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Interaction Between Transmitted Spike-and-wave  
Discharges and Evoked Visual Responses at  
the Secondary Focus Produced by  
Tungstic Acid Gel in Cats

by

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#### INTRODUCTION

This report concerns with a part of study of analyzing a function of so called "mirror focus".

Only a few details are known regarding the underlying mechanisms of the mirror focus, although in clinical and experimental situations, the transmitted paroxysmal discharges in EEG are not infrequently observed at the homologous area contralateral to the original focus. One of the problems of most significance is that of deciding the role of the commissural pathway upon the propagation of the discharges from the original focus to the homotopic contralateral one.

In our present study, interaction between spike-and-wave discharges transmitted from the original focus produced and visual cortical responses elicited by stimulating the optic radiations was observed in order to analyze the neuronal component of cortical elements primarily responsible for the organization of transmitted spike discharges.

For the purpose of making animals epileptogenic, tungstic acid gel produced by BLUM's method (1960)<sup>3)</sup> was topically applied to the left striate cortex in cats. As has been pointed out by BLACK et al. (1967)<sup>2)</sup>, this method provided the advantage of producing a strictly localized epileptogenic lesion.

#### METHOD

Experiments were performed on 16 cats. The animals were anesthetized with ether to allow canulation of the trachea and placed in a stereotaxic head holder, then paralyzed with gallamine triethiodide (Flaxedil) and artificially respired.

A piece of blotting paper 3-4 mm in diameter soaked in the tungstic acid gel was applied to the left striate cortex. As occasion demanded, 2-3 hours after the application of the drug when an atypical spike-and-wave complex (hereafter designated as ASWC) appeared in ECG, the drug soaked blotting paper was removed to prevent the establish-

ment of well matured sustained tonic clonic paroxysms.

Silver wire electrodes were placed on the dura over the homotopic area (the right striate cortex) contralateral to the produced focus to record the evoked potentials as well as elsewhere to record the electrocorticogram (ECG).

Electrodes, used for stimulation, consisted of a pair of enameled stainless steel wires which were stereotaxically inserted into the optic radiations of the right side. The exact location of these stimulating electrodes was ascertained histologically after the completion of a series of experiments.

Square monophasic pulses (30 to 100 microseconds in duration, and between 0.3 to 1.0 milliamperes) were given at a rate of one every 2 sec.

Evoked potentials were observed osciloscopically and they were stored on magnetic tape. Subsequently, wave (or component) 4 and 5 of visual cortical responses were measured, averaged and correlated graphically with other data and comparison was made to the mean amplitude obtained from the total experiments. Seizure activity was recorded with a conventional EEG machine.

The temporal relation between evoked responses, recorded oscillographically, and transmitted ASWC was established by utilizing one EEG channel as a stimulus maker.

On account of the remarkable variations of the amplitude of the evoked potentials even when no apparent changes in ECG could be observed, the comparison was made with the mean amplitude of a large number of responses. Mean amplitude of responses evoked during phases when ASWC was absent and during periods up to one second before the beginning of spike component of ASWC and two seconds after its termination were taken as the control.

## RESULTS

### 1. ECG activity after topical application of tungstic acid gel

Prior to the development of a well organized rapid paroxysmal activity in ECG, atypical spike-and-wave complex (ASWC) appeared at an area where tungstic acid gel had been applied topically and lasted for several hours with a gradual increase in frequency and amplitude ASWC was also observed at the homotopic area contralateral to the original focus (the projected secondary area). The ASWC from the projected secondary area was always preceded by that from the original area, and the temporal relation between the two was calculated as approximately 10-20 msec.

As has been reported in elsewhere, transection of the corpus callosum resulted in the disappearance of the projected secondary ASWC completely remaining ASWC from the original area unchanged (Fig. 1 and 2).

