RULE BASED GRADED ANALYSIS OF AMBULATORY CASSETTE EEGs

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BY

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Dedicated to

Parul, Anuj and Amit

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ABSTRACT

Visual interpretation of prolonged ambulatory cassette EEGs (AEEGs) is time consuming and strenuous. This thesis therefore describes the development and evaluation of approaches for multi-channel context based analysis of 4-channel AEEGs. The algorithms identify spikes/sharp waves (STs), spike-and-wave complexes (SSWs), artifacts and background activity.

The algorithms were trained using 40 segments from a computerized database. Time domain/Mimetic methods were used and semantic rules, based on morphology and contextual information, were developed. Using these rules, the likelihood of STs/SSWs being genuine, was graded from 10 to 1. This approach avoids forced classification of each event as genuine ST/SSW or not.

The algorithms were then evaluated using 60 independent segments. STs/SSWs graded greater than 7 had a significantly higher probability ($P < 0.005$) of being genuine than those graded less than or equal to 7. Less than 4 % of distinct STs/SSWs were missed. Classification of 86 % of waves in the background matched that of one EEGer. The algorithms can now be incorporated into a pattern recognition system.

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1.0. INTRODUCTION

1.1. The Electroencephalogram (EEG).

The EEG is a useful non-invasive procedure for the investigation of neurological problems and has also found applications in the study of physiological states such as sleep staging and maturation of the newborn (Neidermeyer and Lopes da Silva 1982). It has been particularly valuable in the diagnosis and management of epilepsy (Klass and Daly 1979).

Conventionally, EEGs (CEEGs) are done in the laboratory for periods up to an hour with the objective of detecting interictal epileptiform patterns. Epileptiform activity in general, occurs randomly and infrequently. Furthermore, such activity is not diagnostic of epilepsy but only has a statistical association with seizures (Kellaway 1981). In some cases therefore, a diagnosis can only be established by documenting an electrographic ictal event simultaneously with a clinical one. But, as Riley et al. (1981) emphasize, these events occur less frequently in the hospital setting than in the patient's natural environment. Therefore, such events may not occur during CEEGs, even if recordings are done for prolonged periods.

In 1975, Ives and Woods described a 4-channel cassette recorder that could be used to record EEG signals on ambulatory subjects. Such recordings (AEEGs) can therefore be done in the patient's own environment. Twenty-four hours of EEG data can be recorded on one C-120 cassette. The procedure may have to continued for several days in order to capture events (Stores 1984). A number of studies have documented the usefulness of AEEGs in adults (Ives and Woods 1980; Bridgers and Ebersole 1985) and children (Seshia et al. 1984; Stores 1984; Jayakar et al. 1987b). The ambulatory (outpatient) nature of the procedure also makes it a cost-effective one.

The electroencephalographer (EEGer) interprets AEEGs by playing back the cassette and displaying the signals on a videoscreen. Complete examination of the entire recording, the only reliable means of detecting all abnormalities (Bridgers and Ebersole 1987), may take 2 to 4 hours. Interpretation is therefore both time consuming and visually strenuous. An automated system which would scan the entire record, identify and present only significant data to the EEGer for final examination, would facilitate interpretation of AEEGs. Such a system would also have the added advantage of being able to provide quantitative information.

A number of automated systems have been developed to detect selected components of EEG activity; these have been reviewed by Frost (1985), Gotman (1985), Principe and Smith (1985) and Samson-Dollfus and Senant (1985). Most of these systems have concentrated on analysis of waveform characteristics and have tended to ignore contextual information (Frost 1985). Their performance is unpredictable, particularly with respect to poorly defined events and artifacts (Koffler and Gotman 1985); the latter are of particular relevance in ambulatory recordings (Ebersole et al. 1983; Jayakar et al. 1985).

1.2. Objectives of research.

The objective of this thesis was therefore to develop a pattern recognition methodology for multi-channel context based analysis of AEEGs. Specifically, the algorithms had to identify spikes and sharp waves (together called sharp transients-STs in this thesis), spike-and-wave complexes (SSWs), artifacts and background activity. Analysis of background was intended to provide quantitative information.

The main emphasis of this study was to develop approaches that (1) mimicked the processes and principles involved in visual interpretation, (2) overcame/minimized some of the limitations of existing automated systems and (3) would be flexible and interactive so as to be acceptable to a large majority of EEGers.

1.3. Chapter outline.

The background for this study is provided in chapter 2 and the principles of approach and methodology are detailed in chapter 3. The evaluation of the algorithms and the results are given in chapter 4. Discussion of the study is presented in chapter 5 followed by conclusions and recommendations for future investigation in chapter 6.

2.0. BACKGROUND

2.1. Ambulatory Electroencephalography.

The AEEG recording system consists of a set of electrodes, a preamplifier unit, a 4-channel cassette recorder and a calibration unit (Ives and Woods 1980). The tape recorder, powered by batteries, houses a C-120 cassette which at a recording speed of 2 mm/s can contain up to 24 hours of AEEG. The recorder also has an event marker button which when pressed, introduces characteristic pulse signals on channel 1. These signals tag specific sections of the AEEG. These sections can then be correlated with the log of activity kept by the patient or the observer.

The recording procedure was standardized (Seshia et al. 1984; Jayakar et al. 1985). In particular, calibration signals were inserted into the begining of each tape and proper technical performance ensured to minimize technical artifacts.

AEEGs were interpreted using a computer based system (Brusse et al. 1984). The gains on the playback unit were adjusted to the calibration signal inserted into the begining of the tape and the time constant (low frequency filter) on the playback unit was set at 0.1 to 0.05 s (American EEG society guidelines 1986), so that the AEEG signals displayed on the screen were "standardized".

2.2. AEEG Activity.

The wave types seen in AEEGs may be divided into background, epileptiform activity, seizure patterns and artifacts (International Federation of Societies for EEG and Clinical Neurophysiology - IFSECN 1983).

The background activity is subclassified on the basis of frequency into 4 bands. These are Delta (< 4 Hz), Theta (4 to < 8 Hz), Alpha (8 to 13 Hz) and Beta (> 13 to 35 Hz).

Epileptiform activity may be of 2 types. (a) Spikes (20 to 70 ms) or sharp waves (70 to 200 ms), together referred to as sharp transients (STs) in this thesis, are transients "clearly distinguished from background activity", with pointed peaks at conventional paper speed (30 mm/sec) and having variable amplitudes. (b) Spike-and-slow-wave complex (SSW) consists of a spike followed by a slow wave.

Seizure patterns consist of repetitive discharges with relatively abrupt onset and termination and a characteristic pattern of evolution. The component waves vary in form, frequency and topography and are generally rhythmic.

Artifacts are activities of extracerebral origin and may be either physiological (eg., EMG), technical (eg., electrode pop) or environmental (eg., 60 Hz). They may occur transiently or obscure the greater part of the record.

2.3. Visual Interpretation.

The principles of interpretation of AEEGs in general follow those of CEEGs (Gloor 1977; Pedley 1980; Ajmone-Marsan 1984; Engel 1984). Thus, STs/SSWs are identified in complex interactive steps involving morphology, spatial and temporal contextual information. Final interpretation is generally based on the entire record and not on individual events.

Certain aspects of interpretation are unique to AEEGs: (1) The filters in the preamplifier, the tape recorder and the playback unit introduce a cascaded "time constant", which influences the morphology of the signal differently from the single time constant system in CEEGs. This effect may be significant (Shwedyk et al. In Press). The performance of an automated system may therefore be affected if the filter settings are different from those used for the training set of AEEG data. Standardization of the filter settings is therefore important.
(2) The unrestricted activity permitted during recording makes AEEGs prone to artifacts not commonly seen in CEEGs. Some of these artifacts may be morphologically similar to epileptiform activity and pose problems in interpretation (Jayakar et al. 1985).

The EEGer's interpretation is in practice considered to be the "gold standard" for developing and evaluating automated systems. The problem with using this standard is that there is considerable inter-observer variability when EEGers are asked to identify each and every ST/SSW in a record (Gose et al. 1974; Ehrenberg and Penry 1976; Koffler and Gotman 1985). Thus, for example, in a study by Gose et al. (1974), 5 EEGers were given thirty 2 min, 8-channel tracings and asked to mark all spikes. In total, 948 spikes were marked by one or more EEGers, but only 104 (¬ 11 %) were marked by all 5; a total of 466 (¬ 45 %) were marked by only one EEGer and not by the others. This degree of disagreement likely occurred because the EEGers were performing an artificial task, that of identifying every single event, which they never do in day to day practice (Gotman 1985). When the interpretations of the entire record were considered, the agreement was found to be 96 %. Electroencephalography would not be a useful procedure without such overall agreement.

The problem of the "gold standard" is further compounded by intra-observer variability (Woody 1966). But for evaluating automated systems which are expected to be consistent in performance, intra-observer variability is less relevant than inter-observer variability.

2.4. Review of methods.

The rapid advances in computer technology have led to the development of several methods of automatic EEG analysis. Most systems developed for either CEEGs, AEEGs or telemetric EEGs, recognize selective components of EEG activity and have been reviewed recently (Frost 1985; Gotman 1985; Samson-Dollfus 1985; Principe and Smith 1985).

The methods of analysis may examine amplitude relationships as variables in time (time domain methods) or the frequency components (frequency domain) in the EEG signal. Time domain methods are comparable to visual analysis which is mainly "pattern oriented" (Schenk 1976). A classification based on time and frequency domains does not include all methods of analysis. Other classification schemes have therefore also been described (Matousek 1973; Lopes da Silva 1982).

The methods as applied to pattern recognition may be discussed in five groups:

2.4.1. Analysis of background activity.

(A) Time domain based methods.

The amplitude of the signal may be described using a variety of indices such as "baseline" to peak voltage, peak to peak voltage, root mean square voltage or voltage squared (Goldstein 1975; Harner 1977).

Interval or Period analysis (Saltzberg and Burch 1957; Saltzberg 1973) measures the interval between specified "critical data points" on the EEG curve. These critical points may be the times at which:

(i) The signal x(t) passes through a specific amplitude level k; in the special case where k=0, one speaks of zero crossings. The level of the threshold must be defined by continuous computation of the average amplitude (Leader et al. 1967). Otherwise, a slight shift in the baseline produces a large change in the interval detected (Saltzberg 1973). Furthermore, the use of level crossings produce a weighting of the frequency components in the EEG towards those of a higher amplitude. This is because larger waves are more likely to cross the baseline than smaller waves (Harner 1977). Another disadvantage is the sensitivity of the level crossing estimate to high frequency noise (Lopes da Silva 1982).

The time between 2 crossings is used to determine a half-wave and is known as the primary or major period.

(ii) The signal reaches an extremal, ie. the slope is zero. The interval between two extrema which may also be considered to be a segment or a half-wave, is called the intermediate period.

(iii) The signal has an inflection point, ie. the second derivative is zero. The interval between two inflection

points is called the minor period.
The latter two periods often represent superimposed activity (Walter 1972).

Methods which examine both the interval and the amplitude (Interval-amplitude analysis) have been described (Marko and Petsche 1957; Legewie and Probst 1969; Goldberg and Samson-Dollfus 1975; Harner 1975; Remond 1975; Schenk 1976). A method may be biased towards the underlying slow or the superimposed faster activity depending on the criterion used to define the period. Iterative methods (Remond 1975; Schenk 1976) which detect both the underlying and superimposed activity are based on the detection of peaks and troughs and then successively the peaks and troughs of these extreme values and so on. Thus a hierarchy of intervals is obtained; long ones initially, representing background and baseline shifts and then shorter ones in successive iterations, representing high frequency activity and even noise.

A major advantage of interval-amplitude analysis methods is <u>the high degree of data reduction and the speed of computation</u>. This allows the implementation of on-line, real-time analysis on a small computer.

(B) Spectral analysis.

This is an excellent technique for the statistical quantitation of background activity. Both the dominant underlying, as well as the superimposed activity are evaluated independently and accurately. To evaluate the amounts of energy in different frequency bands, the EEG is handled and decomposed as a single realization of a stochastic or random process.

Spectral analysis may be done by either nonparametric or parametric methods. Nonparametric methods, eg., Fourier analysis, analyze EEGs without assuming a specific model for EEG generation. A disadvantage of this technique is the requirement of a fairly long observation time to achieve good spectral estimates. This may conflict with the assumption of stationarity of the EEG signal over that period (Isaksson et al. 1981). Furthermore, in comparison to the time-domain methods this method of analysis loses the temporal dimension of the succession of waves (Samson-Dollfus and Senant 1985). Generally there is only a weak correlation between a certain time domain pattern and the power spectrum (Schenk 1976). Hence, spectral analysis is not ideally suited for identifying individual waveforms.

The parametric methods describe the EEG signals in terms of a mathematical (usually linear) model characterized by a set of parameters and have some advantages over the nonparametric methods (Jansen et al. 1981). The model is strictly empirical and descriptive and does not claim <u>to represent the neurophysiological generation of EEG</u>. It provides a practically useful method, not only to compute the spectra (Wennberg and Zetterberg 1971; Isaksson et al. 1981), but also to subdivide the EEG into quasi-stationary segments, ie., adaptive segmentation (Bodenstein and Praetorius 1977). Bourne et al. (1981) developed spectral estimates from the autoregressive model to classify short segments of EEG background activity and then used syntactic analysis to provide a descriptive summary of the EEG, in patients with renal disorders. Thorne (1981) and Arbez (1984) extended the method, to analyze both the epileptiform patterns and the background activity in AEEGs.

2.4.2. Detection of sharp transients (STs).

Most published methods have concentrated almost exclusively on morphology and have tended to ignore the context (Frost 1985). The main reason for this probably lies in the difficulty of writing programs that precisely mimic human performance (Gotman 1985). Several methods have been explored.

(A) Time domain based or "Mimetic" methods.

The single feature which seems to provide the best discrimination is the peak. The peak is detected by the second derivative (Saltzberg et al. 1967) which is compared to a threshold. The latter need not be fixed, but can be continuously modified by computing the running average of the second derivative within a predetermined preceding window (Carrie 1972a). This is meant to detect events 'clearly distinguished' from the background. Though the second derivative may detect almost 100% of the STs, it is also very sensitive to low amplitude noise and thus needs to be "normalized". In this form it has been used as a key component of more recent schemes which incorporate measurements of other features and multiple thresholds as well (Gevins et al. 1975; Gotman and Gloor 1976; Frost 1979; Glover et al. 1986).

The other features or parameters include slopes, durations, absolute and relative amplitudes (compared to the background) of the up and down strokes and the presence of an after-coming slow wave. The above parameters which were characterized by Ktonas et al. (1981), <u>are not necessarily independent of each other</u> since for instance, a wave with steep rising and falling phases is likely to have a sharp apex (Gotman 1985). Some redundancy may however be helpful in the detection of atypical spikes. As with the computation of the second derivative, these thresholds can be continuously modified by computing the average value of that feature for a preceding window.

The computation of the duration of the ST can pose problems. Gotman and Gloor (1976) defined a feature called "pseudoduration", whereas Frost (1979) defined the begining and end of the ST when the slope fell below a certain fixed threshold.

Guedes de Oliviera et al. (1983) used discriminant analysis to determine which of the several features described above had the best discriminating power. The maximum slope and sharpness, relative to a running average of the background and total wave duration, were the most efficient parameters for ST detection.

The mimetic methods described so far have some limitations:

(1) The average values of the features (eg., amplitude or second derivative) are computed from <u>all preceding waves</u> which may include very slow waves or fast muscle artifact thus contaminating the threshold. Harner and Ostergren (1976) therefore detected waves that were higher in amplitude than the median amplitude of other waves of similar duration found in the background. They however did not measure the sharpness of the waves.

(2) Limited contextual information is obtained only from a <u>small preceding window</u>.

(3) The computer is forced into classifying each event as either a ST or not a ST. The computer's performance like that seen in inter-observer agreement studies (section 2.3), is therefore also variable.

(B) Parametric Methods.

These methods as described earlier, are based on the representation of a section of EEG by a small number of parameters. Rather than describing each wave , the parameters represent the statistical properties of the EEG during the section for which they are determined. ST detection is based on the assumption that ST is an unexpected or statistically improbable event. This concept was proposed by Lopes da Silva et al. (1975,1977) who used the autoregressive filter as a parametric model. In this model it is assumed that the EEG can be represented by linear filtering of white noise. For a section of EEG the filter coefficients are calculated so that the filtered noise and the EEG epoch would have the same second order statistics (would 'look similar'). The original EEG is then passed through the inverse of the calculated filter. The output is expected to be white noise. If the statistical properties of this output deviate from those of white noise, a non-stationarity is said to be present in the EEG.

Many non-stationarities in scalp EEGs, although not concurrent with a spike, are associated with a "spike" in a simultaneous subdural recording (Lopes da Silva 1975, 1977). But there also are non-stationarities that are related to non-epileptiform activity such as vertex sharp waves, EMG artifact and abrupt changes in the background activity. In the absence of subdural recordings it is impossible to decide whether a non-stationarity is epileptiform or not (Gotman 1985).

Approaches similar to the non-stationarity detection method have been described (Samson-Dollfus et al. 1978; Barlow 1980), but suffer from the same basic limitation.

(C) Template Matching or Matched filtering.

A particular ST (template) is chosen and continuously compared to the EEG signal using a measure such as the cross-correlation function (Gotman 1985). Other waveforms which are similar to the template are considered to be STs. This method has only limited application clinically since STs can have a wide variety of configurations in clinical practice (Frost 1985). Barlow and Dubinsky (1976) also discussed the difficulty of choosing the appropriate length of the template; should it include the ST only or also some of the background activity?

Birkemeier et al. (1978) compared the method of non-stationarity detection with that using simple sharpness criterion and found that both performed comparably well. They suggested the use of both methods in succession. Pfurtscheller and Fischer (1978) suggested a combination of inverse and matched filtering for ST detection.

2.4.3. Detection of Spike-and-wave complexes.

SSWs are readily identified in the EEG by their high amplitude and usually regular, bisynchronous appearance. Methods to identify SSWs have been developed mainly as extensions of those used for ST detections (Carrie 1972b;

Frost 1979; Smith et al. 1979; Principe and Smith 1985; Koffler and Gotman 1985). Most use the following scheme: First the individual STs/slow waves are detected. Rules are then applied to recognize a pattern.

Jestico et al. (1976) and Quy et al. (1980) used a simple band-pass filter and threshold logic to detect the slow wave components. Kaiser (1976) used the amplitude and duration of the spikes and slow components. Ehrenberg and Penry (1976) used zero crossing information to build two running sums of data. Each of these sums was obtained from a combination of 4 EEG channels and was compared to a fixed threshold level that was derived heuristically. Others (Carrie and Frost 1977; Gevins et al. 1980; Burr et al. 1981; Principe and Smith 1982;) used amplitude duration criteria based on the configuration of the extrema, either with or without the use of filters. EMG detectors to exclude artifacts were used by Carrie and Frost (1977) and Gevins et al. (1980). The latter "matched" the ST and slow wave components in homologous channels. Whisler et al. (1982) described SSWs detected by the system as "clear" or "marginal" on the basis of slow wave bursts and ST components. Pinon et al. (1982) compared the performance of 8 variables that were related to the energy of the signal and its derivatives using discriminant factor analysis.

