Reperfusion Hyperoxia in Brain after Circulatory Arrest in Humans

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Changes in the electroencephalogram (EEG), mean arterial blood pressure (MABP), and hemoglobin saturation in brain vasculature of lightly anesthetized normothermic humans undergoing induced circulatory arrest for implantation of an automatic internal cardioverting defibrillator were studied. EEG was measured using a four-channel bipolar montage and hemoglobin saturation was measured transcranially using reflectance spectroscopy at 760 nm with an isosbestic reference at 800 nm. Hemoglobin saturation of blood in the quadriceps muscle was also measured. Thirty-two episodes of hypotension due to ventricular fibrillation were studied along with 31 episodes of hypotension related to ventricular tachycardia and rapid ventricular pacing. In a typical fibrillatory event there was a decrease in MABP followed almost immediately by changes in hemoglobin saturation of blood in the brain vasculature. The first changes in EEG were detected an average of 6.5 s ($P < 0.001$, paired t test) after the beginning of change of brain vascular hemoglobin. In some cases changes in hemoglobin saturation could be detected without changes in EEG. Desaturation curves from muscle and brain were significantly different, suggesting that the brain probe was measuring hemoglobin change in a rapidly metabolizing volume of tissue that was dissimilar to the skin, muscle, and bone monitored by the probe over the quadriceps muscle. Examination of the 32 episodes of circulatory arrest revealed a marked response that began immediately with recirculation characterized by an increase of the hemoglobin saturation signal from brain vasculature to above baseline as the duration of circulatory arrest exceeded 37 s, this response is termed reperfusion hyperoxia. When the duration of circulatory arrest was less than 37 s, hemoglobin saturation returned to baseline without a period of reperfusion hyperoxia. An early response to reperfusion after cardiac arrest characterized by a marked increase in brain vascular hemoglobin saturation was identified. This event may have significance in understanding the events leading to brain failure. (Key words: Brain: complete ischemia. Heart: cardiac arrest. Measurement techniques: hemoglobin spectroscopy.)

DESPITE the rapidity with which complete cessation of cerebral circulation produces loss of neuronal function and irreversible brain damage, few studies have examined the changes that occur with brief episodes of circulatory arrest and reperfusion; no such observations have been reported in humans. Experimental reports of specific aspects of neuronal recovery after 1 h of complete ischemia exist; however, normothermic patients having cardiac arrest of greater than 10 min duration often have very poor neurologic outcomes. Examination of the earliest changes that occur with circulatory arrest and reperfusion, particularly following cardiac arrest of brief duration, could provide information that might contribute to an understanding of those factors that lead to brain damage. Because neurologic function and oxygen availability are closely related and loss of oxygen appears to be a key initiator of brain damage, we examined the relationship between a measure of neuronal function and brain oxygenation during 32 episodes of induced ventricular fibrillation lasting 20–80 s in lightly anesthetized, normothermic patients undergoing operation for insertion of automatic internal cardioverting defibrillators (AICD). An additional 31 episodes of hypotension due to pacing and nonfibrillatory tachyarhythms were also studied. Neuronal function was assessed by recording and analyzing the spontaneous EEG. Brain oxygenation was assessed by measuring brain vasculature hemoglobin saturation using dual wavelength in vivo reflectance spectroscopy. This variable is not a measure of arterial saturation as is pulse oximetry; rather, it reflects changes in relative hemoglobin saturation in the "nutritional circulation" (arterioles, capillaries, and venules).

