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RESEARCH ARTICLE

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Understanding language and cognition after brain surgery – Tumour grade, fine-grained assessment tools and, most of all, individualized approach

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Abstract

Cognitive performance influences the quality of life and survival of people with glioma. Thus, a detailed neuropsychological and language evaluation is essential. In this work, we tested if an analysis of errors in naming can indicate semantic and/or phonological impairments in 87 awake brain surgery patients. Secondly, we explored how language and cognition change after brain tumour resection. Finally, we checked if low-tumour grade had a protective effect on cognition. Our results indicated that naming errors can be useful to monitor semantic and phonological processing, as their number correlated with scores on tasks developed by our team for testing these domains. Secondly, we showed that – although an analysis at a whole group level indicates a decline in language functions – significantly more individual patients improve or remain stable when compared to the ones who declined. Finally, we observed that having LGG, when compared with HGG, favours patients' outcome after surgery, most probably due to brain plasticity mechanisms. We provide new evidence of the importance of applying a broader neuropsychological assessment and an analysis of naming errors in patients with glioma. Our approach may potentially ensure better detection of cognitive deficits and contribute to better postoperative outcomes. Our study also shows that an individualized approach in post-surgical follow-ups can reveal reassuring results showing that significantly more patients remain stable or improve and can be a promising avenue for similar reports. Finally, the study captures that plasticity mechanisms may act as protective in LGG versus HGG after surgery.

KEYWORDS

awake brain surgery mapping, brain plasticity, cognition, glioma, language, post-surgical outcomes

INTRODUCTION

Language and cognition have been widely described as key factors of brain tumour patients' quality of life and survival (Rimmer et al., 2023; Salans et al., 2021). Within cognition, better performance in executive functioning, processing speed, working memory (Boele et al., 2014), and divided attention (Svedung Wettervik et al., 2022) have been associated with better health-related quality of life. Thus, the daily life independence of patients with brain tumours is mainly supported by a maximally preserved language and cognitive function (Bergo et al., 2016). However, cognitive impairment is frequently reported in patients with gliomas both before and after surgery (Acevedo-Vergara et al., 2022; Ng et al., 2019; Rijnen et al., 2019) in around 50% of surgically treated patients (Acevedo-Vergara et al., 2022; Boone et al., 2016; Cochereau et al., 2016; Habets et al., 2014; Ng et al., 2021; Santini et al., 2012; van Kessel et al., 2020), especially in those harbouring high-grade gliomas (Yamawaki et al., 2021). Cognitive deficits are mainly reported in executive functions, language (e.g., naming and spontaneous speech difficulties), verbal episodic and visuospatial memory, attention and visuoconstructive abilities, as well as in tonic alertness and processing speed (Antonsson, Jakola, et al., 2018; Antonsson, Johansson, et al., 2018; Boone et al., 2016; Cochereau et al., 2016; Norrelgen et al., 2020; Satoer et al., 2013, 2014; Talacchi et al., 2011; Teixidor et al., 2007; Tucha et al., 2003; Wu et al., 2011), all of them underlaid by whole-brain network disturbances (Derks et al., 2014; Liu et al., 2020). Importantly, neuropsychological impairments are variable depending on the characteristics of the glioma, the type of treatment, the time of measurement, the neuropsychological tests used, and the definition of cognitive dysfunction, all of which substantially varied among studies (see van Coevorden-van Loon et al., 2015 for a systematic review).

In the case of brain tumours located in language-eloquent areas, a detailed assessment of language performance, including testing of different facets of language production is essential for the most adequate postoperative follow-up. In this sense, multiple research groups proposed a variety of fine-grained batteries and selections of perioperative (mainly pre-operative) testing tools (see Rofes et al., 2017 for a survey in this regard). To give an example, Sierpowska and colleagues focused on the importance of assessing phonological and semantic processing to better address language difficulties in patients with lesions occupying perisylvian language networks (e.g., using nonword repetition (Sierpowska et al., 2017) or Semantic Pairs Task (Sierpowska et al., 2019)). However, these last works focused mainly on intra-operative assessments. Moreover, they did not explore the relationships between scores in the tasks tapping into phonology or semantics and the errors produced in naming.

The first aim of the present work is to test if a qualitative analysis of errors during object naming task could come as a handy tool for more in-depth analyses of patients' performance in case phonology and semantics were not/could not be assessed otherwise. The inaccuracies in language that we will investigate in this manner involve different naming errors: semantic paraphasias, phonological paraphasias, circumlocutions, delays and language switching. All these naming errors are demonstrated to arise from widespread regions within perisylvian areas (Corina et al., 2010; Sierpowska et al., 2017). Very recently, Collée et al. (2023), as well as Sarubbo et al. (2020) provided models of localization patterns for different language error types based on a systematic review concluding that the type of naming errors relates to a specific brain localization (Collée et al., 2023; Sarubbo et al., 2020). Hence, it can inform an appropriate selection of intraoperative language monitoring tasks and thus, ensure more precise mapping and potentially result in a better postoperative language outcome. Interestingly, detecting and analysing the type of errors can be useful to predict disrupted language connections as well as language recovery and presumably improve postoperative cognitive performance, if combined with adequate intraoperative mapping. For this reason, it is important to add phonological and semantic aspects of language assessment to standard neuropsychological protocols. In the present work, we hypothesize that these scores can be made available using not only the tasks designed for phonological and/or semantic assessments, but also by appropriately extracting information from the gold standard naming tools. To test this hypothesis, we analyse the type of errors participants produced during object naming in the Boston Naming Test and correlate them with the experimental tasks for phonological and semantic assessment that were used within the neuropsychological assessment protocol.

Several factors can influence language performance and post-surgical recovery. In this sense, language and/or cognitive deficits can appear due to the presence of tumour per se, but it is also intuitive to assume that the neurosurgical resection can further negatively influence a patients' performance. However, this assumption has not yet been fully elucidated. Indeed, a portion of the results showed preservation of neuro-cognitive profile (including language, memory, and executive functions) or even an improvement after surgery both in LGG and HGG patients. In particular, Sarubbo et al. (2011) revealed an unchanged language performance after surgery in LGG patients, in line with Barzilai et al. (2019) who showed an improvement in memory and executive functions in these patients (Barzilai et al., 2019). In a similar way, the results of Bonifazi et al. (2020) illustrate preservation of language after surgery in 80% of HGG patients (Bonifazi et al., 2020) as well as Racine et al. (2015) who described that language skills were generally preserved at 12 months after surgery in patients with LGG. Additionally, van Kessel et al. (2020) described an unimpaired outcome of executive functions, memory, and language in low- and high-grade glioma patients (van Kessel et al., 2020) confirmed by the meta-analysis by Ng et al. (2019). Conversely, results from other groups (Santini et al., 2012; Satoer et al., 2012) describe mild difficulties in the early period after surgery in executive functions, memory, and language of glioma patients. More specifically, results by Tabor and collaborators revealed a post-operative deficit in attention and memory in the HGG group (Tabor et al., 2021). Furthermore, there is some evidence about the presence of a mild decline in the immediate post-operative period, but with an improvement and total recovery in the early period after surgery at around 3 months after surgery in memory and constructional praxis (Zigiotto et al., 2020) and language (Antonsson, Jakola, et al., 2018) in patients harbouring LGG, as well as in executive functions and memory of HGG group (Wolf et al., 2016).

Discrepancies between the aforementioned studies might be explained by a plethora of reasons. Firstly, different research groups may use distinct assessment protocols (e.g., in the study from Racine et al. (2015) or van Kessel et al. (2020), the neuropsychological assessment included a wide cognitive evaluation with memory, visuospatial functioning, executive function, and language evaluation, whereas other studies, such as the one by Bonifazi and colleagues (2020) was mainly focused on language assessment. Secondly, they may assess patients in slightly different periods during post-surgical recovery (e.g., van Kessel et al. (2020) performed their postoperative assessment in a period of 3–6 months after surgery, in contrast with Satoer et al. (2012) who administered it at 3 months or the team of Zigiotto et al. (2020) who assessed postoperative cognition at 1 week and 4 months after surgery). Patients may also represent groups of different ages or grade of a tumour (e.g., Santini et al., 2012, included both patients with LGG and HGG whereas the team of Racine et al., 2015 only recruited HGG patients). Also, the specific language patterns previously introduced and described by Collée et al. (2023) that are underlying specific language errors result in a heterogeneous cognitive and language profile after surgery. Moreover, methodological limitations like small sample size may further aggravate the discrepancies and thus restrict the generalization of the results. Given this lack of general agreement about how cognition evolves after surgery, we propose here an additional method of analysing the post-surgical changes.

