N93-25592
531-52
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p. 7

AUTOMATIC DETECTION OF SEIZURES WITH APPLICATIONS

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ABSTRACT

There are an estimated two million people with epilepsy in the United States. Many of these people do not respond to anti-epileptic drug therapy. Two devices can be developed to assist in the treatment of epilepsy. The first is a microcomputer-based system designed to process massive amounts of electroencephalogram (EEG) data collected during long-term monitoring of patients for the purpose of diagnosing seizures, assessing the effectiveness of medical therapy or selecting patients for epilepsy surgery. Such a device would select and display important EEG events. Currently many such events are missed. A second device could be implanted and would detect seizures and initiate therapy. Both of these devices require a reliable seizure detection algorithm. A new algorithm is described. It is believed to represent an improvement over existing seizure detection algorithms because better signal features have been selected and better standardization methods have been used.

INTRODUCTION

Computerized analysis of electroencephalogram (EEG) data has been the goal of many investigators for years (refs 1-13, 15-28, 31). Such an analysis system could be used for diagnosing seizures, for assessing the effectiveness of medical therapy or for selecting patients for epilepsy surgery. A necessary component of accurate assessment of medical therapy, including safe and effective surgery, requires prolonged EEG monitoring to obtain recordings of seizure activity. One important reason for developing a system is to meet the needs of about one-third of the many patients with complex partial seizures who do not respond to anti-epileptic drug therapy. Computerized systems can be used to collect and store the data, but even with new mass-storage devices, it is not practical to store and review all of the data collected over days. Automatic spike and sharp wave detection and automatic seizure detection algorithms could be used to detect critical events and store just the relevant data for later examination by the neurologist and neural surgeons. This information, in conjunction with clinical observation, is used to localize epileptic form discharges. Many of the references [refs 4, 5, 7, 8, 13, 20] discuss the development of automatic spike and sharp wave detection. Reliable automatic seizure detection is perhaps more challenging and would be a key element of any system designed for analysis of EEG data.

Another use of an automatic seizure detection system derives from the research in the use of electrical stimulation to control epileptic seizures. Hammond, et al. [14], and Wilder, et al. [30], stimulated the vagus nerve, and Velasco, et al. [29], electrically stimulated the centromediam thalamic nucleus. Both groups significantly reduced clinical seizures. Zabara [31] produced, tested and patented an implanted device to control or prevent epileptic seizures. His device proved most effective for the patients who can feel a seizure coming on and then use a small magnet to initiate the stimulation of the vagus nerve. These reports, coupled with the possibility of drug therapy initiated using an implanted device, suggest that an implanted automatic seizure detection device, coupled with a therapeutic device, could be developed and used to significantly reduce the frequency, intensity or duration of seizures.

EXISTING DETECTION SYSTEMS

Five groups of investigators have pursued the goal of automatic seizure detection by implementing a system and publishing their results. Prior, et al. [refs 26, 27] developed a simple system aimed at recording the timing and frequency of seizure discharges. They were able to detect severe seizures by looking for large amplitude signals sustained over a period of time. Their system used a single channel of data recorded on paper running at 5 to 6 cm/hour.

Babb, et al. [1] developed electronic circuits for recording and detecting seizures. Their system used implanted electrodes to detect seizures which might otherwise go unreported. The system identified as seizure high-amplitude EEG signals of sufficient durations. They reported monitoring four patients and detecting 66 seizures, 20 of which were false detections. During this same period of time, the nurses detected 28 seizures, two of which were false detections. Therefore, the automated system detected 20 unreported seizures.

Ives, et al. [refs 15, 16] used implanted depth electrodes and a PDP-12 computer to remotely monitor patients. The system was adjusted or calibrated for individual patients using their seizure patterns. If the EEG signals fell within an amplitude window for a certain period of time, the algorithm identified the event as a seizure and recorded eight channels of EEG data. During two weeks of monitoring, thirteen seizures were detected and recorded by the computer. Only one seizure was reported by the nursing staff and only 3 were noted by the patient.

Gotman [9-13] designed a system to select, from largely uneventful EEG data, the sections which are likely to be of interest. Events, such as seizures, are recorded either because the program detects them or because the event button is pressed. His system was originally implemented in 1975 and has been in use since that time. It detects seizures using both surface and depth electrodes. His system is in use in many centers and has been updated [10]. A study of his latest algorithm used 5303 hours of data and showed that 24 percent of the 244 seizures recorded were missed by the automatic detection system. However, in 41 percent of the seizures, the patient alarm was not pressed, but the computer made the decision to record the event. Like the other systems, Gotman's system detects many seizures which would otherwise be missed. The system experiences about one false detection per hour of recording.

