Title
Evaluation of Somatosensory Evoked Potentials in Temporary Occlusion of Cerebral Artery 2. Intraoperative Monitoring during Internal Carotid and Middle Cerebral Artery Aneurysm Surgery

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Evaluation of Somatosensory Evoked Potentials in Temporary Occlusion of Cerebral Artery

2. Intraoperative Monitoring during Internal Carotid and Middle Cerebral Artery Aneurysm Surgery

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Introduction

Temporary occlusion of parent arteries has been used during surgery for cerebral aneurysm to facilitate the dissection or to control the bleeding due to premature rupture of difficult aneurysms. When the neural function at risk can be evaluated during focal ischaemia caused by iatrogenic temporary occlusion of the arteries intervention to minimize the occurrence of permanent brain damage may be possible.

There have been considerable interests and controversies in the use of somatosensory evoked potential (SEP) for the purpose of monitoring the neural functions during a variety of spinal and cranial operations. Several investigators have recently recorded SEPs during aneurysm operations in an attempt at predicting the neurological outcome and minimizing the postoperative morbidity. Interpretation of SEP during cerebral ischaemia, however, has not been fully established on the basis of quantitative characteristics. A large body of experimental studies on the relationships between SEPs and cerebral ischaemia have mainly dealt with the evaluation of amplitudes, whereas most clinical reports on the use of intraoperative SEP monitoring have described the results in terms of central conduction time (CCT) delay and/or disappearance of the N20 peak.

The following study was therefore undertaken in order to elucidate more fully the appreciable changes in SEPs, not only in the CCT but also in the amplitude, and to determine whether SEP monitoring has any potentials to reduce the morbidity and mortality associated with temporary clipping of the cerebral arteries during aneurysm surgery.

SEP monitoring may be useful in the condition where circulation through the parts of the nervous system related to SEPs generated by median nerve stimulation are jeopardized by temporary occlusion of the parent artery of the aneurysm. In this study, therefore, we have confined the patients to those with the internal carotid and/or middle cerebral aneurysm in whom

Key words: cerebral aneurysm, cerebral ischaemia, recirculation, somatosensory evoked potential, temporary vascular occlusion.
temporary occlusion of the parent artery was necessary.

**Patients and Methods**

Sixteen patients with aneurysms of the internal carotid or middle cerebral arteries underwent operation via a pterional, transsylvian approach using microsurgical techniques and temporary clipping of the parent artery (Table 1). There were twelve middle cerebral artery aneurysms, and six aneurysms of the internal carotid artery. The patients were four men and twelve women, aged between 24 and 72 years (mean 54.1 years). Thirteen operations were carried out 1 to 12 days after a subarachnoid hemorrhage, and five operations were for the nonruptured aneurysms.

Preoperative clinical grading according to the World Federation of Neurosurgical Societies (WFNS) scale was carried out. Nine patients were in grade 1, two were in grade 3, one was in grade 4, and another was in grade 5 with intracerebral hematoma. An arranged neuroleptic anesthetic technique with nitrous oxide was employed after the induction of anesthesia with an

<table>
<thead>
<tr>
<th>No.</th>
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<th>age/sex</th>
<th>location of aneurysm</th>
<th>WFNS score</th>
<th>days to operation</th>
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<td>72/F</td>
<td>Rt ICPC Lt MCA</td>
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<td>11</td>
<td>K.Su</td>
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<td>12</td>
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</table>

intravenous injection of thiopental. We have not used artificial hypothermia or profound induced systemic hypotension during surgery.

Sensory cortical function in the territory of the middle cerebral artery was monitored by recording the SEP to stimulation of the contralateral median nerve at the wrist, using either Medelec MS6 system (Medelec Ltd., Surrey, Great Britain) or Nicolet Compact 4 (Nicolet Instrument Corp., Wisconsin, U.S.A.). Recording skin contact electrodes made of silver were placed over the C3,4 location in the International 10-20 System, and over the skin surface of the C2 spinous process. A frontal reference electrode, Fpz, was used. The median nerve was stimulated by skin contact electrodes, with the cathode 25 mm proximal to the anode at the wrist. Square waves of 0.2 msec duration and of an intensity determined preoperatively that would cause sustained twitching of the thumb (usually in the range of 75-100 V) were delivered at a rate of 5 or 5.1 per second. Two hundred fifty-six (256) responses were averaged and amplified with the filter of time constant 40 msec. The high frequency cutoff of 1.6 kHz and the low frequency cutoff of 32 Hz were used.

