Computer-derived density spectral array in detection of mild analog electroencephalographic ischemic pattern changes during carotid endarterectomy

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The purpose of this prospective study was twofold: 1) to determine the sensitivity and specificity of computer-derived density spectral array in detecting analog electroencephalographic (EEG) ischemic pattern changes during carotid artery cross-clamping in patients undergoing carotid endarterectomy; and 2) to assess the ability of density spectral array to identify such changes in comparison with the degree and type of change seen in the analog EEG ischemic pattern. Sixteen channels of anteroposterior bipolar and two to four channels of referential electroencephalography with four channels of density spectral array were monitored simultaneously during carotid endarterectomy in 103 patients under general anesthesia. Two "observers" interpreted the density spectral array and the analog electroencephalograms, one during and immediately after the operations and the other 6 months after completion of all surgery. Analyses were conducted to establish both the number of patients with analog EEG ischemic changes and the number of ischemia events during carotid artery cross-clamping. Observer A indicated that the density spectral array identified analog EEG ischemic changes in 21 of 29 patients, for a sensitivity of 72% (specificity 99%), whereas Observer B's results showed that the density spectral array identified analog EEG ischemic changes in 16 of 27 patients, for a sensitivity of 59% (specificity 96%). Density spectral array detection of analog EEG ischemic changes based on severity classifications were 61% and 18% in the mild group, 70% and 71% in the moderate group, and 95% in the severe group, indicating a relationship between density spectral array sensitivity and severity of analog EEG ischemic change, with p = 0.02 and p = 0.004 for the two observers. The kappa statistics for observer reproducibility were highly significant, with k = 0.95 for analog EEG ischemic changes and 0.85 for density spectral array changes. It is concluded that density spectral array does not reliably detect mild analog EEG pattern changes of cerebral ischemia and is not a reliable substitute for 16-channel analog EEG monitoring of cerebral ischemia during carotid endarterectomy.

KEY WORDS • cerebral ischemia • carotid endarterectomy • electroencephalography • density spectral array

Electroencephalographic (EEG) changes have been demonstrated to indicate cerebral ischemia during carotid endarterectomy. Several ischemic pattern changes have been described, and some investigators have categorized these changes as mild, moderate, or severe. Computerized devices designed to simplify analog EEG data into compact records of frequency spectra have been proposed as reasonable alternatives to conventional analog EEG interpretation for detecting cerebral ischemia. Previous studies comparing such computerized devices with analog EEG during carotid endarterectomy have identified the presence of analog EEG changes relating to cerebral ischemia and then observed whether similar evidence of cerebral ischemia as defined by the frequency spectra was present.

The purpose of this study was twofold. First, since EEG recording is used at our hospital to monitor cerebral ischemia during carotid endarterectomy, we prospectively chose to determine the sensitivity and specificity of density spectral array, a four-channel Fourier transform technology, for detecting cerebral ischemia defined by ischemic pattern changes found in 16 channels of analog electroencephalography. Second, we sought to determine whether there were differences in the sensitivity of the density spectral array in detecting analog EEG ischemic pattern changes that depended on the type and degree of analog EEG changes.

Clinical Material and Methods

Patient Population

The study protocol was approved by the Subcommittee on Human Studies at the Massachusetts General Hospital. Informed consent was obtained from each...
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Patient for the surgery and the neurophysiological monitoring. Patients were monitored with both analog electroencephalography and density spectral array when personnel were available to operate the two machines simultaneously. From October 5, 1988, to October 17, 1990, 250 carotid endarterectomies were monitored with analog EEG recordings; of these patients, 103 (65 men and 38 women, aged 25 to 86 years, mean age 64 years) underwent simultaneous analog EEG and density spectral array monitoring. Seventy-two patients were symptomatic, with either transient monocular blindness, a transient hemispheric attack, a mild stroke, or exacerbation of an old stroke within 6 months of the planned surgery. Seventeen patients had suffered a previous stroke with new symptoms reflecting disease in the same vascular territory. In two of these 17 patients, the stroke occurred within 3 months before surgery.