Methods

These studies were approved by the University of Pennsylvania Committee on studies involving Human Beings, and written informed consent was obtained from each subject. The subject population consisted of five patients undergoing implantation of AICD. One patient was studied twice during two separate operations so that the data include the results of six studies. No attempts were made to alter the anesthetic management of these patients. Arterial and peripheral venous catheters were inserted preoperatively. Tracheal intubation was performed after induction of anesthesia (table 1) and muscle relaxation with succinylcholine (100 mg) or vecuronium (8–12 mg). Esophageal temperature was measured throughout the operation. Prior to induction of anesthesia, EEG electrodes and optical probes to measure hemoglobin saturation were placed. For the EEG a four-channel bipolar montage consisting of Fp1-C3, C5-O1, Fp2-C4, and C4-O2 was recorded using gold cup electrodes affixed with col...
Table 1. Subject Characteristics and Anesthetic Drugs

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Other Problems</th>
<th>Premedication</th>
<th>Induction TPL (mg)†</th>
<th>Maintenance Isoflurane (%)‡</th>
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</thead>
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<tr>
<td>1</td>
<td>66</td>
<td>M</td>
<td>V tach</td>
<td>CAD</td>
<td>None</td>
<td>250</td>
<td>0.5–3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Cardiac A</td>
<td>MI × 3</td>
<td></td>
<td></td>
<td>MS 5 mg</td>
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<tr>
<td>IA*</td>
<td>21</td>
<td>F</td>
<td>Cardiac A</td>
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<td>None</td>
<td>200</td>
<td>0.2–0.5‡</td>
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<td></td>
<td></td>
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<tr>
<td>3</td>
<td>28</td>
<td>M</td>
<td>Multiple episodes of V tach after MI</td>
<td>Anterior wall MI</td>
<td>MS 7 mg im</td>
<td>300</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td>CHF</td>
<td>MS 10 mg im</td>
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<td>0.4–1.3</td>
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<tr>
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<td></td>
<td></td>
<td></td>
<td>Mild anoxic encephalopathy</td>
<td>MID 1.5 mg iv</td>
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<td>0.3–1.3</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cardiomyopathy</td>
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<td></td>
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<tr>
<td>4</td>
<td>66</td>
<td>M</td>
<td>Replacement of AICD unit Recurrent V tach V tach Cardiac A</td>
<td>CHF</td>
<td>None</td>
<td>By mask‡</td>
<td>0.3–0.6</td>
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<td>83</td>
<td>M</td>
<td>MI</td>
<td>MS 5 mg im</td>
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<td>0.3–1.3</td>
<td>1.2</td>
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<td></td>
<td>Scopolamine 0.3 mg</td>
<td>Fentanyl 0.1 mg iv</td>
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</tbody>
</table>

V tach = ventricular tachycardia; Cardiac A = cardiac arrest; CAD = coronary artery disease; MI = myocardial infarction; CHF = congestive heart failure; TPL = thiopental; MS = morphine sulfate; MID = midazolam.

* Same subject, second operation about 1 week after the first.
† Except as noted.
‡ Required intermittent phenylephrine to maintain arterial blood pressure.
§ Given in the operating room to treat excessive anxiety and movement.
¶ Patient required dopamine infusion to maintain arterial blood pressure, anesthetic induction by mask using nitrous oxide, and up to 0.4% isoflurane. Nitrous oxide was discontinued after induction.

lodion. The EEG locations were measured according to the International 10-20 system. Electrode impedance was less than 5 Kohms. Two optical probes were used to compare the responses of hemoglobin in the brain and muscle vasculature. One optical probe was positioned over the anterior aspect of the quadriceps muscle, and another was placed at the hairline over the left frontal cortex. The placement of the head optical probe varied depending on the hair line, but the probe was placed as high as possible on the forehead or anterior portion of the skull. The probes were covered with opaque towels to decrease potential signal contamination by ambient light. At least 1 h elapsed between induction of anesthesia and the onset of the study. At the time of the study anesthesia in all patients was being maintained with a low dose of a potent inhalational agent in 100% oxygen.

