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Changes in Slow Bioelectrical Potentials of Epileptogenic Foci Produced by Tungstic Acid Gel

by

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INTRODUCTION

Despite the constant growth in pertinent literature, the results regarding the changes in slow bioelectrical potentials (such as steady potentials and tissue impedance) associated with seizure activities are rather conflicting (GOLDRING and O'LEARY 1951; VASTOLA 1955; VANASUPA et al. 1959; MORRELL 1960; O'LEARY and GOLDRING 1960, 1964; MANKE and WARD 1961; GLOOR et al. 1961; GUMNIT and TAKAHASHI 1965; AYALA and WALKER 1965; CASPERS et al. 1966). A steady potential (SP) in itself may be a composite of many factors such as potentials of glial, vascular, humoral, and metabolic as well as of neural origin. Tissue impedance is also a complex phenomenon which may be determined by various factors including fluid volume and electrolyte concentration. In this respect, it is essential to analyze slow potential changes at the different stages during the course of a developing epileptogenic process, because of the great possibility that at the stage when well developed paroxysms begin to appear recurrently, extraneuronal factors such as the accumulated metabolic change will take a primary part in the genesis of these slow bioelectrical potentials.

As to the propagation of seizure discharges, the role of the commissural pathway is not yet definitely established.

In our present study, simultaneous recordings of SP shift and impedance as well as electrocorticograms (ECoGs) were carried out at the original and at the secondary (projected) focus in an attempt to analyze the mechanisms for the development of epileptiform activity.

For this purpose, tungstic acid gel produced by BLUM's method (1960) was topically applied to the cortical surface of one hemisphere. As has been pointed out by BLACK et al. (1967), this method provided the advantage of producing a strictly localized epileptogenic lesion.

METHOD

Experiments were performed on 35 cats. The animals were prepared under ether

anesthesia, then experiments were carried out under local anesthesia, in preparation immobilized with gallamine triethiodide (Flaxidil) and in artificial respiration. The blood pressure was recorded from a femoral artery.

A piece of blotting paper 3-4 mm in diameter soaked in the tungstic acid gel was applied to the cortical surface (usually over the supra- or ectosylvian gyrus) of one hemisphere.

A counter-balanced Ag-AgCl pore electrode was used in recording the SP of the cortical surface in reference to another pore electrode placed on the periostium of the frontal skull. A D. C. coupled system was used for amplification (the band-pass was from D. C. to 100 cycles/sec with a sensitivity of 1 mV/cm).

SP recording in depth was carried out with an glass electrode, about $50\ \mu$ in tip diameter, and the position (depth) within the cortex was determined by reading the distance on the micrometric scale of a mechanically driven micromanipulator. Due to tip potentials and tissue demarcation potentials, the steady D. C. voltages could not be evaluated quantitatively, however, the D. C. transients associated with paroxysms were recorded quite faithfully.

ECoG recordings were obtained by placing silver ball electrode on the pial surface.

Electrical impedance was measured with fine silver acupuncture needles which were insulated except for about 1 mm at the tip. Pairs of such electrodes (interelectrode distance about 1.5-2.0 mm) were stereotactically inserted until only the bared portion of electrodes were within the cortex. Measurement was done mainly with a sine wave signal at a frequency of 10 kc/s. (at which polarization phenomena were quite insignificant) and, with electrode configuration used, the calculated current density did not exceed 10^{-12} amperes per micron of exposed electrode surface.

RESULTS

1. ECoG activity after topical application of tungstic acid gel

a. Prior to the development of a well organized rapid paroxysmal activity in the ECoG, atypical spike-and-wave complex (ASWC) appeared and lasted for several hours with a gradual increase in frequency and amplitude.