Ninety-three of the 103 operations were carotid endarterectomies alone, 47 on the left and 46 on the right. Three patients underwent combined carotid endarterectomy and coronary artery revascularization. Six had carotid endarterectomy and subclavian or innominate artery-to-carotid artery bypass grafts. One patient had a middle meningeal artery-to-middle cerebral artery bypass graft. All surgery required temporary occlusion of the carotid artery by cross-clamping.

Preoperative evaluation of patients scheduled for carotid endarterectomy consisted of a general physical examination with a detailed neurological assessment, an electrocardiogram, and cerebral carotid angiography. The three patients undergoing both carotid endarterectomy and coronary revascularization were also subjected to coronary angiography.

**Anesthetic Regimen**

Preoperative sedation for patients scheduled for carotid endarterectomy consisted of oral diazepam (0.05 mg/kg) given approximately 1½ hours before induction of anesthesia. Each patient was monitored with a radial arterial catheter, electrocardiography, pulse oximeter, capnograph, and oral temperature probe. End-tidal carbon dioxide was maintained between 36 and 42 mm Hg with controlled ventilation. Management of general anesthesia included induction with thiopental (3 to 5 mg/kg) or Propofol (2 to 3 mg/kg), followed by 60% to 70% nitrous oxide in oxygen and boluses of either fentanyl (5 to 8 µg/kg), sufentanil (0.05 to 1.5 µg/kg) or alfentanil (0.15 to 0.5 µg/kg), and a muscle relaxant. Low concentrations of isoflurane or enflurane (0.2% to 0.6%) and phenylephrine infusions were used to maintain systolic blood pressure within 20% of average preoperative readings. Ten minutes before and throughout carotid artery cross-clamping, a constant concentration of inhalational agent was delivered.

The three patients undergoing combined carotid endarterectomy and coronary revascularization were given 1 to 2 mg of oral lorazepam at bedtime, followed by intramuscular scopolamine (0.1 to 0.3 mg) and morphine sulfate (0.01 mg/kg) approximately 1 to 1½ hours before induction of anesthesia. The anesthetic agent was either fentanyl (100 µg/kg) or sufentanil (15 to 20 µg/kg) with oxygen and a muscle relaxant.

**Surgical Procedure**

Surgery for the carotid endarterectomy consisted of angioplasty of the carotid bifurcation and the initial segment of the internal carotid artery. Intracarotid shunts were placed by the surgeons at carotid artery cross-clamping if there were analog EEG pattern changes of cerebral ischemia. Vein patch grafts were placed when considered appropriate.

**Analog Electroencephalography**

Twenty-four gold cup electrodes* were applied to each patient's scalp according to the 10 to 20 system and filled with conduction gel. Electrode impedances were measured at less than 2000 ohms. Sixteen channels of anteroposterior bipolar EEG tracings and either two or four channels of referential tracings were recorded.† The time constant was set at 0.3 seconds and the high-frequency filter at 70 Hz. A 60-Hz notch filter was used when necessary. One channel was used to record the electrocardiogram and another the arterial blood pressure. During the operation, the analog EEG tracing was interpreted by an electroencephalographer and EEG technologist to provide information regarding cerebral ischemia to the surgeons and anesthesiologists. Although EEG recording was continuous from 5 minutes before and throughout the surgery until the patient was awake and responding to simple commands, for purposes of identifying analog EEG ischemic changes in this study, we selectively included only those EEG ischemic patterns that occurred following temporary cross-clamping of the carotid artery during the endarterectomy.

Several types of EEG pattern changes have been correlated with cerebral ischemia. Three modified the criteria for EEG evidence of cerebral ischemia formulated by Blume, et al., to include three components contributing to the definition of "mild," "moderate," and "severe" EEG ischemic changes from the anesthesia-induced baseline established 5 minutes before carotid artery cross-clamping. Mild changes indicating cerebral ischemia were defined as the following: minimal diminution of alpha (8 to 13 Hz) and beta (14 to 30 Hz) frequencies; less than 50% increase in the theta activity (4 to 7 Hz); and no detectable change in amplitude and no increase in delta (0.5 to 3 Hz) activity. Moderate changes denoting cerebral ischemia included: easily detectable loss or absence of fast activity; more than 50% increase in the theta and/or delta activity; and a 30% or less increase or decrease in amplitude. Severe cerebral ischemic changes included: a marked loss or complete absence of alpha and beta frequencies; a predominance of delta activity with little or no theta frequencies; and a greater than 30% increase or decrease in amplitude. In each severity category, the ischemic pattern changes could be focal or generalized. More than one analog EEG ischemic event could take place.

