Anesthesiology
73:821–825, 1990

Electroencephalographic Changes During Brief Cardiac Arrest in Humans

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Slowing and attenuation of the dominant frequency of the electroencephalogram (EEG) are changes commonly used to detect cerebral ischemia. To assess the validity of this method, the EEGs recorded during 93 episodes of circulatory arrest in ten normothermic, lightly anesthetized patients undergoing implantation of automatic internal cardioverting defibrillators (AICDs) were visually inspected for change. The number of events recorded for each patient varied from 5 to 18 and was a function of the duration and success of AICD testing in each patient. In 82 of 93 (88%) episodes, EEG changes were identified, and occurred an average of 10.2 s after the last normal heart beat. Of these 82, 67 (82%) illustrated slowing and attenuation. However, 15 (18%) of the hemodynamic events showed changes not previously described as indicative of cerebral ischemia: 6 (7%) showed a loss of delta-wave activity and 9 (11%) showed an increase in the amplitude of theta activity. Time to onset of these unusual changes (10.6 and 9.2 s, respectively) was not significantly different from that for EEG slowing and attenuation (10.2 s). Five of the ten subjects showed more than one pattern of EEG change. There was no significant difference in the time to onset of EEG change among individual patients, and neither were there differences in patterns of change associated with particular anesthetic agents. These results indicate that in normothermic, lightly anesthetized individuals, cerebral ischemia may cause changes in EEG pattern other than slowing and attenuation of dominant frequencies. These alternative patterns should be recognized as indicative of cerebral ischemia when intraoperative EEG monitoring is performed. (Key words: Brain, ischemia. Monitoring, electroencephalogram. Monitoring, cerebral ischemia.)

CHANGES IN THE PATTERN of electroencephalographic (EEG) activity due to global hypoxic insult to the brain have been recognized for over 100 yr.[1] The majority of studies have been in animals, since appropriate conditions for the study of cerebral hypoxia in humans are not readily available. In the few available human studies, the EEG change classically described as indicative of cerebral ischemia is a progressive slowing and reduction in amplitude followed by relatively high-amplitude delta waves that ultimately become isoelectric.[2–5] This pattern is widely accepted, but its time course and incidence are poorly documented. As continuous intraoperative EEG monitoring to detect cerebral ischemia becomes more common, more precise data regarding the range and character of ischemic EEG changes are desirable. The implantation and testing of automatic internal cardioverting defibrillators (AICDs) provide a unique opportunity to measure the precise onset of circulatory arrest and subsequent ischemic EEG changes in normoxemic individuals receiving modern anesthetic drugs.

Materials and Methods

After approval by the institutional review board, ten subjects were selected from patients scheduled for implantation and intraoperative testing of AICDs at the Hospital of the University of Pennsylvania. The only exclusion criteria was the presence of old focal neurologic injury, although some patients were not studied for administrative or nonmedical reasons.

Ten patients, eight men and two women, were included in the study. The mean age for patients in the study was 58.9 yr (range 21–74 yr). Average height was 177.8 cm (range 167.6–188.0 cm). Average weight was 78.4 kg (range 63.0–115.5 kg). All had documented recurrent ventricular tachycardia and a history of cardiac disease except for a 21-yr old, who had experienced sudden cardiac arrest without identifiable cause. Two patients had a history of postarrest hypoxic encephalopathy. Two other patients had a history of cerebrovascular disease; one was deemed not hemodynamically significant, and the other had undergone carotid endarterectomy. Neither had focal neurologic deficits.

Prior to the induction of anesthesia, gold-cup EEG electrodes were affixed to the scalp with collodion-soaked gauze squares at International 10-20 system positions Fp_1, Fp_2, C_3, C_4, O_1, O_2, and A_1. A four-channel bipolar montage consisting of Fp_1–C_3, C_3–O_1, Fp_2–C_4, and C_4–O_2 grounded to A_1 was continuously recorded with a TM-100 EEG amplifier (Telefactor Corp., Conshohocken, Pennsylvania). The bandwidth was 1–35 Hz. Electrode impedance was measured and maintained below 5 kohm for all leads. EEG, blood pressure (from an indwelling radial artery catheter), and ECG were digitized at 128 Hz per channel and stored for subsequent analysis. Power spectrum analysis (for illustrative purposes only) was performed on a Hewlett-Packard work station (model 310) using 2-s epochs and was displayed in a DSA format.