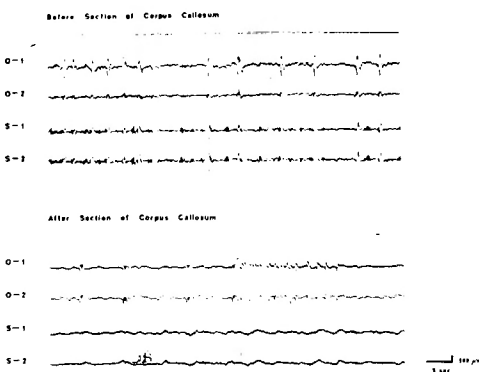
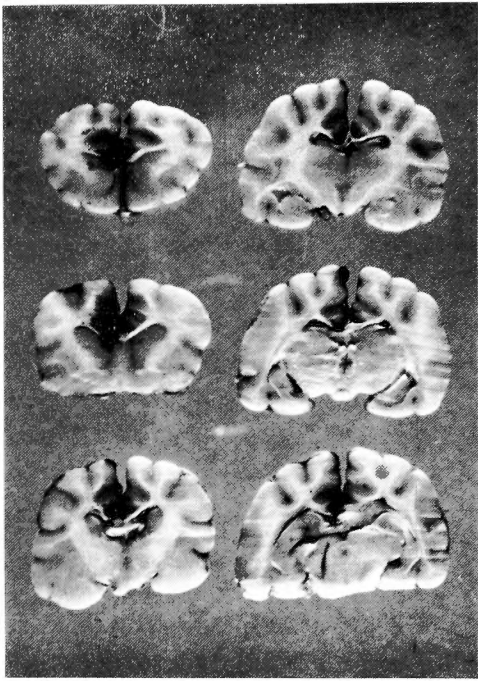
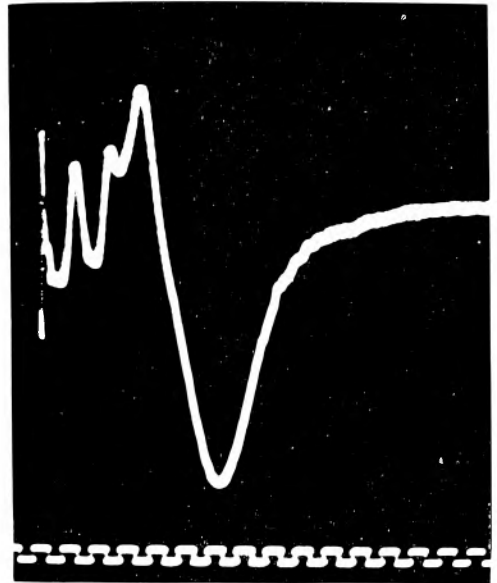


Fig. 1 Before and after section of the corpus callosum : O and S indicate original and secondary (projected) side respectively.



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



**Fig. 3** Primary visual cortical response elicited by the electrical stimulation of the optic radiations in cat. Positive up and negative down. Time marks 1 msec.

## 2. Interaction of ASWC and evoked potentials observed at the projected secondary focus

Fig. 3 shows a typical primary visual cortical response recorded from one of the animals in this series which consists of four successive surface positive spikes followed by a negative wave. The component 4th (C-4) of the response was measured from the point of its initiation to the positive peak and the component 5th (C 5) was measured from the base line to its negative peak (in this and the following Fig., the positive deflection of the evoked response always indicates upward shift from the base line and vice versa).

The results of interactions between the projected ASWCs and the primary visual responses (VRs) are shown in Fig. 4. In our experimental conditions, VR showed considerable variations in its components and the changes in amplitude were observed during various phases of the projected ASWC. However, characteristically, increase in amplitude of VR was observed without fail from immediately before (about 0.5 sec prior to) the appearance of ASWC. In Fig. 5, changes in the overall amplitude of VRs were plotted in relation to the time course of a projected discharge and zero time is indicated by the beginning of the initial negative phase of spike in ASWC.

Fig. 5 and 6 show changes in the mean amplitude of C-4 and C 5 recorded before, during and after the appearance of ASWC respectively. It is indicated that the mean amplitude of both C-4 and C-5 recorded immediately prior to the onset of ASWC was