Given that our second aim was to generate new evidence on post-surgical language/cognitive changes, we will address it not only at a whole sample, but also at an individual level. To do so, we provided a representative sample of 87 subjects with glioma (60 HGG and 27 LGG) located in language-related areas (left-dominant hemisphere) and evaluated using a fine-grained neuropsychological assessment before and after surgery. All the patients underwent intraoperative monitoring of language function to obtain an optimal extent of resection while preserving the neuro-cognitive profile and quality of life as far as possible. It is known that advanced techniques such as awake surgery using electrical stimulation mapping during resection enable to optimize of the quality of lesion removal, with a higher extent of tumour resection, while minimizing the risk of postoperative sequelae including neurological and language deficits (Bu et al., 2021; Duffau et al., 2003). As Bonifazi et al. (2020) reported, 80% of patients with HGG keep their linguistic functions unchanged after awake surgery in eloquent areas with intraoperative monitoring of language using counting and naming tasks. Thus, they considered that the awake procedure is safe and well-tolerated. However, the same study reported discrete impairments in about 50% of patients in memory and executive functions. Importantly, previous evidence indicated that poorer cognitive functioning is associated with lower quality of life (Boele et al., 2014) difficulties in daily functioning (Gonen et al., 2017; Schiavolin et al., 2021, 2022), and worse outcomes after surgery (Schiavolin et al., 2021). In this sense, Moritz-Gasser et al. (2012) showed that the speed of lexical access significantly correlates with the return to professional activities after awake surgery in people with low-grade gliomas. Therefore, a fine-grained cognitive evaluation after surgery is useful in detecting those cognitive deficits essential for optimal quality of life. It has also been shown that the effect of resection surgery on cognition is modulated by other factors like the tumour itself, disease progression, or other comorbidities (Scoccianti et al., 2012). Indeed, a longitudinal study carried out by Dallabona et al. (2017) revealed a general decline at early follow-up in HGG with a following significant recovery at late follow-up, this being dependent on the volume of resected tumour, edema resorption, and patients´ age (Dallabona et al., 2017). Regarding cognitive outcome after surgery, Dallabona et al. (2017) reported that, despite this initial decline, surgery may have a positive influence on cognition as well as on patients' quality of life due to long-term recovery. Furthermore, changes in cognition and language after surgery in HGG may be associated with the concurrent short-term effects of surgery, anaesthesia and/or postsurgical pain treatment (Dallabona et al., 2017).

Importantly, the fact that our sample is composed of a considerable number of participants with either LGG or HGG opens us a special opportunity to test for effects on language plasticity. Indeed, in previous literature (Desmurget et al., 2007; Herbet et al., 2016) it has been suggested that patients with low-grade glioma can benefit from brain plasticity due to a slower tumour growth, and thus manifest a better level of cognitive performance. The third and last aim of this work is to test this hypothesis, by comparing the cognitive scores of participants with tumours of different grades before and after surgery.

In our opinion, a detailed neuropsychological and language evaluation is essential for assessing language and cognitive performance in patients with glioma, as we know that it influences their quality of life and survival. We recommend assessing phonological and semantic aspects of language given both their importance in daily life, as well as the fact that frequently tumours affect dorsal and ventral perisylvian language areas, which may further translate to impairments in these facets of communication. For this reason, we test if including an in-depth analysis of errors in naming can serve as a complementary (or even substitutive) phonological and semantic assessment. To test this hypothesis, we investigate if the analysis of errors in naming tasks can aid in detecting phonological and semantic impairment (at least to a certain degree, for example, in the most affected patients).

Secondly, we explore which post-operative changes occur after brain tumour resection at both whole-group and individual levels. Finally, we investigate the limits of brain plasticity, testing if low-tumour grade may have a protective effect on cognitive performance.

MATERIALS AND METHODS

Participants and population characteristics

Eighty-seven individuals with high- ($N=60$) and low-grade gliomas ($N=27$) on the left-dominant hemisphere who underwent craniotomy for tumour removal were assessed between 2012 and 2022. Among them, the specific anatomical lesion localization under visual inspection was: 19 frontal, 5 fronto-insular, 2 fronto-parietal, 4 fronto-temporo-insular, 1 fronto-temporal, 3 insular, 1 intraventricular-occipital, 3 parietal, 5 parieto-temporal, 30 temporal, 11 temporo-insular, and 1 temporo-occipital (for two patients, information about tumour location was not available). The inclusion criteria were as follows: (1) age between 18 and 70 years (with the exception of one 17 y/o patient who was more suitable for the neurosurgery ward than for the paediatric one), (2) diagnosis of a left hemispheric primary brain glioma, (3) a minimum accuracy of 65% on the simplified naming task adapted from the Boston Naming Test for intraoperative assessment (Havas et al., 2015), (4) a satisfactory level of instruction comprehension in the basic neuropsychological tasks and ability and willingness to cooperate during the surgical procedure while awake (these being understood as the ability to understand the objective of the evaluation, as well as the instructions provided throughout the evaluation), (5) ability and willingness to cooperate during the surgical procedure while awake, and (6) intraoperative monitoring of language during awake surgery. All patients underwent a neuropsychological assessment with cognitive evaluation before surgery which was repeated at the postoperative stage. The postoperative assessment was set to fall at 4 months after surgery, but due to clinical reasons (e.g., radio- and/or chemotherapy, patients´ condition and disposition), the evaluations were carried out as close to this time window as possible and always within the first year of recovery (mean of months post-op = 4.72; $SD=2{,}20$; range: 1.2;11.9). The study protocol was approved by the Local Research Ethics Committee (REC). The study was carried out in accordance with the provisions of the Declaration of Helsinki (Fortaleza, 2013). Patients´ neuropsychological assessment scores were reviewed from standard medical care protocols in a retrospective manner. The informed consent was waived by the REC. The processing of personal data was adjusted to the current legal regulations for data protection.

Our sample included 87 patients with primary brain tumours (high- and low-grade gliomas) in the left-dominant hemisphere that underwent intraoperative monitoring of language functions (see Table 1). Patients' median age was 47.0, with a minimum of 17 years and a maximum of 68 years, and the median years of their formal education was 12.0 [10;15.5]. No differences in the percentage of men and women were observed in clinical groups (LGG and HGG). The presurgical assessment was performed in a median of 19.0 [11.0;47.0] days before the surgery. After surgery, the median of months after the surgery was of 4.3 [3.37;5.7]. A total of 58 patients (42 HGG and 16 LGG) were assessed postoperatively as not all the patients who underwent awake brain surgery completed the postoperative neuropsychological assessment. From the postoperative sample, 40 patients with HGG were submitted to adjuvant treatment (36 of them to chemo and radiotherapy, 2 to radiation and 2 to chemotherapy).

TABLE 1 Demographic variables of the sample.

	ALL (N = 87)	LGG (N = 27)	HGG (N = 60)	Group differences
Age, years	47.0 [38.5;58.0]	40.0 [29.0;47.0]	51.5 [42.0;59.0]	W = 468, p = .002
Gender (female/male)	35/52	11/16	24/36	X^2 = 0, p = 1
Education, years	12.0 [8.0;14.0]	12.0 [10.0;15.5]	11.0 [8.0;13.2]	W = 940.5, p = .225
Days between baseline assessment and surgery	19.0 [11.0;47.0]	29.0 [9.0;76.5]	18.0 [11.0;34.5]	W = 882, p = .51
Months between surgery and follow-up	4.3 [3.37;5.7]	3.72 [2.92;5.3]	4.33 [3.83;5.7]	W = 278.5, p = .38

Note: For numerical variables, the median [1st quartile; 3rd quartile] is indicated; for categorical variables number of observations of each group is indicated. p-value refers to analysis of the Mann–Whitney test for numerical variables and the Chi-square test for categorical data.

Abbreviations: HGG, high-grade glioma; LGG, low-grade glioma.