The anesthetic for each patient was selected by the anesthesiologist assigned to the case, and no limitations on anesthetic management were imposed by the study. The preanesthetic medications included morphine, scopolamine, and midazolam. Thiopental was used as induction agent in six cases. Two patients received fentanyl (8

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Received from the Department of Anesthesia, University of Pennsylvania, Philadelphia, Pennsylvania. Accepted for publication May 17, 1990.

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and 20 μg/kg, respectively) during induction. Anesthesia was maintained with isoflurane alone (two cases), isoflurane and N_2O (five cases), or enflurane and N_2O (three cases). Muscle relaxation was achieved with nondepolarizing agents. End-tidal CO_2 values during AICD testing were stable for each patient, but ranged from 23 to 36 mmHg among patients. The mean esophageal temperature was 35.5° C (range 34.4–36.6° C). The time from induction of anesthesia to study measurements averaged 1 h and 34 min and was never less than 1 h.

Data analysis was performed by a single unbiased observer with no prior knowledge of the study subjects. For each patient, the blood pressure tracing alone was scanned for episodes of sudden and sustained loss of pulsatile pressure. Corresponding ECG data were then reviewed. Only events of sustained ventricular fibrillation were included in the study. Episodes of hypotension induced by cardiac pacing, ventricular tachycardia, and torsade des pointes were excluded, because cerebral perfusion continues under these conditions with a variable degree of impairment, making data analysis more difficult and confusing. EEG data were displayed in analog form and inspected for evidence of change. Usually, Fp_1–C_3 was examined, but other channels were examined if artifact was identified on this channel. For each cardiac arrest event, the time from the last systolic blood pressure to the first change in EEG signal was measured and the type of EEG change noted. For those events in which no EEG change could be identified, the time from last systolic blood pressure to recovery of pulsatile flow was recorded.

Results

The number of events recorded for each patient varied from 5 to 18 and was a function of the duration and success of AICD testing in each patient. A total of 93 events were analyzed. Of these, EEG change was present in 82 (88%) and absent in 11 (12%). For all events showing EEG change, the mean time to onset of change was 10.2 ± 0.4 s (SEM) with a range of 3.3–21.1 s. The mean length of hypotensive events not exhibiting change was 9.2 ± 1.1 s, with a range of 4.7–14.8 s, which was not significantly different from the time to onset of change in those events exhibiting change.

Among the events that exhibited change, three types of EEG change were noted. The majority, composed of 67 events (82%), displayed slowing and attenuation or a sudden loss of activity above the delta range (fig. 1). These changes have been described previously as characteristic of cerebral ischemia.[5] Six events (7%) in two patients showed a loss of low-frequency activity (fig. 2). One of these patients demonstrated this type of change in addition to five events of slowing and attenuation, whereas the

