient's cognitive profile, personality, and needs, which should hopefully result in a better understanding of how to tailor intraoperative tests and to perform intraoperative monitoring procedures. In addition, postoperative follow-up assessments by the same professional are also better suited for a timely detection of cognitive changes over time.

Neuropsychologists and speech therapists have complementary expertise, and their roles and responsibilities may differ across countries and even centres within the same country. However, both skills are desirable and needed in a professional team. Therefore, investing in such professionals is of the uttermost importance for the correct managing of people with DLGGs. Only few reports dealt with this aspect in the literature, but published reports pointed to the pivotal importance of the two disciplines [6; 19; 25]. The role of Occupational Therapists was not examined in this survey, although in some centres they provide very valuable support for ward-based assessments and input for patients needing rehabilitation for cognitive deficits. This aspect can be examined more thoroughly in a future survey.

One of the centres indicated the use of computerised self-testing. This relatively novel assessment method could prove useful in order to collect information on patient-reported outcomes that do not demand the presence of an experienced language and cognitive expert. Examples of these outcomes are health-related quality of life or general service experience questionnaires [54; 40]. Also, it could minimise direct assessment time. Future work could evaluate the validity of computerised self-testing for preoperative and follow-up assessments of cognitive/linguistic skills. Since patients in preoperative sessions are also briefed on the intraoperative procedure, in the same sessions it would be useful to understand their needs, above and beyond strictly psychometric measures. Patients may be enquired about their hobbies, personality, assessed for general compliance with tasks, etc. Then, given a cognitive neuropsychological approach, the investigator may decide to vary the administration of tasks depending on the patient’s performance during the session. Likewise, future work will indicate whether computerised self-testing may be recommended for long-term follow-ups. For example, a professional could be sent an on-line warning on the patient’s performance, and then be asked to call the patient if further assessments or cognitive or language rehabilitation are deemed necessary. Having said that, computerised testing should not substitute a neuropsychologist and/or speech therapist in the operating room. These professionals are experts in the administration and interpretation of the results, and their online interaction with the neurosurgeon and other members of the surgical team is crucial to achieve optimal functional and oncological outcomes of DLGG management.

Core testing battery

Regarding a core of testing, semantic and phonological fluency tests were the most used in the perioperative stages. This could be because these tasks do not require specific materials, are fast to administer (i.e., one minute per test), and have been widely included in test batteries. They also have a good test-retest reliability, which makes them particularly useful to track changes in performance between perioperative stages [e.g., r = 0.74 for phonological fluency in an interval of more than five years in elderly individuals, 89]. Fluency tests are known to assess executive functions, although they also have a strong language component, which makes them useful also in people with left hemisphere lesions. At the neuroanatomical level, performance in both semantic and phonological fluency tasks recruits frontal lobe areas, while semantic fluency tasks typically recruit more areas in the left temporal lobe, which has been long argued to be a hub for semantic processing [1; 35; 62]. Despite their usefulness, fluency tasks alone may not be used to decide whether or not the patient has a cognitive or even executive deficit. In fact, no single task may serve for that purpose, as overreliance on abnormal performance on one task alone could lead to a misleading diagnosis [7]. In other words, understanding the capacities of each individual requires a comprehensive assessment, which can be reduced to a small number of tasks, but must include tasks that tap on different cognitive processes. Furthermore, to obtain an exhaustive picture any results are best discussed in a consensus meeting with other professionals of the team (e.g., radiology, neurosurgery, anaesthesiology, etc).

Choice of tests and questionnaires

A list with common preoperative and intraoperative tests is shown in Table 2. The list is not exhaustive. In fact, no surgical team uses all tasks, and in no case all tasks are used with each individual patient. A description of the tasks and commonly reported areas during intraoperative mapping can be found in the supplementary materials.

[Please add Table 2 around here]

Many teams included tasks that assess language processing, memory, attention, and other executive functions. In addition to fluency tasks, awake surgery centres included at least one language production task (i.e., Object naming), one semantic association task (i.e., Pyramids and Palm Trees test), and two tasks to assess executive functions – such as the Trail Making Test [20] and the Stroop Test (9/16) [12; 84; 90; 94]. Tasks used to assess attention and working memory were more diversified, even though the Forward and Backward Digit Span [52; 57; 87]; and the Rey-Osterrieth Complex Figure Test (11/16) were among the most commonly used. There also seemed to be an interest in using a simple calculation task [28]. The frequent usage of the abovementioned tasks in European awake surgery is similar in neuropsychological services for other neurological disorders [13; 65]. Exceptions to this are the use of the Pyramids and Palm Trees test for semantic association [38] and the use of calculation tasks [28] - these latter tasks are not as commonly used in the assessment of other neurological populations [13; 65].

More centres selected tasks according to tumour location than irrespective of it. This indicates an interest in translating state-of-the-art knowledge in cognitive neuropsychology and cognitive neuroscience into neurosurgical practice [17; 22; 26; 18; 74; 92]. The interest in different areas of language and cognition within the neurosurgical community resembles the assessment practices and test usage patterns in other clinical and experimental contexts [65]. In fact, attention, executive functions, nonverbal memory and language are among the domains most frequently assessed by cognitive professionals, regardless of the population that is being assessed (i.e., range 83-98% of the time).

Preoperative assessments

More centres assessed patients one month or one week before surgery as opposed to one day before surgery. We are unaware of studies that focus on establishing the best timing for preoperative assessments. In general, allowing a longer interval between the cognitive assessment and the operation may be preferable to testing immediately before surgery. In the first place, it is unlikely that a DLGG will significantly increase in size in a matter of 2-4 weeks. In addition, this approach would reduce the likelihood of false positives resulting from immediate preoperative stress, and would give sufficient time to prepare surgery and organise intraoperative testing (intraoperative tasks must be adapted to the patient's profile and cognitive performance). All centres dedicated more than one hour to the assessment of patients, which may resemble reports on general practices in testing services [e.g., 13]. In these reports, centres indicated a mean time of 3.5-4.24 hours to administer, score, and interpret a full battery of tests.

