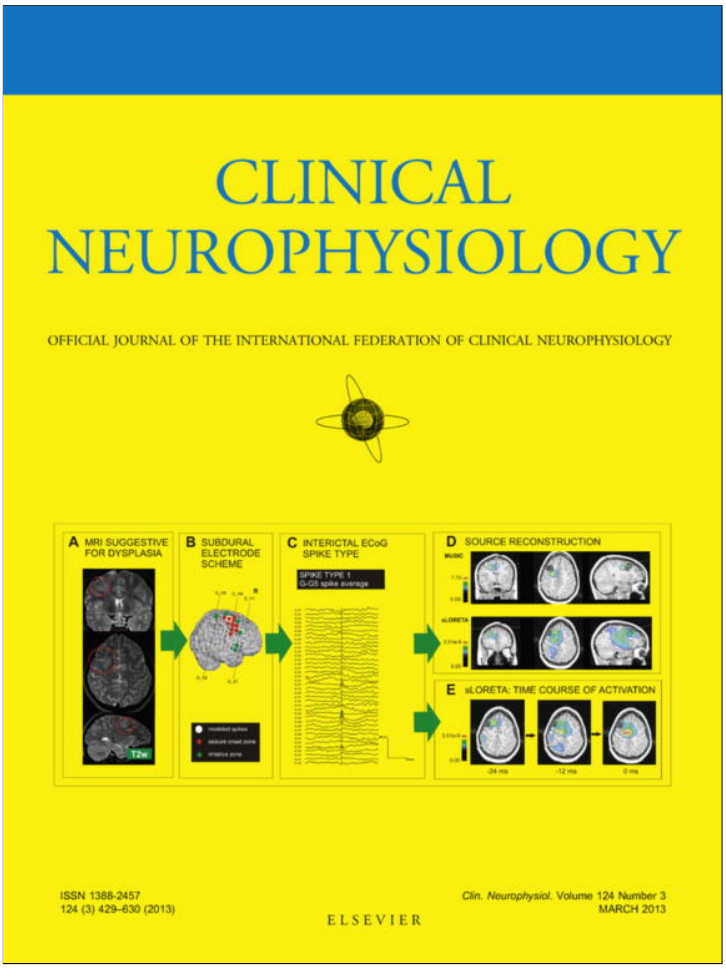

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Presurgical navigated transcranial magnetic brain stimulation for recurrent gliomas in motor eloquent areas

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HIGHLIGHTS

- Navigated transcranial magnetic stimulation (nTMS) and intraoperative direct cortical stimulation (DCS) results correlate well.
- Recurrent tumor does not affect nTMS accuracy despite scarring, plasticity, and edema.
- fMRI results were significantly different, but independent of recurrent tumor or control group.

ABSTRACT

Objective: Navigated transcranial magnetic stimulation (nTMS) has been repeatedly shown to be comparably accurate to direct cortical stimulation (DCS) for rolandic region mapping. However, there are no data on its use for recurrent gliomas in which scarring and radiotherapy can impair nTMS. We therefore evaluated the accuracy of nTMS versus DCS and functional MRI (fMRI) in recurrent gliomas compared to initially operated tumors.
Methods: We examined 8 patients with recurrent gliomas and 23 patients with initially operated lesions in or adjacent to the precentral gyrus by preoperative nTMS.
Results: Preoperative motor mapping correlated well with intraoperative DCS in recurrent gliomas (6.2 ± 6.0 mm), as well as in newly diagnosed tumor patients (5.7 ± 4.6 mm) with no significant difference. Compared to fMRI, the difference was larger for upper (recurrent: 8.5 ± 7.2 mm; new: 9.8 ± 8.6 mm) and lower (recurrent: 17.1 ± 10.6 mm; new: 13.8 ± 13.0 mm) extremities, with no significant differences.
Conclusions: When comparing nTMS with DCS and fMRI, nTMS is as accurate in recurrent gliomas as it is prior to the first operation. It should be considered a helpful modality in recurrent glioma patients as well.
Significance: nTMS is also applicable in recurrent tumors.

