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# Language processing in glioma patients: speed or accuracy as a sensitive measure?

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## ABSTRACT

**Background:** Glioma (brain tumour) patients can suffer from mild linguistic and non-linguistic cognitive problems when the glioma is localised in an eloquent brain area. Word-finding problems are among the most frequently reported complaints. However, mild problems are difficult to measure with standard language tests because they are generally designed for more severe aphasic patients.

**Aims:** The aim of the present study was to investigate whether word-finding problems reported by patients with a glioma can be objectified with a standard object naming test, and a linguistic processing speed test. In addition, we examined whether word-finding problems and linguistic processing speed are related to non-verbal cognitive abilities.

**Methods & Procedures:** We tested glioma patients (N=36) as part of their standard pre-treatment clinical work-up. Word-finding problems were identified by a clinical linguist during the anamnesis. Linguistic processing speed was assessed with a newly designed sentence judgment test (SJT) as part of the Diagnostic Instrument for Mild Aphasia (DIMA), lexical retrieval with the Boston Naming Test (BNT), presence of aphasia with a Token Test (TT), and non-verbal processing with the Trail Making Test A and B (TMT). Test performances of glioma patients were compared to those of healthy control participants (N=35).

**Outcomes & Results:** The results show that many glioma patients (58%) report word-finding problems; these complaints were in only half of the cases supported by deviant scores on the BNT. Moreover, the presence of reported word-finding problems did not correlate with the BNT scores. However, word-finding problems were significantly correlated with reaction times on the SJT and the TMT. Although there were no significant differences between the patient and control group on the SJT, a subgroup of patients with a glioma in the frontal lobe of the language-dominant hemisphere was

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slower on the SJT. Finally, performance on the SJT and TMT were significantly correlated in the patient group but not in the control group.
**Conclusions:** Linguistic processing speed appears to be an important factor in explaining reported word-finding problems. Moreover, the overlap between speed of language processing and non-verbal processing indicates that patients may rely on more domain-general cognitive abilities as compared to healthy participants. The variability observed between patients emphasises the need for tailored neuro-linguistic assessments including an extensive anamnesis regarding language problems in clinical work-up.

## Introduction

### *Gliomas*

Gliomas are the most common type of primary brain tumour. The World Health Organization categorises gliomas into four grades. High-grade gliomas (HGG, grades III–IV) are more aggressive and more common than low-grade gliomas (LGG, grades I–II; Sanai & Berger, 2012). Gliomas are often located in eloquent areas of the brain (Duffau & Capelle, 2004; Gerritsen et al., 2019). In these cases, surgery is aimed at resecting the tumour whilst preserving cognitive functions (Ilmberger et al., 2008; Sanai & Berger, 2008; De Witte & Mariën, 2013). Due to the preferential localisation of gliomas in eloquent areas of the brain, patients may experience neurological and cognitive impairments that can have serious consequences on their quality of life.

### *Sensitivity of assessments*

It is of central importance for quality of life to investigate how patients subjectively experience (loss of) abilities, such as language (Cruice, Worrall, & Hickson, 2006). Word retrieval difficulties are among the most common complaints of people with a glioma (Racine et al., 2015). Importantly, performance on objective cognitive tests may not necessarily reflect the patients' complaints (Gehring et al., 2015; Racine et al., 2015; Taphoorn & Klein, 2004; Van der Linden et al., 2020). More specifically, patients appear to report language complaints that are not supported by lower scores on standard language measures, demonstrating insufficient sensitivity of those tests (Brownsett et al., 2019; Satoer et al., 2012).

For instance, Satoer et al. (2012) compared scores on the Aphasia Severity Rating Scale (ASRS; Goodglass et al., 2001) to the self-reported problems and found that more patients reported issues in daily communication than were shown to have impairments based on the ASRS (57% vs. 39%, respectively). This shows the value of combining standardised tests with an evaluation of self-reported complaints in the assessment of cognitive abilities of glioma patients (Taphoorn & Klein, 2004).

A potential reason for the discrepancy between subjectively experienced language difficulties and objective test performance, is that aphasia assessments are generally designed for patients who suffered a stroke. Glioma patients, with comparable lesion size and location, typically have milder language and/or cognitive deficits (Anderson et al., 1990). These mild impairments can be the result of neural reorganisation (i.e., compensation for loss of function) due to the slow growth rate of gliomas as compared to the sudden onset of neurological damage caused by stroke (Duffau, 2008, 2014). The subtlety of cognitive-linguistic impairments in glioma patients poses a problem for the assessment of their cognitive functions.

### *Processing speed*

Including a measure of response speed in the assessment of glioma patients may increase sensitivity of standard measures and provide a way to objectively measure self-reported word-finding problems. Language processing in patients with a glioma was investigated by Moritz-Gasser et al. (2012), who studied the correlation between naming capacities and the ability to return to work after surgery. They found that naming *speed*, rather than accuracy, significantly predicted return to work, an important marker for quality of life. Importantly, none of the patients in their study was classified as "aphasic" according to the Boston Diagnostic Aphasia Examination (BDAE; Goodglass & Kaplan, 1972), a test battery originally designed for stroke patients. Another recent study has shown that patients with gliomas are significantly slower on a speeded naming test compared to healthy participants (Ras et al., 2020). This difference could not be explained by naming ability measured with the Boston Naming Test (BNT; Kaplan et al., 2001).

As for non-verbal processing speed, previous studies have shown that glioma patients performed significantly worse than a healthy control group (Habets et al., 2014; Wefel et al., 2016). Interestingly, it even appeared to be the most-often impaired cognitive ability in this patient group (Ek et al., 2010). These studies typically operationalise non-verbal processing speed with a Symbol Digit Modalities Test (Smith, 1973) or the Trail Making Test Part A (TMT-A; Army Individual Test Battery, 1944).

Including an assessment of processing speed may not only increase the sensitivity of measures, but may also bear a direct relationship with communicative difficulties experienced by patients in everyday conversations. Everyday communication requires the conversational partners to process information quickly and respond to it in an appropriate manner, and speedy processing of linguistic information is crucial (e.g., Carragher et al., 2012). Subjectively experienced word-finding problems may therefore be the result of not only a lexical retrieval problem, but may also be due to slowed processing.

### *Domain generality of processing speed*

The finding that patients with a glioma are slower on both linguistic (Moritz-Gasser et al., 2012; Ras et al., 2020) and non-linguistic tasks (Ek et al., 2010; Habets et al., 2014; Wefel et al., 2016), raises the question whether slowed performance of a language test is specific to language processing, or whether it has a more domain-general origin. This topic has been investigated in people with aphasia due to stroke. For example, individuals with aphasia (and individuals with left-hemispheric lesions without aphasia) were found to have lower processing speed both within and outside the language domain (Yoo et al., 2021).

Moritz-Gasser et al. (2012) and Ras et al. (2020), on the other hand, found that naming speed of patients with a glioma could not be explained by non-verbal processing speed measured with the TMT-A. Their findings suggest that there is a discrepancy between naming accuracy, naming speed, and general processing speed. However, these two studies investigated processing speed in the *production* of language, leaving *receptive* linguistic processing speed of patients with a glioma open for investigation. It is not self-evident that the influence of processing speed is the same in both language modalities, as a discrepancy between deficits in language production and reception has been described (De Witte et al., 2015b).

From this discussion of the literature it has become clear that the subjectively experienced communication difficulties are not always supported by impaired performance on standard language measures. Measuring processing speed may be useful in objectively assessing subjectively experienced word-finding problems, not only because information processing speed has often been found to be impaired in patients with a glioma, but also because everyday communication relies on speeded integration of linguistic information. Problems in everyday communication may therefore be the result of slower linguistic or non-linguistic processing abilities.