Neuropsychological assessment

A detailed neuropsychological assessment was administered to each participant by a neuropsychologist before and after surgery (within the first year of recovery). The protocol included the assessment of handedness (Edinburgh Inventory; Oldfield, 1971) verbal comprehension (The Token Test; de Renzi & Faglioni, 1971), semantic (animals) and phonological (letter p) verbal fluency, attention/short-term memory and working memory (Digit Span from the Test Barcelona; Peña-Casanova, 2005), object naming (Boston Naming Test; Goodglass et al., 2001), and a simplified naming task (Havas et al., 2015), this last the one being used for mapping language intraoperatively and as a determinant. Additionally, we specified and counted the type of errors produced by participants including: semantic paraphasias (substitution of an intended word with another one, within the same or different category, for example, pear or shoe for apple); phonological paraphasias (inclusion, substitution, or deletion of word phonemes up to 50% of the target word, for example, pable for table); circumlocutions (description of a specific concept or object without using its specific name-label); delays (a delay in the response time, also called “latency”); missing (absence of response in a specific item, also known as “anomia”) and language switching (substitution of an intended word with its analogue with another language). To assess phonological processing, we used repetition of words and nonwords (Sierpowska et al., 2017) and to assess semantic processing, we used two semantic association tasks: Semantic Pairs Task (SPT; Sierpowska et al., 2019) and Pyramids and Palm Trees test (PPT; Howard & Patterson, 1992). SPT was a modified, abbreviated version of the original 96 Synonym Judgement Task (Jefferies et al., 2009) and it included 64 items. SPT task is composed of items of high and low frequency and items of high and low imageability. This composition allowed to create of an additional, conjoined category, where low difficulty (“easy”) items were those of high frequency and high imageability and high difficulty (“difficult”) items were those of low frequency and low imageability. Notice that not all the patients completed all the tasks (see supplementary material, Table S1, table for the exact number of patients completing each of the assessment tasks).

During the surgery, the simplified version of the naming task, (words and nonwords) repetition tasks, the PPT, and SPT were carried out. The tasks were chosen according to tumour localization and involvement of specific white matter tracts. For cortical mapping, the simplified version of naming tasks in all the languages spoken by the patient was administered. For deep white matter intraoperative monitoring, we administer tasks of repetition for lesions located dorsally to the Sylvian fissure and tasks of semantic matching for patients with lesions located ventrally to the latter fissure. For each patient, items were presented on a laptop screen and only items performed correctly during presurgical assessment were displayed during surgery to ensure errors were produced due to electric stimulation or resection and not to previous language difficulties for these items. For singular patients, the intraoperative protocols were further tailored to assess very specific functions (e.g., drum playing).

Statistical analysis

The normative data allowing to score cognitive performance was studied in different ways depending on their availability: (1) Scores on Digit Span (forward and backward), verbal fluency (semantic and phonological), Boston Naming Test and the Token Test were transformed to Scalar Scores (SSs) using results reported in NEURONORMA project, which provides normative data for young (Aranciva et al., 2012; Casals-Coll et al., 2013; Tamayo et al., 2012), and adult Spanish population (Peña-Casanova, Quiñones-Úbeda, Gramunt-Fombuena, Aguilar, et al., 2009; Peña-Casanova, Quiñones-Úbeda, Gramunt-Fombuena, Quintana-Aparicio, et al., 2009; Peña-Casanova, Quiñones-Úbeda, Quintana-Aparicio, Aguilar, et al., 2009). That is, subjects varied from 1 to 19 points, with scores of 6 and below considered pathological, from 6 to 7 as mild difficulties, and above 7 as normal. (2) PPT, SPT, and nonword repetition scores were transformed to *z*-scores, where values equal to or below −2.5 were considered impaired, scores from −1.5 to −2.5 would be a range between deficiency and normality (mild difficulties), and scores above −1.5 were considered normal; (3) words repetition scores were expressed as absolute values (per 40 items). In words repetition normal subjects score at a maximum (40/40) and almost at the maximum for nonwords (98, 56 ± 1.43%). Hence, any score below 100% for word repetition was considered pathological, whereas for nonwords we applied *z*-scores (for more information see Sierpowska et al., 2017). The specific naming errors were expressed as absolute values per 60 (number of items composing BNT).

First, to study the association between naming errors and phonological and semantic processing, the quantity of errors of different types produced during object naming in the Boston Naming Test before and after surgery (separately) were correlated with four experimental tasks: two testing phonological processing (word and nonword repetition), and two testing semantic processing (Semantic Pairs Test (SPT), and Pyramids and Palm Trees Test (PPT)). To study the relationship between the cognitive domains evaluated, baseline and postoperative group scores (separately) were correlated with each other using Spearman's correlation. To assess the effect of the surgery on cognition we compared results on cognitive tasks and errors in BNT at baseline assessment with those at postoperative evaluation through Wilcoxon signed-rank sum test. Further, to assess group differences, we compared patients with HGG and LGG at baseline and postoperative evaluation. We analysed it in the whole sample and the HGG and LGG group separately. For all these analyses, results were considered as significant when $p < .05$, after being corrected for multiple comparisons using Benjamini & Hochberg's correction. For individual analysis – firstly patients' results were plotted individually and the direction of postsurgical changes (declined, stable, improved) as well as the clinical relevance of scores (normal, mildly impaired, pathological) was interpreted qualitatively by visual inspection of data distribution (see Figure 3). Then, it was calculated how many patients significantly declined, improved, or did not change after surgery. Decline was concluded if after surgery a patient scored at least 3 SS or 1 *Z* score lower than at baseline (except for word repetition, where this value was set for 2 words less than in baseline due to ceiling effect in normal sample). The improvement was concluded if a patient improved at least 3 SS or 1 *Z*-score (and 2 words more than in baseline in words repetition task). Further, the "frequency of decline" was analysed (analysis of all patients declining vs. all patients who remained stable or improved) using one sample z proportion test for each task separately, testing against the probability of $p = .5$ ($p = .5$ being the null hypothesis meaning that there is no difference in the proportion of patients who declined vs. these that remained stable or improved). Finally, we checked if there exists a protective effect of low tumour grade on the number of patients declining by applying a Pearson's Chi-square analysis. We also considered gender effect in our sample studying possible differences between men and women in cognition and language at baseline and after surgery using unpaired two-sample Wilcoxon test. Additionally, we assessed the effect of the treatment group (no treatment, chemo-, radio- or chemoradiation) on changes in cognition and language due to surgery using the Kruskal–Wallis test. All the statistical analyses were performed using RStudio Desktop (R Core Team, 2021).

RESULTS

Neuropsychological results at preoperative assessment

Relationship between errors in naming tasks and cognition and language

During the preoperative neuropsychological evaluation, certain naming errors were related to semantic and phonological processing tasks ($p<.05$), as well as to specific cognitive domains (Figure 1a, supplementary material Table S2). The presence of semantic paraphasias was associated with a worse performance in the overall BNT score (r_s (81) = −.47; $p<.001$) and SPT (r_s (70) = −.40; $p=.004$). Phonological paraphasias were related to repetition of both – words (r_s (71) = −.48; $p<.001$) and nonwords (r_s (71) = −.49; $p<.001$), as well as SPT (r_s (68) = −.33; $p=.03$). Circumlocutions were linked to the overall BNT score (r_s (81) = −.43; $p<.001$). Delays in BNT are associated with backward digits (r_s (80) = −.29; $p=.03$) and phonological verbal fluency (r_s (80) = −.29; $p=.045$). Finally, the number of missings detected in BNT was negatively related to semantic verbal fluency (r_s (81) = −.30; $p=.03$), BNT (r_s (81) = −.52; $p<.001$) and semantic knowledge tasks both in SPT (r_s (69) = −.36; $p=.01$) and PPT (r_s (67) = −.44; $p=.002$).

