Title 論文題目	Prediction of Early Postoperative Language Function by Quantitative Evaluation with Visual and Auditory Naming Tasks during Awake Craniotomy for Brain Tumor Resection: Significance of Auditory Naming Task. 覚醒下手術中における視覚性と聴覚性呼称課題を使用した定量的な言語機能評価による術後早期の言語機能予測：聴覚性呼称課題の意義
Author(s) 著者	若松，千裕
Degree number 学位記番号	甲第3207号
Degree name 学位の種別	博士(医学)
Issue Date 学位取得年月日	2023-03-31
Original Article 原著論文	Neurol Med Chir (Tokyo). 2023 May 15;63(5):191-199
Doc URL	
DOI	10.2176/jns-nmc.2022-0319
Resource Version	Author Edition

Title:

Prediction of Early Postoperative Language Function by Quantitative Evaluation with Visual and Auditory Naming Tasks during Awake Craniotomy for Brain Tumor Resection: Significance of Auditory Naming Task

Authors:

Kazuhiro Wakamatsu,[1,2] Sumio Ishiai,[1] Nobuko Aihara,[2] Sho Kurokawa,[2] Yusuke Kimura[3], and Nobuhiro Mikuni[3]

Affiliations:

1. Department of Rehabilitation Medicine, Sapporo Medical University School of Medicine, Sapporo, Hokkaido, Japan
2. Division of Rehabilitation, Sapporo Medical University Hospital, Sapporo, Hokkaido, Japan
3. Department of Neurosurgery, Sapporo Medical University School of Medicine, Sapporo, Hokkaido, Japan

Keywords: awake craniotomy, intraoperative monitoring, aphasia, auditory naming, brain tumor

Running Title: Intraoperative Quantitative Evaluation with VN and AN Tasks

Corresponding Author: Kazuhiro Wakamatsu, SLP., Division of Rehabilitation, Sapporo Medical University, S1W16, Chuo-ku, Sapporo, Hokkaido 060-8543, Japan.

Tel: +81–11–688–9633. Fax: +81–11–618–5220. Email: wakamatsu.k@sapmed.ac.jp

Abbreviations:

AN: auditory naming

AQ: aphasia quotient

AUC: area under the curve

fMRI: functional magnetic resonance imaging

ROC: receiver operating characteristic

PPTT: Pyramid and Palm Trees Test

VN: visual naming

WAB: Western Aphasia Battery

Abstract

Language tasks for monitoring intraoperative language symptoms have not yet been established. This study aimed to examine whether the quantitative evaluation of language function with visual and auditory naming during awake craniotomy predicts early postoperative language function in patients. Thirty-seven patients with brain tumors in the language-dominant hemisphere were included. They underwent visual and auditory naming preoperatively and at the end of tumor resection for intraoperative evaluation. Using the Western Aphasia Battery, their overall language functions were evaluated preoperatively, early postoperatively (within 1 week), and late postoperatively (after 1 month). The preoperative and intraoperative changes in the visual and auditory naming scores were significantly correlated with most of the Western Aphasia Battery score changes between the preoperative and early postoperative evaluations, which was more remarkable for auditory naming. Multiple linear regression analysis showed that changes in the auditory naming score predicted the preoperative to early postoperative changes in the aphasia quotient of the Western Aphasia Battery. Receiver operating characteristics analysis showed a higher area under the curve or discriminative power for auditory than visual naming in predicting the development or exacerbation of aphasia in the early postoperative period. Considering the analyses applied separately for low- and high-grade glioma, auditory naming, which taps into a wider range of linguistic functions, may be more informative than visual naming as language evaluation in awake craniotomy for the early postoperative development of aphasia, especially for patients with high-grade glioma.

Introduction

In neurosurgery for neoplastic lesions in the language-dominant hemisphere, maximizing the removal of neoplastic lesions while preserving language function after surgery improves the patient's quality of life[1–3] and boosts their return to society. Evaluation of language function in awake craniotomy involves functional brain mapping and monitoring language symptoms.[4–10] The most common evaluation of language function is mapping language areas, in which electrical stimulation is used to identify the language function-related areas.[4–6] Historically, neurosurgeons believe that resection excluding the areas where language functions are identified is safe for language preservation, and permanent language disorders do not occur unless the identified language area is removed.[11–13] However, mapping overall language functions is difficult within the limited time to evaluate language function during operation. Intraoperative mapping of language function may result in false-negative or false-positive results owing to various factors, including restriction to a small number of language assessments, fatigue, reduced arousal due to prolonged awake time, and decreased willingness to cooperate. Moreover, when electrical stimulation is intended to suppress the function of a specific cortical area transiently, its effect may not only be limited to the stimulated site but may also cause larger network disturbances distant from the stimulation point.[14]

The development and exacerbation of language disorders during brain tumor removal should also be monitored.[7–10] However, most previous studies have failed to quantitatively evaluate the intraoperative development of language impairments,[7–9] and few studies have linked the appearance and exacerbation of language disorders during surgery to postoperative language function.[10] Chan et al.[10] found that the intraoperative scores of visual (object) naming and the Pyramid and Palm Trees Test (PPTT) significantly correlated with the postoperative language outcome evaluated using an aphasia test battery. Although several tasks other than visual naming (VN) and PPTT have been used in awake craniotomies,[15–17] none are commonly used as intraoperative language tasks. In patients with temporal lobe epilepsy, the auditory naming (AN) task was superior to the VN in retrieving language disorders.[18–20] However, AN is not commonly used in awake craniotomy for patients with brain tumors, and its validity as a tool for monitoring intraoperative language function is largely unexplored.

Therefore, this study hypothesized that introducing a quantitative measurement of language functions with VN and AN would predict postoperative language outcomes. Moreover, we expected intraoperative AN to be an informative prognostic tool to explore a wider range of language functions.

