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Changes of Motor Evoked Potentials in Global and Focal Ischemic Models of Cats

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ABSTRACT

In order to evaluate the significance of motor evoked potentials (MEPs) in central nervous system monitoring, the authors conducted two sets of experiments using feline ischemic models. Twenty-three adult mongrel cats were divided into two groups : global (n=9) and focal ischemic (n=14) groups.

In the case of global ischemia, which was induced by hypovolemic hypotension due to blood letting, deterioration of the D wave began when the mean arterial blood pressure (MABP) approached 45 mmHg, and regional cerebral blood flow (rCBF) dropped to 40% of control. Complete disappearance of the D wave was observed below 30 mmHg in MABP and 20% of control in rCBF. In the case of focal ischemia, which was induced by transorbital occlusion of the middle cerebral artery, the percentages of rCBF at which the D wave disappeared ranged from 9 to 20%. Changes in the amplitude of the D wave – an increase and following decrease – preceded the prolongation of its latency.

In contrast with the D wave I waves were too easily affected by ischemia. Moreover, rCBF at the point of disappearance of the I wave varied greatly.

In conclusion, the D wave is stable in mild ischemia and is a reliable indicator of critically profound ischemia (%rCBF < 40%). Monitoring the D wave of MEPs seems to be a useful method for avoiding the deterioration of motor function by ischemic insult.

Key words: *Cerebral ischemia, Middle cerebral artery, Controlled hypotension, Motor evoked potentials*

Motor evoked potentials (MEPs) are an electrical manifestation of cerebral motor function and are elicited by direct[7,14] or transcranial electrical stimulation[5,8,11,12], or recently, by magnetic stimulation[1]. The wave forms of MEPs consist of two or more components[7,8,11,14]: the initial positive wave, which is called the D wave, is produced by direct activation of the pyramidal cells. The second and further components, called the I waves, are due to the synaptic activation of the pyramidal cells by interneurons. To assess neurological function during cerebrovascular operation and removal of tumors around the motor cortex, MEPs could be used as an intraoperative monitoring method[10]. However, the changes in MEPs due to cerebral ischemia, particularly in the acute phase, are still unclear. We therefore evaluated MEPs under focal and global ischemia in association with regional cerebral blood flow (rCBF) measured by laser Doppler (LDF) flowmetry. The present study was undertaken in an attempt to clarify the effect of acute stroke on the configuration of MEPs.

MATERIALS AND METHODS

Twenty-three adult mongrel cats weighing 2.5–4.0 kg were anesthetized with 30mg/kg of sodium pentobarbital injected intraperitoneally after intramuscular injection of 0.1mg/animal of atropine sulfate. Anesthesia was maintained with an hourly 30mg/kg infusion of ketamine. The femoral artery and vein cannulas were used to administer fluids and monitor systemic arterial pressure. After immobilization with an intravenous injection of 0.08mg/Kg of pancuronium bromide the cats were intubated and placed on a Harvard respirator (Bodine Electric Company, Chicago, ILL, USA). Temperature was measured with a rectal probe and maintained at between 36.5° and 38°C with the use of a heating blanket. A one-level laminectomy was performed at the C2 vertebral segment and then an epidural catheter electrode was inserted into the spinal epidural space (C2–C7). A long rostrocaudal incision was made on the midline scalp. The periostium was scraped toward the sides to reveal the suture lines. A small craniotomy was performed over the left coronal suture and the posterior wall of the

left frontal sinus was removed. A dural incision was made to expose the left precruciate gyrus.

Direct electrical stimulation of the motor cortex was performed by bipolar small silver ball electrodes (4-mm interelectrode distance), with a rectangular pulse (duration, 0.2msec; intensity, 4-6mA) delivered at a frequency of 3Hz. The MEPs were recorded from the epidural catheter electrode. One hundred and twenty-eight signals were averaged by a signal processor (Neuropack 8; Nihon-Kohden, Tokyo, Japan). The bandpass filter was set between 50 and 3000Hz. To monitor rCBF continuously, LDF with a small caliber probe (type OP; Advance, Tokyo, Japan) was placed on the motor cortex using a balancer to avoid indenting the cortex. The probe was slowly rinsed with warmed saline to control the brain temperature. Then, changes in rCBF (percentage) were measured by the LDF monitor (ALF2100; Advance, Tokyo, Japan).