ASWCs were also observed at the contralateral hemisphere. Their amplitude was largest at the area where the tungstic acid gel had been topically applied and at the homotopic area contralateral to the original focus (projected focus) and at greater distances from these foci, the amplitude decreased proportionately. The ASWC from the projected area was always preceded (by 10-20 m sec) by that from the original area. Transection of the corpus callosum resulted in the disappearance of the contralateral (secondary) ASWC completely, although the ipsilateral ASWC remained unchanged (Fig. 1 and 2).

b. Well developed recurrent episodes of rapid paroxysmal discharges followed by electrical silence in the ECoG appeared 10-20 h. after the development of the ASWC. Occasionally, seizure discharges would often show different intensity over various cortical areas. Some areas exhibited more tonic ECoG discharges (referred to as "active" paroxysm) than others. Suddenly developing "active" paroxysms were also seen over the projected area and it was ushered in a sequence of the usual type of paroxysm. As shown in Fig. 3, more intense discharges of ECoG(s) and abrupt negative SP shift (S-SP)

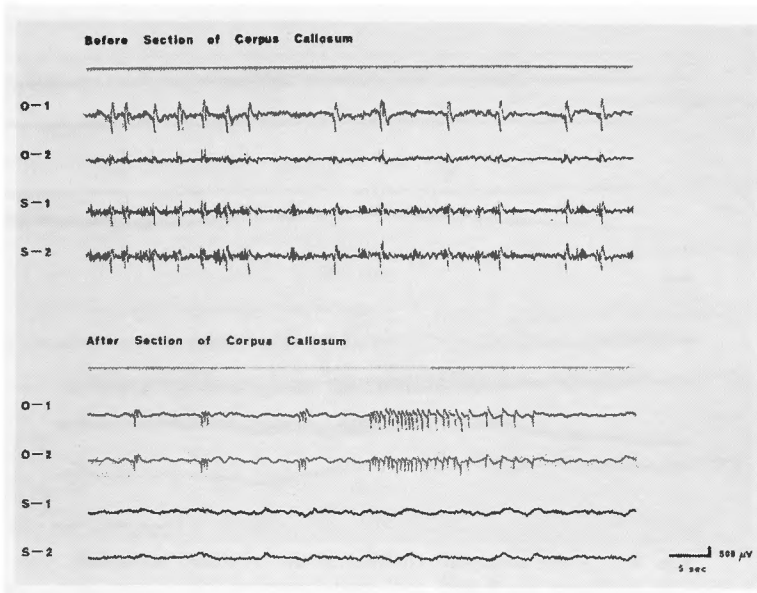


Fig. 1 Before and after section of the corpus callosum. O and S indicate original and secondary hemisphere respectively.

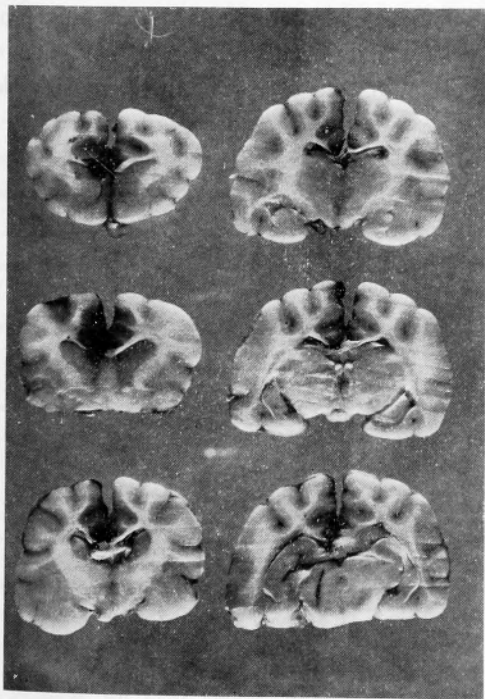


Fig. 2 Successive brain slices of the cat from Fig. 1. The corpus callosum is disconnected in all slices.

(“active” paroxysm) at the secondary focus appeared at the late stage of sustained paroxysm. “Active” paroxysm did not appear soon after the beginning of a usual paroxysm. Neither did it appear if the usual paroxysm lasted but a few seconds. However, in such situations, as some of the cortical areas were involved in “active” paroxysm, electrical silence in the ECoG were found to take place simultaneously throughout all the recorded areas.

