Cortical Evoked Potential and Extracellular K⁺ and H⁺ at Critical Levels of Brain Ischemia

JENS ASTRUP, M.D.,* LINDSAY SYMON, F.R.C.S.,† NEIL M. BRANSTON, PH.D.,† AND NIELS A. LASSEN, M.D.*

SUMMARY As shown previously, the electrical function of the brain is critically dependent on cerebral blood flow in the sense that reduction below an ischemic threshold of approximately 15 ml/100 gm per minute (approximately 35% of control) in the baboon leads to complete failure of the somatosensory evoked response. This study tests the hypothesis that electrical failure in ischemia may be directly associated with a massive release of intracellular K⁺ or with a critical degree of extracellular acidosis. By microelectrode techniques, measurements of blood flow, extracellular activity of K⁺ and H⁺ as well as evoked potential were made in the baboon neocortex. Reductions in blood flow were obtained by occlusion of the middle cerebral artery and depression beyond the ischemic threshold of electrical function achieved by a reduction of systemic blood pressure which, in the ischemic zones, changed local cerebral blood flow proportionally.

Introduction

THE ELECTRICAL FUNCTION of the brain is intimately related to metabolism and blood flow. Large reductions in cerebral blood flow (CBF) may be tolerated as long as oxygen extraction can be increased and normal metabolic rate sustained. However, at very low levels of CBF, metabolic failure develops and neuronal function ceases. If electrical function is assessed as EEG or evoked cortical potential (EP), a threshold-like relationship between blood flow and electrical function has been described in clinical1-4 as well as in experimental5-8 studies. Thus, in a clinical study1 on patients undergoing carotid surgery, a sudden reduction in cortical blood flow (rCBF) to levels between 11 and 19 ml/100 gm per minute was associated with flattening of the EEG. Branston et al.3 have demonstrated that, in the baboon cortex using the model of acute middle cerebral artery occlusion, a somatosensory evoked response is fully sustained above cortical blood flow (rCBF) levels of 20 ml/100 gm per minute. Below this level the EP ceases and there appears to be a fairly sharp threshold for the abolition of the EP at a flow of about 15 ml/100 gm per minute. Subsequent studies6,9 have shown that the suppression of the EP can be reversed if rCBF is promptly increased to above this threshold.

It is clear, therefore, that electrical function is closely related to rCBF, and it has been suggested that the complete electrical failure below the ischemic threshold is due to synaptic depolarization10 subsequent to a release of cellular potassium to the extracellular space.11 Other conditions, however, also known to be concomitants of ischemia such as a change in neurotransmitter metabolism or tissue lactacidosis, have recently been thoroughly discussed in relation to complete electrical failure.7

Abolition of evoked response could not be explained by depolarization by release of intracellular K⁺, nor was it critically dependent on cortical pH. However, the massive release of intracellular K⁺ was by itself critically dependent on cortical blood flow and occurred at 18 > 6 > 2 ml/100 gm per minute (median with 5% confidence limits). Thus a dual threshold in ischemia for neuronal functions is described, the threshold for release of K⁺ being clearly lower than the threshold for complete electrical failure. Further, the findings support the concept of an ischemic penumbra during which the neurons remain structurally intact but functionally inactive. That neurons can survive for some time in this state of lethargy is evidenced by the observations that an increase in rCBF, if sufficient, can restore evoked potential and normalize extracellular K⁺ activity as well as pH.

The aim of this study therefore was to test the association between electrical function and extracellular activities of K⁺ and H⁺ (Kₑ and pHₑ) at the ischemic threshold of electrical failure.

