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Original Article

Outcomes of a novel naming test applied in intraoperative language mapping for awake brain surgery: a preliminary study

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Abstract: Objectives: The selection of intraoperative tasks is important for intraoperative stimulation mapping (ISM), and the pre- and postoperative assessments of language function can be used to investigate the efficacy of these tasks. However, insufficient evidence exists for evaluating the efficacy of intraoperative tasks based on the language outcome. Therefore, we devised a novel intraoperative task and hypothesized that it can be easily applied in ISM and can preserve patients' language function after surgery. Methods: In this retrospective study, awake craniotomy for tumor resection was performed in 28 patients with malignant brain tumors in eloquent areas. The patients' pre- and postoperative language function was assessed using the modified short-form Boston Diagnostic Aphasia Examination (BDAE). Our novel and comprehensive naming task modified from the stimulus sets of the short-form BDAE, including objects, actions, colors, numbers, English letters, Chinese words, and shapes, was employed in ISM. The patients were assigned to three subgroups (normal, mildly impaired and profoundly impaired groups) based on the severity of preoperative language impairment for further analysis. Results: The patient's language function was preserved after surgery or exhibited significant improvement over time. The trend of functional recovery varied in the subtests of complex ideational material, word discrimination, and repeating phrases. Conclusion: The mortified short-form BDAE can indicate preoperative variations in language function. This novel and comprehensive naming task can be applied in ISM and can preserve or improve linguistic outcome. We therefore suggest using this comprehensive but more easily applied intraoperative task in ISM.

Keywords: Naming task, eloquent area, intraoperative stimulation mapping, intraoperative task, linguistic task, Boston Diagnostic Aphasia Examination, language outcome, brain tumor, awake craniotomy, awake brain surgery

Introduction

The main purpose of awake craniotomy in tumor excision is to perform intraoperative stimulation mapping (ISM) in patients with brain tumors located near the eloquent area; therefore, the tumors can be resected more extensively, and brain functions can be preserved as much as possible [1]. In this procedure, intraoperative electrical stimulation combined with linguistic tasks is used to map the language area. Specifically, a brain area is recognized as a putative language-positive site when the site is suppressed by electrical stimulation, and the patient is unable to perform linguistic tasks [2]. Previous research has shown that ISM can yield favorable cognitive outcomes and quality of life for patients receiving brain tumor resection [3, 4], but postoperative neurolinguistic deficits have still been found in a proportion of these patients. Various risk factors, such as preoperative aphasia, intraoperative complications, language-positive sites within the tumor, and nonfrontal lesions, have been suggested to predict the occurrence of postoperative neurolinguistic deficits [1, 5]. However, even in the cases with the resection margins determined in ISM adequately away from the language-positive area, new-onset linguistic deficits could still be observed postoperatively [2, 6]. One possibility is that the repertoire of linguistic tasks applied in ISM is limited; therefore, the sensitivity to detect the eloquent area is determined by the choice of linguistic tasks [2, 6-8].

Only a few simple linguistic tasks, such as number counting, object naming, action naming, reading, spontaneous speech, and semantic and comprehension tasks [7-10], can be applied in awake craniotomy surgery [2, 8], because the duration of each electrical stimulation lasts for only 4 seconds, and awake patients may feel tired after long-term sustained attention. Furthermore, the patient's head is fixed on the operative table; thus, the linguistic tasks are performed in a highly-constrained posture [7, 11, 12]. The selection of intraoperative linguistic tasks is critical [6, 7] and usually depends on the tumor location [7, 9-11, 13, 14]. For example, number counting, object naming, and reading are used for patients with left frontal tumors, whereas object naming and comprehension tasks are used for those with left temporal tumors [7, 11, 14, 15]. However, the sensitivity of intraoperative tasks remains debatable [8, 11, 16], and the guideline for selecting the intraoperative linguistic tasks is still lacking [7, 14, 16]. Even though the validity of linguistic tasks has been reported [1, 2, 6, 8, 16-18], insufficient studies have accounted for the detailed influence of each task on postoperative neurolinguistic outcomes [1, 18, 19].