Hypovolemic hypotension model : Nine cats were given heparin (50 units/kg) and bled via the left femoral artery so that the MABP dropped sequentially until the MEPs disappeared. Then, five minutes after the disappearance of MEPs, blood that had been stored in a warming bath was transfused back into the 6 cats and the return of MEPs was studied for 2 hours.

Focal ischemic model : A left middle cerebral artery (MCA) occlusion was carried out transorbitally in 14 cats using a microclip under direct visualization with an operating microscope. Changes of MEPs were followed for 2 hours.

After the termination of the experiment, all the animals were killed by intravenous administration of a high dose of pentobarbital sodium and potassium chloride.

RESULTS

The typical wave forms of MEPs recorded prior to induced ischemia are shown in Fig. 1. MEPs consist of an initial large positive wave (D wave) followed by small positive waves (I waves). Subsequent analysis on amplitude and latency was carried out on D waves.

[Hypovolemic hypotension model]

The graded drop in MABP to 50 mmHg did not significantly change the wave form of MEPs. In all the animals (N=9), amplitude began to deteriorate when MABP approached 45 mmHg and rCBF reached 40% of control. In all cases an increase in latency was almost simultaneously accompanied by a reduction in amplitude. In all the animals a complete disappearance of MEPs was obtained when MABP was below 30 mmHg, and rCBF below 20% of control (Fig. 2). In 6 animals, a blood transfusion was given 5 minutes after the loss of MEPs. In all the animals the D wave returned within a few minutes after transfusion (Table 1). Typical changes in MEPs are shown in Fig. 3. Two hours after transfusion, the increase in latency of the D wave was 0.13 ± 0.09 msec, and the conduction velocity did not increase significantly. In all the animals no return of the I wave was observed.

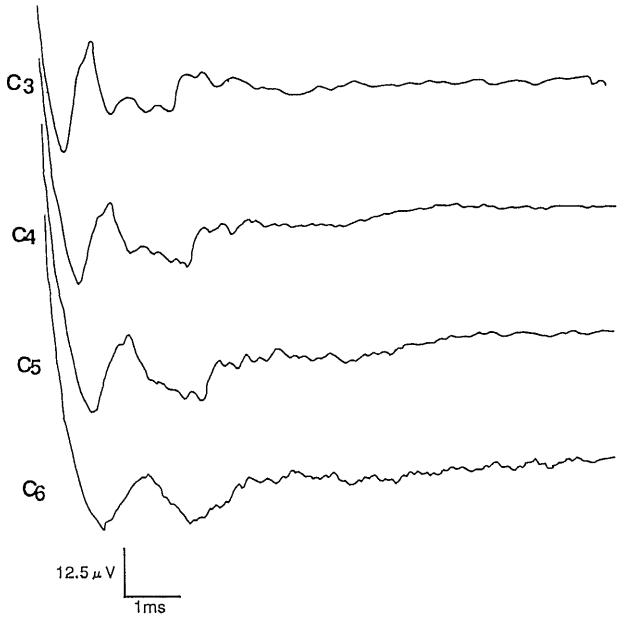

Fig. 1. Motor evoked potentials (MEPs)
Typical MEPs elicited by constant current square wave (intensity, 4mA; duration, 0.2ms; frequency, 3Hz) are shown. After a stimulus artifact, an initial large positive wave (D wave) was followed by a number of later waves (I wave).
C3–C6 : C3–C6 cervical segment