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* Cup electrodes, Model ESCH, manufactured by Grass Instrument Co., Quincy, Massachusetts.
† Electroencephalograph, Model 4321, manufactured by Nihon-Kohden America, Inc., Irvine, California.
during carotid artery cross-clamping; in order to be considered a different analog EEG ischemic event, each subsequent ischemic event after the first had to follow 10 seconds of an interim return to the baseline analog EEG pattern recorded prior to cross-clamping.

Density Spectral Array Technical Parameters

Four bipolar channels of density spectral array were recorded with a frontotemporal, frontoparietal montage. The epoch time was 2 seconds and the frequency window was 0.25 to 20 Hz. The density spectral array display is a 16-level, density-modulated gray scale in which power and frequency on the horizontal axis are plotted against time during each 2-second epoch. The greater amount of EEG activity is represented in the frequency band with the darker display. Density spectral array pattern changes indicating cerebral ischemia were defined as the changes in the gray scale that indicated a shift of power to lower frequencies and/or a diminution or loss of the faster activity at carotid artery cross-clamping.

Analog EEG and Density Spectral Array Data Collection

Double-ended pin-tip patch cords provided the input from a single electrode into two input boxes for both density spectral array and analog EEG data. Internal time clocks for both machines were synchronized, and surgical and anesthesia events were recorded simultaneously. Both analog EEG and density spectral array data were evaluated in the context of the on-going surgery and interpreted in the setting of the events during surgery. Information from the density spectral array was not provided to the surgeons or anesthetists.

Two independent examinations of the records were performed. One analysis was completed by a team consisting of a neurologist/electroencephalographer, an EEG technologist, and a medical student. They read the analog EEG and density spectral array data during and after the operations. These examiners were not blinded to the results of the respective EEG modalities. Subsequent text will refer to these examiners as "Observer A." Six months after completion of all surgery, a second neurologist with training in intraoperative neurophysiology independently and randomly read in a blinded fashion the first analog EEG tracings, then the density spectral arrays. This examiner, aided by the notations specifying the timing of the anesthetic and surgical events, had no knowledge of the first group's assessments and conclusions. We designate this examiner "Observer B." All examiners had identical operating room worksheets.

Statistical Analysis

Two different analyses were performed: the first was based on the patients with ischemic events during carotid artery cross-clamping and the second on the total number of ischemic events that occurred in all patients during carotid artery cross-clamping. In the analysis of patients with ischemic events, we defined sensitivity as the fraction of patients who had ischemic events detected by density spectral array among patients who had analog EEG ischemic changes after carotid artery cross-clamping. Specificity was defined as the fraction of patients without density spectral array ischemic changes who had no analog EEG ischemic changes. The predictive value positive is the fraction of patients who had analog EEG ischemic changes among the patients who exhibited density spectral array ischemic changes. The predictive value negative is the fraction of patients who had no analog EEG ischemic changes among the patients who had no density spectral array ischemic changes. In the analysis of ischemic events among analog EEG severity groups, sensitivity was defined as the fraction of cerebral ischemic events detected by density spectral array criteria among each designated category of "mild," "moderate," and "severe" analog EEG ischemic events that occurred during carotid artery cross-clamping. The relationship of sensitivity to severity type was tested using logistic regression, with the severity type treated as a predictor variable with three equally spaced steps. We defined as false-positives those events measured by density spectral array as cerebral ischemia that were not present as analog EEG evidence of cerebral ischemia.

Since more than one discrete analog EEG ischemic pattern change could occur during cross-clamping of the carotid artery, the procedure of generalized estimating equations described by Zeger and Liang was used to adjust for the multiple events per patient. Because there were two separate "observers," we tested for good observer agreement using the kappa statistic test for reproducibility, with "good" defined as greater than 0.75.

