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Predictive value of fractional anisotropy of the arcuate fasciculus for the functional recovery of language after brain tumor resection: A preliminary study

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ABSTRACT

Objective: The arcuate fasciculus has been recognized as an important pathway for language processing. Brain tumors located in proximity to the fasciculus frequently cause preoperative language impairment, and in some cases, no language recovery occurs after tumor resection. No predictive value has been presented for possible postoperative language recovery after tumor resection. The aim of this study is to analyze the preoperative state of the arcuate fasciculus in the patients with brain tumor from the perspective of its usefulness as a predictive factor for postoperative recovery of language functions.
Methods: For 12 right-handed patients with brain tumors in the left hemisphere, preoperative arcuate fasciculi were analyzed with fractional anisotropy (FA) of the diffusion tensor imaging (DTI) tractography. Language functions were evaluated pre- and postoperatively by using the Western Aphasia Battery (WAB). The preoperative value of the FA of the arcuate fasciculus on the lesion side was examined in relation with the language recovery.
Results: There was a positive relationship between preoperative increasing values of the FA of the left arcuate fasciculus and improvement of the postoperative total WAB score ($p = 0.0056$), and the scores of the naming ($p = 0.018$), reading ($p = 0.029$), and writing subcategories ($p = 0.012$)
Conclusion: The preoperative increasing value of the FA of the arcuate fasciculus in the dominant hemisphere could be a predictor for postoperative language recovery following tumor resection. Meticulous procedure should be performed especially in the cases with higher FA of the arcuate fasciculus harboring high possibility of language recovery.

1. Introduction

Modern in vivo neuroimaging and intraoperative cortical and subcortical stimulation studies have supported the role of subcortical language networks in language function [1–3]. The arcuate fasciculus is a subcortical association fiber tract that can be categorized as part of the superior longitudinal fasciculus [4]. The tract may connect Broca's speech area of the inferior frontal gyrus with Wernicke's speech area of the superior temporal gyrus in the dominant hemisphere, and classically has been recognized to have important roles in conduction aphasia [5–10]. A recent lesion-mapping study in stroke patients found that lesions in the left arcuate fasciculus could be a predictor for impaired speech production [11].

While brain tumors are located in the perisylvian region, the arcuate fasciculus tends to be affected by the tumor mass or tumor invasion. Thus, language function can be impaired due to network disturbance. In case that the tracts are not destroyed but rather compressed and functionally suppressed by the tumor, they can be restored after tumor resection. In such conditions with possible restoration, aiming for postoperative recovery of the language functions, not only the cortical language areas but also subcortical association fiber tracts including the arcuate fasciculus, in proximity to the tumor, should be preserved [12–16]. However, to date, it remains difficult to identify whether the tracts can recover after surgery and to predict language deficit prognoses.

In the present study, we evaluated the preoperative state of the arcuate fasciculus as a predictive factor for possible improvement and recovery of language functions after tumor resection by using diffusion tensor imaging (DTI) tractography. DTI measures the diffusion anisotropy of water molecules often reported as fractional

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anisotropy (FA), which can be a microstructural indicator useful to demonstrate and evaluate the status of the white matter fiber tracts [17]. Then we focused on the FA of the arcuate fasciculus because the FA could be considered as a surrogate marker of white matter integrity.

2. Materials and methods

2.1. Patient profiles and language functions

Twelve right-handed patients who underwent surgical resection of newly diagnosed supratentorial brain tumors at the Department of Neurosurgery of Kanazawa University Hospital were examined in this study. Handedness was assessed in every patient by using the Edinburgh handedness inventory to exclude left-handed patients. All tumors were located in the left frontal, left temporal, or left parietal lobes and were not located in the occipital lobe. Patient age at the time of admission ranged from 28 to 67 years (average, 51.9 years). There were 5 male and 7 female patients. Tumor location and pathological diagnosis after tumor resection are summarized in Table 1. All tumors were totally or subtotally resected using standard microsurgical techniques. Language functions were evaluated by total and subcategory scores of the Western Aphasia Battery (WAB) in all patients, both preoperatively and postoperatively. To evaluate the direct effect of tumor resection and to exclude long-term recovery (including functional reorganization and compensation), postoperative language examination was performed within 12 days after surgery. The Institutional Review Board of Kanazawa University Hospital approved this study.