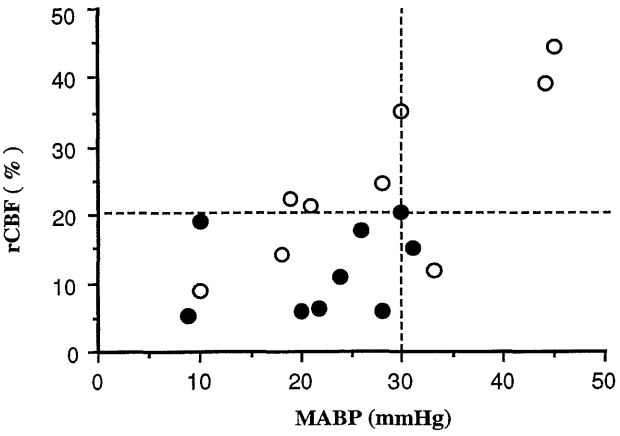

Fig. 2. Changing points in D wave of MEPs due to global ischemia
Open circles show the point at which amplitude of D wave began to deteriorate. Closed circles show the point at which MEPs had completely disappeared. Amplitude began to deteriorate when mean arterial blood pressure (MABP) approached 45 mmHg and regional cortical blood flow (rCBF) reached 40% of control. In all animals complete disappearance of MEPs was obtained below 30 mmHg and 20% of control.

Table 1. Changes in MEPs after transfusion in hypovolemic hypotension model

	Latency (msec) : D wave		Conduction Velocity (m/sec)		
Cat No.	***control***	***2 hours after transfusion***	***control***	***2 hours after transfusion***	**Return of I wave**
1	1.52	1.56	53.5	50	—
2	1.42	1.58	75	75	—
3	1.4	1.52	68	65	—
4	1.74	1.84	58	62.5	—
5	1.74	1.82	65	75	—
6	1.58	1.86	39.5	39.5	—

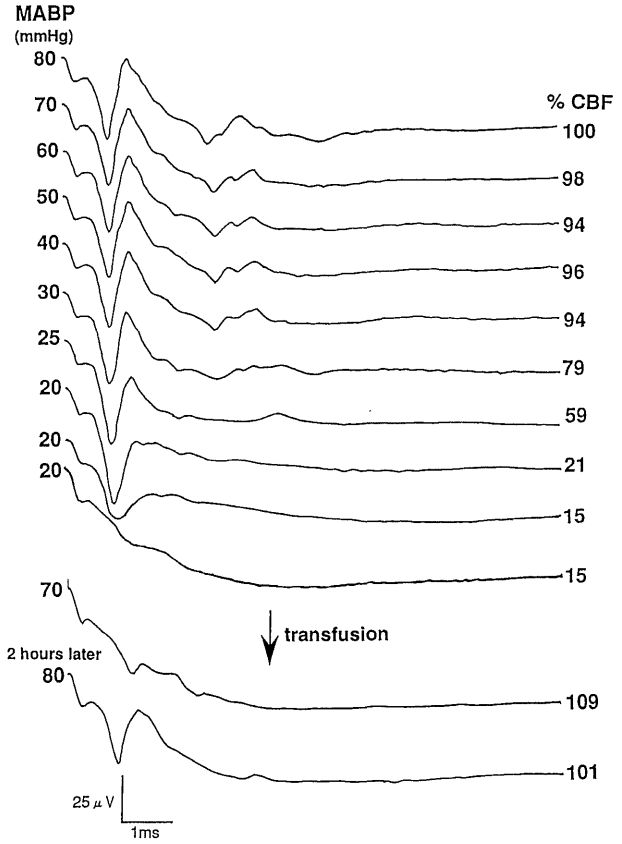

Fig. 3. Changes of MEPs in global ischemia
Sequential changes of MEPs in latency and amplitude in relation to mean arterial blood pressure (MABP) and percentage of cerebral blood flow of control (% CBF) under graded systemic hypotension are shown. Abolition of D and I waves and recovery of D wave are presented.

