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9. Branston NM, Symon L, Crockard HA et al: Relationship between the cortical evoked potential and local cortical blood flow following acute middle cerebral artery occlusion in the baboon. Exper Neurol 45: 195–208, 1974

10. Kwak S, Sasaki M, Takagi K: Dopamine infusion without hypertension for vasospasm after subarachnoid hemorrhage, Proceeding of Eleventh Conference of Surgical Treatment of Stroke. Nyhron Company, Tokyo, p 270–274, 1982 (Jpn)

11. Toda N: Influence of dopamine and noradrenalin on isolated cerebral arteries of the dog. Br J Pharmac 58: 121–126, 1976

12 Edvinsson L, Hardebo JE, McCulloch J et al: Vasomotor response of cerebral blood vessels to dopamine and dopaminergic agonists.

In J Cervö-Navarro et al (eds): Advances of Neurology. Vol 20, Raven Press, New York, p 85–96, 1978

13. Ritchie WL, Weir B, Overton TR: Experimental subarachnoid hemorrhage in the cynomolgus monkey: Evaluation of treatment with hypertension, volume expansion and ventilation. Neurosurgery 6: 57–62, 1980

14 Haraguchi S, Ebina K: Evaluation of the dopamine induced hypertension therapy for vasospasm Surg Neurol (Tokyo) 10: 279–289, 1982 (Jpn)

15 Brown FD, Hanlon K, Mullan S: Treatment of aneurysmal hemiplegia with dopamine and mannitol. J Neurosurg 49: 525–529, 1978

Relationship of Somatosensory Evoked Potentials and Cerebral Oxygen Consumption During Hypoxic Hypoxia in Dogs

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SUMMARY   The effects of hypoxic hypoxia on cerebral hemodynamics and somatosensory evoked potential (SEP) were studied in 10 pentobarbital anesthetized dogs. Cerebral blood flow (CBF) was measured using the venous outflow technique and cerebral oxygen consumption ($CMRO_2$) was calculated from the arterio-cerebro-venous oxygen difference times CBF. SEP was evaluated by percutaneous stimulation of an upper extremity nerve and was recorded over the contralateral somatosensory cortex. The latencies of the initial negative wave (N1), second positive wave (P2) and the amplitude of the primary complex (P1N1) were measured. Animals were breathed sequentially with oxygen concentrations of 21, 10, 6, 5, and 4.5% for five minutes each. Animals were returned to room air breathing when the amplitude of the SEP decreased to < 20% of control and were observed for 30 minutes following reoxygenation. Severe hypoxia (4.5% O_2) increased CBF to 200% of control, decreased $CMRO_2$ to 45% of control, decreased amplitude and increased latency of SEP. Following reoxygenation, as $CMRO_2$ increased toward control, latency of SEP decreased and amplitude increased and CBF returned to baseline within 30 min. During hypoxia and reoxygenation, the latencies of N1 and P2 and the amplitude of P1N1 were correlated with $CMRO_2$ in individual animals. We conclude that changes in SEP amplitude and latency reflect changes in $CMRO_2$ despite high CBF during rapidly progressive hypoxic hypoxia and following reoxygenation.

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SOMATOSENSORY EVOKED POTENTIALS assess the nervous system from peripheral nerve to cortex. Clinical use emphasizes discrete lesions of the nervous system, brachial plexus,[1] brainstem,[2] spinal cord[3] and hemisphere.[4, 5] Somatosensory evoked potential (SEP) is altered by systemic insults such as oligemia[6, 7] anemia,[8] intracranial hypertension,[9] and hypoxia.[10] The changes in superficially recorded waves during systemic oxygen deprivation[6, 8, 10] are similar to those recorded when the cortical region (somatosensory cortex) is directly involved[11] and therefore may be as useful in quantitating the degree of insult in generalized insult as in localized insult.

Previous studies have not explored the relationship between oxygen delivery and changes in brain electrical activity. Verification of the relationship of cerebral oxygen delivery and brain electrical activity allows assessment of adequacy of oxygen availability and utilization when cerebral blood flow (CBF) and other important factors such as blood oxygen carrying capacity cannot be measured. Studies of non-oligemic insults on SEP have failed to include information on CBF or cerebral oxygen consumption ($CMRO_2$).[8, 10] It is therefore unclear if a consistent relationship of changes in $CMRO_2$ and SEP exists.

We studied the relationship of $CMRO_2$ and SEP in a model in which CBF increases in response to cerebral oxygen deprivation to test the hypothesis that somatosensory evoked potentials reflect oxygen availability to the brain regardless of CBF.

Methods

Ten adult mongrel dogs (20–25 kg) of either sex were utilized in this study. Anesthesia consisted of sodium pentobarbital (30 mg/kg, i.v.) supplemented with increments of pentobarbital (60 mg, i.v.) as nec-

essary during the surgical preparation in response to pedal and ocular reflexes. Pancuronium bromide (3–4 mg, i.v.) was administered to minimize muscle contractions related to the electrocautery. Heparin (500 μg/kg, i.v.) was used as the anticoagulant.