Also in line with current advances, the participating centres used timed tasks. This aspect is relevant in people with brain tumours undergoing awake surgery for three main reasons: people with DLGG do not normally present severe language or cognitive impairments, even long after surgery [60; 64; 78; 79]; response times in lexical access tasks correlate with the ability to return to work after surgery [54]; and intraoperative tasks are timed to the maximum safe duration of direct electrical stimulation of the brain (i.e., 4 seconds), as longer electrical stimuli significantly increase seizure risk [85]. The fact that many intraoperative tasks are necessarily timed, poses serious constraints on the tasks that can be implemented during surgery (and especially during language or cognitive mapping). However, the same tasks that cannot be administered during surgery because of time constraints, may be used to assess relevant cognitive processes in the perioperative stages.

Intraoperative assessments

Language tasks

Language tasks are most commonly used for intraoperative mapping. In particular, Object naming [e.g., 16; 24; 51; 75] was used in all centres. It is worth stressing that other centres reported using tasks that tackle other language domains, such as Reading [e.g., 31], Semantic association [38], or naming tasks that use other word categories, such as Action naming tasks [e.g., 46; 74]. These details again indicate an interest in understanding the language components involved in each task and in comparing the intraoperative results of Object naming (the current standard) with newer or less used tasks.

Spontaneous speech tasks may be useful for language monitoring during tumour resection. These tasks resemble communication in everyday life as they require the patient to talk about everyday topics, or in a more controlled setting, picture description, or storytelling. These tasks may be relevant during tumour resection or in instances were brain stimulation is not applied for language mapping, they may be relevant to form an idea of the patient’s language skills, rather than to decide whether a specific brain area is related to a language function. Additionally, it was recently found that stimulation of the perisylvian cortex during a word repetition task can elicit a range of disruptions, such as auditory processing deficits, and errors like word substitutions, phonological paraphasias, neologisms, perseverations and delays [45]. Furthermore, it has been indicated that words are not sensitive enough for intraoperative procedures. Instead, a non-word repetition task, has been pointed as more sensitive than words and object naming in patients whose tumor removal compromised the vicinity of the arcuate fasciculus [82]. This is valuable information as spontaneous speech tasks and repetition tasks are a relatively easy administer in a clinical setting. Further work seems necessary as any task has its advantages and disadvantages [73]

Double tasks

The number of centres that used a motor task together with a language or cognitive task was not significantly different from the number of centres that did not [18]. This may indicate that further work is needed before double tasks are implemented in all centres. Double tasks are used to assess performance throughout surgery (i.e., monitoring of functions). Some proponents of double (and sometimes triple) tasks argue that they are particularly useful when working at the subcortical level, for example, to assess the negative motor network [66; 67], as well as when working in areas close to the associative cortex. Double tasks are particularly relevant to test whether the patient is able to do both tasks together, as opposed to each task separately. A double task requires more planning, working memory, etc. A patient may be unable to do the double task when a specific area is stimulated, while still being able to perform each task separately during stimulation of the same area [47].

Visuospatial and emotion tasks

Finally, and similarly to the use of tests in perioperative stages (see section on General questions), some centres used tasks that tap on visuospatial inattention and tasks that assess emotional recognition when tumours were not located in areas traditionally related to language processing [26; 33; 36; 61; 71].

Hypnosis

Another aspect of the survey that relates to intraoperative assessments is the use of hypnosis. This aspect of the anesthesiological management of the patient was used in one only centre, but many centres expressed interest in this technique. Therefore, it may be relevant to study the effects of hypnosis on intraoperative mapping and patient monitoring. A description of the method along with its psychological impact on patients has been recently reported [96]. To date, there exist no reports on the feasibility of this method for intraoperative mapping of cognitive functions. Perhaps the first question to ask is whether preoperative assessments with and without hypnosis lead to similar results. After that, it would be relevant to assess whether the intraoperative mapping and monitoring procedure is as effective during hypnosis as it is when the patient is not hypnotised. For example, surgical teams may study the number of intraoperative false errors during mapping (e.g., error responses when electrical stimulation is not applied), or the patient's compliance during monitoring (e.g., use of spontaneous speech tasks, such as picture or story description, to assess the general language capacities of the patient during surgery).

Postoperative assessments

The majority of centres performed immediate postoperative assessments 3 to 5 days after surgery. We did not specifically ask about follow-up assessments at 6 to 12 months or more after surgery. However, some centres pose greater weight on assessments of patients early after surgery (<3 days), while others prefer non-acute stages when the patient's performance is possibly more stable (i.e., 3 to 6 months after surgery). Preferring early vs later assessment times could result from the different meaning that various group attach to perioperative evaluations. Some groups may consider early assessments as they are helpful for the immediate post-operative clinical assessment and care (i.e., early rehabilitation therapy) as well as for research (e.g., transient postoperative disorders and brain plasticity). Other may prefer later assessments as critical for clinical care and research. Further work is needed to clarify this issue. For example, a comprehensive assessment can be performed before surgery and 3 to 6 months after surgery and less demanding and time-consuming tasks in the first week or two after surgery. The same, less demanding test battery can also be repeated when a broad but less detailed picture of the patient's cognitive status is required (e.g., language assessment using spontaneous speech and yes/no questions to evaluate language; fluency tasks to examine executive functions). A future survey may also consider how this factor interferes with the fact that, in some countries, patients may be operated on in centres of reference and then referred for follow-up assessments close to their place of residence.

More centres preferred early than late rehabilitative intervention in people with DLGG. Further work is needed in this area. The number of studies that looked at rehabilitation in people with primary brain tumours is particularly small and therefore evidence supporting an optimal time for rehabilitation is scarce [42; 43]. Also, there were no differences in the number of centres that knew and did not know about the rate of work resumption. Yet, the fact that across centres the resumption rate ranged between 50-90% seems positive, as it indicates that many patients may successfully continue with their lives after DLGG surgery.

Towards a European assessment protocol

A European assessment protocol for the managing of DLGGs may include recommendations regarding which core tasks should be used, which additional tasks may be presented for a thorough evaluation, as well as administration strategies for both sets of tasks. The idea behind such a protocol is to decide on a minimum set of measures that are commonly administered by all centres, and reported in their studies. This methodology facilitates comparisons between centres, simplifies the design of new trials, and reduces the risk of biasing the results by reporting on specific outcomes. The development of such a protocol requires the expertise of multiple professionals and should be the outcome of preliminary work, for example, further reviews/surveys of tests and practises, a consensus conference and a position paper. A formal approach to reach this goal is to follow the Core Outcomes Measures in Effectives Trials Initiative [COMET, 95]. This procedure seeks the consensus of medical providers, researchers, and patients. Importantly, it is used to point to a series of outcome measures that should be systematically used, but does not hamper centres to contrast and combine these tasks with other measures [93]. We raise three issues to fuel this conversation: how to reach a shared protocol; where to look for the best materials; and how to reach shared guidelines when facing specific situations in a specific language.