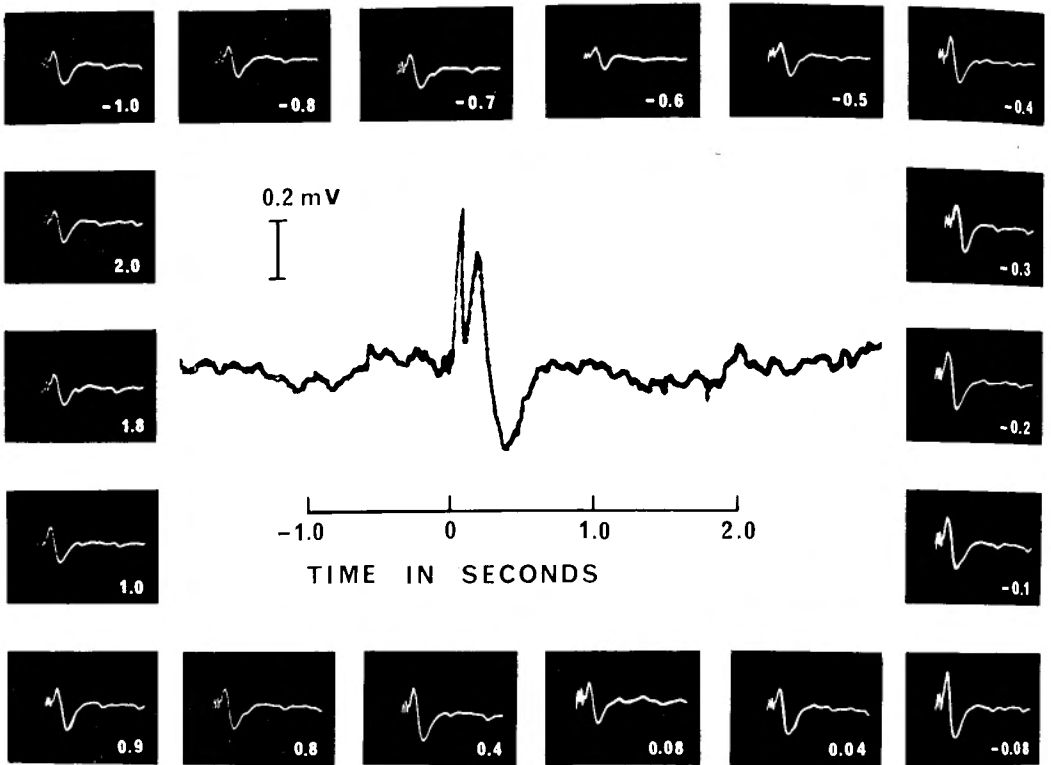
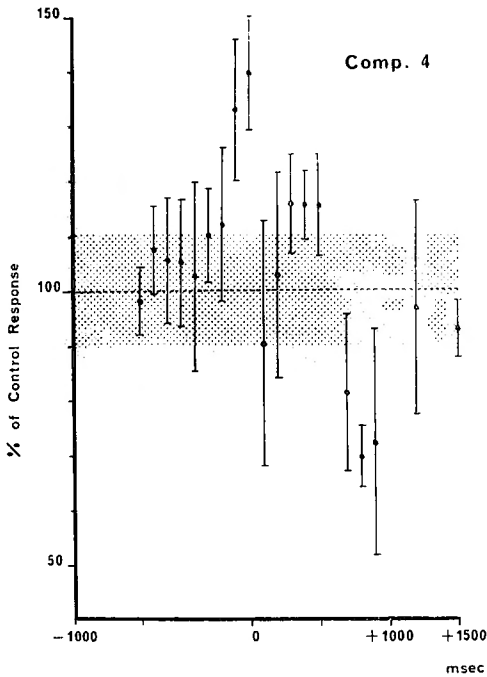


Fig. 4 Alterations in visual responses recorded at the secondary focus occurring during different phases of the projected ASWC (in-set). Augmentation of potentials up to approximately 0.5 sec before the onset of ASWC was observed. Numbers indicate time at which potentials were evoked (zero time is representing an onset of the initial rising phase of spike component of ASWC) and minus indicates that potential was evoked prior to the onset of ASWC.

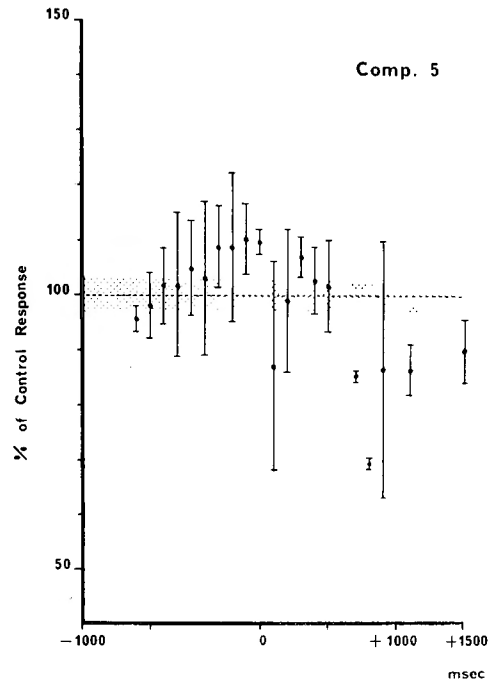
significantly larger as compared with that recorded during the control periods. Especially the augmentation of potentials was much more prominent in C-4, where it was found that the mean amplitude was approximately 33 % larger than that noted during periods of control (Fig. 5), whereas C 5 remained to show about 10 % increase of the mean amplitude (Fig. 6).