Gotman's method uses digitally filtered data broken up into 2-second epochs. He compares features of this data to what he calls "background." The background data is a 16-second long section of data ending 12 seconds prior to the epoch being analyzed. This comparison allows the algorithm to self-scale to account for differences in montage or other settings and is a form of what we will refer to as calibration or standardization. Detection occurs when 1) the average amplitude of half-waves in the epoch is at least three times that of the background, 2) their average duration corresponds to frequencies between 3 and 20 Hz, and 3) the coefficient of variation (ratio of the variance to the square of the mean) of the half-waves is below 0.36. In short the algorithm is based on amplitude, frequency, and the regularity of the half-wave duration. In 1990, Gotman [10] reported modifications to his algorithm including the requirement to look 8 seconds ahead to verify that the amplitude remains high. This modification reduced false detections.

More recently Murro, et al. [23] developed a system using concepts similar to those of Gotman but used spectral concepts for feature development. They used three features from each of two channels. These six features are reduced to four using principal component analysis, and then statistical discrimination is used to develop a detection rule. Their algorithm was developed for intracranial data only.

They address the issue of calibrating for patient differences partly in the way they define their features. They define reference power as the spectral power between 0.15 and 36 Hz averaged over four consecutive EEG epochs from 27 to 55.6 seconds prior to the event being evaluated. One of their features is relative power and is defined as the power between 0.15 and 36 Hz of the current epoch divided by the reference power. The second of their features is the dominant frequency. The third feature is rhythmicity, which is the ratio of the power associated with the dominant frequency to the relative power. Murro, et al.

use a segment of recent EEG data from the patient to influence the definition of their first and third feature. However, Murro, et al. also provide more in the way of custom tailoring their algorithm to the individual by building a separate decision rule for each patient. Their rule is based on normal data from the patient collected at different times and seizure data collected from other patients. These procedures allow for a more careful calibration for patient differences.

The algorithm of Murro, et al. [23] was tested using 8 patients and 43 seizures. Their system was evaluated using different detection thresholds. It detected all seizures allowing for a rate of 2.5 false detections per hour and detected 91% of the seizures with 1.5 false detections per hour.

ALTERNATIVE APPROACHES

The first seizure detection methods relied on amplitude and duration to identify seizures. Gotman's method tends to mimic the EEG readers. He characterizes the signals using features appearing to be motivated by those observed during seizure activity. His self-scaling and his detection rules are simple but effective.

The methods of Murro, et al. are similar to Gotman's but are more statistically sophisticated. Like Gotman, Murro, et al., used recent epochs to self-scale their features. They characterize the epochs of data using relative amplitude, dominant frequency and rhythmicity and then use statistical discriminate analysis to develop a detection rule.

There are three important common elements in these two algorithms and in our own:

1) standardization, calibration or self-scaling
2) feature selection
3) discrimination or a decision rule

We believe that the most critical element in discriminating seizure from other data is the definition and evaluation of features or feature selection. We also believe that other standardization or calibration methods will prove useful. Our algorithm has characteristics which it make fundamentally different from those of other investigators. More emphasis is placed on developing and evaluating a variety of features and on developing an improved approach to standardization.

THE ALGORITHM

Each channel or time series of EEG data is divided into non-overlapping 3-second epochs of data. The first goal is to compute a probability that the patient is having a seizure for each 3-second segment of data and for each of the different channels processed by the system. These probabilities will be combined with probabilities from adjacent epochs to determine if a patient is having a seizure.

To compute the probabilities, several steps are necessary. First the data must be standardized to account for patient, channel and hardware differences. The intent here is different from that of Gotman's self-scaling in that we are not simply evaluating the current epoch relative to background. The methods are very different and the results are different. However, both provide essential calibration necessary to account for patient differences. In our method, a standard deviation of the data is computed and updated for each channel. That is, values are recursively updated as new data enters the system. The current standard deviation is then used to scale the new data to make it consistent with that assumed by the algorithm. A standard deviation is computed and used for each channel.

The next step in developing probabilities of seizures is to characterize each epoch of data using many features and to evaluate these features to determine which can best help separate seizure and normal data. Several hundred features have been evaluated. These include usual time-series characteristics, features which mimic EEG readers' methods and statistical characteristics. We find that all three types of features contribute to the discrimination and algorithms which use all three in combination are better able to detect seizures than those that do not.

Once a set of most-effective features has been identified, then any of the many discriminate techniques can be applied. Our base algorithm uses logistic regression. Neural networks and statistical discrimination techniques such as those described by Murro et al., [23] or Olsen et al., [24] could easily be applied. Logistic regression has the advantage that it provides a meaningful probability of seizure. In our algorithm, the user can adjust the probability levels to reduce false seizure detections or to increase sensitivity. The user may also adjust the standardization for the same purposes.