The responses were evaluated for CCT between the N13 and N20 peaks according to Hume and Cant9, and for the amplitude of the N20 peak. As reported previously, normal value of CCT in our department was 6.1 ± 0.6 msec (mean ± s.d.)12. Prolongation of CCT in excess of 0.6 msec was regarded as a mild delay, and prolongation in excess of 1.2 msec as a severe abnormality. Decrease of the amplitude was considered abnormal, if it exceeds 25% of the control value. Control values of CCT and amplitude were taken from the records preceding either the first application of a temporary clip or the premature rupture.

![Fig. 1](image-url) Case 5 (operation-5). Serial tracings starting from the record taken before premature rupture of the aneurysm to the end of the operation. SEP abruptly became flat on application of a clip to the internal carotid artery. CCT did not elongate until shortly before disappearance of the N20 peaks.
Presentation of Representative Cases

Operation-2 (case 2): This 70-year-old lady with an internal carotid-posterior communicating aneurysm experienced flattening of the N20 peak 11 minutes after the initial temporary clipping of the internal carotid artery in order to control the bleeding due to premature aneurysmal rupture. The second temporary clip was applied before the complete recovery of the amplitude of N20 peak. It caused gradual, further decrease of the N20 peak followed by its abrupt disappearance without showing any appreciable preceding prolongation of the CCT. It took 66 minutes before sufficient recovery of the N20 amplitude was seen (Fig. 1).

Operation-3 (case 3): A 72-year-old lady had a ruptured aneurysm of the right middle cerebral artery and an incidental one of the left middle cerebral artery. The ruptured aneurysm was successfully occluded on day 6 in WFNS scale of grade 1 (operation 9). The patient was operated on the latter one 26 days after the first operation.

The N20 peak disappeared within 1 minute after the application of initial temporary clip on the M1 segment, which was used for control of premature aneurysmal rupture. The clip was released after 2 minutes. The N20 peak recovered to the control level at 7 minutes post-occlusion. The second temporary clip was applied for 8 minutes. The N20 peak once disappeared at 1 minute post-occlusion, but it started to recover gradually during the period of ischaemia. The

Fig. 2 Case 3 (operation-3). Tracings starting from the record taken before premature rupture of the aneurysm to the end of the operation. SEP recovered from flat tracings to the control level after the first two temporary clippings. The third to seventh clippings were necessary to control the bleeding, and it was impossible to wait until a complete recovery of the deteriorated SEP. It took 46 minutes for SEP to recover to the preceding control level.
N20 peak disappeared from the very beginning of the third temporary occlusion, but it reappeared shortly after the recirculation. But the temporary clipping had to be repeated further for control of hemorrhage before a complete recovery of the SEP from the preceding deterioration. The amplitude did not recover to the control level until 46 minutes after the release of the last temporary clip, and the patient showed severe postoperative deficits (Fig. 2).

Results

The effect of temporary occlusions on SEPs are shown in Table 2. Nine of sixteen patients underwent temporary occlusion of the parent artery twice or more for clipping of a single aneurysm. The period of temporary occlusion ranged from 1 to 35 minutes in this series. If any abnormality on SEPs was found by a monitoring staff, it was immediately reported to the surgeon, who made a decision of restoration of circulation.

Overall Changes in SEPs and Outcome of Patients

Immediately after the operation, four patients developed neurological deficits which were attributed to the temporary occlusion of the parent artery (Table 2A). In all these four patients premature rupture of the aneurysm had occurred during the operation. Three of these four patients (cases 1, 2 and 3) showed abnormalities in both the CCT and amplitude; a mild delay of the CCT and reduction of the amplitude in one patient (operation-1, case 1), a mild delay of CCT and sudden disappearance of the wave in two operations (operations-2, 3, cases 2 and 3).

The remaining patient who developed deficit immediately after the surgery (operation-4, case 4) showed false negative recording of SEP during middle cerebral artery occlusion. In this patient, the aneurysm ruptured prematurely and the M1 segment of the middle cerebral artery was occluded for 11 minutes and 45 seconds without showing any abnormal changes either in the CCT or amplitude during the operation. Hemiparesis, however, was worse when the patient recovered from anesthesia, and remained permanent without showing any abnormal findings in SEP throughout the hospital course.