#### DISCUSSION

Visual evoked responses have been widely used in the study of factors modulating or changing in responsiveness in specific sensory pathways. However, studies of a number of investigators have indicated that only C-1, the first positive spike of the primary visual cortical response, represents presynaptic radiation activity and there remains some questions as to whether C-2 and C 3 are reflections of presynaptic or postsynaptic events. Although many authors agree that both C-2 and C 3 reflect postsynaptic cortical activity, several investigators have presented evidence that C-2 and C-3 also represent activity in presynaptic radiation fibers (Chang and Kaada 1950<sup>61</sup> ; Chang 1952<sup>65</sup> ; Bremer and Stoupe<sup>63</sup>).



**Fig. 5** Amplitude changes in C-4 of visual responses evoked prior to, during and after the onset of ASWC. Responses obtained during phases when ASWC was absent were taken as the control and the mean value of responses obtained during control periods was expressed as 100. Then, average amplitudes for responses recorded during various phases of ASWC were calculated in terms of percentage of the control. On ordinate are plotted means and standard deviations to control response and dotted area represents standard deviation of the control responses.



**Fig. 6** Amplitude changes in C-5 of visual responses. Note that mean amplitude of C-5 increases prior to the onset of ASWC, however, this augmentation is less remarkable as compared with that observed at C-4 (Fig. 5).

In contrast, almost all authors agree the Bishop and Clare' identities (1952)<sup>11</sup> that C-4 and C-5 represent the postsynaptic cortical activity of different cortical layers. (C-4: activation of groups of cells in middle cortical layers; C-5: depolarization of superficial apical dendrites) and this is the reason why we chose to use C-4 and C-5 as indicators.

On the other hand, fairly extensive studies have been made regarding the changes in a sensory evoked potential at a cortical epileptogenic focus (primary or original focus) produced by the topical application of various convulsant drugs and many authors have observed the augmentation of negative phase of the evoked responses. This negative potentiation indicates that the action of epileptogenic substances is first exerted upon the superficial cortical structures (probably the dendritic layers) which interfere in the organization of the negative phase of the primary sensory evoked responses. However, scanty data are available regarding interactions between the evoked responses and the projected

seizure discharges transmitted from the original focus (Smith and Purpura, 1960<sup>11</sup> ; Holubar, 1966<sup>7</sup> ; Holubar and Fischer, 1967<sup>8</sup>) and we know of no previous observation performed at the projected focus which was produced secondarily by the topical application of tungstic acid gel to the contralateral homotopic area. In our present study, an attempt was made to analyze the effect of projected discharges (ASWC) upon the amplitude of C-4 and C-5 of evoked visual cortical responses and it was observed that augmentation of C-4 was much prominent as compared with that of C-5 when they were evoked immediately prior to the onset of ASWC.

This result strongly suggests that, at the projected secondary focus, the neuronal aggregate situated within the middle layers of the cortex are activated primarily by the volleys coming from the original focus and in contrast to the results obtained at the primary focus, activation of the superficial dendritic layer is only secondary.

There are many anatomical and physiological grounds for believing that most callosal fibers arise from the fifth and sixth layers, whereas the terminals of these fibers are mainly distributed as free endings in the upper three layers. (Terzuolo et al. 1960<sup>12</sup>). Considering the changes in the evoked visual cortical responses obtained in our study and basing upon the other data reported in elsewhere (Mcrici et al. 1957<sup>10</sup> ; Mori et al. 1958<sup>9</sup>), we postulate that as far as ASWC established by the topical application of tungstic acid gel is concerned, the principal bombardment from the produced focus (primary focus) centers via commissural pathways on the neuron populations situated in the middle layers where callosal axons ramify terminally and subcortical relay system does not play a major role in the propagation of ASWC. Disappearance of ASWC in the projected side after section of the corpus callosum (Fig. 1 and 2) also supports this concept.

#### SUMMARY

Interactions between the projected secondary discharges and the visual cortical response were observed in unanesthetized cats in an attempt to analyze the underlying mechanisms of the so called "mirror focus".

Augmentation in amplitude of both C-4 and C-5 was observed when the visual cortical responses were evoked up to about 0.5 sec prior to the onset of transmitted seizure discharge (ASWC). However, augmentation of C-4 was more prominent as compared with that of C-5 indicating that in contrast to the results obtained at the original focus, the neuronal aggregate situated within the middle layers of the cortex are activated primarily by the coming volleys from the original focus.

ASWC was transmitted via the commissural pathways and the subcortical relay system does not play a principal role in the propagation of ASWC.

#### ACKNOWLEDGEMENT

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#### REFERENCES

- 1) Bishop, G. H. and Clare, M. H. : Sites of origin of electric potentials in striate cortex. *J. Neurophysiol.* 15 : 201-220, 1952.