## Present study

We aim to investigate whether including a measure of response speed in a receptive language test is a sensitive measure for self-reported word-finding problems in patients with a glioma. The presence of self-reported word-finding problems was correlated with lexical retrieval, receptive linguistic processing speed, and non-verbal cognitive abilities. We compared a group of patients with a glioma to a group of age- and education-matched healthy control participants. Individual patients were also described and compared to norm groups. The following research questions were investigated:

RQ1: To what extent can self-reported word-finding problems of patients with gliomas be explained by:

*i. Lexical retrieval as measured with the Boston Naming Test or performance on a Token Test?*

*ii. Linguistic processing speed as measured with a time-pressured sentence judgment test?*

*iii. Non-verbal cognitive abilities as measured with the Trail Making Test A and B?*

RQ2: Is linguistic processing speed of patients with gliomas related to non-linguistic cognitive abilities?

Based on previous findings in the literature, we hypothesised a discrepancy between the subjectively experienced word-finding problems and the objectively measured abilities of patients (Brownsett et al., 2019; Satoer et al., 2012). The addition of reaction time measures to a sentence judgment test is expected to lead to a sensitive measure that can explain anamnestic complaints (Moritz-Gasser et al., 2012; Ras et al., 2020). Finally, if the word-finding problems and slower language processing are the result of a more global cognitive impairment, we expect that patients will also exhibit longer reaction times on a non-linguistic task.

## Methods

### Participants

The study group consists of glioma patients ($N$ = 50) who have undergone awake surgery (between March 2015 and November 2017) at the Erasmus MC University Medical Centre. All patients diagnosed with a glioma, regardless of the hemispheric localisation, were included in the study, as previous research has shown that patients with a glioma in the right hemisphere may also experience language difficulties (Vilasboas et al., 2017; De Witte et al., 2015c). Fourteen patients were excluded due to a recurrent tumour with second or third surgery ($N$ = 10)[1]; too many missing data ($N$ = 2); or co-occurring developmental dyslexia ($N$ = 1) or Noonan Syndrome ($N$ = 1). This resulted in 36 participants in the patient group. All patients were native speakers of Dutch.

Healthy native speakers of Dutch ($N$ = 35) constituted the control group of the study. They were matched to the patient group on age and education but not on gender, as gender has generally not been shown to influence performance on standard language tests (e.g., Snitz et al., 2009; De Witte et al., 2015b). They were included if they had no (history of) cardiovascular, neurological, psychiatric, or developmental language disorders; no toxic substance abuse; normal vision and hearing; no sleep medication, psychotropic, or neuroleptic drugs. The demographic information of the patients and control participants is given in Table 1. None of the participants was financially compensated for his/her participation. The Ethical Committee of the Erasmus MC approved of the study and all participants gave their informed consent.

### Materials

#### Word-finding problems

Information on word-finding problems in patients was based on complaints reported during the preoperative anamnesis. The information in the anamnesis is gathered in an interview with the patient by a clinical linguist, using a standard set of questions about encountered problems with language, memory, attention, and executive functioning. The word-finding complaints were labelled as follows: *0: no complaints; 1: mild complaints*, if the patients only reported difficulties after more targeted questions, if they indicate that they "sometimes" experience problems, or if their partner reported word-finding difficulties; *2: clear complaints*, if the patient presented their word-finding complaints centrally in the anamnesis, or with modifiers such as "often", or "severe". The same coder re-coded the data at a later timepoint and the intra-coder reliability was assessed using an intra-class correlation analysis. The intra-class correlation estimate was based on a single-rating, absolute-agreement, two-way mixed-effects model. The results show that agreement between these two timepoints was good-excellent (intraclass correlation coefficient = .89, $p$ < .001).

**Table 1.** Demographic and tumour characteristics. *Education level based on* Verhage (1964)*: Dutch classification system including 7 categories. 1: did not finish primary school, 2: finished primary school, 3: did not finish secondary school, 4: finished secondary school, low level, 5: finished secondary school, medium level, 6: finished secondary school, highest level, and/or college degree, 7: university degree).*

| Demographic characteristics for patients and control participants<br>Group | | Patients | Control participants |
|---|---|---|---|
| *Gender* | Female | 12 | 20 |
| | Male | 24 | 15 |
| *Mean age (range)* | | 45.37 *(18–73)* | 42.75 *(19–61)* |
| *Mean education (range)* | | 5.36 *(3–7)* | 5.53 *(3–7)* |
| *Handedness* | Right | 28 | N/A |
| | Left | 8 | N/A |
| ***Tumour characteristics for 36 patients*** | | | |
| ***Variable*** | | ***Count (%)*** | |
| *Hemispheric lateralisation* | Left hemisphere | 24 *(67)* | |
| | Right hemisphere | 12 *(33)* | |
| *Tumour localisation: lobe* | Frontal | 19 *(53)* | |
| | Temporal | 7 *(19)* | |
| | Insular | 1 *(3)* | |
| | Parietal | 3 *(8)* | |
| | Frontoparietal | 2 *(6)* | |
| | Parietotemporal | 1 *(3)* | |
| | Temporoparietal | 1 *(3)* | |
| | Frontotemporal | 2 *(6)* | |
| *Tumour histological type* | Astrocytoma | 13 *(36)* | |
| | Oligodendroglioma | 12 *(33)* | |
| | Glioblastoma | 10 *(28)* | |
| | Xanthoastrocytoma | 1 *(3)* | |
| *Tumour grade (WHO classification)* | Grade I | 1 *(3)* | |
| | Grade II | 20 *(56)* | |
| | Grade II | 5 *(14)* | |
| | Grade IV | 10 *(26)* | |

### *An example of a mild complaint*

> "Patient does not report cognitive problems. After additional questions, he reports subtle word-finding difficulties. Handwriting is also a bit messier."

### *An example of a clear complaint*

> "Patient reports word-finding difficulties that result in avoiding talking to people. Word is in mind but cannot be pronounced. Patient also fails in writing and typing. In addition, there are sound changes, and articles and function words that are forgotten."

### *Standard language tests*

The Boston Naming Test (BNT; Kaplan et al., 2001), a standard test to assess anomia in individuals with aphasia was administered. Patients also completed the shortened Token Test (TT; De Renzi & Faglioni, 1978), a standard test to measure aphasia severity.

### *Linguistic processing speed*

The Sentence judgment Test (SJT), a subtest of the Diagnostic Instrument for Mild Aphasia (DIMA; Satoer et al., 2021), was used to test comprehension and language processing on the semantic, syntactic, and phonological level. The SJT was administered in E-Prime software (Psychology Software Tools, 2012) or in Praat (Boersma & Weenink, 2018). The SJT consists of 30 sentences, half of which contain errors in three different linguistic domains. The phonological items aim to assess phonological awareness by including pseudo-words (Example 1). The syntactic items contain errors in verb inflection (tense and agreement), word order, or pronouns (Example 2), and the semantic items include sentences with semantic anomalies (Example 3).

*Example 1 De zanper koopt een blando.*
The zanper buy-AGR a blando
"The zanper buys a blando".

*Example 2 Linda zingt gisteren een lied.*
Linda sing-AGR.PRES yesterday a song
"Linda sings a song yesterday".

*Example 3 De loodgieter repareert de regenboog.*
The plumber repair-AGR the rainbow
"The plumber repairs the rainbow".

The participants read the sentences on a computer screen and rated their correctness by pressing the keys "F" for *fout* "wrong" and "J" for *juist* "right" on the keyboard. Reaction times (RTs) in milliseconds and accuracy were measured. RTs were operationalised as the time between the start of the stimulus presentation and the manual response of the participant. Items were presented in randomised order, and the test contained four practice items to familiarise participants with the procedure.

### Non-language tests

Nonverbal cognitive abilities of the participants were assessed using the Trail Making Test A and B (TMT-A and -B; Army Individual Test Battery, 1944). In the TMT-A, the participant connects numbers (1–25) in an ascending order on a paper sheet. The TMT-B requires the participant to connect alternating numbers and letters (i.e., *1-A-2-B-3* etc.). The score on both tasks consists of the time in seconds it takes to finish. Visuoperceptual speed underlies performance on the TMT-A, while TMT-B relies more heavily on updating and concept-shifting abilities (Sánchez-Cubillo et al., 2009). The difference score TMT-BA, operationalised as the ratio score B:A, provides a relatively pure measure of cognitive flexibility.