To achieve this, rCBF was lowered by middle cerebral artery occlusion to approximately the ischemic threshold for the somatosensory evoked response,4 and then manipulated about the threshold by varying systemic blood pressure, while Kₑ and pHₑ were continuously recorded using extracellular microelectrodes5,9

Methods

Animals, Preparations, EP and Hydrogen Electrodes

Four adult baboons (Papio cynocephalus) of either sex, weighing 10 to 16 kg, were used in this study. The techniques of anesthesia and continuous monitoring of basal functions have been described in detail previously.10,11

After tranquilization with intramuscular phencyclidine (Sernylan), anesthesia was induced with a sleep dose of thiopentone and maintained with alpha-chloralose (60 mg per kilogram i.v.). The animals were paralyzed with gallamine triethiodide (1 mg per kilogram i.v.) and respiration maintained with a Starling pump (C. F. Palmer). Systemic blood pressure, arterial pH, Pco₂ and Po₂, and end-tidal CO₂ were monitored. The exposure of the middle cerebral artery through the orbit and the exposure of the middle cerebral artery was clipped under direct vision close to its origin, with a small Scoville clip. Normal levels of arterial Pco₂ between 38 and 43 mm Hg were maintained by varying the stroke volume of the Palmer pump.
pH and K⁺ Electrodes

Continuous measurements of \( K_e \) and \( pH_e \) were obtained from two double-barreled K⁺ microelectrodes \(^9\) and one miniaturized pH electrode. \(^8\) Tip diameters were 1 to 2 \( \mu m \) for the pH electrode. The electrodes were inserted to a depth of approximately 500 \( \mu m \) in cortical gray matter through a fine slit cut in the pia arachnoid. This was done before the paraffin pool was established. To obtain a corresponding set of measurements of \( K_e \), \( pH_e \), rCBF and EP, one K⁺ electrode and the pH electrode were positioned within a distance of 3 to 6 mm from the EP electrode, also containing the hydrogen electrode No. 1. The other K⁺ electrode was placed close to hydrogen electrode No. 5 in experiments Nos. 1 and 2, and to hydrogen electrode No. 3 in experiments Nos. 3 and 4. In this way paired measurements of \( K_e \), \( pH_e \), rCBF and EP were obtained. In the course of these experiments we had some evidence that withdrawal of an electrode into paraffin appeared to damage K⁺ sensitivity in certain instances, possibly by interference with the liquid K⁺ ion exchanger in the electrode tip. We were particularly careful, therefore, to ensure that the electrodes once introduced remained in the brain and, because of this interference, we also felt it unsatisfactory to recalibrate K⁺ electrodes after the experiment.

Drift and Recording Techniques

Since the usual way of recording drift during the experiment by recalibration was not at hand for the K⁺ electrodes, the absolute terminal values for \( K_e \) should be taken with caution. Rapid changes in reference electrode potential were not observed but could easily have been recognized as identical potential changes in all three electrodes, since the two reference barrels were connected and served as common reference for the two K⁺ electrodes and the pH electrode. Amplifier drift was controlled by recording the zero (short-circuited amplifier inputs) (fig. 1). The three electrodes were sequentially scanned by a low current scanner (Keithley 702/7028) and the signals recorded by a differential high input impedance amplifier (Keithley 604) and a Rikadenki pen recorder.

Precautions Concerning Brain Surface Movements

Swelling or shrinking of the brain with subsequent movements of the brain surface is unavoidable. Regular movements occur with respiration, and surface movements of several millimeters may occur during \( CO_2 \) inhalation, after MCA occlusion and following exsanguination. To keep the K⁺ electrodes in the tissue, the connection to the K⁺ barrel was made by a copper wire (0.3 mm in diameter) which was coiled to serve as a spring in very light compression. To prevent the electrodes from sinking into white matter a small drop of epoxy cement was placed approximately 0.5 mm from the tip. These simple precautions permitted movements of the K⁺ electrodes with the brain surface. The pH electrode was left hanging in the soft connection wire after insertion. No artifacts due to the brain movements synchronous with respiration were noted on the electrode signals.

Electrode Calibration

The K⁺ electrodes were calibrated at room temperature in solutions containing 3, 5 and 50 mmol per liter KCl and 147, 145 and 100 mmol per liter NaCl, respectively. Between 5 and 50 mmol per liter a slope of 50.6 (range 48.5 to 52 mV) was obtained. Calibrations at room temperature were adjusted to 37°C according to the Nernst equation by multiplying the calibration potentials by

\[
\frac{310}{273 + \text{room temperature}}.
\]

Below 5 mmol per liter KCl sensitivity declined. \(^13\) Electrode resistance was approximately 10⁶Ω. The internal solution consisted of 100 mmol per liter KCl and the junction potentials were within a range of +10 to −1 mV.