In this study, we applied a novel and comprehensive naming task modified from the stimulus sets used in the short-form Boston Diagnostic Aphasia Examination (BDAE), denoted as modified BDAE. The task consists of seven naming components, including objects, actions, colors, numbers, English letters, Chinese words, and shapes, and is shorter than the original BDAE. In addition to the naming task, we used number counting for initial intraoperative mapping. The modified BDAE was performed for pre- and postoperative evaluations. We hypothesized that this linguistic task can be easily applied in awake brain mapping, and that its utility is supported by the preservation of patients' language function after awake brain surgery.

Materials and methods

Subjects

Subjects were recruited from the neurosurgery outpatient clinic at a medical center from May 2013 to June 2016. The inclusion criteria were adults aged >20 years who were diagnosed with brain tumors located near the eloquent area and who could cooperate with linguistic assessments. Patients who could not cooperate with preoperative linguistic assessments were excluded. Furthermore, patients who were lost to follow-up before completing the six-month postoperative evaluation or those whose linguistic function deteriorated because of tumor recurrence within 6 months after surgery were excluded from the analysis (to avoid confounding factors that might affect postoperative neurolinguistic outcomes). All aspects of the study were specifically approved by the Human Studies Research Committee of Chang Gung Medical Foundation, and written informed consent was obtained from each subject before recruitment.

Pre- and postoperative evaluations

To simply and easily apply pre- and postoperative linguistic evaluations, we modified and selected several subtests from the Chinese version of the short-form BDAE, which was translated and revised by Taipei Veterans General Hospital, Taipei, Taiwan. The selected subtests, including word discrimination, complex ideational material, repeating phrases (common and rare phrases), responsive naming, and visual confrontation naming, can investigate major speech dimensions, such as auditory and visual naming, comprehension, repetition, articulation, and semantics. In addition, we recorded the total time taken for patients' response for the subtests of complex ideational material and repeating phrases, whereas the other subtests (word discrimination, responsive naming, and visual confrontation naming) were scored according to patients' response time. To simplify the procedure, only the first eight questions in the subtest of complex ideational material were applied in the evaluation.

Intraoperative linguistic tasks

During ISM, number counting and naming tasks were applied sequentially to identify the lan-

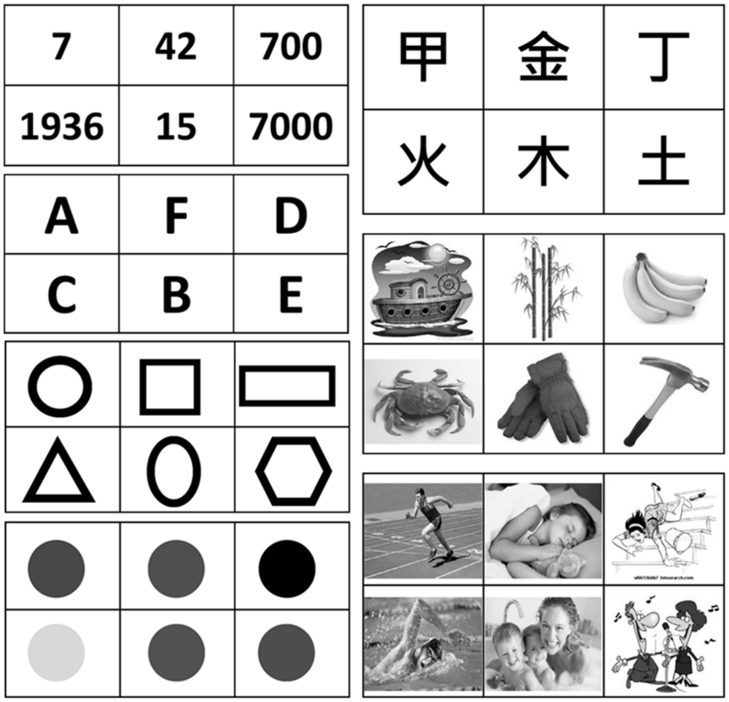

Figure 1. Our novel naming task is consisted of seven naming components, including numbers, English letters, shapes, colors, Chinese words, objects, and actions.

guage area. Specifically, number counting was applied as the first intraoperative task.