## Procedure

The clinical staff at the Erasmus MC University Medical Centre collected the data of the patients. An elaborate neuro-linguistic test protocol was administered as part of the standard clinical work-up, and the tests we report on in the present study are part of this protocol. The results of the preoperative assessment were compared to the performance of healthy control participants, who were tested in a private setting. The BNT, SJT, and TMT were administered in a random order. The entire procedure lasted approximately 15 minutes.

### *Data analysis*

All statistical analyses were carried out in R (R Core Team, 2019) and the graphics were created using R-package *ggplot2* (Wickham, 2016). The results on the SJT, TMT, TT, and BNT constitute the dependent variables. The data were analysed using regression models in the R package *lme4* (Bates et al., 2015) and *lmerTest* (Kuznetsova et al., 2017) to retrieve *p*-values. The accuracy scores and RTs of the SJT were analysed with a (generalised) linear mixed-effects regression model with random slopes for participants and items. The outcomes of the TMT, TT, and BNT were analysed using a linear regression model. The scores on the TMT were log-transformed to meet the model criteria. We adhered to an α-level of 0.05.

The main predictor in each model was *group* (patients vs. control participants), and covariates *age* and *education level* were included in all models. Within the patient group, the effects of *tumour grade* (LGG vs. HGG) and *hemisphere* (left vs. right) and the interaction effect between these factors were estimated. The output of the statistical models is included in the Appendix.

The analysis of the SJT results was carried out with the anomalous sentences.[2] *Linguistic levels* (semantics, syntax, phonology) and *trial-by-trial sequence* (i.e., the position of each item in the test) were included as additional within-participant predictors. We removed outliers before the group analysis of the RTs of the SJT. Items with an RT below 500 milliseconds were removed as it is assumed that participants need at least 500 milliseconds to properly assess an item, so shorter RTs are likely due to slips of attention. In addition, items with an RT above 10 seconds were removed, as the E-Prime experiment included a time limit and any responses longer than 10 seconds were classified as null responses. This led to the exclusion of 13 trials (0.7%). Thereafter, outliers per participant were calculated and removed from the dataset using the *trimr* package (Grange, 2015). An outlier was defined as an RT value of 2 SD above or below the mean for each participant. This led to the exclusion of 87 trials (5%). The remainder of the RTs were log transformed to normalise the data and meet the model criteria. The log-transformed RTs provided a good fit for the raw data ($\rho = .96$, $p < .001$).

To estimate the relationship between the anamnestic complaints and the scores on the objective measures, the correlation between these measures was calculated using Pearson's correlation coefficient.

## Results

### *Lexical retrieval*

The results at the individual patient level are presented in Table 2. Preoperatively, 15 out of 36 patients (42%) did not report any word-finding difficulties. Twenty-one patients (58%) reported word-finding problems of which twelve patients (33%) reported mild word-finding problems, and nine patients (25%) reported serious word-finding problems. Tumour grade did not significantly influence the experienced word-finding problems

**Table 2.** Individual patient scores. Table legend: PP; participant number, Age; age in years at time of assessment, Edu; education level based on Verhage (1964), Sex; male (M) or female (F), Hand; handedness left (L) or right (R), Grade; tumour grade from I–IV based on WHO classification, Location; location of the tumour: left (L) or right (R) hemisphere followed by lobe, WFP; word-finding problems, BNT; score on Boston Naming Test, TT; score on shortened Token Test, TMT-A; score (sec) on Trail Making Test-A, TMT-B; score (sec) on Trial Making Test-B, TMT-BA; ratio of difference score TMT part A and B, SJT; reaction times (ms) and accuracy scores on the Sentence Judgment Test. Deviant scores marked in **bold.**

| PP | Age | Edu | Sex | Hand | Grade | Location | WFP | BNT | TT | TMT-A | TMT-B | TMT-BA | SJT Semantics | Syntax | Phonology | Accuracy |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **1** | 18 | 6 | M | L | I | L Frontal | No | 58 | 36 | 21 | 38 | 1.8 | 1759 | 2459 | 1824 | 15 |
| **2** | 21 | 5 | M | R | III | L Fronto-parietal | Mild | **45** | 34 | **41** | **100** | 2.4 | 3313 | **4473** | **2842** | **12** |
| **3** | 23 | 5 | F | R | II | L Frontal | Clear | 56 | 36 | 28 | 64 | 2.3 | | | | |
| **4** | 23 | 6 | M | R | IV | L Frontal | No | **48** | 36 | 17 | 33 | 1.9 | 1723 | 2088 | 1333 | 15 |
| **5** | 32 | 5 | F | L | III | L Fronto-temporal | Clear | **49** | 31 | **55** | **174** | **3.2** | | | | |
| **6** | 32 | 5 | M | R | III | R Parietal | No | 51 | 28 | 29 | 80 | 2.8 | | | | |
| **7** | 33 | 4 | M | R | II | R Frontal | Mild | **44** | 34 | 37 | **108** | 2.9 | 2696 | 4035 | 2827 | 14 |
| **8** | 34 | 5 | M | L | II | L Frontal | No | **48** | 33 | 29 | 58 | 2.0 | | | | |
| **9** | 36 | 7 | M | R | II | R Frontal | Mild | 58 | 34 | 24 | 34 | 1.4 | 1479 | 1576 | 1327 | 15 |
| **10** | 36 | 5 | M | R | II | L Frontal | Clear | 54 | 33 | 34 | 84 | 2.5 | **6695** | **5977** | 4228 | **11** |
| **11** | 36 | 6 | M | R | IV | L Temporo-parietal | Clear | 54 | 35 | 19 | 46 | 2.4 | 3647 | 3012 | 1491 | 15 |
| **12** | 42 | 5 | F | L | IV | L Temporal | Clear | **34** | **25** | **46** | **127** | 2.8 | 3163 | **4300** | **2991** | 15 |
| **13** | 42 | 5 | F | R | IV | L Frontal | No | **38** | 34 | 23 | 84 | **3.7** | 3648 | 2660 | **2707** | 13 |
| **14** | 42 | 7 | M | R | III | R Parieto-temporal | Mild | 57 | 35 | 22 | 48 | 2.2 | 2404 | 2421 | 1441 | **11** |
| **15** | 43 | 5 | F | R | II | R Frontal | No | 52 | 34 | 17 | 56 | **3.3** | 1578 | 2180 | 1142 | 15 |
| **16** | 45 | 5 | M | R | II | R Fronto-parietal | Clear | 56 | 36 | 24 | 87 | **3.6** | | | | |
| **17** | 46 | 6 | M | L | III | L Frontal | Mild | **50** | 36 | 18 | 40 | 2.2 | 2468 | **4789** | 2271 | 14 |
| **18** | 47 | 3 | F | R | II | L Frontal | No | **48** | 35 | 30 | 103 | **3.4** | | | | |
| **19** | 47 | 5 | M | R | II | R Temporal | Mild | | | | | | 2898 | 2597 | 2211 | **12** |
| **20** | 48 | 5 | M | R | II | R Frontal | No | **49** | 33 | 41 | 52 | 1.3 | 2309 | 3157 | 1405 | 14 |
| **21** | 49 | 6 | F | L | IV | L Frontal | No | 56 | 30 | 27 | 62 | 2.3 | | | | |
| **22** | 49 | 5 | F | R | II | R Temporal | No | 54 | 35 | 31 | 60 | 1.9 | 2506 | 3582 | 1599 | 14 |
| **23** | 50 | 7 | M | R | II | R Frontal | No | 59 | 35 | 14 | 38 | 2.7 | 1596 | 2408 | 1404 | 15 |
| **24** | 51 | 5 | F | R | II | L Parietal | Mild | **35** | 35 | 21 | 34 | 1.6 | | | | |
| **25** | 51 | 6 | M | R | II | L Insular | Clear | **48** | 35 | 33 | 52 | 1.6 | | | | |
| **26** | 51 | 7 | M | R | II | L Frontal | No | 58 | 36 | 19 | 34 | 1.8 | | | | |
| **27** | 52 | 5 | M | R | II | L Temporal | Mild | 54 | | 29 | 80 | 2.8 | | | | |
| **28** | 53 | 4 | M | L | II | L Parietal | No | **34** | 33 | 35 | 79 | 2.3 | | | | |
| **29** | 54 | 5 | F | R | IV | L Temporal | Mild | **44** | | | | | | | | |
| **30** | 57 | 5 | M | R | II | R Frontal | Mild | **36** | 36 | 42 | 56 | 1.3 | 2210 | 2683 | 1853 | **13** |
| **31** | 59 | 6 | M | R | II | R Fronto-temporal | No | 53 | 36 | 15 | 49 | **3.3** | 2586 | 2152 | 2774 | **13** |