Many centres already use a comprehensive approach with similar tasks that tap on various language and cognitive abilities, and that could be implemented in the perioperative stages. Examples of successful sharing of protocols are those used in clinical trials by the European Organisation for Research and Treatment of Cancer [EORTC, 91]. This is a specific protocol for people with brain tumours that includes tasks that have been already adapted in different languages. Testing is supported by a website with forms available in various languages, a training video (in English, but subtitled in some languages) and a certification procedure. Another source is the Fronto Temporal Lobar Degeneration Module of the National Alzheimer's Coordinating Center [NACC FTLD, 3; 44]. This protocol is used by centres working with other neurological disorders, but it could useful because it addresses disorders in which cognitive impairments are particularly mild in initial stages, and evolve slowly. It includes a standardised diagnostic checklist, caregiver and examiner scales, and tasks that tap on different cognitive domains in a comprehensive manner. Above all, further work seems necessary to decide on a general protocol that may be administered to all patients, and on specific tests that may be selected on a patient-specific basis. The later aspect is particularly relevant at the intraoperative level, given that the lack of time and specific needs of each patient reduce the number of tasks to a bare minimum.

It is also essential to decide which tasks are most appropriate for the disorders observed in people with DLGGN. This survey indicated that, despite the abovementioned similarities, in many cases the tasks used across centres are not homogeneous. For example, most centres use Object naming in different surgical stages to tap on semantic access and lexical retrieval. Yet, different centres, even in the same country, may use different tasks or different standardisations of the same task, which creates problems when it comes to comparing the performance of patients across centres. In this regard, an agreement would have to exist as to which cognitive tasks may be used. As regards language, a possibility is to adapt the Dutch Linguistic Intraoperative Protocol [24] in several languages. The DULIP includes tasks that tap on different language levels, and that were developed to be used in DLGGN patients. The work of the Collaboration of Aphasia Trialists (CATs) could be followed for that purpose. The CATs is a European network of language experts that is currently adapting a comprehensive language assessment to more than 10 different languages spoken in Europe [9]. The materials that the CATs is adapting are intended for use in people with aphasia after stroke. Hence, they may not be suitable for use in people with DLGGN. However, some members of the CATs are also members of the ELGGN, and there are also other members that have vast experience adapting excellent test materials in different languages. Some critical issues must be solved if one if to proceed along this route, such as financing the design and publication of test materials and paying for research assistants and healthy individuals to norm the tasks.

Finally, more information is necessary to decide on shared guidelines regarding which clinical and surgical decisions are best taken in any given situation. Specific to cognitive testing, some centres may decide to always use the same basic cognitive work-up for clinical purposes, whereas others may choose to administer additional tasks for more detailed clinical or research purposes. For example, a general protocol may be administered to all patients, and specific tests may be selected on a patient-specific basis (e.g., based on tumour location). Some centres may also wish to administer extra tasks and compare them to current standards to assess their clinical relevance. This approach seems possible given that the current commonalities and shared clinical/scientific interests among centres open the door to the discussion of an agreed-upon assessment protocol across centres.

Conclusion

We described common practices of 21 centres across 11 European countries. We must await replication, possibly through collaboration with more European centres and many other non-European centres. Many commonalities exist regarding the professionals involved in assessing and managing cognitive aspects in people with DLGG. Very clever initiatives are ongoing, and there is ample room for progress. The data indicates an emerging *de facto* standard of care, shared by expert centres in Europe. A future survey may include questions that tackle the relevance of adapting tasks into different languages; cost-effectiveness of different team members; cognitive impact of the therapies for DLGG used after surgery; new language treatment programs aiming at rehabilitating mild cognitive disorders; etc. The ELGGN provides an intellectual network to discuss these commonalities and to understand new aspects that may be implemented in the near future, possibly within a European assessment protocol.

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Tables

Table 1 Cognitive questions of the ELGGN survey

General questions
Q1 In your centre, perioperative cognitive assessments are performed by
Q2 Are perioperative assessments and intraoperative assessments performed by the same person?
Q3 What is your minimal core of tests?
Q4 Do you select tests according to tumour location?
Q5 If yes, what other tests do you use according to tumour location?
Q6 Do you use a Quality of life questionnaire?
Preoperative assessments
Q7 Timewise, the preoperative cognitive assessment is performed
Q8 How long does the preoperative cognitive assessment last?
Q9 Are preoperative tasks timed?
Intraoperative assessments
Q10 Does your team practise hypnosis to patients during awake surgery?
Q11 Do you think it would be interesting to introduce hypnosis in your practice of awake surgery?
Q12 Which tasks do you use for intraoperative language assessment?
Q13 Which of the following tasks do you add depending on tumour location? Line bisection (spatial consciousness); Visual field Reading the Mind in the Eyes (low-level emotion recognition); Double task (ie adding motor task to one of the previous tasks); Other
Postoperative assessments
Q14 Immediate postoperative cognitive assessment is performed: Between postoperative day 1 or 2; Between postoperative day 3 and 5; After postoperative day 5
Q15 Do you recommend starting rehabilitation: Right after surgery; 1 to 3 months after a recovery period; only in case of permanent deficit after a 6 to 12 months follow-up
Q16 Do you know the rate of work resumption after awake surgery in your institution?

Table 2 Commonly reported tasks per cognitive domain, as reported in the survey

<u>Perioperative assessments</u>	
Language	Object naming Pyramids and Palm Trees Test (semantic association) Phonological and semantic verbal fluency
Attention and working memory	Forward and Backward Digit Span Rey-Osterrieth Complex Figure Test Free and Cued Selective Reminding Test D2 Attention test Paced Auditory Serial Addition Test Calculation (addition, subtraction, multiplication)
Executive functions	Trial Making Test Stroop Test Phonological and semantic verbal fluency
Visual inattention	Bell's Cancellation Test
Emotion recognition	Reading the Mind in the Eyes test
<u>Intraoperative assessments</u>	
Language	Object naming Action naming Reading Pyramids and Palm Trees Test (semantic association) Word Repetition
Visual inattention	Line bisection Visual field task
Emotion recognition	Reading the Mind in the Eyes Test

Survey on current cognitive practices within the European Low Grade Glioma Network: towards a European assessment protocol

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Abbreviations:
ELGGN = European Low Grade Glioma Network;
DLGG = Diffuse Low Grade Glioma;

Abstract

Background: The European Low Grade Glioma network indicated a need to better understand common practices regarding the managing of Diffuse Low Grade Gliomas. This area has experienced great advances in recent years.