- 2) Black, R.G., Abraham, J. and Ward, A.A. Jr. : The preparation of tungstic acid gel and its use in the production of experimental epilepsy. *Epilepsia*, **8** : 58-63, 1967.
- 3) Blum, B. and Liban, E. : Experimental basotemporal epilepsy in the cat. Discrete epileptogenic lesions produced in the hippocampus or amygdaloid by tungstic acid gel. *Neurology*, **10** : 546-554, 1960.
- 4) Bremer, F. and Stoupe, N. : Interpretation de la réponse de laire visuelle a une volée d'influx sensoriels. *Arch. int. physiol.*, **64** : 234-250, 1956.
- 5) Chang, H.T. : Cortical response to stimulation of lateral geniculate body and the potentiation there of by continuous illumination of the retina. *J. Neurophysiol.*, **15** : 5-26, 1952.
- 6) Chang, H. T. and Kaada, B. : An analysis of primary response of visual cortex to optic nerve stimulation in cats. *J. Neurophysiol.*, **13** : 305-318, 1950.
- 7) Holubar, J. : Different mode of activation of the penicillin and mirror cortical foci in rats. In *Comparative and Cellular Pathology of Epilepsy*, edited by Z. Servit, Amsterdam, 204-213, 1966.
- 8) Holubar, J. and Fischer, J. : Electrophysiological properties of the epileptogenic cortical foci produced by a new cobaltgelatine method in rats. An attempt to correlate the electrophysiological, histological and histochemical data. *Physiol. Bohemoslov.*, **16** : 278-284, 1967.
- 9) Mori, K., Kako, M. and Handa, H. : Changes in slow bioelectrical potentials of epileptogenic foci produced by tungstic acid gel. *Electroenceph. Clin. Neurophysiol.*, In press.
- 10) Mori, K., Kako, M., Iwayama, K. and Yonekawa, Y. : A case with the "projected" EEG disturbances due to minute unilateral epileptic focus. *Arch. Jap. chir.*, **36** : 874-880, 1967.
- 11) Smith, G. and Purpura, D.P. : Electrophysiological studies on epileptogenic lesions of cat cortex. *Electroenceph. clin. Neurophysiol.*, **12** : 59-82, 1960.
- 12) Terzuolo, L.A. and Adey, W.R. : Sensorimotor cortical activities. In *Handbook of Physiology*, 817 p. Am Physiol. Soc., Washington, D.C., 1960.

## 和文抄録

# Tungstic acid gel による癲癇二次性 (鏡) 焦点部における視性誘発電位の変動

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癲癇の鏡焦点の機能の分析に関する研究の一環として、二次性焦点 (鏡焦点) の部において痙攣波による視性誘発電位の振幅の変化、及び両者の時間的相関について検討を加えた。即ち Blum (1960) の方法に準じて tungstic acid gel を作製し、これを無麻酔猫の左側視領野皮質上におき眼局性癲癇原性焦点を形成、次いで反対側大脳半球同名部 (右視領野) への痙攣波の投射による所謂鏡焦点を形成、一方、右側視放線の電気刺激による皮質誘発電位をこの鏡焦点部で記録、atypical spike and wave complex (ASWC) が原焦点より二次性焦点に伝播した時、視性誘発電位の第四及び第五成分が、いかに修飾されるかを分析した。

誘発電位が ASWC の出現に先行 (ほぼ 500 msec まで) する時、その第四及び第五成分の振幅の増大をみるとめるが、特に第四成分の振幅の augmentation が著明であり、control の振幅のほぼ 1.3 倍に達するに対し、第

五成分の振幅の増大はそれほど著明ではない。この事実は原焦点からの volley が二次性焦点部の皮質中層の細胞集団を先ず発火させる事を示唆するものである。

二次性 (鏡) 焦点における痙攣波と誘発電位の相関に関する研究は非常に少なく、今回報告の如き tungstic acid gel による二次性焦点での観察は、著者等の知る限りにおいて未だなされていらない。又従来、各種薬剤貼布、局所冷却等により作製された癲癇の原焦点部では、諸家により誘発電位の陰性相の強調が主な変化として認められているが二次性焦点部では上記の如く視性誘発電位の第四陽性成分の増大が最も著明である。

我々の今回の成績はまた、既に他紙に発表した諸所見と共に、tungstic acid gel により作製した原焦点から二次性焦点への ASWC の伝播は、皮質下 relay nucleus を経由せず、直接 commissural pathways が主役を演ずるとする我々の説を更に支持するものである。