After induction of anesthesia, animals were intubated and ventilated utilizing a positive pressure respirator (Harvard respiration pump 607). Tidal volume and respiratory rate were adjusted to give an alveolar (end-expiratory) carbon dioxide of 4% as monitored by a CO_2 analyzer (Beckman LB2). The CO_2 analyzer was calibrated regularly with mixtures of CO_2 in air analyzed to a precision of 0.1%. Electrocautery was used to expose one femoral artery and both femoral veins. The femoral artery was cannulated for continuous monitoring of mean arterial blood pressure (MABP). One femoral vein was cannulated and was utilized to return cerebral venous outflow while the other femoral vein was cannulated and used for infusion of fluids and drugs. Rectal temperature was maintained at 38° ± 1 centigrade using heating lamps. All pressures were measured with Statham P-23 transducers, and all data were recorded on a Gould-Brush recorder.

Measurement of Cerebral Blood Flow

The technique used to measure cerebral venous outflow has been described by Rapela and Green.[12] The confluence of the cerebral sinuses was cannulated and the lateral sinuses and occipital emissary veins were occluded with bone wax to minimize communication between intracranial and extracranial venous circulations. From the confluence of the sinuses blood then passed through a previously calibrated electromagnetic flow probe, before returning to the dog via the femoral vein. With this technique approximately 50–70% of the mass of the brain is drained at the confluence of the sagittal and straight sinuses.[12] Cerebral venous outflow pressure was measured upstream from the flow probe. This pressure measures the resistance to the flow of blood induced by the flow transducer because the outflow cannula was set at the level of the right atrium and all pressures were referred to this common zero reference plane. Brain perfusion pressure was estimated as systemic arterial pressure minus cerebral venous outflow pressure. Intracranial vascular resistance was calculated by dividing brain perfusion pressure by cerebral venous outflow.

The verification of the measurement of CBF utilizing this venous outflow technique has been described in detail elsewhere.[13] In addition, the viability and responsivity of the cerebral vasculature to hypercapnia,[13] hypoxia,[14, 15] and ability to autoregulate[12] using this technique has been previously demonstrated.

Measurement of Somatosensory Evoked Potential (SEP)

Stimulating needle electrodes were placed percutaneously in the volar surface of a foreleg in a location which caused a distinct digital twitch and the stimulus intensity just sufficient for a motor response (motor threshold) was determined. The needles were secured and a large surface ground pad was attached to the

extremity proximal to the stimulating electrodes. Silver ball electrodes with shielded cables were placed in depressions drilled in the skull over the contralateral somatosensory cortex. A needle electrode with shielded cable was placed in the snout and acted as reference. The junction of the lambdoidal and sagittal suture is an easily indentifiable landmark in the dog and was chosen as an anatomical reference point. Two parallel rows of electrode locations were examined in each animal. One row consisted of electrode locations 2 cm from the midline, with electrode locations 4, 6, and 7.5 cm anterior to the lambdodial suture. A second row was located 4 cm from the midline posteriorly and 3.5 cm from the midline anterior. Electrodes were placed at 4, 6, and 7.5 cm anterior to the lambdoidal suture. In each animal, the electrode location with maximum amplitude was considered to be nearest the somatosensory cortex and was analyzed for this study.

The SEP was developed using a 4 channel signal averager (Nicolet Med 80, Nocolet Biomedical, Madison, Wisc). A stimulus intensity twice motor threshold and a stimulus duration of 150 usec was used. One hundred twenty eight stimuli were delivered at a rate of 5.9/sec and averaged. Upper and lower band pass filters were 5 and 1500 Hz respectively. Waveforms were stored on magnetic disk for later analysis. In the control period, replicate waves were generated to ensure stability of the waveform. High amplitude electrical artifact was automatically rejected by the computer. The peripheral nerve was stimulated only during study periods (approximately 45 sec each).

This active electrode and reference system yields a consistent wave-form in the dog. The waveform consists of a small positive wave (P1) and 15 ms after stimulus, a large negative wave (N1) and about 20–25 ms after stimulus and a large positive wave (P2) occurring 35–45 ms after stimulation. The amplitude and latency of the waveform were evaluated using the cursor mode of the computer. The latencies of the first negative (N1) and second positive (P2) waves were determined. The latency was measured at the midpoint of the wave. The amplitude of the initial complex (P1N1) was measured from the maximum positive deflection of the initial postive wave (P1) to the maximum negative deflection at N1. A representative wave is provided (fig. 1).

A single bipolar EEG channel was monitored ipsilateral to the stimulated extremity. One electrode was placed posteriorly and the anterior electrode was placed in the same coronal plane as the active SEP electrode.