(*Continued*)

**Table 2.** (Continued).

| PP | Age | Edu | Sex | Hand | Grade | Location | WFP | BNT | TT | TMT-A | TMT-B | TMT-BA | SJT Semantics | Syntax | Phonology | Accuracy |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **32** | 62 | 5 | F | R | II | L Temporal | Mild | 55 | | 17 | 37 | 2.2 | 1414 | 2097 | 1103 | 12 |
| **33** | 63 | 5 | M | R | IV | L Frontal | Mild | 53 | 35 | | | | 3329 | 3614 | 3225 | **13** |
| **34** | 66 | 5 | M | R | IV | L Frontal | No | | 32 | 53 | 106 | 2.0 | | | | |
| **35** | 69 | 6 | F | L | IV | L Temporal | Clear | **20** | 32.5 | 38 | **199** | **5.2** | | | | |
| **36** | 73 | 6 | M | R | IV | L Frontal | Clear | 54 | 35 | 48 | **318** | **6.6** | **5595** | **6030** | **4928** | **14** |

(ß = −0.26, SE = 0.34, p = .45), neither did the hemispheric localisation (ß = 0.58, SE = 0.62, p = .36). There was no significant interaction between grade and hemispheric localisation (ß = 0.36, SE = 0.72, p = .62).

At the group level, patients (*M* = 48.9, 82%) deviated from the control participants (M = 52.9, 88%) on the BNT (ß = 3.54, SE = 1.62, p = .03). The patients' BNT scores were not significantly influenced by tumour grade (ß = 4.41, SE = 3.71, p = .24), hemispheric localisation (ß = 8.57, SE = 6.78, p = .22), or an interaction between these factors (ß = −7.23, SE = 7.87, p = .37). The experienced word-finding problems were not always accompanied by deviant scores on the BNT and these outcomes were not correlated (ρ = −.15, p = .40). Of the patients who reported word-finding difficulties, one did not perform the BNT. Ten out of the remaining twenty patients with reported word-finding problems (50%) also showed deviant scores on the BNT.

The scores on the shortened Token Test did not correlate with the reported word-finding difficulties (ρ = −.07, *p* = .71). The mean score of the patient group was 33.8 out of 36 points. Adhering to the cut-off score of 29 (De Renzi & Faglioni, 1978), only one patient showed a deviant score on the Token Test. The Token Test scores were not significantly influenced by tumour grade (ß = 1.79, SE = 1.08, p = .11), or hemispheric localisation (ß = −1.38, SE = 1.86, p = .47). And there was no significant interaction effect between these variables (ß = 1.43, SE = 2.19, p = .52).

### *Linguistic processing speed*

At the group level, there were no significant differences for RTs between patients and control participants (ß = −0.02, *SE* = 0.08, *p* = .84), but the difference between the two groups on accuracy scores in all linguistic domains combined was significant (ß = 1.16, *SE* = 0.41, *p* = .01). The differences between the groups are presented in Figure 1. Tumour grade, hemispheric localisation, or the interaction between these factors, did not significantly affect RTs nor accuracy scores. The reported word-finding problems were strongly correlated with the RTs on the SJT averaged over all linguistic domains (ρ = .64, $p < .01$), and with each linguistic level separately (*syntax*: ρ = .61, *p* = .003; *semantics*: ρ = .64, *p* = .002; *phonology*: ρ = .55, *p* = .01). However, the word-finding complaints did not correlate significantly with the accuracy scores on the SJT over all linguistic domains (ρ = −.23, *p* = .31).

At the individual patient level, it appears that there is a subgroup of patients with deviant RTs in the SJT compared to normative data (Satoer et al., 2021). Six out of twenty-one (29%) patients had slightly deviant RTs (≥1.5 SD from population mean) in at least one of the three linguistic domains (phonology, semantics, syntax). All six patients with deviant RTs on the SJT had a glioma in the left hemisphere, and all but one (83%) in the frontal lobe. One patient (17%) had a grade-II glioma, two patients (33%) a grade-III glioma, and three patients (50%) had a grade-IV glioma. Eight out of twenty-one (38%) patients showed deviant accuracy scores on the SJT. Nine out of 35 control participants (26%) had deviant RTs on one of the language domains of the SJT, and two control participants (6%) showed deviant accuracy scores.

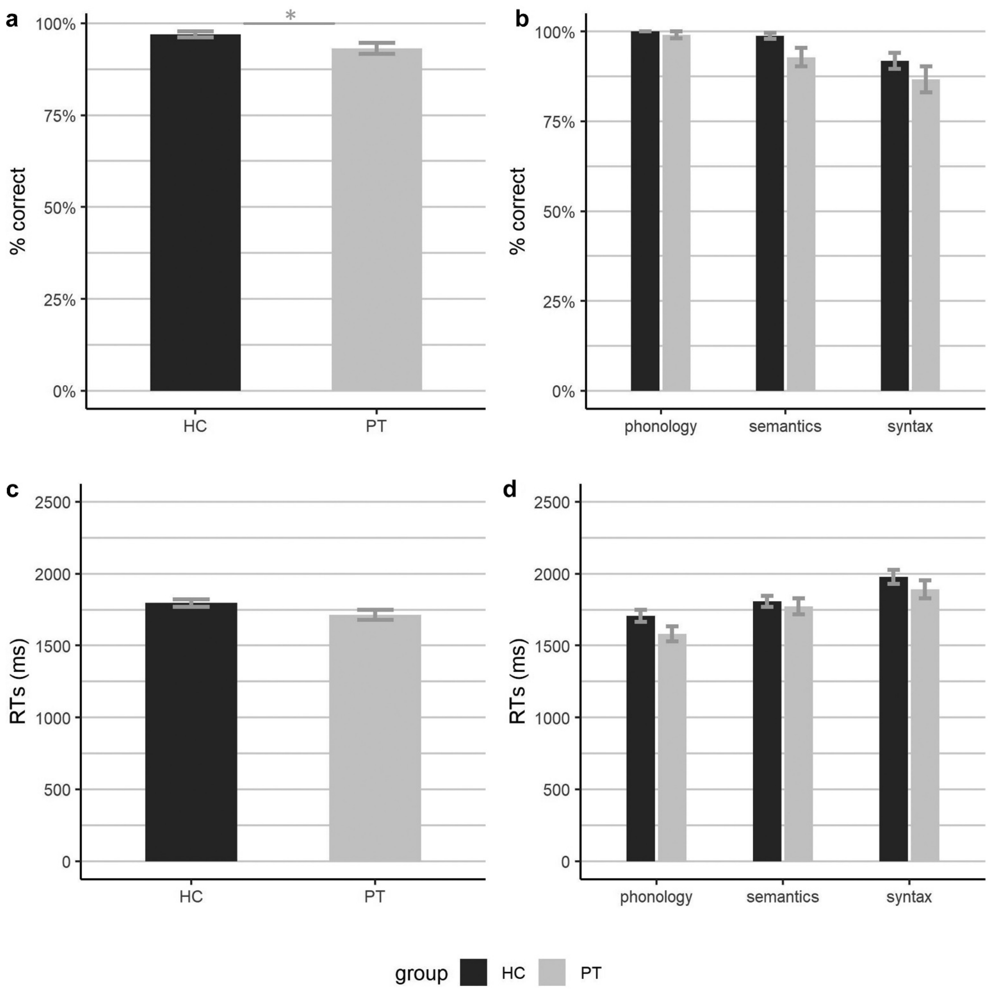


**Figure 1.** Reaction times (in milliseconds) and accuracy (percentage correct) on the SJT for healthy control participants (HC) and patients (PT) and per linguistic domain. Error bars represent the standard error.