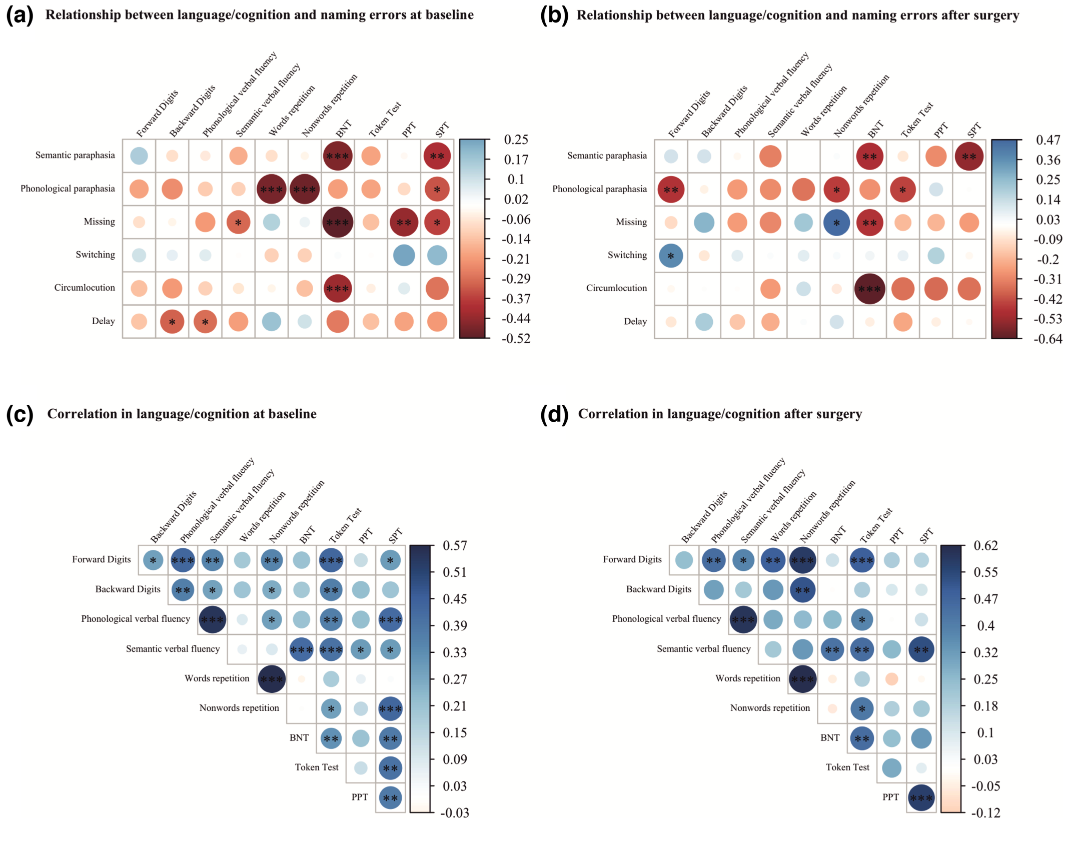

FIGURE 1 Matrix of correlations between cognitive/language domains and between cognitive/language domains and naming errors. (a) Relationship between language/cognition and naming errors at baseline. (b) Relationship between language/cognition and naming errors after surgery. (c) Correlation in language/cognition at baseline. (d) Correlation in language/cognition after surgery. *Indicates the level of significance of p-value result from Spearman's correlation test: *$p<0.05$; **$p<0.01$; ***$p<0.001$. Colour scale indicates the value of Spearman's correlation parameter. BNT, Boston Naming Test; PPT, Pyramids and Palms Tree Test; SPT, Semantic Pairs Test.

Association between language and cognitive domains

Results in the preoperative assessment revealed several positive relationships ($p < .05$) among cognitive domains evaluated (see Figure 1c, supplementary material Table S3). Regarding executive functions, forward and backward digits were related to both semantic (forward digits: r_s (84) = .35; $p = .002$; backward digits: r_s (84) = .28; $p = .01$) and phonological verbal fluency (forward digits: r_s (83) = .43; $p < .001$; backward digits: r_s (84) = .37; $p = .001$), nonword repetition (forward digits: r_s (72) = .35; $p = .005$; backward digits: r_s (72) = .26; $p = .04$) and Token Test (forward digits: r_s (84) = .43; $p < .001$; backward digits: r_s (84) = .37; $p = .001$). Forward digits also correlated with SPT (r_s (70) = .30; $p = .02$). Furthermore, semantic and phonological verbal fluency was correlated to SPT (semantic verbal fluency: r_s (70) = .30; $p = .02$; phonological verbal fluency: r_s (69) = .42; $p < .001$) and Token Test (semantic verbal fluency: r_s (85) = .40; $p < .001$; phonological verbal fluency: r_s (84) = .37; $p = .001$) but with different relationships depending on the verbal fluency subtype assessed: phonological verbal fluency was related to nonword repetition (r_s (71) = .29; $p = .02$), and the semantic verbal fluency with BNT (r_s (83) = .42; $p < .001$). BNT was also associated with Token Test (r_s (83) = .32; $p = .007$) and semantic selection was assessed with SPT (r_s (70) = .38; $p = .003$).

Additionally, we encountered a positive relationship between forward and backward digits (r_s (84) = .29; $p = .01$), phonological and semantic verbal fluency (r_s (84) = .55; $p < .001$), both measures of repetition: word and nonword repetition (r_s (72) = .57; $p < .001$) and semantic processing tasks: SPT and PPT (r_s (68) = .38; $p = .003$).

Neuropsychological results at postoperative evaluation

Relationship between language/cognition and naming errors

After surgery, and if compared to baseline, the type of errors present in naming was associated with cognition slightly differently and some effects described before surgery disappeared (see Figure 1b, supplementary material Table S4). As previously, and overall, errors in BNT were negatively correlated with the performance in specific cognitive tasks. In this sense, the presence of semantic paraphasias was associated with a worse performance in the overall BNT score (r_s (50) = −.49; $p = .005$) and SPT (r_s (35) = −.55; $p = .005$). Phonological paraphasias were related to a lower score in nonword repetition (r_s (38) = −.45; $p = .03$), forward digits (r_s (49) = −.48; $p = .005$), and in the Token Test (r_s (47) = −.44; $p = .02$). Regarding errors of a compensatory character (circumlocutions), these revealed a robust association with overall BNT score (r_s (50) = −.64; $p < .001$). Finally, the number of missings detected in BNT was negatively related to overall BNT (r_s (50) = −.48; $p = .005$). Interestingly, only two positive relationships were found – between the number of missings in BNT and the score in the nonword repetition task (r_s (38) = .47; $p = .02$), as well as between the presence of switching errors and forward digits (r_s (49) = .38; $p = .04$).

Association between language and cognitive domains.

Results in the postoperative assessment revealed a series of positive relationships ($p < .05$) between either semantic or phonological processing and a selection of language and cognitive tasks (see Figure 1d, supplementary material Table S5). Forward and backward digits were associated with nonword repetition (forward digits: r_s (41) = .58; $p < .001$; backward digits: r_s (41) = .52; $p = .002$). Moreover, a relationship emerged between forward digits and semantic verbal fluency (r_s (52) = .38; $p = .01$), phonological verbal fluency (r_s (53) = .45; $p = .002$), repetition of word (r_s (41) = .49; $p = .003$) and Token Test (r_s (50) = .49; $p < .001$). Overall, verbal fluency was related to Token Test (semantic verbal fluency: r_s (50) = .45; $p = .002$; phonological verbal fluency: r_s (50) = .38; $p = .01$) and forward digits (semantic verbal fluency: r_s (53) = .38; p = .01; phonological verbal fluency: r_s (52) = .45; p = .002), whereas semantic verbal fluency was specifically related to BNT (r_s (52) = .43; p = .004) and semantic selection assessed with SPT (r_s (39) = .53; p = .002). Both word and nonword repetition tasks, were associated with attention/short-term memory (word repetition: r_s (41) = .49; p = .003; nonword repetition: r_s (41) = .58; p < .001). Nonwords alone were also associated with Token Test (r_s (40) = .42; p = .02). Regarding BNT, the relationships were found with semantic tasks - semantic verbal fluency (r_s (52) = .43; p = .004), and Token Test (r_s (50) = .42; p = .003). Similarly, SPT was related to semantic verbal fluency (r_s (38) = .53; p = .002). As previously described in the baseline evaluation, and intuitively, we also confirmed positive relationships between pairs of analogue tasks that are: phonological and semantic verbal fluency (r_s (53) = .60; p < .001), word and nonword repetition (r_s (43) = .62; p < .001) and SPT and PPT for semantic knowledge (r_s (37) = .57; p < .001).

Influence of grade of tumour on cognition

When both timepoints were analysed separately, there was no effect of tumour grade either baseline or in the postoperative cognitive and language performance.

Cognition in the late postsurgical recovery

Considering all patients together, the post-operative evaluations revealed a decline in cognitive performance in language domains when compared with pre-surgical assessment. Repeated measures analysis indicated that cognitive performance after surgery significantly worsened for semantic verbal fluency (V = 668.5, p = .03), word (V = 148, p = .01), nonword repetition (V = 352, p = .049) and BNT (V = 534, p = .01). Moreover, errors in BNT increased after surgery in the form of circumlocutions (V = 103; p = .03; see Figure 2).

For patients harbouring HGG, a significant decline was detected in overall BNT score (V = 275.5, p = .036), and word repetition (V = 73, p = .047). Additionally, there was a significant change in the number of missings in BNT (V = 105.5, p = .047) after surgery. By contrast, LGG patients' results revealed no change after surgery.

