Thesis points of a Ph.D.

The importance of somatosensory and motor evoked potentials in intraoperative electrophysiological monitoring

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Debrecen, 2002

1.Introduction

The neurosurgeon has to use all possible means to avoid surgical risks. One of the effective means of reducing surgical risks is continuous intraoperative neurophysiologic monitoring. The pre-condition of success is to make it possible to check the function of the neural generators within, as well as the pathways and nerves running through and near the operative field during surgery. In the past three decades prominence has been given to electrophysiological methods, particularly to the examination of the evoked potentials. The evoked potential is the synchronised discharge of a particular part of the central nervous system, as a response to a specific sensory stimulus. The action potential can be directly recorded in the representative areas (nuclei and pathways) of the given sense organ. Evoked potentials can be recorded with the digital averaging technique, from the skin surface, as well. The motor evoked potential method is different in that recording is possible following stimulation of the motor area of the brain without averaging, directly from the muscles. Intraoperative monitoring of the evoked potentials is most widely used in spinal surgery, primarily when the operation is performed for intramedullary disorders or to correct major spinal deformities. In the neurosurgery the main filed of application is cerebrovascular surgery (e.g. aneurysms) and carotid endarterectomy. It has proved very useful in tumour surgery in any part of the central nervous system from tumours in the hemispheres to the cauda aequina.

The possibilities of intraoperative electrophysiological monitoring are limited by a number of factors. The most significant of these are the ones that result from narcosis and muscle relaxation. During surgery there may occur technical problems in monitoring which give rise to false positive responses misleading the surgeon. This is why there is need of the elaboration of newer and safer methods of stimulation and recording, and continuous standardisation of drugs for inducing narcosis and the electrophysiological parameters.

2. Objectives

The aim of the study is to give answers to the following questions:

1. What objectively verifiable benefits can somatosensory evoked potentials (SSEP) monitoring yield, beyond information available from the literature, for everyday practice, in surgery for cerebral aneurysms?
2. What prognosis can be assumed from the analysis of data on the patient's state, from data obtained by intraoperative SSEP monitoring for the outcome of the operation?
3. Do the data from intraoperative SSEP monitoring give information on the outcome of acute or delayed surgery for cerebral aneurysms?
4. Do the data from intraoperative SSEP monitoring refer to the impact of temporary clipping on the outcome of the operation?
5. What conclusions can be drawn when comparing the data gained through traditional intraoperative SSEP monitoring and those given by ventral SSEP recording?
6. Can the response evoked by transtracheal spinal motor pathway stimulation be applied for intraoperative MEP monitoring?

3. Patients material and methods

3.1. Somatosensory evoked potential (SSEP)

SSEP examination is an everyday procedure in our department. The pieces of equipment used, in chronological order, for the examinations: Amplaid MK-25, Amplaid EMG-15 (Madaus, Freiburg, Germany) and Neuropack-Sigma MEB-5504 K (Nihon-Kohden, Tokyo, Japan). SSEP was elicited by stimulating median (ICA and MCA aneurysms) or tibial (ACA and AcoA aneurysms) nerves or both with bipolar surface electrodes. Repeated rectangular electrical stimuli were delivered at a rate of 4/sec using supramaximal stimulation (40-50mA). Cortical SSEP was recorded with subcutaneous needle electrodes, from the centroparietal region (C3΄ and C4΄ (American EEG Society)) opposite the stimulation against midfrontal reference (Fz΄). Early SSEP was recorded from the neck above the C II spinous process. Central conduction time (CCT) was determined as the latency-difference of cortical and neck potentials. In case of tibial nerve stimulation the active electrode was inserted over the postcentral reference (Cz΄). 200 signals were averaged in each session. During the period of vascular occlusion, 100 responses were accepted in order to update the recording as rapidly as possible, generally within an interval of one minute. Body temperature was continuously monitored and all changes were taken into account.

3.1.1 SSEP monitoring during surgery for cerebral aneurysms

The use of intraoperative monitoring of SSEP as an indicator of brain ischemia is particularly valuable during operations on aneurysms in which the anterior circulation of the brain mybe affected. Brain ischemia can be manifested in the decreased amplitude of cortical potential and in the prolongation of latency and central conduction time. Intraoperative electrophysiological monitoring is especially important when using temporary clipping of major vessels.

Alterations in SSEP results were distributed into 5 types as previously described by Friedman and co-workers. 1: no significant change 2: significant change with complete return to the baseline 3: significant change with incomplete return to the baseline 4: complete loss with no return 5: no response at baseline.

Successful operative treatment of intracranial aneurysms following subarachnoid haemorrhage (SAH) can be influenced by numerous factors such as:

I. Results of SSEP changes were correlated to

II. the preoperative Hunt and Hess's grade of patients,

Grade	**Description**
0	unruptured aneurysm or asymptomatic
1	asymptomatic, or mild headache and slight nuchal rigidity
2	moderate to severe headache and nuchal rigidity
3	mild focal deficit, lethargy, or confusion
4	stupor, moderate to severe hemiparesis, early decerebrate rigidity
5	deep coma, decerebrate rigidity, moribund appearance.

III. timing of surgery,

Acute surgery (0-48 hours after SAH)

delayed surgery (10-14 days after SAH)

IV. intraoperative aneurysm rupture,

V. temporary clipping,

VI. postoperative vasospasm,

VII. postoperative ischemic cerebral lesions.

3.1.2. Patients material

Somatosensory evoked potential monitoring performed during 186 operation for intracranial aneurysms of the anterior part of circle of Willis has been analysed retrospectively by the joint evaluation of the above seven parameters. All patients were operated on by 4 experienced surgeons during the regular working hours. There were 118 women and 68 men. The patients' average age was 48 years (range, 23-76 years). The locations of the aneurysms were as follows: middle cerebral artery (MCA) 65; internal carotid artery (ICA) 57; anterior cerebral artery (ACA) or anterior communicating artery (ACoA) 44; multiple 20. The preoperative clinical grades, determined according to Hunt and Hess, were as follows:

Grade 0: 13 patients, Grade 1: 79 patients, Grade 2: 52 patients, Grade 3: 33 patients, Grade 4: 8 patients and Grade 5: 1 patient. The patients had been selected from the point of view of timing of surgery in two groups: 1. patients with acute surgery (0-48 hours after SAH), 2. patients with delayed surgery (10-14 days after SAH).

