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Technical contribution

A TOPOGRAPHICAL DISPLAY OF EPILEPTIFORM TRANSIENTS BASED ON A STATISTICAL APPROACH

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In any method of automatic classification of EEG epileptiform transients account has to be taken of the graphical presentation of the relevant information. This involves making a graphical display of the detected transients which should be synthetic, statistically valid and easy to interpret clinically. We present here such a display based on a novel approach. The basis of the method is that the epileptiform events are considered to be realizations of a multichannel point process. The present method may be seen as an improvement of our previously published spatial maps (Lopes da Silva et al. 1977) on two accounts: statistical analysis has been added and topographical representation has been made more general since the method provides a quantification of the time associations between epileptiform events occurring not only in pairs of derivations, but also in groups of 3 (triads) and in higher order groups. Such displays are of practical use for the evaluation of interictal EEGs, particularly in partial epilepsy where the localization of an epileptogenic focus is a question of importance. The present method differs from previously published ones (Rossi 1973; Rosadini et al. 1974; Gotman and Gloor 1976; Lieb et al. 1978) in that the time relationships between events occurring in pairs of derivations or in groups of 3, 4, etc. derivations can be estimated in a statistical way, independently of the wave forms of those events.

The statistical method used is based on that published recently by Gerstein et al. (1978) for the analysis of functional assemblies of neurones based on simultaneously recorded spike trains. The objects for their analysis were the impulses produced by different neurones; in our case they are epileptiform transients, which are also discrete events. The method is applied to scalp EEGs recorded in standard conditions from 16 bipolar derivations using the 10-20 system. EEGs are digitized after being passed through anti-aliasing filters (cut-off, 3 dB; 70 Hz) at a rate of 200 samples/sec. From the sampled EEGs epileptiform transients are detected by a suitable algorithm (for example that described by Lopes da Silva et al. 1975).

Statistical analysis

In a period T we may find N_i events (i.e., epileptiform transients) in channel i and N_j events in channel j. We may define as N_{ij} the number of events occurring simultaneously in channels i and j within a time window Δt. This window should be kept small, so that there is a low probability of two events occurring within the same window in the same channel.

We may then build the following 2-way contingency table, which gives the necessary information as regards the number of times an event occurs in any window in channel i (N_i) and in channel j (N_j) or jointly in both channels (N_{ij}) with $k = T/\Delta t$.

	in i	not in i	
in j	N_{ij}	$N_j - N_{ij}$	N_j
not in j	$N_i - N_{ij}$	$k - N_i - N_j + N_{ij}$	$k - N_j$
	N_i	$k - N_i$	k

To test the null hypothesis that the events in channel i and j occur independently, we use the test statistic with the continuity correction as advised for $k \geq 40$ (Cochran 1954)

$$\chi^2_{ij} = \frac{k(|kN_{ij} - N_iN_j| - \frac{1}{2}k)^2}{N_iN_j(k - N_i)(k - N_j)}$$

which for the null hypothesis and k large enough has a χ^2 distribution with 1 df.

We have followed in this the approach proposed by Gerstein et al. (1978) including, however, one new feature. Instead of using contiguous time windows we

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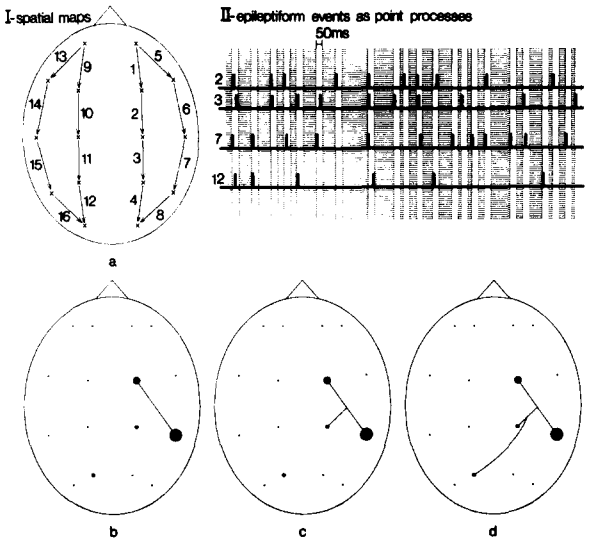