Hypoxia Administration and Blood Gas Analysis

Animals were subjected to hypoxic hypoxia by administration of a mixture of air and nitrogen. The inspired oxygen concentration was measured utilizing an oxygen analyzer (Beckman LB-2). The inspired oxygen concentration was decreased sequentially from 21 to 10, 6, 5, and 4.5% and each level of hypoxia was maintained for approximately 5 minutes or until the SEP was suppressed to < 20% of control. Endtidal
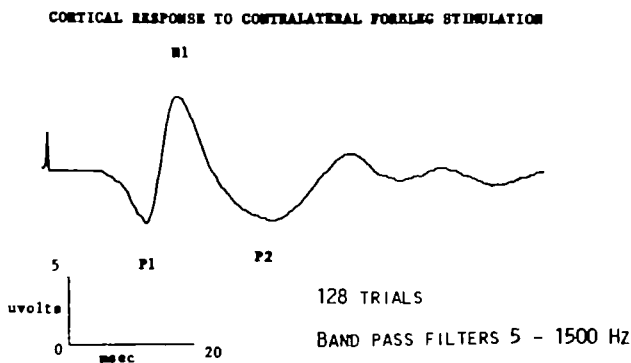
CORTICAL RESPONSE TO CONTRALATERAL FORELEG STIMULATION

N1

5
uvolts

0

P1   P2

128 TRIALS

BAND PASS FILTERS 5 - 1500 Hz

20

msec

FIGURE 1. *A representative response recorded over the somatosensory cortex to contralateral foreleg stimulation is shown. The period evaluated was 80 msec following stimulation. The response was recorded from a 2 mm silver ball electrode placed in a depression drilled into the skull over the somatosensory cortex. The response shown was generated by averaging 128 stimuli delivered at 5.9/sec.*

CO_2 was maintained at 4% by altering the ventilator rate and sodium bicarbonate (1 meq/ml) was given slowly to prevent metabolic acidosis. SEP waveforms were obtained at the end of the 5 min periods at each level of hypoxia and simultaneous arterial and cerebral venous blood samples were obtained from the femoral artery and cerebral venous cannulae respectively at the mid-point of the SEP determination. SEP acquisition required 30–45 seconds.

A final set of data (for hypoxia) was obtained when SEP amplitude was decreased to < 20% of control. This degree of SEP suppression usually occurred when the EEG was flat or showed burst suppression. This degree of hypoxia (between 6 and 4.5% inspired oxygen) caused a decrease in MABP. The animals were then returned to room air breathing. Arterial and cerebral venous blood samples and SEP waveforms were obtained 2, 4, 6, 8, 10, 15, 20, and 30 minutes following reoxygenation. Again, blood samples were obtained at the midpoint of each SEP determination.

Arterial O_2 tension (PaO_2), CO_2 tension ($PaCO_2$) and pH were measured at 37°C immediately after the samples were obtained by use of Radiometer BMS-3 electrodes and analyzer. The electrodes were calibrated with air (20.8% O_2) and mixtures of O_2 in N_2 (8%) and CO_2 in air (5 and 10% CO_2) were analyzed to a precision of 0.1%. The pH electrode was calibrated with standard phosphate buffers (6.840; 7.381). O_2 saturation and hemoglobin were also measured immediately after samples were taken with an Instrumentation Laboratories Co-Oximeter (Model 282). Electrodes were calibrated before and after each set of samples were analyzed. This instrument computes oxygen content from the saturation and hemoglobin. Cerebral oxygen consumption ($CMRO_2$) was calculated by multiplying the arterial (CaO_2) to cerebrovenous (CvO_2) O_2 content difference by CBF. Fractional O_2 extraction was calculated using the formula:

$$\frac{CaO_2 - CvO_2}{CaO_2}$$

Data in the text and figures are presented as mean ± standard error. Regression analysis was performed using a microcomputer to compare changes in waveform parameters (latency of N1, P2 and amplitude of N1P2) with changes in $CMRO_2$. Because the absolute rate of change in $CMRO_2$ was similar during hypoxia and recovery, a single slope was estimated for each animal. Variance components analysis[16] was used to calculate confidence intervals for each parameter. This statistical technique acknowledges two sources of uncertainty in the slope estimate for a given animal: the first being the measurement errors in that animal's data; the second being the naturally occurring differences in the rates among animals.