To evaluate SSEP, data after anaesthesia induction but before the start of surgery were considered as baseline. A more than 50% fall of the amplitude of N20 or P40 and/or 25% prolongation of the central conduction time (CCT) or latency were defined as significant changes when compared to the baseline.

24 hour postoperative status and clinical outcome at discharge were scored according to the following scheme:

Good outcome:

no symptoms pre- and postoperatively

improved preoperative symptoms

unchanged preoperative status

no preoperative symptoms, postoperative deficit that improved

Bad outcome:

no preoperative symptoms, residual postoperative deficit

progression of preoperative symptoms

vegetative state

death

3.2 .Other possibilities of intraoperative monitoring

3.2.1. Examination of SSEP recordings in dogs

There are instances, especially during surgery of the central regions of the scalp and the neck, (e.g., the craniospinal junction and on the cervical spinal cord) when SSEP recording is disturbed by the surgical approach or manipulation. In such situations, standard monitoring of SSEP is not reliable. It is, therefore, desirable to find another useful SSEP recording method that can be used in everyday surgical practice. Because general anaesthesia usually involves orotracheal or nasotracheal intubation, SSEP recordings obtained by use of pharyngeal and oesophageal SSEP recording methods, may be advantageous. Therefore, the purpose of the study presented here was to investigate the value of nasopharyngeal and tracheal recordings of SSEP in anesthetized dogs. To determine applicability for intraoperative neurophysiologic monitoring, SSEP recordings obtained by this method were compared with SSEP recordings obtained from the scalp and neck.

Materials and Methods

Animals- Ten healthy research mixed-breed dogs (5 males and 5 females), which weighed 18. 6 to 24 kg and were 1 to 2 years old were examined under veterinary surveillance. The study was approved by the Regional Scientific

Ethical Council for the protection of animal rights. Dogs were anesthetized by IM administration of xylazine hydrochloride (1 mg/kg) and ketamine hydrochloride (10 mg/kg). After the insertion of a venous cannula, the dogs received atracurium besylate IV (0. 1 mg/kg) for relaxation and were intubated with tubes suitable for SSEP recording (intratracheal tube, Pulmonx, Palo Alto, California). Dogs were artificially ventilated with a 2: 1 mixture of air and oxygen. During the entire experiment rectal temperatures were taken and maintained within the range of 37 to 39 C degree, using a heating pad and external radiator. An ECG, arterial blood pressure, pulse, and blood gases were continuously monitored. On completing the experiments, anaesthesia was suspended by IV administration of atropine hydrochloride (0. 25 mg), neostigmine methylsulfate (0. 5 mg), and galantamine (2. 5 mg). After return of spontaneous breathing, tubes were removed.

Electrophysiologic method and measurements-

Soft web- electrodes were placed on the balloon of the tracheal tube and the balloon of the nasally introduced probe pressing against the epipharynx. Inflation of the balloon ensured the stable position of the electrode and good contact with the surrounding tissues. The exact placement of the nasopharyngeal balloon was the uppermost portion of the epipharynx, which was checked by fluoroscopy. The balloon of the tracheal tube was fixed at level C6-C7, and its position was monitored by conventional radiography. Standard recordings of SSEP were measured SC from the scalp region corresponding to the left somatosensory cortex of the brain and from the neck at the level of the C2-C3 interspinous ligament, using 2-cm-long 0. 8 mm-diameter stainless-steel needle electrodes. The reference electrode was placed in the midline on the forehead. For all measurements, the impedance of the electrodes was < 2 kΩ.

After shaving and degreasing of the area, the median nerve of the right forelimb was stimulated with a series of supramaximal stimuli, using a bipolar stimulator with 2-cm interelectrode distance. The duration of single stimuli was 50 microseconds, the strength of the current 7 to 12 mA with a frequency of 4 Hz. Results of 100 recordings were averaged using automatic artefact rejection. Examinations were performed by an evoked potential measuring system (Neuropack- Sigma MEB-5504 K - Nihon-Kohden, Tokyo, Japan).
Mean (±) values of latency and amplitude of the individual waveforms were determined.

3.2.2. Transtracheal electrical stimulation of the spinal cord for intraoperative monitoring of the motor pathway in dogs

Monitoring of descending motor pathways is of importance during orthopaedic and neurosurgical spinal operations as well as during reconstructive aortic surgery. Transcranial electrical and magnetic stimulations are generally employed. These methods of stimulation are generally easy in alert patients, but can be problematic during anaesthesia. Motor evoked potentials (MEP) in response to both magnetic and electrical stimulations are usually recorded from peripheral nerves or skeletal muscles. However, electrical stimulation with the voltage that produces reproducible potentials is painful in alert patients. It is difficult to discharge the lower motoneurons with single stimuli conveyed by the efferent long tracts. Repeated stimulation may facilitate the lower motoneuron and makes motor responses highly independent of anaesthesia but quick repetition of transcranial stimuli is technically difficult. Stimulation of the spinal cord and recording from a peripheral nerve is another appropriate technique of motor pathway monitoring. As the spinal cord lies deep under the surface, successful stimulation requires invasive techniques. In this study we made an attempt to stimulate the spinal cord in a non-invasive way and tried to record both compound myogenic and averaged neural responses of the motor pathway.

Materials and Methods

Animals- Transtracheal stimulation of the spinal cord was carried out in 14 healthy research mixed-breed dogs (7 males and 7 females) that weighed 14 to 22 kg and were 1 to 2 years old were examined under veterinary surveillance. The study was approved by the Regional Scientific Ethical Council for the protection of animal rights. Dogs were anesthetized by IM administration of xylazine hydrochloride (1 mg/kg) and ketamine hydrochloride (10 mg/kg). After the insertion of a venous cannula, the dogs received atracurium besylate IV (0.1 mg/kg) for relaxation and were intubated with tubes (intratracheal tube, Pulmonx, Palo Alto, California). Dogs were artificially ventilated with a 2: 1 mixture of air and oxygen. Atracurium besylate was maintained by 0. 2 mg/ kg/ h. This dose of relaxant resulted in partial neuromuscular blockade, yet enabled muscle action potentials to be recorded. The right femoral nerve and vein were exposed and the latter was cannulated. During the entire experiment rectal temperatures were measured and maintained within the range of 37 to 39 C degree, using a heating pad and external radiator. An ECG, arterial blood pressure, pulse, and blood gases were continuously monitored. On completing the experiments, anaesthesia was suspended by IV administration of atropine hydrochloride (0. 25 mg), neostigmine methylsulfate (0. 5 mg), and galantamine (2. 5 mg). After return of spontaneous breathing, tubes were removed.