While observing the post-surgical changes at an individual level (see Figure 3), we may fathom that their direction (e.g., improvement or decline) may not apply to all patients as it was predicted while analysing all the groups together. Indeed, we can see that every individual patient may decline, stay stable, or even improve after surgery in a particular task. The visual introspection of data distribution in Figure 3 also allows us to acknowledge that for some patients, the post-operative changes are minimal and clinically non-significant (e.g., participants decline, but stay within the range of normal values), while for other people the decline may mean a drastic change from normal values to severe impairment. Interestingly, even though word repetition showed the most dramatic change post-surgery at a group level, we can observe this was due to the severe decline of a handful of patients. For nonword repetition, this pattern changed slightly, as it showed a decline in a greater number of participants. Finally, while inspecting data distribution for the PPT, we can see that only a few individuals with HGG declined in the task after surgery and the only LGG individual with pathological baseline scores, improved in a clinically significant manner (from pathological to mildly impaired). In the SPT task carried out in patients with HGG, we can see that, although a great number of individuals preserved results close to their baseline, there also exist a considerable number of participants who declined dramatically. Similarly to what was observed in PPT, the only LGG individual with pathological SPT scores before surgery, improved by changing the score from pathological to mildly impaired. To acknowledge these differences in post-surgical changes at an individual, clinically meaningful level, we report here also an analysis of frequency in patients who declined versus those who did not decline and remained stable or improved (Table 2, see methods for details on considering a change meaningful). For all cognitive and language

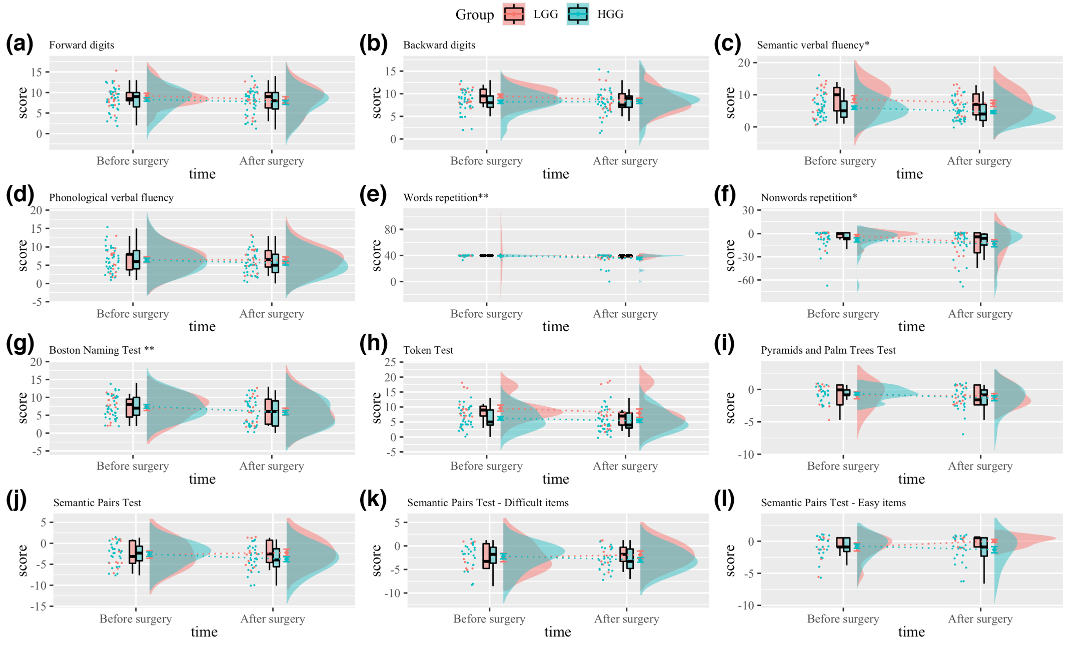

FIGURE 2 Effect of surgery on language and cognition. Comparison between baseline and postoperative performance. Results are represented in Scalar Score (a–d,g,h), *z*-scores (f,i,j,k,l) and direct scores (e). *Indicates the level of significance of *p*-value result from the Wilcoxon signed rank sum test used to analyse differences between preoperative and postoperative results of the entire sample (HGG and LGG) analysis: *$p<0.05$; **$p<0.01$; ***$p<0.001$.

domains tested, significantly more patients remained stable or improved after surgery as compared to patients who declined.

When comparing two groups with different grades of tumour (high vs. low), no effect of tumour grade was observed.

Additionally, no effect of treatment (radio-, chemo- or chemoradiation) was observed. However, these results should be interpreted with caution. Firstly, the sample size was extremely unbalanced (radiotherapy group: $N=2$, chemotherapy: $N=2$, chemoradiation: $N=36$). Secondly, and most importantly, we must consider that the majority of patients under chemoradiation were harbouring HGG (35 HGG vs. 1 LGG). Thus, it was difficult to disentangle the effects of treatment from the effects of tumour grade.

Regarding the possible gender effects in our sample, men and women performed similarly in language and cognitive tasks, both before and after surgery.

DISCUSSION

In this study, we described how the analysis of naming errors can aid to detect phonological and semantic processing impairments before and after brain surgery. Furthermore, we investigated how other language and cognitive functions contribute to phonological and semantic processing. We checked the effects of awake surgery on language cognition using a whole sample and an individualized approach in our analyses. Finally, we tested if plasticity mechanisms favour LGG patients in their language/cognitive outcome both before and after surgery.

Our results indicated that phonological and semantic processing tasks (e.g., SPT or nonword repetition) correlate with language and cognitive domains that are designed to assess similar domains (e.g., semantic fluency and SPT). They also suggested that naming errors can be useful to evaluate and monitor

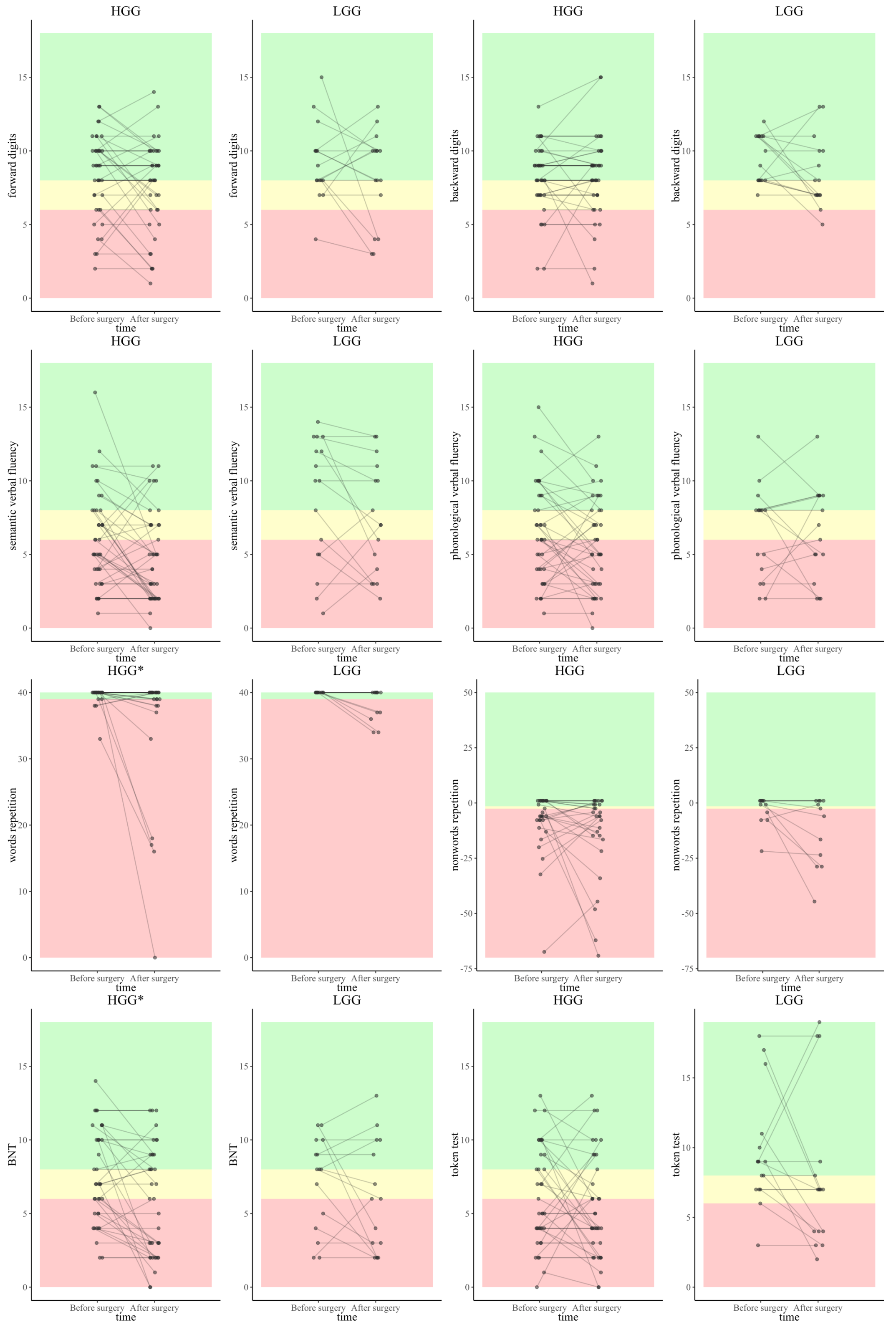

FIGURE 3 (Continued)