Fig. 1. Schematic representation of the statistical method of analysis of associations of epileptiform transients based on Gerstein et al. (1978). I: the growth of a spatial map in 3 phases; in the maps the location of the derivations is midway between the corresponding electrodes (following the 10-20 system as shown above). II: the epileptiform transients which have been detected are shown as point processes for 4 derivations only. Note that a time window of 50 msec is open by one transient occurring in any derivation. In the 1st time window of this example a tetrad can be seen. The pair 2 and 7 has in this example the largest number of common events; therefore it is the pair which is shown in the spatial map b. The most significant triad is between 1 and 7 *and* 3, as shown in spatial map c. The most significant tetrad is between (1 and 7) and 3 *and* 12 as shown in d.

TABLE I

No. of SSW = number of spikes and sharp waves per EEG derivation, and number of significant pairs, triads and tetrads. The number of phase reversals found in significant pairs is indicated (PH.REV). GOT 700-704. Threshold $P < 0.5\%$, $\chi^2 > 7.88$. Time window = 50 msec.

Derivation	No. of SSW	Significant associations			
		Derivations	No.	χ^2	PH.REV.
1	21	10, 1	8	8.86	6
2	19	11, 2	9	8.12	3
3	15	10, 9	13	37.76	10
4	17	11, 9	15	33.98	13
5	8	11, 10	14	38.51	3
6	12	9 (10, 1)	5	8.46	
7	16	11 (10, 1)	7	19.40	
8	13	10 (11, 2)	7	25.51	
9	22	11 (10, 9)	11	32.45	
10	18	15 (10, 9)	6	9.77	
11	25	10 (11, 9)	11	41.50	
12	17	14 (11, 9)	5	9.18	
13	13	1 (11, 10)	7	9.47	
14	11	2 (11, 10)	7	11.45	
15	17	9 (11, 10)	11	34.72	
16	10	14 (11, 10)	5	10.31	
Total	122 windows	11 (9(10, 1))	5	15.46	
		9 (11(10, 1))	5	10.75	
		9 (10(11, 2))	5	10.75	
		11 (15(10, 9))	5	11.51	
		9 (1(11, 10))	5	10.75	
		9 (2(11, 10))	5	10.75	

decided to open a time window only whenever an epileptiform transient occurred in any of the 16 derivations. This procedure is shown in Fig. 1. This was done because in most cases the mean rate of epileptiform activity is low and therefore the procedure proposed by Gerstein et al. (1978) would result in many windows without any event. Based on our experience we chose a time window $\Delta t = 50$ msec (this corresponds approximately to the mean duration of an epileptiform event).

The χ^2 values were compared with a selected threshold corresponding to a determined probability level in order to test whether the null hypothesis (no time relation between the events of channel i and those of channel j) could be rejected or not. This was done for all pairs of derivations. The probability level in our algorithm was chosen interactively; normally we started at $P < 0.001$; this level could be increased or decreased at will.

Whenever a pair of derivations showed a significant χ^2, the next step was to search for the relation between each of those pairs taken as a unit and all other derivations. The test of whether this triad association was significant or not was done in a similar way to that for the pairs. If significant triads were found the analysis was continued for the tetrads in a similar way and so forth. The analysis was continued until no χ^2 could be found above the threshold or no group of common events (N_{ij} for the case of pairs) contained at least 5 events.

Table I shows the number of epileptiform events per derivation determined in an EEG epoch together with the degree of time association between groups of derivations. It should be noted that in this type of analysis any set of more than two elements is not commutative. Any new element is associated with the previous set considered as a whole; in this way we note a triad when C has shown relation to pair AB as C(AB). If a tetrad is found with element D we write D(C(AB)) and so forth. In any case the initial pair is the one which represents the most significant association of all the elements considered; this means, for example, that if among all possible pairs the association AB is that which attains the largest χ^2 value, this one is chosen to start a triad. Alternatively one could also use a 3 entry contingency table for triads and so forth, but this would increase the number of combinations without leading to an important advantage as regards the determination of the most significant sets of association.

Table I shows the results of the analysis of 50 sec of EEG, the graphical display of which is shown in Fig. 2. In this table the number of epileptiform transients (SSW) per derivation is shown. A list of the significant pairs, triads and tetrads is given jointly. Furthermore, the number of phase reversals encountered among the events forming a pair has been indicated.