Materials and Methods

Participants

The participants were patients who underwent surgery for brain tumor diagnosis in the language-dominant hemisphere and evaluation of language function during awake craniotomy at the Department of Neurosurgery of Sapporo Medical University Hospital from December 2012 to May 2022. The inclusion criteria were as follows: (1) adults (aged ≥ 20 years); (2) diagnosed with a first-ever primary intra-axial brain tumor in the language-dominant hemisphere; (3) able to undergo preoperative, intraoperative, and postoperative evaluation of language function; and (4) able to tolerate intraoperative evaluation of language function until the end of tumor resection. We excluded patients who were considered to exhibit language symptoms due to complications of postoperative stroke, which was rare in the present collection of participants. This retrospective study was approved by the Ethics Review Committee of the Clinical Research

Support Center of Sapporo Medical University Hospital (No. 342–101). As this study had a retrospective design, the requirement for informed consent by patients was waived, and an opt-out policy was used as a proxy for informed consent in this study.

Preoperative and postoperative evaluation of language function

The patients underwent the Western Aphasia Battery (WAB) Japanese edition, a comprehensive test battery of language functions. We included the aphasia quotient (AQ) provided by the WAB as an overall measure of aphasia and the WAB subtest scores of spontaneous speech, comprehension, repetition, and naming (composed of object naming and word fluency) in the analyses.

Language evaluations were conducted at three time points relative to the operation: preoperative, early postoperative (within 1 week after surgery), and late postoperative (after 1 month) periods. As this study included patients with high-grade glioma and late postoperative evaluation may lead to deterioration of language function due to recurrence of glioma, we set the postoperative observation period basically up to one month. For patients who underwent the WAB more than 1 month after surgery; however, we adopted the latest one for the late postoperative evaluation.

For the early postoperative changes in overall language function, the difference between the preoperative and early postoperative AQs of the WAB (ΔAQ = early postoperative AQ − preoperative AQ) was used as an index. Additionally, early postoperative changes were calculated for the WAB subtest scores (Δcomprehension, Δrepetition, Δnaming total, Δobject naming, and Δword fluency) and included in the analyses.

The aphasia severity of each patient was classified into five levels according to the AQ ranges proposed by Forkel et al.[21]: AQ 91.3 (mean −2 standard deviation [SD]) or higher as non-aphasia, 91.2–76 as mild, 75–51 as moderate, 50–26 as severe, and 25–as the most severe. If a patient's AQ level decreased by one or more, it was considered a worsening of aphasia severity.

Intraoperative quantitative evaluation of language function

VN and AN were performed as intraoperative evaluations of language function (Supplementary Table 1).[22]

In VN, the participants were presented with 20 colored drawings with familiar names for Japanese (familiarity mean 6.39 SD 0.20)[23] individually and were required to name the drawings individually. Patients' responses, other than the correct name for each drawing, were recorded as errors. VN requires cognitive processes, such as visual object perception, semantic access, lexical selection, and phonological processing.

In AN, the participants were presented with verbal descriptions (as sentences) of 30 highly familiar words (familiarity mean 6.38 SD 0.24)[23] individually and were required to say the target words the sentences meant. Responses other than the target word were recorded as errors. AN requires cognitive processes of auditory phonological processing, lexical retrieval, semantic access, and syntactic comprehension, followed by lexical and phonological processing for target word production. AN is a more demanding task for language functions than VN is.

VN and AN were also administered to the patients preoperatively to record their baseline performance. To represent the exacerbation of naming in awake craniotomy, the preoperative–intraoperative changes in the VN and AN scores were calculated and designated as ΔVN (intraoperative VN score − preoperative VN score) and ΔAN (intraoperative AN score − preoperative AN score). Three speech language pathologists (KW, NA, and SK) participated in this study. For one patient, one of the three consistently assessed the WAB and the naming tasks throughout the preoperative, intraoperative, early postoperative, and late postoperative periods.

Statistical analysis

Statistical analysis was performed using the JMP Statistical Analysis Software Fair (JMP Pro Version 15.1.0). Correlation analyses were conducted between the intraoperative exacerbation of naming (ΔVN and ΔAN) and the early postoperative changes in the WAB (ΔAQ, Δspontaneous speech, Δcomprehension, Δrepetition, Δnaming total, Δobject naming, and Δword fluency) in language function. Stepwise linear regression analysis was used to examine whether the intraoperative exacerbation of naming (ΔVN and ΔAN) could predict the postoperative changes in language function, with ΔVN and ΔAN as independent variables and the early postoperative language function changes as dependent variables. Receiver operating characteristics (ROC) analysis was used to investigate the discriminative power and optimal cutoff values of ΔVN and ΔAN, or the intraoperative exacerbation of naming, to predict postoperative aphasia exacerbation. The area under the curve (AUC) and Youden index were used to determine the discriminatory ability of ΔVN and ΔAN in predicting the appearance or exacerbation of aphasia in the postoperative period. The statistical significance level was set at 5%. The analyses described above were performed on all participants, as well as on the high-grade glioma and the low-grade glioma patient.

Results

The participants were 39 patients who underwent surgery for brain tumor diagnosis in the language-dominant hemisphere that was determined with functional magnetic resonance imaging (fMRI). Three were excluded from the study because of postoperative complications: complications of cerebral infarction in two and encephalitis in one. Electroencephalography revealed no epileptic discharges postoperatively in the 36 selected patients. Table 1 shows the demographic data of the 36 patients. Their age range was 21–82 years (mean, 49.1 years; SD, 16.4), and most (33/36) were right-handed. Brain tumors were mostly located in the left hemisphere, and the most common intrahemispheric site was the frontal lobe, followed by the parietal and temporal lobes and insula. Nineteen patients had high-grade glioma.

