ELECTROENCEPHALOGRAPHIC STUDIES IN DIFFUSE ENCEPHALOPATHIES

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It is a well-known fact that electroencephalograms of patients suffering from diffuse encephalopathies of inflammatory, degenerative, or metabolic origin have many features in common. The recordings are diffusely abnormal and most frequently show diffuse disturbance of cerebral background activity, diffuse slow waves, and bilaterally synchronous paroxysmal discharges.

This study was prompted by our impression that these diffuse cerebral pathological processes leading to diffuse neuronal disease at the cortical level were often associated with bilaterally synchronous paroxysmal discharges and we therefore asked whether a mechanism of origin of diffuse bilateral synchrony may not depend upon the presence of diffuse neuronal disease or widespread neuronal loss affecting the cortex of both hemispheres without necessarily involving any subcortical mechanisms. It was mainly with the purpose of verifying this impression that the present study was undertaken. The initial working hypothesis of the study was that the diffuse bilateral synchrony seen in the E.E.G. was probably produced by diffuse neuronal disease involving cortical and subcortical grey matter and that perhaps in some cases diffuse cortical involvement alone was sufficient to produce this bilateral synchrony. In contrast to this, diffuse involvement of the white matter would not be expected to lead to this type of disturbance.

In order to test these hypothetical views, a number of cases with diffuse pathological lesions involving cortical and subcortical matter as well as white matter of both hemispheres, were studied. Since the purpose was to try to correlate certain electrographic phenomena, especially bilateral synchrony, with the involvement of either cortical and subcortical grey matter, the material was divided into four groups

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(Table 1). In order to classify the observations in this manner, only complete postmortem examinations of the brain could be used.

TABLE 1
DIFFUSE ENCEPHALOPATHIES
CLASSIFICATION OF CASES

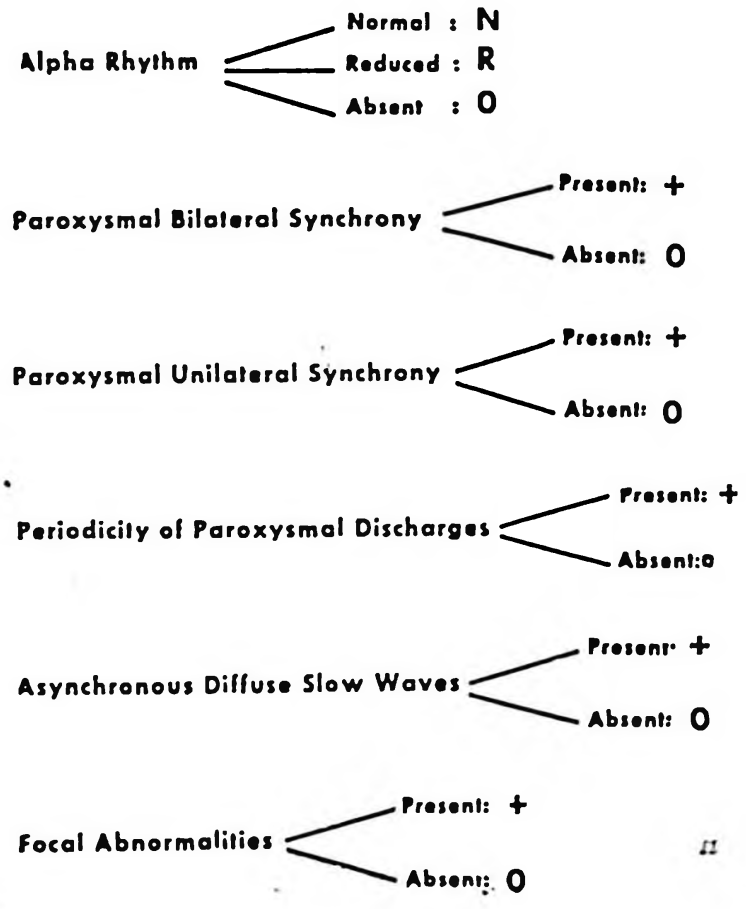
GROUP I	**Diffuse cortical grey matter disease**	**8 Patients**
GROUP II	**Diffuse cortical and subcortical grey matter disease**	**10 Patients**
GROUP III	**Diffuse white matter disease**	**7 Patients**
GROUP IV	**Diffuse cebebral disease with predominant white matter pathology and some cortical and subcortical grey matter involvement**	**7 Patients**

Encephalographic features analyzed in these records are summarized in Table 2.