## *Non-verbal cognitive measures*

At the group level, there was no statistically significant difference between the patient group and the control group on the TMT-A and B (ß = 0.08, SE = 0.08, p = .30 for TMT-A and ß = 0.13, SE = 0.09, p = .16 for TMT-B). However, patients had a larger difference score on the TMT-BA compared to healthy participants (ß = 0.56, SE = 0.19, p = .004). The differences between the groups are presented in Figure 2. Within the patient group, patients with an HGG were slower to finish the TMT-B (ß = −0.51, SE = 0.22, p = .03) and had a larger ratio score on TMT-BA (ß = −0.96, SE = 0.45, p = .04) compared to patients with an LGG. This was not the case for the TMT-A (ß = −0.22, SE = 0.16, p = .17). There were no significant main effects of hemispheric localisation or interaction effects between these factors on any of the TMTs.

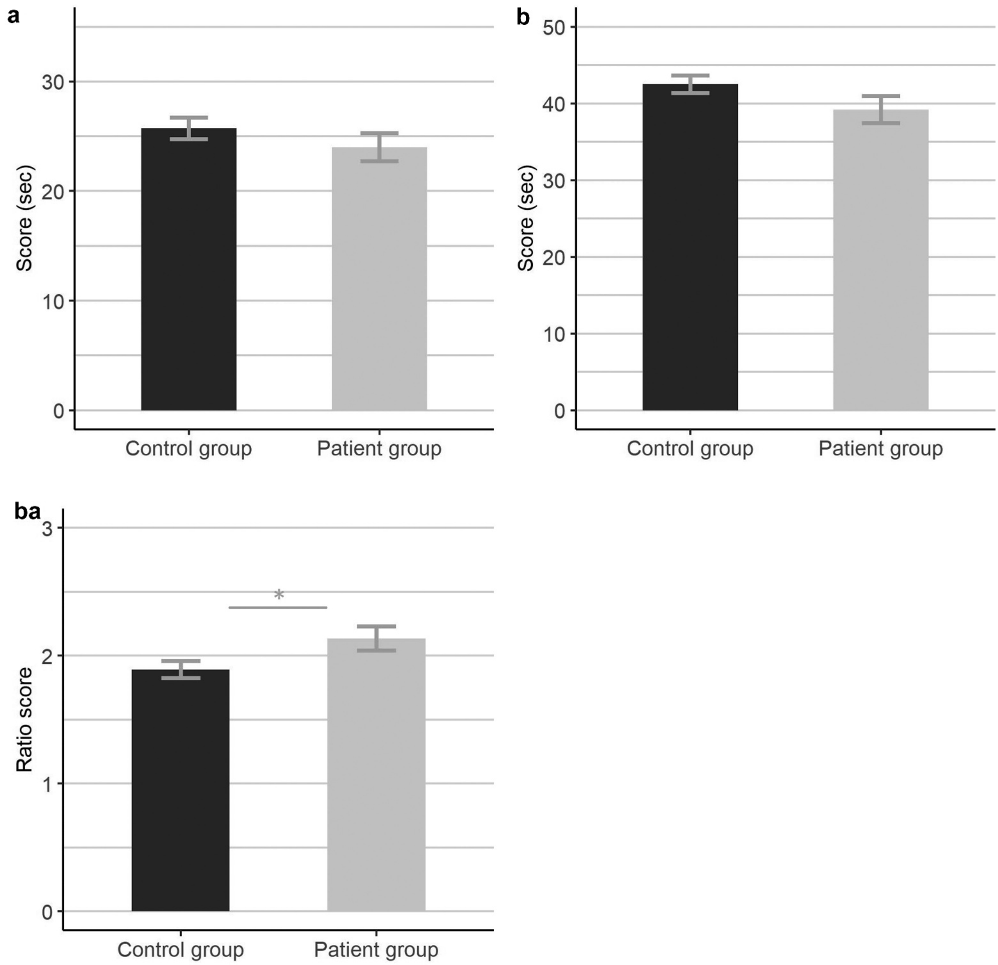


Figure 2. Scores (in seconds) on the TMT-A and TMT-B and ratio scores on TMT-BA per participant group. Error bars represent the standard error.

In the patient group, performance speed on the TMT-A and -B strongly correlated with the RTs on the SJT (ρ = .61, $p$ = .01 for TMT-A and ρ = .74, $p$ < .001 for TMT-B), indicating that longer RTs on the SJT were accompanied by longer completion time on the TMT-A and -B. The ratio of the difference score TMT-BA also correlated moderately with the RTs on the SJT (ρ = .59, $p$ = .01), indicating a shifting component in the SJT independent of speed. Interestingly, in the control group significant correlations between the RTs on the SJT and the TMT-A and -B were absent (ρ = .20, $p$ = .256 and ρ = .10, $p$ = .58, respectively). In the control participants, the ratio score of the difference TMT-BA also did not correlate significantly with the RTs on the SJT (ρ = −.07, $p$ = .682). These correlations are presented in Figure 3.

There was a weak but significant correlation between the reported word-finding problems and the TMT-B (ρ = .44, $p$ = .01) and a marginally significant correlation between the word-finding problems and the TMT-A (ρ = .34, $p$ = .052). The correlation between word-