1. Introduction

Resection of gliomas in eloquent motor areas remains a surgical challenge and can only be safely achieved with the aid of intraoperative neuromonitoring. While continuous transcranial, cortical motor evoked potentials (MEP) monitoring and subcortical electrical stimulation are well-established techniques to monitor functional integrity of the motor strip and corticospinal tract, a reliable method that functionally identifies motor cortex prior to surgery is not currently in use. Modalities for non-invasive preoperative brain mapping, such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) are unable to adequately identify motor functional areas because metabolic and electrical activity do not necessarily correlate with neurophysiological pathways. Therefore, its usefulness for functional motor cortex mapping is limited (Rutten and Ramsey, 2010).

Several studies have shown that navigated transcranial magnetic brain stimulation (nTMS) correlates well with intraoperative direct cortical stimulation (DCS) and is a useful tool for surgical planning (Forster et al., 2011; Krieg et al., 2012a,c; Picht et al., 2009, 2011a). However, it has only been assessed in newly diagnosed tumors. Scar formation and commonly suggested cerebral plasticity in recurrent tumors could potentially impair nTMS applicability (Ius et al., 2011; Robles et al., 2008). Therefore, this study aimed to prospectively evaluate nTMS accuracy in recurrent gliomas with relation to the established mapping methods of intraoperative DCS and preoperative fMRI. We also compared nTMS accuracy in recurrent gliomas and newly diagnosed brain tumors, which served as a control group.

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2. Methods

2.1. Patients

We performed presurgical nTMS mapping in 8 patients prior to recurrent glioma resection and in 23 patients who underwent resection of newly diagnosed tumors (control group) between May 2010 and September 2011. All tumors were located in or near the precentral gyrus or the CST (Fig. 1). Demographic data and the clinical neurological status of every patient was assessed and documented. Tumor location was determined from imaging data, and tumor histology was acquired.

2.2. Magnetic resonance imaging

Pre- and postoperative MRI scans were performed in all patients on a 3 Tesla MR scanner in combination with an 8-channel phased array head coil (Achieva 3T, Philips Medical Systems, The Netherlands B.V.) for contrast-enhanced 3D gradient echo sequence, T2 FLAIR, diffusion tensor imaging (DTI), and fMRI (Fig. 1). For blood oxygen level-dependent (BOLD) functional imaging (fMRI), each subject underwent 4 fMRI block designed paradigms: upper limb fine motor control (alternating-limb bilateral finger tapping for the right and left hand) and lower limb motor control (alternating extension and flexion of the right and left toes). Data were later processed using the IViewBOLD package (Philips Medical Systems, The Netherlands B.V.) by a neuroradiologist blinded to the patients nTMS mapping results. The contrast-enhanced 3D gradient echo sequence dataset was transferred to the nTMS system (eXimia 3.2, Nexstim, Helsinki, Finland).

The day after surgery, each patient underwent another MRI to evaluate the extent of resection, including T1 sequences with and without contrast enhancement, T2 FLAIR and additionally diffusion-weighted imaging (DWI) to detect any postoperative ischemic incidents.

2.3. Navigated brain stimulation

The Nexstim eXimia 3.2 nTMS system and later the Nexstim eXimia 4.3 nTMS system (Nexstim, Helsinki, Finland) were used for navigated transcranial magnetic stimulation. A biphasic figure-of-eight TMS coil with a 50 mm radius is the magnetic stimulator, which is attached to an infrared tracking system (Polaris Spectra, Waterloo, Ontario, Canada) as reported earlier (Forster et al., 2011; Picht et al., 2011a,b). During anatomical registration of the MRI data set we paid special attention that the registration points were not in areas of interference with the metal plates for cranioplasty. One day prior to surgery, all enrolled patients underwent primary motor cortex mapping as described previously (Picht et al., 2011a). Briefly, for the upper extremity, mapping began at the lateral hand knob identifying the most susceptible point of stimulation, termed the 'hot spot', where motor threshold was determined as described previously (Picht et al., 2011a). Upper-extremity mapping was performed using 110% of motor threshold intensity and covered the entire precentral gyrus, the tumor, and adjacent gyri until compound muscle action potential (CMAP) was no longer detected. The lower extremity required a higher stimulation intensity of up to 130% of motor threshold intensity. As shown in previous works of our and other groups, which were refered to in the manuscript, mapping of the lower extremity by increasing stimulation intensity to reach deeper cortex. For mapping purposes, CMAP above 50 μV was considered significant if latency was within the commonly described latency range of monosynaptic MEP for each muscle (Kombos et al., 2000). After postprocessing, positive motor mapping points were exported to the neuronavigation unit (BrainLAB iPlan® Net Cranial 3.0.1 and Vector Vision 2® or Vector Vision Sky®, BrainLAB AG, Feldkirchen, Germany) and fused to a continuous sagittal image set of a T1-weighted 3D gradient echo sequence.