Results

Hypoxia

Decreasing the inspired O_2 concentration from control (21%) to 10, 6, 5 and 4.5%, decreased PaO_2 from 92 ± 5 to 31 ± 1, 19 ± 1, 17 ± 1 and 14 ± 1 mmHg, respectively (table 1). Fractional O_2 extraction increased markedly from control (.47 ± .02) at a PaO_2 of 92 ± mmHg, to .74 ± .02 at a PaO_2 of 14 ± 1 mmHg. pH and $PaCO_2$ were unchanged throughout the different O_2 levels. The cerebral hemodynamic changes with hypoxia are shown in figure 2. MABP increased from 127 ± 4 to 150 ± 6 mmHg as PaO_2 was lowered from control to 31 ± 3 mmHg but decreased markedly when PaO_2 was lowered to 14 ± 1 mmHg. CBF increased markedly to 240% of control at

TABLE 1 *Blood Gas Changes During Hypoxia and Recovery*

Hypoxia				
Inspired oxygen concentration	pH	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)	Fractional extraction
21%	7.40 ± 0.01	92 ± 5	30 ± 1	0.47 ± 0.02
10%	7.43 ± 0.01	31 ± 1*	31 ± 1	0.55 ± 0.02*
6%	7.46 ± 0.01	19 ± 1*	30 ± 1	0.56 ± 0.03*
5%	7.43 ± 0.01	17 ± 1*	31 ± 1	0.65 ± 0.04*
4.5%	7.37 ± 0.01	14 ± 1*	31 ± 1	0.74 ± 0.02*

Recovery				
Time after return to room air (min)	pH	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)	Fractional extraction
2	7.28 ± 0.01*	71 ± 7*	36 ± 2*	0.13 ± 0.02*
4	7.29 ± 0.01*	86 ± 4	33 ± 2	0.15 ± 0.03*
6	7.30 ± 0.01*	85 ± 4	33 ± 2	0.20 ± 0.03*
8	7.31 ± 0.01*	87 ± 5	31 ± 1	0.23 ± 0.04*
10	7.31 ± 0.01*	88 ± 5	32 ± 1	0.25 ± 0.02*
15	7.32 ± 0.01*	86 ± 6	31 ± 1	0.35 ± 0.04*
20	7.33 ± 0.01*	86 ± 5	30 ± 1	0.44 ± 0.04
30	7.35 ± 0.01	87 ± 5	31 ± 1	0.47 ± 0.04

* = $p < 0.05$.

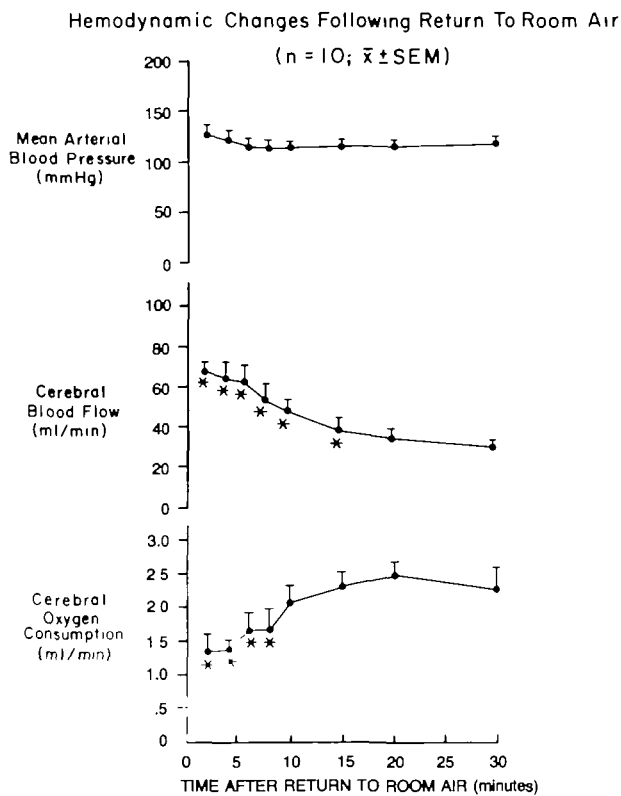Hemodynamic Changes Following Return To Room Air

(n = 10; x̄ ± SEM)

FIGURE 2. Hemodynamic and cerebrovascular changes to a progressive decrease in inspired oxygen concentration (21, 10, 6, 5, and 4.5% O_2) is shown (n = 10, mean ± SEM). Animals were returned to room air when the amplitude of SEP decreased to less than 20% of control. Differences from control value (* = p < .05) were evaluated using analysis of variance for repeated measures.

Hemodynamic Changes During Hypoxia (n=10; x̄ ± SEM)

FIGURE 3. Hemodynamic and cerebrovascular changes following return to room air are shown (n = 10, mean ± SEM). Animals were returned to room air after the SEP amplitude had decreased to < 20% of control. Determinations were made 2, 4, 6, 8, 10, 15, 20 and 30 minutes after reoxygenation. Differences from control value (* = p < .05) were evaluated using analysis of variance for repeated measures.

PaO_2 of 19 ± 1 mmHg but then decreased to 160% of control as PaO_2 was reduced to 14 ± 1 mm Hg. $CMRO_2$ was reduced (75% of control) at PaO_2 of 19 ± 1 mmHg and was 54 and 36% of control at PaO_2 of 17 ± 1 and 14 ± 1 mmHg, respectively. Two minutes following the return of the animal to room air breathing, PaO_2 was increased to 71 ± 7 mmHg and by 4 minutes was at the control value (86 ± 4 mmHg) (table 1). Brain oxygen extraction did not return to normal until 20 minutes after reoxygenation (table 1). Following reoxygenation, CBF was elevated and required 20 min to return to its control value, whereas $CMRO_2$ had returned to control by 10 min (figure 3). MABP decreased immediately after reoxygenation and remained unchanged over the 30 minute period.

