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Electrophysiological Considerations Regarding Electrical Stimulation of Motor Cortex and Brain Stem in Humans

Author(s): Cedzich, Cornelia MD; Pechstein, Ulrich MD; Schramm, Johannes MD; Schäfer, Sonja MD

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Neurosurgical Clinic of Nürnberg (CC), Nürnberg, and Neurosurgical Clinic (UP, JS), University of Bonn, Bonn, Germany, and Department of Medicine, Stiftshospital, Andernach, Germany (SS)

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Reprint requests: Cornelia Cedzich, M.D., Neurosurgical Clinic of Nürnberg, Klinikum Süd, Breslauer Str. 201, 90340 Nürnberg, Germany.

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Abstract

Abstract

OBJECTIVE: To provide information about activation of descending motor pathways in humans, motor evoked potentials were obtained from 16 patients without

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any sensorimotor deficit, after both cortical and brain stem stimulation.

METHOD: Total anesthesia was achieved in all patients through intravenous administration. Short trains of one to five electrical pulses were delivered separately to the motor cortex and the brain stem. Compound muscle action potentials were recorded from the contralateral upper extremity. Threshold intensity, stimulus polarity, latencies, and effect of increased stimulus intensity on latencies were analyzed.

RESULTS: The threshold intensity was significantly lower when stimulating the brain stem than when stimulating the cortex. A monophasic anodal stimulus was better for cortical stimulation than for brain stem stimulation. Conversely, a monophasic cathodal stimulus was more effective for brain stem stimulation. The rate of unsuccessful stimulations was higher with brain stem stimulation and with increased stimulation intensity. The variability of latencies was so high that a calculation of the conduction velocity of the motor pathways was not possible.

CONCLUSION: The results indicate that cortical surface and brain stem stimulation act on different nervous elements. Because of the condensation of motor pathway fibers at the brain stem level, much less stimulus intensity for eliciting compound muscle action potentials was necessary. On the other hand, the higher rate of unsuccessful brain stem stimulations may be caused by a block of conduction at either the anterior horn cell pool or the neuromuscular junction. Thus, for cortical and for brain stem stimulation, different stimulating parameters seemed to be necessary with the patient under general anesthesia.

Direct cortical electrical stimulation for eliciting movements of the contralateral extremities has been practiced since 1874, as presented in the report by Bartholow (4). A transcranial electrical stimulation method was described by Gualtierotti and Paterson (7), and the magnetic transcranial stimulation was introduced by Barker et al. (3). The comparison of the compound muscle action potentials (CMAPs) after electrical and magnetic transcranial stimulation showed differences, especially in latencies. Thus, different elements of the central nervous system must have been stimulated by the different techniques. The discussion regarding which elements of nervous structures are excited by the different stimulation methods was opened. The following study was performed to evaluate stimulation parameters for cortical and brain stem stimulation with the patient under general anesthesia and to find out whether different nervous elements are excited by cortical and brain

stem stimulation. A modified stimulation method was used, which is described elsewhere (5,12).