TRAINING AND TESTING THE ALGORITHM

The critical measure of an algorithm's performance is not how well it detects seizures, but how well it detects seizures without producing false detections. It is a simple matter to demonstrate an algorithm correctly identifies seizures on a limited span of data. Our algorithm has been applied to several spans of seizure data from different patients and all seizures were detected with no false detections. The difficulty comes when extending an algorithm's use to days of data. Thus, while our algorithm performed admirably on many data sets, the only true test is that which comes from extensive testing on large representative data sets or from continuous monitoring of patients in a real-time environment.

Five-minute segments of data were collected from each of two patients, both day and night, over a five-day period. The segments were sampled at least once per hour with an effort being made to record a variety of activity and sleep stages. Nine seizures (some lasting over 10 minutes) were recorded, five from one patient and four from the other. Seven and one-half hours of sampled data were saved. An initial algorithm was developed for two channels from one patient and was successfully applied to the second. All seizures in both patients were detected and there were no false detections.

Our algorithm was developed using all 35,000 epochs of standardized data from both patients. Seizure onset for one patient was on the left temporal region and for the second was on the right. As a result, data from FP1-F7, F7-T3, T3-T5, and T5-O1 from the first patient and data from FP2-F8, F8-T4, T4-T6, and T6-O2 from the second were used as example data to build the algorithm. When the algorithm was applied to the sampled data, *all seizures were detected and there were no false detections.*

Our algorithm used logistic regression to identify the most useful features and to form a decision rule. Unlike neural networks, logistic regression selects only about 5-15 constants and therefore cannot over-train or memorize even with much smaller data sets. As a result, the testing on 35,000 epochs of data described above provides significant evidence of the discrimination capability of the algorithm. It remains to test the algorithm on other large data sets and in a real-time environment.

APPLICATIONS OF AUTOMATIC SEIZURE DETECTION

In the United States alone, there are over two million people with epilepsy. Each year 100,000 new cases are diagnosed. The most common type of seizures are complex partial seizures and of these, 35% of the patients fail to respond to anti-epileptic drug therapy [14]. Since for these patients, long-term monitoring is necessary for localization of epileptic activity (for possible local resection), the need is clear for a system which will process the massive EEG data collected and decide which data to save. Such a system would also be used to evaluate various drug therapies. Automatic spike and seizure detection capability is an essential part of developing a microcomputer based monitoring system.

As noted in the introduction, the first application of the seizure detection algorithm will be to monitor patients in long-term epilepsy monitoring units. Most of these data will be from surface electrodes.

A more ambitious application, in some respects, is to automatically detect seizures and reduce their intensity or duration. Since the data for this application would be from implanted electrodes, the seizure detection algorithm would not need to deal with muscle and other artifacts or the effects of the skull on the electrical signals. The algorithm could be adapted to the patient. Based on experience with more difficult surface detection algorithms, we believe that a highly reliable detection algorithm can be developed.

SEIZURE DETECTION IMPLANT HARDWARE

It is somewhat difficult at this stage of the program to predict accurately what the configuration of an implanted monitoring device will be. This is due to the fact that the algorithm would not be finalized until extensive on-line testing is complete. However, the development of such a device is not beyond the "state of the art" and certain aspects of the implant can be predicted, which are discussed here. The physical configuration will be very much like a modern-day pacemaker. There will be a titanium case about 1.5" x 1.5" x 0.3" thick that will be implanted subcutaneously just below the clavicle. This case will hold the electronics as well as a lithium battery which should allow an implant life of 5-6 years. There will be a lead containing at least 4 conductors connecting to the case. This lead will be tunneled subcutaneously over the clavicle, up the neck and under the scalp to the point of entry into the skull. This is the same technique which is currently used for hydrocephalus shunt systems. Once the leads enter the skull, they will travel under the skull to the surface locations on the brain which were selected by the surgical team at implant.

The circuitry for this device will probably use subthreshold CMOS analog circuitry rather than digital CMOS circuitry. The analog circuitry uses less power for the large number of computations which will be required by this device. The analog approach also eliminates the analog-to-digital (A/D) converters which would be required in the digital approach.

CONCLUSION

The development of new medical procedures has enabled neurologists and neural surgeons to provide safe and effective treatment of otherwise intractable epilepsy. At the same time, the development of computer technology has made it possible to collect and process more information than ever before. Key elements to improving the general care of patients with intractable epilepsy are the algorithms which will enable the computers to efficiently reduce the data collected to information useful in planning therapy or possibly to initiate treatment in a timely fashion. Systems for the long-term EEG monitoring have been developed at the Johns Hopkins Hospital and elsewhere. Some of these systems automatically save spike and seizure data for later analysis by neurologists. Commercial development of such a system is possible.

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