TABLE 2

DIFFUSE ENCEPHALOPATHIES

EEG SIGNS ANALYZED



Group I was composed of patients with diffuse cortical grey matter disease. There were eight patients in this group and their specific diseases are given in Table 3. The electroencephalographic abnormalities of these patients are tabulated in Table 4.

TABLE 3

DIFFUSE ENCEPHALOPATHIES

GROUP I

Diffuse Cortical Grey Matter Disease
8 Patients

Jakob-Kreutzfeldt disease	**2**
Acute necrotizing encephalitis	**2**
Diffuse arteriosclerotic aortical atrophy	**1**
Alzheimer's disease	**1**
Pick's disease	**1**
Unknown disease process with diffuse involvement of cortical grey matter	**1**

TABLE 4

DIFFUSE ENCEPHALOPATHIES

GROUP I Diffuse Cortical Grey Matter Disease

CASE	PATHOLOGY	ALPHA	PAROXYSMAL BILATERAL SYNCHRONY	PAROXYSMAL UNILATERAL SYNCHRONY	PERIODICITY	DIFFUSE ASYNCHRONOUS SLOW WAVES	FOCAL ABNORMALITIES
E.S.	J.K.D. (parieto-occ. cort. spared)	N (low volt.)	0	0	0	0	0
E.T.	J.K.D.	0	+ (Frontal only)	+	+	0	0
W.B.	A.N.E.	0	0	0	+ (focal)	+	+
L.S.	A.N.E.	0 (unilat.)	0	+	+ (unilat. diff.)	+	0
C.W.	D.A.C.A.	0	+ (intermittent)	+	+	0	0
L.McD.	Alz.D.	0	0	0	0	0	0
M.C.	P.D. (parieto-occ. cort. spared)	N	0	0	0	0	0
J.R.	U.D.P.	0	+ (intermittent)	+	0	+ (not prominent)	0
TOTAL : 8		6:0 (unilat. in one) 2:N	5:0 3:+ (intermittent or frontal only)	4:+ 4:0	4:+ 4:0	5:0 3:+ (not prominent in one)	7:0 1:+

Alpha activity was normal in only two cases. In both of these, the parieto-occipital cortex was relatively uninvolved in the pathological process. Bilateral paroxysmal discharges were infrequent. They were completely absent in five cases, intermittenty present in two cases, and localized to the frontal region in one case only. Some degree of synchronization, however, was apparent in four of the eight patients in this group, but the synchrony was confined to one hemisphere. Periodicity of discharges was present in four of the eight patients. Diffuse asynchronous slow waves were not a prominent feature in this group. They were seen in only three patients, in one of whom it was a rather minor abnormality. The incidence of focal abnormalities was not remarkable, there being only one patient with this abnormality. Examples of the electroencephalograms from which these observations were made are seen in Figures 1 and 2.