Considerable or severe abnormalities of the CCT were found in operations-2, 3, 13, 16, 18, and those of amplitude were found in operations-1, 2, 3, 6, 10, 18. If patients with normal values in either the CCT or amplitude are excluded, abnormalities in both the CCT and amplitude were found only in operations-1, 2, 3, 18. Namely, postoperative deficits were correctly predicted either by the CCT or amplitude with a sensitivity of 50% or 75%, respectively, and a specificity of 78.6%. If prediction was made by combination of the CCT and the amplitude, sensitivity remained 75%, but the specificity increased to the higher level of 92.9%.

Comparison between Central Conduction Time and N20 Amplitude

The CCT showed elongation in 17 occasions of temporary occlusion in 12 patients; elongation up to 1.2 msec was seen in 11 and that exceeding 1.2 msec in 6 recordings during temporary ischaemia. There were found sudden disappearances of the N20 peak twice during temporary occlusions (operations-2, 3). In operation-2 (case 2, Fig. 1) disappearance of the N20 peak was preceded by a decrease of the amplitude, but not by any delay of the CCT.
Table 2 "SEP and outcome of the 18 temporary occlusions in 16 patients with aneurysms"  

A. SEP records in the patients with deficits due to temporary occlusion

<table>
<thead>
<tr>
<th>No. Op/Pt</th>
<th>site of occlusion</th>
<th>rupture</th>
<th>CCT delay</th>
<th>T to delay</th>
<th>T for recovery</th>
<th>range of N20 amplitude</th>
<th>T to reduce</th>
<th>T to disappear</th>
<th>length of disappearance</th>
<th>T for recovery</th>
<th>total T of occlusion</th>
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<td>7</td>
<td>66</td>
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B. SEP records in the patients without deficits due to temporary occlusion

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<th>site of occlusion</th>
<th>rupture</th>
<th>CCT delay</th>
<th>T to delay</th>
<th>T for recovery</th>
<th>range of N20 amplitude</th>
<th>T to reduce</th>
<th>T to disappear</th>
<th>length of disappearance</th>
<th>T for recovery</th>
<th>total T of occlusion</th>
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</thead>
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Pt: patient. CCT: central conduction time. T: time. F: flat. IC: internal carotid artery. AC: anterior cerebral artery. M1: M1 segment of middle cerebral artery. ①: premature rupture from aneurysm during operation. ②: period from the start of occlusion to the onset of elongation of CCT longer than 0.6msec. ③: period from the last abnormal measurement during temporary ischaemia, or from recirculation if abnormal record continues throughout the occlusion, to the first normal recording. ④: period from the start of occlusion to the onset of reduction of amplitude more than 25% of the control value. ⑤: This patient unfortunately suffered from severe hypotension not related to the intracranial manipulation after permanent clipping of the aneurysm, and her consciousness did not recover after the operation, associated with flattening of the SEP peaks.
Six recordings did not show abnormal delay of the CCT exceeding 0.6 msec. Three of them (operations-4, 7, 8, cases 4, 7, and 8) did not show decrease of the $N_{20}$ amplitude, either, and the patients recovered without neurological deficit immediately after the surgery. But three other recordings (operations-5, 6, 15, cases 5, 6, and 3) showed decreased $N_{20}$ amplitudes without evidence of CCT elongation. For example, at operation-5 (case 5) the patient showed a decrease of the amplitude to 76% of the control value 5 minutes after temporary clipping followed by a bolus injection of 250 mg of thiopental. The reduction of the amplitude recovered within 25 minutes, and the patient showed excellent outcome despite a total occlusion period of up to 35 minutes.

To the contrary, the CCT elongated without any changes of the amplitude in two occasions (operations-11, 17, cases 10 and 15), and with the paradoxical increase of the amplitude in two other occasions (operations-10(3), 16(2), cases 9 and 14). Such changes in the CCT were recorded during temporary occlusion of the middle cerebral artery but not during the internal carotid artery occlusion. Discrepancies between the changes of the CCT and of the amplitude were observed at different stages of occlusion even in a single patient (operation-10, case 9) as shown in fig. 3.