2.4. Intraoperative neurophysiological mapping and monitoring via MEP

To allow for IOM, intravenous anesthesia with propofol and remifentanyl without neuromuscular blockade was used.

IOM was performed by MEP mapping/monitoring as outlined in earlier reports (Krieg et al., 2012d). CMAP was detected over the same muscles, which were preoperatively mapped with nTMS. After opening the dura, motor threshold for DCS was determined at the hand knob, and rolandic region mapping was performed by anodal monopolar DCS (Inomed Medizintechnik, Emmendingen, Germany) with an electrode tracked by the navigation system. Surgeons were blinded to pre-operative TMS data during the procedure. Stimulation intensities for DCS ranged between 5 and 14 mA, a square-wave pulse with a duration of 0.2–0.3 ms and a frequency of 350 Hz was applied in a train of 5 pulses as described previously (Cedzich et al., 1996; Taniguchi et al., 1993). By using BrainLAB iPlan® Cranial Unlimited in combination with a navigation stimulation probe, we are able to save every point of stimulation where we obtained a CMAP in the navigational data set. Every positive stimulation point was saved to the navigation system. Following DCS mapping, a strip electrode (Inomed Medizintechnik, Emmendingen, Germany) was positioned over the precentral gyrus for continuous MEP monitoring.

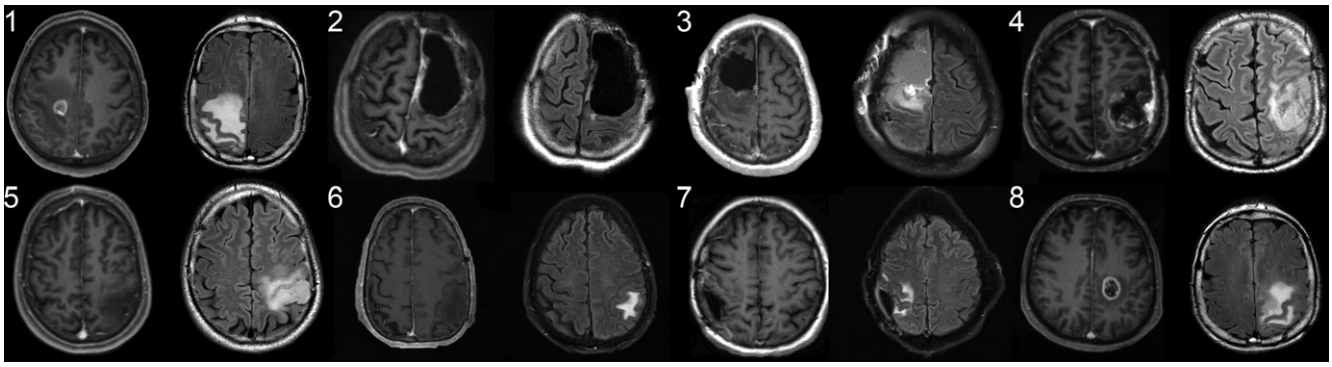

Fig. 1. Preoperative MRI of all patients with recurrent glioma. Patient 1: central region and CST are affected by tumor and edema; patient 2: central region shows edema; patient 3: edema and recurrent glioma within the rolandic cortex; patient 4: edema and tumor affecting the central region and CST; patient 5: recurrent low-grade glioma affecting the hand knob and CST; patient 6: rolandic region is infiltrated by recurrent astrocytoma WHO°II; patient 7: edema affecting the CST; patient 8: recurrent GBM affecting the CST and edema within the rolandic cortex.

2.5. Correlation between nTMS, intraoperative DCS and fMRI

Preoperative motor cortex mapping was compared to intraoperative DCS with the navigation system. Borders between positive and negative stimulation points of both modalities were compared by directly measuring the distances of the mapped borders in 2D axial images via BrainLAB iPlan® Cranial Unlimited (BrainLAB AG, Feldkirchen, Germany) as described previously (Krieg et al., 2012b,c).