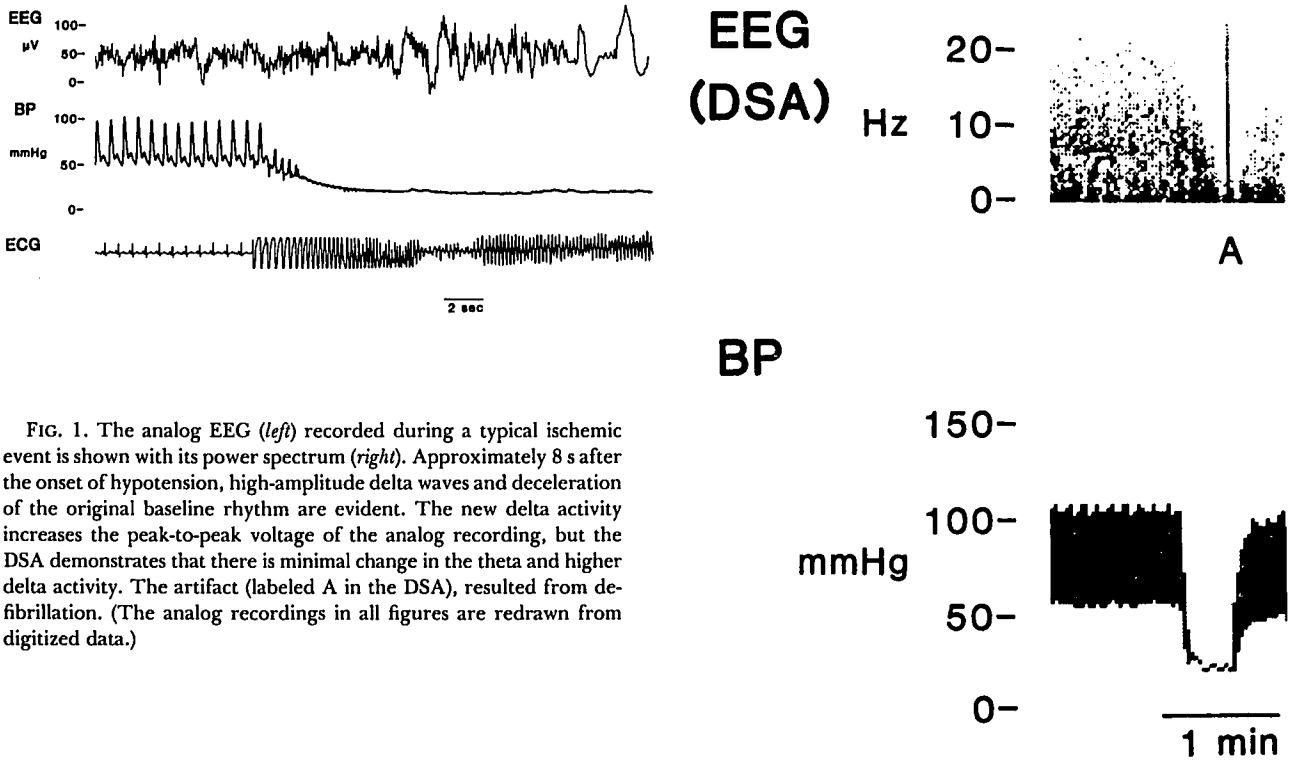
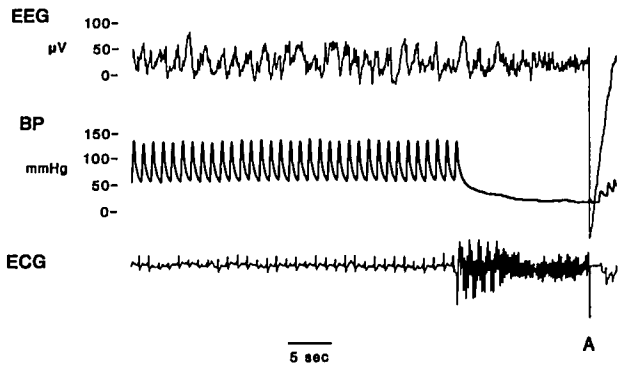


FIG. 1. The analog EEG (*left*) recorded during a typical ischemic event is shown with its power spectrum (*right*). Approximately 8 s after the onset of hypotension, high-amplitude delta waves and deceleration of the original baseline rhythm are evident. The new delta activity increases the peak-to-peak voltage of the analog recording, but the DSA demonstrates that there is minimal change in the theta and higher delta activity. The artifact (labeled A in the DSA), resulted from defibrillation. (The analog recordings in all figures are redrawn from digitized data.)