PATIENTS AND METHODS

We studied 16 patients who underwent resection of the anterior two-thirds of the temporal lobe and hippocampectomy to treat pharmacoresistant epilepsy. All examinations were permitted by the local ethical committee, and all patients provided informed consent. After the anterior two-thirds of the temporal lobe was exposed via a frontotemporal trepanation, a strip (4-8 contacts arranged in series) or grid electrode (20 contacts arranged in four rows of five electrodes each) (Ad-Tech, Racine, WI) was pushed on the unexposed sensorimotor cortex subdurally for localization of the central sulcus, recording the phase reversal phenomenon. Therefore, from each contact point, evoked potentials were recorded after median nerve stimulation of the contralateral side. Recordings were performed in a referential mode using a reference electrode at Fpz (Table 1). A good phase reversal of N20/P30 to P20/N30 was obtained only when the recording electrode was exactly placed over the sensorimotor cortex. Because the sensorimotor cortex was not exposed, several positions of the recording electrode were tried to span the central sulcus and to thus obtain a good, reliable phase reversal. A Nicolet Pathfinder I (Nicolet Instruments, Biomedical Division, Madison, WI) was used for all examinations. After somatosensory recording, the motor cortex was stimulated directly using the contact of the strip or grid electrode from which the best P20/N30 potentials were recorded. A monophasic, anodal stimulus was delivered from a constant current electrical stimulator (ES Toennis-Jäger GmbH, Würzburg, Germany) to the motor cortex. The reference electrode was placed on Fpz. The duration of each stimulus was 400 microseconds, and the interstimulus interval was 2 milliseconds. One train of stimuli contained one to five pulses. Stimulation intensity was increased stepwise until CMAPs were elicited in the target muscles or when the stimulation intensity reached 20 mA. CMAPs were recorded with a pair of subdermal needle electrodes from forearm flexor muscles, thenar and hypothenar contralateral to the side of stimulation in a belly-tendon fashion. Our recording device was a Nicolet Pathfinder I(Nicolet Instruments), which was triggered by the stimulating device. The detailed stimulation and recording parameters are presented in Table 1. The parameters used in this study resulted from earlier researchers and are published elsewhere (5,12). After temporal lobe resection, i.e., when uncus, hippocampal gyrus, and hippocampus had been removed, the surgeon was able to lift the pial membrane. The cerebral peduncle, optic tract, and midbrain, which constitute the brain stem at the level, could then be seen. Sometimes, the pial membrane was not intact overall. A silver plate electrode (1.13 cm^2) (TS90-030; Unique Medical Corp., Ltd., Tokyo, Japan) was placed on the ventrolateral aspect to the peduncle, and the brain stem was stimulated directly via this electrode. To compare both the cortical and the brain

parameters evaluated differed at least in polarity and intensity of the delivered stimuli. A cathodal stimulus was delivered to the brain stem, and the anode was at Fpz. The stimulus intensity varied from 2 to 10 mA. The detailed parameters of stimulation and recording are listed in Table 1.

TABLE 1. Stimulation and Recording Methods*a*

SEP	
Stimulation	Bipolar
Intensity	20 mA
Frequency	5.3 Hz
Duration	300 μs
Recording	Strip-/gridelectrode
Filter	30 Hz–3 kHz
Repetition	50–250
Sensitivity	10–20 μV/Div
MEP (cortical stimulation)	
Stimulation	Monopolar, anodal, rectangular
Intensity	6–20 mA
Interstimulation interval	2 ms
Duration	400 μs
Recording	Needle electrodes
Filter	30 Hz–3 kHz
Repetition	1–5
Sensitivity	50–200 μV/Div
MEP (brain stem stimulation)	
Stimulation	Monopolar, cathodal, rectangular
Intensity	2–10 mA
Interstimulation interval	2 ms
Duration	400 μs
Recording	Needle electrodes
Filter	30 Hz–3 kHz
Repetition	1–5
Sensitivity	50–200 μV/Div

a SEP, somatosensory; MEP, motor evoked potential.

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Primarily, threshold intensity for eliciting CMAPs was evaluated. Therefore, the stimulus intensity was increased from 4 to 20 mA in a stepwise manner of 2 mA for cortical surface stimulation and from 1 to 10 mA in a step-by-step manner of 1 mA for brain stem stimulation. The latencies of these evoked potentials were compared. Additionally, the latencies of motor evoked potentials (MEPs) after brain stem and cortical stimulation were compared, using increasing stimulation intensities; i.e., the stimulus intensities were increased 1 to 2 mA over the threshold intensity. According to the distance between the motor cortex and the brain stem, i.e., 8 to 10 cm, and the latencies of MEPs after cortical stimulation and brain stem stimulation, calculation of the conduction velocity of the motor tract in humans was attempted.

Total anesthesia was achieved in all patients through the intravenous administration of propofol and alfentanil. Anesthesia was induced in all patients with a bolus of propofol (60 mg), alfentanil (1 mg), and atracrium(0.3 mg/kg of body weight). Simultaneously, a continuous infusion of propofol(16 mg · min^{-1}), alfentanil (0.3 mg · min^{-1}), and atracrium (0.3 mg/

kg) was started. The infusion rate of propofol and alfentanil was reduced after 30 minutes to 6 mg · minute^{-1} and 0.1 mg · minute^{-1}, respectively. The level of neuromuscular block was monitored by observing the motor response after stimulation with the train of four and was maintained at a level at which two responses were elicited after electrical stimuli on the posterior tibial nerve.