In addition, fMRI and nTMS data were imported to the neuronavigation system, and the distances between borders of motor BOLD areas and areas of positive nTMS stimulation were measured on axial slices.

2.6. Ethical standards

The study was performed in accordance with the ethical standards of the Technical University of Munich, the local ethics committee (registration number: 2793/10), and the Declaration of Helsinki. Informed consent was obtained for every participating patient.

2.7. Statistical analysis

Differences between groups were tested by Friedman's test for non-parametric one-way analysis of variance (ANOVA), followed by Dunn's post hoc test. Differences between the two groups were tested using Wilcoxon signed-rank test for comparisons of related samples. All results are presented as box plots (SigmaStat 3.5, Jandel Scientific, Erkrath, Germany). A value of $p < 0.05$ was considered significant.

3. Results

3.1. Patients

For recurrent gliomas, the mean age was 50.1 ± 11.1 years (median 45.2 years; range 40.5–69.1 years); 5 patients (62.5%) were female and 3 (37.5%) were male. All patients were right-handed and had a history of seizures, and 6 of the 8 (75.0%) were on antiepileptic drugs (AED). Mild preoperative motor deficits were present in 2 cases (25.0%), and two tumors (25.0%) were in the dominant hemisphere. Out of 8 cases, there were 6 glioblastomas (WHO°IV), 1 anaplastic astrocytoma (WHO°III), and 1 diffuse astrocytoma (WHO°II). Time span between first and recurrent surgery was 26.8 months (range 9–60 months).

For primarily diagnosed lesions, the mean age was 58.4 ± 17.0 years (median 65.7 years; range 18.7–78.8 years); 10 patients (43.5%) were female, and 13 (56.5%) were male. Fourteen patients (60.9%) had a history of seizures, and 12 of those 14 (85.7%) were on AED. Nineteen patients (82.6%) were right-handed and 4 patients (17.4%) were left-handed while none showed bilateral handedness. Mild preoperative motor deficits were present in 10 cases (43.5%). Fourteen tumors (60.9%) were in the dominant hemisphere. Out of 23 cases, there were 10 glioblastomas (WHO°IV), 2 anaplastic astrocytomas (WHO°III), 1 diffuse astrocytoma (WHO°II), 1 DNET (WHO°I), and 9 metastases. Table 1 provides a detailed overview.

3.2. Preoperative nTMS mapping

Preoperative mapping of the primary motor cortex was performed in all 31 patients. The mean resting motor threshold (rMT) was 35.7 ± 9.2% maximum stimulator output and did not differ in patients on AEDs. Levetiracetam was used as AED in all but one case of recurrent glioma, in which lamotrigin was used. Between 121 and 253 stimulation points were needed for complete mapping. Lower extremity mapping was possible in 45.2% of cases. Out of 31 patients, one patient experienced nTMS mapping as unpleasant, but none found it painful. Mean rMT did not differ between patients with recurrent gliomas (36.0 ± 8.9%; median 34.0%; range 26.0–55.0%) and control patients (34.2 ± 9.0%; median 33.0%; range 23.0–65.0%). Successful lower extremity mapping was possible with comparable differences in both groups (recurrent: 50.0%; primarily: 43.5% of cases). A detailed overview is provided in Table 1. The area of the mapped primary motor cortex was slightly smaller in patients with recurrent gliomas (mean 3.69 ± 1.87 cm^2; median 3.18 cm^2; range 0.87–6.53 cm^2) compared to the control group (mean 4.52 ± 3.12 cm^2; median 3.59 cm^2; range 0.86–12.71 cm^2), but this difference was not significant (Fig. 2).

3.3. Correlation between nTMS, intraoperative DCS and fMRI

Preoperative motor mapping correlated well with intraoperative DCS mapping in recurrent gliomas (mean distance 6.2 ± 6.0 mm; median 3.2 mm; range 0.0–18.2 mm) and newly diagnosed tumors (5.7 ± 4.6 mm; median 4.5 mm; range 0.0–22.5 mm). No significant difference or monodirectional systematic deviation could be observed between groups (Fig. 3).

One recurrent glioma patient did not tolerate fMRI due to claustrophobia, and the general condition of a patient in the control group was too poor to tolerate fMRI. Therefore, a comparison of nTMS and fMRI was available for 7 patients with recurrent gliomas and 22 patients with newly diagnosed tumors.