Throughout the surgeries, the amplitude of the $N_{20}$ peak showed variations by $\pm 20\%$ of the value at the start of the operation. However, the amplitude remained rather constant with variation of about $\pm 10\%$ during intradural manipulation. The amplitude of $N_{20}$ showed an increase by more than $20\%$ of the control value in seven recordings during temporary occlusion.

![Fig. 3 Case 9 (operation-10). Serial tracings starting from just before the first temporary occlusion to the end of the fourth one. CCT and $N_{20}$ amplitude show no appreciable changes during the first two temporary occlusions. CCT delay was not associated with a decrease in amplitude during the third occlusion. But the fourth occlusion caused a decrease in amplitude without any prolongation of CCT.](image-url)
of the middle cerebral or the internal carotid arteries. Those increases of the amplitude were associated with a mild elongation of the CCT in 4 occasions, and with a severe elongation of the CCT in one case, but not associated with any abnormalities of the CCT in two events. The cases that simply showed an increase in the amplitude during temporary occlusion had a good immediate outcome, whichever change did the CCT show.

Time necessary for recovery of the CCT and the amplitude after removal of the temporary clip varied widely: from 7 to 46 minutes and from 3 to 75 minutes, respectively. There seems no definite relationships either between the period of occlusion and the time necessary for recovery of SEP, or between the time to appearance of changes in SEP and time to recover. There were found discrepancies between the total time of arterial occlusion and the final neurological outcome of patients. However, there was found correlations between the severity of changes either in the CCT or the amplitude and the time to its recovery, and also between the time to recovery and outcome of patients. The correlation coefficient ($R$) was 0.32 between absolute value of CCT delay and the time for recovery, and 0.60 between reduction of the amplitude in terms of percentage and the time for recovery.

**Discussion**

Irreversible neuronal damage during temporary occlusion of the cerebral artery is determined both by severity and duration of the ischaemia of the brain. The threshold of cerebral blood flow for synaptic transmission failure has been demonstrated experimentally to be 5 to 10 ml/100 g. brain min higher than that for membrane failure. Loss of the SEP at flows well above the threshold for membrane failure implies the presence of a margin of safety when the SEP is used as an indicator of focal cerebral ischaemia. If prompt action is taken to restore the blood flow and to protect the brain as soon as the SEP deteriorates, it is expected to avoid permanent ischaemic cerebral damage.

The technique of Hume and Cant of measuring changes in the CCT, the interval between N13 and N20, eliminates the possible contribution of peripheral nerve and spinal conduction times and their variations from latency measurements of the cortical peaks. Intraoperative monitorings of SEP have been performed during aneurysm surgery, carotid endarterectomy, and spinal surgery, evaluating the CCT and, or disappearance of the cortical peak. Grundy described that loss of the signal in SEP is an ominous sign, but that they lack quantitative measures to pick up subtle changes in wave forms that may be associated with loss of function. Intraoperative comparison of the information from the CCT and the amplitude of SEP has not yet been done, probably because it is technically difficult to get a clear SEP records in the operating theatre, and also because it is complicated to measure and evaluate both of the CCT and amplitude at the venue.

This is the first report comparing the changes in the CCT and the $N_{20}$ amplitude of the SEP during intracranial surgery. In this study, the correlation between the deterioration of SEP and the time of recovery seems to be more clearly demonstrated by reduction of the amplitude of the $N_{20}$ peak than by prolongation of the CCT. This clinical experience elucidates that the
decrease in the amplitude of N20 peak has more information than the CCT changes in predicting a recovery of SEP after recirculation. Results of the animal experiment support the fact that the amplitude of cortical component of SEP has more definitive correlation than the CCT to the decrease in cerebral blood flow in the territory of the middle cerebral artery.

LJUNGGREN et al. temporarily occluded the proximal M1 segment in 5 cases and the distal M1 segment in 5 cases without SEP monitoring. They concluded that either procedure was well tolerated for up to 20 minutes during aneurysm operation. In six cases where temporary middle cerebral artery occlusion was monitored by SEP, SYMON concluded that, when the CCT did not exceed 10 msec, no permanent neurological deficit was likely to follow. MCPHERSON also reported a case in whom 12 minutes occlusion of the middle cerebral artery was necessary because of aneurysmal rupture. The SEP became unrecordable after 10 minutes of occlusion, and this was followed by a neurological deficit that fortunately resolved over 24 hours when the SEP was symmetrical in the hemispheres.