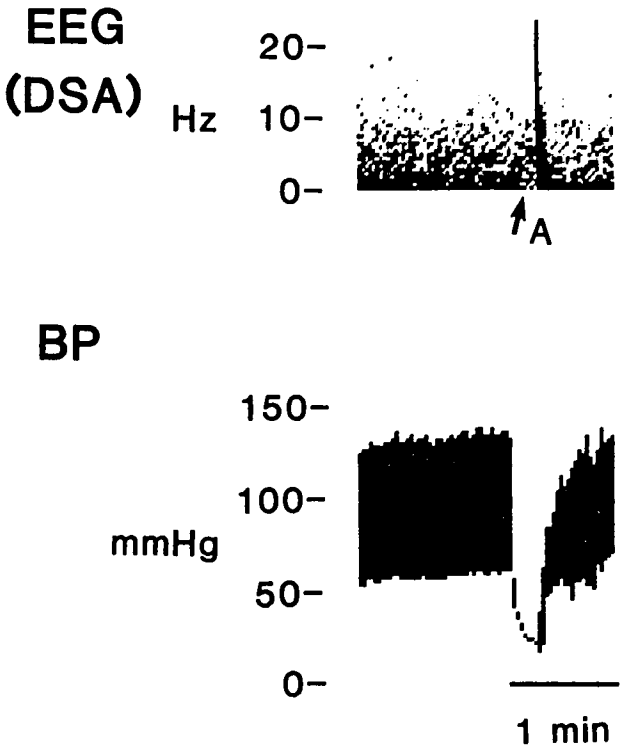


FIG. 2. An example of loss of delta activity with ischemia is shown in analog (*left*) and power spectral (*right*) form. Note that the time scale differs from that of figure 1 in order to emphasize the slow wave activity. Approximately 12 s after the last pulse, the delta activity diminishes. In the DSA, this occurs at the arrow. The DSA clearly shows that the high-frequency activity is unchanged in amplitude up to the defibrillation artifact (labeled A), which is evident in both the analog and power spectral recordings.

other patient demonstrated predominantly the unusual pattern of change. The third pattern of change, an increase in amplitude of theta-frequency activity without associated attenuation, was observed in 9 hypotensive events (11%) (fig. 3). Examples of this type of change occurred among the hypotensive events of four of the ten study patients. Five of the ten patients showed two patterns of change. Unusual patterns of change were not associated with frequent or repeated events or particular anesthetic agents.

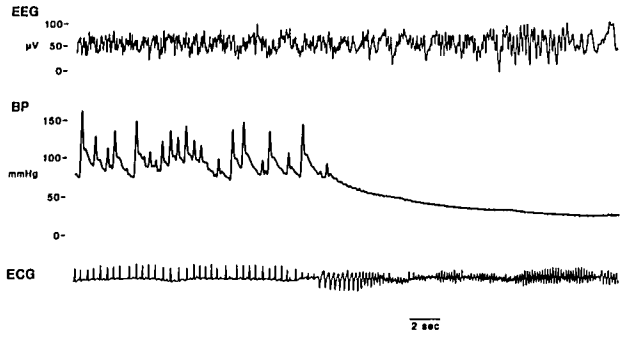
For events showing slowing and attenuation, the mean time from the last systolic blood pressure to the onset of EEG change was 10.2 ± 0.5 s. For events showing loss of delta activity, this delay was 10.6 ± 0.4 s, and for events showing increased theta activity the delay was 9.2 ± 0.5 s. These times were not significantly different by analysis of variance (ANOVA). In addition, mean time to onset of EEG change was compared among patients by ANOVA, and no significant difference was found, despite their varied medical histories, physical conditions, and the variety of anesthetic combinations used.

The average mean blood pressure before ventricular fibrillation was 81 mmHg, which decreased (on average) to 28 mmHg. There was no difference in the mean decrease in blood pressure (53 mmHg) whether or not EEG changes occurred, although individual patients differed in blood pressure at points when EEG changes were observed ($P < 0.01$ by ANOVA).