Electrophysiologic method and measurements

The upper cervical part of the spinal cord was stimulated with single and serial stimuli. One of the stimulating electrodes (a 20 μm x 1. 5 cm^2 thin sheet of Ag-AgCl) was attached to the balloon of the intratracheal tube and pressed against the dorsal wall of the trachea by the inflated balloon. The other electrode (a 0. 5 mm thin bent Ag-AgCl plate 4 cm^2 in area) was fixed to the shaven and cleaned skin above the 2nd cervical spinous process. The impedance of stimulating electrodes was kept below 2 kΩ. The recording electrodes were a pair of Teflon- insulated Dantec sensory needles, the active one inserted into the epineurium of the femoral nerve, the reference electrode subcutaneously 2 cm apart. Recordings were also obtained from the quadriceps muscle with bipolar needle electrodes.

Two kinds of stimulation were applied:

1. Single electric shock with the Digitimer D 180A constant- voltage stimulator (Digitimer, L. Welwyn Garden City, UK). Reproducible responses could be evoked with 2. 5 – 10 % of the maximum output (1000 V) and with 100 µs time constant. The endotracheal electrode was used as a cathode in single stimulation.
2. Serial stimulations with the constant current stimulator unit of the Amplaid EMG 15 (Madaus, Freiburg, Germany). Rectangular impulses of 100 µs duration and 11- 16 mA were delivered at a stimulus rate of 4 Hz.

Recordings were made with an Amplaid EMG 15 amplifier in single or superimposed mode, with a band pass of 50- 2500 Hz and an analysis time of 200 ms. The gain was adjusted between 2000- 20000 in order to obtain optimum vertical resolution of the compound action potentials. In the cases of serial stimulations one hundred responses were averaged.

In two animals C4 laminectomy was performed and the spinal cord was directly stimulated with epidural plate- electrodes. Responses evoked by direct epidural and transtracheal stimulations were compared.

3.3. Statistical analysis

The SPSS program was used for data analysis. Hierarchical log linear analyses were performed to investigate the interactive effects, for analysing the structure of discrete variables with no normal distributions. A special class of statistical techniques, i.e., log linear models, has been formulated for the analysis of categorical data.

The tests of hypotheses explaining how the log linear models fit the observed data are based on the likelihood ratio chi squared statistic. In order to explore the relationship between the factors found to interact with one another we used multiple logistic regression analyses. The Fisher exact test is applicable to either one-tailed or two-tailed hypotheses.

4. Results

4.1. Surgery for cerebral aneurysms and SSEP monitoring

4.1.1. Central conduction time (CCT) and amplitude changes of SSEP

In 66 cases we did not observe any change in either amplitude or CCT. Amplitude decreased significantly in 53 cases, CCT prolonged in 37 cases and both values changed significantly in 26 cases. There was no difference in the improvement rate of patients with SSEP type II and III if only the amplitude changed (Fisher p=0. 249) or if only CCT changed (Fisher p=0. 313). However, the improvement rate of patients with SSEP type II and III significantly differed (66%, n=17 and 34%, n=9, respectively, Fisher p=0. 046) when both amplitude and CCT changed.

4.1.2. Preoperative Hunt- Hess's grade and SSEP type

In order to explore the relationship between the factors found to interact with one another we used multiple logistic regression analyses. 24-hr status was significantly influenced by preoperative HH's grade (p=0. 026), but not by SSEP type (p=0. 192). In contrast, both factors showed a marginally significant effect on postoperative outcome at discharge (preoperative HH's grade, p=0.070, SSEP type, p=0. 058). The 24-hr improvement rate of patients with SSEP type I and II (n=126) was 80%, whereas for patients with SSEP types III-V (n=60) it was 65% (Fisher exact probability test, p=0. 03). The improvement rate at discharge was also higher for SSEP types I and II (85%, n=126) than for types III- V (67%, n=60, Fisher p=0. 007). The improvement rate of Hunt-Hess's grade 1 patients marginally differed by SSEP type for 24-hr status (p= 0.051) and significantly for status at discharge (p<0.001).

4.1.3 Correlation between timing of surgery and type of SSEP

The 24-hr improvement rate after acute surgery (66%, n=88) was lower than after delayed surgery (84%, n=98, Fisher p=0. 006). Similarly, for status at discharge, delayed surgery resulted in a better improvement rate than acute surgery (88%, n=98 vs. 69%, n=88, Fisher p=0. 002). Patients with SSEP type II undergoing delayed surgery showed a better 24-hr improvement rate compared to patients with the same SSEP type who underwent acute surgery (93% vs. 66%). Otherwise, patients with SSEP type I and delayed surgery had a higher improvement rate at the time of discharge (88% vs. 69%). There was no significant difference between delayed and acute operations in cases with other types of SSEP (Fisher p>0.1) neither at 24hr status nor at status at discharge.

4.1.4. Simultaneous analysis of perioperative conditions

We evaluated the importance of perioperative factors such as preoperative HH's grade, timing of surgery, type of SSEP, temporary clipping, intraoperative rupture, postoperative cerebral ischemia and postoperative 24-hr status or status at discharge as variables by using a log linear model. Postoperative vasospasm was also analysed as a factor in correlation with the status at discharge. There was a significant interaction between postoperative 24-hr status and the following factors investigated: preoperative HH's grade, SSEP type, temporary clipping, and ischemia (p=0. 007). Postoperative outcome (status at discharge) was significantly associated with the SSEP type, temporary clipping, intraoperative rupture, postoperative vasospasm and postoperative cerebral ischemia (p<0. 0001).

4.1.5. Factors influencing postoperative 24-hr status

24-hr status was significantly influenced by the use of temporary clipping (logistic regression, p<0. 0001) and was marginally affected by postoperative cerebral ischemia (p=0. 0898). Intraoperative aneurysm rupture, which occurred in 39 cases, did not affect 24-hr status (p>0.5). When no temporary clipping was used, the improvement rate was 83%, whereas it was 57% in patients with intraoperative temporary clipping (total n=186, Fisher p=0. 0006).