Our novel naming task was modified from the stimulus sets of short-form BDAE and consisted of seven naming components, including objects, actions, colors, numbers, English letters, Chinese words, and shapes, each comprising six items (**Figure 1**). The number of items included is lower than that used in the original BDAE. Each naming component with six items was organized on a sheet of A4 paper. The items for object, action, and color naming were printed in color, and the others were printed in black and white.

ISM procedure

After each patient woke up, the optimal intensity of ISM was determined by the minimal intensity that elicited observed motor responses of the contralateral face by electrically stimulating the primary motor area [16, 20]. Specifically, a bipolar electrode with 5-mm spaced tips was applied for delivering biphasic current stimulation (pulse frequency, 50 Hz; single pulse phase duration, 1 ms; amplitude, 2-10 mA) (Model OCS2 Ojemann Cortical Stimulator, Integra Life Sciences Corporation, Saint Priest, France). The intensity of electrical stimulation was increased gradually until oral twitching, speech arrest, dysarthria, or the motor response of a limb was observed, and electrical stimulation at this amplitude was used for subsequent stimulation for the naming test. For the naming task, each electrical stimulation lasted for 4 seconds, as the patient named each item on the naming sheet. As a control, at least one stimulation-free naming task was performed between the episodes of electrical stimulation. All seven naming components were applied in the seven rounds of ISM, each of which covered the whole mapping area. Language-positive sites were defined if the subject showed abnormality in naming, such as anomia, speech arrest, or misnaming. Moreover, the abnormality in naming was confirmed if the patient had the same abnormal responses in two consecutive tests. If patients could tolerate it, subcortical mapping was performed.

Statistical analysis

We assessed the demographic data by using descriptive statistics and analyzed the trend of changing language function in line charts. From the findings of the trend of language function, we assigned the patients into three subgroups based on the severity of preoperative language impairment, as follows: normal, mildly impaired (MI), and profoundly impaired (PI) groups. We performed subgroup analysis, disclosed the trend comparison of subgroups in each language subtest in line charts, and compared the change in linguistic measurements by using a paired t test. Statistical significance was set at $P<0.05$.

Results

In this study, 42 patients with brain tumors located near the eloquent area were recruited from May 2013 to June 2016. Among these