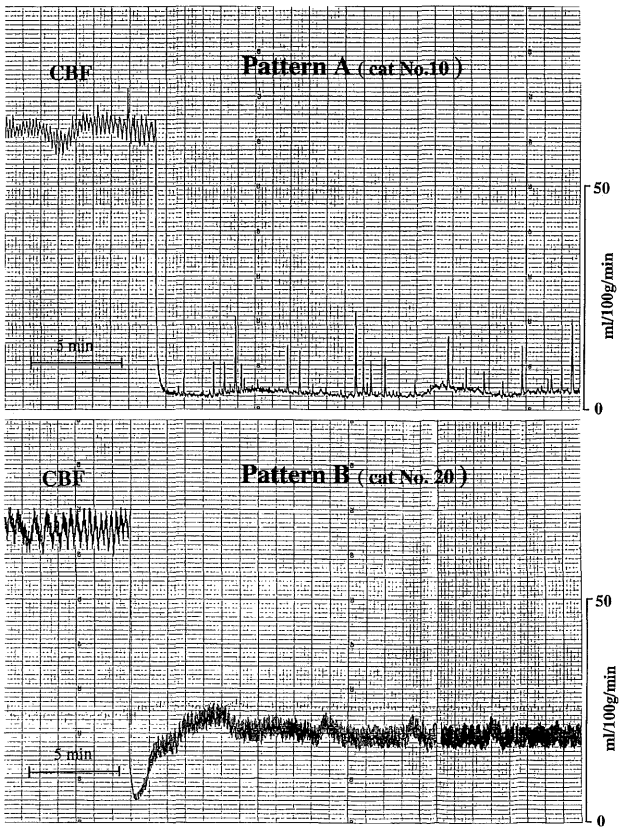

Fig. 4. The cortical flow patterns by laser-Doppler flowmetry after middle cerebral artery (MCA) occlusion
The cortical flow significantly reduced immediately after MCA occlusion and stayed at the same level (Pattern A) in all animals of Group 1. It also reduced significantly but soon recovered to some extent (Pattern B) in 5 out of 6 animals of Group 2

[Focal ischemic model]

According to the depth of the drop in rCBF due to the occlusion of MCA, the animals (N=14) were divided into two groups: Group 1 (N=8) in which rCBF was reduced to below 20%, and Group 2 (N=6) in which rCBF did not fall below 20%. Cortical flow reduced significantly immediately after MCA occlusion and stayed at the same level (Pattern A) in all the animals of Group 1. It was also reduced significantly but soon recovered to some extent (Pattern B) in 5 out of 6 animals in Group 2 (Fig. 4). The D wave disappeared after MCA clipping in all the animals in Group 1, but in no animals in Group 2. The relation of rCBF to the amplitude, latency and conduction velocity of the D wave is given in Table 2. The percentage of rCBF of the 8 animals, in which the D wave disappeared, ranged from 9 to 20% (mean = 14.3%),

Table 2. %rCBF in relation to amplitude, latency and conduction velocity of D wave after MCA clipping*

Cat No.	%rCBF	Relative amplitude			Latency (msec)				Increase or decrease	Disappearance	
	after 5 min	*1min*	*5*	*10*	*control*	*1min*	*5*	*10*	of conduction velocity	*D wave*	*I wave*
Group 1 (rCBF ≦ 20%)											
10	9	1.31	1.08	0.62	1.32	1.32	1.32	1.32	increase	+	+
11	10	2	2.36	—	1.62	1.66	1.66	—	decrease	+	+
12	11	1.1	0.67	—	1.24	1.24	1.24	—	NC	+	+
13	14	1.2	—		1.56	1.56	—		NC	+	+
14	15	1.15	—		1.48	1.48	—		NC	+	+
15	16	1.14	0.68	—	1.4	1.38	1.42	—	decrease	+	+
16	19	0.2	—		1.46	1.48	—		NC	+	+
17	20	1.11	—		1.24	1.26	—		NC	+	+
Group 2 (rCBF > 20%)											
18	34	0.87	0.72	0.58	1.28	1.28	1.34	1.4	increase	−	+
19	36	1.45	0.45	0.18	1.4	1.34	1.3	1.3	increase	−	+
20	36	1	1.21	0.93	1.62	1.62	1.66	1.74	increase	−	+
21	60	0.92	0.23	0.15	1.2	1.24	1.24	1.28	increase	−	+
22	61	1	1	1.09	1.26	1.24	1.24	1.46	NC	−	+
23	125	0.87	0.87	0.84	1.16	1.18	1.18	1.2	NC	−	+