The improvement rate was significantly higher without temporary clipping in patients with type I SSEP (n=66, 86% vs. 50%, respectively, Fisher p=0. 02), and in patients with SSEP type III (n=56, 79% vs. 52%, respectively, Fisher p=0. 046). There was no difference in cases with SSEP type II (n =60, 83% vs. 74%, Fisher p=0. 493). Following acute surgery (n=88) the improvement rate was 78% when no temporary clipping was used and it was 41% with temporary clipping (Fisher p=0. 0015). After delayed surgery (n=98) the improvement rate was 86% without temporary clipping and was 76% with temporary clipping (Fisher p=0. 229).

4.1.6. Postoperative cerebral ischemia

CT and/or MRI confirmed that postoperative cerebral ischemia occurred in 40 cases (22%). The occurrence of postoperative cerebral ischemia was influenced by temporary clipping (multiple logistic regression, p=0. 006), timing of surgery (p=0. 037), whereas it was not correlated with the occurrence of vasospasm (p=0. 303) or preoperative Hunt-Hess's grade (p=0. 542). The occurrence of postoperative cerebral ischemia highly influenced whether the status of the patients improved or deteriorated. The postoperative status deteriorated in 38 of the 40 patients with postoperative cerebral ischemia (95%), whereas there was only one deterioration out of 146 patients without ischemia (Fisher p<0. 0001). The frequency of postoperative cerebral ischemia was higher when temporary clipping was used (n=54) compared to the cases when it was not used (n=132) (39% vs. 14%, respectively, Fisher p=0. 0006). There was no difference in the frequency of postoperative cerebral ischemia either in patients with type I or II SSEP when temporary clipping was used versus not used (SSEP type I cases: 13% vs. 30%, SSEP type II cases: 12% vs. 21%, Fisher p>0. 05). However, in patients with SSEP type III the frequency of postoperative cerebral ischemia was higher when temporary clipping was used (15% vs. 52%, Fisher p=0. 007). After acute surgery (n=88), the frequency of postoperative cerebral ischemia was 32%, whereas after delayed surgery (n=98) it was 12% (Fisher p=0. 001). Postoperative vasospasm (proven by transcranial doppler sonography, measured velocity > 120 cm/sec) occurred in 97 cases (52%). The occurrence of vasospasm, however, did not influence the frequency of postoperative cerebral ischemia (see above), probably due to adequate therapy.

4.1.5. Status at discharge

The status at discharge was affected by timing of surgery (multiple logistic regression, p=0. 014) and the use of temporary clips (p=0. 019). The occurrence of intraoperative rupture or postoperative vasospasm did not influence the status at discharge (p>0. 2). The improvement rate at discharge was 69% after acute surgery (n=88) and 88% after delayed surgery (n=98, Fisher p=0. 002). When temporary clipping was used (n=54), the improvement rate was 61%, whereas without temporary clipping (n=132), it was 86% (Fisher p=0. 0003). The improvement rate of patients with SSEP type I (n=66) was significantly different when acute surgery was performed (71%) from the results of delayed surgery (92%, Fisher p=0. 043). In this group of patients the improvement rate was similar regardless of whether temporary clipping was used or not (86% vs. 70%, respectively, Fisher p=0. 351). There was no difference in the improvement rate of patients with SSEP type II (n=60) by either timing of surgery (acute: 80%, delayed: 93%, Fisher p=0. 254) or the use of temporary clipping (when used: 79%, when not used: 90%, Fisher p=0. 249). Similarly, the timing of surgery did not affect the improvement rate of patients with SSEP type III (n=56) (acute: 59%, delayed: 79%, Fisher p=0. 147). However, when temporary clipping was used, this group of patients had an improvement rate of 48%, but it was 85% (Fisher p=0. 007) when temporary clipping was not applied.