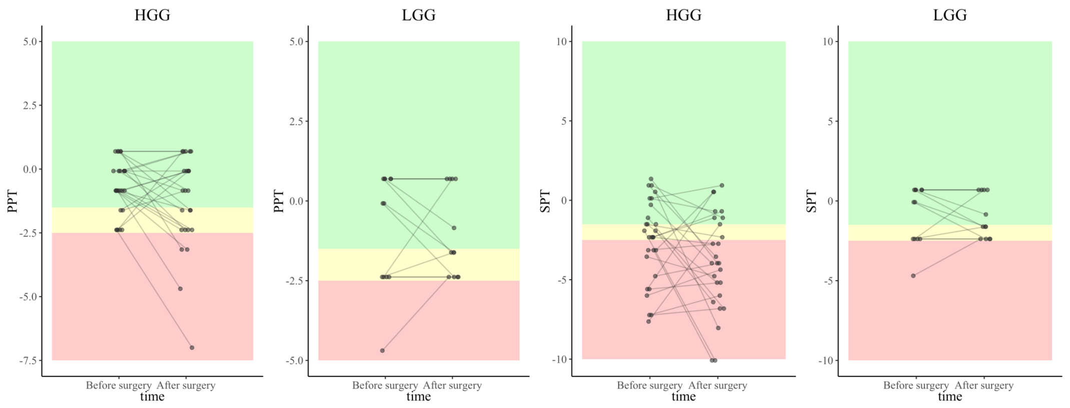

FIGURE 3 Effect of surgery on language and cognition in LGG and HGG group. Comparison between baseline and postoperative individual scores. Results are represented in Scalar Score for forward and backward digits, verbal fluency, Token Test, and BNT; in *z*-score for nonword and word repetition, SPT, and PPT; and in direct scores for words repetition. Colour of background: green: normal scores; yellow: mild impairment scores; red: impaired scores. *Indicates the level of significance of *p*-value result from the Wilcoxon signed rank sum test to analyse differences between preoperative and postoperative results of the entire sample (HGG and LGG) analysis: $*p<0.05$; $**p<0.01$; $***p<0.001$.

semantic and phonological processing (see relationships between nonword repetition and phonological paraphasia or between SPT and semantic paraphasias). Furthermore, we show that although patients decline in a handful of tasks postoperatively overall, the decline is significantly less frequent than stability/improvement when postoperative changes are considered on an individual, clinically meaningful basis. Finally, while analysing LGG and HGG groups separately, we observed that having LGG may favour patients' outcomes after surgery, as patients with LGG manifested no postoperative changes, meanwhile their HGG counterparts did so in certain language/cognitive domains, which could, most probably, occur thanks to brain plasticity mechanisms.

Phonological and semantic processing assessed with naming errors and standard neuropsychological tasks before and after surgery

Following the first aim of our study, we tested the usefulness of naming errors to determine phonological and semantic deficits at baseline and after surgery. Results showed that phonological naming errors (phonological paraphasias) are associated with phonological processing tasks, that is word and nonword repetition at baseline. The number of these errors also correlated with the scores of nonword repetition after surgery, and to a lesser degree with semantic processing at baseline, and with working memory and verbal comprehension after surgery. Our results suggest that phonological errors in naming (phonological paraphasias) may be a sensitive measure of phonological processing, also addressed with repetition tasks. A previous study by Sierpowska et al. (2017) proposed nonword repetition task as a complement to word repetition and naming that allows more careful monitoring of language, especially in the intraoperative setting (Sierpowska et al., 2017). In that study, the authors detected phonological paraphasias only in three patients (25% of the sample), who were already unable to correctly repeat words and nonwords. This suggested that these naming errors could be useful only when the impairments are already very severe. Thus, the authors concluded that adding tasks of repetition of word and especially nonword to the neuropsychological assessment protocols could be recommendable for detecting phonological difficulties in different grades of impairment. In cases where it is not possible to administer a repetition task, preferably of nonwords, the specific analysis of the type of errors in naming can be used as a proxy for phonological processing and more specifically phonological paraphasias.

TABLE 2 Individual analysis for post-surgical changes.

	Decline	Stability	Improvement	Decline	Stability or Improvement	Equality of proportions[a]	Pearson's chi-squared test[b]
Forward digits ($N = 55$)	16 (29.09%)	26 (47.27%)	13 (23.64%)	16 (29.09%)	39 (70.1%)	**$X^2 = 9.62$ $p = .009$**	
HGG	12 (21.82%)	19 (34.55%)	8 (14.55%)	12 (21.82%)	27 (49.09%)		$X^2 = .01$ $p = .92$
LGG	4 (7.27%)	7 (12.72%)	5 (0.09%)	4 (7.27%)	12 (21.82%)		
Backward digits ($N = 55$)	8 (14.55%)	42 (76.36%)	5 (9.09%)	8 (14.55%)	47 (85.45%)	**$X^2 = 26.65$ $p < .001$**	
HGG	3 (5.46%)	32 (58.18%)	4 (7.27%)	3 (5.46%)	36 (65.45%)		$X^2 = 3.35$ $p = .07$
LGG	5 (9.09%)	10 (18.18%)	1 (1.82%)	5 (9.09%)	11 (20%)		
Semantic verbal fluency ($N = 57$)	20 (35.09%)	29 (50.88%)	8 (14.03%)	20 (35.09%)	37 (64.91%)	**$X^2 = 5.07$ $p = .03$**	
HGG	14 (24.56%)	22 (38.6%)	5 (8.77%)	14 (24.56%)	27 (47.37%)		$X^2 = 0$ $p = 1$
LGG	6 (10.53%)	7 (12.28%)	3 (5.26%)	6 (10.53%)	10 (17.54%)		
Phonological verbal fluency ($N = 55$)	17 (30.91%)	29 (52.73%)	9 (16.36%)	17 (30.91%)	38 (69.09%)	**$X^2 = 8.02$ $p = .01$**	
HGG	12 (21.82%)	21 (38.18%)	6 (10.91%)	12 (21.82%)	27 (49.09%)		$X^2 = 0$ $p = 1$
LGG	5 (9.09%)	8 (14.55%)	3 (5.45%)	5 (9.09%)	11 (20%)		
Word repetition ($N = 41$)	13 (31.71%)	28 (68.29%)	0 (0%)	13 (31.71%)	28 (68.29%)	**$X^2 = 5.48$ $p = .02$**	
HGG	8 (19.51%)	21 (51.22%)	0 (0%)	8 (19.51%)	21 (51.22%)		$X^2 = .26$ $p = 1$
LGG	5 (12.20%)	7 (17.07%)	0 (0%)	5 (12.20%)	7 (17.07%)		
Nonword repetition ($N = 41$)	21 (51.22%)	11 (26.83%)	9 (21.95%)	21 (51.22%)	20 (48.78%)	$X^2 = .02$ $p = .88$	
HGG	14 (34.15%)	7 (17.07%)	8 (19.51%)	14 (34.15%)	15 (36.58%)		$X^2 = 1.87$ $p = 1$
LGG	7 (17.07%)	4 (9.76%)	1 (2.44%)	7 (17.07%)	5 (12.20%)		

TABLE 2 (Continued)

	Decline	Stability	Improvement	Decline	Stability or Improvement	Equality of proportions[a]	Pearson's chi-squared test[b]
BNT ($N=52$)	16 (30.77%)	33 (63.46%)	3 (6.77%)	16 (30.77%)	36 (69.23%)	**$X^2=7.69$ $p=.01$**	
HGG	13 (25%)	22 (42.31%)	2 (3.85%)	13 (25%)	24 (46.15%)		$X^2=.55$ $p=.94$
LGG	3 (5.77%)	11 (21.15%)	1 (1.92%)	3 (5.77%)	12 (23.08%)		
Token test ($N=53$)	18 (33.96%)	26 (49.06%)	9 (16.98%)	18 (33.96%)	35 (66.04%)	**$X^2=5.45$ $p=.02$**	
HGG	11 (20.76%)	19 (35.85%)	7 (13.21%)	11 (20.75%)	26 (49.06%)		$X^2=.45$ $p=.94$
LGG	7 (13.21%)	7 (13.21%)	2 (3.77%)	7 (13.21%)	9 (16.98%)		
PPT ($N=37$)	11 (29.73%)	22 (59.46%)	4 (10.81%)	11 (29.73%)	26 (70.27%)	**$X^2=6.08$ $p=.02$**	
HGG	7 (18.92%)	16 (43.24%)	2 (5.40%)	7 (18.92%)	18 (48.65%)		$X^2=0$ $p=1$
LGG	4 (10.81%)	6 (16.22%)	2 (5.41%)	4 (10.81%)	8 (21.62%)		
SPT ($N=39$)	11 (28.21%)	19 (48.72%)	9 (23.07%)	11 (28.21%)	28 (71.79%)	**$X^2=7.41$ $p=.01$**	
HGG	11 (28.21%)	10 (25.64%)	6 (15.38%)	11 (28.21%)	16 (41.02%)		$X^2=4.95$ $p=.26$
LGG	0 (0%)	9 (23.08%)	3 (7.69%)	0 (0%)	12 (30.77%)		

Note: The bold font in the table indicates a significant result with a p-value $<.05$.