Compared to the continuous nTMS motor area of upper and lower extremity, fMRI determination of the primary motor cortex yielded distinct areas for upper and lower extremity motor areas. Therefore, comparisons of nTMS and fMRI are presented separately for upper and lower extremities (Fig. 4). In patients with recurrent tumors, as well as in the control group, differences between the nTMS positive areas and fMRI were larger for the upper (recurrent: mean 8.5 ± 7.2 mm, median 6.7 mm, range 0.0–37.6 mm; control: mean 9.8 ± 8.6 mm, median 7.6 mm, range 0.0–44.0 mm) and lower extremity (recurrent: mean 17.1 ± 10.6 mm, median 14.8 mm, range 3.6–36.7 mm; control: mean 13.8 ± 13.0 mm, median 10.3 mm, range 0.0–49.2 mm) than the spatial difference between nTMS and DCS. However, there were no significant differences between the groups (recurrent vs. control). Again, no monodirectional systematic deviation could be observed (Fig. 4).

3.4. Patient outcome

Of 8 patients with recurrent gliomas, two (25.0%) had contralateral preoperative motor weakness. Three patients (37.5%) showed increased weakness at the first postoperative day and did not show immediate motor improvement. At discharge, one patient (12.5%) still suffered from aggravated paresis, 6 patients (75.0%) were unchanged from their preoperative status, and one patient (12.5%) improved from surgery. Long-term follow up was achieved in all patients (25.1 ± 11.8 weeks, median 27.6 weeks, range 4.9–38.6 weeks). The patient with postoperatively aggravated paresis at discharge still presented with persistent motor deficit at long-term follow up. Intraoperative MEP monitoring of this patient showed an amplitude decline of more than 50% during resection, and postoperative DWI showed an ischemic lesion within the fibers of the dorsal part of the CST. Compared to the preoperative motor status, 6 patients (75.0%) remained unchanged in long-term follow up, and one patient (12.5%) showed significant motor function improvement.

With regard to the 23 patients in the control group, 10 (43.5%) suffered from preoperative paresis. At the first postoperative day, 12 patients (52.2%) showed aggravated weakness, and none

Table 1
Patient data. Detailed overview on neurological status as well as mapping properties.

Pt no.	Age (years)	WHO°	Radiotherapy	Chemotherapy	AED	Paresis pre-OP	New paresis post-OP	RMT	Lower extremity possible	Resection	Affection of CST by	Size of ROI (cm^3)
Recurrent glioma												
1	69.1	4	Y	Y	LTZ	Y	N	32	Y	STR	T, E	4.38
2	40.5	4	Y	Y	LTZ	N	N	29	Y	STR	E	3.10
3	50.2	4	Y	Y	–	N	N	38	N	GTR	T, E	6.53
4	46.9	3	Y	Y	–	Y	N	55	N	GTR	T, E	5.97
5	41.5	2	N	N	CBZ	N	N	35	Y	STR	T	3.08
6	43.5	2	N	N	LTZ + LTN	N	N	40	Y	STR	T	2.36
7	43.1	4	Y	Y	LTZ	N	Y	33	N	GTR	E	3.25
8	65.6	4	Y	Y	LTZ	N	N	26	N	GTR	T, E	0.87
Pt no.	Age	Tumor type	Radiotherapy	Chemotherapy	AED	Paresis pre-OP	New paresis post-OP	RMT	Lower extremity possible	Resection	Affection of CST by	Size of ROI (cm^3)
Primary tumor												
1	53.6	met	N	Y	–	Y	N	34	Y	STR	E	2.10
2	69.3	GBM	N	N	–	N	N	27	Y	GTR	T, E	7.46
3	50.6	met	N	Y	–	Y	Y	65	Y	STR	E	8.49
4	78.8	GBM	N	N	LTZ	Y	Y	25	Y	STR	T. E	1.94
5	55.0	GBM	N	Y	LTZ	N	N	28	N	GTR	T	2.10
6	48.7	met	N	Y	LTZ	Y	N	31	Y	GTR	E	1.24
7	78.1	meningeoma	N	N	LTZ	Y	N	36	N	GTR	T	0.86
8	76.3	GBM	N	N	–	Y	N	28	N	STR	E	12.71
9	59.9	met	Y	N	LTZ	N	Y	34	Y	STR	T. E	2.77
10	31.8	DNET °I	N	N	LTN	N	N	33	N	GTR	T	5.09
11	66.5	AA	N	N	LTZ	N	N	26	Y	GTR	T	4.14
12	18.7	OA	N	N	–	N	N	37	N	GTR	T	6.00
13	67.5	met	N	Y	LTZ	N	N	30	N	STR	E	5.94
14	75.2	GBM	N	N	–	N	Y	48	Y	STR	T	7.59
15	67.2	met	N	Y	–	N	N	29	N	GTR	T, E	5.00
16	65.7	met	N	Y	–	N	N	32	Y	GTR	E	2.60
17	67.6	GBM	N	N	–	Y	Y	45	N	STR	T, E	5.04
18	70.5	GBM	N	N	LTZ	N	N	36	N	STR	T, E	3.00
19	73.6	GBM	N	N	LTZ	Y	Y	39	N	GTR	T	1.85
20	44.6	GBM	N	N	CBZ	N	0	35	Y	GTR	T, E	10.47
21	59.2	GBM	N	N	–	Y	0	32	N	GTR	T, E	3.59
22	41.9	AA	N	N	LTZ	Y	–	33	N	STR	T, E	1.78
23	23.9	met	Y	Y	–	N		23	N	GTR	E	2.25