4.2. Other possibilities of intraoperative monitoring

4.2.1. With „ ventrally" located electrodes (nasopharyngeal and tracheal) recorded SSEP examinations in dogs

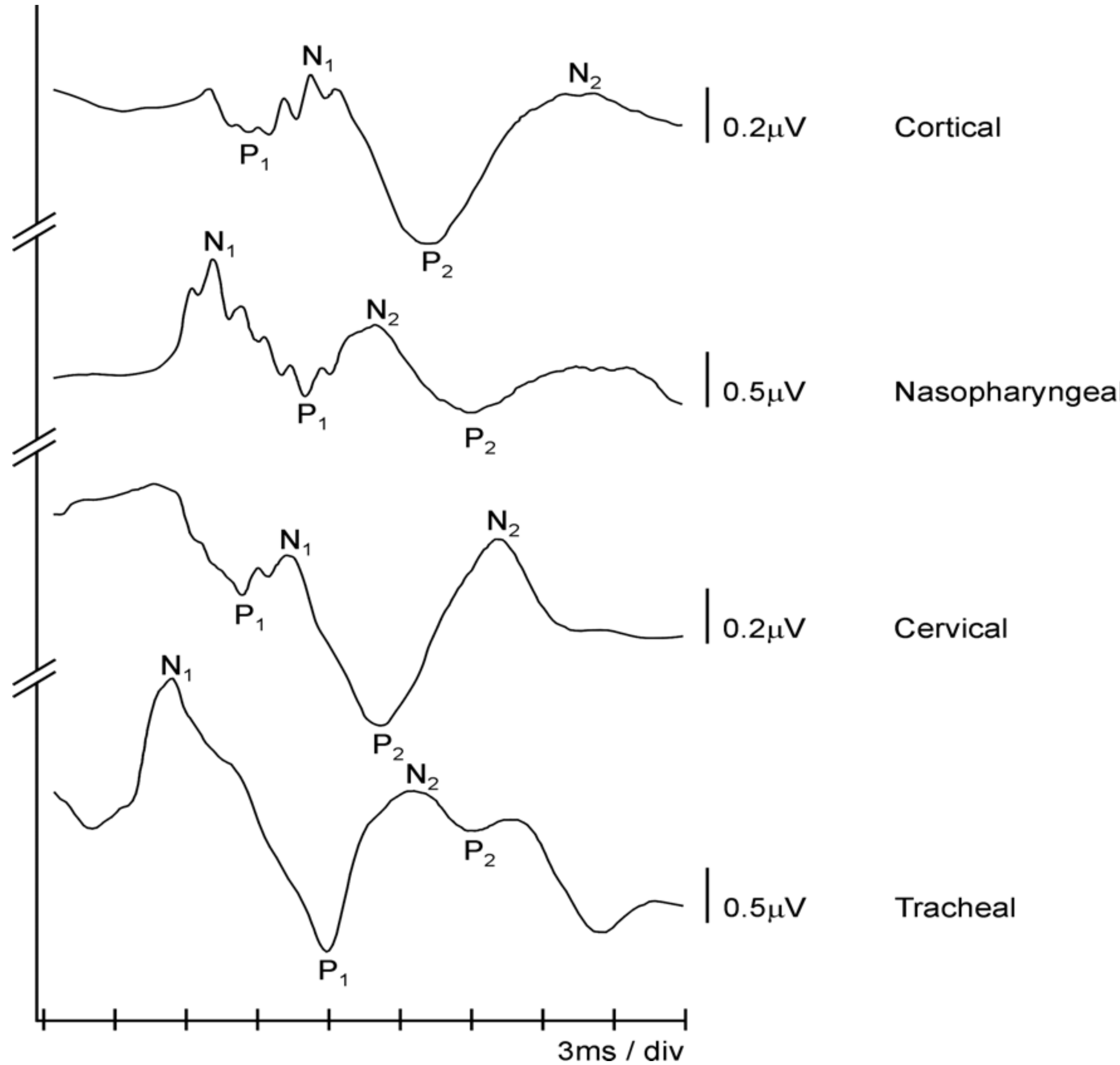

Figure 1 – Somatosensory evoked potential recording from the scalp (brain cortex), nasopharynx, neck (cervical spinal cord), and trachea following stimulation of the median nerve of the right forelimb in a dog.

By electrically stimulating the peripheral nerve, multiphase potentials were derived from all 4 recording sites.These potentials could be evoked consistently, and their appearance was not influenced by longer periods of narcosis (Fig 1). Recorded waveforms were labelled, depending on polarity, by the notation of P1, N1, P2, N2 (positive [P]; negative [N]

Mean (± SD) latency and amplitude values of individual waveforms of multiphase recordings from various sites were determined (Table 1 and 2).

Table 1—Mean (± SD) latency values of somatosensory evoked potentials recorded from the scalp (brain cortex), nasopharynx, neck (cervical spinal cord), and trachea in 10 dogs.

	Recording sites			
Waveforms	**Scalp (cortical)**	**Nasopharyngeal**	**Neck (cervical)**	**Tracheal**
P1 (ms)	9.1±2.5	7.8±3.8	6.6±1.7	5.3±1.5
N1 (ms)	13.1±4.5	13.5±4.6	11.1±1.4	10.5±4.2
P2 (ms)	19.4±5.5	18±6.8	15.6±2.6	14.9±3.5
N2 (ms)	24.4±6.6	22.9±6.3	23±6.4	21.3±8.6

Table 2—Mean (± SD) amplitude values of somatosensory evoked potentials recorded from the scalp (brain cortex), nasopharynx, neck (cervical spinal cord), and trachea in 10 dogs.

	Recording sites			
Waveforms	**Scalp (cortical)**	**Nasopharyngeal**	**Neck (cervical)**	**Tracheal**
P1 (μV)	0.8±0.5	0.9±0.4	1.1±0.8	3.7±3.4
N1 (μV)	1.2±0.9	1.1±0.9	1.2±1.0	4.5±3.8
P2 (μV)	1.4±1.1	1.1±0.5	2.2±1.6	1.8±1.3
N2 (μV)	1.2±0.9	0.5±0.4	1.2±0.6	2.4±2.1

Some of the potentials recorded from the scalp region and the nasopharynx, as well as from the neck and the trachea had similar values with opposite polarity (Table 1). On the basis of the rostrocaudal position relative to the axes of the somatosensory pathways of the cerebrum, brain stem, and spinal cord, the nasopharyngeal and tracheal recording of potentials corresponded to the somatosensory cortical and cervical potentials respectively. Opposite directions of propagation of the far-field potentials were indicated by opposite polarities of identical peaks. For example, nasopharyngeal recording of P1 corresponded to somatosensory cortical N1 and the tracheal recording N2 corresponded with somatosensory cervical P2. Latencies between some opposite-polarity peaks shifted.

In several dogs intermediate peaks of low amplitude were observed within and between potentials. Most of these peaks were found in the nasopharyngeal recordings. In the tracheal recordings the dominating potential was early, which corresponded presumably to Erb's potential of humans. (Erb's point is where the brachial plexus crosses the clavicle.) The later potentials (of more rostral origin) did not always develop sharp peaks in these recordings. Mean values of amplitudes had large SD (Table 2), which may have been attributable to a low number of dogs in our study.

4.2.2 Transtracheal electrical stimulation of the spinal cord for intraoperative monitoring of the motor pathway in dogs

High-voltage single electric impulses elicited reproducible bi- or triphasic responses from both the femoral nerve and muscle (Figure 2). Depending on the stimulus intensity, latencies varied between 15 and 18 ms. The amplitudes showed an interindividual variation ranging between 150-850 μV. The first potential was frequently followed by a polyphasic second response with longer latency and duration (Figure 3). No significant difference was seen between recordings of direct epidural and transtracheal stimulations (Figure 4).

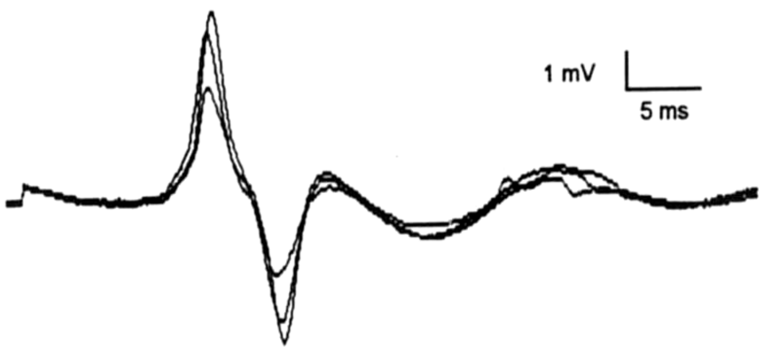

Figure 2. Motor responses evoked by transtracheal electrical stimulation of the spinal cord and recorded from the femoral nerve. Tree superimposed action potentials were elicited with 5 % of the maximum output of the Digitimer stimulator.