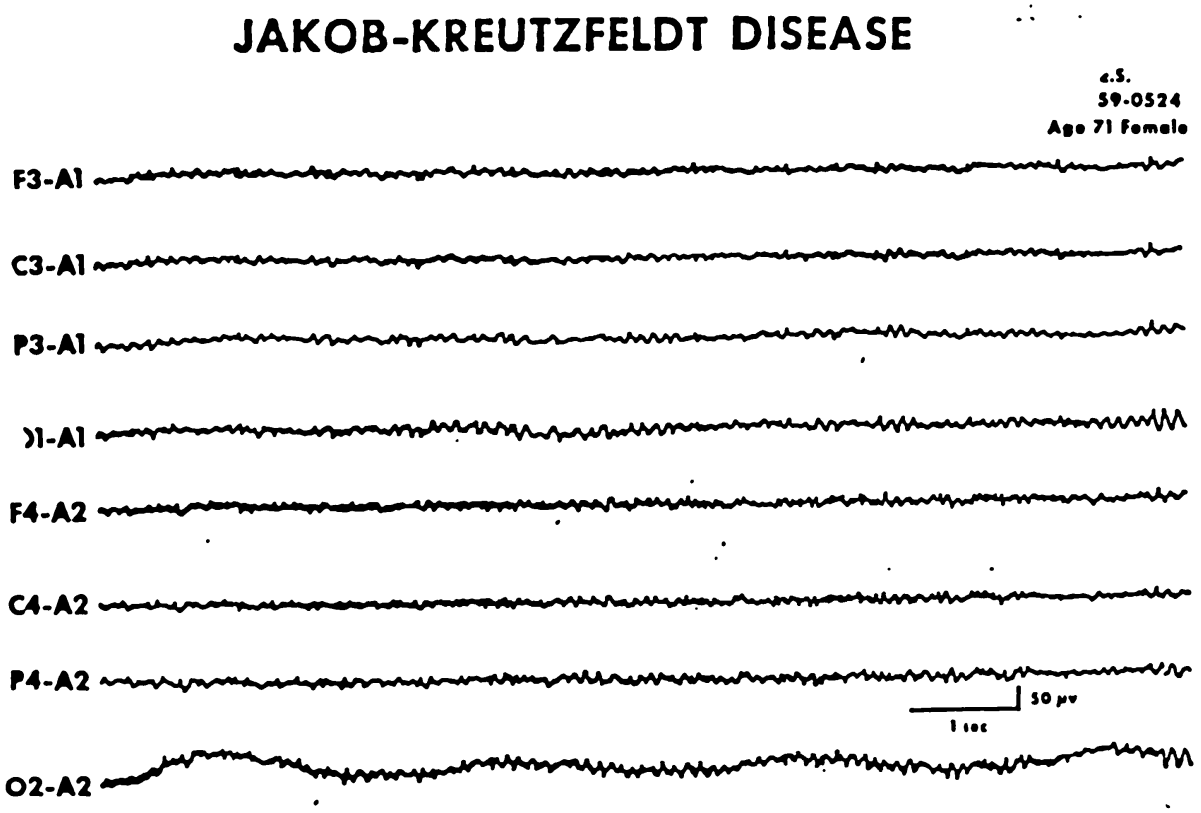


Figure 1.

Group II was composed of patients who had diffuse cortical and subcortical grey matter disease (Table 5). Electroencephalographic features of the ten patients in this group are tabulated in Table 6.

None of these patients had normal alpha activity, although a reduced alpha rhythm was found in two of these patients. The most

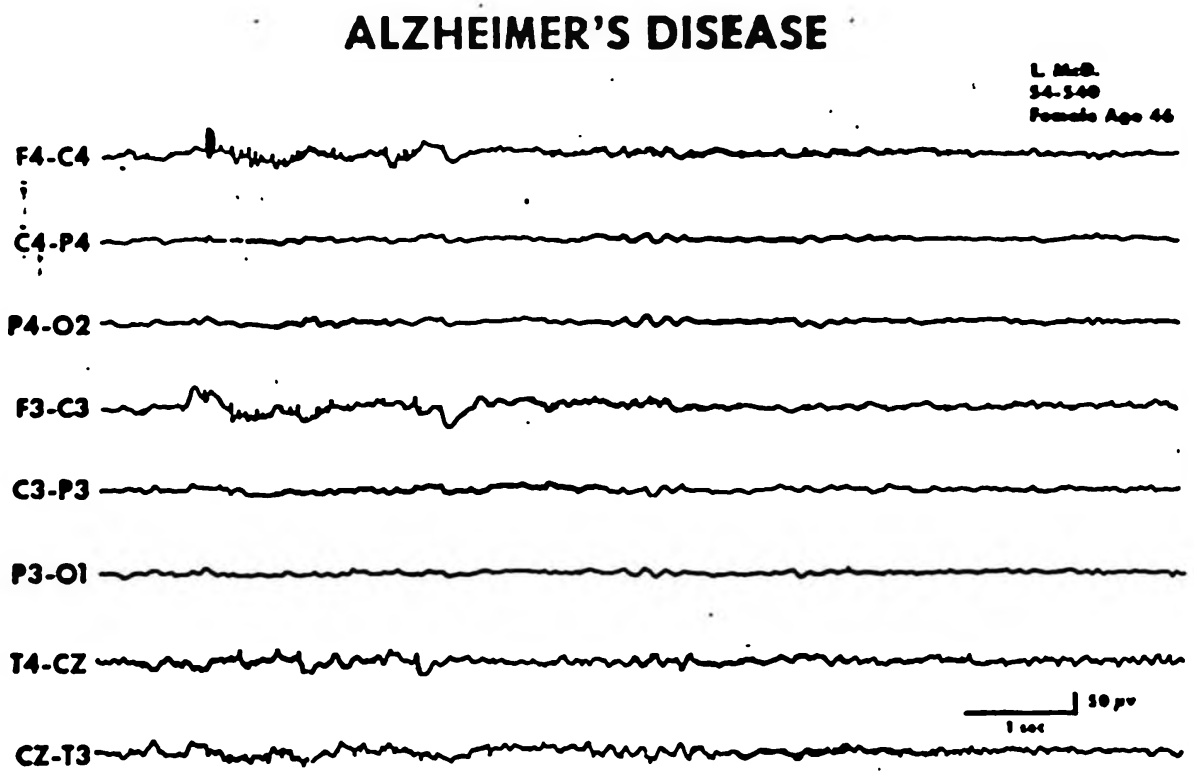


Figure 2.