AED = antiepileptic drug, LTZ = Levetiracetam, CBZ = Carbamazepine, LTN = Lamotrigin, RMT = resting motor threshold, CST = corticospinal tract, ROI = region of interest (primary motor cortex), STR = subtotal resection, GTR = gross total resection, met = metastasis, GBM = glioblastoma multiforme, AA = anaplastic astrocytoma, OA = Oligo-astrocytoma, T = tumor, E = edema.

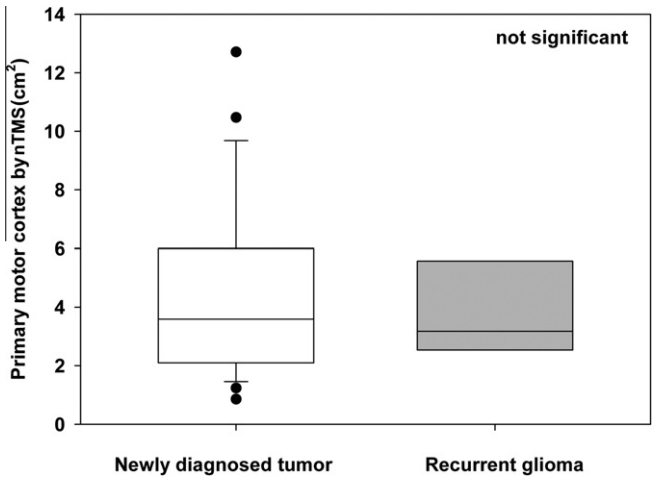

Fig. 2. Area of the primary motor cortex measured by nTMS Box plot showing the motor cortex area measured by nTMS in recurrent gliomas and primarily diagnosed lesions. No statistically significant difference was observed.

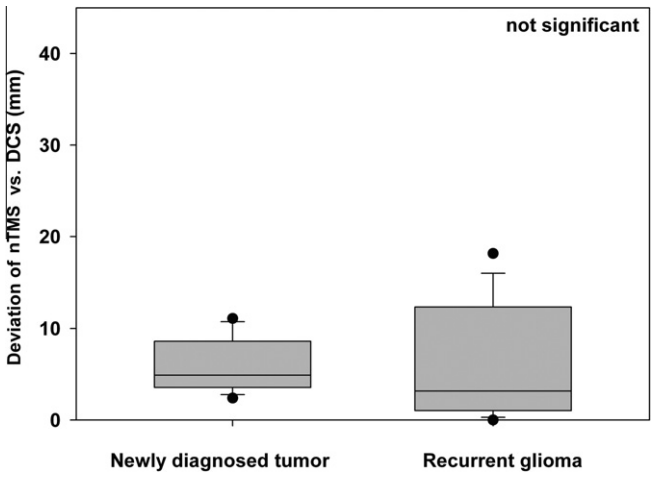

Fig. 3. Deviation of nTMS compared to DCS Box plot outlining the correlation between nTMS and DCS in recurrent gliomas and primarily diagnosed brain tumors. No statistically significant difference was observed.

showed immediate motor improvement. By discharge, 7 patients (30.4%) still had increased surgery-related paresis, 15 (65.2%) did not change due to surgery, and one patient (4.3%) improved due to surgery. For long-term follow up, two patients without postoperative deficits were lost. The mean follow up period for all others was 17.5 ± 14.9 weeks (median 13.1 weeks, range 0.7–46.7 weeks).