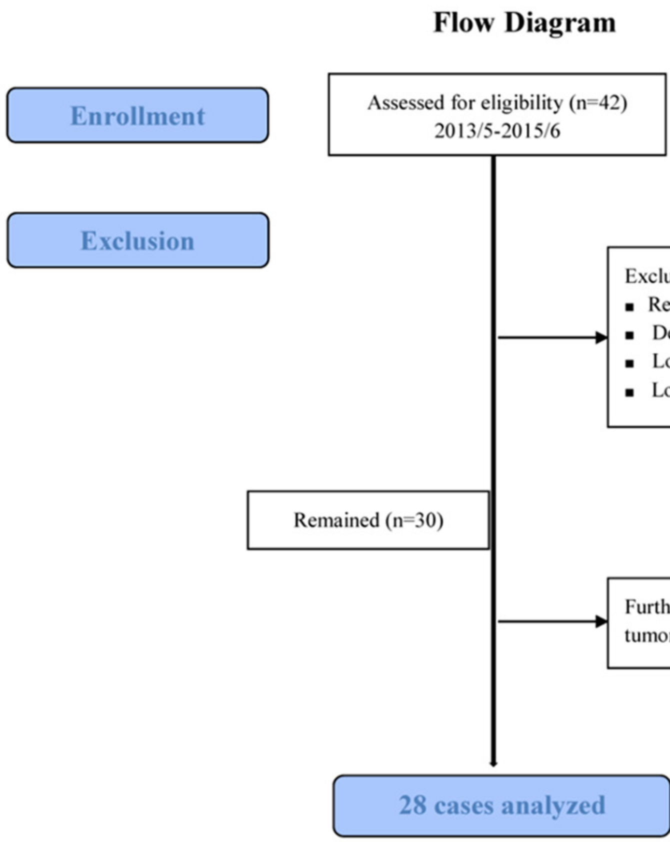

Figure 2. Flowchart for subject enrollment, exclusion, and analysis.

patients, 12 were excluded from the analysis because they were lost to follow-up within 6 months, among whom six had tumor recurrence within 6 months, two died within 6 months and two had a poor medical condition. Two patients were further excluded from the analysis because of a late decline in language function caused by confirmed tumor recurrence. As a result, the remaining 28 patients were analyzed (**Figure 2**). The demographic data (**Table 1**) demonstrated that 21 patients (75%) received gross total resection (>95%), and three (11%) received subtotal resection (95%-85%) [5]. Their histological results revealed that oligodendroglioma (n = 8, 29%), glioblastoma (n = 6, 21%), and anaplastic oligoastrocytoma (n = 4, 14%) were the most common categories. The brain tumors were most commonly located in the frontal (n = 13, 46%) and temporal (n = 7, 25%) lobes.

Trend of language function over time

We analyzed the language function data by evaluating the temporal change in linguistic performance as a function of time. We defined the composite score as the summation of scores from all the subtests (word discrimination, complex ideational material, repeating phrases, responsive naming, and visual confrontation naming) of short-form BDAE. **Figure 3A** and **3B** show the change in the composite score in pre- and postoperative assessments; the three subgroups had different temporal change patterns. The major findings are that (1) patients with significantly impaired language function preoperatively showed significant improvement over time; (2) patients with MI language function preoperatively regained normal language function; and (3) patients with normal preoperative language function retained normal language function. The three subgroups had nonoverlapping preoperative composite scores, and a strong correlation (R = -0.987, *P* = 0.000) was observed between the preoperative composite score and the 6-month postoperative composite score (**Figure 3C**, **3D**). According to these observations, the patients can be assigned to three subgroups for further analysis based on their preoperative language function.

Patients were assigned to the three subgroups based on their preoperative language function:

Table 1. Demographics and resection rate, pathology, and location of tumors by total cases and subgroups

N or mean±std	Total cases	Normal group	MI group	PI group
Sex (male/female)	13/15	6/7	5/5	4/1
Age (year)	28-76	42.5±10.0	47.1±11.7	60.3±14.3
Grade				
II	12	6	5	1
III	10	5	3	2
IV	6	2	2	2
Resection rate	44%-100%	85.5±20.1%	99.4±1.0%	97.4±2.6%
>95%	21	7	10	4
85-95%	3	2		1
<85%	4	4		
Histologic results				
Glioblastoma	6	2	2	2
Anaplastic oligoastrocytoma	4	2	2	0
Anaplastic oligodendroglioma	3	1	0	2
Anaplastic astrocytoma	2	2	0	0
Anaplastic papillaryglioneuronal tumor	1	0	1	0
Oligoastrocytoma	2	1	1	0
Astrocytoma	1	1	0	0
Oligodendroglioma	8	4	4	0
Mixed glioma of oligodendroglioma and ependymoma	1	0	0	1
Location				
Frontal lobe	13	6	4	3
Temporal lobe	7	3	2	2
Parietal lobe	1	0	1	0
Frontotemporal & insular lobes	4	2	2	0
Frontotemporal lobe & corpus callosum	3	2	1	0

MI: mildly impaired, PI: profoundly impaired, n: number.