Method: A general survey on the managing of diffuse low grade gliomas was answered by 21 centres in 11 European countries. Here we focused on specific questions regarding perioperative and intraoperative cognitive assessments.

Results: More centres referred the same Speech and Language therapist and/or Neuropsychologist across all assessments; a core of assessment tools was routinely used across centres; fluency tasks were commonly used in the perioperative stages, and Object naming during surgery; tasks that tapped on attention, executive functions, visuospatial awareness, calculation and emotions were sparsely administered; preoperative assessments were performed one month or one week before surgery; timing for postoperative assessments varied; finally, more centres recommended early rehabilitation, whenever needed.

Conclusion: There is an emerging trend towards following similar practices for the management of low grade gliomas in Europe. Our results are descriptive and formalize current discussions in our group. Also, they contribute towards the development of a European assessment protocol.

Keywords: diffuse low-grade-glioma, surgery, cognition, assessment, survey, protocol

Introduction

The European Low Grade Glioma Network (ELGGN) is a discussion group for research and management of primary brain tumours, particularly, diffuse low grade gliomas (DLGG). Access to the collaboration is free and open to professionals working in neurosurgery, anaesthesiology, molecular biology, radiotherapy, oncology, occupational therapy, neurology, neuroimaging, cognitive and language assessment, and related topics[1]. Since 2006, the collaboration has quadrupled its size (currently, 208 registered members). The ELGGN organises an annual meeting that each year takes place in a different European site. The meetings are an excellent opportunity for interdisciplinary and intergenerational discussion and learning. These include talks by relevant keynote speakers; hands-on courses on varied topics such as cadaveric brain dissection, and tractography; and small-group discussions led by leaders in the field.

In this article we summarise the results and follow-up discussions of the cognitive part of a survey on current practices among members of the ELGGN. A review and discussion of the whole survey, which was presented at the 11th meeting of the collaboration (June 2015), can be found in another manuscript [50]. For the first time, we review the common practices of a wide number of European awake surgery teams regarding language and cognition in people with DLGG [for general reviews see 13 and 65]. These areas have experienced great advances in recent years – many of which have been put forward by members of the Network. For example, seminal neurosurgical papers have been revisited and evaluated from a cognitive neuropsychological and neuroscientific perspective, also indicating which tests may be more suitable for intraoperative brain mapping depending on tumour localisation and/or the desired surgical approach [17; 22; 26; 74; 92]; new tests, test batteries and methods for perioperative (i.e., pre- and postoperative) and intraoperative assessments have been developed and standardised in different European languages [24; 29; 31; 32; 36; 48; 49; 53; 59; 70; 75; 76; 77; 83; 86; 94]; the role of cortical and subcortical brain structures has been looked at to scrutinise the types of errors that are more likely to appear during direct brain stimulation in individual subjects [4; 5; 21; 23; 27; 36; 69; 80; 81]; and the behavioural profile of people with

[1]More information and registration can be obtained in the ELGGN website: www.braintumours.eu

DLGG has been comprehensively studied at all stages, including long term follow-up and quality of life assessments [40; 54; 60; 64; 78; 79].

In this article we review the common practices adopted for intraoperative and perioperative assessment by the ELGGN peers. This work contributes to a better understanding of the current state-of-the-art in this field. Its main aim is descriptive, not prescriptive. This implies that frequent answers to one or more of the questions describe current practises, not necessarily recommendations to other centres. Future research may be planned to indicate assessment baselines from which to recommend effective postoperative rehabilitation protocols; to explain and to predict the patient's performance over time; and to report tests that other centres may consider in order to assess, map and monitor the patient while minimising postoperative functional injury. Future discussions within the ELGGN should lead towards the development of a European assessment protocol that could allow comparisons across different centres, languages, and cultures.

Methods

In May 2015, a Google Forms survey was sent to 28 centres where members of the ELGGN are located. Only one survey form could be filled in by each centre, and it was recommended that each centre would complete it in an interdisciplinary consensus meeting. The complete survey contained 69 questions. It was divided in 10 sections following the common pathway of events that a person with a DLGG typically undergoes (i.e., preoperative cognitive assessment; neuroimaging; initial management; intraoperative anaesthetic management; intraoperative cognitive assessment; postoperative cognitive assessment; molecular biology and neuropathology; postoperative strategy; choice and follow-up chemotherapy; and radiation therapy). The full list of the questions can be found in the general manuscript, which has been published elsewhere [49]. In this article, we discuss replies to the 15 questions of the survey that are most relevant to cognitive assessments (see Table 1). Non-parametric statistics were performed to decide whether any response was significantly more frequent than others.

[Please add Table 1 around here]

Results

Complete answers to the survey were obtained from 21 centres in 11 European countries: Austria (Innsbruck); France (Besançon, Montpellier, Nancy, Nice, Paris Lariboisière, Paris Saint-Anne, Poitiers); Germany (Frankfurt); Greece (Thessaloniki); Italy (Brescia, Catania, Udine, Milan); Netherlands (Tilburg); Portugal (Lisbon); Spain (Santander); Sweden (Uppsala); Switzerland (Lausanne); and UK (Cambridge, Leeds). This corresponds to 75% of the centres that we contacted, 23% of which were based in France (7/21). Some questions were not answered by all centres. Therefore, we performed statistical analyses based on the number of total respondents for each question, which we indicated in parenthesis as follows (i.e., number of respondents/total number of respondents).

Personnel involved

In all centres, perioperative assessments were commonly pursued by a Neuropsychologist and/or a Speech and Language Therapist. We encountered no significant differences regarding the type of professional that centres appointed to perform the assessments (Fisher's Exact Test[5]=8.42, p=0.116, two-tailed). The majority of centres appointed only a Neuropsychologist (6/21); a Speech and Language Therapist or a Neuropsychologist (6/21); or both a Speech and Language Therapist and a Neuropsychologist (6/21) to perform these assessments. Less centres appointed only a Speech and Language Therapist (2/21) or a Neuropsychologist alone with the addition of self-computerised testing (1/21). We did not specifically ask about the role of Occupational Therapists and other professionals in this survey. Perioperative assessments were administered more often by the same person who performed the intraoperative assessment, as opposed to a different person (always the same person: 13/21; almost always the same person: 6/21; not so often the same person: 2/21; Fisher's Exact Test =13.12, p=0.002, two tailed).