Johnson et al. (1978) and Principe and Smith (1985) implemented a SSW detector based on the repetitive properties of the pattern. Two analog filters (22 to 45 Hz, 1.5 to 4 Hz) were used to detect the basic components (spikes and slow waves) morphologically in the initial stage. This was followed in a second stage by pattern rules to distinguish the random sequences of similar waveforms present in artifacts from the orderly sequence of these elements in SSW bursts. Koffler and Gotman (1985) described a system based principally on ST detection in successive 1/3 s epochs and across channels in AEEGs. The slow wave components were considered only for low amplitude STs.

Most of these methods perform satisfactorily for SSWs of long duration (> 3sec) but have a higher error rate for short bursts (Frost, 1985). The systems have an all-or-none approach, the limitations of which as discussed for ST detection methods in section 2.4.2, also hold true for SSW detection.

2.4.4. Detection of seizures.

Few publications have dealt with automatic recognition of seizures not characterized by 3 Hz SSW. From the point of pattern recognition these other seizure patterns pose a problem, as the patterns to be recognized are often poorly defined and can be extremely variable. Techniques based on large changes in amplitude (Prior et al. 1973; Ives et al. 1974) are not very sensitive. Gotman (1982) using average amplitude, duration and coefficient of variation (indicating rhythmicity), found that about 20% of the detections were true seizures in scalp recordings. Though the false detection rates are high a considerable amount of data reduction is still achieved.

2.4.5. Artifact rejection.

Artifacts pose a major problem in prolonged monitoring especially when the patient is ambulatory (Gotman et al. 1979). Several criteria have been used to eliminate gross artifacts (Gotman 1985). These are:

(1) Waves with a duration less than 18 to 30 msec are assumed to be EMG artifact.

(2) Waves with an amplitude which exceeds 500 uv and persists above that level for more than 100 msec are assumed to be movement artifact.

(3) If the amplitude difference between two adjacent samples (slope) exceeds 15 uv/msec, a technical artifact is assumed to be present.

Gevins et al. (1975,1977) described a method based on spectral analysis to eliminate artifacts. Bourne et al. (1981) found that the syntactic approach was useful in differentiating artifact from the background activity in patients with renal disorders.

Despite these approaches, it is practically impossible to automatically eliminate all false positive detections due to artifacts (Gotman 1985).

2.5. Evaluation methods.

Gotman (1985) discusses some of the problems associated with evaluation of automated systems. These are related to the "gold standard" used for evaluation and to the type of data selected.

The EEG background activity is not a pure sinusoid. The classification of each wave into one frequency range is therefore based on the identification of the most dominant frequency component. This task may be extremely difficult when there is a combination of frequencies and would depend on the choice of the 'level crossing'. One cannot therefore expect a perfect agreement between any two independent classifications.

Lopes da Silva et al. (1975) evaluated their method by comparing the non-stationarities detected in scalp EEGs with simultaneous subdural recordings. The latter are not influenced by inhomogeneities of the skull and scalp and are not contaminated with muscle artifact. One expects that these factors would allow the EEGer to identify epileptiform activity more reliably in subdural recordings than in scalp EEGs. However, such evaluations would not be readily feasible in general.

Gotman et al. (1978) evaluated their method by using EEGs obtained from normal adults, non-epileptic abnormal adults and epileptic patients. Detections in the first two groups were considered to be truly false positive errors.

Most studies compare the performance of the system with annotations done by EEGers. Three different approaches have been used:

(1) Simple comparisons with one EEGer (Birkemeier et al. 1978) or a consensus of several EEGers. The consensus was variably defined as the agreement between 2 out of 5 (Gevins et al. 1975), 7 out of 8 (Guedes de Oliveira et al. 1983) or 3 out of 3 (Ehrenberg and Penry 1976) EEGers. The criteria used were false positive or negative errors. Gotman et al. (1978) defined these errors as those detections which could be unambiguously visually identified as or not as EMG , eyeblinks and alpha "artifacts".

(2) Comparing the system with the EEGers performances taking observer variability into account. Guedes de Oliveira et al. (1983) used arbitrary definitions to design sensitivity and specificity criteria. They compared the maximum and minimum values of sensitivity and specificity obtained by a set of EEGers and by the computer. Ehrenberg and Penry (1976) compared the number of times a reader or a computer stood alone in detecting or rejecting a SSW.

(3) Comparing the overall performance of the system. Gotman et al. (1978) evaluated their method by comparing the interpretation of the EEG tracing done by 2 EEGers on one hand and the results of the analysis by the computer on the other hand. Bourne et al. (1981) compared the results of syntactic analysis with overall interpretations of the EEGers.

EEG data selection may vary from study to study making comparison of system performances difficult (Koffler and Gotman 1985). The duration of recording may be short or prolonged. The latter increases the probability of finding artifacts (eg., by electrode drying). The recording may be done either at rest or on ambulant subjects. Those on ambulant subjects are prone to artifacts and may affect the results of analysis. The state of the subject during a recording may differ. Recordings during sleep or active awake periods (eg., eating) present different transients and artifacts from those during awake resting periods.

2.6. Principles of Pattern Recognition (Duda and Hart 1973).

"Recognition" is a basic attribute of humans who can be regarded as very sophisticated information systems with superior pattern recognition capability (Tou and Gonzalez 1974).

Gevins et al. (1975) emphasize the need for and the importance of, standardized databases for the development of pattern recognition systems. A database is essential for both training (learning set) and evaluation (test set) of the algorithms. The set of features which give the best possible discrimination between classes is determined from the learning set. The system's performance will be satisfactory only if the size of the learning set is large enough. Although there is no theoretical answer to the size of the learning set required, Demartini and Vincent-Carrefour (1977) suggest that the number of samples N, must be greater than the following limit:

N= 5*n*k where n = dimension of the feature space
k = number of classes

Thereafter the best set of features is used to classify other data forming the test set. The performance of the system can be evaluated by error rates, preferably the error rates for <u>new patterns which do not belong to the learning set</u>. The confidence in the estimation of performance again depends on the test set sample size. Thus as a guideline, for a two class problem with a minimum of 100 samples, an apparent error rate of 0.05 has a 95 % confidence interval of (0.02, 0.12) (Highleyman 1962).

3.0. RULE BASED GRADED ANALYSIS

Having reviewed the literature on automated EEG analysis this chapter presents, explains and discusses the pattern recognition methodology developed in this thesis. Before discussing the methodology a brief overview of the hardware, software and data used for training and evaluating the algorithms is given.

3.1 Hardware and Software.

The algorithms were developed on a DEC PDP-11/73 microcomputer with a 30 MB fixed Winchester (RD52) hard disc and A/D and D/A converters. The operating system is micro/RSX. The programs were written in Fortran 77 and Assembly languages.

3.2. Database.

A computer database of AEEG signals (Jayakar et al., 1987a) was developed before the current study was planned. It now contains 100 thirty second segments from the AEEGs of 50 children. Data, sampled at 128/sec, is stored on a hard disc.

The AEEGs, done on subjects aged 1-22 years, were recorded either to aid in the diagnosis of epilepsy or to assess seizure frequency in patients with epilepsy. Bipolar derivations employing standard inter-electrode distances were used for all recordings; the choice of montage was based on clinical information. All recordings were done according to a set protocol (Jayakar et al. 1985). All tapes were calibrated.

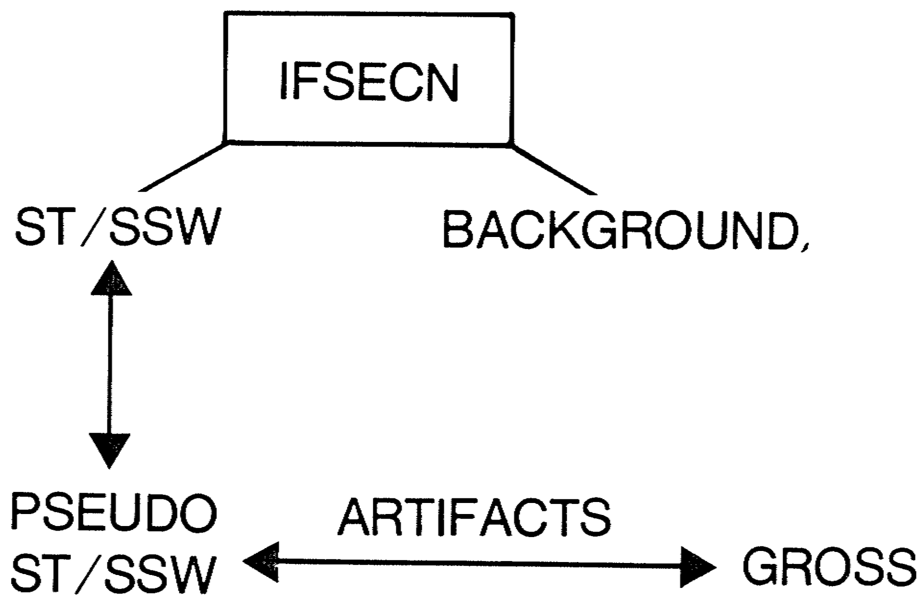
A classification scheme was developed to include background activity, epileptiform patterns and artifacts (Figure 1). The terminology was based on the recommendations made by the IFSECN (1983). The complexity of differentiating epileptiform activity from some artifacts prompted the annotation of artifacts into two groups: one of <u>gross or easily differentiable artifacts and the other of "pseudo" STs/SSWs which morphologically resemble STs/SSWs</u>, <u>but can be differentiated as such by contextual information</u>.

Two segments were selected from each tape during the awake and sleep sections of the record. The segments were selected by an individual other than the EEGers who annotated the data, to minimize selection bias. The selected segments were written out on a strip chart recorder and annotated independently by 2 EEGers. After every 10 segments or so, the contents of the database were examined and subsequent selections done so as to obtain a relatively uniform number of epochs in all classes, especially in ST/SSW and pseudo-ST/SSW.

The data base is structured so that a specific class or groups of classes can be recalled independently, thus facilitating its role in training of algorithms. Forty of

Figure 1. Database classes. Artifacts resembling epileptiform activity were classed separately as pseudo-ST/SSW.

DATABASE CLASSES



the 100 segments were used for training the algorithms and the remaining 60 for evaluation. Thus the EEG data and the subjects were independent in the two groups.

The database has some limitations: (i) The sampling rate of 128/sec may affect the performance. For example, this sampling rate does not provide adequate resolution to differentiate a 10 Hz. wave from a 10.5 Hz. wave (Harner 1977). Higher sampling rates (200 to 256) may therefore be considered in future. (ii) The problem of inter-observer variability cannot be entirely eliminated because the data base has been annotated by only two EEGers. It should be pointed out that 5 EEGers had agreed to participate in the database project but the annotation procedure was so time-consuming, that 3 of them dropped out (Jayakar et al. 1987a). (iii) Background activity may also occasionally resemble STs (sharply contoured theta or alpha) or SSWs (bursts of slow waves in drowsy state). These patterns were not classified separately as was done in the case of artifacts.

3.3 Principles of Approach.

The choice of the method of EEG analysis should be guided mainly by the goal of its application. Practical considerations for the appropriate strategy include the number of derivations to be analyzed, the duration of the records and whether the results must be made available in real time or may be presented off-line.

The objective of this study was to develop algorithms for the off-line analysis of 4-channel AEEGs in a manner comparable to the EEGer. The EEGer analyzes the morphology of individual waveforms and the context in which they occur in an attempt to classify them. Some epileptiform and non-epileptiform activity may have similar features. Specific events (waves of interest) may be considered to be either <u>definitely epileptiform</u>, <u>possible</u>, <u>questionable</u> <u>or</u> <u>definitely non-epileptiform</u> (Ajmone-Marsan 1984, Frost 1985) (Figure 2).

Time domain / Mimetic methods were therefore used for morphological analysis. Semantic rules based on morphology and multi-channel contextual information were developed to mimic the processes and principles involved in visual interpretation (section 2.3). Using these rules, detections were graded from 10 to 1 <u>to indicate the likelihood of their being genuinely epileptiform</u>. The principle of such grading is illustrated diagramatically in Figure 3.

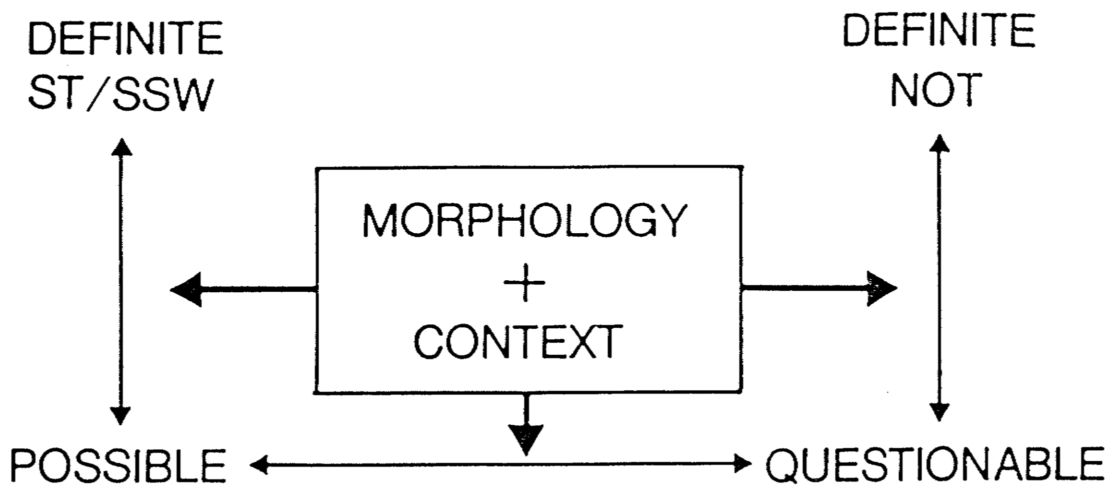
<u>3.4. Methods</u>.

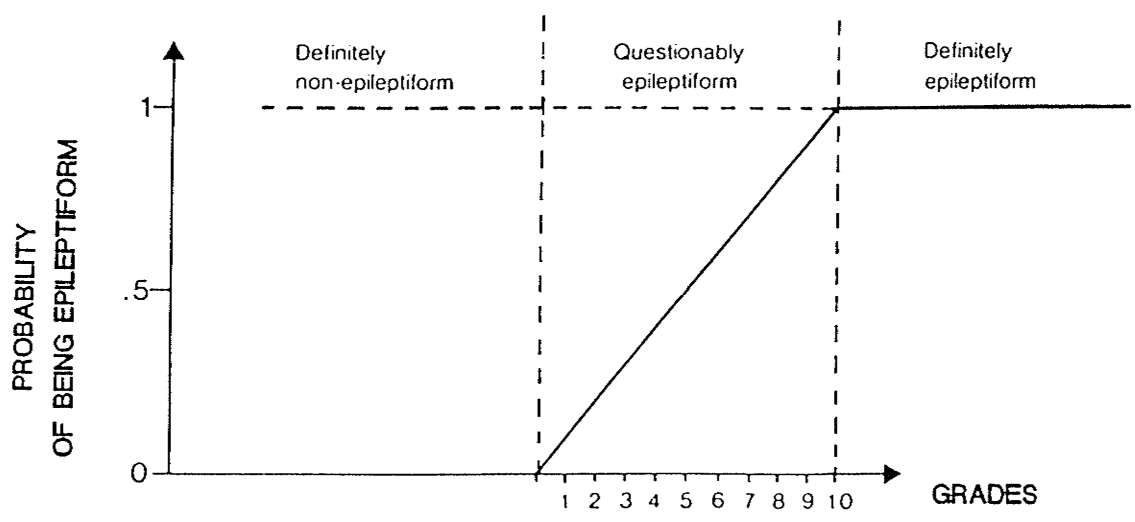
Some of the methods used here have been described in the literature. Several new ones have been developed to mimic visual interpretation. A flow chart of the detection algorithms is shown in Figure 4. The algorithms analyze AEEG signals in 2 sequential stages.

Figure 2. Spectrum of activity recognized by the EEGer during day to day visual interpretation of EEG.

Figure 3. Principle of grading. STs/SSWs are graded on the basis of morphology and context, to indicate the likelihood of their being genuine. Definitely epileptiform events (probability of 1) are graded 10 and questionably epileptiform events are graded from 1 to 9 (probabilities 0.1 to 0.9).

"SPECTRUM" OF ACTIVITY





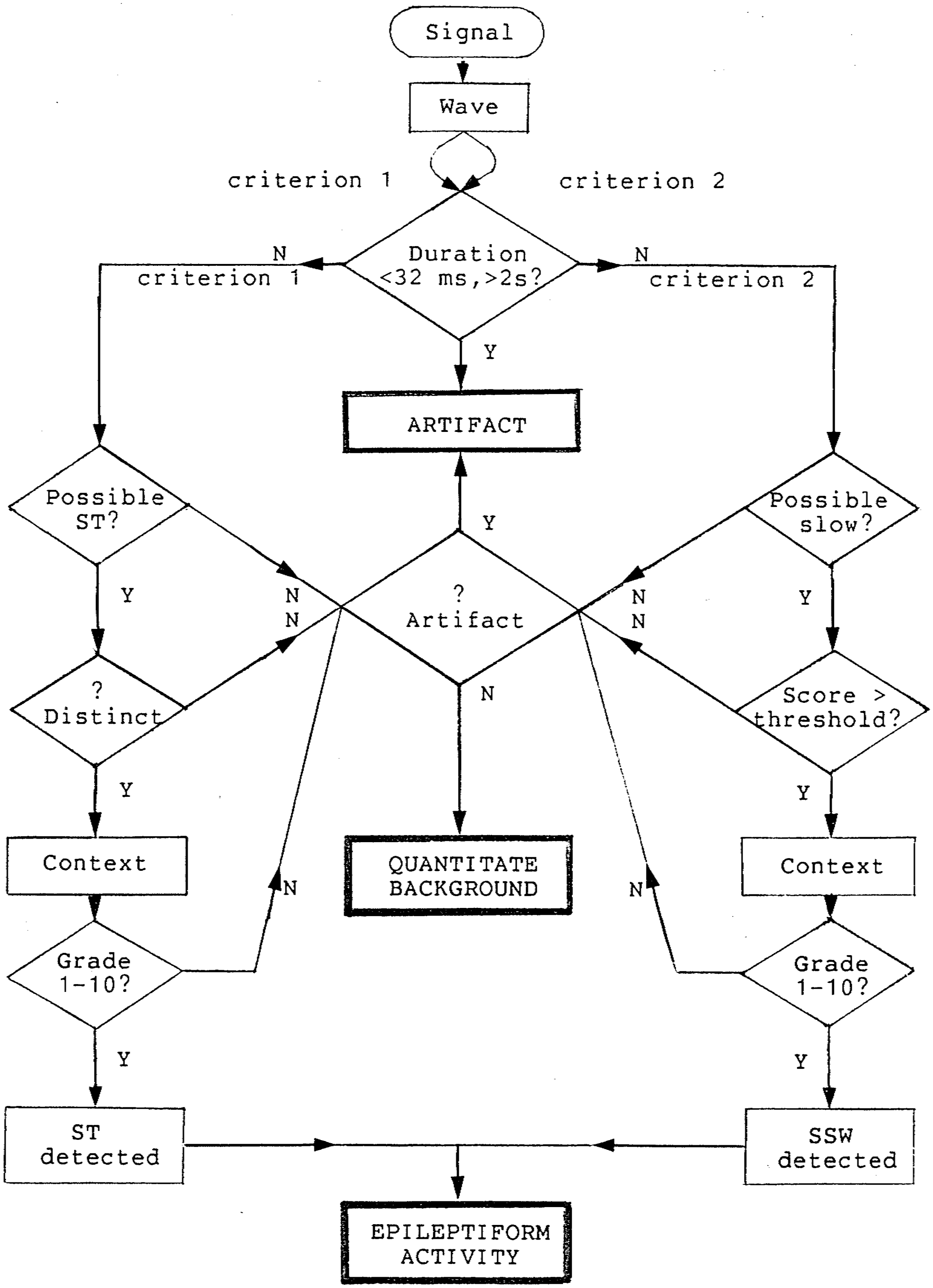


Figure 4. Flow diagram of the algorithms.