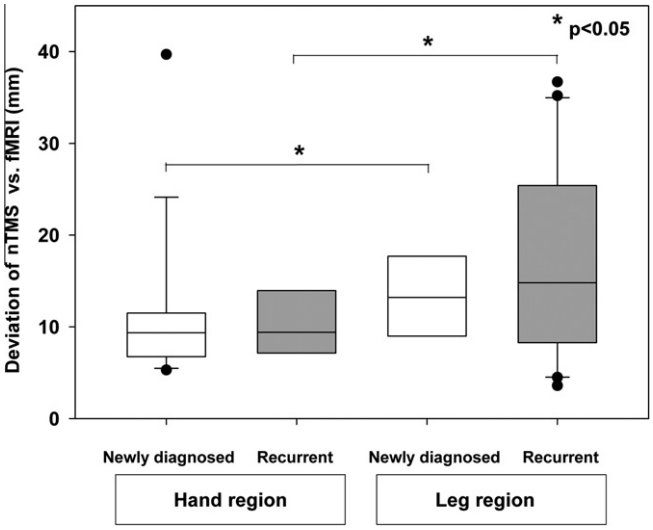

Fig. 4. Accuracy differences between nTMS and fMRI Box plots showing differences in primary motor cortex delineation between nTMS and fMRI for upper and lower extremities. Although no difference was observed between recurrent gliomas and newly diagnosed lesions, there were significant differences between nTMS vs. fMRI.

Out of the 7 patients with postoperatively aggravated deficit at discharge, 3 patients (13.0%) still showed persistent motor deficit at long-term follow up. All 3 patients showed MEP amplitude loss >50% during resection within the CST fibers. Compared to their preoperative motor status, 15 patients (65.2%) remained unchanged, and 2 patients (8.7%) improved.

4. Discussion

The present study aimed to assess the feasibility and accuracy of nTMS in patients with recurrent gliomas near or in motor eloquent areas. Therefore, motor areas outlined during preoperative non-invasive nTMS were compared to intraoperative DCS. Spatial errors for recurrent gliomas were compared to a series of newly diagnosed gliomas, in which the same comparison between presurgical nTMS and DCS was performed. The central finding of the present study is that nTMS in patients with recurrent tumors is as feasible and accurate as in patients with newly diagnosed gliomas.

Electrophysiological methods are accepted as standards to assess motor pathways during resection of motor eloquent tumors. For identification of the cortical representation of motor function SEP phase reversal is widely performed.

However, apart from intraoperative mapping and monitoring of motor pathways, preoperative identification of motor areas by nTMS was proofed to be helpful in surgical planning for motor eloquent tumors (Picht et al., 2012). This is especially the case in recurrent tumors because recently suggested brain plasticity might lead to a mismatch of cortical motor presentation and anatomy (Ius et al., 2011; Robles et al., 2008). A method available for presurgical delineation of subcortical motor pathways is DTI fiber tracking, which has gained increasing attention in recent years and was also proofed to show reduced interobserver variability when combined with nTMS (Krieg et al., 2012a). Magnetencephalography (MEG) and fMRI are currently available methods of non-invasive cortical motor representation mapping; MEG is rarely used, but fMRI is frequently applied. However, both techniques have significant limitations. fMRI does not measure electrophysiological function *per se*; rather, the BOLD effect measures increased metabolism as surrogate parameter of neurological function. However, metabolism might be altered independent of brain function, which is partially attributable to an altered vascular pattern. This is especially relevant in the vicinity of tumors. Several publications have shown that fMRI does not show sufficient sensitivity or specificity to identify eloquent brain function in the vicinity of tumors; therefore, it is not reliable for surgical planning (Hou et al., 2006; Krishnan et al., 2004; Lehericy et al., 2000; Rutten and Ramsey, 2010; Yetkin et al., 1997). MEG was also shown to correlate with nTMS (Vitikainen et al., 2009). However, many hospitals do not have the necessary equipment, and the costs are high.