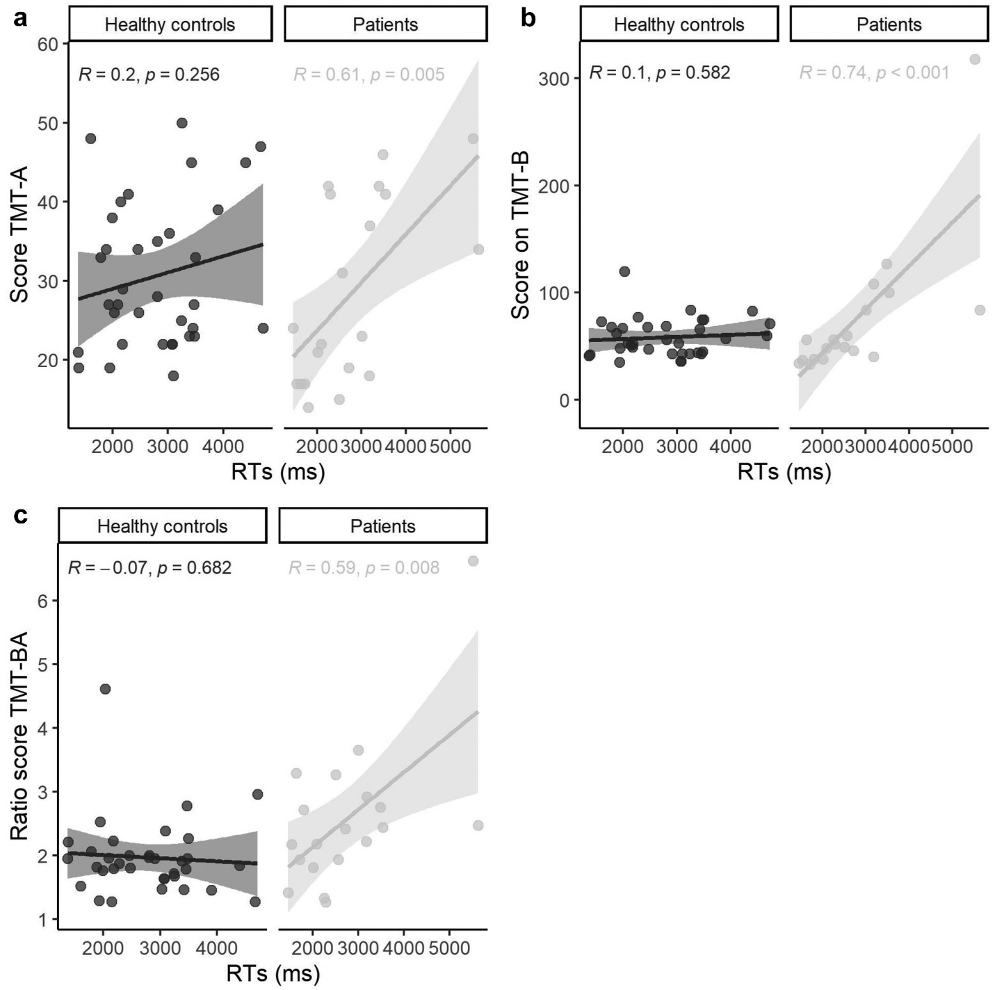


**Figure 3.** Correlations between the reaction times (milliseconds) on the SJT and the TMT-A (A), TMT-B (B), and TMT-BA (C).

finding problems and the TMT-BA was not significant (ρ = .32, $p = .07$). Model comparison showed that the linear regression model with only the RTs in the SJT as a predictor (and no TMT measure) yielded the best fit for the word-finding problems (Figure 4).

Eleven out of 33 patients (33%) had an impaired score on at least one of the subcomponents of the TMT (Tombaugh, 2004). Three patients (9%) scored >1.5 SD from the normal score on both the TMT-A and B. Three patients (9%) had problems with the TMT-B and a deviant difference score TMT-BA (cut-off ratio score >3, Arbuthnott and Frank, 2000). Five out of 33 patients (15%) had a selective problem with concept shifting (cognitive flexibility), exemplified by a deviant difference score TMT-BA.

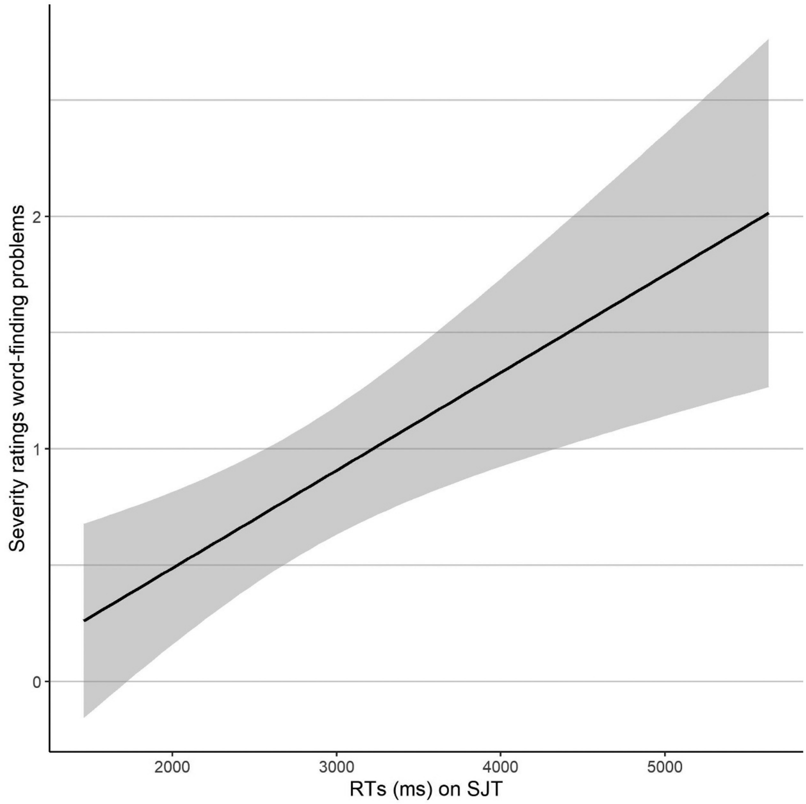


Figure 4. Visualisation of linear regression model of the reported severity of word-finding problems predicted by the reaction times (milliseconds) on the SJT.

## Discussion

### *Linguistic processing speed and word-finding complaints*

We aimed to examine whether assessment of processing speed in a receptive language test would provide a sensitive measure to objectively determine reported language problems, and whether it is related to non-verbal processing speed. First, we showed that 58% of glioma patients experience word-finding difficulties in daily life, but that their reported problems were supported by deviant BNT scores in only 50% of the cases. The reported word-finding problems also did not correlate with the accuracy scores on the SJT. The Token Test proved to be insensitive to detect language problems in this patient group; only one patient scored below the cut-off level and the scores were not correlated with the reported word-finding problems. At the group level, however, glioma patients scored significantly worse on the BNT and had worse accuracy scores on the SJT compared to the control group.

The discrepancy between reported language complaints and scores on objective language measures has been described in previous research (Satoer et al., 2012). In addition, there is evidence that impaired linguistic variables found in spontaneous speech of glioma patients do not correlate with performance on standardised language tests (Satoer et al., 2018, 2013). At the same time, Brownsett et al. (2019) found that after surgery, 58% of glioma patients reported communication difficulties, which did not correspond with the Aphasia Quotient of the Western Aphasia Battery-Revised (Kertesz, 2006, 27% of patients scoring below normal cut-off), but could be explained with the scores on the Comprehensive Aphasia Test (Swinburn et al., 2004, 77% of patients scoring below normal cut-off). The inconsistency between the BNT scores and the language complaints we found in the current study could indicate that the word-finding problems originate from an issue other than a pure lexical retrieval deficit.

We investigated the relationship between the reported complaints and linguistic processing speed. Previously, productive language tasks with a time constraint have been reported to be difficult for glioma patients, illustrated by longer response times on naming tasks (Moritz-Gasser et al., 2012; Ras et al., 2020). In contrast to our expectations, the results of the current study did not show deviant group-level performance on the RT measure of the SJT, which assesses speed of receptive language processing. However, glioma patients had significantly lower accuracy scores compared to the control group. This could be due to a deviant speed/accuracy trade-off, in which higher response speed is favoured over accurate responding.

In a subsequent analysis, we looked at the individual RT scores in the SJT and found that all patients with long RTs had a glioma in the language-dominant hemisphere, mostly in the frontal lobe. This seems to suggest that assessing speed of language processing in patients with left frontal damage may be particularly useful, although data from more patients is necessary to further investigate this observation.

In contrast to the absence of a significant correlation between the word-finding problems and BNT and accuracy scores, more severe word-finding complaints were accompanied by longer RTs on the SJT. We found that the presence of word-finding problems was significantly correlated with the overall RTs in the SJT, but also with each linguistic level separately. The commonalities between the different linguistic levels may point to a shared underlying attentional component required to perform this task. This is in accordance with the finding that the reported complaints also correlated with performance of the TMT. Although the TMT is not a perfectly matched non-verbal equivalent of the linguistic processing speed task, it provides a measure of visuoperceptual speed and relies on attention. Therefore, our findings could imply that domain-general attentional mechanisms underlie experienced word-finding problems. This aligns with previous research in which attentional deficits were observed in persons with self-reported mild anomia, who performed within normal limits on standard language assessments (Hunting-Pompon et al., 2011).

At the same time, it must be noted that the observed correlations between reported word-finding problems and the TMT were weaker than the correlations with the SJT. A model with linguistic processing speed as a sole predictor best fit the word-finding complaints of the patients, compared to models also including scores on the TMT as predictors. This indicates that, despite an important role for more domain-general processing abilities in lexical retrieval, there appears to be an indispensable linguistic factor to word-retrieval difficulties.