TABLE 5

DIFFUSE ENCEPHALOPATHIES

GROUP II

Diffuse Cortical and Subcortical Grey Matter Disease

10 Patients

Subacute inclusion body encephalitis	3
Lipid storage diseases	3
Heidenhain's disease	2
Wilson's disease	1
Glycogen storage disease	1

TABLE 6

DIFFUSE ENCEPHALOPATHIES

GROUP II Diffuse Cortical and Subcortical Grey Matter Disease

CASE	PATHOLOGY	ALPHA	PAROXYSMAL BILATERAL SYNCHRONY	PAROXYSMAL UNILATERAL SYNCHRONY	PERIODICITY	DIFFUSE ASYNCHRONOUS SLOW WAVES	FOCAL ABNORMALITIES
Y.P.	S.I.B.E.	R	+	0	0	0	0
J.D.	S.I.B.E.	0	+	0	+	0	0
R.D.	S.I.B.E.	0	+	0	+	+	0
M.v.R.	H.D.	0	+	0	+	0	0
H.P.	H.D.	R	+ (intermittent)	+	0	+	0
G.C.	W.D.	0	+	0	0	+	0
D.H.	L.S.D.	0	+	0	0	0	0
Y.S.	L.S.D.	0	+ (post. head reg.)	0	0	+ (minimal)	0
D.L.*	L.S.D.	— (young infant)	+	0	0	0	0
J.C.	G.S.D.	— (young infant)	+ (intermittent)	0	0	+	0
TOTAL: 10		6:0 2:R (0:N)	10: + (2 intermittent) (0:0)	9:0 1: +	7:0 3: +	5:0 5: + (1 minimal)	10 : 0

* Max. Path. subcortical grey matter

prominent feature of this group, seen in all the patients, was paroxysmal bilaterally synchronous discharges which in eight of these ten patients were continuously present, and in two were intermittent. Paroxysmal unilateral synchrony was present in one patient in whom bilateral synchrony was intermittent. Periodicity of discharges was seen in three of ten patients, but was most remarkable in one patient with Heidenhain's disease (Figure 3). Diffuse asynchronous slow waves were present in five patients of this group. No focal abnormalities were seen.

The main difference between the second group (combined cortical and subcortical grey matter disease) and the first group (diffuse cortical disease) is the invariable occurrence of paroxysms of bilateral synchrony in the former and the relatively infrequent occurrence of this abnormality in the latter. Sample tracings of patients in this second group are seen in Figures 3, 4, 5, and 6.

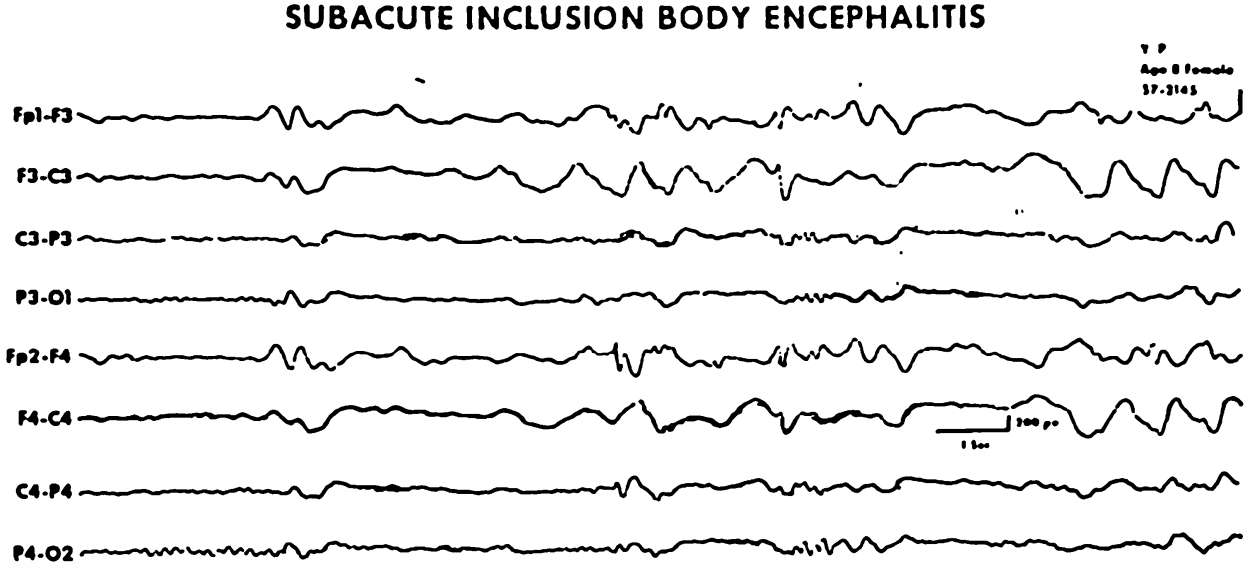


Figure 3.