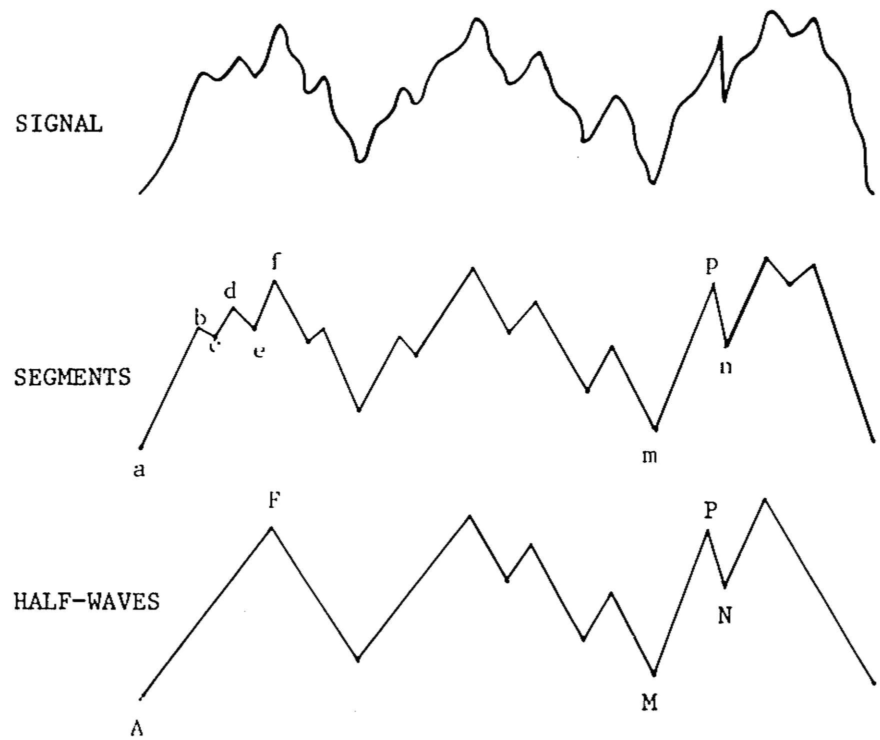
3.4.1. Stage I.

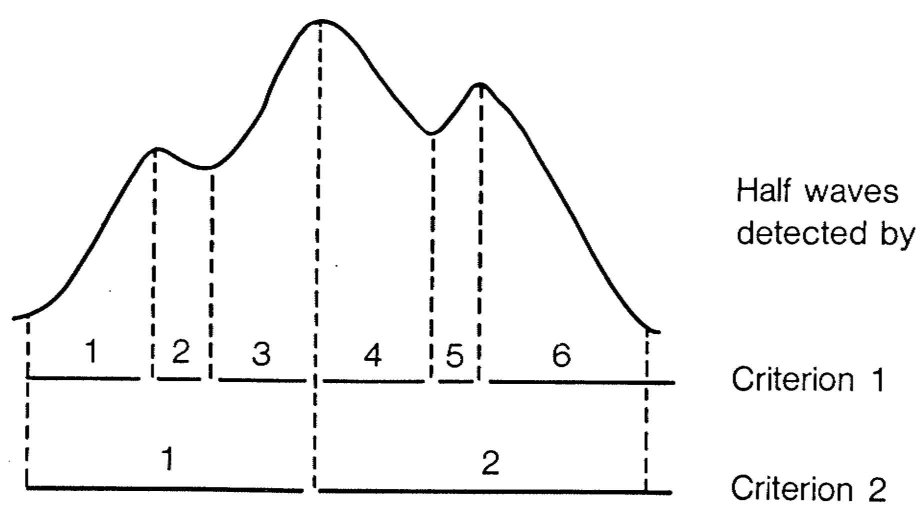
Each channel is analyzed individually. The signal is broken down into segments in order to facilitate the computation of features (Figure 5). A segment is a section between two consecutive extrema of amplitude and is characterized by duration, amplitude and direction (Leader et al. 1967; Gotman and Gloor 1976). Hence segments alternate in direction. An undesirable feature of such breakdown is that low amplitude "noise" superimposed on other activity, is identified as separate segments thus obscuring the underlying activity of interest. Adjacent low amplitude segments of no significance are therefore merged with larger segments to define a half-wave with a specific direction. A half-wave is thus composed of one or more segments (Figure 5) and is also characterized by a set of quantities such as time of occurrence, amplitude, duration and slope. Note that for well defined rhythmic activity or a ST, a segment and a half-wave are identical.

Half-waves are defined using a modification of the criteria described for background activity analysis (Goldberg and Samson-Dollfus 1975) and for ST detection (Gotman and Gloor 1976). As both superimposed and underlying activity could be of interest, separate criteria are used to identify the two. Thus a half-wave composed of one or more segments is terminated if a succeeding half-wave of opposite direction has an

Figure 5. Diagramatic illustration of breakdown of EEG signal into segments and half-waves. Half-wave AF corresponds to the 5 segments ab, bc, cd, de and ef. Some half-waves (eg., MP and PN) are identical to the corresponding segments.

Figure 6. Diagramatic illustration of six half waves detected by the criterion 1 and two by the criterion 2.


SIGNAL
SEGMENTS
HALF-WAVES
a
b
c
d
e
f
m
p
n
A
F
M
P
N


Half waves
detected by
1
2
3
4
5
6
Criterion 1
1
2
Criterion 2

amplitude exceeding 10 uv (criterion 1) or greater than one half the amplitude of the current half-wave (criterion 2). The first criterion mainly detects the superimposed activity, whereas the second mainly detects the underlying slow waves (Fig 6). Some waves may be detected by both criteria. Note that only superimposed segments with an amplitude greater than 10 uv are "ignored". The durations, amplitudes and positions of half-waves detected by both these criteria are stored separately.

The method has some advantages. It obviates the need for the continuous complex computation of an average zero level, using only the succeeding half-wave to establish the threshold. Furthermore, the method provides information on the amplitudes and durations of the half-waves and the positions of the peaks (troughs) ; features which could be used directly for the initial detection of STs, SSWs and gross artifacts (Harner 1977).

There is one disadvantage. The choice of the thresholds (eg., midpoint of the current half-wave) influences the intervals detected. This disadvantage is also shared by other interval-amplitude analysis methods.

3.4.2. Stage II.

In this stage the half-waves are analyzed further to identify STs, SSWs, artifacts and to quantitate background activity. STs/SSWs are identified in a series of steps.

In the first step of screening, simple features are computed and used to reject a large portion of the data that are unlikely to contain any epileptiform activity. The remaining EEG sections are then tested in a second step with progressively more stringent criteria based on intra- and inter-channel information. This procedure allows both rapid and detailed analysis of sections likely to contain epileptiform activity (Gotman and Gloor 1976).

(A) Identification and grading of STs.

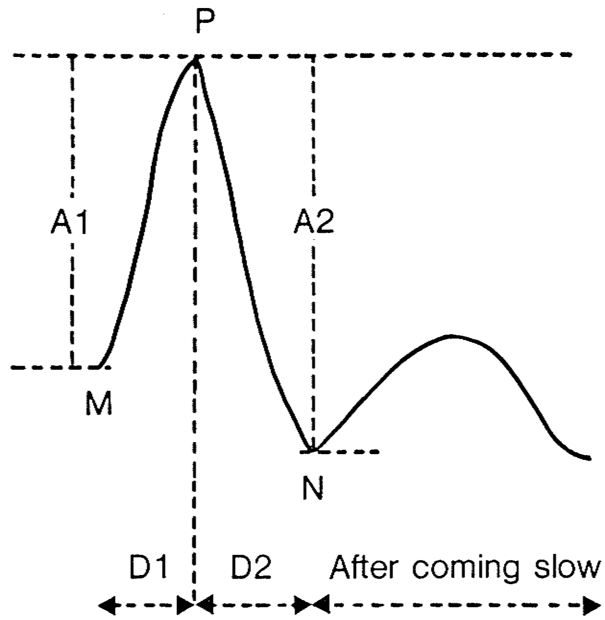
STs may sometimes be superimposed on background activity. Half-waves detected in stage I by criterion 1 are therefore analyzed.

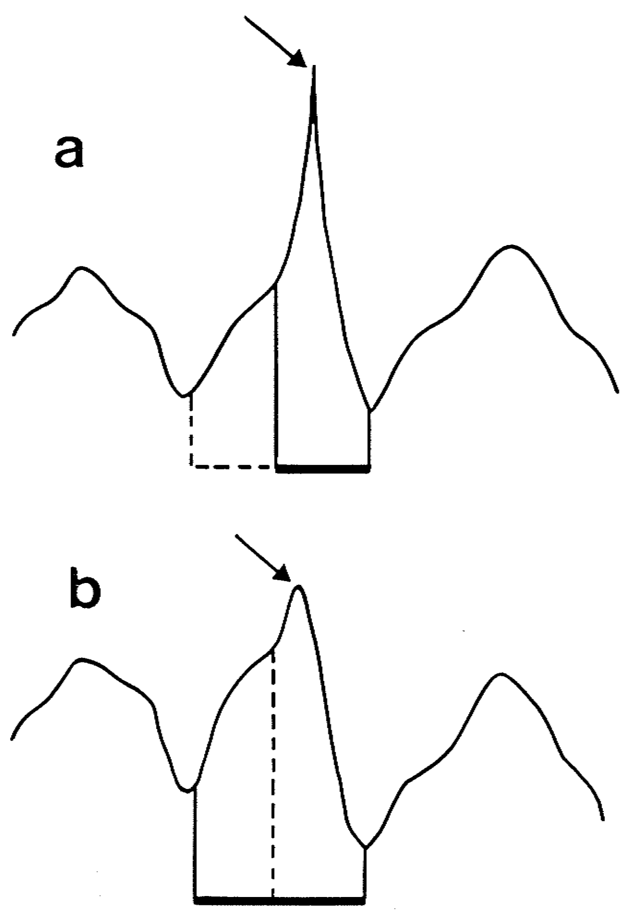
(1) Screen for STs.

STs have a wide range of morphological features (Frost 1985). A typical ST is illustrated in Fig 7. Sharpness, a single feature which provides the most discrimination, is used initially. The junction P, of two half-waves MP and PN (Figs 5,7), is tested for sharpness using a modification of the method described by Frost (1979). Two measures $s1 = v(P) - v(P-2)$ and $s2 = v(P) - v(P+2)$, where $v(i)$ is the voltage of sample position i, are computed. The slopes immediately adjacent to point P ie., $v(P) - v(P-1)$ and $v(P) - v(P+1)$, are not used because of the variability produced by digitization. Peak (trough) P is considered to be sharp if the absolute values of both

Figure 7. Diagramatic representation of a typical ST.

Figure 8. The "correct" duration (solid bar) of a wave is computed by using different criteria in (a) and (b).


P
A1
A2
M
N
D1
D2
After coming slow


a
b

s1 and s2 exceed 8 uv/ 16msec.

Points M and N as detected in stage I are located where the signal reverses direction (Fig 5). They may not therefore accurately delineate a ST which is superimposed on slower background activity (Fig 8a). Frost (1979) redefined M and N as points beyond which the slopes fell below a threshold. However, with the use of a similar criterion in this study it was observed that the duration (points M to N) of some sharply contoured slow activity was erroneously computed (Fig 8b). A further constraint is therefore added. If the absolute value of the sum s1+s2 exceeds 40 uv indicating a very sharp peak (eg., a spike), M and N are redefined as points beyond which the slopes fall below 0.6 uv / msec (Fig 8a). If the absolute value of s1+s2 is less than 40 uv, as may be the case with some sharply contoured theta activity, points M and N are left unchanged (Fig 8b).

The durations (D1 and D2) and amplitudes (A1 and A2) of wave MPN are then measured. Constraints are placed on these measurements or parameters as shown in Table I. These constraints ensure that a wave which is to be evaluated further has a duration of a ST and an amplitude of at least 20 uv; waveforms of smaller amplitude usually represent noise. The constraints also exclude muscle artifact (which usually has a duration of < 32 msec) and grossly asymmetrical waveforms. The amplitude A2 of most

Table I

Thresholds used for screening potential STs

Feature	Threshold
Amplitude	
A1 and A2	A1,A2 > 20 uv
A1 / A2	1/4< A1/A2 < 2
Duration	
D1 and D2	D1,D2 > 8 msec
D1 + D2	32 msec< D1+D2< 240 msec
|D1 - D2|	|D1-D2|< (D1 + D2)/2

STs is larger than A1 (Gotman and Gloor 1976) (Fig 7) although the converse may occasionally be seen. The range of the threshold for the ratio A1 / A2 is therefore biased in favour of a larger A2. Waves with grossly asymmetrical amplitudes or durations of the upstroke and downstroke are highly unlikely to be STs. Note that the thresholds for all these parameters are kept "low", in order to allow the detection of STs with a wide range of morphological characteristics.

(2) Intra- and Inter-channel comparisons.

Wave MPN which has not been rejected so far has the morphology of a ST. However STs by definition are also clearly distinguished from the background (IFSECN 1983). "Background" may consist of activity with a wide range of morphology (amplitude, duration and sharpness) and may include artifacts (eg., muscle artifact). No single feature can therefore be expected to successfully and consistently help distinguish a ST from the "background".

In an attempt to mimic visual interpretation, two features and their thresholds are used selectively to determine if wave MPN is clearly distinguished from the "background". "Background" is defined as 3 seconds of activity on either side of, but excluding wave MPN. This duration was chosen as a compromise between stationarity of the signal and adequate representation of the background activity.

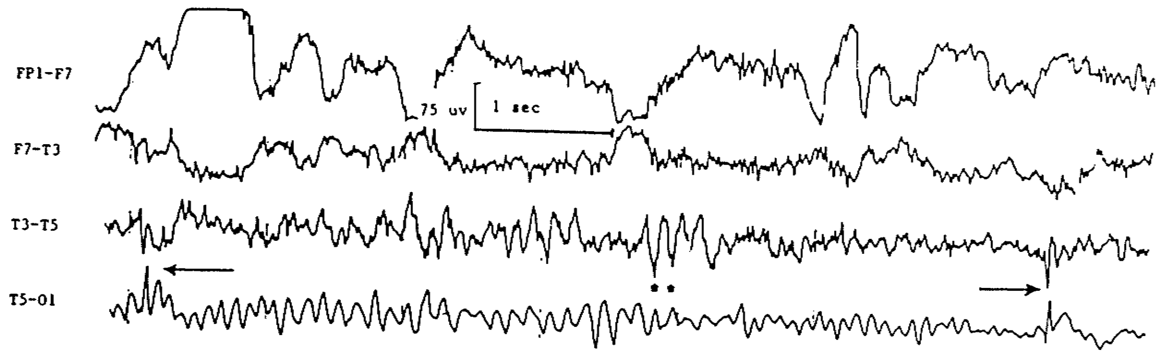
The first feature, a ratio F1 = amplitude / duration defines the prominence of a wave and contains some information about the shape, the sharpness and the two slopes. Amplitude is defined as the larger of A1 and A2 and duration as the sum of D1 and D2. Feature F1 is computed for the wave MPN as well as for all other waves in the frequency range 5 to 13 Hz in the neighbouring 3 seconds. The value of F1 for the wave MPN, X1, is then compared with the mean (M1) of F1 obtained from these other waves. This ratio, I1 = X1 / M1 indicates how dissimilar wave MPN is with respect to alpha-theta activity in the background (Fig 9a). Note that X1 will be larger than M1 if the wave's amplitude is bigger and/or duration much smaller than alpha-theta waves in the background.

The second feature, a product F2= amplitude X duration defines approximately the area under the wave. The value of F2 for wave MPN, X2, is compared with the corresponding mean (M2) obtained from all waves with a frequency greater than 13 Hz. The ratio, I2 = X2 / M2 then indicates how dissimilar wave MPN is from beta-muscle activity in the background (Fig 9b).

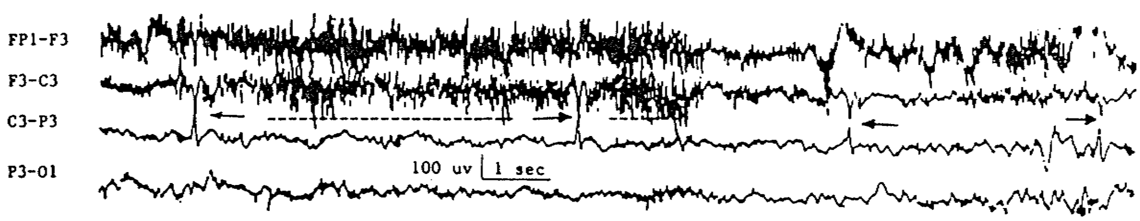
Note that sharpness of a wave which is implicit in feature F1 and is useful to distinguish a ST from theta-alpha activity, has no role in distinguishing it from beta or muscle activity. Note further that the indices I1 and

Figure 9. STs (arrows) are clearly distinguished from (a) 5-13 Hz activity (examples marked '*') by index I1 and (b) from > 13 Hz activity (marked '---') by index I2.

a


FP1-F7
F7-T3
T3-T5
T5-O1
75 uv
1 sec

b


FP1-F3
F3-C3
C3-P3
P3-O1
100 uv
1 sec

I2 are relative measures (compared to the means of the background) and thus not influenced by recording factors such as minor errors in gains setting or inter-electrode distances.

For computational efficiency the values of M1 and M2 for 5-13 Hz and greater than 13 Hz activity respectively, are computed and stored in 1 second blocks during stage I. Values of an event under consideration are then compared to those of the 3 second block; the one including the event and one second on either side.