normal (n = 13), MI (n = 10), or PI (n = 5) (**Figure 3A-C**). The cutoff values of 235 and 225 were chosen to define the three subgroups because these values can yield a more obvious distinction between preoperative composite scores. The differences among the three subgroups are illustrated in **Figure 3B**, showing distinct trends of functional recovery. Comparison of demographic data revealed no difference in sex, age, or grade among the three subgroups (all $P>0.05$) (**Table 1**). Borderline differences were observed in the resection rate among the three subgroups ($P = 0.06$), with the normal group showing the lowest resection rate. **Figure 4** displays the temporal changes in subtest scores among the three subgroups. In the normal group, the trend of functional recovery varied in subtests of complex ideational material and its duration. The trend of the linguistic outcome did not decline compared with the preoperative status in all subtests (all $P>0.05$), except the duration of complex ideational material and repeating phrases, for which the trend changed at the 6-month postoperative follow-up ($P = 0.049$). In the MI group, the trend of the linguistic outcome mildly declined at the 1-week postoperative follow-up but returned to normal or preoperative levels at the 3-month and 6-month postoperative follow-up. Comparison between preoperative and postoperative data by using the paired t test revealed no significance for all subtests (all $P>0.05$). In the PI group, language function improved substantially by the 1-week and 3-month postoperative follow-up but then declined by the 6-month postoperative follow-up. Compared with the preoperative score, the score of word discrimination at the 1-week postoperative follow-up significantly increased ($P = 0.044$). Moreover, the duration for complex ideational material at all follow-up points