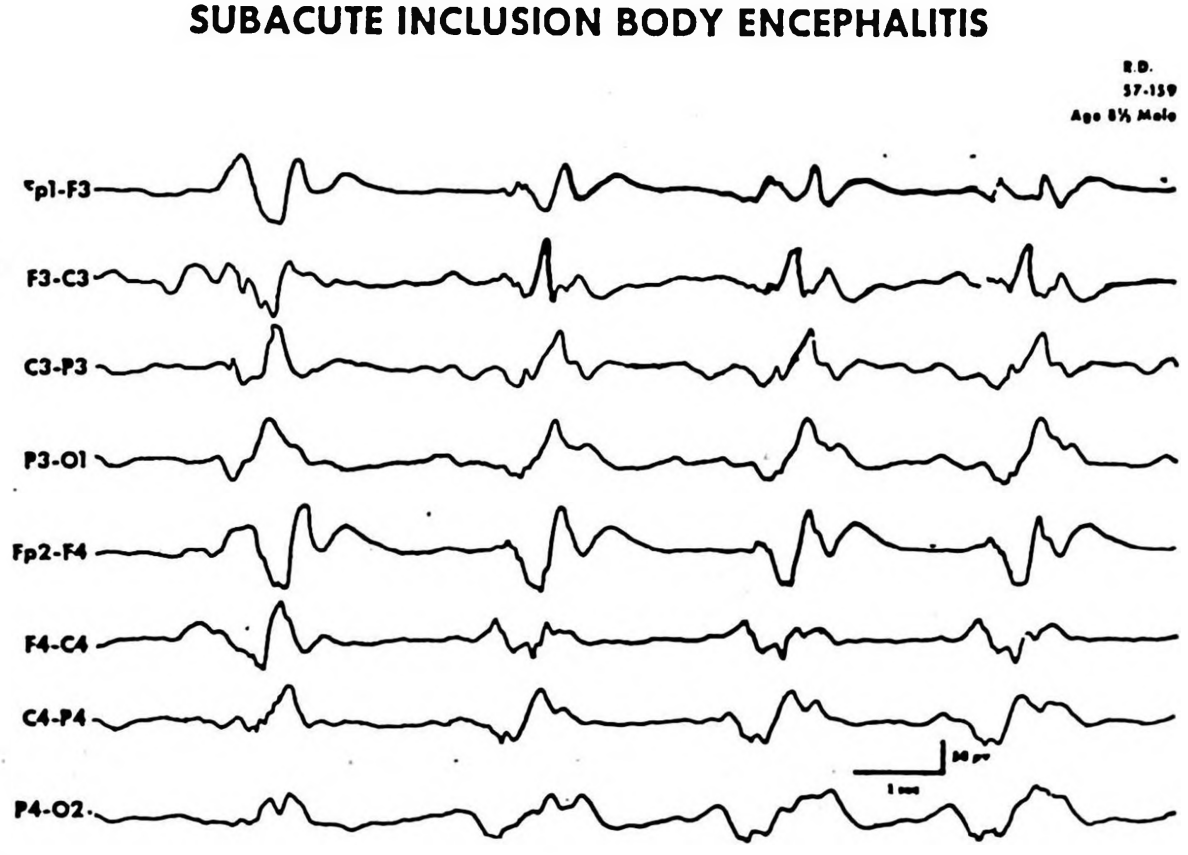


Figure 4.