Discussion

Previous studies have attempted to assess the effects of acute decreases in cerebral perfusion on EEG activity; however, safe and reproducible experimental human models are uncommon. In 1943, Rossen *et al.*[6] used an inflatable cervical collar to acutely interrupt cerebral blood flow without compromising ventilation on healthy awake male volunteers—an experimental design clearly unacceptable today. They noted an average time of 6.8 s from arrest of cerebral circulation to loss of consciousness, which was accompanied by the sudden appearance of delta waves on the EEG.[6] Studies in anesthetized patients have been limited to case reports and to hypoperfusion during carotid endarterectomy and cardiopulmonary bypass—situations that necessarily include several confounding variables, such as preoperative neurologic deficit, hemodilution, incomplete ischemia, and hypothermia, all of which may modify the EEG change produced by ischemia.[7–10]† The advent of AICD implantation operations has created the opportunity to monitor EEG activity during repeated episodes of cerebral ischemia in patients whose physiologic parameters are otherwise stable.

† Levy WJ, Parcella PA: Electroencephalographic evidence of cerebral ischemia during acute extracorporeal hypoperfusion. Journal of Cardiothoracic Anesthesia 4:300–304, 1987.



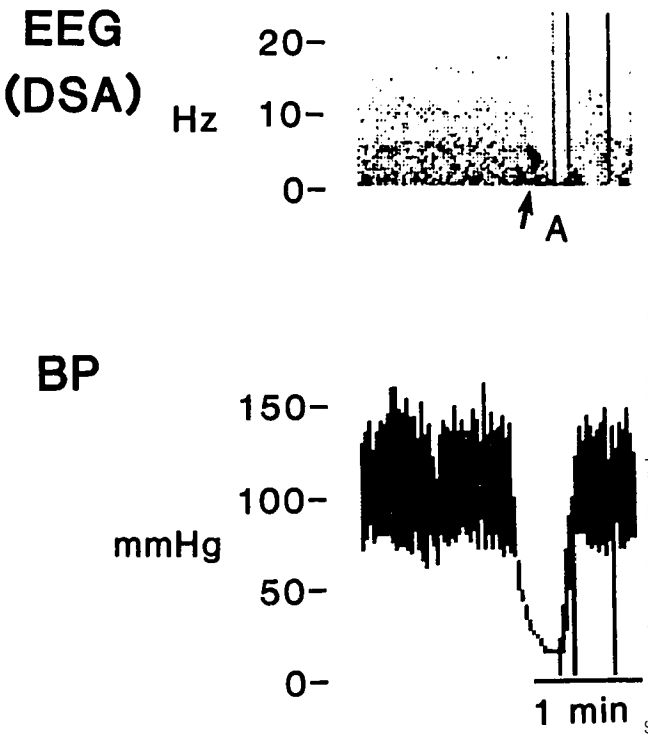


FIG. 3. This recording exemplifies the increased theta activity seen in some cases. In the analog recording (*left*), there is the suggestion of slowing approximately 8 s after the last pulse. The amplitude of this activity increases and becomes more rhythmic for the next 6–8 s until diffuse, very slow activity occurs at the end of the analog strip. This activity produces the appearance of a marked increase in EEG power in the DSA as the first evidence of the ischemic changes (arrow, *right*). Defibrillation artifact (labeled A) also is evident in the power spectral recording.

Previous work has compared the incidence of EEG changes in a similar population during episodes of ventricular tachycardia and ventricular fibrillation in patients receiving AICDs.‡ A lower incidence of change was observed when ventricular tachycardia was present, suggesting that there is a small amount of continued cerebral perfusion during ventricular tachycardia and that in some patients this continued perfusion may avert EEG change. For this reason, we restricted our study to episodes of ventricular fibrillation only. The mean time to onset of EEG change in our study was 10.2 s, which is longer than the 6.8 s observed by Rossen *et al.*[6] Although this difference may represent an effect of anesthesia, it is equally likely that perfusion ceased more quickly with inflation of the cervical collar than with cardiac arrhythmia. Differences in position (sitting *vs.* supine) and oxygenation may also be factors.