Results

Analog EEG Ischemic Events During Carotid Artery Cross-Clamping

Observer A identified 57 analog EEG ischemic pattern changes in 29 patients during carotid artery cross-clamping. Fifty of these episodes were associated with cross-clamping of the common and the internal carotid arteries, three with a gradual decrease in systolic blood pressure 5, 13, and 17 minutes after carotid artery cross-clamping, two with carotid artery back-bleeding maneuvers, one with a flow obstruction within the carotid artery shunt, and one with dislodgment of the shunt from the carotid artery. Of the 57 episodes of EEG ischemic pattern changes, 18 met the criteria for mild changes, 20 were considered moderate, and 19 were thought to be severe.

Observer B identified 53 analog EEG ischemic changes during carotid artery cross-clamping in 27 patients. Forty-six of these ischemic events were associated with carotid artery cross-clamping, three with gradual decreases in systemic blood pressure 12, 13, and 79 minutes into the cross-clamping period, two with carotid artery back-bleeding measures, one with flow

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EEG 1 density spectral array manufactured by Noran Instruments, Inc., Middleton, Wisconsin.
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![Figure 1](image)

**FIG. 1.** A and B: Sections of analog electroencephalographic (EEG) tracings after carotid artery cross-clamping (A) and after relative hypotension occurred (B) in a 73-year-old man undergoing right carotid endarterectomy (RCEA). Only the leads ipsilateral to the endarterectomy are shown. Note the generalized diminution of the fast activity and slight increase in the slower frequencies during hypotension. C: Density spectral array display showing frequency on the right axis with the range between 0 and 20 Hz for each channel. Time is on the y-axis and reads from bottom to top. Arrows indicate the time of cross-clamping of the right carotid artery. Note that the ischemic changes seen on the analog EEG tracing during hypotension cannot be distinguished on the density spectral array. BP = blood pressure.

obstruction within the intracarotid shunt, and one with shunt dislodgment from the carotid artery. Eleven were categorized as mild, 21 were identified as moderate, and 21 were considered severe.

**Density Spectral Array Detection of Analog EEG Changes of Cerebral Ischemia**

On the patient level analysis, Observer A indicated that density spectral array detected analog EEG ischemic pattern changes in 21 of 29 patients, for a sensitivity of 72%. The specificity was 99%, predictive value positive 95%, and predictive value negative 91%. Observer B's results showed a density spectral array sensitivity of 59% (16 of 27 patients) with a specificity of 96%, predictive value positive of 84%, and predictive value negative of 87%.

On the event level analysis, Observer A found that density spectral array identified 43 of the 57 analog EEG ischemic events, for a sensitivity of 75%. The sensitivity of density spectral array for detecting analog EEG cerebral ischemia in the mild group was 61%, in the moderate group 70%, and in the severe category 95%. Observer B found that 37 density spectral arrays defined ischemic changes in 53 analog EEG ischemic events, for a sensitivity of 70%. Density spectral array identified analog EEG evidence of cerebral ischemia in two of 11 mild analog EEG changes (sensitivity 18%), in 15 of 21 moderate EEG ischemic changes (sensitivity 71%), and in 20 of 21 severe analog EEG changes, (sensitivity 95%).

The logistic regressions showed that the trend of higher density spectral array sensitivity for the detection of more severe analog EEG pattern changes of cerebral ischemia was significant, with p = 0.02 for Observer A and p = 0.004 for Observer B. These values were further confirmed by generalized estimating equations, with p = 0.004 and p = 0.0003, respectively, for Observer A and Observer B. The kappa statistics for examiner reproducibility were highly significant, with k = 0.95 for analog EEG changes (p < 0.001) and 0.85 for density spectral array changes (p < 0.001). Thus, there was highly significant reproducibility between blinded and unblinded examiners in detecting both density spectral array identification of cerebral ischemia and analog EEG ischemic change among patients at carotid artery cross-clamping.

**Density Spectral Array and Analog EEG Tracing Differences**

The greatest discrepancy between analog EEG ischemic change and simultaneous density spectral array detection of such analog changes of ischemia was in the mild category. Since mild analog EEG ischemic changes consisted of diminution of the fast activity, close analysis of the correlated density spectral array activity revealed that the postinduction beta and alpha frequencies, although prominent on the analog EEG tracings, were scattered and minimal at baseline on the density spectral array, making detection of mild changes in the activity of these frequency bands during the ischemic events impossible. Figure 1 illustrates the differences in mild analog EEG ischemic change and density spectral array recordings.