Table 1

The WAB results are presented in Table 2 (Supplementary Table 2 shows the WAB results separately for the low- and high-grade glioma patients). The WAB was performed preoperatively in all 36 patients, in the early postoperative period in 34 and the late postoperative period in 34. The WAB was not performed in two patients who showed no language disorder immediately after surgery. Moreover, two patients who were transferred to a local hospital or discharged did not also undergo late postoperative evaluation of the WAB. In the preoperative evaluation, most patients were diagnosed as non-aphasic, and a small number (one case with low-grade glioma and seven cases with high-grade glioma) had mild to severe aphasia. For all patients, the mean AQ of the WAB and the mean scores of the subtests decreased in the early postoperative evaluation compared with those in the preoperative evaluation. However, they recovered nearly to the preoperative level in the late postoperative evaluation. Regarding individual patients, the severity of aphasia worsened in 13 (38.2%) patients in the early postoperative evaluation and only in two (5.9%) patients in the late postoperative evaluation compared with the preoperative severity. One of the latter two patients was a 51-year-old right-handed woman with glioblastoma.

Table 2

She showed a change in AQ from 93.3 preoperatively to 88.3 early postoperatively, and her AQ further declined to 85.1 two months postoperatively even after 1 month of radiation and chemotherapy for the recurrence of brain tumor depicted by MRI. The other patient, an 82-year-old right-handed woman, had a ganglioglioma on pathology. She had mild dysarthria preoperatively and then exhibited apraxia of speech postoperatively. Her AQ worsened from 97.3 preoperatively to 78.4 early postoperatively and improved to 83.6, which was still the level of mild aphasia at 33 days postoperatively.

For VN and AN, we focused mainly on their last evaluation during craniotomy. Intraoperatively, VN was performed in 29 patients, and the remaining seven were excluded because they could not see the drawings because of eye closure or other reasons. The VN scores were 18.9 ± 4.2 preoperatively and 15.2 ± 6.4 intraoperatively; the difference between the preoperative and postoperative values, or ΔVN, was -4.1 ± 6.1. The intraoperative AN was recorded in 35 patients. The AN scores were 27.7 ± 5.1 preoperatively and 19.2 ± 11.1 intraoperatively; the difference between the preoperative value and the postoperative value, or ΔVN, was -8.4 ± 9.6. Fig. 1 shows the individual VN and AN changes from the preoperative to intraoperative evaluations. The number of evaluated patients tended to be higher in the AN than in the VN group (Fisher's exact test, $p = 0.055$). Fig. 1

Intraoperative evaluation of language function was repeated with at least one of VN and AN in 34 cases (excluding two cases that underwent quantitative evaluation only at the end of resection). The number of quantitative language function assessments performed varied for individual patients. VN was repeated in 28 cases, of whom 20 showed no or minor decline (decrease of correct responses from 0 to 5) and eight major declines (from 6 to 30). AN was repeated in 33 cases, of whom 20 showed no or minor decline (from 0 to 5) and 13 major declines (from 6 to 30).

The neurosurgeons monitored the patient for the appearance of intraoperative language symptoms. They made a comprehensive decision on the extent of resection with reference to age, preoperative symptoms, intraoperative rapid pathological diagnosis, and intraoperative neurologic symptoms.

Correlation between intraoperative naming exacerbation and early postoperative changes in WAB score

Table 3 shows the correlations between intraoperative exacerbation of naming (ΔVN and ΔAN) and early postoperative changes in the WAB scores. ΔVN was significantly correlated with ΔAQ, Δspontaneous speech, Δrepetition, Δnaming total, Δobject naming, and Δword fluency ($p < 0.05$) but not with Δcomprehension ($p = 0.17$). ΔAN was significantly correlated with ΔAQ, Δspontaneous speech, Δcomprehension, Δrepetition, Δnaming total, Δobject naming, and Δword fluency ($p < 0.05$). No correlation was found between intraoperative naming exacerbation (ΔVN and ΔAN) and late postoperative changes in the WAB scores.

Table 3

Table 3 also presents the results of separate analyses for low- and high-grade patients. In low-grade glioma patients, ΔVN and ΔAN were significantly correlated with ΔAQ, Δspontaneous speech, Δcomprehension, Δrepetition, Δnaming total, Δobject naming, and Δword fluency ($p < 0.05$). In high-grade glioma patients, ΔVN was not significantly correlated with all WAB scores, but ΔAN was significantly correlated with ΔAQ, Δspontaneous speech, Δcomprehension, Δrepetition, Δnaming total, Δobject naming, and Δword fluency ($p < 0.05$). For late postoperative changes of the WAB scores, intraoperative naming exacerbation (ΔVN and ΔAN) was correlated only with the change of repetition score in low-grade patients ($p < 0.05$).

Prediction of early postoperative changes in language function

Table 4 shows the results of stepwise multiple regression analysis with VN and AN as independent variables and the early postoperative language function changes (ΔAQ, Δspontaneous speech, Δcomprehension, Δrepetition, Δnaming total, Δobject naming, and Δword fluency) as dependent variables. ΔVN predicted Δnaming total and Δobject naming, and ΔAN predicted ΔAQ, Δspontaneous speech, Δcomprehension, Δrepetition, and Δword fluency ($p < 0.05$).

Table 4

In low-grade glioma patients, stepwise multiple regression analysis performed in the same way as the previous analysis showed that ΔVN predicted Δcomprehension, Δnaming total, Δobject naming, and Δword fluency, and ΔAN predicted ΔAQ, Δspontaneous speech, and Δrepetition ($p < 0.05$). In high-grade glioma patients, stepwise multiple regression analysis performed in the same way showed that only ΔAN predicted ΔAQ, Δcomprehension, Δrepetition, Δnaming total, Δobject naming, and Δword fluency ($p < 0.05$).

Intraoperative exacerbation of naming and ROC analysis to identify cutoff values for postoperative appearance and worsening of aphasia

We performed ROC analysis to determine the discriminative ability of ΔVN and ΔAN to predict the appearance and worsening of aphasia in the postoperative period and to identify the cutoff values. In the early postoperative period, the AUC of ΔVN was 0.86 ($p = 0.03$), and that of ΔAN was 0.88 ($p < 0.01$), indicating that ΔAN had a higher discriminative power against the appearance and exacerbation of aphasia. For early postoperative appearance and worsening of aphasia, a cutoff value of −4 for ΔAN had a sensitivity of 92% and specificity of 63%, and a cutoff value of −1 for ΔVN had a sensitivity of 100% and specificity of 72%. For the late postoperative appearance or worsening of aphasia, the AUC of ΔVN was 0.44 ($p = 0.66$), and the AUC of ΔAN was 0.84 ($p = 0.45$), both of which were not statistically significant.