The pH electrode was calibrated at room temperature in phosphate buffers in which \( pH \) measured at 37°C was 6.48 and 7.22, respectively. Sensitivity was 55.4 mV/pH. Electrode resistance was 10⁷ to 10⁸Ω. Calibrations were done using the reference barrel of the K⁺ electrodes, later serving as reference during the experiment to avoid a change in junction potential. The internal solution was 0.1 N HCl.

Results

Response to \( CO_2 \) Inhalation

To test the pH electrode \( CO_2 \) was added at the respirator inlet. This was performed in experiments Nos. 1 and 2. The electrode responded within one to two minutes. At steady-state arterial \( P_{CO_2} \) values from 34 to 60 and from 37 to 54 mm Hg, \( pH_e \) changed from 7.33 to 7.07 and from 7.21 to 7.07, respectively. No changes in \( K_e \) occurred.

Initial and Terminal Recordings of \( K_e \) and \( pH_e \)

\( K_e \) and \( pH_e \) recorded immediately after insertion, just before MCA occlusion, and after terminating the ex-
TABLE 1  Initial and Terminal Measurements of rCBF (ml/100 gm/min), Arterial Pco2 (mm Hg), Ke (mmol/l) and pHx

<table>
<thead>
<tr>
<th>Exp. no.</th>
<th>rCBF</th>
<th>Ke</th>
<th>pHx</th>
<th>Before MCA occlusion</th>
<th>&quot;Drift&quot;</th>
<th>Terminal measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>46</td>
<td>3.5</td>
<td>7.33</td>
<td>29</td>
<td>3</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>70</td>
<td>36</td>
<td>57</td>
<td>55</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>86</td>
<td>3.4</td>
<td>5.5</td>
<td>10</td>
<td>13</td>
<td>285</td>
</tr>
<tr>
<td>5</td>
<td>30</td>
<td>50</td>
<td>42</td>
<td>10</td>
<td>176</td>
<td>84</td>
</tr>
<tr>
<td>Pco2</td>
<td>34</td>
<td>36</td>
<td>38</td>
<td>10</td>
<td>196</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>63</td>
<td>55</td>
<td>102</td>
<td>65</td>
<td>132</td>
<td>318</td>
</tr>
<tr>
<td>2</td>
<td>76</td>
<td>4.8</td>
<td>7.36</td>
<td>13</td>
<td>50</td>
<td>216</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>3.4</td>
<td>7.37</td>
<td>11</td>
<td>44</td>
<td>318</td>
</tr>
<tr>
<td></td>
<td>44</td>
<td>5.8</td>
<td>7.37</td>
<td>13</td>
<td>50</td>
<td>216</td>
</tr>
<tr>
<td></td>
<td>48</td>
<td>41</td>
<td></td>
<td>78</td>
<td>50</td>
<td>216</td>
</tr>
<tr>
<td></td>
<td>81</td>
<td>75</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>102</td>
<td>85</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>94</td>
<td>79</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pco2</td>
<td>46</td>
<td>41</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>150</td>
<td>2.4</td>
<td>7.26</td>
<td>10</td>
<td>40</td>
<td>6.34</td>
</tr>
<tr>
<td></td>
<td>111</td>
<td>4.9</td>
<td>7.26</td>
<td>10</td>
<td>40</td>
<td>6.34</td>
</tr>
<tr>
<td></td>
<td>102</td>
<td>5</td>
<td></td>
<td>78</td>
<td>50</td>
<td>216</td>
</tr>
<tr>
<td></td>
<td>94</td>
<td>79</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pco2</td>
<td>40</td>
<td>41</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

"Drift" refers to observed changes in electrode potential in mV from time of insertion to MCA occlusion. Observation time and total length of experiments are given in minutes. The terminal Ke values were still increasing at time of disconnection.

Experiments by inhalation of N2 (in experiment No. 1: air), are given in table 1. The changes in Ke and pHx, during the time of observation between insertion and MCA occlusion were within 0 to 13 mV (table 1). Changes in Ke and pHx subsequent to insertion are likely to occur from cell damage, bleeding and arterial Pco2 changes. This leaves only a proportion of the "drift" listed in table 1 to electrode drift. No identical changes in all electrode signals indicating drift in junction potential were observed.