RESULTS

In each of the 16 patients, a monophasic anodal stimulation needed less stimulus intensity with cortical stimulation than with brain stem stimulation. With brain stem stimulation, less stimulus intensity was necessary for eliciting CMAPs using a cathodal stimulation (Fig. 1). the threshold intensity was between 5 and 18 mA for the direct cortical stimulation and between 2 and 10 mA for the brain stem stimulation. The mean values were 3.3, 3.5, and 3.1 mA versus 11.3, 11.5, and 10.4 mA (Table 2) (Fig. 2 and 3). Thus, to elicit an MEP, markedly less intensity was necessary with brain stem stimulation than with cortical stimulation. As demonstrated in Tables 3 and 4, CMAPs from all muscle groups were not available in all cases. A potential was available in 15 of 16 cases with cortical stimulation, in 14 of 16 cases with brain stem stimulation for the forearm flexors, in 14 of 16 cases with cortical stimulation, in 12 of 16 cases with stem stimulation for the thenar, in 10 of 16 cases with cortical stimulation, and in 11 of 16 cases with brain stem stimulation. The analysis of latencies showed a high interindividual variability but a stable intraindividual variability during the measurement period. Latencies varied widely using direct cortical or brain stem stimulation. Additionally, the latencies of the different muscle groups showed high variability (Table 3).

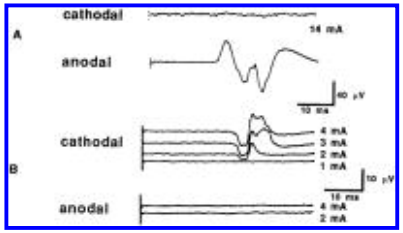

FIGURE 1. Electromyographic responses from the forearm flexors after cortical anodal and cathodal stimulation (*A*) and brain stem anodal and cathodal stimulation (*B*). With cortical stimulation, the anodal stimulation was more effective; with brain stem stimulation, the cathodal stimulation was more effective.

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n = 36	Cortical Stimulation (mA)			Brain Stem Stimulation (mA)		
	Flexor	Thenar	Hypothenar	Flexor	Thenar	Hypothenar
1	6	5	5	2	2	2
2	12	18	–	2	2	3
3	9	9	–	2	2	3
4	18	15	18	2	2	2
5	18	16	–	3	–	–
6	–	14	–	–	5	–
7	10	8	9	–	9	–
8	10	15	15	2	2	2
9	14	14	12	2	2	2
10	10	8	8	10	6	6
11	12	–	–	3	–	–
12	9	9	9	3	4	4
13	8	6	6	2	4	4
14	12	12	12	3	2	2
15	10	12	10	6	–	4
16	12	–	–	4	–	–
Mean	11.33	11.50	10.40	3.29	3.50	3.09
Standard deviation	3.22	3.87	3.77	2.15	2.14	1.24

TABLE 2. Threshold Intensity for Eliciting Electromyographic Responses

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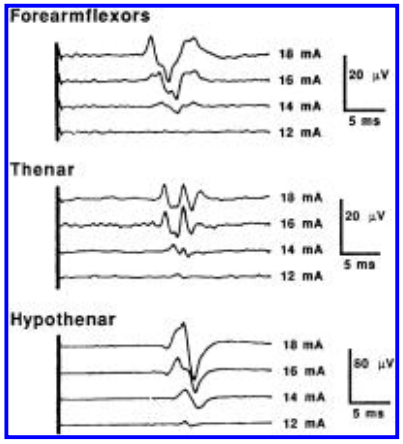

FIGURE 2. Studies for the evaluation of the minimal necessary stimulus intensities to evoke a motor potential after cortical stimulation from forearm flexors and hypothenar and thenar muscles. With increasing intensities, the latencies decreased and the amplitudes increased.

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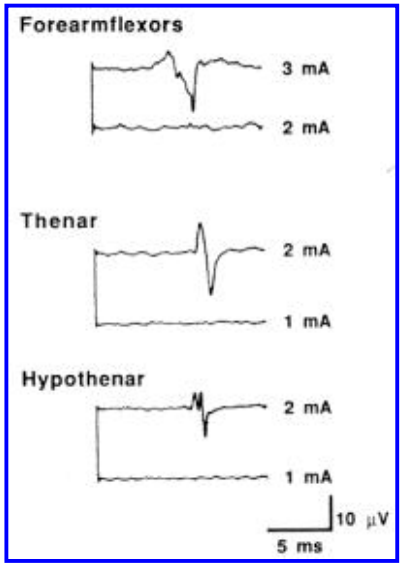

FIGURE 3. Studies to evoke the minimal necessary stimulus intensities to evoke a motor potential after brain stem stimulation from forearm flexors and hypothenar and thenar muscles.