Value X1 and indices I1 and I2 are used for the detection of STs as shown in Table II. Wave MPN with values of either X1 or I1-I2 below those shown, is rejected. Thus STs which are detected not only satisfy the morphological requirements, but also the measures of being distinct from background. Note that STs occurring synchronously in 2 or more channels have lower thresholds to allow detection of less clearly distinguished STs.

(3) Grading of STs.

STs detected above are initially graded from 1 to 6 on the basis of (i) value X1 (1 to 3) and (ii) the dissimilarity indices, I1 and I2 (up to +3) (Table II). I1 and I2 are biased in favour of STs which occur synchronously. Thus, STs which have a prominent morphology (large value of X1) and/or are clearly distinct

Table II

Criteria for detection and initial grading of STs

Feature	Grade	
X1=		
< 3	–	
3-5	1	
6-8	2	
> 9	3	
Adjust grade based on minimum of I1 and I2	**	*
< 1.5	–	–
1.5 - 2.5	+1	–
2.5 - 3.5	+2	+1
> 3.5	+3	+2

Events with synchrony (**) and without (*)
Events in regions marked (-) are rejected

from the background get a higher grade than those that are not.

Semantic rules are then used to consider the intra- and inter-channel contextual information in that 30 second segment. The initial grade is adjusted (increased or decreased) using these rules. The maximum grade obtainable is 10. Detections with grade less than 1 are rejected. The rules to increase or decrease the grades are considered in two separate passes over the STs. Particular attention is given to avoid the creation of a feedback loop in the determination of the grades.

The grade is increased in the presence of the following contextual information: (i) It is increased (by 2) if STs occur synchronously in more than one channel. This finding, suggestive of a "phase reversal" or a ST with a "field" is one of the important characteristics of genuine STs. (ii) It is incremented by 1 if the ST is followed by a slow wave, a pathophysiological association seen in some STs (Fig 7). The slow wave is identified as a wave immediately following the ST and having a frequency less than 8 Hz. (iii) It is also increased if 3 or more STs of grade greater than 6 are detected in the same channel in that 30 second segment. The increment "I" is calculated as I=(Max-5), where Max is the maximum grade of a ST in that channel. This rule, based on "peer comparisons" done during visual interpretation (Frost 1985) helps upgrade less prominent STs.

The grade is decreased (by up to 6) in presence of the following contextual information: (i) Presence of artifacts, depending on their number and type (slow, large amplitude or fast "muscle" artifacts). The grade is reduced by 3 for every single slow or large amplitude artifact and/or every 15 fast artifacts occurring in the 3 second "background" but is reduced by only 1 if the same artifacts occur elsewhere in that 30 second segment. (ii) Presence of similar alpha/beta waves in the 3 second "background". The grade is decremented by 1, for every 4 waves which are similar. Similarity here is defined as amplitude of at least 1/2 that of the ST and a duration difference of less than 32 msec. This rule is used since the presence of such alpha/beta activity increases the likelihood of the detected event also being sharply contoured background activity.

The weights given to morphological and contextual features were derived using the "learning " set of the database and are based on the logic involved in visual interpretation. Furthermore, they are adjusted so that a ST which is distinct may not be missed even if it occurs amidst considerable artifact. STs occurring synchronously in more than one channel are not only graded, but in addition also coded and stored separately. This was done to capitalize on the importance given to phase reversal or to a field during visual interpretation.

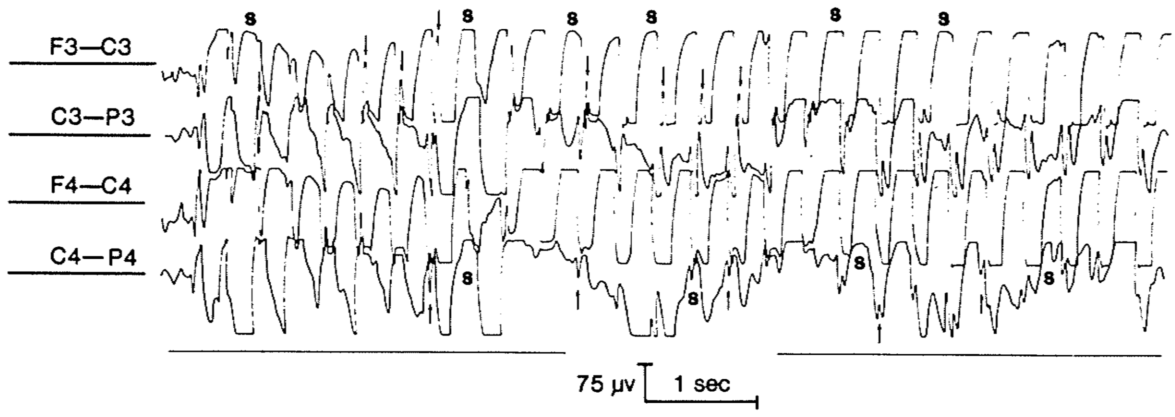
Indices I1 and I2 used above are measures of dissimilarity of wave MPN with respect to corresponding averages of alpha-theta and beta-muscle activity. However, it is possible that visual analysis employs more complex processes to decide if a wave is distinct. An alternative measure of dissimilarity was therefore also evaluated. Thus, let the value of feature F1 for wave MPN be x_0 and the values of for example, 9 waves in alpha-theta range in the background be $x_1, x_2, .., x_9$. The mean I3 of the ratios x_0/x_1, $x_0/x_2, ..,$ x_0/x_9, then gives a measure of the average of the 9 individual dissimilarities. Similarly using feature F2 for wave MPN and beta-muscle activity the mean I4 is obtained. I3 and I4 are then used for the initial grading (from 1 to 6) in exactly the same manner as I1 and I2.

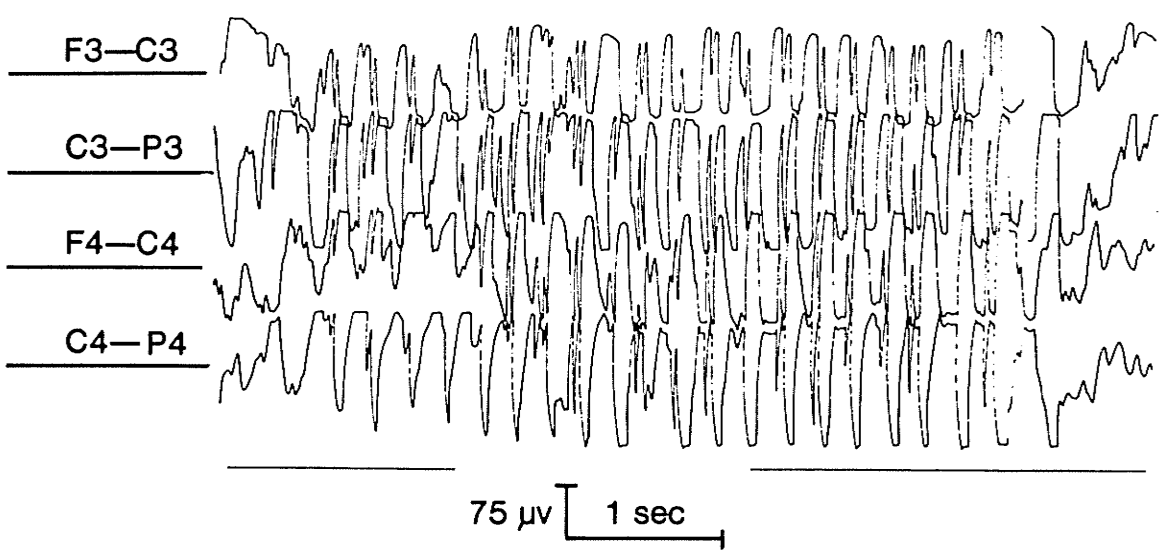
(B) Identification and grading of SSWs.

The definition of a SSW (IFSECN 1983) implies alternate repetition of ST and slow waves. However, the repetition pattern and the duration of SSWs can be very variable (Koffler and Gotman 1985). Thus the ST component may not precede each slow wave component (Fig 10). Only 18.5 % of SSW activity in our database had a typical pattern (class

Figure 10. An example of a generalized SSW. Some ST (arrows) and slow (S) components are marked.

Figure 11. An example of a generalized SSW with a fast repetition rate.


F3—C3
C3—P3
F4—C4
C4—P4
75 µv
1 sec


F3—C3
C3—P3
F4—C4
C4—P4
75 µv
1 sec

No. 24, "typical SSW")(Jayakar et al. 1987a). A combination of features is therefore used to identify SSWs.

(1) Screen for slow wave components of SSWs.

Half-waves detected by criterion 2 in stage I are analyzed as these mainly represent the underlying slow activity. A slow wave is identified if a wave comprised of 2 consecutive half-waves has a duration between 125 msec and 0.7 sec and an amplitude (larger of the two half-waves) greater than 30 uv. Note that waves with a duration of 125 msec are in the alpha frequency and are not slow activity. However, the "slow" component of a SSW with a fast repetition rate (eg., 6 Hz) may fall in the alpha frequency range (Fig 11) and is "slow" only relative to the ST component of the SSW.

The slow wave component of a SSW is usually "smooth" (Fig 10), ie., it has little or no superimposed activity. Slow waves in the background (eg., delta activity) are unlikely to be "smooth". Thus, only 7.5 % of all delta waves in our database were smooth (class No. 1-3,"pure" delta)(Jayakar et al. 1987a). The number of half-waves superimposed on the slow wave are measured using the zero-crossings of the slope of the signal. The latter indicate a change in the direction (upwards or downwards) of the EEG signal. The slow wave is considered to be smooth if there are less than 10 superimposed half-waves.

(2) Intra- and inter-channel comparisons.

Rhythmicity of the ST and slow wave in a SSW is a characteristic though not consistent feature. Even when the ST component is absent, the repetitive slow waves are almost uniform in duration.

The algorithms therefore attempt to identify a sequence of slow-ST-slow waves. Each channel is initially analyzed individually. For each slow wave under consideration (current slow wave) the preceding two waves are scanned to detect the occurrence of another slow wave and/or a ST. The absolute difference in the durations of the preceding and current slow waves should be less than 1/3 the duration of the current slow wave. The ST should have a duration less than one half that of the current slow wave component and satisfy the screening criteria for STs (section 3.4.2 (A(1))). The current slow wave is considered to show intra-channel "organization" if preceded by a ST and/or slow wave as specified. The process is repeated for all slow waves in all channels.

This approach is similar to those reviewed by Principe and Smith (1985).

The slow wave components across channels in a SSW are usually uniform in duration and the ST components synchronous (Fig 10). All four channels are therefore scanned by the program to detect the synchrony of the ST components and to compare the durations of the slow components. The slow waves are considered to be synchronous if they occur in the same 1/4 sec window. If the absolute difference between the durations of the slowest and fastest of the slow waves is less than 1/3 the duration of the slowest wave, the slow wave components are considered to show inter-channel "organization".

In order to identify SSWs that have a wide range of morphology, the threshold for detection must not place rigid restrictions on any individual feature such as frequency, rhythmicity or synchrony of the components (Koffler and Gotman 1985).

To allow this threshold to be flexible, scores are given to the following features individually: (i) the morphology (amplitude, duration and degree of "smoothness") of the slow components, (ii) the intra- and inter-channel "organization" of the slow components and (iii) the presence and synchronous occurrence of the ST components.

The limits of a paroxysm are then defined as points beyond which there are no ST components or well organized (smooth and/or synchronous and/or repetitive) slow waves for a duration of 1 second in any channel.

The total scores (sum of the individual scores) for the slow and ST components are then computed for the entire paroxysm. These scores thus reflect the overall degree of "organization" and/or the duration (number of ST and slow components) of a paroxysm. Paroxysms with total scores below a threshold are rejected. Detected paroxysms thus need to have both slow and ST components. At the same time the threshold is low enough to allow the detection of SSWs with a wide range of ST and slow wave characteristics.

(3) Grading of SSWs.

Paroxysms with scores above the threshold are then graded from 10 to 1, based on the total scores of the paroxysm. Paroxysms which are well organized and/or of longer duration receive higher grades than those which are not. The grade may then be increased by the presence of other SSWs of grade greater than 6 in the same 30 second segment. The increment "I" is calculated as I=(Max-6), where Max is the maximum grade obtained by any other SSW in that segment. This rule helps "upgrade" short duration SSWs which may have received a low score. The grade is decreased (by up to 6) by the presence of high frequency (> 32 Hz) activity for example, chewing artifact in the same segment. The grade is decremented by 1 for every 4 seconds of high frequency activity.

Bursts with grade less than 1 are rejected. Note that as with ST grading, typical well organized SSWs should be detected even in the presence of considerable artifact.

The durations of the SSWs along with their grades are then stored.

(C) Detection of artifacts.

One expects some artifacts morphologically resembling STs (pseudo-STs) or SSWs (pseudo-SSWs) to be detected as STs or SSWs of low grades. Detections resembling STs/SSWs which on considering contextual information were rejected (grade < 1) because of neighbouring artifacts, are considered to be artifacts. The latter rule was used so that these artifacts may not be included in the quantitative analysis of background activity.

A wave which does not satisfy criteria in A or B is considered to be a gross artifact if it has an amplitude greater than 300 uv and/or duration greater than 2 s or less than 32 ms. These thresholds are similar to those described by Gotman (1985).

(D) Quantitative analysis of background activity.

A wave which does not fulfill criteria in A, B or C above, is assumed to be part of the background activity. Its duration (trough to trough) and amplitude (larger of the upstroke or downstroke) are measured. The number of waves and the amplitudes in each frequency band are then stored.

4.0 RESULTS AND EVALUATION

Epileptiform activity identification and background analysis were evaluated separately in this study. The algorithms were evaluated using 60 segments from the database; the subjects from whom they were obtained were independent from those used in development.

4.1. Epileptiform activity.

The algorithms grade the detections based on the likelihood of these being epileptiform. Traditionally used measures of performance such as false positive and false negative error rates were therefore inappropriate. Furthermore, the 2 EEGers had annotated the events as ST/SSW or pseudo-ST/SSW rather than grading them. An evaluation scheme was therefore designed based on the assumptions that:

(i) An event, marked genuine by both EEGers was more likely to be so than an event marked by only one of the two.

(ii) An artifact marked either as pseudo-ST or as pseudo-SSW, would have greater morphological resemblance to the corresponding genuine events than waves left "unclassified". "Unclassified" events were those that were not considered to be ST/SSW or pseudo-ST/SSW by either EEGer. The four groups as shown in column 1 of Tables III to VI, were thus assumed to represent events with decreasing probabilities of being epileptiform.

Based on these assumptions, the grades given by the computer to each event were compared with the annotations done by the 2 EEGers. For each range of grades, the probability of an event being ST/SSW was estimated as the ratio of events classified as STs/SSWs by one or both EEGers to the total number of events in that range.

4.1.1. ST detection evaluation (Table III).

The probability of a detection being a genuine ST is significantly higher ($P < .005$) for those given a high grade and decreases for successively lower grades (see APPENDIX). The probabilities are higher for STs with synchrony than for those without in the same grade range. Note that synchronous events in a particular grade range have a probability comparable to that of non-synchronous events in a higher grade range. This suggests that the "weight" given to synchrony during the grading of STs can be increased. However, this may also upgrade some artifacts that may also occur synchronously.

The computer detected 254 out of 293 (86.6 %) STs identified by one or both EEGers, including some that were small and indistinct. In comparison only 126 / 293 (43.0 %) STs had been identified by both EEGers. Only 4 of these 126 STs were missed by the computer. Examples of STs detected or missed are shown in Figs 12 a to f.

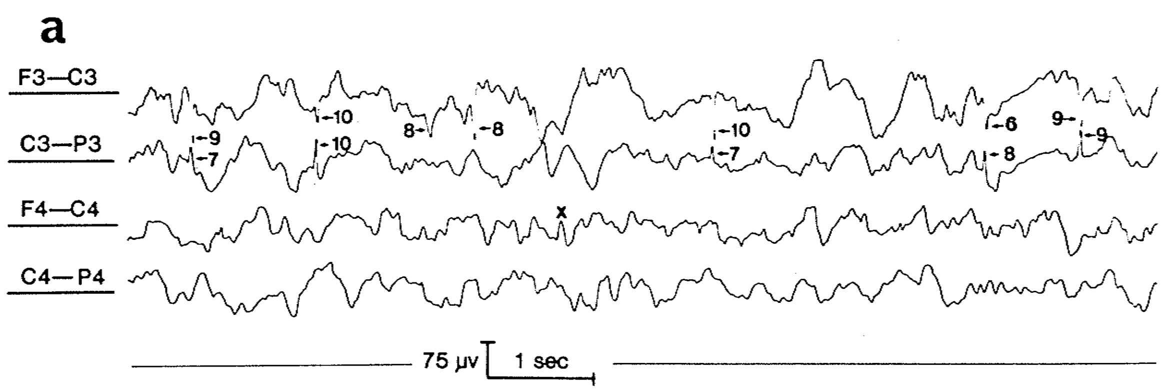
Table III

Results of ST detection by the automated system

	Total No.	No. detected in each grade range								No. Undetected
		10-8		7-6		5-4		3-1		
		**	*	**	*	**	*	**	*	
Classif. by EEGers STs by both	126	28	13	14	19	7	20	8	13	4
ST by one	167	1	6	3	22	13	32	14	41	35
PST by one or both	103	0	0	3	12	2	25	13	36	12
Unclassified by both	357	1	0	2	9	15	97	30	203	-
Probability of detection being a ST		.97	1	.77	.66	.54	.29	.33	.15	

Events with synchrony (**) and without (*)

Figure 12 a to f. Examples of STs identified by the EEGer. Grades of STs detected by the automated system are indicated by arrows whereas STs undetected are marked "X". Note that none of the latter is very prominent or distinct.


a
F3—C3
C3—P3
F4—C4
C4—P4
75 µv
1 sec

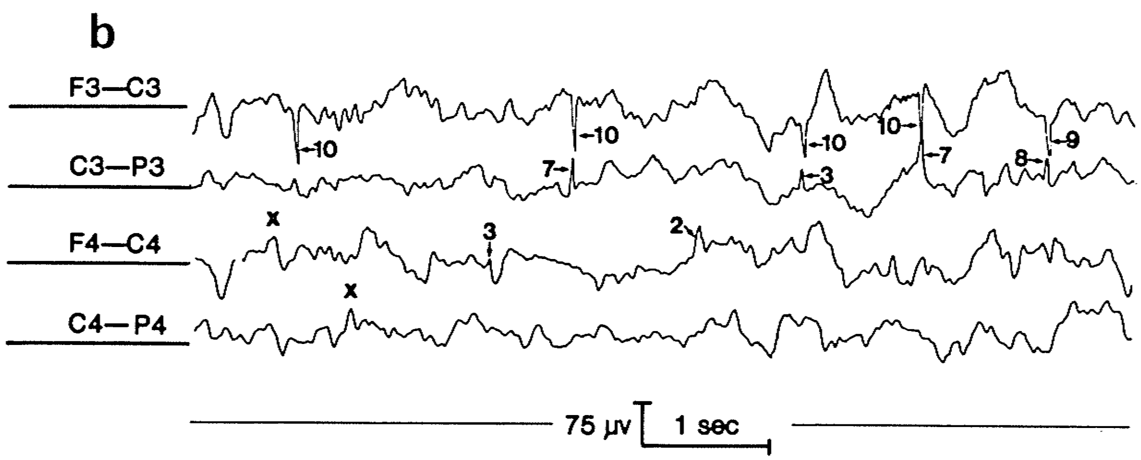

b
F3—C3
C3—P3
F4—C4
C4—P4
75 µv
1 sec

Figure 12 (continued).