The terminal recordings of Ke and pHx are given in table 1. By recording the anoxic release of cellular K+ at the end of the experiment, the K+ electrode was proved to respond...
adequately. Thus, the electrode tip buried in the tissue was protected from paraffin contamination. The anoxic K+ release occurred gradually and a steady-state was not obtained even after 20 minutes of N2 inhalation (18, 24 and 27 minutes, respectively).

MCA Occlusion

In all four experiments, MCA occlusion caused an immediate drop in rCBF and a subsequent moderate elevation of Ks, an extracellular acidosis and a decline in EP amplitude. The changes in Ks, pHc and EP following MCA occlusion were similar in time and occurred more rapidly in the experiments with the largest initial drops in rCBF (experiments Nos. 1 and 2 compared to Nos. 3 and 4, figs. 2 and 3). Corresponding values of EP, Ks and pHc and of rCBF following occlusion are given in table 2. It is seen from table 2 that abolition of EP is not necessarily associated with the biggest increase in Ks nor with the most severe extracellular acidosis. But, consistent with previous studies, abolition of EP is associated with the lowest rCBF values.4 Thus it appeared that no critical value of Ks nor pHc could be associated with onset of electrical failure.

Effect of Blood Pressure on rCBF After MCA Occlusion

A good correlation (r = 0.93) was found between the relative changes in MABP and rCBF, as shown in figure 4. This indicates a passive vascular bed in the ischemic zones. The regression line has a slope of 1.23 and the intercept of 19.5 ±21.1 MABP% (5% confidence limits) is not significantly different from zero.

Effect of Blood Pressure on EP, Ks and pHc After MCA Occlusion

By varying systemic blood pressure and hence rCBF after MCA occlusion, the interrelations between rCBF, EP, Ks and pHc at critical low levels of rCBF were studied further.

Recovery by Increase in MABP

By increasing MABP (by infusion of aramine or noradrenalin) a complete recovery of EP and a partial recovery of Ks and pHc were obtained in experiments Nos. 3 and 4 (table 3, fig. 3). The recovery of EP, Ks and pHc was closely related in time to the changes in MABP. In experiments Nos. 1 and 2, a partial recovery in Ks and pHc but no recovery of EP were obtained by an increase in MABP. However, in experiment No. 2, EP, Ks and pHc were normalized by release of the MCA occlusion accompanied by a large increase in rCBF (table 3, fig. 2). That normalization of pHc and Ks is obtained in this situation is in accordance with the study by Heuser et al.4 Again, no critical levels of Ks and pHc for electrical failure or recovery could be identified since comparisons between experiments as well as within the individual experiments show that a good recovery in EP is not necessarily associated with the lowest Ks values or with a less severe extracellular acidosis (table 3, fig. 3).

Massive Cellular Release of K+ by a Decrease in MABP

Reductions in MABP by exsanguination led to abolition of EP, to higher values of Ks and to more severe acidosis (table 3, figs. 2 and 3). Again, the changes were closely related in time to MABP. At MABP levels as low as 59, 60 or 70 mm Hg in the three animals so studied, a massive release of intracellular K+ noted as a steep rise in Ks occurred. The closest corresponding rCBF values were obtained at MABP of 57, 55 or 45 mm Hg, respectively (table 3), i.e., later in the exsanguination procedure when MABP and hence rCBF was even further reduced. The rCBF values

![Figure 4](http://stroke.ahajournals.org/)

**Figure 4.** Correlation between relative changes in rCBF and MABP indicating a completely passive vascular bed in areas of cerebral ischemia. Omitted since MABP could not be assessed accurately due to cardiac arrhythmia.
so obtained were 11 > 5 > 2 ml/100 gm per minute and (after adjustment according to fig. 4) 18 > 6 > 2 ml/100 gm per minute (median with 5% confidence limits). The adjusted reductions in rCBF required to enter the state of K+ release from the state of electrical failure were 17 > 10.5 > 2 ml/100 gm per minute (median with 5% confidence limits). This indicates the ischemic threshold of K+ release.