For low-grade glioma patients, the AUC of ΔVN in the early postoperative period was 0.91 ($p = 0.07$), which was not statistically significant. That of ΔAN was 0.87 ($p < 0.01$), indicating that ΔAN had a high discriminative power against the appearance and exacerbation of aphasia. In the late postoperative period, the AUC of ΔVN was 0.25 ($p = 0.91$) and that of ΔAN was 0.93 ($p = 0.13$), both of which were not statistically significant. For high-grade glioma patients, the AUC of ΔVN in the early postoperative period was 0.72 ($p = 0.44$), which was not statistically significant. By contrast, that of ΔAN was 0.81 ($p = 0.03$), indicating that ΔAN had a high discriminative power against the appearance and exacerbation of aphasia. In the late postoperative period, the AUC of ΔVN was 0.54 ($p = 0.58$) and that of ΔAN was 0.50 ($p = 0.61$), both of which were not statistically significant.

Discussion

The results showed that the exacerbation of naming evaluated quantitatively with VN and AN during awake craniotomy correlated with changes in language function and predicted the severity of aphasia within 1 week after surgery. In low-grade glioma patients, VN and AN during awake craniotomy correlated with changes in language function in the early postoperative period. In high-grade glioma patients, only AN during awake craniotomy correlated with changes in early postoperative language function. In awake craniotomy especially for high-grade glioma, intraoperative evaluation of language function with AN adding to VN may prevent early postoperative impairments of language function in wider aspects. Additionally, AN has the advantage of being easily adapted to surgical or patient situations where visual perception is limited, as shown by the greater number of patients evaluated in AN than in VN.

Our results support the findings of Chan et al.[10], in which intraoperative quantitative evaluation of language function correlates with postoperative language function and predicts the severity of postoperative aphasia immediately after surgery. In their study, 13 of the 19 patients had cerebral infarction on MRI immediately postoperatively, which may have influenced the appearance and worsening of language disorders in the postoperative period. The present study increased the number of participants to 37 and excluded those with postoperative complications of cerebral infarction, which may have resulted in the appearance of language symptoms.

Intraoperative language tasks are selected according to the language function assumed in or near the area to be removed.[17,24] Naming deficits commonly occur after damage to the language-dominant hemisphere, and evaluation of language function with VN is commonly used in awake craniotomy.[2,6–8,10–13,15–17,24] Cognitive processing of VN proceeds in the order of visual object perception, semantic access, lexical selection, and phonological processing, which mainly loads the ventral and dorsal systems of the linguistic network in the language-dominant hemisphere.[25,26]

AN has also been adopted especially for temporal lobe epilepsy in mapping with chronic subdural electrode implantation[27–30] and is reported to be a sensitive measure for language disorders.[18–20] Because of the additional requirement of sentence comprehension, more cognitive demands are involved in AN, which is accomplished through auditory phonological processing, lexical retrieval, semantic access, and syntactic comprehension, followed by lexical and phonological processing for target word production.[29–32] AN depends on a broader neural network connecting the frontal and temporal-parietal lobes involved in more than just language.[33–35] Thus, VN and AN are processed differently and have different neural bases.[27–32]

The present study suggests that AN predicts early postoperative language impairment better than VN during awake craniotomy in patients with brain tumors. The intraoperative exacerbation of AN (ΔAN) more accurately predicted the early postoperative change of the WAB AQ (ΔAQ) or a comprehensive measure of aphasia compared with that of VN (ΔVN). Additionally, ΔAN predicted changes in the WAB subtests (spontaneous speech, comprehension, and repetition), except for the naming subtest. However, when ΔAN was analyzed separately for object naming and word fluency, which consists of the naming subtest, ΔAN predicted Δword fluency but not Δobject naming. Word fluency is a task that measures spontaneous word retrieval and can detect mild aphasia,[36] whereas object naming is rather easy, and its score does not significantly decrease postoperatively. ROC analysis showed that ΔAN was a better predictor than ΔVN for discriminating the appearance and worsening of aphasia in the early postoperative period. Chan et al.[10] reported that PPTT performed better intraoperatively to predict postoperative language function than VN. AN and PPTT have common characteristics that tap into a wider range of linguistic aspects than VN, and using these tasks in awake craniotomy may contribute to predicting postoperative language function.

In low-grade glioma patients, AN predicted AQ scores that represent the overall severity of early postoperative aphasia, but VN predicted language function only in a few subtests. On the other hand, in high-grade glioma patients, ΔAN but not ΔVN correlated with early postoperative language function, and only ΔAN predicted ΔAQ. These results show that for high-grade glioma patients, evaluation of language function with AN may be more informative than VN. We consider that AN that covers a wider range of language evaluation may be suitable for the more infiltrating nature of high-grade glioma that affects the neural network of language.[37,38) However, VN has the advantage of being simple as a task and can be performed in a short time for assessment. VN and AN should be used flexibly for the impairment of input regarding sensory modalities and profiles of language impairment during awake craniotomy.

Immediately after tumor resection, edema, brain shift, and subclinical epileptic discharges can impair language function. By contrast, a period of 1 month or longer leads to functional recovery of the neural network of language through neuroplasticity.[39,40)] In this study, AQ decreased immediately after surgery but recovered to nearly the preoperative level 1 month or more postoperatively. In two patients with no improvement in aphasia 1 month after surgery, which may have resulted from the recurrence of brain tumors and the advanced age. The mean preoperative to intraoperative exacerbation of the naming score was only in the range of −4.3 ± 6.1 for VN (maximum score = 20) and −8.7 ± 9.6 for AN (maximum score = 30). Whether these changes in scores are useful in determining the extent of resection of brain tumors must await further research.