* Amplitude was measured from valley to peak; latency was measured from stimulus onset to peak. Abbreviations : %rCBF = percentage of regional cerebral blood flow of control, NC = no change

and 7 (88%) animals of these had an increase in amplitude soon after MCA occlusion, although it was not necessarily accompanied by an increase in latency. Changes in the conduction velocity were variable and there was no obvious tendency. In all of the animals of both Groups, the I wave disappeared regardless of rCBF.

DISCUSSION

There have been many investigations concerning the relationship between CBF and the cerebral electrical activity under developing ischemia[2,3,16]. Coyer[3] presented the extreme sensitivity of the evoked response to blood flows at a value of 40% of control or 20ml/100g/min in the gray and 12ml/100g/min in the white matter by monitoring the somatosensory evoked potential (SEP) in cats. Branston[2] suggested a threshold-type relationship between the amplitude of the SEP and CBF and showed that the SEP began to decay at a CBF of 16ml/100g/min and abolished at less than 12ml/100g/min in baboons. Yamagata[16] found that the thresholds for attenuation and loss of direct cortical response (DCR) were 21.3 and 8.7 ml/100g/min respectively in cats.

As for MEPs, Haghighi[6] reported that the decay in the evoked responses occurred at 30mmHg in blood letting hypovolemic hypotension models. However, monitoring of rCBF was not conducted in his experiment. The use of laser-Doppler flowmetry (LDF), which allows continuous, noninvasive and accurate measurement of microcirculatory blood flow, enabled us to ascertain the thresholds of decay and disappearance of MEPs[4]. Our finding that the latency of the D wave began to decrease at 40% of control blood flow and disappeared at 20% is similar to the results for SEP and DCR. It is reassuring to note that these thresholds of approximately 20ml and 10ml/100g/min hold true in a variety of experimental conditions, despite the use of different species and different techniques for measuring the blood flow.

The significance of changes in the D and I waves during ischemia have been discussed in previous literature. Hossmann[7] reported that I waves were suppressed after 2.5 min of ischemia and that the D wave was suppressed after less than 4 min. Patton[14] observed that I waves were more affected than the D wave by cortical injury, asphyxia and anesthesia. Our results showed that I waves were not recovered by the transfusion and that the disappearance of I waves due to MCA occlusion occurred regardless of the severity of ischemia. Therefore I waves are too fragile to stand as an appropriate monitor of the motor function. On the other hand, the D wave seems to be a better indicator of serious ischemia than I waves.

Concerning the change in amplitude, Simpson[15] showed the immediate attenuation of all components after infarction. However, meticulous evaluation of our results showed that an increase in the amplitude of the D wave preceded a decrease at the early phase of profound ischemia. A few authors have already reported that a brief facilitation in spinal motor evoked potential amplitude occurred following cerebral ischemia[9,11,13]. However, in our experiment, this facilitation of the D wave turned out to depend upon the severity of ischemia, because the facilitation was rarely observed under moderate ischemia.

In general, during SEP examination, extension of the latency of the cortical component of the evoked response seems to be a sensitive and stable indicator of reduced blood flow. However, amplitude changes are too variable and unpredictable to determine blood flow in global ischemia[3]. On the other hand, the data concerning MEPs obtained from our experiment suggest that the increase in latency in the acute phase of ischemia is not an adequate means of detecting the severity of ischemia, whereas the increase in amplitude is more sensitive. The detection of changes in the amplitude of the D wave would be more useful than latency for providing against acute ischemic insult.