2. SP and impedance changes associated with ASWC

On the side of the tungstic acid gel application, the ASWC was usually but not invariably associated with a negative SP shift amounting about 2-5 mV with respect to the indifferent electrode placed on the frontal skull. In the presence of recurrent ASWCs, the negative SP shift would tend to increase stepwise (see also GUMNIT and TAKAHASHI 1965). Conversely, the SP shift observed at the contralateral cortical surface was positive in almost all the cases (i.e. 32 out of 35

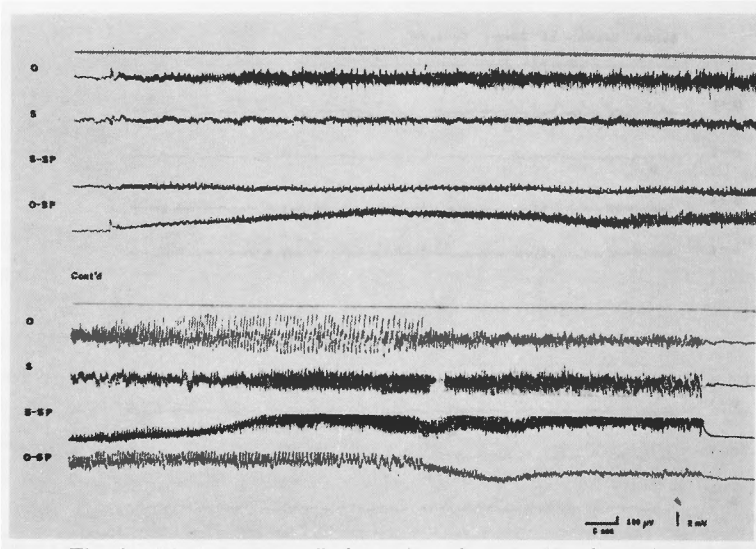


Fig. 3 "Active paroxysm" observed at the secondary hemisphere. ECoG (upper two traces) and steady potential (SP) (lower two traces) were recorded from an area where tungstic acid gel was applied (O) and from the contralateral homotopic area (S).

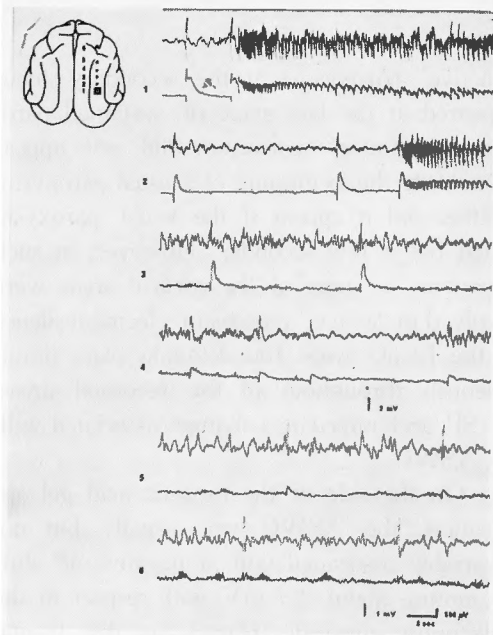


Fig. 4 SP shift associated with ASWC recorded from the original hemisphere. Both ASWC and SP shift are maximum around the produced focus (point 1) and with increasing distance from this point (point 2, 3 and 4), they become smaller. In this and the following Figs., an upward deflection of the D. C. base line indicates a negativity against the indifferent electrode, and vice versa.

studied). These changes in potential were maximum around the original and the projected focus, their amplitudes decreasing progressively a distance from such foci (Fig. 4 and 5). In contrast with these remarkable

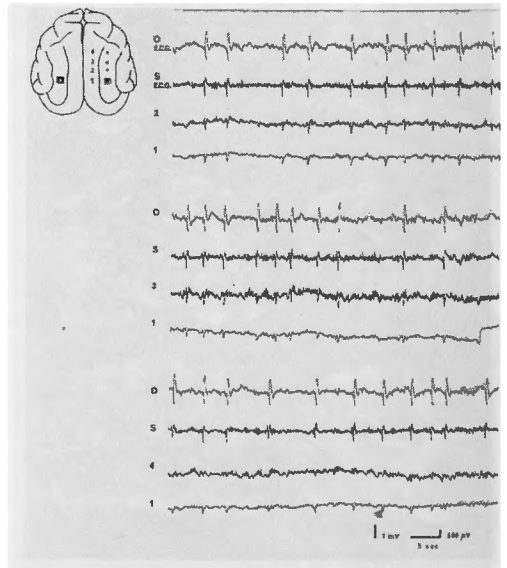


Fig. 5 SP shift recorded from the secondary hemisphere. Positive SP shift (downward deflection of the base line) is maximum around the secondary focus (point 1).

SP shifts, no definite impedance changes associated with the ASWC at the cortex of either hemisphere could be detected under our experimental conditions (Fig. 6).