This study has five limitations. First, the VN and AN used were not standardized language tests. However, this limitation has a minor effect on the overall results because we compared the score changes of these tasks between the preoperative and intraoperative evaluations for individual patients. Second, the study was conducted retrospectively, and the participants were recruited from a single institution. Therefore, a prospective, observational, multicenter study with a larger number of participants is needed to confirm the validity of the present results. Third, intraoperative changes in VN and AN scores did not correlate with language function after 1 month postoperatively. From these results, it is not possible to conclude whether a quantitative evaluation of language function intraoperatively with VN and AN can contribute to the long-term preservation of language function. Fourth, the intraoperative quantitative evaluation of language function shown in this study was limited to a single time point after resection. Quantitative assessment of language function during tumor resection is less common, and there is not sufficient consensus to determine the extent of resection based on the appearance of intraoperative language impairment. It remains to be examined whether quantitative language assessment, which is applicable during tumor resection, can reliably improve the postoperative prognosis of brain tumor patients. Lastly, intraoperative language disorders and their postoperative recovery may depend on patients' age and the grade of the brain tumor. Most neurosurgeons consider these factors to determine the extent of resection. In the determination of resection limits for the patients of this study, the intraoperative levels of AN and VN were additionally referred to. This may have had some effect on the observed correlations between the intraoperative naming exacerbation and the early postoperative changes of the WAB scores.

In conclusion, AN, which taps into a wider range of linguistic functions, may be more informative than VN as language evaluation in awake craniotomy for the early postoperative development of aphasia, especially for patients with high-grade glioma. AN has the advantage of being easily adapted to surgical or patient situations in which visual perception is limited.

Acknowledgments

This study was supported by the Japanese Society for the Promotion of Science (Grant-in-Aid for Young Scientists, Wakamatsu).

Disclosure of Conflict of Interest

There are no conflicts of interest.

References

1) Sanai N, Berger MS: Glioma extent of resection and its impact on patient outcome. Neurosurgery 62: 753–766, 2008

2) Yordanova YN, Moritz-Gasser S, Duffau H: Awake surgery for WHO grade II gliomas within "noneloquent" areas in the left dominant hemisphere: toward a "supratotal" resection: clinical article. J Neurosurg 115: 232–239, 2011

3) Groshev A, Padalia D, Patel S, *et al.*: Clinical outcomes from maximum-safe resection of primary and metastatic brain tumors using awake craniotomy. Clin Neurol Neurosurg 157: 25–30, 2017

4) Berger MS, Kincaid J, Ojemann GA, Lettich E: Brain mapping techniques to maximize resection, safety, and seizure control in children with brain tumors. Neurosurgery 25: 786–792, 1989

5) Silbergeld DL, Mueller WM, Colley PS, Ojemann GA, Lettich E: Use of propofol (Diprivan) for awake craniotomies: technical note. Surg Neurol 38: 271–272, 1992

6) Duffau H, Gatignol P, Mandonnet E, Peruzzi P, Tzourio-Mazoyer N, Capelle L: New insights into the anatomo-functional connectivity of the semantic system: a study using cortico-subcortical electrostimulations. Brain 128: 797–810, 2005

7) Meyer FB, Bates LM, Goerss SJ, *et al.*: Awake craniotomy for aggressive resection of primary gliomas located in eloquent brain. Mayo Clin Proc 76: 677–687, 2001

8) Picht T, Kombos T, Gramm HJ, Brock M, Suess O: Multimodal protocol for awake craniotomy in language cortex tumour surgery. Acta Neurochir (Wien) 148: 127–138, 2006

9) Trinh VT, Fahim DK, Shah K, *et al.*: Subcortical injury is an independent predictor of worsening neurological deficits following awake craniotomy procedures. Neurosurgery 72: 160–169, 2013

10) Chang WH, Pei YC, Wei KC, *et al.*: Intraoperative linguistic performance during awake brain surgery predicts postoperative linguistic deficits. J Neurooncol 139: 215–223, 2018

11) Sanai N, Mirzadeh Z, Berger MS: Functional outcome after language mapping for glioma resection. N Engl J Med 358: 18–27, 2008

12) Haglund MM, Berger MS, Shamseldin M, Lettich E, Ojemann GA: Cortical localization of temporal lobe language sites in patients with gliomas: Neurosurgery 34: 567–576, 1994

13) Peraud A, Ilmberger J, Reulen H-J: Surgical resection of gliomas WHO grade II and III located in the opercular region. Acta Neurochir (Wien) 146: 9–18, 2004

14) Logothetis NK, Augath M, Murayama Y, *et al.*: The effects of electrical microstimulation on cortical signal propagation. Nat Neurosci 13: 1283–1291, 2010

15) Aabedi AA, Kakaizada S, Young JS, *et al.*: Balancing task sensitivity with reliability for multimodal language assessments. J Neurosurg 135: 1817–1824, 2021

16) Rofes A, Spena G, Miozzo A, Fontanella MM, Miceli G: Advantages and disadvantages of intraoperative language tasks in awake surgery: a three-task approach for prefrontal tumors. J Neurosurg Sci 59: 337–349, 2015

17) Morshed RA, Young JS, Lee AT, Berger MS, Hervey-Jumper SL: Clinical pearls and methods for intraoperative awake language mapping. Neurosurgery 89: 143–153, 2021

18) Bell BD, Seidenberg M, Hermann BP, Douville K: Visual and auditory naming in patients with left or bilateral temporal lobe epilepsy. Epilepsy Res 55: 29–37, 2003

19) Hamberger MJ, Tamny TR: Auditory naming and temporal lobe epilepsy. Epilepsy Res 35: 229–243, 1999

20) Hamberger MJ, Seidel WT: Auditory and visual naming tests: normative and patient data for accuracy, response time, and tip-of-the-tongue. J Int Neuropsychol Soc 9: 479–489, 2003