The relationship between amplitude (P1N1) and latency (N1, P2) of the SEP and $CMRO_2$ during hypoxia and recovery is shown in figure 4. Hypoxia (PaO_2 = 14 ± 1 mmHg) decreased P1N1 amplitude to 17% of control, increased N1 latency to 111% of control, and increased P2 latency to 107% of control. As PaO_2 decreased to the lowest level (14 ± 1 mmHg), EEG progressively slowed and showed electrocortical silence or prolonged burst suppression (5–10 sec) occurred when the SEP amplitude was decreased to 17% of control. Two minutes after reoxygenation, P1N1
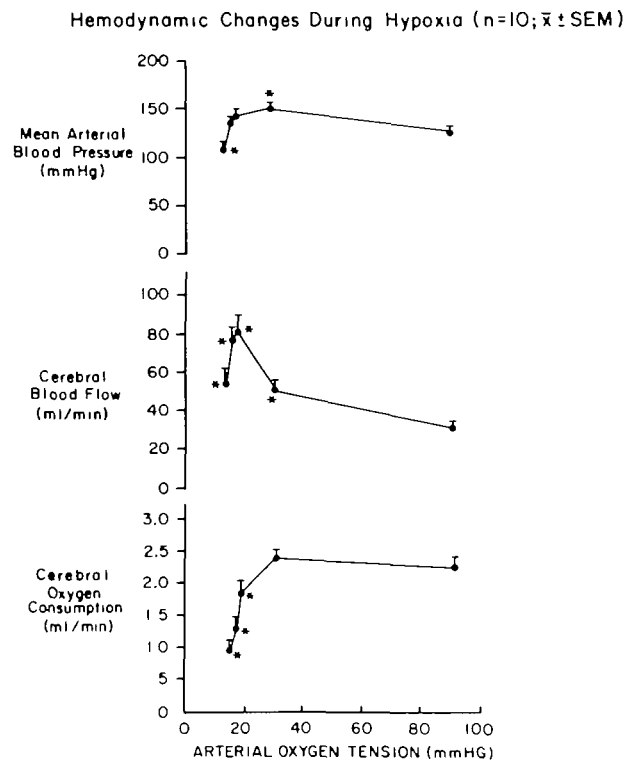
amplitude had increased to 53% of control while N1 latency was still elevated at 112% of control, and P2 latency was 109% of control (fig. 4). Thirty minutes after reoxygenation, P1N1 amplitude, and N1 and P2 latency had returned to control values.

Table 2 shows the slope of changes in $CMRO_2$ and changes in latency of N1 and P2 and amplitude P1N1 in individual animals during both hypoxia and recovery. It can be seen that the slopes of these responses are similar in the group of animals and that a correlation exists in each animal. The values during hypoxia and recovery were pooled in each animal. The average slope of latency N1 versus $CMRO_2$ is −0.46 ± 0.19 (95% confidence interval), P2 versus $CMRO_2$ is −0.19 ± 0.13, and amplitude vs $CMRO_2$ N1P2 is 0.15 ± 0.06.

Discussion

The model of cerebral oxygen deprivation (hypoxic hypoxia) differs from other models used to assess changes in SEP, oligemia,[6] and increased tissue pressure[11] because increases in CBF may preserve oxygen delivery to the brain despite low oxygen content of blood. Previous studies have related SEP and CBF without assessment of $CMRO_2$.[6, 11] In those studies, the insult was delivered over a prolonged period of time and the experimental design excluded cerebral com-
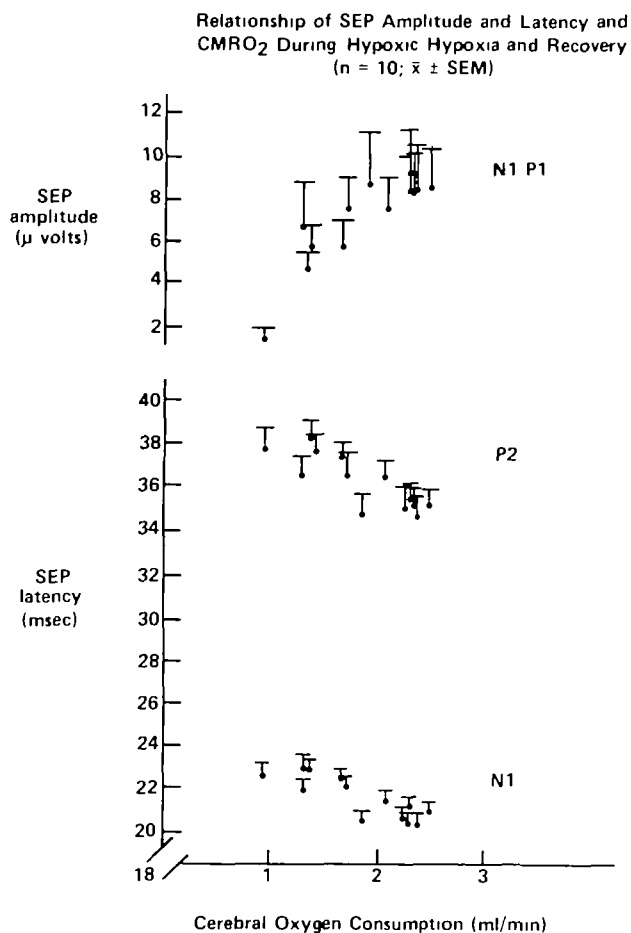
Relationship of SEP Amplitude and Latency and
CMRO₂ During Hypoxic Hypoxia and Recovery
(n = 10; x̄ ± SEM)