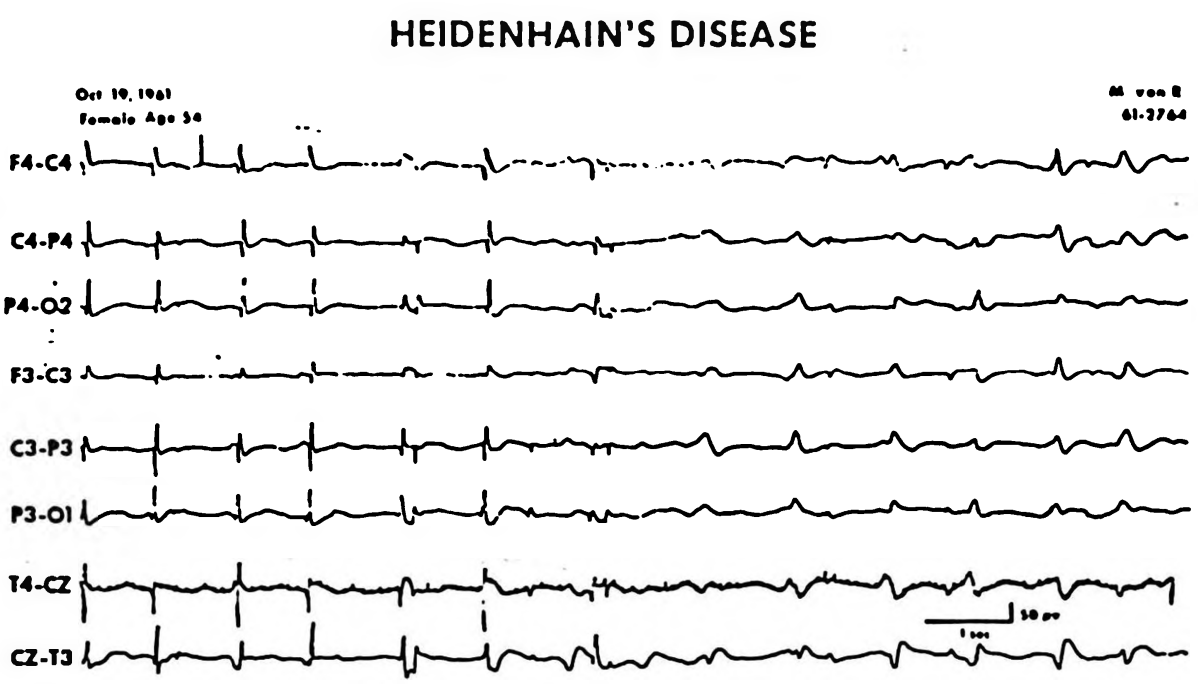


Figure 5.

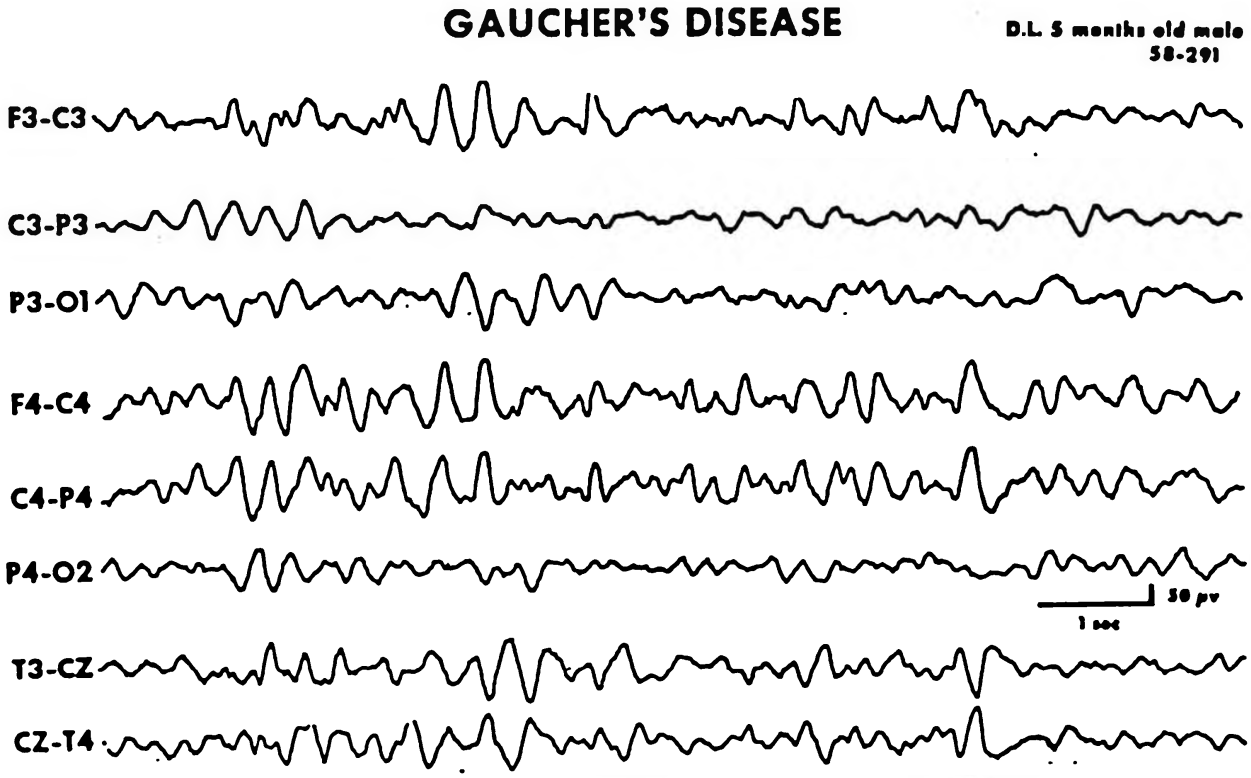


Figure 6.