21) Forkel SJ, Thiebaut De Schotten M, Dell'Acqua F, *et al.*: Anatomical predictors of aphasia recovery: a tractography study of bilateral perisylvian language networks. Brain 137: 2027–2039, 2014

22) Kayama T; The guidelines for awake craniotomy guidelines committee of the Japan awake surgery conference: The guidelines for awake craniotomy guidelines committee of the Japan awake surgery conference. Neurol Med Chir (Tokyo) 52: 119–141, 2012

23) Amano S, Kondo T: NTT data base series. Lexical properties of Japanese. ed 1. Tokyo, Sanseido, 2000

24) Middlebrooks EH, Yagmurlu K, Szaflarski JP, Rahman M, Bozkurt B: A contemporary framework of language processing in the human brain in the context of preoperative and intraoperative language mapping. Neuroradiology 59: 69–87, 2017

25) Hickok G, Poeppel D: Dorsal and ventral streams: a framework for understanding aspects of the functional anatomy of language. Cognition 92: 67–99, 2004

26) Duffau H: Stimulation mapping of white matter tracts to study brain functional connectivity. Nat Rev Neurol 11: 255–265, 2015

27) Cervenka MC, Corines J, Boatman-Reich DF, *et al.*: Electrocorticographic functional mapping identifies human cortex critical for auditory and visual naming. NeuroImage 69: 267–276, 2013

28) Forseth KJ, Kadipasaoglu CM, Conner CR, Hickok G, Knight RT, Tandon N: A lexical semantic hub for heteromodal naming in middle fusiform gyrus. Brain 141: 2112–2126, 2018

29) Nakai Y, Sugiura A, Brown EC, *et al.*: Four-dimensional functional cortical maps of visual and auditory language: intracranial recording. Epilepsia 60: 255–267, 2019

30) Ikegaya N, Motoi H, Iijima K, *et al.*: Spatiotemporal dynamics of auditory and picture naming-related high-gamma modulations: a study of Japanese-speaking patients. Clin Neurophysiol 130: 1446–1454, 2019

31) Farias ST, Harrington G, Broomand C, Seyal M: Differences in functional MR imaging activation patterns associated with confrontation naming and responsive naming. AJNR Am J Neuroradiol 26: 2492-2499, 2005

32) Hamberger MJ, Habeck CG, Pantazatos SP, Williams AC, Hirsch J: Shared space, separate processes: neural activation patterns for auditory description and visual object naming in healthy adults: description and visual naming activation patterns. Hum Brain Mapp 35: 2507–2520, 2014

33) Brennan J, Pylkkänen L: The time-course and spatial distribution of brain activity associated with sentence processing. Neuroimage 60: 1139–1148, 2012

34) Acunzo DJ, Low DM, Fairhall SL: Deep neural networks reveal topic-level representations of sentences in medial prefrontal cortex, lateral anterior temporal lobe, precuneus, and angular gyrus. Neuroimage 251: 119005, 2022

35) Humphries C, Binder JR, Medler DA, Liebenthal E: Syntactic and semantic modulation of neural activity during auditory sentence comprehension. J Cogn Neurosci 18: 665–679, 2006

36) Faroqi-Shah Y, Milman L: Comparison of animal, action and phonemic fluency in aphasia. Int J Lang Commun Disord 53: 370–384, 2018

37) Agnihotri S, Burrell KE, Wolf A, *et al.*: Glioblastoma, a brief review of history, molecular genetics, animal models and novel therapeutic strategies. Arch Immunol Ther Exp (Warsz) 61: 25–41, 2013

38) Yuan B, Zhang N, Yan J, Cheng J, Lu J, Wu J: Tumor grade-related language and control network reorganization in patients with left cerebral glioma. Cortex 129: 141–57, 2020

39) Duffau H, Moritz-Gasser S, Mandonnet E: A re-examination of neural basis of language processing: proposal of a dynamic hodotopical model from data provided by brain stimulation mapping during picture naming. Brain Lang 131: 1–10, 2013

40) Wilson SM, Lam D, Babiak MC, *et al.*: Transient aphasias after left hemisphere resective surgery. J Neurosurg 123: 581–593, 2015

Figure Legends

Fig.1 Results of preoperative and intraoperative evaluation of language function

Table 1 Demographic data of 36 patients

	n (%) or mean ± std
Sex (men/women)	21/15
Age (years)	49.1 ± 16.4 (21–82)
Handedness (Lt/Rt)	3/33
Tumor location side	
Left side	33
Right side	3
Lesion location	
Frontal	15 (42)
Parietal	9 (25)
Temporal	6 (16)
Temporo-insula	3 (8)
Fronto-insula	1 (3)
Insura	1 (3)
Temporoparietal	1 (3)
WHO tumor grade	
I	4 (11)
II	13 (38)
III	4 (11)
IV	15 (40)

Table 2 WAB AQ and subtest scores and aphasia severity in preoperative, early postoperative, and late postoperative periods

	Preoperative	Early postoperative (within a week)	Late postoperative (after a month)
Numbers	36	34	34
Inspection date	−8.5 ± 8.1	4.6 ± 2.1	50.1 ± 33.3
WAB scores			
AQ (/100)	92.5 ± 11.9	81.8 ± 22.3	95.0 ± 7.3
Spontaneous speech (/20)	18.5 ± 2.4	16.0 ± 5.2	19.0 ± 1.8
Comprehension (/10)	9.3 ± 1.0	8.4 ± 1.8	9.5 ± 0.7
Repetition (/10)	9.5 ± 1.2	8.6 ± 2.7	9.7 ± 0.7
Naming total (/10)	9.0 ± 2.0	7.9 ± 2.5	9.4 ± 0.8
Object naming (/60)	56.6± 12.7	51.4 ± 16.0	58.6 ± 5.6
Word fluency (numbers)	15.6 ± 6.5	10.6 ± 6.9	15.8 ± 5.5
Number of participants in each aphasia severity, n (%)			
Non-aphasia (AQ ≥ 91.3)	28 (78)	18(53)	28(80)
Mild aphasia (AQ = 91.2–76)	5 (14)	5(15)	4(14)
Moderate aphasia (AQ = 75.9–51)	2 (5)	9(26)	2(6)
Severe aphasia (AQ = 50–26)	1 (3)		
Most severe aphasia (AQ = 25–0)		2(6)	