There has been no established criteria of the abnormalities in the amplitude of SEP. Based on our findings, good clinical outcome would be expected if the N20 amplitude recovers within 25 minutes after the onset of reduction more than 25% of the preceding reference value. And it also seems that an increase in the amplitude during temporary occlusion means a good recovery as well, even if it is associated with the elongation of the CCT. In this connection, we also emphasize that a combined evaluation of the CCT and the amplitude significantly increases the specificity of the SEP monitoring.

There were no correlations between the total time of occlusion and outcome immediately after the surgery, between the total time of occlusion and the time to recover, or between the time to appearance of SEP change and the time of recovery. On the other hand, there were correlations between the overall severity of the SEP changes, especially the changes in the amplitude, and the time of recovery, and also between the time of recovery and the immediate outcome of patients. Therefore, close observation of changes in the course of recovery after recirculation as well as of changes during a temporary ischaemic period, is of utmost importance in prediction of outcome of patients.

Changes of the N20 amplitude proved more reliable than delay of the CCT to predict neurological deterioration immediately after surgery. CCT and amplitude are two different kinds of factors in SEP, that is, the N20 amplitude is derived from physiological activity of the cortical neuron, but the CCT reflects axonal and junctional function including the pathways from the upper spinal cord to the cortex. It may be that cortical ischaemia caused by an occlusion of the internal carotid and middle cerebral arteries has more direct influences on the N20 amplitude than on the CCT.

SEP recording proved to be false negative in only one case (operation-4, case 4). Mild hemiparesis had been found at the presentation of the patient with subarachnoid hemorrhage, and it became more severe and persisted after the operation. However, the SEP in this particular patient showed neither lateralities nor other abnormalities throughout the hospital course. It was probable that her sensory pathway escaped from damage by subarachnoid hemorrhage or
by iatrogenic temporary ischaemia, in spite of the permanent damage to somewhere in the intracranial motor pathway.

In conclusion, monitoring of SEPs offers promise as a noninvasive means of minimizing intraoperative damage to the nervous system, but several limitations and prerequisites must be considered. Naturally, ischaemic changes only in topographically appropriate areas or pathways stimulated by the peripheral nerve would be detected by the SEP. Physiological and pharmacological environments have considerable influences on the SEP during surgery. Quantitative definitions of the acceptable limits for the intraoperative SEP abnormalities are still to be refined and individual variations in the CCT and/or amplitudes are considerable. Nevertheless, we are convinced that the change in the amplitude of N20 is more reliable and it predicts more accurately the functional recovery than a delay in the CCT, at least during the aneurysmal operation using temporary clipping, and that the combined evaluation of the CCT and the amplitude provides the most reliable information than either of them alone.

References


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和文抄録

一時的脳血流遮断における体性知覚誘発電位

2. 内頸動脈，中大脳動脈の脳動脈瘤手術中記録における評価

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脳動脈瘤根治術中に正中神経刺激による体性知覚誘発電位（SEP）を時的に記録し、内頸動脈、または中大脳動脈の一時的遮断を必要とした16例、18例の手術において、術中の SEP の変化を手術前後の神経学的所見と比較して予後の判定における SEP の有用性を検討した。

SEP の皮質成分 N20 の振幅と，N12 と N20 間の伝導時間（CCT）を比較すると，振幅はその減少量と再灌流後の回復時間に相関が認められ（R=0.6），術後の神経学的悪化の指標としても CCT もも優れた感度を持っていた。また，振幅と CCT を組み合わせて正常所見を観察することにより，選択性が向上した。

振幅の異常な減少（20%以上）が25分以内に回復した例，また，CCT が延長しても振幅の増大の観察された例では，術後神経学的に悪化を見なかった。しかし，術後に悪化を認めた4症例のうち，1例は SEP の変化を全く示さなかった。

以上から，術中の一時的脳血流遮断の指標として，SEP の振幅さらには振幅と CCT との組み合わせによる判断は，神経学的異常を予知するうえで重要な指標となることが明らかになった。但し，灌流後と虚血領域の一致と，生理学的，薬理学的な環境の安定が常に考慮されなければならない。また，虚血中の SEP の変化に対する絶対的な安全限界の決定は困難と考えられた。