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Case report

Plastic reshaping of cortical language areas evaluated by navigated transcranial magnetic stimulation in a surgical case of glioblastoma multiforme

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1. Introduction

Navigated repetitive transcranial magnetic stimulation (nrTMS) is a novel technology that, unlike the other non-invasive methods used to map language, applies a methodology ("virtual lesions") that is identical to that of the gold standard direct electrical stimulation (DES) during awake surgery [1].

The induction of brain plasticity due to pathological conditions is an established observation and has been studied extensively in stroke [2]. In brain tumor surgery, a small number of reports have demonstrated that brain plasticity can occur in slow-growing lesions and may enable the resection of tumors that were previously deemed inoperable due to their infiltration of areas that carry essential language or motor function [3]. This article reports for the first time a subacute reshaping of the language network within 7 months after surgery for a left fronto-opercular glioblastoma detected by nrTMS.

2. Case report

2.1. Preoperative course

A 51-year-old right-handed woman presented with a 4-week history of short episodes (<5 min) of transient motor aphasia. MRI scanning revealed a contrast-enhancing tumor (6 cc) in the operculum of the left frontal lobe. Formal language testing revealed no language deficit.

2.2. nrTMS methodology

Cortical language mapping was performed using repetitive nrTMS (Nexstim Oy, Helsinki, Finland). The language network was activated by an object-naming task (122 black and white drawings of common objects). The pictures were displayed with an inter picture interval of 2.5 s. The 1 s stimulation train started 300 ms after the picture presentation onset at a frequency of 5 Hz. The stimulation coil was randomly moved in approximately 10 mm steps over the perisylvian cortex, and the stimulation sites were allocated to respective anatomical areas based on a recently described cortical parcellation system (Fig. 1). Any disturbance of speech processing during the object-naming task was categorized into no-response errors, performance errors, neologisms, semantic errors, phonologic errors or circumlocution errors during the offline

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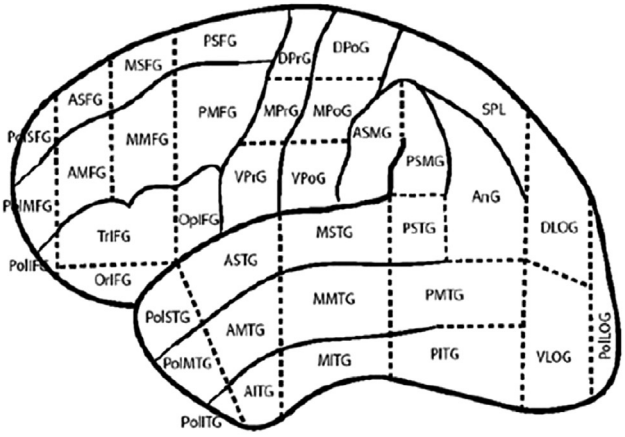

code	cortical area
AITG	anterior inferior temporal gyrus
AMFG	anterior middle frontal gyrus
AMTG	anterior middle temporal gyrus
AnG	angular gyrus
ASFG	anterior superior frontal gyrus
ASMG	anterior supramarginal gyrus
ASTG	anterior superior temporal gyrus
DLOG	dorsal part of lateral occipital gyrus
DPoG	dorsal part of postcentral gyrus
DPrG	dorsal part of precentral gyrus
MITG	middle inferior temporal gyrus
MMFG	middle part of middle frontal gyrus
MMTG	middle part of middle temporal gyrus
MPoG	middle postcentral gyrus
MPrG	middle precentral gyrus
MSFG	middle superior frontal gyrus
MSTG	middle superior temporal gyrus
OpIFG	opercular part of inferior frontal gyrus
OrIFG	orbital part of inferior frontal gyrus
PITG	posterior inferior temporal gyrus
PMFG	posterior middle frontal gyrus
PMTG	posterior middle temporal gyrus
PolIFG	polar part of inferior frontal gyrus
PolITG	polar part of inferior temporal gyrus
PolLOG	polar part of lateral occipital gyrus
PolMFG	polar part of middle frontal gyrus
PolMTG	polar part of middle temporal gyrus
PolSFG	polar part of superior frontal gyrus
PolSTG	polar part of superior temporal gyrus
PSFG	posterior superior frontal gyrus
PSMG	posterior supramarginal gyrus
PSTG	posterior superior temporal gyrus
SPL	superior parietal lobule
TrIFG	triangular part of inferior frontal gyrus
VLOG	ventral part of lateral occipital gyrus
VPoG	ventral part of postcentral gyrus
VPrG	ventral part of precentral gyrus

Fig. 1. Cortical areas and abbreviations.

analysis. Further details of the methodology are described elsewhere [1].

2.3. nrTMS before 1st operation

A total of 320 nrTMS trains were applied in a pattern that was distributed evenly over the perisylvian cortex of both hemispheres. On the left hemisphere, a relative error rate of 10.2% was observed. Errors were elicited in the middle precentral gyrus (MPrG), the opercular inferior frontal gyrus (OpIFG), the posterior middle frontal gyrus, the ventral post-central gyrus (VPoG), and the ventral precentral gyrus (VPrG), with performance and phonological errors forming the predominant error category. No errors were elicited over the tumor, but several errors were observed immediately adjacent to the tumor border. In contrast, the error rate on the right hemisphere was 0% (Fig. 2A, B).

2.4. First operation

During intraoperative language mapping, the intensity for the bipolar 50 Hz stimulation was set to 12 mA, just below the after discharge threshold that had been measured using electrocorticography. Each stimulation train lasted 4 s, during which the patient was presented with the same set of images used during the preoperative mapping. In addition, a trigger sentence ("This is a. . .") was added to each picture. Within the exposed cortex, speech arrests were reproducibly observed in the OpIFG and in the VPrG, whereas DES in triangular inferior frontal gyrus (TrIFG) showed no symptoms, confirming the nrTMS results (Fig. 2C). Consequently, corticotomy was performed in the posterior part of the TrIFG. A gross total resection was performed, and language function remained stable throughout the course of the operation.

2.5. Postoperative course

The histopathological findings revealed a WHO Grade IV glioblastoma. Adjuvant therapy included radiotherapy (fractionated focal irradiation, 60 Gy over 6 weeks) plus continuous daily temozolomide (125 mg per day), followed by cycles of adjuvant temozolomide (125 mg for 5 days during each 28-day cycle). The patient did not report any subjective language problems during the later course, and formal testing after 6 months failed to reveal any deterioration of language function. However, MRI 6 months after the operation revealed a small (1 cm × 1.5 cm × 2 cm) recurrent tumor in the anterior to medial border of the resection cavity.

2.6. nrTMS before second operation

In contrast to the first mapping result, we now observed 7 months later only 4.3% errors when stimulating the left hemisphere but 6.3% errors on the right hemisphere. In addition, the left hemisphere showed new involvement of the temporal and postcentral regions: hesitations were observed in the anterior superior temporal gyrus (ASTG), semantic errors in the dorsal post-central gyrus, and performance errors in the anterior middle temporal gyrus (AMTG) and the ASTG. No errors were induced during stimulation over the TrIFG, and the OpIFG was also insensitive to stimulation. Stimulation of the right hemisphere caused a widespread pattern of errors: hesitation errors in the AMTG and performance errors in