Core testing battery

Sixteen of twenty-one centres answered to this question. All sixteen centres used phonological and semantic verbal fluency tasks (16/16), which evaluate executive functions and have a strong verbal component [e.g., 14; 55; 88]. Language processing was evaluated with Object Naming (10/16) [e.g., 16; 24; 51; 75] and a semantic association task, particularly, the Pyramids and Palm Trees Test (9/16) [i.e., PPTT, 38]. Attention and working memory were evaluated with the Forward and Backward Digit Span (12/16) [52; 57; 87]; the copy and the long-term reproduction of the Rey-Osterrieth Complex Figure Test (11/16), which are also used to assess planning, problem-solving strategies, organisational skills, as well as motor, perceptual, and episodic memory functions [58; 68]; and the Free and Cued Selective Reminding test (8/16), which also assesses learning [11; 39]. One team indicates that in the follow-up, they change the Rey-Osterrieth Complex Figure Test we use the Modified Taylor complex figure [15]. Other measures of attention and concentration included the D2 Attention test (5/16) [10]; and the Paced Auditory Serial Addition Test (4/16) [34], which also requires calculation. Another task to assess calculation has involved asking participants to do one addition, one subtraction and one multiplication (9/16) [28]. *Executive functions* (i.e., cognitive control, attention, response inhibition) were evaluated with the Trail Making Test (11/16) [20], and the Stroop Test (9/16) [12; 84; 90; 94].

Choice of tests and questionnaires

Most centres tailored the choice of tasks according to tumour location, (yes: 15/21; no: 6/21; chi-square(1)=6.10, p=0.014, two tailed). Centres that chose tasks according to tumour location sometimes included additional perioperative tasks. The most common addition to the perioperative battery was the Bell’s Cancellation Test [30], which was used to assess visual inattention and spatial neglect (8/15). The Reading the Mind in the Eyes test was also frequently added [2], in order to assess low-level emotion recognition/mentalising (7/15). Finally, the number of centres that used quality of life was higher than those that did not use them (yes: 13/19, no:6/19). However, these values fell just short of statistical significance (chi-square[1]=3.79, p=0.052, two tailed).

Preoperative assessments

With regards to preoperative assessments, most centres systematically assessed patients one month (7/21) or one week before surgery (7/21), compared to centres that perform assessments one day before surgery (3/21), or on a more varied schedule: between one month or one week before surgery (4/10), one day or one month before surgery (1/10), one day or one week before surgery (1/10), or one day, one week, or one month before surgery (1/10) (Fisher's Exact test[6]=16.76, p=0.004, two tailed). The total time dedicated to the preoperative assessment amounted to more than one hour in all centres (21/21). The majority of centres used timed tasks (i.e., any task where stimulus presentation is 4 seconds and the patient is asked to respond in 4 seconds) in the preoperative assessments, although these differences were not significant (used timed tasks 12/19; did not use timed tasks 7/12, chi-square[1]=1.68, p=0.194, two tailed).

Intraoperative assessments

Regarding tests for intraoperative mapping, Object naming [e.g., 16; 24; 51; 75] was used in all centres (21/21), followed by reading (12/21) [e.g., 31], a semantic association task (11/21) [38], repetition (9/21), and action naming (2/21) [e.g., 46; 72]. Twelve centres asked participants to perform a motor task whilst giving answers to object naming or carrying out another intraoperative task (i.e., a double task [18]). This number was not significantly different from that of centres which did not include a motor task (included a double task: 12/21; did not include a double task: 9/12; chi-square[1]=0.38, p=0.537, two tailed). Depending on tumour location, for example, for temporoparietal lesions in the right hemisphere as well as lesions in the optic radiations, centres added a line bisection task (12/17) where patients are asked to indicate the centre of one or more straight black lines [8; 41]; also, a visual field task (12/17) where patients are instructed to fixate a red cross located in the midpoint of the screen and name (or read the name of) objects located in two or four quadrants of the image [33; 71]. For patients harbouring other lesions, for example, those located in the right frontal lobe, a smaller number of centres included a Reading the Mind in the Eyes test (4/17) [2]. Some centres also indicated the use of a double task depending on tumour location (11/17).

For the awake surgery, the majority of centres did not use hypnosis (no hypnosis: 19/20; yes hypnosis: 1/20, Fisher's Exact test[1]=30.85, p=0.001, two tailed). However, seven centres expressed interest in developing this technique (considers hypnosis interesting for awake surgery: 7/18; does not consider hypnosis interesting for awake surgery: 11/18; chi-square[1]=1.00, p=0.317, two tailed).

Postoperative assessments

Most centres performed immediate postoperative assessments within 3 to 5 days after surgery, although comparable numbers of centres referred patients for postoperative assessments earlier or later than 3 to 5 days (1 to 2 days after: 4/20; 3 to 5 days after: 10/20; more than 5 days after: 6/20; Fisher's Exact test[2]=4.02, p=0.160, two tailed). Regarding the issue of cognitive rehabilitation, significantly more centres recommended to start rehabilitation immediately after surgery, as opposed to centres that recommended commencing 1-3 months after surgery (rehabilitation right after surgery: 15/20; rehabilitation 1-3 months after: 5/20; chi-square[1]=8.10, p=0.004, two tailed). The number of centres that did and did not know about work resumption was not significantly different (knew about work resumption: 8/20; did not know about work resumption: 12/20; chi-square[1]=0.90, p=0.343, two tailed). Among the 8 centres that knew about it, resumption rate was estimated at 80-90% by four, and 50 to 65% by two others. The remaining two centres did not respond to this question.

Discussion

Fifteen questions regarding cognitive aspects of the ELGGN survey were analysed [see 50 for a summary of the whole survey]. Survey compliance was high, as evidence by complete responses from 21/28 centres, spanning 11 European countries. This work regarding commonalties among expert centres in the managing of DLGG in Europe and further discussions within the ELGGN should bring us towards the development of a European assessment protocol.