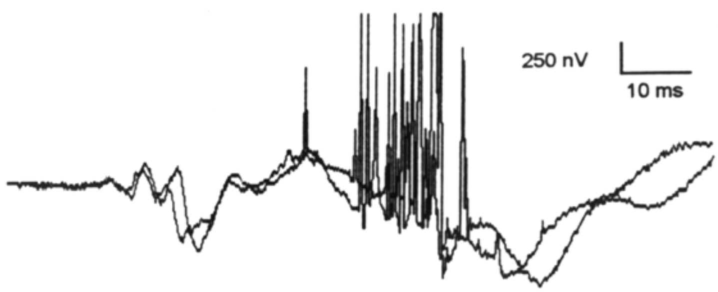

Figure 3. Early and late responses evoked by transtracheal single electrical stimulation of the spinal cord and recorded from the femoral nerve with slower sweep speed. Two responses are superimposed on

Serial stimulation resulted in a double potential complex starting with a negative peak at 20 ms when recording from the femoral nerve (Figure 5).

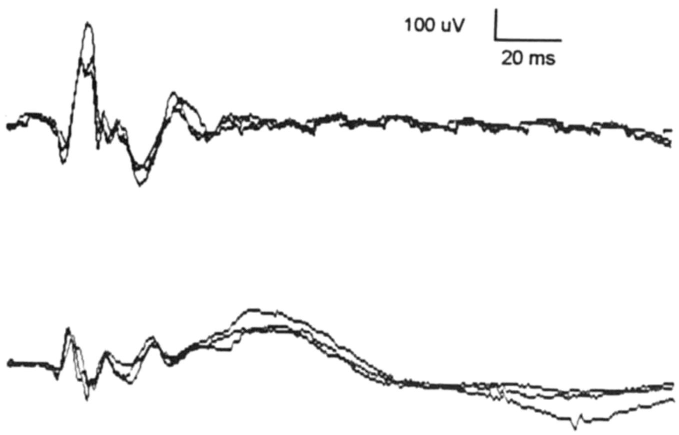

Figure 4. Motor responses recorded from the right femoral nerve of anesthetized dog. Top: direct epidural stimulation with a single electrical impulse at C 4. Bottom: Responses to transtracheal stimulation of the upper cervical cord.

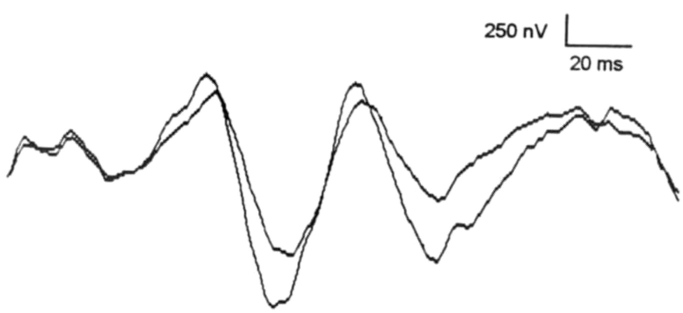

Figure 5. Neurogenic evoked potential elicited by serial transtracheal stimulation of the upper cervical cord. The average of 100 responses was recorded from the right femoral nerve.

5. Discussion

5.1. Clinical outcome following surgery for cerebral aneurysms and intraoperative SSEP

No statistical evaluation of SSEP changes related to preoperative HH’s grading was found in the literature. As expected, there was a strong correlation between preoperative HH’s grade and 24 hour status in our material. The 24 hour status proved to be worse than the status at discharge. This suggests that part of the patients improved during postoperative therapy.

Our results also show that the outcome was worse with SSEP type III than with SSEP type I or II. Furthermore, our results suggest that patients with SSEP type III require exceptional care during the postoperative period, especially when operated in a low grade of HH`s.

5.2. Clinical outcome following delayed surgery and SSEP

The statistical analysis of our patients showed that even the early outcome (24 hour status and status at discharge) was better in case of delayed operations as compared to acute surgery. Considering SSEP changes, the different prognosis of acute and delayed surgery was conspicuous in types I and II. There was no difference of outcome between early and late operations with type III of SSEP. Type III reflects a worsening itself, because the basic SSEP will not recover by the end of the operation. SSEP monitoring type III can be considered as an electrophysiological manifestation of a cerebral stroke.

5.3. Temporary clipping and SSEP

Among all factors that we analysed, the effect of temporary clipping was the most important that influenced both 24 hour outcome and status at discharge. A negative effect of temporary clipping on the 24 hour outcome was significant in patients with types I and III, but not in patients with type II of SSEP. The explanation for this virtual controversy is that the intraoperative alteration of SSEP does not always reflect ischemic lesion of all subcortical structures. Thus, false negative monitoring probably belongs into the group of SSEP type I. We experienced postoperative deterioration (24 hr- status) in 13 patients with uneventful monitoring. Two of them improved**.** The ratio of false negative monitoring in our material is 6%. False positive monitoring belongs into the SSEP group of type IV. In the present material one of three patients with this type of monitoring improved. The ratio of false positive monitoring is < 1 %. There was no controversy regarding status at discharge and SSEP changes with temporary clipping. In cases of types I and II the improvement rate was the same with or without temporary clipping. Significant difference could be observed (Fisher p=0. 007) in patients with type III of SSEP, that is between patients whose SSEP deteriorated after temporary clipping and those who showed deterioration of intraoperative SSEP without a temporary clip. The outcome was better in patients without temporary clip.

Multifactorial analysis: We analysed the effect of SSEP changes and temporary clipping on the outcome, separately, in acute and delayed operations. Both 24 hour status and status at discharge proved to be significantly worse in patients operated on within 48 hours after SAH using a temporary clip. Temporary clipping of major vessels during acute surgery probably involves more risk than its use during delayed surgery. The explanation for it is possibly the changed permeability of the arterial wall following SAH. A swollen, oedematous vessel wall is more liable to be damaged by the clip. Any lesion of the endothelial layer starts the haemostatic mechanism, which is manifested by increased ET-1 secretion, augmented platelet adherence and increased permeability. Later, several days or weeks following SAH, permeability and intramural oedema decreases making the vessel wall more resistant against clamping forces.