3. Depth SP recording associated with ASWC

In order to analyze more precisely the electrical field gradient associated with the surface ASWC, SP recording was performed within the original and the projected foci by means of minute glass electrodes inserted at depth by steps of about 100μ .

Quite striking differences in respect to the distribution of the D. C. field were observed (Fig. 7). In the region of the tungstic acid gel lesion (original focus), the D. C. polarity of the cortical surface showed predominantly negative and no reversal of polarity was observed until the electrode reached a point of about 2.5-3.0 mm in

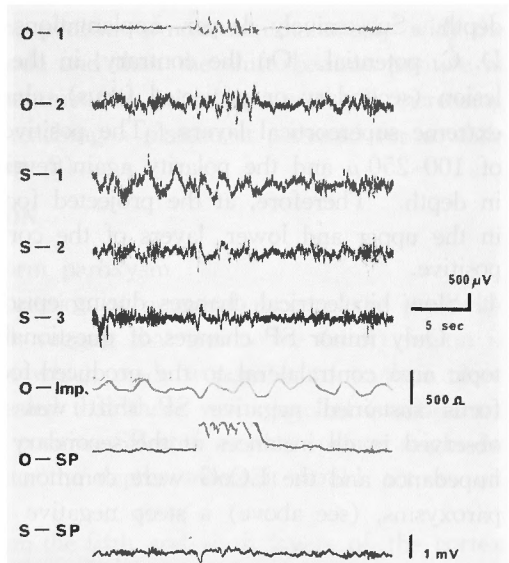


Fig. 6 Simultaneous recordings of ECoG, SP and impedance. Note that impedance (Imp.) recorded from an area close to the original focus shows no significant changes when ASWCs, accompanied by negative (at original) and positive (at secondary) SP shifts, are observed in ECoG.

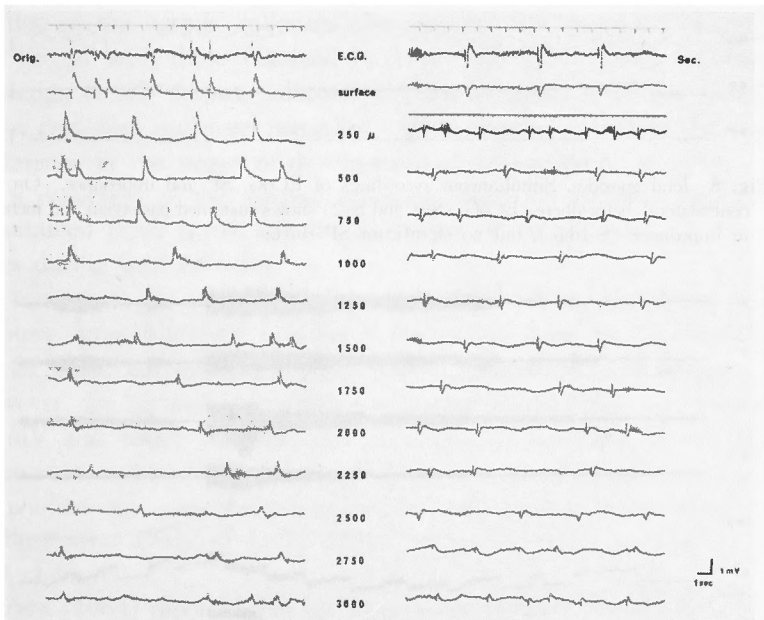


Fig. 7 SP changes associated with ASWC at different depths of the cortex (in μ). The top of each column shows ECoG. SP shifts associated with ASWC at the original area (left column) are negative throughout the depth of cortex. At the secondary area (right column), surface positive SP shifts revert to negative within the limit of 250μ and positive again at a point approximately 2500μ in depth. Negative up and positive down.

depth. Successively deeper implantations of the electrodes resulted in a positive shift in D. C. potential. On the contrary, in the homotopic region contralateral to the produced lesion (secondary or projected focus), changes in D. C. polarity were noticed within the extreme supercortical layers. The positive D. C. shift turned to negative within a depth of 100-250 μ and the polarity again reversed itself at a point approximately 2.5-3.0 mm in depth. Therefore, at the projected focus, an electrical field of the opposite sign arose in the upper and lower layers of the cortex: surface positive, middle negative, and deep positive.