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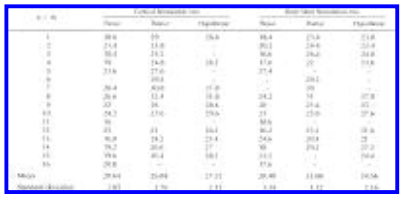

TABLE 3. Latencies of Electromyographic Responses at Threshold Stimulation Intensity

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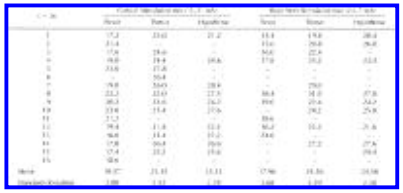

TABLE 4. Latencies of Electromyographic Responses with Increased Intensity

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Mainly (i.e., in 10 of 14 patients), the latencies of MEPs of forearm flexors decreased after brain stem stimulation, between 0.2 and 8.8 milliseconds. The mean was 20.64 and 20.4 milliseconds. However, we observed in four patients (Patients 5, 11, 13, and 15) an increase of latencies after brain stem stimulation of 2.6 to 7.8 milliseconds. Standard deviations of cortical stimulation values were 2.85 and of brain stem stimulation values were 3.34 (Table 3).

An analysis of the results of the CMAPs recorded from thenar muscles revealed the same phenomenon as that described for the forearm flexors. Mainly, a decrease of latencies was obtained after brain stem stimulation. The values lay between 0.4 and 5.6 milliseconds. Standard deviations were 2.76 and 3.32. Additionally, however, in this muscle group, the paradoxical increase of latencies (0.6-2.6 ms) after brain stem stimulation (Patients 2, 3, 12, and 14) was observed (Table 3).

For the analysis of the CMAPs recorded from the hypothenar muscles, 11 patients could be included. A decrease of latencies was observed in 10 of 11 patients. The values varied between 2 and 3.8 milliseconds. Standard deviations were 2.13 and 2.16. One patient had an increase of latency after brain stem stimulation of 0.2 milliseconds (Table 3).

Thus, although a high interindividual variability of latencies was observed, the latencies generally decreased after brain stem stimulation, as was expected. In a few patients, however, an unexpected increase of latencies was observed.

An increase of stimulus intensity over the threshold intensity was usually followed by a decrease of latency (Table 4), especially using cortical stimulation. For the forearm muscles, the mean value decreased from 20.64 to 19.57 milliseconds, for the thenar muscles, from 26.84 to 25.35 milliseconds, and for the hypothenar muscles, from 27.52 to 25.12 milliseconds; a decrease of mean values was observed after brain stem stimulation from 20.4 to 17.96 milliseconds for the forearm flexors and from 25.68 to 24.56 milliseconds for the thenar muscles. No difference was observed in comparing the values of hypothenar muscles with threshold intensity stimulation and increased intensity stimulation (Tables 3 and 4).

Although the amplitudes varied much more than those of the latencies, they generally increased with increasing stimulus intensity and also with brain stem stimulation (Figs. 2 and 3), compared with cortical stimulation. The rate of unsuccessful stimulations increased with increasing stimulation intensity using brain stem stimulation (two versus seven for the forearm muscles, four versus six for thenar, and five versus seven for hypothenar). With the cortical stimulation, no such phenomenon was observed. The attempt to calculate the conduction velocity of the motor tract was not possible because of the high interindividual variability of latencies, especially the paradoxical results of increasing latencies after brain

stem stimulations.

DISCUSSION

We demonstrated that a monophasic, anodal stimulation was always more effective than a monphasic, cathodal stimulation for cortical stimulation. On the other hand, a monophasic cathodal stimulation was more effective for brain stem stimulation. This phenomenon was already studied in animals and described in several publications (1,2,8-11). Hern et al. (8) were the first authors to explain the effectiveness of an anodal stimulation at the level of the motor cortex by direct stimulation of the pyramidal cells. In 1975, Ranck (11) reported some electrophysiological considerations regarding electrical stimulation of different nervous structures and determined that the best stimulation of the pyramidal cells seemed to be an anodal current and for the fibers, a cathodal current; a bipolar stimulation may result in an anodal block. In 1966, Gorman (6) studied the different polarities of stimulation for a direct cortical stimulation. He also determined that using a monopolar, anodal direct cortical stimulation, less stimulus intensity was necessary for eliciting a potential. The values of latencies were thereby lower than when using a cathodal or bipolar stimulation; i.e, an anodal direct cortical stimulation seemed to be more effective than a cathodal or bipolar cortical stimulation. The explanation for these results was published by Hern et al. (8), demonstrating that a monopolar pial anodal stimulation directly stimulates pyramidal cells.