[a] p-value from one-sample test for equality of proportions.

[b] p-value from Pearson's Chi-squared test.

Regarding semantic processing, our results illustrate a negative association between specific naming errors (these include semantic paraphasias, circumlocutions, and missings) and semantic association tasks. Specifically, the more semantic paraphasias at baseline and after surgery a patient produces, the lower the score in naming and SPT. However, these results should be interpreted with caution by considering previous, intraoperative findings (Sierpowska et al., 2019), which suggested that paraphasias (of any kind) occur (or co-occur with other errors) once the impairment is already severe. Furthermore, while observing the direction of the correlations overall, we can appreciate that participants with high numbers of paraphasias also show a severe impairment overall. Our results indicate that semantic errors detected in naming can be used to assess semantic processing and consequently, a higher presence of semantic errors can be used as an indicator of a greater semantic impairment. However, since semantic paraphasias appear once the semantic processing is already severely impaired (and comparably to the results found in phonological paraphasias), we recommend using more fine-grained tasks (e.g., SPT) together with naming. Overall, the present and past results illustrate that the simple analysis of paraphasias may be helpfully used as a proxy to assess semantic and phonological processing, only when more fine-grained tests are not available.

In our study, and still addressing the first research question, we also defined specific contributions of cognitive and language domains to phonological and semantic processing analysing the correlations among neuropsychological tasks used. The neuropsychological assessment revealed a positive relationship between specific semantic processing tasks (PPT and SPT), attention/short-term memory, and language. Our results revealed a positive relationship between SPT and attention/short-term memory and language and between PPT and semantic verbal fluency at baseline. In postoperative evaluation, semantic processing assessed using SPT was associated with semantic verbal fluency. The association between SPT and BNT at baseline and the relationship with semantic verbal fluency both before and after surgery, and between PPT and semantic verbal fluency illustrates how semantic processing and access relate to dealing with word meaning (Rodríguez-Fornells et al., 2009). Moreover, the findings from the current study are consistent with previous results by Sierpowska et al. (2019) who found that all three tasks: SPT, PPT, and BNT were associated with the loss of integrity of the ventral language pathways. This previous evidence, together with our present study supports the relevance and usefulness of these tasks in the assessment of semantic processing. Regarding phonological processing, the nonword repetition task was associated with attention/short-term memory, working memory, as well as with language – expressed by measures of verbal fluency, semantic selection, and verbal comprehension at baseline. At the postoperative evaluation, the nonword repetition task correlated with attention/short-term memory, working memory, and verbal comprehension. Word repetition was only associated with attention/short-term memory in postoperative evaluation. The implication of attention/short-term memory and working memory in the phonological process is in line with the results described by Saito & Baddeley (2004), who observed a close relationship between speech errors and digit span. Moreover, this association may be also explained by the fact that these processes share functional streams related to phonological processing but also to the respective working memory connections (e.g., the arcuate fasciculus or frontal aslant tract; Papagno et al., 2017; Shallice & Papagno, 2019; Vavassori et al., 2023; Zigiotto et al., 2022). Interestingly, word repetition at baseline was not significantly related to any neuropsychological task administered, apart from nonword repetition, enhancing the importance of additional and more specific tasks to those traditionally administered for better monitoring of cognition. Interestingly (and intuitively) our study results indicated that the presence of delays in naming at baseline is associated with lower scores in working memory. This result yet again confirms the notion that working memory grounds language in space and time (Baddeley, 2003), linking linguistic and visuo–spatial representations (Huettig & Janse, 2016). Moreover, this association is also the picture of common functional streams of language and working memory networks. To give an example, the arcuate fasciculus has been related to both working memory (Vavassori et al., 2023) and verbal fluency (Zigiotto et al., 2022). Hence, due to the topography of the lesion present in our sample, mainly around perisylvian areas, networks we can observe impairments in more than one cognitive process that they subserve. Even if we did not include hypotheses on working memory associations in our set of research questions, we dedicate this separate subsection for this accidental result to emphasize, once again, the importance of interpreting neuropsychological testing results in a conjunction. We believe, and our results support an opinion, that very few assessment tasks assess a single and "pure" neuropsychological function. Overall, these results emphasize the importance of a neuropsychological assessment battery including both standard tests used but also a fine-grained assessment of naming errors in patients with glioma in language-related areas.

Besides the clinical contribution of our results, the presence of a specific association between phonological and semantic domains, both assessed through neuropsychological tasks but also with type of errors in denomination, may be illustrative of the involvement of language-related WM tracts, in particular of the dual language pathway model widely described and applicated in clinical practice (Herbet & Duffau, 2020; Middlebrooks et al., 2017). Specifically, at a subcortical level, on one hand, it has been observed that the deficits in phonological processes, e.g., repetition errors and phonological paraphasias were related to the stimulation or damage of the arcuate fasciculus (Hickok & Poeppel, 2007; Saur et al., 2008; Sierpowska et al., 2017), while low scores in phonological verbal fluency were related to the loss of integrity at the level of the left frontal aslant tract and the left frontal part of the IFOF at 1 week and 1 month after surgery (Zigiotto et al., 2022). On the other hand, semantic errors in naming, and resulting impairment in semantic processing, suggest that these impairments co-occur mainly with the malfunction of the white matter ventral pathway that includes the inferior longitudinal and the inferior fronto-occipital fasciculus (Mandonnet et al., 2007; Sierpowska et al., 2019) as well as the left arcuate and the uncinate fasciculus (Zigiotto et al., 2022). All in all, our results, and the existing evidence about the importance of mapping WM tracts (Duffau et al., 2003; Sarubbo et al., 2020; Young et al., 2021), confirm the need for specific neuropsychological and neurosurgical protocols based on the tumour site. Moreover, these assessments may be helpful not only in neuropsychological perioperative follow-up to detect both semantic and phonological difficulties in language processing but also in surgical preparation.

Cognition and language after surgery: Whole-sample, group and individual analysis

Responding to the second research question, we analysed the consequences that surgery may have on the cognition and language of subjects with either high- or low-grade glioma. Our results in the group of all patients showed a decline in semantic verbal fluency, word and nonword repetition, and naming, as well as in the number of circumlocutions in naming. In a more specific analysis, and the context of our third research question, we could observe that the HGG group results showed a decreased performance in word repetition, naming and an increased number of missings in naming. By contrast, the LGG group did not show any significant difference after surgery in language and cognition. These results from the second and third research questions bring us conclusions that need a cautious interpretation because deficits observed in the whole sample are partially explained by those presented in the HGG group, specifically. For this reason, the results of the second and third research questions will be discussed altogether, and we consider that when analysing the effects of surgery on the cognition of glioma patients, the type of glioma is an unavoidable factor to take into account.