The polarity reversal was found just by examining the directions of the slopes of the leading edges of those epileptiform events which were encountered in a pair of derivations which was considered to be significant.

Graphical displays

At first a computer drawing [3] of a head with the derivations indicated by points half way between the corresponding electrode placements (we are assuming bipolar derivations according to the 10-20 system) is made (Fig. 1); on this drawing a segment is drawn joining each significantly associated pair of derivations. The segment which links the pair to the third element of a triad is drawn from the middle point of the previous segment to the placement of the third element of the triad. The same method is used for higher order groups. To avoid the link between two channels overwriting a third one, inducing a false connection, the channel coordinates as well as the middle point of previously drawn lines form a 'protected' array. Any new line has to keep a minimum distance from the points of the array; this is achieved by drawing hyperbolic curves (Fig. 1d).

Finally a dark circle centred at each channel is drawn with a diameter proportional to the number of transients detected in that channel. This has only a relative meaning since in this drawing it is normalized to the channel with maximal activity. The scaling factor is given in the numerical table. An example from a clinical case is shown in Fig. 2 and the corresponding numerical data are indicated in Table I. In this case it can be seen that the pairs of derivations where significant associations were encountered included derivations 9 ($F_{p1} - F_3$), 10 ($F_3 - C_3$) and 11 ($C_3 - P_3$) on the left hemisphere; there were also significant interhemispheric pairs formed between 10 and 1 ($F_{p2} - F_4$) and 11 and 2 ($F_4 - C_4$). It should be noted that all significant pairs, triads or tetrads included either derivation 10 or 11 or both. A remark should be made regarding the strength of the associations: it can be noted that the associations within the left hemisphere (9, 10 and 11) had generally larger χ^2 values than the inter-hemispheric ones, and that the triad 10 (11 and 9) reached the largest χ^2 encountered. This can also easily be seen in the graphical display of Fig. 2, right, where the threshold has been set a higher level ($P < 0.1\%$).

It can also be seen from Table I that most epilepti-

[3] Both the programs for statistical analysis and graphical display run in a PDP 11-20 computer with 24K of core memory, two disk (RKØ5) units and a Calcomp plotter. Programs were written in Fortran IV.

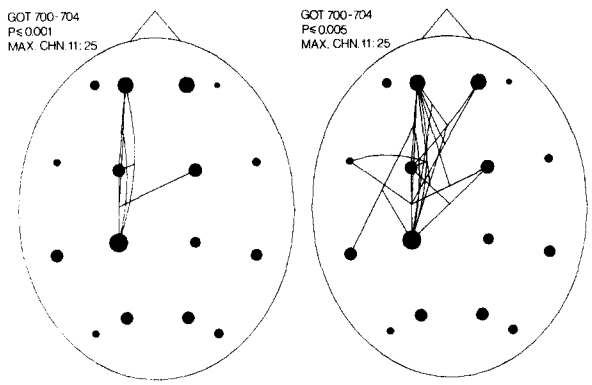

Fig. 2. A spatial map representing the epileptiform activity of an EEG analysed according to the statistical method presented here. On the right side the association between derivations which are significant above the $P < 0.5\%$ level is represented. On the left those which are significant above the level $P < 0.1\%$ are shown. Note the strong association between derivations 9 ($F_{p1} - F_3$), 10 ($F_3 - C_3$), 11 ($C_3 - P_3$) and 2 ($F_4 - C_4$); these include 3 pairs (10 and 9, 11 and 9 and 11 and 10) and 2 triads (10 (11 and 9) and 2 (11 and 10)). The spatial map at a lower level shows a significant spread of epileptiform activity from the central core indicated above towards derivation 1 ($F_{p2} - F_4$) on the right hemisphere and towards derivation 14 ($F_7 - T_3$) and 15 ($T_3 - T_5$).

form events presented phase reversals between derivations 10 ($F_3 - C_3$) or 11 ($C_3 - P_3$) and 9 ($F_{p1} - F_3$), but not between 10 and 11. This indicates that the epileptogenic area was most likely to be located between derivations 9 and 10, i.e., at and around F_3.

In the case illustrated in Fig. 2 visual inspection of the same EEG record by an experienced EEGer who had no knowledge of the computer analysis results led to the following description: 'The EEG shows epileptiform activity over the left hemisphere, which spreads to the right side. Maxima tend to occur at the left fronto-central (derivations 9, 11) areas and/or at the left occipito-parietal (derivations 12, 16) areas spreading to the right side (derivation 4).'