At the level of the brain stem, nerve fibers are present, and therefore, a monopolar cathodal current was more effective for eliciting action potentials (8,11). These results, evaluated by animal experiments and described in the available literature, could be confirmed for humans in the above described study.

As demonstrated for brain stem stimulation, much less stimulus intensities were necessary compared with cortical surface stimulation. This phenomenon can be explained in that motor pathways are more focussed at the level of the brain stem than at the cortical surface.

The high variability of latencies may be surprising and therefore must be discussed. The variability between the values determined by cortical stimulation may be explainable in that the sensorimotor cortex was not exposed and sometimes an exact position over this area was not possible. A second explanation of the high variability may be that within the peduncle, the nerve fibers are very focussed, and therefore, when stimulating at this level, both excitatory and inhibitory fibers could be activated so that, finally, an increase of latency can result. Additionally, the effects of anesthesia may have caused

some differences in latencies whereby the intraindividual variability was not so high.

The results of this study can be concluded as follows. Different nervous structures are stimulated at the cortical surface and at the brain stem level by different polarities and different intensities of stimulus. A short train of monophasic stimuli with a stimulus duration of 40 microseconds and an interstimulus interval of 2 milliseconds would be the best for cortical stimulation but may result in a potential loss of stimulation at the level of the brain stem. Thus, different interstimulus intervals must be evaluated for brain stem stimulation to establish the best parameters. A calculation of conduction velocities was not possible because of the high variability of latencies and would also not be possible if further investigations show that really different stimulation parameters must be used for cortical and brain stem stimulations.

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The intraoperative recordings were done at the Neurosurgical Clinic of Bonn during the first author's working period at his hospital.

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COMMENTS

The ability to record compound muscle action potentials from peripheral muscles in response to stimulation in the central nervous system could be a major help in monitoring motor pathway function during surgery. The authors have begun to define some of the critical issues in this difficult task. The study demonstrates that such recordings can be made, but a number of additional issues need to be resolved before we will know how to obtain clinically useful motor evoked potentials during surgery.

Jasper R. Daube

Neurologist; Rochester, Minnesota

This is an interesting study that provides important information about activation of descending motor pathways in humans by electrical stimulation. These investigators used the opportunity to stimulate the motor cortex and the surface of the brain stem that presented when these structures became exposed in patients undergoing temporal lobe resections and hippocampectomy for resistant epilepsy. They compared the threshold of motor responses to electrical stimulation of the cortical surface with that of stimulation of the descending tracts of the brain stem at the midbrain level by recording electromyographic potentials from specific muscle groups.

This study is a good example of how specific surgical procedures may offer possibilities for conducting

meaningful neurophysiological studies that can increase our understanding of the function of the human nervous system. Transcranial cortical stimulation is gaining increasing use in intraoperative monitoring, and knowing more about the motor responses from electrical stimulation of the motor cortex is therefore important. The authors interpret their results critically, and they are aware that providing detailed information about such factors as anesthesia and stimulus and recording techniques that may affect the responses is important.

Aage R. Møller

Neurophysiologist; Dallas, Texas

The authors attempt to show differences between stimulation parameters in evoking distal muscle responses when stimulating the motor cortex and the cerebral peduncle. Presumably, stimulating the motor cortex activates neuronal dendrites and complex neurocircuitry, whereas peduncular stimulation activates axons. Therefore, it is not unreasonable that different parameters, as well as pulse phases, are more effective in one area than the other. More importantly, however, this is another example of how basic science can be incorporated into the clinical practice of medicine. It is through such studies that a clear understanding of central nervous system neurophysiology can be obtained.

Allen R. Wyler

Seattle, Washington

Key words: Brain stem stimulation; Cortical surface stimulation; General anesthesia; Motor evoked potentials; Stimulation parameters

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