Personnel involved

Centres typically identified one or two Neuropsychologists or Speech and Language Therapists as responsible for perioperative and intraoperative assessments for a particular patient. Having the same professional assessing the patient at all stages seems relevant to achieve a more accurate picture of the patient's cognitive profile, personality, and needs, which should hopefully result in a better understanding of how to tailor intraoperative tests and to perform intraoperative monitoring procedures. In addition, postoperative follow-up assessments by the same professional are also better suited for a timely detection of cognitive changes over time.

Neuropsychologists and speech therapists have complementary expertise, and their roles and responsibilities may differ across countries and even centres within the same country. However, both skills are desirable and needed in a professional team. Therefore, investing in such professionals is of the uttermost importance for the correct managing of people with DLGGs. Only few reports dealt with this aspect in the literature, but published reports pointed to the pivotal importance of the two disciplines [6; 19; 25]. The role of Occupational Therapists was not examined in this survey, although in some centres they provide very valuable support for ward-based assessments and input for patients needing rehabilitation for cognitive deficits. This aspect can be examined more thoroughly in a future survey.

One of the centres indicated the use of computerised self-testing. This relatively novel assessment method could prove useful in order to collect information on patient-reported outcomes that do not demand the presence of an experienced language and cognitive expert. Examples of these outcomes are health-related quality of life or general service experience questionnaires [54; 40]. Also, it could minimise direct assessment time. Future work could evaluate the validity of computerised self-testing for preoperative and follow-up assessments of cognitive/linguistic skills. Since patients in preoperative sessions are also briefed on the intraoperative procedure, in the same sessions it would be useful to understand their needs, above and beyond strictly psychometric measures. Patients may be enquired about their hobbies, personality, assessed for general compliance with tasks, etc. Then, given a cognitive neuropsychological approach, the investigator may decide to vary the administration of tasks depending on the patient’s performance during the session. Likewise, future work will indicate whether computerised self-testing may be recommended for long-term follow-ups. For example, a professional could be sent an on-line warning on the patient’s performance, and then be asked to call the patient if further assessments or cognitive or language rehabilitation are deemed necessary. Having said that, computerised testing should not substitute a neuropsychologist and/or speech therapist in the operating room. These professionals are experts in the administration and interpretation of the results, and their online interaction with the neurosurgeon and other members of the surgical team is crucial to achieve optimal functional and oncological outcomes of DLGG management.

Core testing battery

Regarding a core of testing, semantic and phonological fluency tests were the most used in the perioperative stages. This could be because these tasks do not require specific materials, are fast to administer (i.e., one minute per test), and have been widely included in test batteries. They also have a good test-retest reliability, which makes them particularly useful to track changes in performance between perioperative stages [e.g., r = 0.74 for phonological fluency in an interval of more than five years in elderly individuals, 89]. Fluency tests are known to assess executive functions, although they also have a strong language component, which makes them useful also in people with left hemisphere lesions. At the neuroanatomical level, performance in both semantic and phonological fluency tasks recruits frontal lobe areas, while semantic fluency tasks typically recruit more areas in the left temporal lobe, which has been long argued to be a hub for semantic processing [1; 35; 62]. Despite their usefulness, fluency tasks alone may not be used to decide whether or not the patient has a cognitive or even executive deficit. In fact, no single task may serve for that purpose, as overreliance on abnormal performance on one task alone could lead to a misleading diagnosis [7]. In other words, understanding the capacities of each individual requires a comprehensive assessment, which can be reduced to a small number of tasks, but must include tasks that tap on different cognitive processes. Furthermore, to obtain an exhaustive picture any results are best discussed in a consensus meeting with other professionals of the team (e.g., radiology, neurosurgery, anaesthesiology, etc).

Choice of tests and questionnaires

A list with common preoperative and intraoperative tests is shown in Table 2. The list is not exhaustive. In fact, no surgical team uses all tasks, and in no case all tasks are used with each individual patient. A description of the tasks and commonly reported areas during intraoperative mapping can be found in the supplementary materials.

[Please add Table 2 around here]

Many teams included tasks that assess language processing, memory, attention, and other executive functions. In addition to fluency tasks, awake surgery centres included at least one language production task (i.e., Object naming), one semantic association task (i.e., Pyramids and Palm Trees test), and two tasks to assess executive functions – such as the Trail Making Test [20] and the Stroop Test (9/16) [12; 84; 90; 94]. Tasks used to assess attention and working memory were more diversified, even though the Forward and Backward Digit Span [52; 57; 87]; and the Rey-Osterrieth Complex Figure Test (11/16) were among the most commonly used. There also seemed to be an interest in using a simple calculation task [28]. The frequent usage of the abovementioned tasks in European awake surgery is similar in neuropsychological services for other neurological disorders [13; 65]. Exceptions to this are the use of the Pyramids and Palm Trees test for semantic association [38] and the use of calculation tasks [28] - these latter tasks are not as commonly used in the assessment of other neurological populations [13; 65].

More centres selected tasks according to tumour location than irrespective of it. This indicates an interest in translating state-of-the-art knowledge in cognitive neuropsychology and cognitive neuroscience into neurosurgical practice [17; 22; 26; 18; 74; 92]. The interest in different areas of language and cognition within the neurosurgical community resembles the assessment practices and test usage patterns in other clinical and experimental contexts [65]. In fact, attention, executive functions, nonverbal memory and language are among the domains most frequently assessed by cognitive professionals, regardless of the population that is being assessed (i.e., range 83-98% of the time).

Preoperative assessments

More centres assessed patients one month or one week before surgery as opposed to one day before surgery. We are unaware of studies that focus on establishing the best timing for preoperative assessments. In general, allowing a longer interval between the cognitive assessment and the operation may be preferable to testing immediately before surgery. In the first place, it is unlikely that a DLGG will significantly increase in size in a matter of 2-4 weeks. In addition, this approach would reduce the likelihood of false positives resulting from immediate preoperative stress, and would give sufficient time to prepare surgery and organise intraoperative testing (intraoperative tasks must be adapted to the patient’s profile and cognitive performance). All centres dedicated more than one hour to the assessment of patients, which may resemble reports on general practices in testing services [e.g., 13]. In these reports, centres indicated a mean time of 3.5-4.24 hours to administer, score, and interpret a full battery of tests.