Measurement of hemoglobin saturation in brain and muscle vasculature was made noninvasively using separately balanced and calibrated, time-shared, dual wavelength (760 and 800 nm) reflectance spectrometers that were based on designs of Chance et al.9,10 Wan et al.11 demonstrated the passage of a significant fraction of light in the 750–800 nm range through 9–13 mm of human skull and scalp. The penetration depth of this deep red light (800 nm) through brain (without hemoglobin) is 3 times that of light in the blue/green part of the spectrum.12,13 (The penetration depth is defined as the distance at which optical power is reduced by 63% of the incident power.) Recent data from our laboratory has demonstrated that red laser light will migrate 21 ± 1 cm through adult human brain before reemerging when input and output are separated by 3 cm (unpublished observations). In the spectrometer used for this study, light is supplied by a probe (fig. 1) containing two small incandescent bulbs arrayed 30 mm from two 2 mm² silicon diode photodetectors. This probe is placed on the skin overlying the organ of interest. The two photodiodes are juxtaposed and rubber dams between the light emitters and detectors and around the circumference of the probe minimize light leaks and specular reflections. Increasing absorbance at 760 nm represents increases in deoxyhe-

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**Fig. 1.** A side view of the optical probe in relation to skin, skull, and brain. The arrows suggest several of many potential reflected photon paths from emitter to detector. Reprinted from NIM, Inc., patents pending, with permission.
moglobin while increasing absorbance at 800 nm (an isosbestic point) represents increases in total hemoglobin (oxy plus deoxy). The difference between the absorbances at the two wavelengths is directly related to deoxyhemoglobin concentration corrected for increases in total hemoglobin (such as would occur with vasodilation). The technique assumes that other heme absorbing compounds are absent or present in negligible concentrations (i.e., <5%) and that the contribution from cytochrome aa₃ is small (a reasonable assumption for the wavelengths used).¹⁴

The device is sensitive to all hemoglobin present in the tissue of interest (arterial, arteriolar, capillary, venular, and venous) and thus differs from pulse oximetry, which measures only arterial hemoglobin saturation. However, in view of the much larger volume of arterioles, capillaries, and venules, the probability of a photon entering a larger pulsating vessel is small¹⁵⁻¹⁷; thus, the majority of emerging photons represent passage through the nutritional circulation. The emerging signal represents the summed absorbances of all tissues through which the light passes, though the brain would make a significantly larger contribution than the skin, muscle, and bone overlaying the brain because of its larger mass and greater vascular volume.¹⁸⁻²⁰ Hemoglobin saturation calculated with this technique correlates well with saturation determined from sagittal sinus hemoglobin saturation in the hypoxic dog (unpublished data) and with mixed venous saturation in infants during cardiopulmonary bypass.²¹,²² The extraction of oxygen from the nutritional circulation by actively metabolizing tissue ensures that the measured saturation will be less than 100% even when a subject is breathing 100% oxygen (unlike arterial hemoglobin saturation measured with a pulse oximeter), and in some situations (as will be shown) saturation can increase to above the baseline measurement. In addition, because path length is not known, the absolute saturation is also unknown, but rather a relative saturation, calculated from the minimal and maximal measurable values, is obtained. Our experience suggests that these values appear to be consistent for a given subject, and Kurth et al.²¹,²² have demonstrated good between-subject reproducibility in the neonate.

Each patient underwent as many as 20 brief episodes of hypotension secondary to induced ventricular arrhythmias, including ventricular fibrillation, ventricular tachycardia, and rapid ventricular pacing. EEG, arterial blood pressure, and reflectance changes were recorded continuously during these episodes. The signals from all four sources were digitized continuously at 128 Hz allowing simultaneous comparison of rapid changes in blood pressure, brain and muscle hemoglobin saturation, and EEG.

