Author's response to reviews

Title: Intraoperative electrocortical stimulation of Brodman area 4: A 10-year analysis of 255 cases.

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Author’s response to reviews: see over
Intraoperative Electrocortical Stimulation of Brodman Area 4: A 10-year Analysis of 255 Cases.
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Answers to the Reviewer’s comments:

Dear Reviewers:

Thank you for your comments and inspiring critics concerning the above mentioned manuscript. Please find enclosed our respond and the changes made in the manuscript.

Yours sincerely,
O. Suess, Berlin May 10, 2006

Red = corrections/changes made in the manuscript

Reviewer: Ricarda I. Schubotz

What is new given to the study of Cedzich et al. 1996?

The major interest of this paper is to report an analysis of a much larger group (n=255) of patients than published by Cedzich et al. (n=58 and n=70). We hope that this will strengthen the acceptance of MCS by giving a good overview on which stimulation parameters can be successfully used.

Can MCS be used to quantify or validate the grade of paresis?

(p20) However, there is no statistical prove that MCS can be used to quantify or validate the grade of paresis.

Does the time since the lesion exists affect or interact in any way with the effect or effectiveness of MCS mapping or monitoring?

(p15) ... whereas the presence and duration of a pre-existing preoperative paresis BMRC grade 3/5 or better has no significant influence on repetitive MCS as a monitoring procedure [23].


Please give a reference for the statement on page 5 saying that 85% of the fibers are crossing to the opposite side.


Definition of CMAPS could be already given in the introduction.

(p4/5) Using a high-frequency anodal square-wave pulse, compound muscle action potentials (CMAPs, a group of almost simultaneous action potentials from several muscle fibers in the same area)
were evoked by stimulation of the supplying cortical motor area and are recorded as one multipeaked summed action potential in muscles of the contralateral extremities during surgery under general anesthesia.

It should read “authors are of the opinion that” on page 17.

(p17) Having performed a detailed analysis of the 232/255 monitoring cases, the authors are of the opinion that a latency prolongation of > 15 % and/or amplitude reductions of > 80 % should be established as significant potential changes requiring action.

Reviewer: Hugues Duffau

The authors should comment their higher rate of complications (8% vs. approx. 5% in literature) and explain this discrepancy with the literature.

(p18) Permanent motor deficits (clinically unchanged on 3- and 6-month follow up) occurred in 19/232 cases (8.2%) of this study. Two cases (2/232, 0.9%) with uneventful MCS were caused by territorial infarction, in the other 17 cases (17/232, 7.3%) abnormal MCS was to be noticed during the phase of lesion resection. MCS was irreversible in all of these cases. Post-operative control CTs demonstrated total tumor resection within the anatomical and electrophysiologically confirmed precentral gyrus in 15 of the 17 cases. In comparison, Neuloh and Schramm [31] report about 9% new permanent deficits in a group of 140 central and insular space-occupying lesions, operated on under direct monopolar electrocortical stimulation, if only the monitored muscle groups and limbs are considered. This perfectly demonstrates the ethical dilemma between preserving function and the goal of total tumor resection, as this might correlate with a better survival rate.

(p19) However, damage to neural structures during brain tumor surgery can only be prevented if appropriate measures are taken while functional changes are reversible. That is why several authors [32,33,34] started using subcortical stimulation in addition to cortical mapping and monitoring. A number of high-quality publications give prove of the reliability of this intraoperative neurophysiological tool, although its limited specificity, its lack of quantifiable results and continuous monitorability seem to be a drawback of that method in the hand of the inexperienced user [31]. Keles et al [32], using bipolar cortical and subcortical stimulation in a group of 294 cases, calculated the risk of permanent motor deficits to be 7.6% if both stimulation sites demonstrated that the lesion was located within or adjacent to motor tracts. Noteworthy, the risk of permanent deficit decreased significantly in their study (down to 2.3%) when subcortical pathways could not be identified but cortical stimulation confirmed a functionally intact status – demonstrating, that eloquent cortex sites were close but not in direct contact with the lesion (>2-3 mm distance [31]). In a recently published paper by Eisner et al. [33] the authors report a 10% morbidity (1/10) if the lesion was found within the primary motor cortex and close to the pyramidal fiber tract. Post-operative CT- and MRI-scan verified radical tumor resection in all of their cases.