Cerebral Oxygen Consumption (ml/min)

FIGURE 4. *Relationship of SEP amplitude and latency and cerebral oxygen consumption during hypoxic hypoxia and recovery (n = 10; mean ± SEM). The relationship of SEP amplitude and latency are plotted for each level of hypoxia (21, 10, 6, 5, and 4.5% O₂) and following reoxygenation (2, 4, 6, 8, 10, 15, 20 and 30 minutes).*

pensatory mechanisms such as an increase in CBF in response to cerebral oxygen deprivation. Adequate cerebral O₂ delivery and utilization (CMRO₂) can be maintained at low PaO₂ if oxygen carrying capacity is adequate and CBF can increase sufficiently.[15] In addition to an increase in CBF, an increase in fractional oxygen extraction also serves to maintain cerebral oxygen delivery constant in a variety of circumstances.[17]

Since the venous outflow assesses both blood flow and metabolism from the cerebral hemispheres, values determined by this method should reflect the environment in the cortical area of generation of the cortical SEP waves.

In this study, parameters used to generate the SEP (band pass filter; number of stimuli) were chosen to emphasize the cortically generated waves. A recent report demonstrates that cortical components of the SEP are more sensitive to oligemia than are subcortical components.[18] Additionally, failure of cortical SEP components and spontaneous cortical activity (EEG) at a similar level of oxygen deprivation is consistent with previous reports.[19] Transient loss of SEP with rapid

return with normalization of O₂ delivery and good correlation with neurological outcome has been shown.[20]

The present experiments evaluated the adequacy of O₂ delivery and its effect on SEP in a rapidly changing situation. The stress of O₂ deprivation was rapid and reoxygenation was accomplished quickly at a point of exhaustion of cerebral compensatory mechanisms (increased CBF). Lack of equilibration could appear to decrease the relationship of the changes in cerebral O₂ uptake and parts of the SEP waveform. However, despite the potential for a non steady state condition, changes in SEP were well correlated with CMRO₂. The parameters used to acquire SEP data allowed data acquisition in 30–45 seconds and should minimize the effect of changes of neural function occuring during the data acquisition period. It is unlikely that oxygen deprivation of peripheral structures (peripheral nerve or spinal cord) contributed to the SEP changes noted. The spinal cord components of SEP are less sensitive than cortical components during ischemia[21] and during hypoxic hypoxia.[22]

The SEP was evaluated for changes of both amplitude and latency. Latency of waves from peripheral nerve to the cortex is a function of white matter and the amplitude of the cortical waves is primarily a function of gray matter. Amplitude of SEP is easier to evaluate visually than latency, particularly in a situation of rapid change. Early parts of the SEP wave, representing arrival of the afferent volley at the cortex, were chosen for evaluation because of their constancy in this preparation and the resistance of these early wave to anesthetic drugs[23, 24] which make them preferable to later waves for intraoperative or intensive care monitoring. Our studies demonstrate that changes in wave latency correlated well with CMRO₂. The delay from peripheral nerve to cortex increased as O₂ availability was decreased and then decreased toward normal as O₂ became available following reoxygenation. The change in latency N1 from room air to severe hypoxia was 11% and the latency of P2 was changed by 8%. The magnitude of amplitude change was much greater (84% decrease) and changes in amplitude (p1N1) appears to be a more reliable indicator than changes in latency (as indicated by a more narrow confidence interval of the slope). For rapid assessment of CMRO₂ change, amplitude appeared preferable because of the much larger change.