The moderate analog EEG changes of cerebral ischemia not recognized by density spectral array consisted of a loss of beta activity and a greater than 50% increase in theta and delta slowing ipsilateral to the carotid artery during cross-clamping. These changes were not reflected in the density spectral array gray scale. No apparent shift of the background frequencies of the density spectral array to lower frequencies and no distinguishable attenuation of the beta activity could be identified. As
Two patients, both undergoing right carotid endarterectomy, developed new postoperative neurological deficits consisting of a left-sided neglect syndrome and weakness of the face and arm in one, and weakness of the face, arm, and leg in the other. Both patients experienced transient hemispheric attacks in the week before surgery, and one had residual weakness from a mild stroke.

In the patient with no neurological deficits before surgery, the preoperative baseline analog EEG tracing obtained while awake was normal. On three occasions during surgery, the analog EEG tracing showed mild and moderate transient increases in theta slowing and diminution of beta activity on the right. The first analog EEG ischemic pattern change was associated with a rapid decrease in systolic blood pressure of 20 mm Hg, the second with compression due to retraction of the carotid artery, and the third with a gradual lowering of the blood pressure while the carotid artery was cross-clamped. The first two episodes of analog EEG patterns of cerebral ischemia were also portrayed on the density spectral array, but the third event during carotid artery cross-clamping was a mild analog EEG ischemic change that was not detected by the density spectral array. Because of a high carotid artery bifurcation, the surgeon elected not to place a shunt, and the analog EEG ischemic change persisted. The postoperative neurological deficit was immediately evident and was unchanged when the patient was transferred to a rehabilitation center 5 days after surgery.

In a patient who had suffered a stroke prior to the surgery, the baseline analog EEG tracing was abnormal with decreased amplitude and an underlying background of irregular 4- to 5-Hz theta slowing and intermittent 2- to 3-Hz delta slowing on the right. After induction of anesthesia, there was severe amplitude depression on the right. At cross-clamping of the carotid artery, there was no significant change in the analog EEG data from the postinduction tracing. However, with the placement of the shunt, a predominant 1- to 3-Hz rhythmic delta pattern developed on the right and persisted throughout the operation. The analog EEG ischemic change was also evident on the density spectral array. The postoperative neurological examination showed exacerbation of the patient's left arm and hand weakness. These findings, however, completely resolved over 3 days.

**Discussion**

A significant relationship was found between the severity of the analog EEG ischemic pattern change (from mild to moderate to severe) and the probability that the change would be detected by density spectral array. The more severe the analog EEG ischemic pattern change, the more likely the density spectral array would show an ischemic change. The density spectral array's lack of sensitivity to mild analog EEG ischemic events demonstrates a major limitation in the ability of density spectral array to provide accurate information concerning the well-being of cerebral activity. The
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Changes represented 32% and 21% of the total cerebral ischemic events by Observers A and B, respectively, and the density spectral array sensitivity for those mild analog ischemic events was 61% and 18%, respectively. Therefore, we conclude that density spectral array, although highly specific for the absence of analog EEG evidence of cerebral ischemia, is not sufficiently sensitive in detecting mild analog EEG changes of cerebral ischemia for this technique to be a reliable substitute for 16 channels of analog EEG data as an intraoperative monitor of cerebral ischemia during carotid endarterectomy.

Our study was limited by the specific density spectral array device and its display. In our analysis, we did not include the trend charts or the four-channel analog EEG display, both of which were available on our model. These additions may have allowed greater accuracy in interpreting the density spectral array. We compared the analog EEG recording and density spectral array during carotid endarterectomy because both require interpretation of displays reflecting cerebral activity. A method of accentuating or highlighting the fast activity on the density spectral array may have improved its ability to detect mild analog EEG ischemic changes consisting of a diminution of the beta and alpha frequencies. A broadening of the delta and theta bands to make differentiation of slower frequencies possible may have improved sensitivity of the density spectral array in detecting cerebral ischemia in the moderate and severe groups. However, in our analysis, the ischemic analog EEG changes that the density spectral array did not detect were of a type that would not have been detected even if more channels were added to the density spectral array.

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