The authors should provide precise data with regard to the diffusion of MCS. ... In the present article, there is no data given concerning the policy of the authors with regard to the distance that they have taken from the motor sites.

For Taniguchi et al. muscle activity recording seemed suitable especially for intraoperative monitoring as it can be recorded without causing obvious movement of the patient (which might be especially meaningful during microneurosurgery), as well as its potential size (which allows recording without averaging) and its latencies (which might supply the surgeon with quantitative and qualitative information about the motor system's integrity) [17]. The physiological basis of such motor effects following a transient stimulus to the cerebral cortex is in detail described by Amassian et al. [22] in the animal model, showing that the response to a surface stimulus applied to Brodman area 4 is a direct (D-) wave conducted in fast axons followed by several indirect (I-) waves if recorded from the cortico-motoneural cord and a specific motor action potential if recorded from certain muscle groups [22]. With an anodal stimulus applied to the cortex, current is assumed to enter at the apical dendrites, leading to depolarization at the proximal Ranvier internodes of the corticospinal tract axons [22]. Unfortunately, little is still known concerning the effect of the total charge and the total charge density of a number of pulses in train on the cortex excitability. One major concern is, that far field depolarization and current spread are more likely to occur with this technique. Therefore, MCS monitoring differs from the bipolar stimulation technique in that action must be taking immediately when potential changes are observed, assuming that they occur before motor function is damaged irreversibly, whereas repetitive bipolar mapping gives a more spatial information, e.g. on the anatomical localization of the motor pathways, allowing the surgeon to define margins which have to be preserved around the motor sites.


Why the authors have never used subcortical stimulation, which enables a direct information regarding the exact location of the pyramidal pathways, in addition to CMAP monitoring, which give only indirect data ...?

(p19) ... That is why several authors [32,33,34] started using subcortical stimulation in addition to cortical mapping and monitoring. A number of high-quality publications give prove of the reliability of this intraoperative neurophysiological tool, although its limited specificity, its lack of quantifiable results and continuous monitorability seem to be a drawback of that method in the hand of the inexperienced user [31]. ...

(p20) In conclusion, surgical morbidity for lesions immediately within the precentral gyrus or with direct contact to subcortical motor pathways seems to be dependent on more than the location and the intraoperative monitoring technique used alone. Other factors such as tumor histology (metastases vs. gliomas), surrounding edema or aggressiveness of tumor resection play an important role in the outcome as well. A detailed multivariate meta-analysis should give more information on this important topic. Furthermore, studies combining MCS with subcortical stimulation techniques (such as already performed with bipolar stimulation techniques [32,33,34]) should investigate the potential of subcortical mapping and/or monitoring in reducing the rate of permanent morbidity for operations in these high-risk eloquent motor areas.

The authors mapped and monitored the upper limb and the leg: what about the face?

(p16) Depending on the exact location of the target lesion, additional muscles, such as the orbicularis oris muscle of the face, may be included in the recording scheme. However, in the author's
experience, recordings from the limbs picked up basically all motor impairment that could be found on postoperative examination.

What about the pre- and postoperative somesthetic examination in the 55 patients with lesions dorsal to Brodman Area 4? Was the somatosensory function mapped or monitored intraoperatively?

All patients underwent a routine neurological examination pre- and post-operative (day 1 and 7 post-op) as well as on their 3- and 6-month follow up. Somatosensory function was controlled and evaluated, but not described in detail in this paper as main focus of this study was motor function. Somatosensory function was not monitored as in intraoperative parameter in any of the cases.

Can the authors explain why the multi-pulse technique … differs from Penfield’s technique in that it calls for only 5-7 stimuli with up to 2Hz …?

Sorry for that typing mistake. It should read: “… only 5-7 stimuli with up to 500 Hz …”

This multi-pulse technique essentially differs from Penfield’s technique in that it calls for only 5-7 stimuli with up to 500 Hz of stimulation rate, while Penfield’s technique calls for continuous stimulation during a few seconds with a frequency of 50-60Hz.

First report on direct motor cortex stimulation under general anesthesia.

Thank you for that important correction! Text and reference were changed to:

(p4) It was only in the year 1990 that Berger et al. [7] described a modification of that bipolar technique already used by Penfield.