The recovery phase of this experiment is particularly important. In this circumstance, changes in SEP correlated with decreased CMRO₂ due to metabolic impairment, when cerebral O₂ delivery was normal. Hence, alteration in CBF and cerebral O₂ availability do not alter SEP unless CMRO₂ is decreased whether due to limited O₂ availability or metabolic impairment. A potential area of usefulness of SEP monitoring is the brain injured patient. Since SEP is related to brain metabolic function, regardless of CBF or cerebral oxygen availability, it may be a useful tool to assess brain function during the period following brain injury in which hyperemia may be followed by oligemia. Hence a measure of function (SEP) might be more useful than

TABLE 2 *Correlation of $CMRO_2$ with Wave Parts in Individual Animals*

Dog	Latency N1			Latency P2			Amplitude P1N2		
	Slope	T	P	Slope	T	P	Slope	T	P
1	−0.45	−6.60	0.001	−0,08	−1.02	NS	0.19	3.76	0.003
2	−0.36	−2.57	0.03	−0.28	−3.11	0.01	0.16	3.40	0.005
3	−1.28	−3.29	0.01	−0.51	−2 97	0 02	0.18	1 29	NS
4	−0.28	−1.65	NS	−0.10	−2.14	0.05	0.13	0.85	NS
5	−0 46	−17.30	0.001	−0.30	−5.39	0.001	0.09	5 18	0 001
6	−0.27	−2.26	0.05	−0.18	−1.53	0 14	0.20	2.32	0.04
7	−0.21	−2.48	0.04	−0.19	−3.26	0.01	0 10	2.10	0.05
8	−0 53	−2.85	0.02	−0.30	−1.55	NS	0.24	2 08	0.05
9	−0.57	−4.19	0.001	−0.13	−1.94	0.07	0.70	1.54	NS
10	−0.77	−5.59	0.001	−0.35	−4.36	0.001	0.26	2.99	0.01

The slope of comparisons of $CMRO_2$ and amplitude and latency for each animal was assessed by combining values during hypoxia and reoxygenation and a regression line determined using a microcomputer. The difference of the slope from zero was determined using a student's t-test.

CBF measurement in such circumstances. Validation of a clinically useful non-invasive method of assessing return of CNS function regardless of CBF will allow therapeutic manipulation to be based on such evaluation. The use of the SEP as a monitor gives more information than intracranial pressure, cerebral perfusion pressure or even CBF concerning brain function.

The cerebrovascular, cerebral metabolic and electrical (EEG) responses and recovery to hypoxic hypoxia are similar to those noted previously[25] although we produced a more severe degree of hypoxia. The degree of hypoxic stress in our study was greater than in that study by effects on both $CMRO_2$ and EEG amplitude. The time course of return of brain high energy compounds to control reported previously[25] are similar to the return of the brain's ability to use O_2 (fractional oxygen extraction) in the present study. We have shown that the SEP reflects cerebral O_2 deprivation, even in a non-steady state situation.

It is important to note that both return of CBF and the ability of the brain to extract oxygen (fractional extraction) returned slowly toward control. Indeed, correlation of SEP components with $CMRO_2$ when the brain was metabolically impaired (increase CBF, decrease ability to extract oxygen) substantiates the importance of SEP as a monitor of O_2 adequacy. Studies using oligemic methods stress a pressure threshold of CBF resulting in changes of either spontaneous (EEG) or evoked electrical activity (SEP). The information developed during the recovery period verifies that SEP reflects brain function regardless of CBF.

These data are relevant to clinical assessment of the brain injured patient. Although severe hypoxia was necessary to alter the SEP, the SEP was depressed only when cerebral oxygen availability was limited. In addition to lowered PaO_2, decreased oxygen carrying capacity (Anemia), and lowered cerebral blood flow may lower cerebral oxygen delivery. Our study supports the concept that any combination of oxygen carrying and cerebral blood flow which limits cerebral oxygen delivery will be demonstrated by alteration in

SEP and correction of the abnormality will return the SEP toward normal. Indeed, uses of changes of SEP to evaluate therapy appears useful when other currently used methods are inadequate or not feasible. SEP evaluation is possible without movement of the patient to special facilities, and is useful at a stage of disease when other methods are too complicated (PET Scanner), or provide inadequate information concerning CBF, $CMRO_2$, or cerebral perfusion pressure.

In the brain injured patient, normal and acceptable values of MABP, ICP, CBF are determined based on the expected values for the patient rather than knowledge of normal, "control", values for that patient. In the same context, "normal" values for brain electrical activity must frequently be presumed and therapy maneuvers undertaken to return the values toward that presumed normal value. Indeed, we and others,[1-15] have used non-normal, that is SEP altered by anesthetic agents to prevent or diagnose neurological injury.

We have shown that evoked electrical activity of the brain is progressively altered by O_2 deprivation when $CMRO_2$ is decreased and returns to normal as the brain's ability to utilize oxygen is restored. This suggests that SEP monitoring may be useful during oxygen deprivation and recovery to assess adequacy of cerebral O_2 delivery and the ability of the brain to use available oxygen.