Group III is composed of patients with white matter disease (Table 7). Electroencephalographic features of this group are tabulated in Table 8.

Alpha rhythm was abnormal in all cases, but still present in the four patients with multiple sclerosis. No patients with diffuse cerebral sclerosis either of the Schilder or Scholz type had alpha rhythm.

TABLE 7
DIFFUSE ENCEPHALOPATHIES
GROUP III

Diffuse White Matter Disease
7 Patients

Multiple scelerosis (with widespread involvement of cerebral white matter)	4
Diffuse cerebral sclerosis (Schilder Type)	2
Diffuse cerebral sclerosis (Scholz Type)	1

TABLE 8

DIFFUSE ENCEPHALOPATHIES

GROUP III Diffuse White Matter Disease

CASE	PATHOLOGY	ALPHA	PAROXYSMAL BILATERAL SYNCHRONY	PAROXYSMAL UNILATERAL SYNCHRONY	PERIODICITY	DIFFUSE ASYNCHRONOUS SLOW WAVES	FOCAL ABNORMALITIES
S.P.	M.S	R	0	0	0	+	+
V.C.	M.S.	R	0	0	0	+	0
W.V.	M.S.	R	0	0	0	+	0
R.B.	M.S.	R (unilateral)	0	0	0	+ (unilateral)	0
J.M.	D.C.S. (Schi.)	0	0	0	0	+ (max. post.)	0
D.B.	D.C.S. (Schi.)	0	0	0	0	+ (max. post.)	0
A.P.	D.C.S. (Scho.)	0	0	0	0	+ (max. post.)	0
TOTAL: 7		4:R (unilat. in one) 3:0	7:0 (0:+)	7:0 (0:+)	7:0 (0:+)	7:+ (3 max. post.) (1 unilat.)	6:0 1+

It should be mentioned that the pathological involvement of the white matter in these cases was maximal in the posterior part of the cerebral hemisphere. None of these patients showed either bilateral or unilateral synchrony. Neither was there periodicity of discharge. On the other hand, diffuse synchronous slow waves were a constant feature in all these patients. In one case of multiple sclerosis they were present only intermittently. The incidence of focal abnormality was unremarkable, being one out of seven.

The main difference between this group and the two previous ones is the complete absence of synchronization, bilaterally or unilaterally, of paroxysmal discharges. It also seems that the presence of periodic discharges is dependent on either cortical or subcortical grey

matter involvement and does not occur in pure white matter disease. In contrast to this, diffuse asynchronous slow waves seem to be a main feature of the electroencephalograms of diffuse involvement of white matter. Examples of tracings from patients in this group are seen in Figures 7, 8, and 9.