WAB: Western Aphasia Battery, AQ: aphasia quotient

Table 3 Prediction of early postoperative changes in language function with a stepwise multiple regression analysis

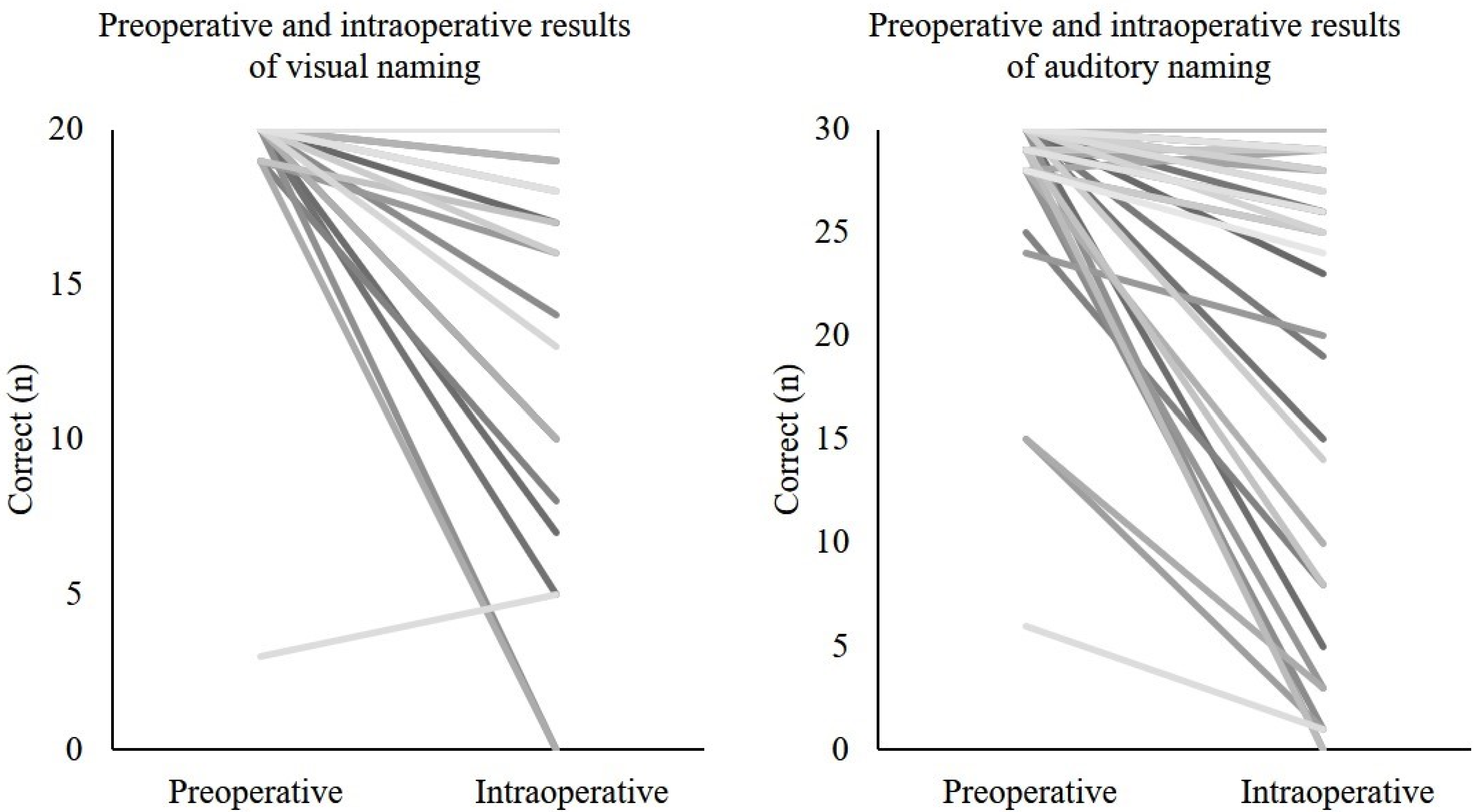
	Intraoperative naming reductions			
	ΔVN score		ΔAN score	
	r	*p* value	*r*	*p* value
All patients				
ΔAQ	0.53**	<0.01	0.73**	<0.01
Subtest scores				
Δspontaneous speech	0.51**	<0.01	0.77**	<0.01
Δcomprehension	0.27	0.17	0.61**	<0.01
Δrepetition	0.40*	0.04	0.59**	<0.01
Δnaming total	0.58**	<0.01	0.61**	<0.01
Δobject naming	0.54**	<0.01	0.59**	<0.01
Δword fluency	0.43*	0.02	0.51**	<0.01
Low-grade glioma				
ΔAQ	0.83**	<0.01	0.89**	<0.01
Subtest scores				
Δspontaneous speech	0.74**	<0.01	0.92**	<0.01
Δcomprehension	0.78**	<0.01	0.77**	<0.01
Δrepetition	0.74**	<0.01	0.81**	<0.01
Δnaming total	0.91**	<0.01	0.79**	<0.01
Δobject naming	0.89**	<0.01	0.78**	<0.01
Δword fluency	0.63**	<0.01	0.60**	<0.01
High-grade glioma				
ΔAQ	0.38	0.22	0.69**	<0.01
Subtest scores				
Δspontaneous speech	0.37	0.24	0.72**	<0.01
Δcomprehension	−0.07	0.82	0.56**	0.02
Δrepetition	0.24	0.44	0.54**	0.03
Δnaming total	0.49	0.10	0.62**	0.01
Δobject naming	0.46	0.13	0.59*	0.02
Δword fluency	0.50	0.09	0.64**	<0.01