The word-finding problems may be the most salient issue that glioma patients experience in everyday communication. Dialogues require conversational partners to process verbal information quickly and respond to it promptly in an appropriate manner. This entails the integration of a range of different abilities, which may be challenging for individuals with aphasia. For example, they have been shown to experience more difficulties with language production on a story retelling task, when they have to perform another task simultaneously (Harmon et al., 2019). Apart from linguistically meaningful and grammatically correct output, other cognitive functions, attention and executive functioning in particular, have been shown to play a crucial role in the successful everyday communication of aphasic speakers (Fridriksson et al., 2006; Olsson et al., 2019). This may be an explanation for the relationship between word-finding complaints and slower processing of both linguistic and non-linguistic tasks. Given the characteristics of functional communication, their experienced word-finding problems could be the result of slowed processing rather than lost function.

### *Underlying mechanism of linguistic processing speed*

The significant correlation between performance of the TMT and the presence of reported word-finding difficulties could imply that there is a domain-general attentional basis for the experienced language difficulties. This is corroborated by the significant correlation between RTs on the language task (SJT) and performance on the non-verbal tasks (TMT-A and B), indicating that longer completion time on the TMT co-occurred with longer reaction times on the SJT. The cognitive abilities known to underlie performance speed on the TMT are visuoperceptual speed (TMT-A and -B) and concept shifting (TMT-B and -BA).

Remarkably, a significant correlation only existed in the patient group and was absent in the control group. This suggests that linguistic and non-linguistic functions are more heavily interconnected in glioma patients as compared to healthy participants. In addition, the contribution of domain-general abilities in performing language tasks could explain why the outcomes on the BNT and SJT were not influenced by hemispheric tumour localisation. If patients recruit domain-general cognitive abilities to perform language tasks, lesions in the left or right hemisphere may lead to impairments.

These results show that the receptive linguistic processing speed partially constitutes a more general cognitive speed. This is in accordance with the literature on persons with aphasia due to stroke. For example, Yoo et al. (2021) found that persons with aphasia show domain-general cognitive slowing, as indicated by slower processing speed on linguistic and non-linguistic tasks. However, our finding is in contrast with Ras et al.'s (2020) and Moritz-Gasser et al.'s (2012) results for patients with a glioma, who did not find a significant correlation between the RTs on a rapid naming test and overall processing speed measured with the TMT-A.

One potential explanation for this discrepancy lies in the difference between modalities of the used language tests. In the present study, we measured receptive reading abilities, whereas Ras et al. and Moritz-Gasser et al. administered a speeded naming test, assessing language production in a more isolated manner. As Sánchez-Cubillo et al. (2009) noted, the TMT-A mainly relies on visual search and perceptual speed. Therefore, a comparison between a reading task such as the SJT (both perceptual and visual) and the TMT-A may result in stronger relationships than with a naming task. Importantly, Moritz-Gasser et al. did find naming speed to be highly correlated with executive tasks that require lexical access (fluency and the Stroop test), and argue that the decreased naming speed, in absence of impaired naming accuracy, is due to the cognitive functions involved in language processing.

We found that linguistic processing speed was correlated with the ratio score of the TMT-BA, a measure of concept shifting. This could be because multiple linguistic levels are combined in the SJT. The participants assessed correct sentences and sentences that contain a semantic, syntactic, or phonological error. The correct and incorrect items are presented in a randomised order. It could thus be argued that there is constant task switching within the SJT, placing a higher demand on cognitive flexibility (Rubinstein et al., 2001) and explaining the significant correlation with the ratio score of the TMT-BA. Combining various tests and presenting them in a rapidly alternating way has previously been shown to be a good way to assess brain tumour patients (De Witte et al., 2015b). The SJT requires the participant to simultaneously integrate various processes, such as sentence processing, sentence evaluation, and task switching.

## *Limitations of the present study*

A first limitation is that there was missing information on the language lateralisation via fMRI for the left-handed patients ($N$ = 8). All left-handed patients had a glioma in the left hemisphere. Previous research has shown that while language lateralisation is more mixed, the majority of non-right-handed people nevertheless show typical language lateralisation in the left hemisphere (Szaflarski et al., 2002). Secondly, we could not perform analysis on the specific tumour location and its effects on linguistic and non-linguistic functions due to small group sizes. This is an important direction for future work. Thirdly, although the reported word-finding problems were coded twice at different timepoints, allowing for an intra-coder reliability analysis, having multiple independent coders assess the complaints would have further increased the reliability of the scoring. A fourth limitation is the task choice of the present study. Considering that data collection took place in a clinical context, we were bound by the tasks that are part of the standard clinical work-up. While the TMT and SJT are good measures of visuoperceptual processing speed and linguistic processing speed, respectively, and both tasks rely on attentional processes, the two tasks are not perfectly matched verbal and non-verbal variants. A final limitation of the study is that a pure reading task was not part of the test protocol. Consequently, we could not verify whether reading issues interfered with performance on the SJT. While this should be addressed in future studies, previous research has shown that reading performance is generally unaffected in glioma patients (Satoer et al., 2014, 2012).

## *Clinical implications and future directions*

In clinical practice, demands for brevity generally compete with needs for sensitivity (e.g., Ek et al., 2010). Therefore, critical evaluation of the sensitivity of tests can guide the selection of materials for a patient group. The SJT is part of the DIMA (Satoer et al., 2021), which is designed to be both short and sensitive enough to detect mild language difficulties in patients with neurological diseases. The finding that deviant RTs in the SJT were most often observed in glioma patients with a lesion in the frontal lobes of the dominant hemisphere suggests that the task may be particularly suitable for this patient group. This is in accordance with De Witte et al. (2015b) who also suggest the administration of sentence judgment tests in patients with gliomas in the frontal and temporal (sub)cortical areas. Including measures of RTs, as was done for the SJT in the DIMA, could further increase the value of such judgment tests.

The finding that, despite a significant correlation between the TMT and the RTs on the SJT, not all patients with deviant scores on the SJT show impaired performance on the TMT (or vice versa) is an indication that both tests are necessary for a reliable interpretation of cognitive functioning. Additionally, considering that at the group level, patients do not show significantly lower processing speed than healthy control participants, demonstrates the need for elaborate anamnesis and assessment tailored to the individual patient.

Our results imply that administering the SJT could be beneficial for patients who report word-finding problems, but do not show deviant scores on Token tests or standard naming tests. Assessing linguistic processing speed provides a way to objectively assess these complaints. The finding that word-finding problems were significantly, but weakly correlated with the TMT-A and – B, shows that lexical retrieval has a general processing speed component but cannot be fully explained by this. This is an important observation that deserves attention in the clinical setting. Clinicians could try to gain additional information on the distinction between delayed and failed lexical access by administering a naming test under time pressure. The anamnesis is another valuable source of information; clinicians could ask patients more targeted questions about word retrieval. Patients differ in how they present their complaints during the anamnesis, which emphasises the importance of asking more thorough questions. Examples of such questions are whether difficult words surface eventually or not at all, or whether there are specific circumstances (noisy environments, time pressured conversations, etc.) under which word-finding problems are more prominent.

Finally, investigating the relationship between the performance of the SJT and non-linguistic functions in populations with different neurological diseases, such as stroke or traumatic brain injury, is a potential direction for future work. The result that response speed of the SJT only correlates with visual search speed and concept shifting in the patient group, and not in healthy participants, suggests that patients may recruit a wider network to perform language tasks. It is interesting to see if similar relationships can be observed in patients with other neurological impairments. Moreover, this finding can serve as a starting point for therapy. Previous work on cognitive rehabilitation of glioma patients has found that in-person training (Locke et al., 2008), and telerehabilitation (Van der Linden et al., 2018) of cognitive functions is feasible and evaluated positively. Cognitive rehabilitation has short-term positive effects on subjective cognitive functioning and longer-term objective benefits for attention and verbal memory (Gehring et al., 2009). However, detailed individual assessment of the patient's impairments should guide the choice of therapy.