Discussion

Reliability of Methods

The pH electrode used in this study measures extracellular pH (pHₑ) in neocortex and does not merely reflect plasma pHₑ since blood-brain barrier integrity toward H+ and HCO₃ ions is not interrupted by electrode insertion. 4 Further, the time response is more than adequate since a step increase in arterial PₐCO₂ is followed by a change in electrode signal within five seconds. 15 With these previous observations and with the present finding of an adequate response so obtained, it was concluded that, during the experiment, the tip buried in the tissue was protected from possible paraffin contamination.

Sudden changes in junction potential including that of the reference electrodes, as would be easily detectable as identical changes in all electrode signals, did not occur, but electrode drift is an unavoidable though only modest disadvantage of this technique (table 1). Experience from the rat shows that after insertion for two to three hours, sensitivity is preserved and the drift is within ±9 mV, 16 but the absolute values recorded at the end of the experiments must be interpreted with this precaution in mind.

Mechanism of the Complete Electrical Failure in Ischemia

On the basis of several studies, clinical as well as experimental, we will consider the critical dependence of cortical electrical function (EEG, EP or single neuron discharges) on rCBF as a physiological fact. 14 In the present ischemic model, the EP is totally abolished at rCBF values of about 15 ml/100 gm per minute. 9

Recently, Marshall et al. 7 have discussed the various hypotheses possibly explaining the electrical failure in ischemia. These have been primarily depletion of high energy phosphates, synaptic depolarization by release of intracellular K+, severe lactacidosis and impaired neurotransmitter metabolism.

The results of both Branston et al. 3 and Marshall et al. 7 suggest the hypothesis of a synaptic depolarization subse-
sequent to release of cellular K⁺. However, the results obtained in this study demonstrate that only the possibility of highly localized release of K⁺ at synaptic sites and therefore perhaps not seen by the electrode cannot be definitely excluded. Only slight elevations in K⁺ were found at levels of ischemia producing complete electrical failure. These elevations in K⁺ must be considered too small to produce inexcitability, because full electrical activity is seen at K⁺ values as high as 10 to 12 mmol per liter during epileptic discharges and following electrical stimulation. Thus, the potassium hypothesis (association of massive K⁺ release with electrical failure in ischemia) cannot be supported by the present study. Further evidence against the potassium hypothesis has been provided by previous studies. In asphyxiated rats, EEG becomes isoelectric one to two minutes before the massive K⁺ release. Furthermore, recovery from the terminal state of hypoglycemia by intravenous glucose leads to a rapid normalization in K⁺, but to a much slower recovery in EEG, and in a study on cats by Heuser et al. it was found that in the recovery from total ischemia by reperfusion, K⁺ may normalize while EEG stays isoelectric. The conclusion of these results is that the state of complete electrical failure need not be associated with a high K⁺ value; in fact K⁺ may stay normal or normalize at onset of isoelectricity. This has recently been observed in rats with epileptic seizures and hypotensive ischemia. On the other hand, a massive release of intracellular K⁺ is always associated with electrical failure, and in the phenomenon of spreading depression the potassium hypothesis may fully explain the local transient isoelectricity.

A causal relationship between tissue lactacidosis and complete electrical failure is discounted also by the present study. It is clearly demonstrated that neither abolition of EP nor recovery of EP could be associated with a critical level of tissue extracellular acidosis. Neither could the study of Heuser et al. relate EEG recovery after total ischemia to a critical pH value. The close relationship in time between changes in pH and EP is striking (figs. 2 and 3), but does not necessarily indicate a causal interrelationship. Rather, the changes in pH as well as in EP are concomitants of the general ischemic metabolic pattern, the pH drop being related to lactic acid production and the EP abolition possibly to intermediates acting as neurotransmitters. The possible role of the reduction in glutamate and the rise in GABA for electrical function has been emphasized by several investigators.

Release of K⁺ and the Existence of Two Ischemic Thresholds

The massive release of intracellular K⁺ recognized as a steep rise in K⁺ did not occur at the threshold of electrical failure of about 15 ml/100 gm per minute. K⁺ release first occurred only when systemic blood pressure and hence rCBF was further reduced by exsanguination to a level of about 6 ml/100 gm per minute. We have thus demonstrated that the ischemic threshold for K⁺ release is below that for complete electrical failure.