Also in line with current advances, the participating centres used timed tasks. This aspect is relevant in people with brain tumours undergoing awake surgery for three main reasons: people with DLGG do not normally present severe language or cognitive impairments, even long after surgery [60; 64; 78; 79]; response times in lexical access tasks correlate with the ability to return to work after surgery [54]; and intraoperative tasks are timed to the maximum safe duration of direct electrical stimulation of the brain (i.e., 4 seconds), as longer electrical stimuli significantly increase seizure risk [85]. The fact that many intraoperative tasks are necessarily timed, poses serious constraints on the tasks that can be implemented during surgery (and especially during language or cognitive mapping). However, the same tasks that cannot be administered during surgery because of time constraints, may be used to assess relevant cognitive processes in the perioperative stages.

Intraoperative assessments

Language tasks

Language tasks are most commonly used for intraoperative mapping. In particular, Object naming [e.g., 16; 24; 51; 75] was used in all centres. It is worth stressing that other centres reported using tasks that tackle other language domains, such as Reading [e.g., 31], Semantic association [38], or naming tasks that use other word categories, such as Action naming tasks [e.g., 46; 74]. These details again indicate an interest in understanding the language components involved in each task and in comparing the intraoperative results of Object naming (the current standard) with newer or less used tasks.

Spontaneous speech tasks may be useful for language monitoring during tumour resection. These tasks resemble communication in everyday life as they require the patient to talk about everyday topics, or in a more controlled setting, picture description, or storytelling. These tasks may be relevant during tumour resection or in instances were brain stimulation is not applied for language mapping, they may be relevant to form an idea of the patient’s language skills, rather than to decide whether a specific brain area is related to a language function. Additionally, it was recently found that stimulation of the perisylvian cortex during a word repetition task can elicit a range of disruptions, such as auditory processing deficits, and errors like word substitutions, phonological paraphasias, neologisms, perseverations and delays [45]. Furthermore, it has been indicated that words are not sensitive enough for intraoperative procedures. Instead, a non-word repetition task, has been pointed as more sensitive than words and object naming in patients whose tumor removal compromised the vicinity of the arcuate fasciculus [82]. This is valuable information as spontaneous speech tasks and repetition tasks are a relatively easy administer in a clinical setting. Further work seems necessary as any task has its advantages and disadvantages [73]

Double tasks

The number of centres that used a motor task together with a language or cognitive task was not significantly different from the number of centres that did not [18]. This may indicate that further work is needed before double tasks are implemented in all centres. Double tasks are used to assess performance throughout surgery (i.e., monitoring of functions). Some proponents of double (and sometimes triple) tasks argue that they are particularly useful when working at the subcortical level, for example, to assess the negative motor network [66; 67], as well as when working in areas close to the associative cortex. Double tasks are particularly relevant to test whether the patient is able to do both tasks together, as opposed to each task separately. A double task requires more planning, working memory, etc. A patient may be unable to do the double task when a specific area is stimulated, while still being able to perform each task separately during stimulation of the same area [47].

Visuospatial and emotion tasks

Finally, and similarly to the use of tests in perioperative stages (see section on General questions), some centres used tasks that tap on visuospatial inattention and tasks that assess emotional recognition when tumours were not located in areas traditionally related to language processing [26; 33; 36; 61; 71].

Hypnosis

Another aspect of the survey that relates to intraoperative assessments is the use of hypnosis. This aspect of the anesthesiological management of the patient was used in one only centre, but many centres expressed interest in this technique. Therefore, it may be relevant to study the effects of hypnosis on intraoperative mapping and patient monitoring. A description of the method along with its psychological impact on patients has been recently reported [96]. To date, there exist no reports on the feasibility of this method for intraoperative mapping of cognitive functions. Perhaps the first question to ask is whether preoperative assessments with and without hypnosis lead to similar results. After that, it would be relevant to assess whether the intraoperative mapping and monitoring procedure is as effective during hypnosis as it is when the patient is not hypnotised. For example, surgical teams may study the number of intraoperative false errors during mapping (e.g., error responses when electrical stimulation is not applied), or the patient's compliance during monitoring (e.g., use of spontaneous speech tasks, such as picture or story description, to assess the general language capacities of the patient during surgery).

Postoperative assessments

The majority of centres performed immediate postoperative assessments 3 to 5 days after surgery. We did not specifically ask about follow-up assessments at 6 to 12 months or more after surgery. However, some centres pose greater weight on assessments of patients early after surgery (<3 days), while others prefer non-acute stages when the patient's performance is possibly more stable (i.e., 3 to 6 months after surgery). Preferring early vs later assessment times could result from the different meaning that various group attach to perioperative evaluations. Some groups may consider early assessments as they are helpful for the immediate post-operative clinical assessment and care (i.e., early rehabilitation therapy) as well as for research (e.g., transient postoperative disorders and brain plasticity). Other may prefer later assessments as critical for clinical care and research. Further work is needed to clarify this issue. For example, a comprehensive assessment can be performed before surgery and 3 to 6 months after surgery and less demanding and time-consuming tasks in the first week or two after surgery. The same, less demanding test battery can also be repeated when a broad but less detailed picture of the patient's cognitive status is required (e.g., language assessment using spontaneous speech and yes/no questions to evaluate language; fluency tasks to examine executive functions). A future survey may also consider how this factor interferes with the fact that, in some countries, patients may be operated on in centres of reference and then referred for follow-up assessments close to their place of residence.

More centres preferred early than late rehabilitative intervention in people with DLGG. Further work is needed in this area. The number of studies that looked at rehabilitation in people with primary brain tumours is particularly small and therefore evidence supporting an optimal time for rehabilitation is scarce [42; 43]. Also, there were no differences in the number of centres that knew and did not know about the rate of work resumption. Yet, the fact that across centres the resumption rate ranged between 50-90% seems positive, as it indicates that many patients may successfully continue with their lives after DLGG surgery.

Towards a European assessment protocol

A European assessment protocol for the managing of DLGGs may include recommendations regarding which core tasks should be used, which additional tasks may be presented for a thorough evaluation, as well as administration strategies for both sets of tasks. The idea behind such a protocol is to decide on a minimum set of measures that are commonly administered by all centres, and reported in their studies. This methodology facilitates comparisons between centres, simplifies the design of new trials, and reduces the risk of biasing the results by reporting on specific outcomes. The development of such a protocol requires the expertise of multiple professionals and should be the outcome of preliminary work, for example, further reviews/surveys of tests and practises, a consensus conference and a position paper. A formal approach to reach this goal is to follow the Core Outcomes Measures in Effectives Trials Initiative [COMET, 95]. This procedure seeks the consensus of medical providers, researchers, and patients. Importantly, it is used to point to a series of outcome measures that should be systematically used, but does not hamper centres to contrast and combine these tasks with other measures [93]. We raise three issues to fuel this conversation: how to reach a shared protocol; where to look for the best materials; and how to reach shared guidelines when facing specific situations in a specific language.