Both analog and quantitative EEG data were used for the data analysis. The EEG data were collected using a bandwidth of 1–35 Hz. The data were digitized at 128 Hz and power spectrum analysis was performed on 2-s epochs of data and displayed as a density modulated spectral array (DSA).²³⁻²⁵ Hemoglobin saturation is presented as relative optical density. The half-times for hemoglobin desaturation and resaturation were calculated for each episode. In some patients an optical signal was observed to exceed baseline following restoration of cardiac output. This increase in hemoglobin saturation to greater than control values was quantified by computing the ratio of the area of the hemoglobin signal above the baseline level of hemoglobin saturation (reperfusion) to the area below the baseline (circulatory arrest). This ratio, expressed as a per cent, helped correct for inter-subject differences in the absolute value of signal change.

Comparisons were made between the times of onset of EEG change and change in hemoglobin saturation. The time course of changes in hemoglobin saturation in brain and muscle were compared for similarity using the mean-square successive difference test.²⁶ Statistical analysis of desaturation and recovery half-times and onset of variable change was done using the paired t test, and comparisons of EEG to arrhythmia type were made using the chi-square test.

Results

Patient Characteristics

There were five patients in the study. They varied greatly in age and cardiovascular status (table 1). For example, one patient was a previously healthy 21-yr-old woman who had an arrhythmia followed by cardiac arrest during exercise and another patient was a 66-yr-old man with 100% occlusion of the left carotid artery. Mean arterial blood pressure (MABP) prior to induced fibrillation was always greater than 60 mmHg. Arterial oxygen saturation as measured by pulse oximetry was between 99% and 100% during the nonarrest portions of the study period. Esophageal temperature during the studies was 36.4 ± 0.3°C (mean ± SE). No new neurologic deficits were recorded in any of the patients postoperatively.

Relationship Between Blood Pressure, Brain and Muscle Hemoglobin Saturation, and EEG

Figure 2 shows EEG (both DSA and analog, top two panels), MABP (third panel), and hemoglobin saturation from vessels of both brain (fourth panel) and muscle (bottom panel) obtained from one patient during two consecutive episodes of ventricular fibrillation. Defibrillation artifacts are noticeable in the DSA traces. The MABP decreased from approximately 63 mmHg to about 20 mmHg, and no pulsatile pressure waveforms were seen during either episode. During the first episode of ven-
tricular fibrillation there was a rapid decrease in MABP due to the arrhythmia. Almost immediately there was a rapid decrease in hemoglobin saturation from brain. Hemoglobin desaturation from muscle began about 2 s after the onset of changes in the brain and the changes in optical density in muscle were of lesser magnitude. The signals from both probes rapidly returned toward baseline with restoration of MABP. EEG changes began 10 s after the onset of hypotension (about 8 s after the onset of changes in brain hemoglobin saturation). Note that the EEG appears to be nearly isoelectric during part of the ischemic episode, confirming the severity of the ischemia.

Figure 3 shows data from another patient. Overall, the response was similar to that described previously; however, in this case signal changes from the head clearly preceded both the EEG changes and the hemoglobin changes from muscle. With recovery of MABP there was a marked hyperoxic response in which the optical signal from the head exceeded the baseline, indicating that hemoglobin oxygen saturation in the vessels of the brain had increased. No comparable response was recorded by the probe overlying the muscle.

**Hyperxia During Reperfusion**

Figure 4 summarizes 32 episodes of circulatory arrest from the six studies and demonstrates that episodes greater than about 37 s duration were associated with hyperxia during reperfusion. This figure includes all episodes of ventricular fibrillation that occurred in the six studies. Four of the six subjects had ventricular fibrillation durations greater than 37 s, and those longer duration events tended to show reperfusion hyperxia. In contrast, none of the fibrillation events lasting less than about 37 s showed reperfusion hyperxia.
LOCALIZATION OF THE OPTICAL SIGNAL

The mean times from the onset of hypotension to the first change in the hemoglobin saturation recorded from head and muscle vascularization were 8.3 ± 0.4 s (mean ± SE) and 11.4 ± 2.0 s, respectively; differences that were not statistically significant. The half-times for desaturation and recovery determined for brain and muscle, 13.1 ± 1.0 s (brain) compared with 15.8 ± 1.9 s (muscle, mean ± SE, desaturation) and 16.4 ± 1.8 s compared with 17.1 ± 1.8 s (recovery), were not statistically different. Even though these specific measures were similar, when the entire desaturation response from brain and muscle was compared for the 63 episodes of ventricular fibrillation or tachycardia, in no case were the response curves similar (P < 0.0001), suggesting that the tissues interrogated by the two probes had different characteristics. This suggests that tissue other than skin, muscle, and bone was being transilluminated by the probe over the head.