## Conclusions

This research studied the linguistic processing speed in glioma patients and investigated whether these abilities could be a more sensitive measure to capture word-finding complaints. We found that patients' reported word-finding problems were not correlated with the BNT, a well-known test to assess lexical retrieval difficulties, nor with accuracy scores on the SJT. However, the word-finding problems were correlated with linguistic processing speed, operationalised as response speed in the SJT. At group-level, apart from patients with a glioma in the frontal lobe of the dominant hemisphere, response speed of the SJT was not deviant in glioma patients compared to the healthy control group. Furthermore, a relationship between linguistic processing speed and non-verbal functioning was found in the glioma patients but not in the healthy control group, suggesting that patients rely on more domain-general abilities to perform the task. These results indicate that the SJT, a time-constrained task assessing receptive language abilities, appears to be influenced by non-verbal processing speed, and that processing speed may contribute to subjectively experienced problems. This demonstrates the importance of administering tasks that assess language as well as non-verbal cognitive processing speed for the interpretation and dissociation of impairments.

## Notes

1. Patients with a recurrent tumour are excluded because it is impossible to attribute their preoperative impairments to the presence of the tumour alone, as their impairments may also be the result of the previous surgery.
2. An analysis including both correct and incorrect target items showed that there was a significant main effect of *correctness* of the item on the reaction times across both groups (ß = 0.25, $SE$ = 0.05, $p < .001$). Participants responded significantly faster to anomalous sentences than to correct target sentences.


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## Disclosure statement

No potential conflict of interest was reported by the author(s).



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## Appendices

Outcomes of the statistical models.

*Influence of participant characteristics*

The demographic factors *age* and *education level* were included in the statistical models as covariates. These factors contributed significantly to the outcomes of the BNT, TMT, and the RT measures of the SJT. The effect of age and education level on these tests has been corroborated in earlier studies (Snitz et al., 2009; Tombaugh, 2004; De Witte et al., 2015b). In addition, significant interaction effects between age, education, and group on the SJT RTs, TMT-B, and TMT-BA, seem to suggest that older patients with lower education are more affected by their glioma than younger patients with a higher education when it comes to linguistic processing speed, visuoperceptual speed, and concept shifting.

**Table A.** BNT Score by group, age, and education level.

| | Estimate | Std.Error | *t*-value | *p*-value |
|---|---|---|---|---|
| (Intercept) | 51.082 | 0.812 | 62.908 | 0.000 |
| Group | 3.543 | 1.624 | 2.182 | 0.033* |
| Age | −0.022 | 0.061 | −0.352 | 0.726 |
| Education level | 3.422 | 0.945 | 3.621 | 0.001* |
| Group x Age | 0.275 | 0.122 | 2.249 | 0.028* |
| Group x Education level | −0.963 | 1.890 | −0.510 | 0.612 |
| Age x Education level | −0.049 | 0.086 | −0.574 | 0.568 |
| Group x Age x Education level | 0.093 | 0.172 | 0.542 | 0.590 |

**Table B.** Reaction times on the sentence judgment test.

| | Estimate | Std.Error | df | *t*-value | *p*-value |
|---|---|---|---|---|---|
| (Intercept) | 7.612 | 0.054 | 40.535 | 141.781 | 0.000 |
| Group | 0.016 | 0.081 | 47.968 | 0.201 | 0.841 |
| Education level | −0.131 | 0.050 | 48.042 | −2.623 | 0.012* |
| Age | 0.000 | 0.003 | 47.937 | 0.157 | 0.876 |
| Order | −0.010 | 0.002 | 722.384 | −5.320 | 0.000* |
| Semantics-Phonology | 0.165 | 0.051 | 11.803 | 3.206 | 0.008* |
| Syntax-Phonology | 0.357 | 0.052 | 11.957 | 6.920 | 0.000* |
| Group x Education level | 0.008 | 0.100 | 48.023 | 0.081 | 0.936 |
| Group x Age | −0.003 | 0.006 | 47.951 | −0.438 | 0.663 |
| Education level x Age | 0.015 | 0.005 | 47.996 | 3.222 | 0.002* |
| Order x Condition Sem-Phon | 0.007 | 0.003 | 722.336 | 2.450 | 0.015* |
| Order x Condition Syn-Phon | 0.009 | 0.003 | 724.654 | 3.109 | 0.002* |
| Group x Education x Age | −0.018 | 0.009 | 48.001 | −1.947 | 0.057 |

**Table C.** Summary accuracy scores Sentence Judgment Test.

| | Estimate | Std.Error | *z*-value | *p*-value |
|---|---|---|---|---|
| (Intercept) | 6.850 | 2.154 | 3.180 | 0.001 |
| Group | 1.156 | 0.414 | 2.790 | 0.005* |
| Education level | 0.431 | 0.248 | 1.740 | 0.082 |
| Age | 0.010 | 0.014 | 0.706 | 0.480 |
| Order | 0.201 | 0.200 | 1.009 | 0.313 |
| Semantics-Phonology | −3.351 | 2.169 | −1.545 | 0.122 |
| Syntax-Phonology | −4.485 | 2.155 | −2.081 | 0.037* |
| Group x Education level | −0.136 | 0.497 | −0.273 | 0.785 |
| Group x Age | 0.023 | 0.029 | 0.810 | 0.418 |
| Education level x Age | −0.008 | 0.020 | −0.413 | 0.680 |
| Order x Condition Sem-Phon | −0.233 | 0.204 | −1.143 | 0.253 |
| Order x Condition Syn-Phon | −0.128 | 0.202 | −0.637 | 0.524 |
| Group x Education x Age | −0.011 | 0.039 | −0.285 | 0.775 |

**Table D.** TMT-A Score by group, age, and education level.

| | Estimate | Std.Error | *t*-value | *p*-value |
|---|---|---|---|---|
| (Intercept) | 3.351 | 0.039 | 86.054 | 0.000 |
| Group | 0.082 | 0.078 | 1.048 | 0.299 |
| Age | 0.002 | 0.003 | 0.541 | 0.591 |
| Education level | −0.131 | 0.045 | −2.886 | 0.005* |
| Group x Age | −0.006 | 0.006 | −1.090 | 0.280 |
| Group x Education level | 0.132 | 0.091 | 1.454 | 0.151 |
| Age x Education level | 0.006 | 0.004 | 1.373 | 0.175 |
| Group x Age x Education level | −0.004 | 0.008 | −0.479 | 0.633 |

**Table E.** TMT-B Score by group, age, and education level.

| | Estimate | Std.Error | *t*-value | *p*-value |
|---|---|---|---|---|
| (Intercept) | 4.100 | 0.044 | 93.613 | 0.000 |
| Group | −0.125 | 0.088 | −1.431 | 0.158 |
| Age | 0.004 | 0.003 | 1.175 | 0.245 |
| Education level | −0.181 | 0.051 | −3.562 | 0.001* |
| Group x Age | −0.011 | 0.007 | −1.683 | 0.098 |
| Group x Education level | 0.188 | 0.101 | 1.851 | 0.069 |
| Age x Education level | 0.018 | 0.005 | 3.831 | 0.000* |
| Group x Age x Education level | −0.028 | 0.009 | −2.988 | 0.004* |

**Table F.** Ratio score TMT-BA score by group, age, and education level.

| | Estimate | Std.Error | *t*-value | *p*-value |
|---|---|---|---|---|
| (Intercept) | 2.249 | 0.094 | 23.900 | 0.000 |
| Group | −0.558 | 0.188 | −2.966 | 0.004* |
| Age | 0.013 | 0.007 | 1.790 | 0.079 |
| Education level | −0.101 | 0.109 | −0.926 | 0.358 |
| Group x Age | −0.027 | 0.014 | −1.891 | 0.063 |
| Group x Education level | 0.129 | 0.218 | 0.593 | 0.555 |
| Age x Education level | 0.033 | 0.010 | 3.307 | 0.002* |
| Group x Age x Education level | −0.067 | 0.020 | −3.345 | 0.001* |