2.2. Imaging acquisition and arcuate fasciculus measurements

Diffusion-weighted (DW) magnetic resonance (MR) images were acquired using a 3.0-T MR imager (Signa Excite HDx 3.0T; General Electric Medical Systems) with a single-shot, spin echo, echo planar, diffusion-weighted sequence, in addition to a full conventional MR image. A series of axial DW images with a diffusion-sensitizing gradient (b-value = 1000 s/mm^2) along 6 directions was obtained, as well as a series of axial images without DW (b-value = 0). The other diffusion parameters were as follows: time of repetition (TR) = 12,000 ms; time of echo (TE) = 74.1 ms; matrix = 128 mm × 128 mm; field of view (FOV) = 200 mm × 200 mm; number of excitations (NEX) = 2; 37 axial slices; and slice thickness = 3 or 4.5 mm with no inter-slice gap. The DW-MR image was transferred to an Advantage Workstation (General Electric Medical Systems) for data processing using a commercial software program (Functool 4; General Electric Medical Systems) that generated qualitative maps. A seed region of interest (ROI) for use of a deterministic fiber-tracking approach was manually placed on subcortical regions under the supramarginal gyrus, which were defined as the vertical part of the arcuate fasciculus and were separated from the major location of each tumor. Tractography was carried out with fiber propagation stopped at a FA threshold of less than 0.18. The arcuate fasciculus was depicted by a probabilistic approach.

To evaluate the FA value of the arcuate fasciculus, the ROI of the FA of the arcuate fasciculus was placed at the vertical segment of the fiber tract that was located under the supramarginal gyrus [9]. Because the expected main function of the tract is connecting the 2 major speech centers (Broca's and Wernicke's areas located in the inferior frontal gyrus and superior temporal gyrus, respectively), the vertical segment between the 2 terminal cortices of Broca's and Wernicke's areas should be considered as the most appropriate part connecting the 2 speech centers.

A sample control of a normal volunteer is shown in Fig. 1. Next, the average FA value of voxels in the ROI was analyzed. To account for the different slice of DTI conditions, the right part of the non-affected side was adopted as a control, and the relative score of FA value was calculated in each subject according to the following formula: relative FA = (average FA value of the preoperative left arcuate fasciculus region/average FA value of the preoperative right arcuate fasciculus region).

2.3. Statistical analyses

Statistical analyses were performed using JMP statistical discovery software (JMP Version 8; SAS Institute Inc., Cary, NC). The Pearson product-moment correlation coefficient was used to assess the relationship between the preoperative relative FAs of the left arcuate fasciculus and changes in language functions (ΔWAB score, [postoperative score in WAB] − [preoperative score in WAB]), and then patients were clustered into 2 groups according to the preoperative relative FA using a k-means 2-step cluster analysis. All relationships were considered significant at p-values less than 0.05.

3. Results

In each patient, both arcuate fasciculi could be reconstructed in tractography in the preoperative MR study (data not shown). None of the 12 patients had complications that affected postoperative examinations, and WAB examinations were successfully performed within 12 days postoperatively. The total WAB score evaluated both pre- and postoperatively, ΔWAB score and preoperative average FA value of both arcuate fasciculi, and the relative FA values are summarized in Table 1. Representative cases are shown in Fig. 2.

The Pearson product-moment correlation coefficient depicted a positive relationship between increasing preoperative relative FA score of the arcuate fasciculus and increasing ΔWAB score (p = 0.0056, correlation coefficient = 0.77) (Fig. 3A). Using a k-means 2-steps cluster analysis, the 12 samples could be classified into 2 groups: group 1 included 4 cases with highly increasing relative FA score, and group 2 included 8 cases with less increasing/decreasing relative FA score (Fig. 3B). In group 1, total WAB score highly improved postoperatively in all patients. In contrast, total WAB score improved, but less significantly, in 4 of the 8 patients in group 2. Unfortunately, postoperative relative FA could be evaluated in not every case, but in case no. 1, 4 and 10 which were classified into group 1 and postoperative DTI data could be obtained, postoperative relative FAs were decreased to 1.182, 1.058 and 0.944 respectively and approximating to 1.0. These results highlighted that cases with high relative FA were expected to have a higher possibility of improving language functions with the increased relative FA decreasing, i.e. normalizing, postoperatively.

WAB and ΔWAB scores of each subcategory pre- and postoperatively are shown in Table 2. There were significant relationships between the relative FA and ΔWAB scores in the naming (p = 0.018), reading (p = 0.029), and writing subcategories (p = 0.012), but not in the fluency, comprehension, and repetition subcategories (Fig. 4).

4. Discussion

4.1. Fractional anisotropy and brain tumors

Recently, the number of studies that evaluate preoperative DTI tractography of white matter association fibers in patients with brain tumors has increased [18–22]. The tumor can affect fiber tracts and related functional regions by shifting them from expected anatomical locations as well as by destroying their integrity due to tumor invasion. With the effects of tumor