Discussion

The adaptation of the method of Gerstein et al. (1978) to the statistical analysis of epileptiform transients provided a new way of displaying EEG interictal epileptiform events in a quantitative and statistically relevant way. The procedure used here avoids the difficulties of determining precise time relations between epileptiform transients with different wave forms, which commonly occur. Furthermore, it avoids the influence of jitter in the time relations between the events occurring in different derivations within, of course, the length of the window chosen (50 msec). The graphical display provides synthetic information easy to interpret in a clinical setting. In the case illustrated in Fig. 2 it can be seen that over the right hemisphere and over the posterior regions there were no significant associations noted. However, this was only the case when the results were tested at the levels $P < 0.001$ or $P < 0.005$. At lower probability levels significant associations were also found in other pairs than those shown in Fig. 2 and in Table I. It should be noted that the method used here provides essentially a way of comparing the strengths of associations between events. This form of analysis should preferably be conducted in an iterative way, starting from the highest level at which significant associations are still encountered (e.g., $P < 0.001$), down to a low level such as $P < 0.05$ or $P < 0.10$. It should also be stressed that within each EEG record the statistical analysis has the same power for all pairs of events (triads, etc.) since for each case the total number of time windows is constant. A direct comparison between EEG records in absolute terms, however, can only be made whenever the total number of time windows is approximately the same. In other cases only a comparison in relative terms is allowed, i.e., the spatial distributions of the strongest associations can be computed over different records, but it makes no sense to consider whether in one particular case the highest probability level attained is higher or lower than in another one. In all clinical cases where this method has been applied so far, useful information of practical interest as regards the localization of an epileptogenic focus has been obtained. It should be added that in these cases we used EEG segments of the same length, obtained in awake conditions, which had been carefully selected as representative of the presence and distribution of interictal epileptiform events. A clinical trial in a large and unselected population is in course. It should be stressed that the information obtained from the spatial maps is complementary to that based on phase reversals between pairs of derivations obtained using a bipolar montage. By means of the phase reversals one can decide, for example in Fig. 2, where precisely the centre of the focus is located within the group of derivations in which significant associations were encountered, using the statistical method proposed here. However, the spatial maps give extra information regarding the amount and the pattern of spread of epileptiform transients over the whole area. The statistical analysis employed here should be seen simply as a way of arranging in an hierarchical manner the number of associations between derivations as regards the occur-

rence of epileptiform events. The basic assumption is that the associations which reach the highest probability (χ^2) values represent those EEG derivations which share epileptogenic activity originating from the same brain source.

Summary

A method for the analysis of topographical relations of EEG epileptiform transients based on a statistical approach is described. The degree of time association of those transients recorded in pairs of derivations, or in 3 (triads), 4 (tetrads) or more derivations is estimated, using the χ^2 statistic. Pairs of derivations which are found to be significantly associated are tabulated. This information is also graphically displayed on a computer drawing of the head (10-20 system). The same is done for triads, tetrads or higher order associations. The number of phase reversals between epileptiform transients found in significantly associated pairs of derivations is also computed. The resulting spatial displays enable a visualization of the location of the dominant epileptogenic area and of the spread of epileptiform activity over the head.

Résumé

Visualisation topographique des événements épileptiformes, basée sur une approche statistique

Une méthode statistique pour l'analyse des relations topographiques des grapho-éléments épileptiformes de l'EEG est décrite. La valeur de l'association dans le temps entre des grapho-éléments enregistrés sur des pairs de montages ou sur 3 (triads), 4 (tétrads) ou plusieures montages est determinée employant la statistique du χ^2. Les pairs de montages où on trouve une association significative sont tabulés. Cette information est aussi présentée graphiquement au moyen d'un schéma de la tête dessiné par l'ordinateur (système 10-20). La même chose est faite pour les 'triads', les 'tétrads' et les autres associations. Le nombre des inversions de polarité trouvées entre des grapho-éléments sur des pairs de montages associés significativement est aussi calculé. Les cartes spatiales ainsi obtenues permettent une visualisation de la localisation de l'aire épileptogène dominante ainsi que la diffusion de l'activité épileptiforme sur la tête.

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