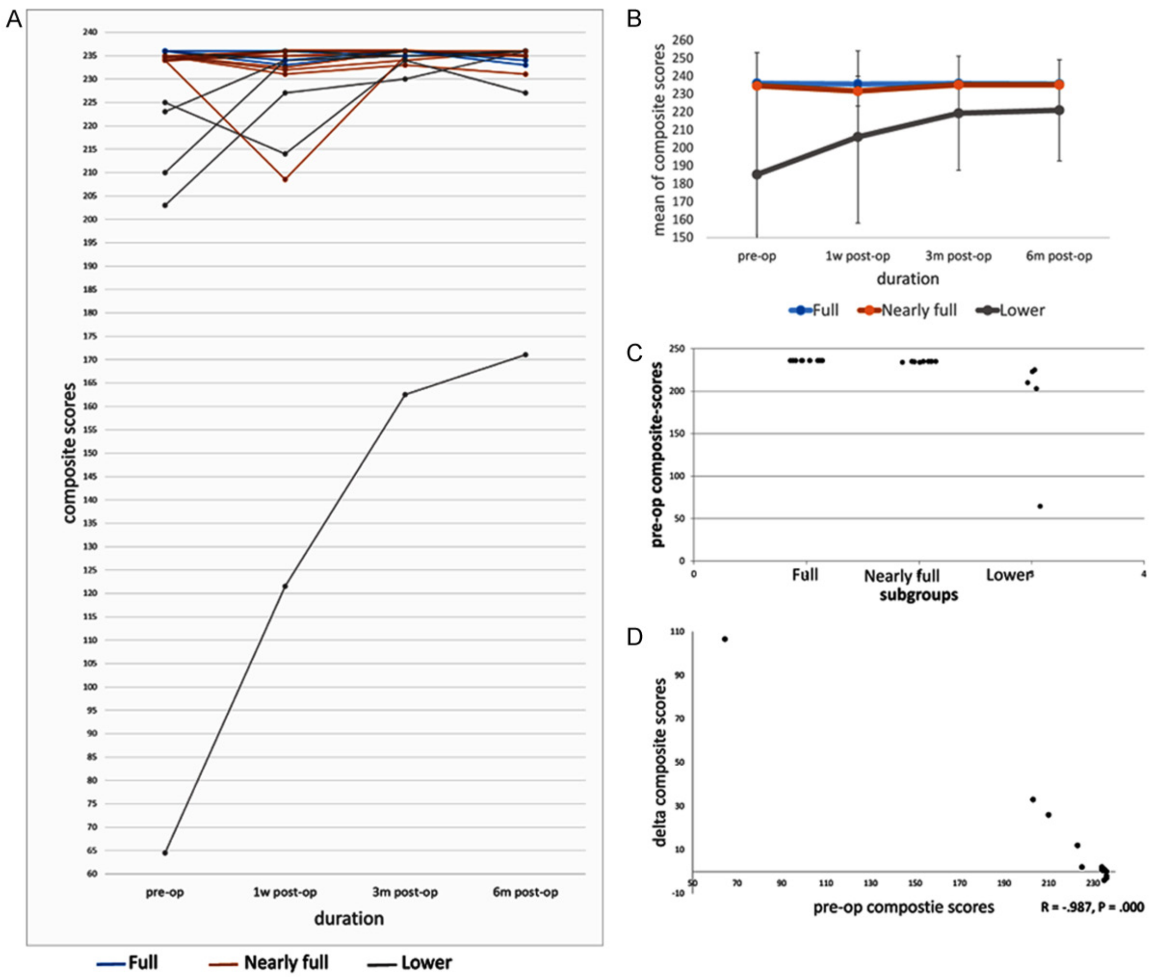

Figure 3. Distribution and temporal changes in composite scores from short-form BDAE. A. Composite score as a function of time. Each line represents the data obtained from a patient; three patterns were observed, each of which was color-coded. B. Mean±SD of the three subgroups, including the full, nearly full, or lower composite-score subgroups. C. Preoperative composite score of the three subgroups showing nonoverlapping preoperativevalues. D. Positive correlation between the preoperative composite score and the 6-month postoperative composite score.

decreased (all $P<0.05$) compared with the preoperative scores. Furthermore, the scores for complex ideational material ($P = 0.07$) and repeating rare phrases ($P = 0.07$) at the 6-month postoperative follow-up and the duration of repeating phrases ($P = 0.07$) at the 1-week postoperative follow-up showed borderline differences compared with the preoperative scores.

Discussion

In the present study, all 28 patients showed stationary or substantial improvement in their language function at the 3-month and 6-month follow-up, indicating that awake brain surgery combined with the intraoperative tasks modified from the stimulus sets of short-form BDAE can preserve a patient's language function. These results are consistent with those of previous studies [1, 5, 9, 18, 21-24], demonstrating that high-quality intraoperative mapping can identify the eloquent area and thus avoid language impairment. The most novel finding of this study is that preoperative language function determined the trajectory of language function following surgery. We found that short-term postoperative language decline mostly occurred in the MI group than in the other two groups, which is consistent with findings of Ilmberger *et al*. and Kim *et al*. [1, 5]. Specifically, Ilmberger *et al.* reported that the risk factors for early language impairment included preoperative aphasia, language-positive stimulation