Many centres already use a comprehensive approach with similar tasks that tap on various language and cognitive abilities, and that could be implemented in the perioperative stages. Examples of successful sharing of protocols are those used in clinical trials by the European Organisation for Research and Treatment of Cancer [EORTC, 91]. This is a specific protocol for people with brain tumours that includes tasks that have been already adapted in different languages. Testing is supported by a website with forms available in various languages, a training video (in English, but subtitled in some languages) and a certification procedure. Another source is the Fronto Temporal Lobar Degeneration Module of the National Alzheimer's Coordinating Center [NACC FTLD, 3; 44]. This protocol is used by centres working with other neurological disorders, but it could useful because it addresses disorders in which cognitive impairments are particularly mild in initial stages, and evolve slowly. It includes a standardised diagnostic checklist, caregiver and examiner scales, and tasks that tap on different cognitive domains in a comprehensive manner. Above all, further work seems necessary to decide on a general protocol that may be administered to all patients, and on specific tests that may be selected on a patient-specific basis. The later aspect is particularly relevant at the intraoperative level, given that the lack of time and specific needs of each patient reduce the number of tasks to a bare minimum.

It is also essential to decide which tasks are most appropriate for the disorders observed in people with DLGGN. This survey indicated that, despite the abovementioned similarities, in many cases the tasks used across centres are not homogeneous. For example, most centres use Object naming in different surgical stages to tap on semantic access and lexical retrieval. Yet, different centres, even in the same country, may use different tasks or different standardisations of the same task, which creates problems when it comes to comparing the performance of patients across centres. In this regard, an agreement would have to exist as to which cognitive tasks may be used. As regards language, a possibility is to adapt the Dutch Linguistic Intraoperative Protocol [24] in several languages. The DULIP includes tasks that tap on different language levels, and that were developed to be used in DLGGN patients. The work of the Collaboration of Aphasia Trialists (CATs) could be followed for that purpose. The CATs is a European network of language experts that is currently adapting a comprehensive language assessment to more than 10 different languages spoken in Europe [9]. The materials that the CATs is adapting are intended for use in people with aphasia after stroke. Hence, they may not be suitable for use in people with DLGGN. However, some members of the CATs are also members of the ELGGN, and there are also other members that have vast experience adapting excellent test materials in different languages. Some critical issues must be solved if one if to proceed along this route, such as financing the design and publication of test materials and paying for research assistants and healthy individuals to norm the tasks.

Finally, more information is necessary to decide on shared guidelines regarding which clinical and surgical decisions are best taken in any given situation. Specific to cognitive testing, some centres may decide to always use the same basic cognitive work-up for clinical purposes, whereas others may choose to administer additional tasks for more detailed clinical or research purposes. For example, a general protocol may be administered to all patients, and specific tests may be selected on a patient-specific basis (e.g., based on tumour location). Some centres may also wish to administer extra tasks and compare them to current standards to assess their clinical relevance. This approach seems possible given that the current commonalities and shared clinical/scientific interests among centres open the door to the discussion of an agreed-upon assessment protocol across centres.

Conclusion

We described common practices of 21 centres across 11 European countries. We must await replication, possibly through collaboration with more European centres and many other non-European centres. Many commonalities exist regarding the professionals involved in assessing and managing cognitive aspects in people with DLGG. Very clever initiatives are ongoing, and there is ample room for progress. The data indicates an emerging *de facto* standard of care, shared by expert centres in Europe. A future survey may include questions that tackle the relevance of adapting tasks into different languages; cost-effectiveness of different team members; cognitive impact of the therapies for DLGG used after surgery; new language treatment programs aiming at rehabilitating mild cognitive disorders; etc. The ELGGN provides an intellectual network to discuss these commonalities and to understand new aspects that may be implemented in the near future, possibly within a European assessment protocol.

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Tables

Table 1 Cognitive questions of the ELGGN survey

General questions
Q1 In your centre, perioperative cognitive assessments are performed by
Q2 Are perioperative assessments and intraoperative assessments performed by the same person?
Q3 What is your minimal core of tests?
Q4 Do you select tests according to tumour location?
Q5 If yes, what other tests do you use according to tumour location?
Q6 Do you use a Quality of life questionnaire?
Preoperative assessments
Q7 Timewise, the preoperative cognitive assessment is performed
Q8 How long does the preoperative cognitive assessment last?
Q9 Are preoperative tasks timed?
Intraoperative assessments
Q10 Does your team practise hypnosis to patients during awake surgery?
Q11 Do you think it would be interesting to introduce hypnosis in your practice of awake surgery?
Q12 Which tasks do you use for intraoperative language assessment?
Q13 Which of the following tasks do you add depending on tumour location? Line bisection (spatial consciousness); Visual field Reading the Mind in the Eyes (low-level emotion recognition); Double task (ie adding motor task to one of the previous tasks); Other
Postoperative assessments
Q14 Immediate postoperative cognitive assessment is performed: Between postoperative day 1 or 2; Between postoperative day 3 and 5; After postoperative day 5
Q15 Do you recommend starting rehabilitation: Right after surgery; 1 to 3 months after a recovery period; only in case of permanent deficit after a 6 to 12 months follow-up
Q16 Do you know the rate of work resumption after awake surgery in your institution?

Table 2 Commonly reported tasks per cognitive domain, as reported in the survey

Perioperative assessments	
Language	Object naming Pyramids and Palm Trees Test (semantic association) Phonological and semantic verbal fluency
Attention and working memory	Forward and Backward Digit Span Rey-Osterrieth Complex Figure Test Free and Cued Selective Reminding Test D2 Attention test Paced Auditory Serial Addition Test Calculation (addition, subtraction, multiplication)
Executive functions	Trial Making Test Stroop Test Phonological and semantic verbal fluency
Visual inattention	Bell's Cancellation Test
Emotion recognition	Reading the Mind in the Eyes test
Intraoperative assessments	
Language	Object naming Action naming Reading Pyramids and Palm Trees Test (semantic association) Word Repetition
Visual inattention	Line bisection Visual field task
Emotion recognition	Reading the Mind in the Eyes Test