5.4. Advantages of „ventral" (nasopharyngeal and tracheal) SSEP recording

Results of our investigation indicate that nasopharyngeal recordings of potentials correspond to standard recordings of cortical and the cervical (early) SSEP. Thus it becomes possible to determine central conduction time with the application of a single electrode. Nasopharyngeal recording is not used for routine SSEP examinations, because placing the electrodes is inconvenient in patients who are awake and there are a lot of disturbing artefacts (concerning the muscles, respiration, swallowing, etc.). However, this method is excellent for monitoring patients under general anaesthesia. No reports on tracheal SSEP recording were found in the literature. From interpeak latency variations of waveforms obtained by tracheal recordings, it is possible to infer on the propagation of stimulation (i.e., on the functioning of the ascending pathways of the spinal cord in the neck). Tracheal recordings allow the examination of the section of the SSEP pathway between the Erb's point and the craniospinal junction. Because the electrode is attached to the tracheal tube, a tracheal recording of SSEP does not interfere with surgery that involves ventral or the dorsal approaches to the cervical spinal cord.

5.5. Studying motor responses evoked by transtracheal stimulation is a possible novel method of the intraoperative monitoring of the spinal cord

The advantage is of transtracheal stimulation that the spinal cord lies between the two electrodes in the middle of the electric field so that each part of the cord receives the same stimulus intensity. It is disadvantageous however that the excitation of the upper cervical roots may cause a slight movement of the head. Short latency responses to high voltage single stimuli are probably direct responses of the lower motoneurons excited by the upper ones. Late responses to single electric stimulation recorded either from the femoral nerve or quadriceps muscle may represent multisynaptically activated spinal reflexes. With the transtracheal stimulation, both efferent and afferent long tracts of the spinal cord get excited at the time of stimulation. The excitement spreads in both rostral and caudal directions. The following possibilities can be considered for the explanation of the origin of evoked compound potentials recorded from the femoral nerve. **1/** Direct excitation of the pyramidal tract (motor responses of short latency). **2/** Antidromic excitation of the pyramidal tract is reflected back from the cortical pyramidal cells evoking double responses from the alpha motoneurones, as indicated by the F response of the peripheral nerve. The reflected potential repeatedly stimulates the lower motoneurone and elicits peripheral motor response. **3/** Antidromic activation of the dorsal white column afferent tracts may produce direct sensory evoked potentials and also motor responses of longer latency via centrally activated H- reflex. **4/** Flexor reflexes, crossed flexor - extensor reflexes or other polysynaptically elicited motor responses of longer latency and duration may be responsible for the late components.

6. Conclusions, new scientific results

Regarded as the most important results of the present study are the scientific observations and conclusions that have not been reported on in the literature. In addition, when composing the thesis it was always kept in mind that the new results be suitable for use in clinical practice, to help the more exact diagnoses and successful operations. The results can be summarised in the following:

1. By immediate detection of ischemic cerebral lesion during surgery for cerebral aneurysms the relevance of SSEP monitoring is 94 %.
2. Simultaneous presence of important risk factors such as poor preoperative clinical grade, acute surgery, temporary clipping and deterioration of intraoperative SSEP allows the prediction of a problematic postoperative course and outcome.
3. Temporary clipping is to be avoided as far as possible, especially during acute operations and in case of low HH's grade.
4. By electrically stimulating the peripheral nerve, multiphase and well reproducible potentials can be derived from the scalp region, nasopharynx as well as from the neck and the trachea in dogs. These potentials can presumably be bound to different neural generators.
5. Recommended for brain operations rostral from the craniospinal junction is the nasopharyngeal recording, for cervical spinal cord operations caudal from the craniospinal junction is the tracheal recording. For intraoperative SSEP monitoring either of the two recordings is appropriate.
6. By transtracheal stimulation of the spinal cord reproducible potentials can be recorded from the peripheral nerve and the skeletal muscles. Part of these potentials can correspond to the synchronous action potentials of the descending motor system.

7. List of publications

7.1. Author's publications on the subject of the PhD thesis

Mikó, L., Csécsei, Gy., Székely, Gy.jr., Molnár, Cs., Balogh, A., Furka, I., Mikó, I.: Intraoperative monitoring of the motor pathway using transtracheal stimulation of the cervical spine in dogs. Acta Chirurgica Hung 1997; 36 (1-4): 240-242.

Csécsei, Gy., **Mikó, L.**, Székely, Gy.jr., Molnár, Cs., Balogh, A., Furka, I., Mikó, I.: Transtracheal electric stimulation of the spinal cord for intraoperative monitoring of the motor pathways. Neurosurg Rev 1998; 21: 232-236.
(**IF: 0. 327**)

Mikó, L., Székely, Gy.jr., Dobai, J.G., Mikó, I., Csécsei, Gy.: Examination of nasopharyngeal and tracheal somatosensory evoked potential recordings in dogs. Am J Vet Res 2002; 63: 669-672. (**IF: 1. 04**)

7.2. Other publications by the author

Rózsa, L., Szabó, S., Balázs, E., Székely, Gy. jr., **Mikó, L.**: Importance of transcranial Doppler sonography in the diagnostics of angiostenoses and cerebrovascular syndromes caused by vascular occlusion. Clin Neurosci 1990; 43: 167-174.

Tóth, Sz., **Mikó, L.**, Kollár, J., Sikula, J., Várallyay, Gy.: Are intra- and suprasellar masses detected by CT and MR really tumours? Acta Neurochir 1995; 137: 54-57. (**IF: 0. 656**)

Szabó, S., **Mikó, L.**, Novák, L., Rózsa, L., Székely, Gy. jr.: Correlation between central somatosensory conduction time, blood flow velocity and delayed cerebral ischemia after aneurysmal subarachnoid haemorrhage. Neurosurg Rev 1997; 20: 188-195. (**IF: 0. 161**)

Székely, Gy. jr., Csécsei, Gy., **Mikó, L**.: Somatosensory and motor evoked potentials in patients with tumours in the spinal canal. Acta Neurochir 1998; 140: 533-539. (**IF: 0. 748**)

Csécsei, Gy., Székely, Gy.jr., Szabó, S., **Mikó, L.**, Berényi, E., Gyarmati, J., Klekner, Á.P.: Radical removal of meningeomas invasing superior sagittal sinus. In: Book of Proceedings, 12th World Congress of Neurosurgery, Openbook Publishers, Adelaide, South Australia 2001

Kisely, M., Emri, M., Lengyel, Z., Kálvin, B., Horváth, G., Trón, L., **Mikó, L.**, Sziklai, I., Tóth, A.: Changes in brain activation caused by caloric stimulation in the case of cochleovestibular denervation- PET study. Nuclear Med Com 2002; 23: 967-973. (**IF: 1. 13**)