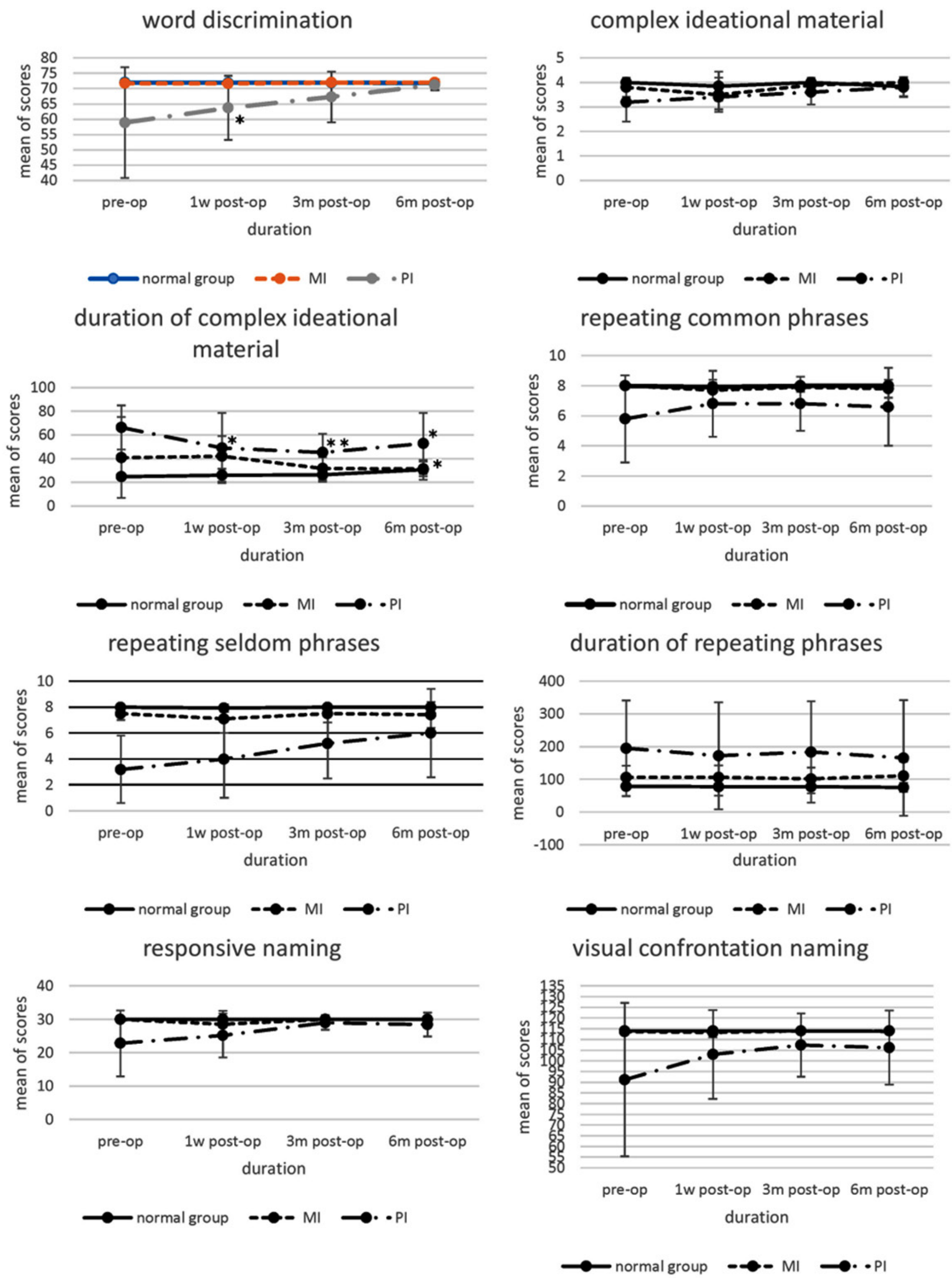

Figure 4. Temporal change in subtest scales for the three subgroups. Asterisks indicate statistically significant differences as compared with preoperative scores. **P*<0.05; ***P*<0.01; ****P*<0.001. MI: mildly impaired, PI: profoundly impaired.

sites within the tumor, a nonfrontal tumor location, and intraoperative complications, among which preoperative aphasia was the major risk factor. Nevertheless, Kim *et al.* stated that cortical mapping results, the extent of resection, and intraoperative neurological changes predicted the immediate neurologic outcome, rather than preoperative neurological deficits. The difference can be partly attributed to the assessment tools used. Ilmberger *et al*. defined preoperative aphasia as any disturbance in the numerous subtests of the Aachener Aphasia Test, whereas Kim *et al*. defined it as any impairment in motor, language, or both functions.

Several studies have reported worsening language function immediately postoperatively but continuing recovery after long-term follow up [1, 5, 9, 18, 22], ranging from 3 to 12 months. To the best of our knowledge, this study is the first to categorize patients based on their preoperative language status. We found the language function of the PI group continually improved and mildly declined at the 6-month follow-up. The mild decline at 6 months may be attributed to more severe preoperative deficits [1, 9] and a higher percentage of high-grade histology in this group.