Acknowldgments

References

1. Mahla ME, Long DL, McKennett J, Green C, McPherson RW: Detection of brachial plexus dyfunction by somatosensory evoked potential monitoring. A report of two cases Anesthesiology 60: 248–252, 1984
2. McPherson RW, Szymanski J, Rogers MC. Somatosensory evoked potential changes in position related brainstem ischemia. Anesthesiology 61: 88–90, 1984
3. McPherson RW, North RB, Udvarhelyi GB, Rosenbaum AE: Mi-

grating disc complicating spinal decompression in an achondroplastic dwarf. Intraoperative demonstrating of spinal cord compression by somatosensory evoked potentials. Anesthesiology **61:** 764–767, 1984

4. Symon L, Wang AD, Costa DeSilva IE, Gentile F: Perioperative uses of somatosensory evoked responses in aneurysm surgery. J Neurosurg **60:** 269–275, 1984

5. McPherson RW, Niedermeyer EF, Otenasek RJ, Hanley DF: Correlation of transient neurological deficit and somatosensory evoked potentials after intracranial aneurysm surgery. J Neurosurg **59:** 146–159, 1983

6. Branston NM, Symon L, Crockard HA, Pasztor E: Relationship between cortical evoked potential and local cortical blood flow following acute middle cerebral artery occlusion in the baboon Experimental Neurology **45:** 195–208, 1974

7. Meldrum BS, Brierley JB: Brain damage in the rhesus monkey resulting from profound hypotension. Changes in spontaneous and evoked electrical activity of the neocortex. Brain Research **13:** 101–118, 1969

8. Nagao S, Roccaforte P, Moody RA: The effects of isovolemic hemodilution and reinfusion of packed erythrocytes on somatosensory and visual evoked potentials. J Surg Research **25:** 530–537, 1978

9. McKay AR, Hosbrichi Y, Williston JS, Jewett D: Brainstem auditory evoked response and brainstem compression. Neurosurgery **6:** 632–638, 1980

10. Colin F, Bourgain R, Maril J: Progressive alterations of somatosensory evoked potential waveforms with lowering of cerebral tissue PO_2 in the rabbit. Archives Internationales de Physiologie et de Biochimie **86:** 677–679, 1978

11. Bennett MH, Albin MS, Bunegin L, Dujovny M, Hellstrom H, Janetta PJ. Evoked potential changes during brain retraction in dogs. Stroke **8:** 487–492, 1977

12. Rapela CE, Green HD: Autoregulation of canine cerebral blood flow Circ Res **14:** 1205–1211, 1964

13. Traystman RJ, Rapela CE: Effect of sympathetic nerve stimulation on cerebral and cephalic blood flow in Dogs. Circ Res **36:** 620–630, 1975

14. Traystman RJ, Fitzgerald RS. Cerebrovascular response to hypoxia in baroreceptor and chemoreceptor denervated Dogs. Am J Physiol **241:** H724–H731, 1981

15. Traystman RJ, Fitzgerald RS, Loscutoff SC: Cerebral circulatory responses to arterial hypoxia in normal and chemodenervated dogs. Circ Res **42:** 649–657, 1978

16. Scheffe H: The Analysis of Variance, John Wiley and Sons, New York, 1959, p 221–258

17 Jones MD Jr, Traystman RJ: Cerebral oxygenation of the fetus, newborn and adult Seminars in Perinatology **8:** 205–216, 1984

18. Branston NM, Ladds A, Symon L, Wang AD. Comparison of the effects of ischemia on early components of the somatosensory evoked potentials in brainstem, thalamus and cerebral cortex. J Cerebral Blood Flow and Metabolism **4:** 68–81, 1984

19. Gregory PC, McGeorge AP, Fitch W, Graham DI, MacKenzie ET, Harper AM: Effects of hemorrhagic hypotension on the circulation. Electrocortical function. Stroke **10:** 719–723, 1979

20. Dong WK, Bledsoe SW, Eng DY, Nearner JE et al: Profound arterial hypotension in dogs. Brain electrical activity and organ integrity. Anesthesiology **58:** 61–71, 1983

21. Sato M, Pawlik G, Umbach C, Heiss W Comparative studies of regional CNS blood flow and evoked potentials in the cat. Stroke **15:** 97–101, 1984

22. Kobrine AI, Evans DE, Rizzoli HV: Relative vulnerability of the brain and spinal cord to ischemia. J Neurological Sciences **45:** 65–72, 1980

23. Clark DL, Rosner BS: Neurophysiologic effects of general anesthetics Anesthesiology **38:** 564–582, 1973

24. Sutton LN, Freiven T, Marsh R, Joggi J, Bruce DA: The effects of deep barbiturate coma on multimodality evoked potential. J Neurosurg **57:** 178–185, 1982

25. Artru AA, Michenfelder JD: Canine cerebral metabolism and blood flow during hypoxemia and normoxic recovery from hypoxia J Cerebral Blood Flow and Metabolism **1:** 277–283, 1981