Recent attempts to evaluate the prognoses of comatose patients with MEPs have failed[17] but MEPs may be a valuable prognostic indicator of the recovery of motor function in the acute stage of paralytic stroke[5]. This work confirmed that MEPs are very sensitive and reliable monitor of cerebral ischemia, particularly in the acute phase. An understanding of the relationship between patterns of MEPs and blood flow reduction will be usefull for further study of the motor function of the central nervous system.

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REFERENCES

1. **Barker, A.T. and Freeston, I.L.** 1985. Non-invasive magnetic stimulation of human motor cortex. Lancet **11:** 1106–1107.
2. **Branston, N.M., Symon, L., Crockard, H.A. and Pasztor, E.** 1974. Relationship between the cortical evoked potential and local cortical blood flow following acute middle cerebral artery occlusion in the baboon. Exp. Neurol. **45:** 195–208.
3. **Coyer, P.E., Simeone, F.A. and Michele, J.J.** 1987. Latency of the cortical component of the somatosensory evoked potential in relation to cerebral blood flow measured in the white matter of the cat brain during focal ischemia. Neurosurgery **21:** 497–502.
4. **Dirnagl, U., Kaplan, B., Jacewicz, M. and Pulsinelli, W.** 1989. Continuous measurement of cerebral cortical blood flow by laser-Doppler flowmetry in a rat stroke model. J. Cereb. Blood Flow Metab. **9:** 589–596.
5. **Dominkus, M., Grisold, W. and Jelinek, V.** 1990. Transcranial electrical motor evoked potentials as a prognostic indicator for motor recovery in stroke patients. J. Neurol. Neurosurg. Psychiatry **53:** 745–748.
6. **Haghighi, S.S. and Oro, J.J.** 1989. Effects of hypovolemic hypotensive shock on somatosensory and motor evoked potentials. Neurosurgery **24:** 246–252.
7. **Hossmann, K.A. and Sato, K.** 1971 Effect of ischaemia on the function of the sensorimotor cortex in cat. Electroenceph. clin. Neurophysiol. **30:** 535–545.
8. **Inghilleri, M., Berardelli, A., Cruccu, G., Priori, A. and Manfredi, M.** 1989. Corticospinal potentials after transcranial stimulation in humans. J. Neurol. Neurosurg. Psychiatry **52:** 970–974.
9. **Konrad, P.E., Tacker, W.A., Levy, W.J., Reedy, D.P., Cook, J.R. and Geddes, L.A.** 1987. Motor evoked potentials in the dog: effects of global ischemia on spinal cord and peripheral nerve signals. Neurosurgery **20:** 117–124.
10. **Levy, W.J.** 1987. Clinical experience with motor and cerebellar evoked potential monitoring. Neurosurgery **20:** 169–182.
11. **Levy, W.J. and York, D.H.** 1983. Evoked potentials from the motor tracts in humans. Neurosurgery **12:** 422–429.
12. **Merton, P.A. and Morton, H.B.** 1980. Stimulation of the cerebral cortex in the infarct human subject. Nature **285:** 227–228.
13. **Oro, J. and Levy, W.J.** 1987. Motor evoked potential as a monitor of middle cerebral artery ischemia and stroke. Neurosurgery **20:** 192–193.
14. **Patton, H.D. and Amassian, V.E.** 1954. Single and multiple unit analysis of cortical stage of pyramidal tract activation. J. Neurophysiol. **17:** 345–363.
15. **Simpson, R.K. and Baskin, D.S.** 1987. Early component changes in corticomotor evoked potentials following experimental stroke. Stroke **18:** 1141–1147.
16. **Yamagata, S., Carter, L.P. and Erspamer, R.** 1982. Cortical ischemia: effect upon direct cortical response. Stroke **13:** 680–686.
17. **Zenter, J. and Rohde, V.** 1992. The prognostic value of somatosensory and motor evoked potentials in comatose patients. Neurosurgery **31:** 429–434.