Previous studies commonly used the BDAE, Aachener Aphasia Test, their respective naming tests, the Boston Naming Test, or the Dénomination Orale 80 for pre- and postoperative assessments [7]. In the present study, we proposed using a tool modified from the short-form BDAE that can measure multiple language dimensions, including auditory and visual naming, comprehension, repetition, articulation, and semantics. The short-form BDAE is unlike the long-form BDAE or other language test batteries that can comprehensively evaluate language function; it can detect the trend of the linguistic outcome and is much less time-consuming (an entire assessment requires only 20 minutes). However, few studies have reported comprehensive linguistic outcomes with individual subtests of language test batteries and have discussed their significance in assessing the linguistic outcome [1, 18, 19, 21, 24]. Among them, only two studies have focused on discussing the usefulness of the subtests. Santini *et al*. [18] investigated the language outcome through picture naming, comprehension, reading, and writing and found that picture naming, rather than the other subtests, reflected the difference between pre- and postoperative assessments. Analogously, Ilmberger *et al*. [1] reported that the naming test and the Token test, rather than writing, repetition, or comprehension, could reflect postoperative language deficits. To the best of our knowledge, the present study is the first to intensively show the temporal change in subtest scores over long-term follow-up. We thought this assessment model can evaluate the efficacy of intraoperative tasks. According to our subgroup analysis, we found that word discrimination (visual naming), complex ideational material (semantics), and repeating phrases (particularly complex ideational material) more sensitively indicated the linguistic change pre- and postoperatively. Specially, complex ideational material showed most significance in paired t test of each subgroup. Therefore, we suggest that semantics should be used as the major assessment dimension, and that naming and repetition should also be included to form an adequate assessment.

The present study is the first to apply naming tasks modified from the stimulus sets of short-form BDAE for ISM. Our naming task includes seven components: objects, actions, colors, numbers, English letters, Chinese words, and shapes. This task seems comprehensively to evaluate patients' language function, including naming, semantics (object and action naming), grammatical processes (action naming), and reading (Chinese words) and can be simply applied in ISM. Moreover, the task can actually preserve or improve patients' language function. Numerous linguistic tasks have been applied in ISM [7-10, 14, 16], but the most commonly used task is object naming [7, 9, 10, 17]. Although object naming usually involves both semantic and lexical processing [8, 16] and is suitable for both cortical and subcortical ISM [16], its sensitivity in isolation remains debatable. The literature has increasingly reported that object naming alone is inadequate for identifying the entire language area, given the extent of functional anatomy for object naming and other language dimensions [8, 11, 16, 17, 25-30]. For example, only a partial overlap in the area of reading and naming has been demonstrated [11, 25], and Roux *et al.* [25] and Bilotta *et al.* [26] suggested that reading tests should be included in intraoperative tasks. Distinct functional anatomy for object and action naming have also been identified [27-30]; Rofes *et al.* [8, 16] and Ojemann *et al*. [17] have found that action naming (a verb test) drives more language components than object naming (a noun test). Even with the considerable evidence of the neuroanatomy of language, it is still challenging to establish the selection guidelines for intraoperative tasks because of the variations in language processing and language anatomy in individual patients [7, 8, 16].

The present study is a preliminary study. We intensively analyzed the trend of linguistic outcome over time. The limitations are the small sample size and the high dropout rate. Overcoming the high dropout rate is problematic because of the high recurrent and mortality rates of malignant brain tumor; however, stricter criteria for subject selection may mitigate this problem.

Conclusively, the pre- and postoperative assessment tool modified from the short-form BDAE can indicate the variation in language function, and we suggest semantics (complex ideational material) combined with naming and repetition as major assessment tools. The comprehensive naming test reported in this study can be applied in ISM and can preserve or improve linguistic outcomes. Therefore, before establishment of the selection guideline for intraoperative tasks, we suggest using the comprehensive but more easily applied intraoperative task in ISM.

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Disclosure of conflict of interest

None.

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