4. Slow bioelectrical changes during episodes of rhythmically organized ictal paroxysm

Only minor SP changes of questionable significance could be observed at the homotopic area contralateral to the produced focus during such episodes although at the original focus sustained negative SP shift was noticed. In contrast, increase in impedance was observed in all instances at the secondary focus although some divergences between the impedance and the ECoG were common at onset (Fig. 8). During periods of "active" paroxysms, (see above) a steep negative steady potential shift and increase of impedance

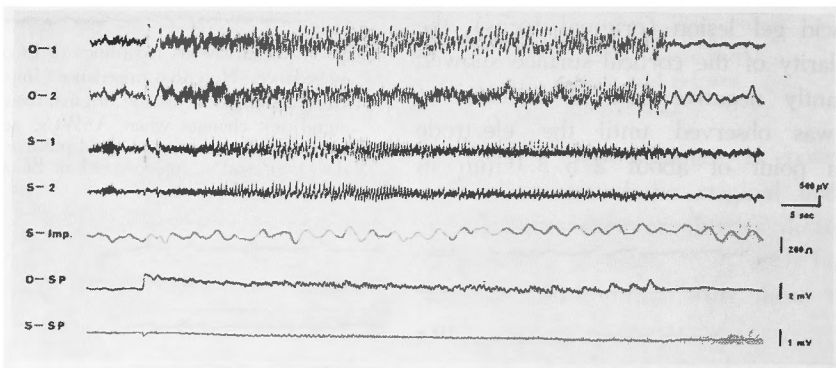


Fig. 8 Ictal episodes. Simultaneous recordings of ECoG, SP and impedance. On the contralateral hemisphere, ECoG (S-1 and S-2) shows sustained paroxysm and increase in impedance (S-Imp.), but no significant SP shift.

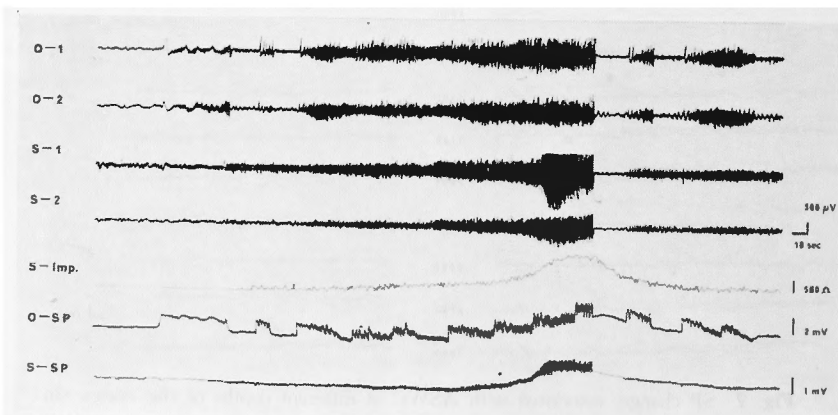


Fig. 9 "Active" paroxysmal ictal episodes observed on the contralateral hemisphere (S-1 and S-2). Steep negative SP shift (S-SP) and increase in impedance (S-Imp.) are noted. Note that the negative SP shift reaches its plateau almost simultaneously with the appearance of the clonic phase of the "active" paroxysmal episode, whereas impedance keeps increasing at the beginning of the clonic phase and upon reaching its plateau, it remains high for a while after the end of the ictal episode during the phase of ECoG quiescence.

were noted. The negative SP shift reached the plateau almost simultaneously with the appearance of the clonic phase of the ictal episode and then the shift became positive at the beginning of the post-ictal quiescence. In contrast, the impedance was still increasing at the beginning of clonic phase and then after reaching a plateau, it persisted for a while even during the period of ECoG depression (Fig. 9).

DISCUSSION

1. SP changes associated with isolated epileptiform paroxysm

On the assumption that SP shifts be the expression of neuronal process, the positivity observed at the contralateral hemisphere, would suggest that the active (sink) region is deep within the cortex and our depth recordings which made it possible to analyze more precisely the location of the current source, revealed that there was a level of (maximum) negativity at the depth of 0.5-1.0 mm. The positive SP shift at the surface might be explainable as the sequelae of a current flow into the depths where it would act as an electrical sink.