Navigated TMS directly assesses electrophysiological function rather than a surrogate parameter, thereby increasing accuracy in comparison to fMRI and MEG. Recently, we and others have shown its feasibility and accuracy for presurgical motor cortex identification (Forster et al., 2011; Krieg et al., 2012a,c; Picht et al., 2011a, 2012). The present study now verifies the feasibility and accuracy of nTMS in recurrent tumors despite significant edema and tumor infiltration of the rolandic cortex as shown in Fig. 1.

nTMS and DCS correlated in recurrent gliomas and initially diagnosed lesions, despite potential cerebral plasticity, edema, and scar formation which can be typical in recurrent tumors (Duffau, 2006; Ius et al., 2011; Lonjon et al., 2010; Martino et al., 2009; Robles et al., 2008). However, in our current study, we were not able to find any proof for plasticity of the motor cortex because location and size of the mapped primary motor area were comparable to initially operated tumors (Fig. 2). As previously argued, DCS and nTMS are similar techniques based on MEPs via neuronal activation. Today, DCS is still the most precise method for functional mapping but is limited to intraoperative use (Berger et al., 1990; Kombos et al., 2000; Neuloh et al., 2007; Sanai and Berger, 2008; Suess et al., 2006). Navigated TMS can also elicit CMAPs to characterize the primary motor cortex, but in contrast to DCS, it can be performed transcranially in an awake patient prior to surgery. By opening this new possibility, nTMS was shown to have a significant impact on surgery but also on preoperative decision making when applied routinely (Krieg et al., 2012c; Picht et al., 2012).

When considering the spatial variation between DCS and nTMS, our results are within the calculated precision of the nTMS system (eXimia 3.2, Nexstim, Helsinki, Finland), which is 5.73 mm according to the manufacturer (Ruohonen and Karhu, 2010). Additionally, brain shift might contribute to the slight spatial difference between nTMS and DCS because DCS positive stimulation points were recorded by a neuronavigation system and a tracked DCS electrode.

As a direct comparison between two preoperative non-invasive methods, nTMS and fMRI were compared as well. However, we found a poor spatial correlation between fMRI and nTMS for both recurrent tumors and newly diagnosed tumors which is well in accordance with other data showing differences between electrophysiological (i.e., true functional) and metabolic mapping; not only shown in nTMS studies (Forster et al., 2011; Krings et al., 2001; Rutten and Ramsey, 2010). Additionally to the above-mentioned mechanisms of impairment, scar tissue might also potentially hamper fMRI. However, we could not detect any differences between recurrent and newly diagnosed tumors between nTMS and fMRI. Moreover, fMRI is more dependent on patient cooperation; poor condition, paresis, or claustrophobia can make fMRI mapping impossible. In contrast, nTMS was reported to be possible in a hemiplegic patient (Picht et al., 2011b). Although one patient experienced nTMS to be unpleasant, none experienced it as painful, and it was successful in all patients, which is in accordance with previous studies (Forster et al., 2011; Picht et al., 2009, 2011a).

Navigated TMS mapping depends on various confounding factors, such as the definition of rMT, the voltage at which CMAP is considered significant, registration errors, navigation errors, and brain shift after durotomy (Hastreiter et al., 2004; Suess et al., 2007). Therefore, we must keep in mind that the level of

agreement between nTMS and DCS shown here is possible only with considerable nTMS experience. Despite these limitations, our results were more accurate than previously published data, despite the supposed additional confounders in recurrent tumors (Krings et al., 1997a,b; Picht et al., 2009). However, the number of cases in our series is considerably small and therefore may not rule out that some patients are not able to get mapped by nTMS.

Preoperative nTMS mapping also allowed us to inform the patient of possible transient postoperative motor weakness, as we now knew how close the primary motor region was to the intended resection border. Thus, we were able to assess the operative risks for permanent paresis more precisely and used this information to prepare the patient preoperatively. However, we have to remember that patient outcome is the most essential parameter in evaluating the usefulness of a new technique.

Disclosure

The study was completely financed by institutional grants through the Department of Neurosurgery. SK has been involved in Nexstim Oy workshops but is not a contracted consultant. Therefore, the authors report no conflict of interest concerning the materials or methods used in this study, or the findings specified in this paper.

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