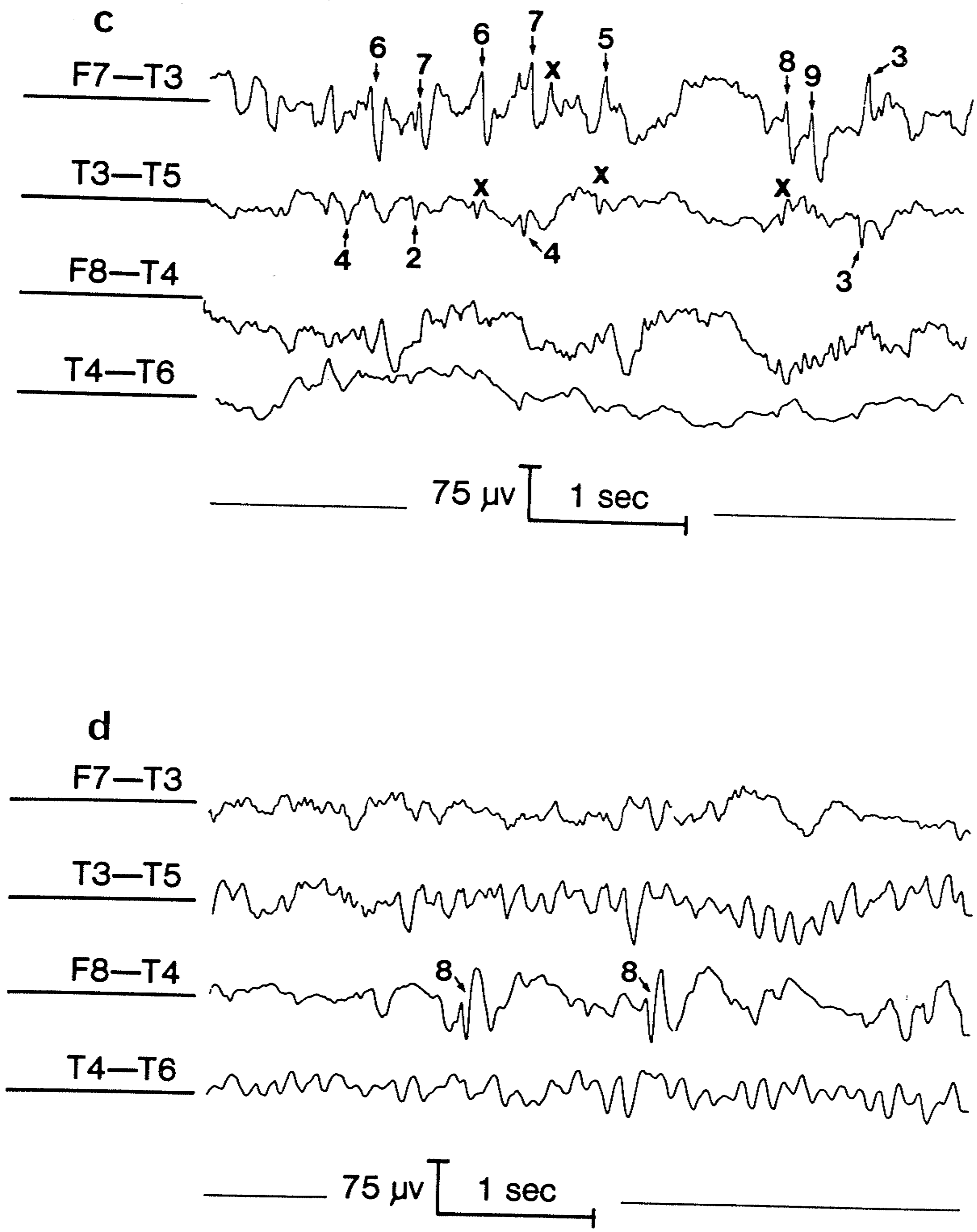
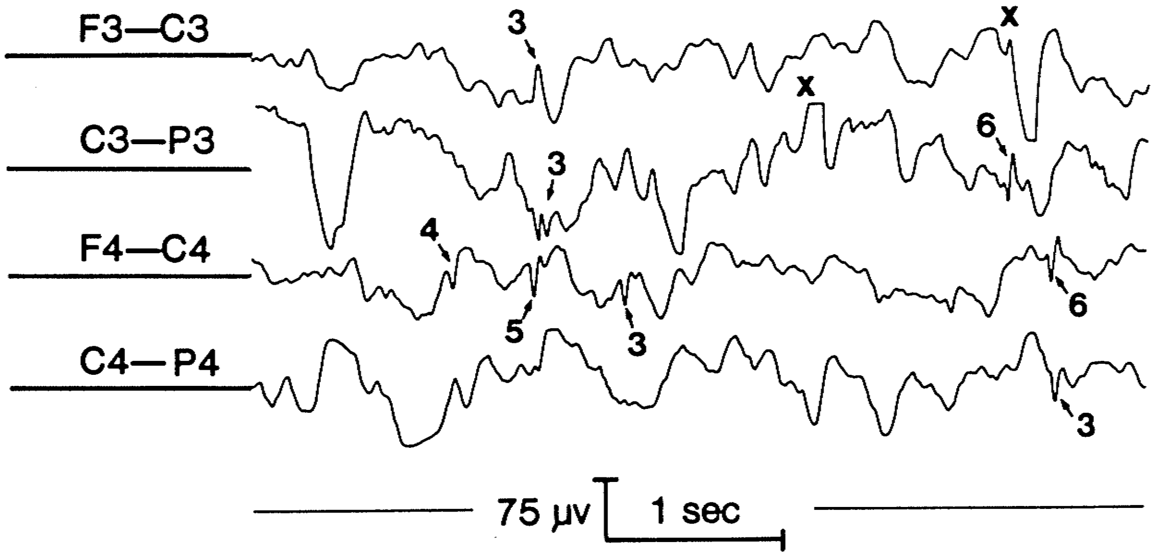

c
F7—T3
T3—T5
F8—T4
T4—T6
6
7
6
7
x
5
8
9
3
x
x
x
4
2
4
3
75 µv
1 sec
d
F7—T3
T3—T5
F8—T4
T4—T6
8
8
75 µv
1 sec

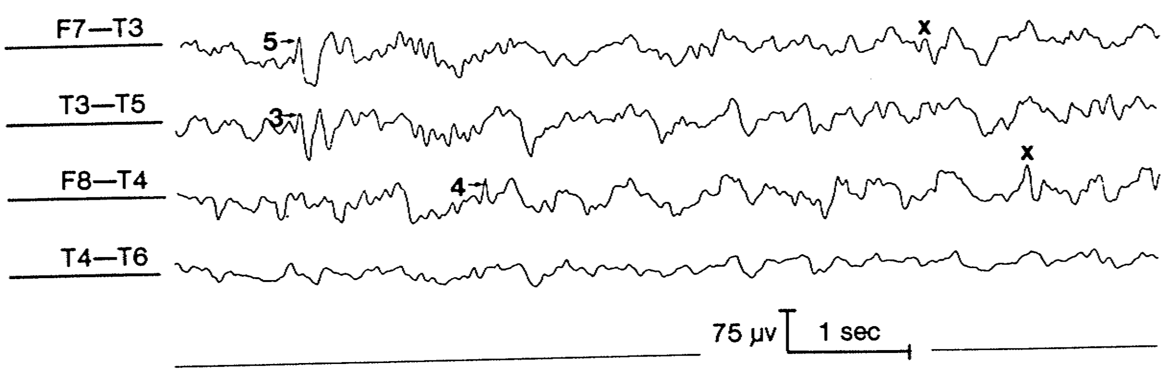
Figure 12 (continued).

e



F3—C3
C3—P3
F4—C4
C4—P4
3
x
x
6
3
4
5
3
6
3
75 µv
1 sec

f



F7—T3
T3—T5
F8—T4
T4—T6
5
x
3
4
x
75 µv
1 sec

None of the STs missed is prominent or distinct. One ST (Fig 12c, channel 1) was missed because its amplitude ratio A1/A2 was greater than 2. Some of those missed were part of a run of repetitive sharp waves. Others were either small in amplitude, too broad or too blunt.

Four hundred and forty eight detections were not classified as STs by either of the 2 EEGers. Examples of events left unclassified by the EEGers and those classified as pseudo-STs are shown in Figures 13 a to f and 14 a to d respectively. Only 1 of the 49 detections given a grade greater than 7 by the computer had been left unclassified by both EEGers. This detection had some features of a ST (Fig 13 a). Eighty eight out of 103 pseudo-STs were either rejected or identified as low grade (< 5) STs. None was graded greater than 7. Note that some of the "false" detections have resemblance to genuine STs and may fall into the questionably epileptiform category. Some of these detections may have been classified as STs by other EEGers. Also note that some detections are quite definitely sharply contoured background activity (Fig 13 c and f).

Thirteen small STs (eg., Fig 12c,e) identified by both EEGers were given a low grade of 1 to 3. None of these 13 was "isolated"; all were associated with other STs graded greater than 5 by the computer in the same channel. Such small STs may therefore be upgraded by modifying the

Figure 13 a to f. Examples of detections by the computer (open arrows), which had been left unclassified by both the EEGers.

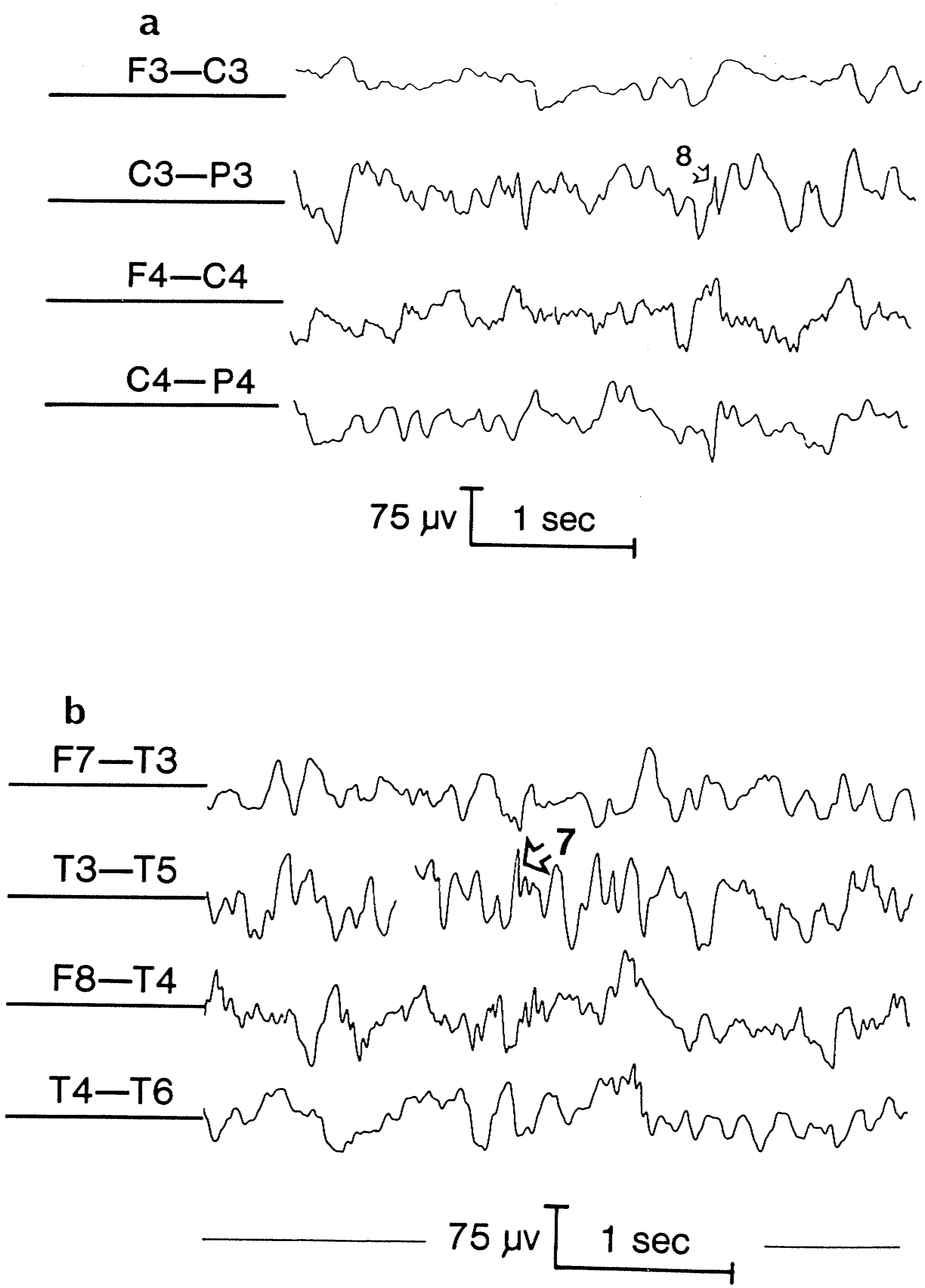

a
F3—C3
C3—P3
8
F4—C4
C4—P4
75 µv
1 sec
b
F7—T3
T3—T5
7
F8—T4
T4—T6
75 µv
1 sec

Figure 13 (continued).

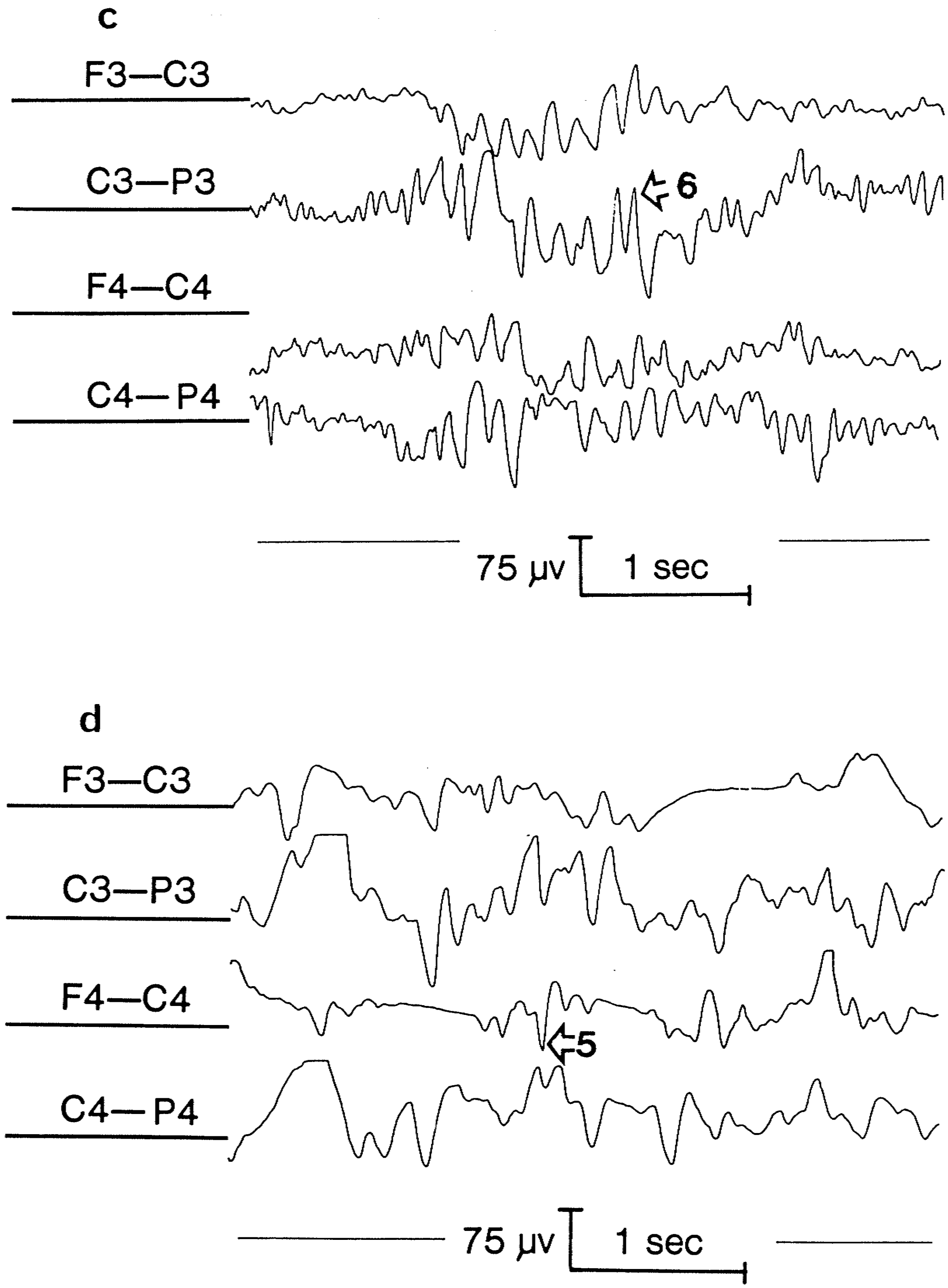

c
F3—C3
C3—P3
6
F4—C4
C4—P4
75 µv
1 sec
d
F3—C3
C3—P3
F4—C4
5
C4—P4
75 µv
1 sec

Figure 13 (continued).