Most callosal fibers are thought to arise from the fifth and sixth layers of the cortex whereas their terminals are mainly distributed as free endings in the upper three layers (see TERZUOLO 1960). Considering the field gradient observed at the contralateral cortex, we postulate that the principal bombardment from the primary focus centers, via the commissural pathways, on the neuron populations situated in the superficial cortical layers, where the callosal axons terminally ramify. Disappearance of the ASWC in the projected side after section of the corpus callosum also supports this concept. In this respect, our results do not accord with those obtained by HOLUVÁŘ (1965) who demonstrated that a previous transection of the corpus callosum did not interfere with the development of a mirror focus in rats with unilateral penicillin. This discrepancy could be due, at least in part, to a difference in the stages of development of the epileptogenic focus. In fact, also in our study, a dissection of the corpus callosum could not prevent the contralateral appearance of sustained rapid paroxysms in later stage of experiment.

2. SP changes during ictal episodes

Previous reports on SP shift with sustained rapid seizure discharges are conflicting. Most investigators agree that such episodes at the cortical level are accompanied by a surface negative SP shift, but others have reported a positive SP shift associated with seizure activity. However, an "active" paroxysm was always accompanied by a negative SP shift of about 3-5 mV and which was preceded by a smaller positivity similar to that observed by VAN HARREVELD and SCHADÉ (1962) in Metrazol induced seizures in rabbits. As these authors have pointed out, such changes are suggestively akin to those observed in the case of spreading depression (SD) of LEÃO (1944).

3. Impedance changes

ALADJALOVA (1964) reported that an increase in cortical impedance occurs simultaneously with the onset of paroxysmal activity and the appearance of high frequency tonic discharges would coincide with the phase of increased resistance while the 'clonic' stage would coincide with its decreased. In our present experiment, no such definite correlations between the phase of ECoG paroxysm and shift in impedance were observed. Furthermore, no quantitative correlations could be found between SP shifts and impedance

changes. Isolated discharges are accompanied by definite SP shifts, but show no impedance changes. In contrast, during organized ictal episode, impedance recorded from the projected focus would increase by 10-15% without showing any definite swing in SP. Only with "active" paroxysmal ictal episode, shifts in these two potentials were recognized, although the course of the two events was not always parallel.

To evaluate our results, however, certain limitations in our experimental conditions should be pointed out: (1) exact temporal correlations between these slow potentials could not be made, because they were not recorded from exactly the same site. (2) our measuring technique did not distinguish between the two components of impedance, ohmic and capacitive, although it was postulated that in our conditions, the ohmic component should play a greater role in producing the impedance changes.

But even with these limitations in our mind, the lack of a direct link between these two bioelectrical potentials associated with paroxysm might be apparent.

On the basis of our results and the absence of more crucial experimental evidence, we suggest that SP might reflect the neuronal excitation process, whereas impedance is more probably related primarily to the metabolic process.

SUMMARY

In cats, (acute experiments under local anesthesia and artificial respiration), simultaneous SP, impedance and ECoG recordings were made at different stages of a local and contralateral developing epileptogenic focus produced by the topical application of tungstic acid gel to the exposed cortex of one hemisphere. An attempt was also made to assess the role of the commissural pathway in the projection of discharges and SP shifts.

1. The contralateral (mirror area) isolated paroxysmal discharges seemed to be conducted through the corpus callosum and the subcortical relay system did not play a major role in its propagation.

2. SP shifts appeared to reflect neuronal processes, whereas impedance was more likely related to the metabolic process secondary to the neuronal excitation.

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和文抄録

タンゲステン酸ゲルによる癲癇原性焦点における Slow Bioelectrical Potentials の変動

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森 和 夫

タンゲステン酸ゲルをネコの一侧視領野に塗布することにより、実験的癲癇原性焦点を作製し、焦点が成熟するに至るまでのいろいろの stage における皮質脳波、Steady Potential (SP) 及び Impedance の同時記録を行ない下記の結論を得た。

(1) 形成された焦点から、その反対側脳表への isolated paroxysmal discharge の伝播は、主として corpus

callosum を介し、subcortical relay system は主役を演ずるものではない。

(2) 皮質脳波における癲癇性放電の出現は、SP 及び Impedance の変動を伴うが、SP の変動は、neuronal process をかなり忠実に反映するに対し、Impedance の変動は、neuronal excitation による二次的な代謝過程とより密接な関連を有する。