VN: visual naming, AN: auditory naming, WAB: Western Aphasia Battery, r: correlation coefficient, AQ: aphasia quotient, *$p < 0.05$, **$p < 0.01$

Table 4 Intraoperative changes in language function predict early postoperative changes in language function

	Predictors					
	ΔVN score		ΔAN score		Selected model	
	β	*p* value	*β*	p value	Adjusted R^2	*p* value
All patients						
ΔAQ			0.73**	<0.01	0.44**	<0.01
Δspontaneous speech			0.77**	<0.01	0.54**	<0.01
Δcomprehension			0.61**	<0.01	0.21**	<0.01
Δrepetition			0.59**	<0.01	0.21**	<0.01
Δnaming total	0.58**	<0.01			0.30**	<0.01
Δobject naming	0.54**	<0.01			0.26**	<0.01
Δword fluency			0.51**	<0.01	0.20**	<0.01
Low-grade glioma						
ΔAQ			0.87**	<0.01	0.78**	<0.01
Δspontaneous speech			0.88**	<0.01	0.84**	<0.01
Δcomprehension	0.79**	<0.01			0.57**	<0.01
Δrepetition			0.82**	<0.01	0.63**	<0.01
Δnaming total	0.86**	<0.01			0.82**	<0.01
Δobject naming	0.82**	<0.01			0.77**	<0.01
Δword fluency	0.62**	<0.01			0.36**	<0.01
High-grade glioma						
ΔAQ			0.69**	<0.01	0.44**	<0.01
Δspontaneous speech			0.72**	<0.01	0.48**	<0.01
Δcomprehension			0.56**	0.02	0.27*	0.02
Δrepetition			0.54**	0.03	0.24*	0.03
Δnaming total			0.62**	0.01	0.33*	0.01
Δobject naming			0.59*	0.02	0.30*	0.02
Δword fluency			0.64**	<0.01	0.36**	<0.01

VN: visual naming, AN: auditory naming, β: standardized partial regression coefficient, AQ: aphasia quotient, *$p < 0.05$, **$p < 0.01$



Preoperative and intraoperative results of visual naming
Correct (n)
20
15
10
5
0
Preoperative
Intraoperative
Preoperative and intraoperative results of auditory naming
Correct (n)
30
25
20
15
10
5
0
Preoperative
Intraoperative

Supplementary Table

List of visual and auditory naming issues

Visual naming	Auditory naming
Grape	What is your name?
Ear	What color is the snow?
Ant	What color are sunflowers?
Potato	What color are crows?
Train	What color are the bananas?
Strawberry	What color is the fire truck?
Eye	How many days are in a week?
Cat	How many minutes per hour?
Truck	How many legs does the dog have?
Bus	What day of the week is next Tuesday?
Scissors	What is the next season after spring?
Police car	What month is New Year's Day?
Carrot	What month is Obon?
Airplane	Which direction is the sun setting?
Chicken	What is a frog child?
Pencil	What is a chicken's offspring?
Motorcycle	Mother is a woman. Father is…
Apple	My brother is a man. And my sister is…
Cup	When is the sun daytime and when are the stars visible?
	Cherry blossoms are in spring. When are the autumn leaves?
	Where do you buy stamps?
	What is the tool used to cut vegetables?
	What do you use to cut paper?
	What is your tool for looking at time?
	Hot water is hot. Ice is…
	Iron is a thought. Feathers are…
	The sea is deep. The mountains…
	Clothes on. Shoes on…
	The bird flies. The fish…
	Music is listening. Pictures are…

Supplementary Table 2 WAB AQ and subtest scores and aphasia severity in preoperative, early postoperative, and late postoperative periods

	Low-grade glioma			High-grade glioma		
	Preoperative	Early postoperative (within a week)	Late postoperative (after a month)	Preoperative	Early postoperative (within a week)	Late postoperative (after a month)
Numbers	17	17	16	19	17	18
Inspection date	−7.2 ± 6.1	4.2 ± 1.7	40.1 ± 41.3	−9.7 ± 9.5	5 ± 2.4	58.9 ± 21.9**
WAB scores						
AQ (/100)	97.6 ± 3.1	88.5 ± 20.6	97.4 ± 4.2	88.0 ± 14.8	75.2 ± 22.4	92.9 ± 8.8
Spontaneous speech (/20)	19.6 ± 0.6	17.8 ± 4.1	19.4 ± 1.5	17.5 ± 3.0	14.2 ± 5.6	18.6 ± 2.0
Comprehension (/10)	9.6 ± 0.5	8.9 ± 1.6	9.8 ± 0.3	9.0 ± 1.3	7.9 ± 1.9	9.2 ± 0.9
Repetition (/10)	9.9 ± 0.5	8.9 ± 2.7	9.9 ± 0.3	9.2 ± 1.5	8.3 ± 2.7	9.5 ± 0.9
Naming total (/10)	9.7 ± 0.4	8.5 ± 2.3	9.6 ± 0.3	8.3 ± 2.5	7.2 ± 2.7	9.1 ± 1.1
Object naming (/60)	59.8 ± 1.0	53.6 ± 14.5	59.8 ± 0.7	53.8 ± 17.1	49.1 ± 17.6	57.5 ± 7.6
Word fluency (numbers)	20.0 ± 5.1	14.0 ± 6.6	18 ± 5.0	11.7 ± 5.1	7.2 ± 5.5	13.8 ± 5.3
Number of participants in each aphasia severity, n (%)						
Non-aphasia (AQ ≥ 91.3)	16 (94)	13 (76)	15 (94)	12 (63)	5 (29)	13 (72)
Mild aphasia (AQ = 91.2–76)	1 (6)	2 (12)	1 (6)	4 (21)	3 (18)	3 (17)
Moderate aphasia (AQ = 75.9–51)		1 (6)		2 (11)	8 (47)	2 (11)
Severe aphasia (AQ = 50–26)				1 (5)		
Most severe aphasia (AQ = 25–0)		1 (6)			1 (6)	

WAB: Western Aphasia Battery, AQ: aphasia quotient