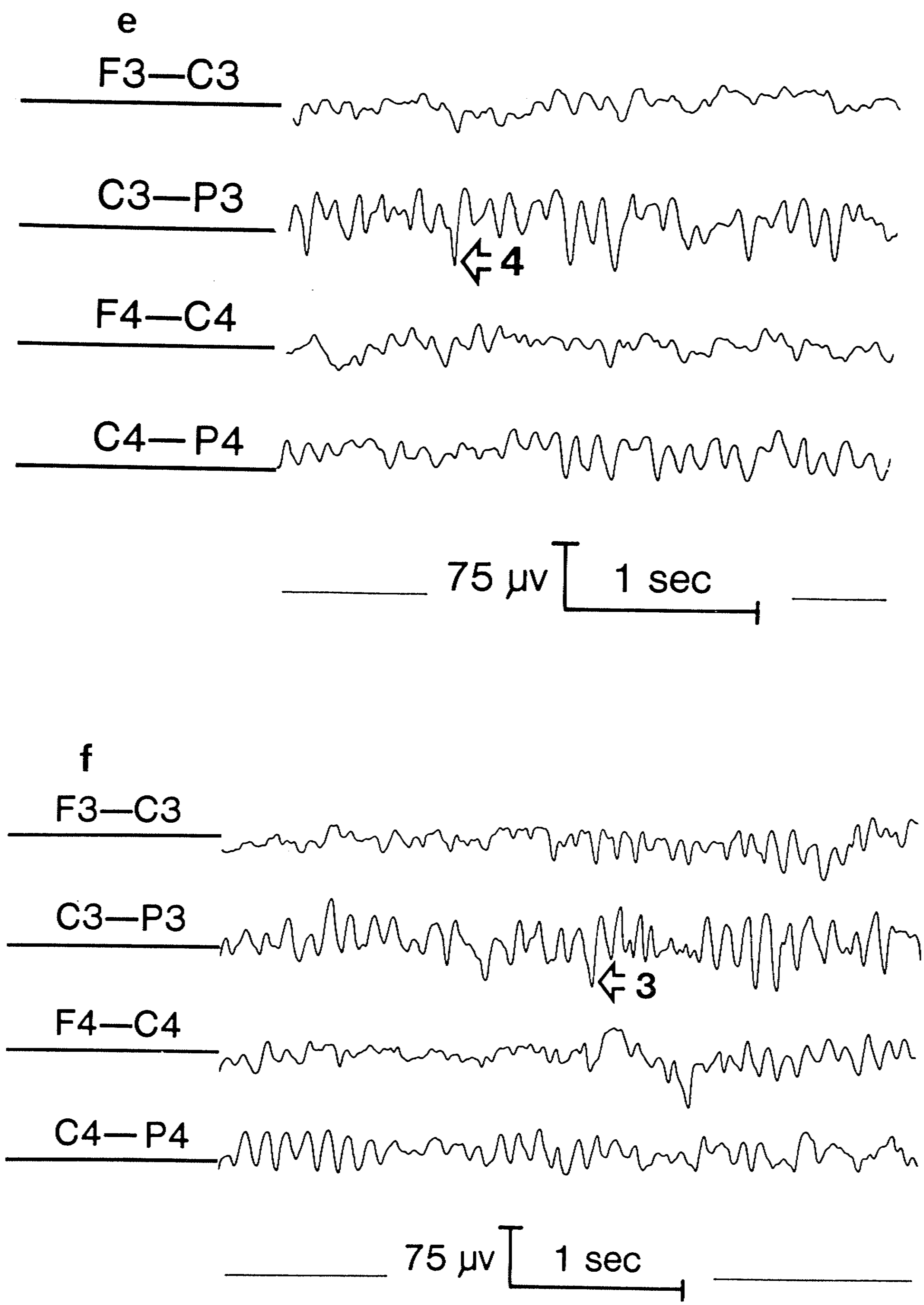
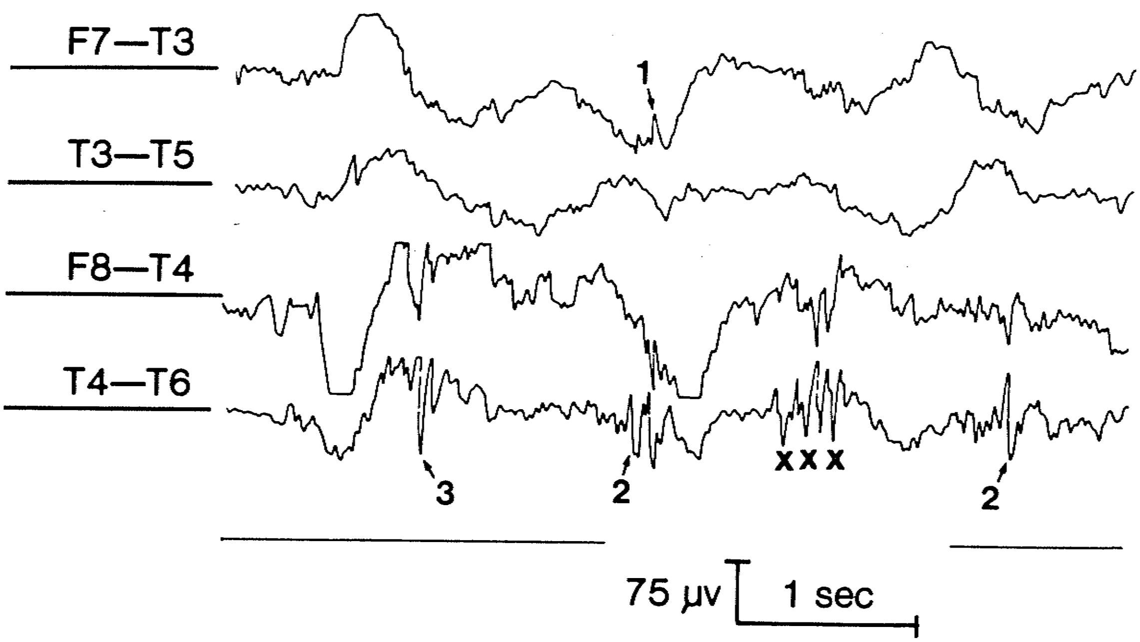

e
F3—C3
C3—P3
4
F4—C4
C4—P4
75 µv
1 sec
f
F3—C3
C3—P3
3
F4—C4
C4—P4
75 µv
1 sec

Figure 14 a to d. Examples of pseudo-STs identified by the EEGers. The computer either rejected them (X), or detected them as STs with a low likelihood (arrows) of being genuine.

a


F7—T3
T3—T5
F8—T4
T4—T6
1
3
2
x x x
2
75 µv
1 sec

b

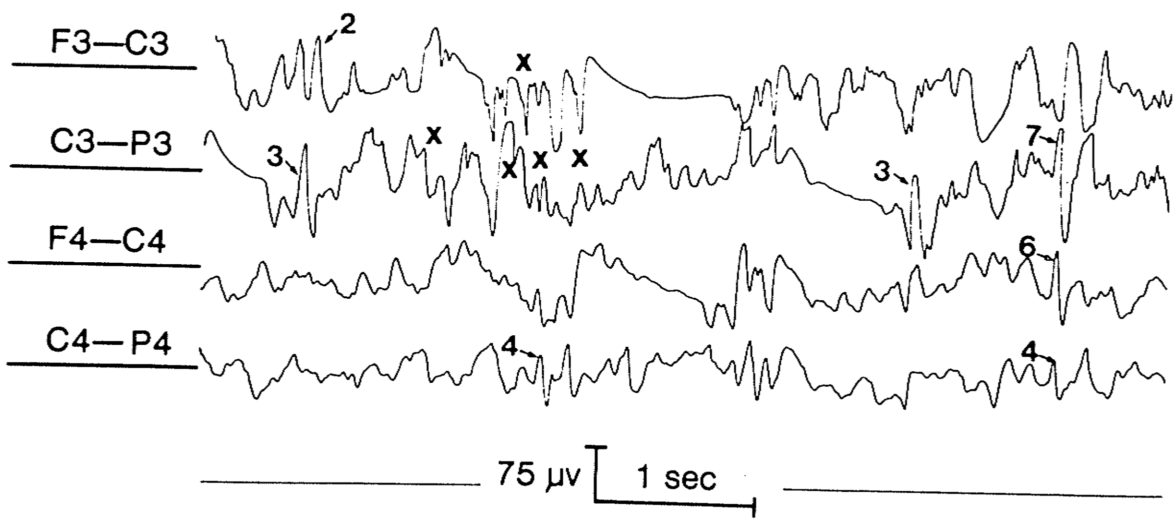
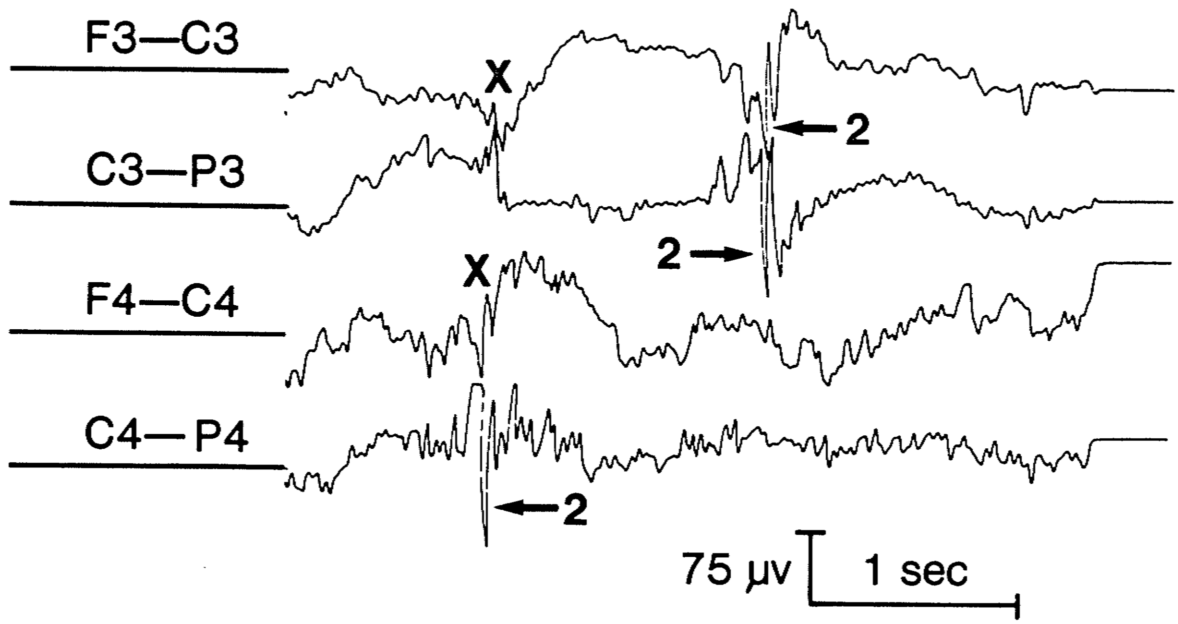
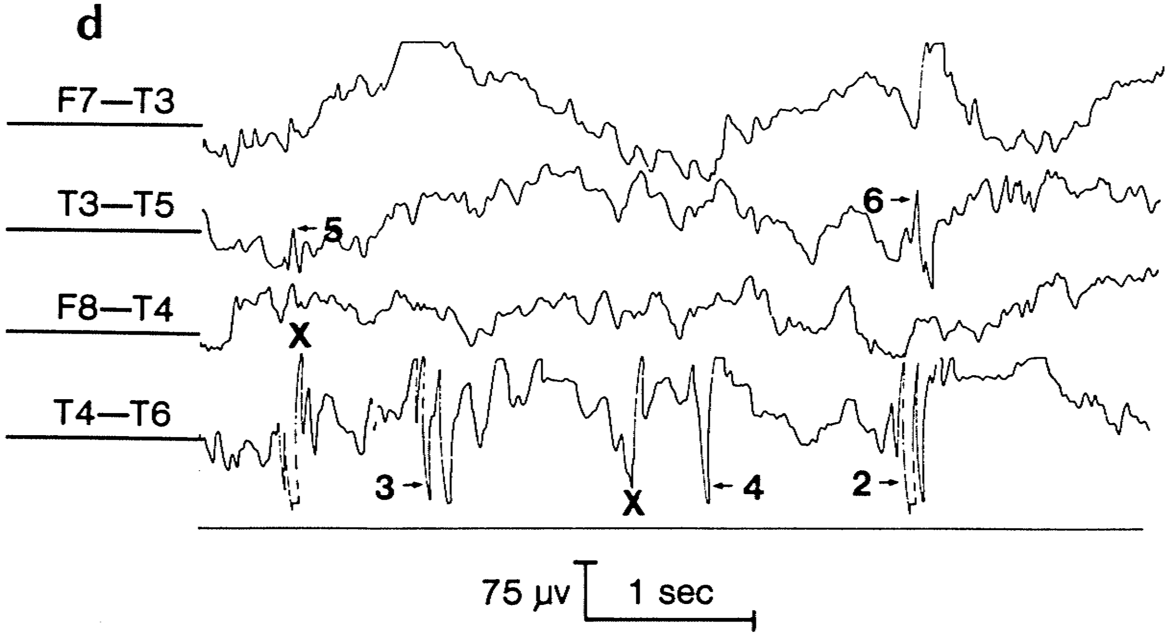

F3—C3
C3—P3
F4—C4
C4—P4
2
x
3
x
x
x
x
3
7
6
4
4
75 µv
1 sec

Figure 14 (continued).

c


F3—C3
C3—P3
F4—C4
C4— P4
X
X
2
2
2
75 µv
1 sec

d


F7—T3
T3—T5
F8—T4
T4—T6
5
6
X
X
3
4
2
75 µv
1 sec

semantic rules which deal with the presence of neighbouring STs. Once again however, such modification may also upgrade some artifacts.

Additional evaluation was also done to:

(i) Determine if taking contextual information into account improved performance.

(ii) Compare the performances of the 2 dissimilarity measures I1-I2 and I3-I4.

The proposed statistic for this component evaluation required a square matrix. Table III has 5 columns and 4 rows. The two grade ranges 7-6 and 5-4, were therefore collapsed into one range. The results of initial grading (from 1 to 6) obtained from indices I1-I2 and I3-I4 were grouped in 4 columns as shown in Tables IV and V.

An ideal system of grading would only give high grades to all definite STs, intermediate grades to events in rows 2 and 3 and not detect any event which had been left unclassified by the EEGers. The distribution of the numbers in the table would therefore ideally be along the principal diagonal. A statistic "scatter index" (SI) was therefore designed to measure the "spread" of numbers away from the principal diagonal.

$$SI = \frac{A+B}{T}$$

where A is the sum of numbers in the principal diagonal, B is the sum in the 2 paradiagonals and T is the grand total

Table IV

Results of ST detection by Indices I1-I2.

	Total No.	No. detected in each grade range 6-5	4-3	2-1	No. Undetected
Classif. by EEGers					
ST by both	126	35	45	42	4
ST by one	167	5	68	62	32
PST by one or both	103	12	42	45	4
Unclassified by both	427	19	162	246	–
Probability of detection being a ST		.56	.35	.26	

Table V

Results of ST detection by Indices I3-I4.

	Total	No. detected in each grade range			No.
	No.	6-5	4-3	2-1	Undetected
Classif. by EEGers					
ST by both	126	32	45	46	3
ST by one	167	6	71	58	32
PST by one or both	103	17	40	41	5
Unclassified by both	445	25	169	251	-
Probability of detection being a ST		.47	.35	.26	

in the entire table (Fig 15). A perfect system would give a SI value of 1. The values of the index SI for Tables III, IV and V, were 0.86, 0.67 and 0.61 respectively.

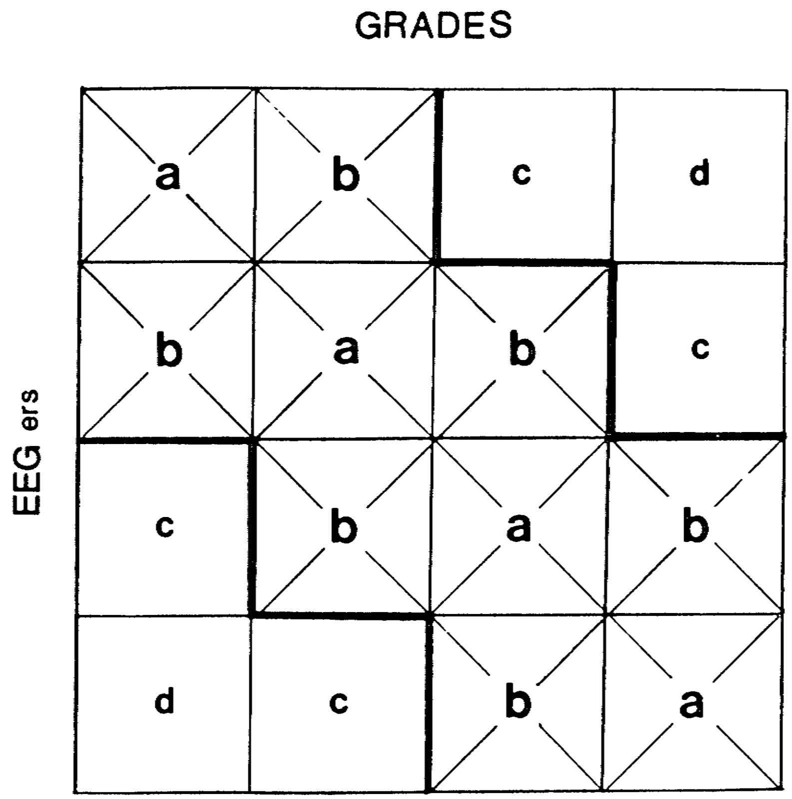
The SI values suggest that there is an improvement in the performance by considering contextual information. Contextual information helped to upgrade distinct STs (Fig 16 a) and also to correctly identify or downgrade distinct non-epileptiform activity (Fig 16 b). Three of the STs identified by one EEGer had been detected by the dissimilarity index I1-I2 (Fig 17). These were erroneously rejected on considering contextual information. All of these 3 STs were from the same segment.

There was a difference of only 0.06 in the SI values obtained for the two dissimilarity measures I1-I2 and I3-I4. The grades were usually comparable, neither measure consistently gave a higher grade than the other. Examples are shown in Fig 18. In some cases (eg., Fig 18) both measures falsely considered an event to be distinct from the background.

<u>4.1.2. SSW detection evaluation</u> (<u>Table VI</u>).

The probability of a burst being a genuine SSW is significantly higher (P <.005) for detections given a high grade and decreases for subsequent lower grades (see APPENDIX).

Figure 15. Computation of the scatter index SI.



$$SI = \frac{A+B}{T}$$

Figure 16. Examples of (a) STs upgraded and (b) detections downgraded, by considering contextual information. The initial (small print) and final (bold print) grades of each event are indicated.