Impact factor: 4. 062

7.3. Author's congress presentations and posters on the subject of the PhD thesis

Mikó L. Subarachnoidealis vérzés miatt kezelt betegek követése SSEP monitorozással. 1991. Szeged, Magyar EEG és Klinikai Neurophysiologiai Társaság 34. Kongresszusa

Mikó L., ifj. Székely Gy. Szomatoszenzoros kiváltott válasz (SSEP) monitorozás agyi aneurysma műtétek alatt. 1992. Jászberény, Magyar Ideg- és Elmeorvosok Tiszántúli Tagozat Kongresszusa

Mikó L., ifj. Székely Gy. Szomatoszenzoros kiváltott válasz (SSEP) monitorozással nyert tapasztalatok agyi aneurysma műtétek során. 1993. Siófok, Magyar Ideg- és Elmeorvosok Tiszántúli Tagozat Kongresszusa

Mikó, L., Balogh, A., Erdődy, K., Molnár, Cs. Electrophysiological monitoring during spinal surgery. 1995. Budapest, 7th International Conference on Lumbar Fusion and Stabilisation

Mikó, L., Székely, Gy.jr., Csécsei, I. Gy. Electrophysiological monitoring during surgery for cerebral aneurysms. 1997. Kassa (Kosice), International Neurosurgical Conference

Székely, Gy.jr., **Mikó, L.**, Csécsei, I. Gy. Electrophysiological investigation in patients with tumor in the spinal canal. 1997. Kassa (Kosice), International Neurosurgical Conference

Mikó, L., Csécsei, Gy., Székely, Gy.jr., Molnár, Cs., Balogh, A., Furka, I., Mikó, I.: Intraoperative monitoring of the motor pathway using transtracheal

stimulation of the cervical spine in dogs. 1997. Debrecen, XVI. Kísérletes Sebészeti Kongresszus

Mikó L. Gerincvelői és ideggyöki működés intraoperatív monitorozása. 1997. Debrecen-Budapest-Győr- Miskolc-Pécs Videokonferencia

Mikó, L., Csécsei, Gy., Székely, Gy.jr. Transtrachealis gerincvelő ingerléssel történő motoros pálya működésvizsgálat. 1998. Debrecen, Magyar Idegtudományi Társaság V. Konferenciája

Mikó, L., Lengyel, Sz., Székely, Gy.jr., Dodai, G.J., Ruszti, P., Klekner, Á., Csécsei, I.Gy. Monitoring of somatosensory evoked potentials during surgery for cerebral aneurysms. Part.I. Correlation of postoperative outcome, Hunt-Hess's grading and type of SSEP during aneurysm surgery. 2000. Neuro 2000, Miskolc, XVth Congress of the Hungarian Neurosurgical Society

Mikó, L., Lengyel, Sz., Székely, Gy.jr., Dodai, G.J., Ruszti, P., Klekner, Á., Csécsei, I.Gy. Monitoring of somatosensory evoked potentials during surgery for cerebral aneurysms. Part.II. Relationship of postoperative outcome, intra- and postoperative complications. 2000. Neuro 2000, Miskolc, XVth Congress of the Hungarian Neurosurgical Society

Mikó, L., Székely, Gy.jr., Dodai, G.J., Sárkány, P., Szűcs, I., Molnár, Cs., Csécsei, I.Gy. Monitoring of SSEP with ventrally located electrodes. 2000. Berlin, First Interdisciplinary World Congress on Spinal Surgery

Mikó L. Szomatoszenzoros kiváltott válasz monitorozása carotis endarterectomia alatt. 2001. Debrecen, Konszenzus Konferencia

7.4. Congress presentations and posters by the author not on the subject of the PhD thesis

Mikó L., Rózsa L. Koponyasérültek CT vizsgálata. 1989. Zalaegerszeg, Fiatal Neurológusok VI: Országos Fóruma

Mikó L., Rózsa L., Kollár J., Sikula J., Molnár L. Traumás agyduzzadás CT vizsgálata. 1991. Szeged, 2nd Annual Meeting of the Hungarian Neuroradiological Society

ifj. Székely Gy., **Mikó L.** A centrális motoros pálya sebessége nyaki porckorongsérvek és daganatok esetében. 1992. Jászberény, Magyar Ideg- és Elmeorvosok Tiszántúli Tagozat Kongresszusa

Mikó L., Tóth Sz., Kollár J., Sikula J., Várallyay Gy. Valóban tumor-e a CT, MR vizsgálattal kimutatott intra-suprasellaris térfoglalás? 1992. Győr, III. Magyar Neuroradiológiai Vándorgyűlés

ifj. Székely Gy., **Mikó L.** A motoros rendszer vizsgálata mágneses ingerléssel a központi idegrendszer daganatos megbetegedéseiben. 1993. Siófok, Magyar Ideg- és Elmeorvosok Tiszántúli Tagozat Kongresszusa

Székely, Gy.jr., Csécsei, Gy., **Mikó L.** Multimodális kiváltott válaszok szerepe az idegsebészeti diagnosztikában. 1998. Debrecen, Magyar Idegtudományi Társaság V. Konferenciája

Mikó, L., Csécsei, Gy., Székely, Gy.jr. Electrophysiological examinations in patints suffering from tumour of the third ventricle. 1998. Debrecen, XIVth Congress of the Hungarian Neurosurgical Society

Székely, Gy. jr., Csécsei, Gy., **Mikó, L**. „Brown-Sequard type" electrophysiological results in a patient with lateralised spinal tumour. 1998. Debrecen, XIVth Congress of the Hungarian Neurosurgical Society

Dobai, J.G., Hargitai, Z., Szakáll, Sz., **Mikó, L.**, Székely, Gy.jr., Klekner, Á., Csécsei, I.Gy. Intracerebellar haemorrhage due to an AVM after lumbar discectomy. A case report. 2000. Neuro 2000, Miskolc, XVth Congress of the Hungarian Neurosurgical Society

Klekner, Á., Csécsei, I.Gy., Molnár, P., Székely, Gy.jr., **Mikó, L**., Dobai, G.J., Módis, L. Possible role of proteoglycans int he pathomechanism of cerebral aneurysms (preliminary study). 2000. Neuro 2000, Miskolc, XVth Congress of the Hungarian Neurosurgical Society