SENSITIVITY OF THE OPTICAL MEASUREMENTS

Figure 5 shows changes in EEG, MABP, and optical signals from the head probe during two episodes of ventricular fibrillation and one episode of rapid ventricular pacing (right-most event). Note the presence of pulsatile waves in the blood pressure trace confirming the presence of effective cardiac ejection. It can be seen that a decrease in MABP from 75 to about 40 mmHg was mirrored by changes in the head probe signal consistent with hemoglobin desaturation. In contrast, no change was seen in the EEG. Of 32 episodes of hypotension due to ventricular fibrillation, EEG changes could be identified in 23 (72%). For the entire study population (63 events), EEG changes were observed during only 48% of the hypotensive events that produced changes in the brain probe; 80% of these changes occurred during episodes of ventricular fibrillation. This incidence of EEG change in relation to the type of arrhythmia is statistically significant (P < 0.001 by chi-square) and is similar to that reported previously.27 In addition, changes in the optical signal recorded from brain vascularization preceded EEG changes by 6.5 s (P < 0.001 by paired t test).

Discussion

We have demonstrated that a new noninvasive transcranial reflectance spectrometer can track changes in brain hemoglobin saturation during circulatory arrest and hypotension in humans. The changes in optical signals correlate with changes in MABP and EEG, and there is sufficient time resolution (an instrument time constant of 1 s) so that the rapidly evolving events that occur during 20–60 s of circulatory arrest can be resolved. In addition, we have described a hyperoxic response during reperfusion after circulatory arrest lasting longer than 37 s. Before discussing the implications of these findings, a brief discussion of the instrument and its limitations is appropriate.

DUAL-WAVELENGTH REFLECTANCE HEMOGLOBINOMETRY

The spectrophotometry of cell suspensions or tissues was facilitated by the invention of the dual-wavelength spectrophotometer in 1951.28 This was immediately applied to the study of absorbance changes during stimulation in the perfused frog sartorius muscle29,30 and in other muscles.31 These studies showed that the redox states of cytochromes could be clearly delineated in resting and stimulated perfused tissues. Reflectance spectrophotometry of hemoglobin of blood in rat brain showed deoxygenation of hemoglobin to precede the reduction of nicotine adenine dinucleotide (NAD).32

The advances in this area of research were furthered by the development of time-sharing dual-wavelength spectrophotometers capable of quantitating small changes in absorption in highly scattering media.3,10 The use of deep red or near-infrared light was suggested by the work of Butler and Norris33 who measured light transmission through dense light scattering samples. The application of these techniques to noninvasive in situ tissue monitoring, particularly of brain, was pursued by Jobsis et al.34,35 who developed a multiwavelength near-infrared device to estimate hemoglobin saturation, brain blood volume, and the redox state of cytochrome aa3, which is the ter-
minal oxygen acceptor of the cytochrome transport chain. This approach relies (as does ours) on the relative transparency of tissue at wavelengths between 750 and 900 nm, a region that contains specific absorption maxima for oxyhemoglobin, deoxyhemoglobin, and cytochrome aa3. Despite scattering, the concentration of these absorbing compounds is proportional to absorbance if the changes are small.\textsuperscript{56,57} Measurement of absorbance by either transmission or reflectance gives similar results,\textsuperscript{38} although reflectance techniques are best for the large human brain. Overlying skull and skin contribute little to the cytochrome aa3 signal and less than 5% to the hemoglobin signal.\textsuperscript{18,19} Our results confirm these findings in humans in that signals from the probe over the brain were statistically different from the signals arising from the muscle probe and that the brain signals were associated with changes in the EEG. Note that the change in saturation of vasculature hemoglobin in the quadriceps muscles was small compared with that seen in brain. A much larger change in saturation of muscle vasculature has been observed with 5–10 min of tourniquet ischemia.\textsuperscript{39}