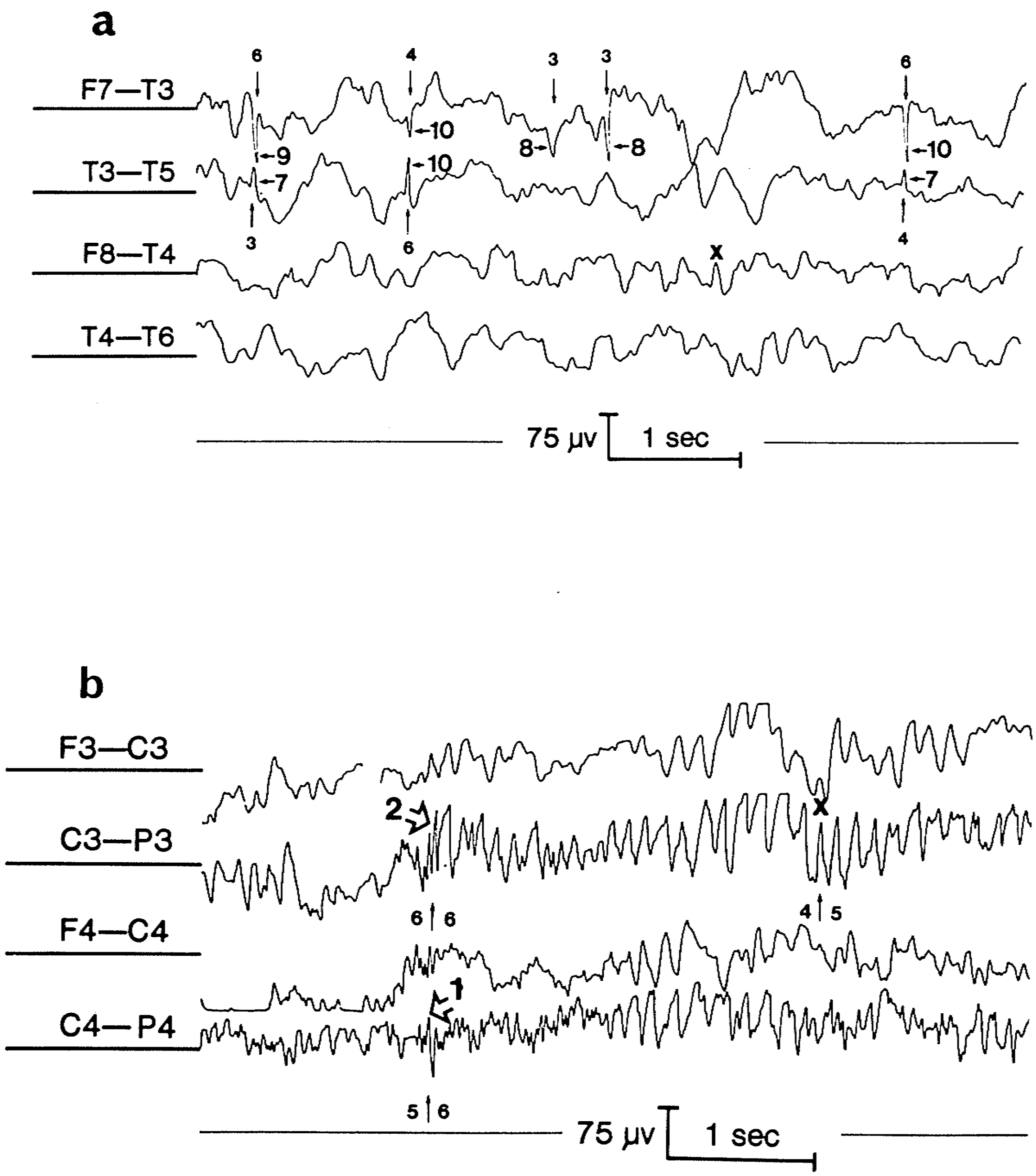
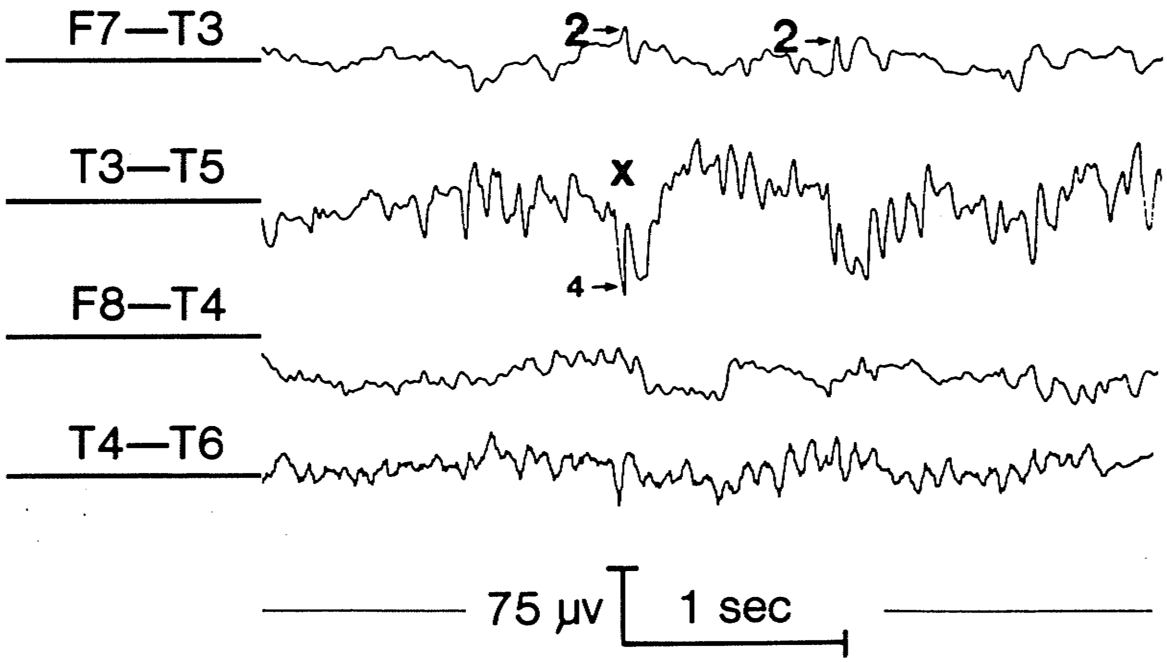

a
F7—T3
T3—T5
F8—T4
T4—T6
75 µv
1 sec
b
F3—C3
C3—P3
F4—C4
C4—P4
75 µv
1 sec

Figure 17. Example of a ST erroneously rejected (X) on considering contextual information. The initial grade is shown below the event.

Figure 18. Example showing events (arrows) and their grades obtained by the two dissimilarity measures I1-I2 (left) and I3-I4 (right).


F7—T3
2
2
T3—T5
X
4
F8—T4
T4—T6
75 µv
1 sec

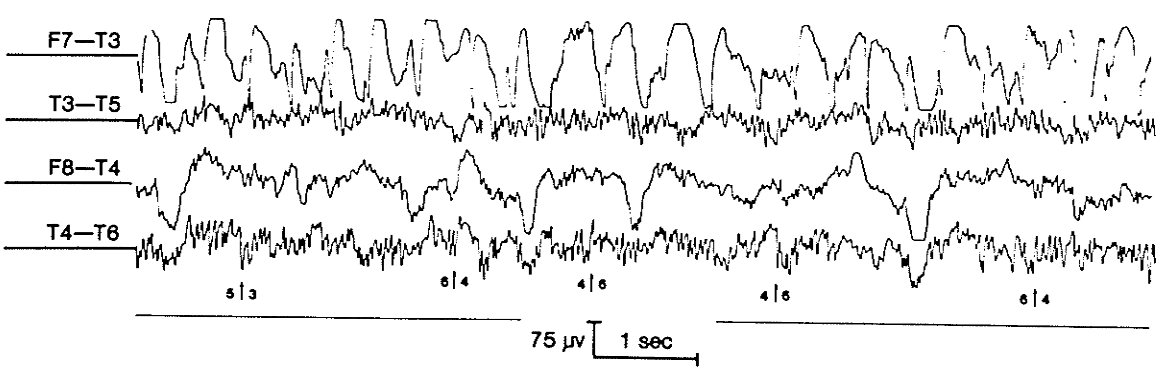

F7—T3
T3—T5
F8—T4
T4—T6
5 | 3
6 | 4
4 | 6
4 | 6
6 | 4
75 µv
1 sec

Table VI

Results of SSW detections by the automated system.

	Total	No. detected in each grade range			No.
	No.	10-8	7-4	3-1	Undetected
Classif. by EEGers SSW by both	9	6	3	0	0
SSW by one	7	1	5	1	0
PSSW by one or both	10	0	2	6	2
Unclassified by both	4	0	0	4	-
Probability of detection being a SSW		1	.8	.1	

All 16 SSWs which had been identified by either EEGer were detected by the computer. Only 9 of these 16 had been identified by both EEGers. SSW bursts ranged in duration from 1 sec to 10 seconds (Fig 19 a to d). Some had high amplitude slow components that saturated the preamplifiers. SSWs varied in morphology, amplitude and spatio-temporal distribution; some were present in only 1 or 2 channels (Fig 19 d).

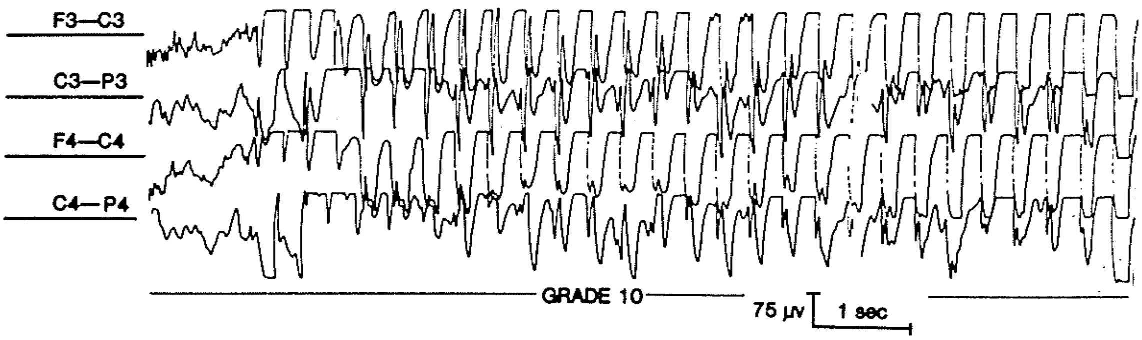
Twelve bursts detected by the computer had not been classified as SSWs by either EEGer (Fig 20 a,b). None of these was graded greater than 7. Detections that had been left unclassified by both EEGers were mainly related to bursts of slow activity with some sharply contoured activity. Most of the 10 pseudo-SSWs were related to rhythmic movements. Two of these were rejected by the computer (Fig 21 a,b).

4.2. Background activity.

Although automated methods are expected to be highly accurate in measuring durations and amplitudes the complexity of the EEG signal dictated the need for objective evaluation. The frequencies and amplitudes of the waves detected by the automated analysis were compared to the annotations done by one EEGer. The EEGers had coded only epochs greater than 3/8 sec into specific classes, whereas the algorithms defined the duration and amplitude of each wave individually. Error in frequency

Figure 19 a to d. Examples of SSWs identified by both EEGers (a and b) and by only one EEGer (c and d). All of these were detected by the computer, the grades of each are shown.

a


F3—C3
C3—P3
F4—C4
C4—P4
GRADE 10
75 µv
1 sec

b

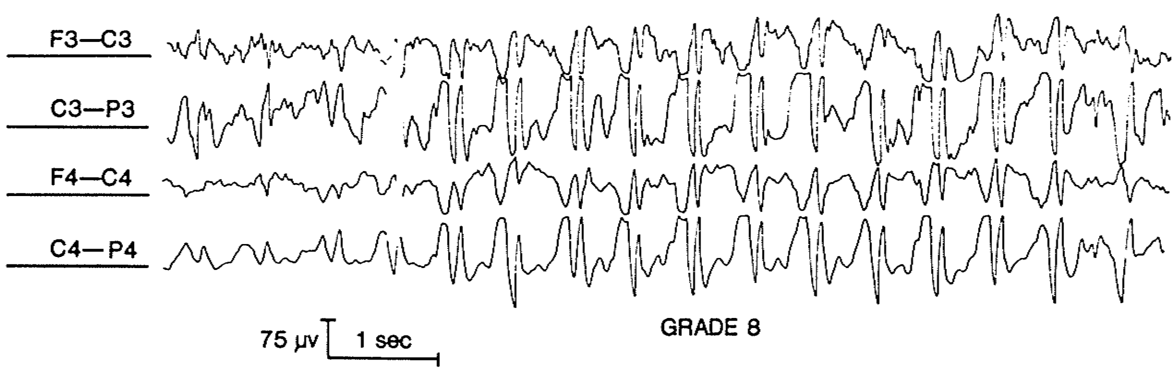
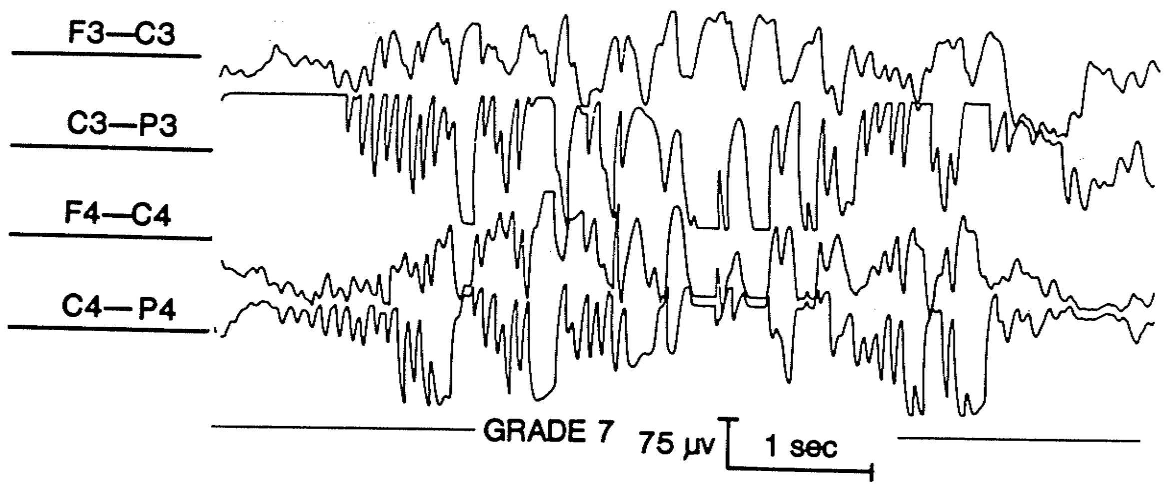

F3—C3
C3—P3
F4—C4
C4—P4
75 µv
1 sec
GRADE 8

Figure 19 (continued).

c


F3—C3
C3—P3
F4—C4
C4—P4
GRADE 7
75 µv
1 sec

d

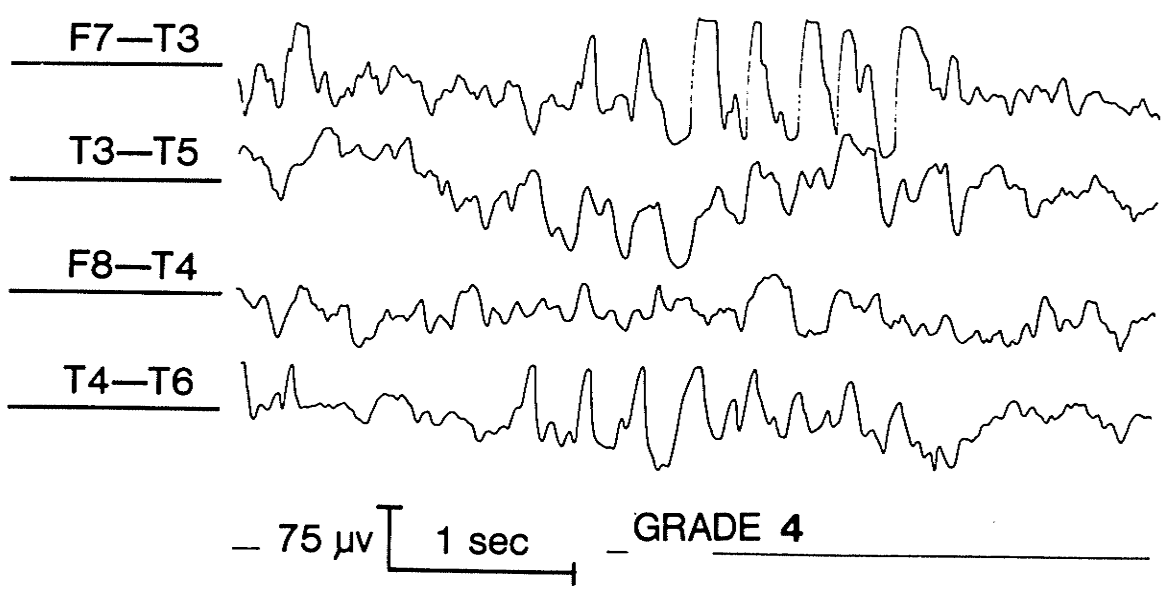
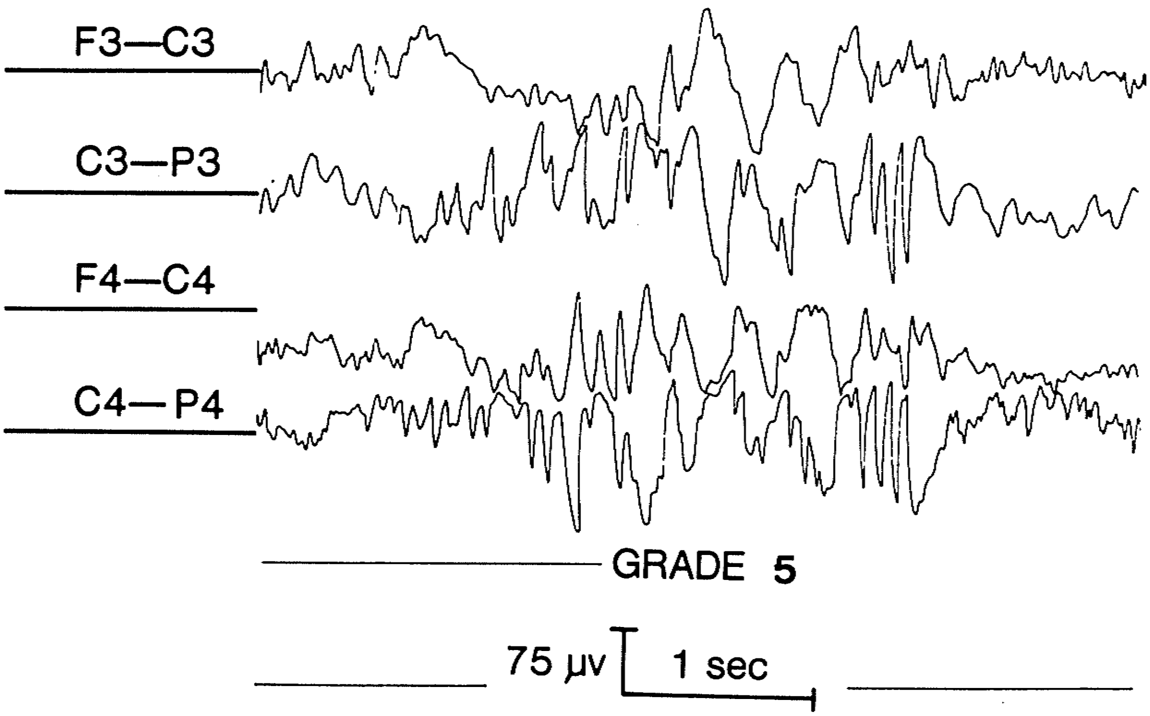

F7—T3
T3—T5
F8—T4
T4—T6
75 µv
1 sec
GRADE 4

Figure 20 a,b. Examples of bursts detected by the computer which had not been classified as SSWs by either EEGer. Note that they have some resemblance to genuine SSWs.