Cognitive difficulties after resection of glioma are frequently reported in adult patients (Antonsson et al., 2017; Bonifazi et al., 2020; Ng et al., 2019; Tabor et al., 2021; van Kessel et al., 2020; Wolf et al., 2016). At a whole sample level, and in line with existing evidence (Satoer et al., 2012, 2013), our results revealed a decline in language after surgery (as compared to baseline), in particular in a BNT score, semantic verbal fluency and word repetition, as well as in a greater number of circumlocutions in naming. When analysing the two groups differing in tumour grade separately, a decline in naming and word repetition and the increase in the presence of missings in naming was detected only in the HGG group whereas the LGG group did not show any significant changes after surgery. These results add further evidence to the previous evidence showing that clinical variables (e.g., grade of tumour) influence cognition (Gehring et al., 2015; Yamawaki et al., 2021; Yuan et al., 2020). They are also a key prognosis factor in glioma patients (Gehring et al., 2011). Our results are in line with the revision made by Acevedo-Vergara et al. (2022), who found that HGG is responsible for significant alterations in the cognition of patients. The rapid growth associated with HGG limits the possibility of compensatory processes, which negatively influences prognostics of survival. As described by Cargnelutti et al. (2020), HGG displays less frequent compensatory functional activation in the right-sided homologues of language essential areas like IFG or STG ("Broca" and "Wernicke"), and this is associated with higher language dysfunction. By contrast, low-grade glioma presents with slow and progressive growth and has a lower degree of cell infiltration and proliferation (Lv et al., 2022) facilitating restructuration of peritumoral neural networks (Krishna et al., 2021), as well as a progressive redistribution of eloquent areas (Duffau, 2008), in this way allowing greater plasticity mechanisms before surgery to counteract post-surgery impairments. Overall, the findings of the present study illustrate that patients with HGG after surgery decline in certain facets of cognitive functioning, while patients with LGG do not. Therefore, one may assume that different patterns of functional brain reshaping occur within diffuse glioma patients before surgery (Duffau, 2017) and may determine the functionality of peritumoral areas and hence, the postoperative impairment. In particular, patients with LGG showed increased functional connectivity of the default mode network (DMN) essential for several cognitive processes, and this is associated with the neurocognitive profile after surgery (Saviola et al., 2022). Specifically, longitudinal post-surgical changes in functional connectivity of DMN are associated with higher performance in short-term memory and divided attention. The results presented here, as compared with the existing evidence, show that plasticity mechanisms according to the type of tumour can be determinant in the cognitive status of the patient before and after surgery.

When observing Figure 3, there are pre- to postoperative differences that may be relevant from a clinical point of view, as they impact significantly particular patients, but these differences are not detected in the whole sample as the analysis does not turn out significant. Importantly, we need to keep in mind that the results provided above are based on the results from the entire group (with the only differentiation based on tumour grade) and it is important to interpret the post-operative changes also at an individual level. Indeed, in clinical practice, we acknowledge the importance of tailoring intrasurgical tasks and their items selection for every person individually, and we also observe that patients manifest different directions of post-surgical changes. This is extremely relevant clinically, as we may erroneously predict that glioma patients do not decline post-surgery in a certain task simply because the effects of one patient's improvement cancel out another patient decline (for example, see results of the Token Test in Figure 3). Thanks to the analysis of the frequency of patients who declined versus those who did not, we found rather comforting news – there are significantly more patients who remain stable or even improve in all tasks carried out at our institution (see Table 2). Furthermore, we also proved that this effect can be relevant for all patients (both LGG and HGG), as no effect of tumour grade was found while comparing the number of declines in language and cognitive scores.

With this exploration we could also see those certain tasks, for example, word repetition, can only be suitable for the detection of a severe impairment, and in a reduced number of participants. This means that this task could be interpreted as superfluous if our sample of glioma patients were smaller and we would not encounter anyone with phonological processing impairment severe enough to detect it. In the same vein, we can also see that the pattern of impairments detected using nonword repetition is somehow like the one in word repetition, but with a capacity to point to the phonological difficulties in a greater number of individuals (something that is also easily interpretable given than words have meaning which can potentially provoke a compensatory effect). We could observe that the tasks designed to test phonological and semantic processing (e.g., nonword repetition and SPT) have a great potential to detect difficulties, especially in patients with HGG (see Figure 3 to observe how many individuals are in the pathological range of points as compared to those within the normal). We need to notice that not every decline means the same for an individual. Indeed, some of the patients from our sample declined in a way in which their score changed from normal to pathological (see Figure 3 patients with HGG and

BNT), while some others simply scored less, while still staying within the normal range (see patients with LGG and SPT, Figure 3). We can conclude from these observations that it is recommendable to use a wide range of language and cognition assessment tasks as some facets may be preserved while others decline and it is beneficial for the patient to cherish as complete a neuropsychological profile, as possible. It is also important to always tailor the assessments (and their interpretations) according to the individual patients. We also believe that the distinct directions of post-surgical cognitive and language changes at an individual level may explain why the field did not yet reach a consensus regarding how surgery impacts language and cognition overall.

Strengths and limitations of the study

The main strength of this study includes a large number of patients, offering a representative sample of the population with brain tumour placed in eloquent areas for language, and the specific and detailed neuropsychological assessment applied. Importantly, all participants underwent awake brain surgery with language mapping. Moreover, we presented a group of people with either HGG or LGG. However, our study also has limitations. Firstly, the proportion of people with HGG (69%) was significantly higher than the one with LGG (31%; $X^2 = 23.54$; $p < .001$). Although we know that, ideally, we would have a more balanced number of patients with different pathologies, we wish to reiterate that our number reflects upon the real prevalence of glioma in the adult population, as glioblastoma (WHO Grade 4) is the most common glioma subtype in adult (Ostrom et al., 2014), and thus also the reality of our clinical practice. For this reason, we keep in mind this limitation and account for it in statistical analyses. For example, we have considered the type of tumour in the analyses (e.g., by specifically performing the analyses in each group) to take into account the heterogeneity of the sample with this higher proportion of HGG.

Secondly, although the overall group results showed protective effects of LGG on language and cognition, these were not confirmed while analysing patients' scores individually. This brings yet another interesting piece of evidence to the puzzle of post-operative recovery and tumour grade effects. Thirdly, not all participants were able (or willing) to perform the post-surgery evaluation and our initial sample size was reduced in the follow-up. We have considered that the preoperative group differs from the postoperative one and hence, relationships observed between language and cognition and naming errors after surgery (see Figure 1) may be different depending on the sample of study (mainly sample size). To account for this, we have analysed the relationship between language and cognition and naming errors at baseline only in these participants who have performed the postoperative evaluation as well. Results from this analysis did not substantially differ from the effects that we first reported in the whole group. Therefore, we concluded that this result remains stable regardless of sample size and decided to show the results from a more representative sample ($N = 87$ instead of $N = 58$) in the preoperative comparisons. Moreover, not all the participants completed all the tasks. However, despite not having all the scores per patient, we have included a participant in our postoperative sample even if they fulfilled only a few tasks, as we considered each variable as an independent one. Indeed, given that some patients cannot complete the entire protocol (e.g., due to fatigue), we considered that all the available data was of value, independently of the number of tasks the subject has completed. Finally, our study includes only evaluations performed during the first year of recovery, but more long-term evaluations in the postsurgical follow-ups would help to better define long-term plasticity mechanisms. Additionally, the postoperative assessment during this first year after surgery coincides with the most impactful phase of adjuvant treatments in the case of HGG and this may influence cognition and language. However, our results revealed no effect of treatment on changes after surgery. Future studies should envisage the reasons why patients abandon post-surgical follow-ups. New lines of research should also contemplate including long-term evaluations (e.g., 1 year after surgery, see also (Sierpowska et al., 2022)).

CONCLUSIONS

This study adds to a minor body of research addressing language and cognitive evaluations in patients undergoing awake brain surgery for tumours in left-hemispheric language-eloquent areas with a special focus on errors in naming and individual-level analysis. The first research question of this study concludes that naming errors can be used as a proxy of the semantic and phonological processing assessment and completes previous intraoperative work in this regard. According to the results of the second research question, we observed that, after surgery, a decline in language can be observed if the entire sample is analysed. However, after the data was subjected to an analysis where we treated patients individually – we observed that a greater number of patients remained stable or even improved after surgery than declined. Finally, we further confirm that compared to people with HGG, patients with LGG are less prone to cognitive and language decline after surgery. The latter effect is most probably due to brain plasticity mechanisms. The results presented are relevant to plan adequate assessment protocols and may aid in an optimal interpretation of them. Therefore, and potentially, they may also aid in adequately designing neurorehabilitation programs promoting patients' professional reincorporation and personal well-being.

AUTHOR CONTRIBUTIONS

AGR: conceptualization, methodology, software, data curation, investigation, validation, formal analysis, visualization, project administration, resources, writing – original draft preparation, writing – review & editing; AR: supervision writing – original draft preparation, writing – review & editing; MS: conceptualization, data curation, writing: review & editing; MJ: data curation, investigation, project administration, resources, writing – review & editing; IR: data curation, investigation, project administration, resources, writing – review & editing, project administration; AC: data curation, investigation, project administration, resources, writing – review & editing, project administration; AG: conceptualization, data curation, investigation, validation, supervision, funding acquisition, project administration, resources, writing – review & editing; ARF: conceptualization, methodology, data curation, investigation, validation, supervision, funding acquisition, project administration, writing – original draft preparation, writing- review & editing; JS: conceptualization, methodology, software, data curation, investigation, validation, formal analysis, supervision, visualization, project administration, resources, writing – original draft preparation, writing – review & editing, project administration.

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CONFLICT OF INTEREST STATEMENT

MS has participated in lectures by Pfizer. All other authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Authors elect not to share data.

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