Considerable attention has been given to the measurement of cytochrome aa3 because this cytochrome is the mitochondrial oxygen receptor and changes in its redox state should directly reflect the adequacy of cell oxygenation.\textsuperscript{54,55} However, the wavelength for cytochrome aa3 absorbance overlaps that of hemoglobin, and cytochrome aa3 absorption is less than 10% of the hemoglobin absorption. Thus, even at the most appropriate wavelengths for deconvoluting signals from the two compounds, a correction is needed for hemoglobin overlap. Algorithms to deconvolute cytochrome and hemoglobin absorption changes have been developed, but the success of this approach is a matter of continuing controversy.\textsuperscript{40,41}

Despite these continuing problems, measurement of cytochrome aa3 has been reported for monitoring brain oxygenation during cardiopulmonary bypass\textsuperscript{49} and other operations.\textsuperscript{43} In addition, Glaister \textit{et al.}\textsuperscript{44} reported measurement of brain hemoglobin and cytochrome aa3 in volunteers undergoing high gravity acceleration, and others have used similar approaches to monitor preterm infants in intensive care units.\textsuperscript{45–48}

Our approach has been to return to the simple dual-wavelength method in which one of the wavelengths is at an isobestic point between oxyhemoglobin and deoxyhemoglobin and the other is at a nearby maximum of the difference spectrum. This simplifies the instrument required and the hemoglobin dominance virtually eliminates the need to correct for interfering signals.

The choice of hemoglobin as an indicator of oxygen delivery to the tissue is well founded in physiology and biochemistry. Photons can travel through a number of capillaries and emerge in the detector area without excessive attenuation; thus, changes in deoxyhemoglobin concentration will produce proportional changes in the intensity of the reflected light. Because oxygen gradients between capillaries and mitochondria are thought to be steep, the degree of deoxygenation of hemoglobin in the capillary bed would be expected to be linked closely to the oxygen demand of the tissue.

**Quantification of Hemoglobin Changes**

At present this instrument cannot determine absolute concentrations of deoxyhemoglobin, a problem shared by all continuous light spectrometers. Thus, there is the assumption that the initial hemoglobin saturation is adequate and that one is detecting changes from this presumed normal. Quantitation of hemoglobin saturation requires knowledge of path length, and in none of the continuous light spectrophotometers employed in any laboratory has the correct value of the optical path been determined by physical measurements. Most recently, we and others have used picosecond laser pulses to determine the optical path length and penetration depth of light for continuous light instruments of similar geometry, making it theoretically possible to calculate hemoglobin changes from continuous wave optical absorbance recordings.\textsuperscript{20,59,49}

**Neurophysiologic Changes during and after Cardiac Arrest**

There are few studies of cardiac arrest with which to compare our findings. Todd \textit{et al.}\textsuperscript{50} studied 12 min of cardiac arrest in cats. The EEG became flat within 22 s, and after resuscitation it required an average of 26 min for the EEG to reappear. Blomqvist and Wieloch\textsuperscript{51} used intracardiac potassium chloride to produce 5–6 min of cardiac arrest in rats. They noted that the EEG was isoelectric within 15 s, and although the EEG reappeared 15 min after resuscitation, it remained abnormal for at least 6 h. Korf \textit{et al.}\textsuperscript{55} studied cardiac arrest induced with intracardiac magnesium chloride in unanesthetized rats. They found that brain impedance, a marker of decreased extracellular space, increased after 1.5 min of cardiac arrest. In all of these studies the duration of cardiac arrest was considerably longer than in our patients who had rapid return of EEG and developed no new neurologic deficits.