a


F3—C3
C3—P3
F4—C4
C4—P4
GRADE 5
75 µv
1 sec

b

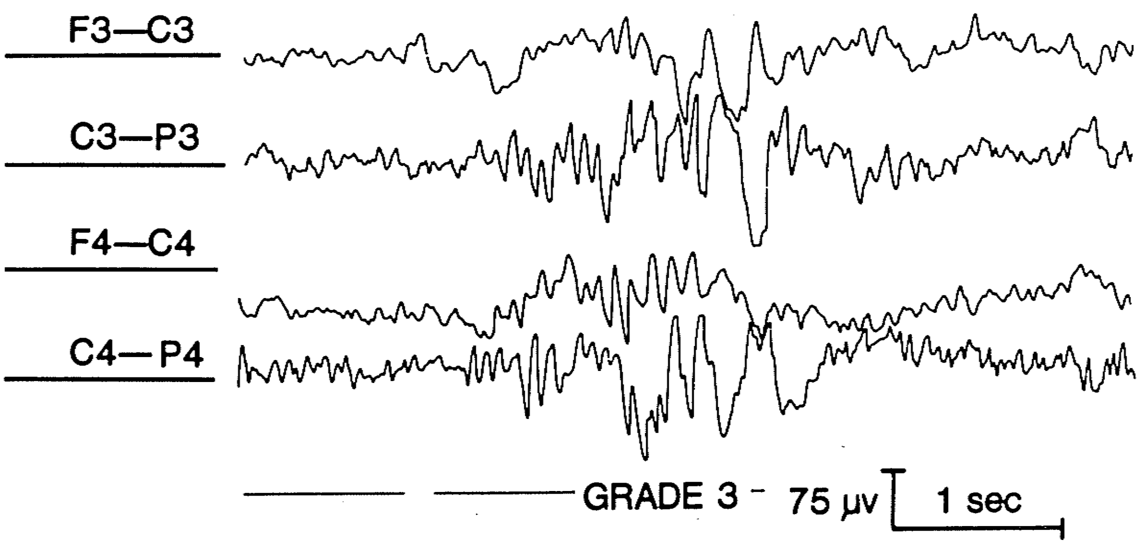
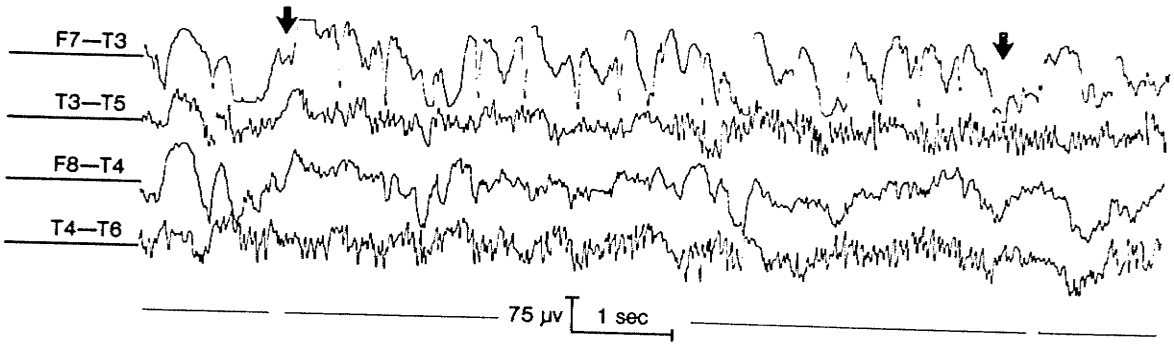
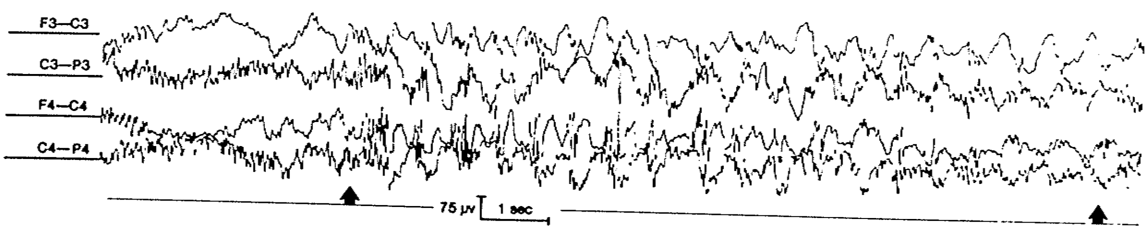

F3—C3
C3—P3
F4—C4
C4—P4
GRADE 3
75 µv
1 sec

Figure 21 a,b. Examples of pseudo-SSWs identified by the EEGers, which were correctly rejected by the computer.

a



b



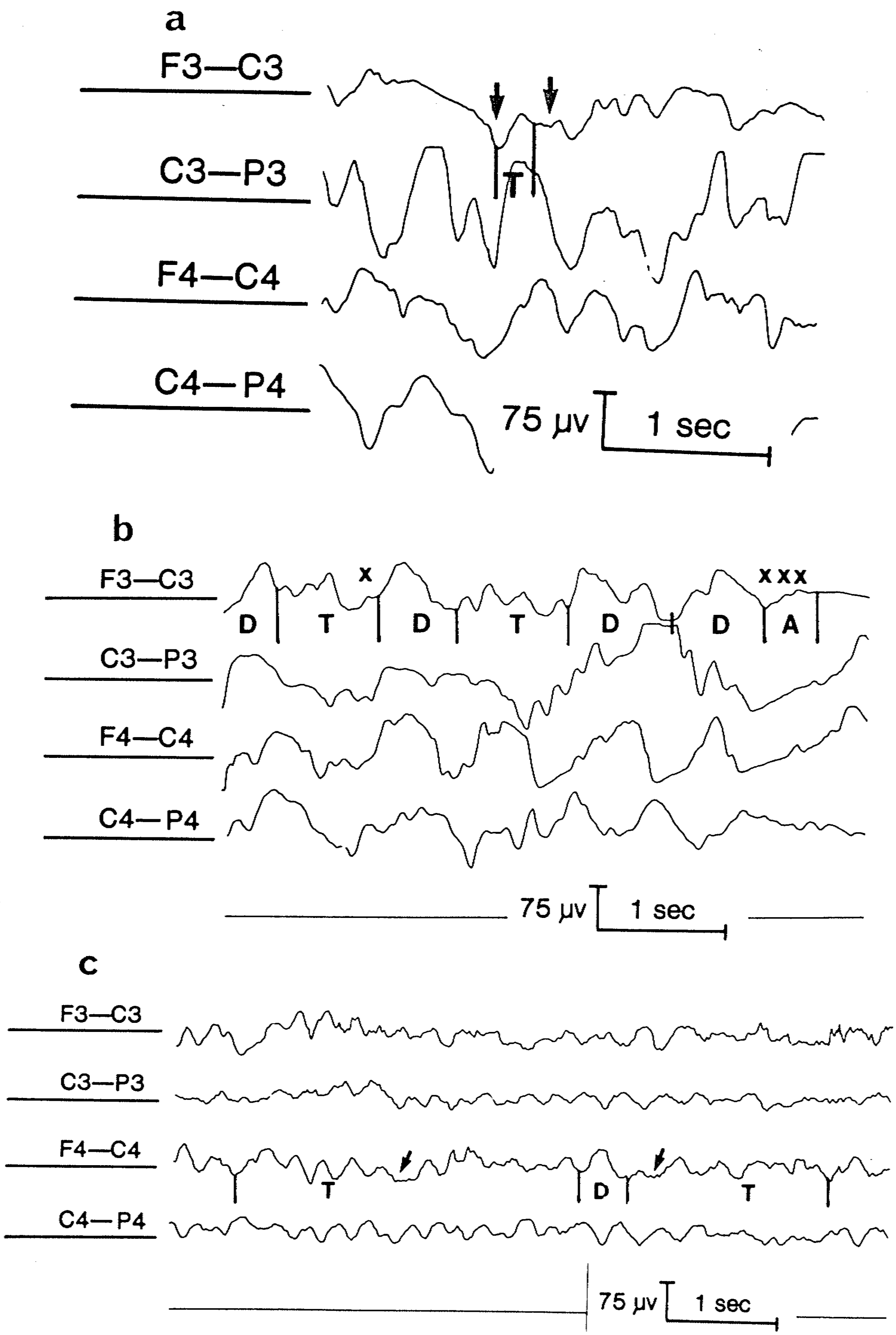
measurement was defined as the difference between the frequency limit of the class identified by the EEGer and the frequency detected by the computer. Eight segments were analyzed. Misclassification occurred in 148 out of 1117 (14 %) waves. "Baseline sway" and superimposed activity were the major causes of misclassification, which was of 3 types:

(1) Sixty seven waves were classified in a different frequency, from that done by the EEGer. In all of these cases, the difference was less than 5 Hz. An example is shown in Fig 22 a.

(2) The computer did not detect 45 low amplitude (< 10 uv) superimposed waves (example in Fig 22 b). This was expected because the algorithms were programmed only to detect superimposed half-waves with an amplitude greater than 10 uv.

(3) The computer detected 36 low (< 20 uv) amplitude beta waves near the "baseline" which had been "missed" or "overlooked" by the EEGer. An example is shown in Fig 22c.

Figure 22. Examples of background missclassification. (a) Theta (T) activity identified by the EEGer was classified as a 3.2 Hz. wave (demarcated by arrows). (b) Low amplitude theta and alpha (A) activity superimposed on delta (D) was missed (marked "X") and (c) low amplitude beta activity overdetected (arrows).


a
F3—C3
C3—P3
T
F4—C4
C4—P4
75 µv
1 sec
b
F3—C3
x
xxx
D
T
D
T
D
D
A
C3—P3
F4—C4
C4—P4
75 µv
1 sec
c
F3—C3
C3—P3
F4—C4
T
D
T
C4—P4
75 µv
1 sec

5.0. DISCUSSION

The study describes algorithms to identify STs/SSWs and analyze background activity in 4-channel AEEGs. The algorithms were developed using a database of AEEG signals annotated by two EEGers. The inter-observer variability seen between the 2 EEGers was comparable to that observed in other studies (Gose et al. 1974).

The AEEGs were done on patients aged 1-22 years using bipolar montages, this being the only type of derivation permitted by commercially available AEEG systems. The performance may be different if the algorithms are used to analyze EEGs obtained (i) on a different patient sample, (ii) with a different type of recording system or (iii) using other derivations. The database segments were selected from AEEGs by a person other than the EEGers who annotated the data and the segment collection was completed before the current study on automated analysis was planned, thus minimizing bias. Selection bias could have been eliminated by choosing segments at some predetermined, fixed time intervals. Instead, an attempt was made to select segments so as to obtain a relatively uniform number of epochs, especially in ST/SSW and pseudo-ST/SSW classes; a feature felt to be important for estimation of the performance of any automated system.

5.1. System Performance.

The computer performed just as well as the EEGers, in identifying STs/SSWs and background activity. The results show that the probability of an event being genuinely epileptiform, was high for events graded high and decreased progressively for lower grades. The low rate of missed events may be at least partly, credited to the grading. Distinct STs or SSWs were not missed. Some STs that were not detected were either too small, too broad or to blunt. This is possibly a limitation of the use of absolute values as screening criteria. Such STs may however be the only ones present in some patients. To allow the detection of such STs, the algorithms would have to be modified so that the thresholds for the screening criteria are lower. Non-epileptiform events which exceed the threshold, may possibly then be rejected by the dissimilarity indices (I1 and I2) which are used to determine if a wave is distinct from the background (section 3.4.2).

Some sharply contoured background activity was identified as STs/SSWs by the computer. A separate classification of such background activity in the database may have been useful in training the algorithms and thereby minimizing such errors.

The indices I1-I2 and I3-I4 were useful in differentiating a ST from the background. However, some

STs which were within a run of repetitive STs, may have been missed because the thresholds for indices I1-I2 were elevated by the neighbouring STs. On the other hand, in some cases both measures falsely considered an event to be distinct from the background. This may be because the measures are based on computation of the average. The average may be inappropriately lowered by a few waves with very low values of features F1/F2. <u>This may well be a limitation of all previously described systems based on computation of the average</u>. Additional contextual information obtained from the total number of "similar" waves in the background, was therefore also included in the algorithm and helped downgrade some definite, non-epileptiform activity. It is possible that visual analysis also employs a combination of similar "measures".

The misclassifications of background activity may be considered to be disagreements between the EEGer and the computer, rather than as errors by the computer. As emphasized in section 2.5, one cannot expect total agreement between the computer and the EEGer. Some low amplitude background activity was missed. The algorithms could be modified to detect even very low amplitude (< 10 uv) superimposed activity. This may be undesirable in an AEEG, since such systems may have a noise level of about 5-10 microvolts. This noise generally has a very high frequency. It may therefore be possible to identify even low amplitude activity by placing constraints on the duration of the waves.

Several studies have described automated systems to identify STs or SSWs. However, the graded detection of STs/SSWs in this study, makes comparison of performance with the other systems difficult. Although the computer performed well on an independent set of AEEG segments, evaluations based on short segments of data may not provide accurate estimates of the performance (Gotman et al. 1979). The value of the system has therefore to be tested for analyzing prolonged, continuous AEEGs.

The system may be biased towards the 2 EEGers who annotated the database. But the basis for the semantic rules are robust and should make it acceptable.

5.2. The main contributions of this research are:

(1) Grading of STs/SSWs is a unique feature which has not been described in most of the previous automated systems. Whisler et al. (1982) described SSWs detected by their system as either "clear" or "marginal".

The gradation of STs and SSWs conceptually has several advantages: (a) It mimics day to day visual interpretation since EEGers consciously or subconsciously use probabilities. (b) It avoids the forcible classification of each event as genuinely epileptiform or not, a possible limitation of existing automated systems. (c) It is practically impossible to automatically eliminate all false positive detections due to artifacts (Gotman 1985). The grading of events therefore provides a method of probabilistically differentiating between artifacts and genuine epileptiform events. (d) It provides flexibility in the use of the system. Thus for example, the EEGer has the option of displaying or obtaining a writeout of all grades of events or of only those that are graded high. The burden of examining and interpreting a large number of detections may therefore be reduced. (e) It permits selectivity in the storage of detections. Thus for example, if the memory in the computer is exhausted, one may choose to keep only the detections which have a higher grade and discard the remaining.

(2) The algorithms identify all major waveform types. Most systems described recently have been developed to identify specific type of activity eg., STs or SSWs; Goldberg et al. (1973) described a system to identify background and epileptiform activity. It may be argued that detection of all waveform types may not be necessary in all cases. Nevertheless, a composite system such as the one presented here has some advantages: (a) False negative errors of most SSW detection methods are related to short (< 1 sec) duration bursts (Frost 1985). A composite system may detect such bursts as STs and thus would not "miss" them. (b) Quantitative analysis of background activity can be done after the exclusion of

epileptiform activity and artifacts.

(3) The algorithms attempt a more detailed definition of STs/SSWs and a more thorough consideration of intra- and inter-channel contextual information, than previously described systems.

6.0. CONCLUSIONS

The objective of this thesis was to develop approaches for multi-channel context based analysis of AEEGs. Algorithms have been developed to identify STs, SSWs and to analyze background activity in 4-channel AEEGs. Time domain methods and semantic rules were used to consider morphology and multi-channel contextual information. The algorithms have been evaluated on an independent set of AEEG segments. The computer performed just as well as the EEGers. The algorithms can now be incorporated into an automated system for off-line analysis of 4-channel AEEGs.

The main contribution of the thesis, is the approach of grading the detected STs/SSWs, to indicate the likelihood of the detection being genuinely epileptiform. The grading is done using semantic rules based on morphology and multi-channel contextual information, in a thirty second segment.

6.1. Recommendations for future work.

(1) Extend to 8/16 channel EEGs.

Prolonged EEG recordings with either AEEG or telemetry are established methods of neuro-intensive monitoring. The approaches developed in this study can be applied for the analysis of either 8/16 channel AEEGs, CEEGs or telemetric EEGs. A 16 channel data base with annotation of only epileptiform and pseudo-epileptiform activity, can complement the 4-channel data base used in this study.

(2) Specific improvements to the algorithms.

The algorithms can be improved in several ways. The rules may consider the region of the brain over which each channel records. This can allow the definition of a "field" for a ST and help to reject some non-epileptiform activity. Identification of vertex spikes which are distinct from the vertex sharp transients of sleep (Neidermeyer and Lopes da Silva 1982) is a challenge for automated systems.

The rules used in this study considered only the contextual information in the same 30 second segment. However, the EEGer may during interpretation compare events which occur over longer sections of the record (Frost 1985). The possibility of storing specific types of events separately so as to allow such comparisons automatically may be explored.

(3) Detection of seizures without STs.

Gotman (1982) described separate algorithms for the detection of seizures without ST components. However, only 20 % of the detections were genuine seizures. Applying the principle of grading to such detections may prove useful.

(4) Statistical Derivation of Rules.

The semantic rules in this study were based on "EEGer's knowledge" and logic; the weights to some extent were arbitrarily defined. The role of mathematical/statistical approaches such as Bayesian or Discriminant analysis in developing the rules was considered. It was felt that the basic assumptions in these methods made them inappropriate for the problem. But such approaches could be explored.

7.0. REFERENCES

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8.0. APPENDIX

Statistical analysis of the grading in Tables III and VI.

The probability (more appropriately termed "relative frequency") of an event being ST/SSW was computed as the proportion of events considered to be ST/SSW by either EEGer (sum of rows 1 and 2), out of the total number of events in that grade range (section 4.1). This probability is observed to be higher for events given high grades as compared to those graded lower (Tables III and VI). The objective was to test whether this difference in probability is significant.

One would expect the "cell" probabilities of the two classifications, epileptiform (rows 1+2) and non-epileptiform (rows 3+4) done by the EEGers, to be alike, if the computer graded events randomly. To test the null hypothesis, that in each grade range, the two "cell" probabilities are equal, a Chi-square test of homogeneity in a contingency table was used (Johnson and Bhattacharya 1985). The Chi-square statistic measures the overall discrepancy between the observed frequencies and those expected under the null hypothesis.

The expected frequencies and the total Chi-square values were computed for Table III and VI (Johnson and Bhattacharya 1985). The data were regrouped as epileptiform (rows 1+2) and non-epileptiform (rows 3+4).

The last column of undetected events in each table was not included.

Tables VII to X show the results of the analysis. The observed Chi square values for Tables III and VI are larger than the expected value ($P < 0.005$). Therefore one concludes that there is a significant difference in the "cell" probabilities of each grade range. Thus, the observed difference in the probability for the grade ranges, is significant.

Table VII.

Observed and expected frequencies of data in Table III.

	Grades				Total
	10-8	7-6	5-4	3-1	No.
ST	48 (17)	58 (29)	72 (76)	76 (130)	254
Non-ST	1 (32)	26 (53)	139 (135)	282 (228)	448
					702

Table VIII

The value of $(O-E)^2 / E$ for Table VII

56	29	0	22
30	13	0	12
		Total Chi-square = 162	

Observed (O) and expected (E) frequencies.

Table IX.

Observed and expected frequencies of data in Table VI.

	Grades 10-8	7-4	3-1	Total No.
SSW	7 (4)	8 (5)	1 (7)	16
Non-SSW	0 (2)	2 (4)	10 (4)	12
				28

Table X.

The value of $(O-E)^2 / E$ for Table IX.

2	2	5
2	1	9
	Total Chi-square = 21	

Observed (O) and Expected (E) frequencies.