Although the average delay before EEG change was 10.2 s, the range of times was 3.3–21.1 s. This wide variation suggests that time of onset may have been influenced by other variables. Unfortunately, the results of this study give little indication of what those variables might have been. Patient demographic data, type of anesthetic received, and end-tidal CO_2 appeared to have no significant effect on time to EEG change, although an effect might be demonstrated with better control of these variables. Blood pressure may have been a factor, but its contribution is not clear; the decrease in mean arterial pressure was the same whether or not EEG changes occurred. Thus, the individual variability in events may reflect a parameter more difficult to elucidate, such as the adequacy of brain tissue oxygenation at the time of initiation of fibrillation or the magnitude of the oxygen reservoir in the cerebral vessels. These would be a function of cerebral blood flow, volume, hemoglobin concentration, saturation, and metabolic demand.

Examination of the events not followed by EEG change did not help to elucidate the confounding variables. Some events were very short and perhaps less likely to cause ischemia on that basis. Others, however, were longer than events causing change in the same patient. We are left with the impression that some unidentified and uncontrolled factor may play an important role in determining the delay before EEG evidence of cerebral ischemia occurs during cardiac arrest.

The most surprising finding of this study was the relatively high incidence (18%) of changes in EEG pattern that have not been previously described as indicative of cerebral ischemia in humans. In early studies on cats subject to cerebral anoxia, Sugar and Gerard[11] noted that, prior to the disappearance of electrical activity, cortical rhythms increased in frequency and amplitude temporarily, an effect they postulated was due to the accumu-

‡ Boretsky RH, Levy WJ: Cerebral hypoxia during ventricular dysrhythmias (abstract). ANESTHESIOLOGY 67:3A, 1986.

lation of carbon dioxide. All EEG studies during cerebral ischemia in humans have described progressive slowing of signal accompanied by a decrease in high-frequency activity and a generalized attenuation of voltage, and ultimately becoming an isoelectric EEG with prolongation of ischemia.

We detected two alterations in EEG activity, a loss of delta activity and an increase in amplitude of theta activity, that have not been previously described in relation to human cerebral ischemia. Both of these patterns of change occurred at times consistent with time to onset of EEG patterns accepted as marking ischemia. With one exception, these changes occurred in one or several hemodynamic events of patients manifesting progressive slowing and attenuation of electrical activity during other ischemic episodes. There was no change in anesthetic state or drugs that explained the occurrence of the previously undescribed ischemic changes in a particular patient. Therefore, we conclude that in response to arrest of cerebral circulation, the EEG may manifest several different types of change, including loss of delta-wave activity and increased amplitude of theta activity, as early evidence of cerebral ischemia.

These findings may have relevance for the use of intraoperative EEG monitoring to detect cerebral ischemia during carotid endarterectomy. The value of such monitoring is the early detection of ischemia in order to place a bypass shunt in a timely manner and prevent permanent tissue damage. Selective shunting is believed to provide optimal balance between the complications of shunting and the presence of ischemia,[12-14] although it is not clear that EEG change is the criterion on which this decision should be made. The extrapolation of the findings from this complete ischemia model to the incomplete ischemia present during carotid endarterectomy may also be questioned, and we have not demonstrated that these unusual patterns can occur in a state of stable incomplete cerebral ischemia. Nonetheless, these findings in complete ischemia raise the possibility that unusual patterns of EEG change may be observed during incomplete ischemia. Further investigation of the conditions producing these unusual patterns is warranted.

In summary, the study of 93 brief hypotensive events produced by ventricular fibrillation during AICD implantation under anesthesia demonstrated EEG evidence of cerebral ischemia in 88% of events, occurring at an average of 10.2 s after the last normal heart beat. In 18% of the events demonstrating change, the initial EEG change was not slowing and attenuation. The severity of the ischemia represented by these changes and their value for predicting outcome during conditions of incomplete ischemia remain to be demonstrated.

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