Winn \textit{et al.}\textsuperscript{53} demonstrated a significant increase (2.5-fold) in brain adenosine and a decrease (29%) in phosphocreatine 5 s after aortic transection in rats anesthetized with pentobarbital, and at 10 s there was a significant increase in brain lactate. Five minutes of cardiac arrest in rats\textsuperscript{51} and 5 min of global ischemia in dogs\textsuperscript{54} and rabbits\textsuperscript{55} were associated with markedly increased cerebral blood flow upon restoration of circulation. Whether this is also true for our patients, who had a significantly shorter insult, cannot be determined from our current data because indices of cerebral blood flow were not measured.
In addition, the rapid time course of these intraoperative events would make standard approaches for measuring cerebral blood flow in humans difficult to apply.

Reports of complete ischemia by decapitation, by increasing intracranial pressure, and a variety of reversible techniques for stopping blood flow to the brain that include neck tourniquets and major vessel ligation all suggest that our patients should have had significantly decreased levels of brain energy metabolites during their episodes of circulatory arrest. However, it is difficult to extrapolate further from these animal models, with their higher metabolic rates and differing anesthetic levels, to humans; thus, the exact degree of brain energy compromise in our study cannot be determined.56,57

HYPOXIA DURING REPERFUSION

Of particular interest is the rapid development of reperfusion hypoxia of hemoglobin in brain after circulatory arrest lasting more than 37 s. In contrast, with circulatory arrest of shorter duration, brain vasculature hemoglobin saturation returned to the pre-insult value without this overshoot. Rosenthal et al.68 reported brain vasculature hemoglobin saturation returning to levels above baseline in the brains of cats subjected to 1 min of complete ischemia induced by ligation of major thoracic vessels. They also noted that brain blood volume increased; however, the maximal change in brain blood volume preceded the maximal hemoglobin saturation. Lang et al.69 noted increased oxygen availability (suggesting hyperemia) with as little as 1 min of complete ischemia in the isolated perfused dog brain, and Nair et al.66 showed that brain oxygen tension (as measured with intracerebral microelectrodes) increased above baseline in many gerbils subjected to bilateral carotid ligation for as little as 10–15 s. Previously we have shown a reperfusion hyperoxic response during reperfusion of the ischemic human forearm.60 Inspection of the limb during this hypoxia showed hyperemia as indicated by marked reddening and sensations of warmth noted by the subjects. However, hyperemia may not be the only explanation for our reported increase in brain oxyhemoglobin. A reduced tissue utilization of oxygen may also lead to increased tissue oxygen tension and could explain some of the observations during the earliest stages of reperfusion; however, by itself, reduced oxygen consumption is insufficient to explain the entire time course and duration of the hyperoxic phase.

In summary, we have used a newly developed reflectance spectrometer to measure changes in brain hemoglobin saturation during intraoperative circulatory arrest. This instrument shows changes that correlate well with changes in MAPB and EEG. It is a more sensitive indicator of decreased cerebral perfusion than the EEG. However, it is nonquantitative and its ultimate utility relies on developments that may allow future quantitation of brain oxyhemoglobin. Despite this limitation we have demonstrated a marked increase in brain vasculature hemoglobin saturation upon reperfusion after circulatory arrest lasting longer than about 37 s. The etiologic and physiologic significance of this response is unclear, although it represents the earliest change described during reperfusion after circulatory arrest in humans.

The authors wish to thank the cardiac surgeons and cardiologists for their cooperation and support in making their patients readily available for this study: Iris R. Karasin for her expert secretarial assistance; and NIM, Inc. (Philadelphia, Pennsylvania) who provided the continuous wavelength spectrometers used in this study.

References

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