No data seem yet at hand which strictly relate the K⁺ release to the energy metabolism. We have not assigned the term "failure of the ionic pump" to the phenomenon of K⁺ release, since other mechanisms such as an increase in ionic permeability of the cell membranes might well be of importance.

Our conclusions are illustrated in figure 5. We have restricted the use of the term ischemia to a reduction in local blood flow of a degree leading to impaired tissue function, while oligemia is taken to mean a reduction in local blood flow which leaves functions unaltered. When electrical activity ceases, a further reduction of about 50% in rCBF is required to move the functional state of the tissue from isoelectricity to K⁺ release. In figure 5 we have indicated not only the absolute rCBF values describing the present experimental condition, but we have also given a percentage rCBF scale. This is done to indicate that the concept of ischemic thresholds of various functions as shown in figure 5 should not be restricted to the present acute preparation which must unavoidably involve some depression of metabolic rate. We assume that in ischemia the functional inactivations occur subsequent to a failure of oxygen supply and utilization. Even if oxygen utilization is extremely high as in epilepsy, or extremely low as in hypothermia or barbiturate anesthesia, the concept of clearly separate ischemic thresholds of various functions may still apply as a general pattern independent of experimental conditions. Evidence for this has recently been provided by the demonstration of clearly separated thresholds of complete electrical failure and of K⁺ release in rats with generalized epileptic discharges and systemic hypotension. The actual threshold values in ischemia may thus cover a large range dependent on cerebral metabolic rate.

Possible reversibility of the functional inactivation in ischemia is the key problem of interest here. Neither the state of complete electrical failure nor the state of K⁺ release of severe extracellular acidosis per se indicates irreversible tissue damage since recovery of EP and normalization of K⁺ and pH can be obtained simply by increasing local blood flow above ischemic levels. In experiment No. 2, the occlusion was released and an almost complete recovery in EP and a normalization in pH occurred, while K⁺ was about normal all the time (fig. 2). In experiment No. 1, rCBF was increased by an increase in MABP but stayed below the ischemic threshold of electrical function, with recovery only of K⁺ and pH. That a completely normal K⁺ can be regained after the massive K⁺ release has occurred is not shown in

---

**FIGURE 5.** Ischemic thresholds for electrical failure and for release of cellular K⁺. For further details see text.
this study, but is known from the study of Heuser et al.\textsuperscript{14} as well as from other studies from our group.\textsuperscript{9,17}

According to figure 4, it is likely that in patients with clinical stroke, blood flow in the ischemic zone varies in parallel with systemic blood pressure. A clinical implication of a drop in blood pressure in the stroke patient is seen in figure 5, which suggests the conversion of zones with spared electrical function into a state of electrical failure, and the conversion of zones with electrical failure into a state in which a massive cellular K\textsuperscript{+} release with subsequent increase in K\textsubscript{e} may occur. That such extensions of the areas of impaired brain function, produced by hypotension, may be reversed with subsequent clinical improvement simply by the reestablishment of normotension is not unknown in clinical work. The zones of complete electrical failure and K\textsuperscript{+} release lie in the ischemic penumbra, with functional inactivation but not yet cell death.

Acknowledgment
We wish to thank Paul Preston for skilled technical assistance.

References
16. Astrup J, Heuser D, Nilsson B, et al: Epileptic discharges and extracellular K\textsuperscript{+} and H\textsuperscript{+} in rat cortex at critical levels of ischemia. (in preparation)
18. Lux HD, Neher E: The equilibrium time course of (K\textsuperscript{+})o in cat cortex. Exp Brain Res 17: 190-205, 1973

ELECTRICAL FUNCTION OF BRAIN IN ACUTE ISCHEMIA/Astrup et al. 57
Cortical evoked potential and extracellular K+ and H+ at critical levels of brain ischemia.
J Astrup, L Symon, N M Branston and N A Lassen

*Stroke*. 1977;8:51-57
doi: 10.1161/01.STR.8.1.51

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1977 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/8/1/51

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org/subscriptions/