MULTIPLE SCLEROSIS

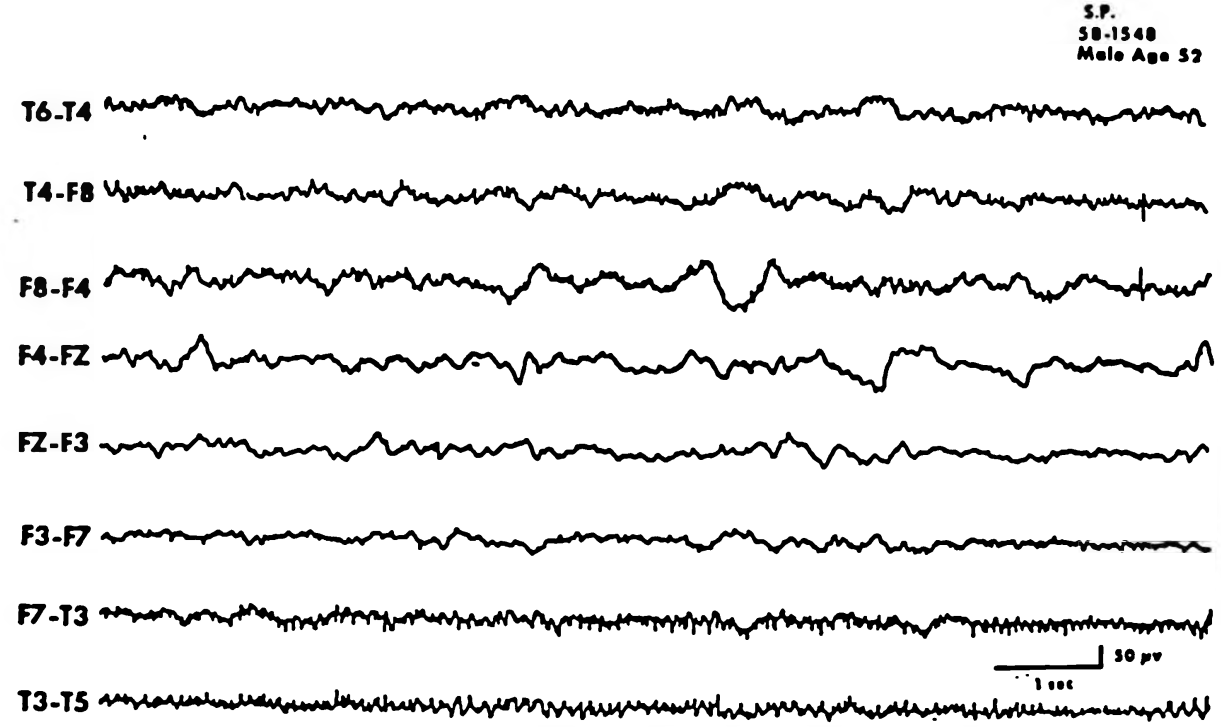


Figure 7.

SCHILDER'S DISEASE

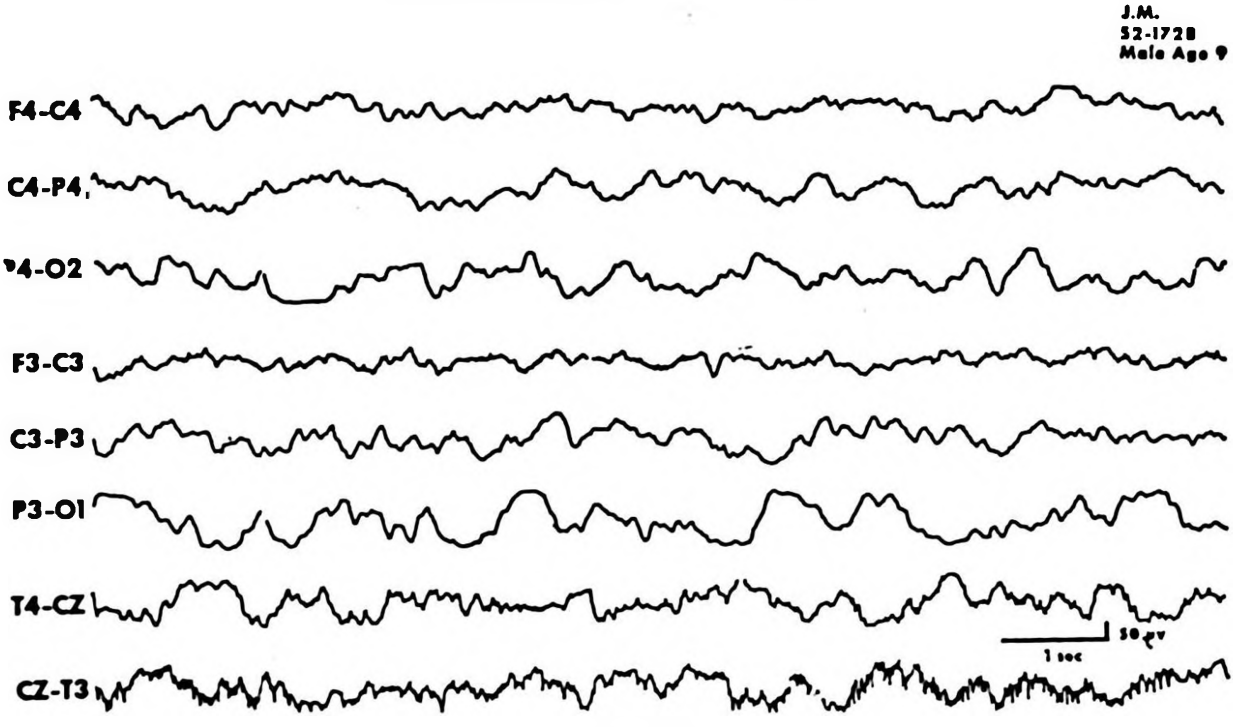


Figure 8.

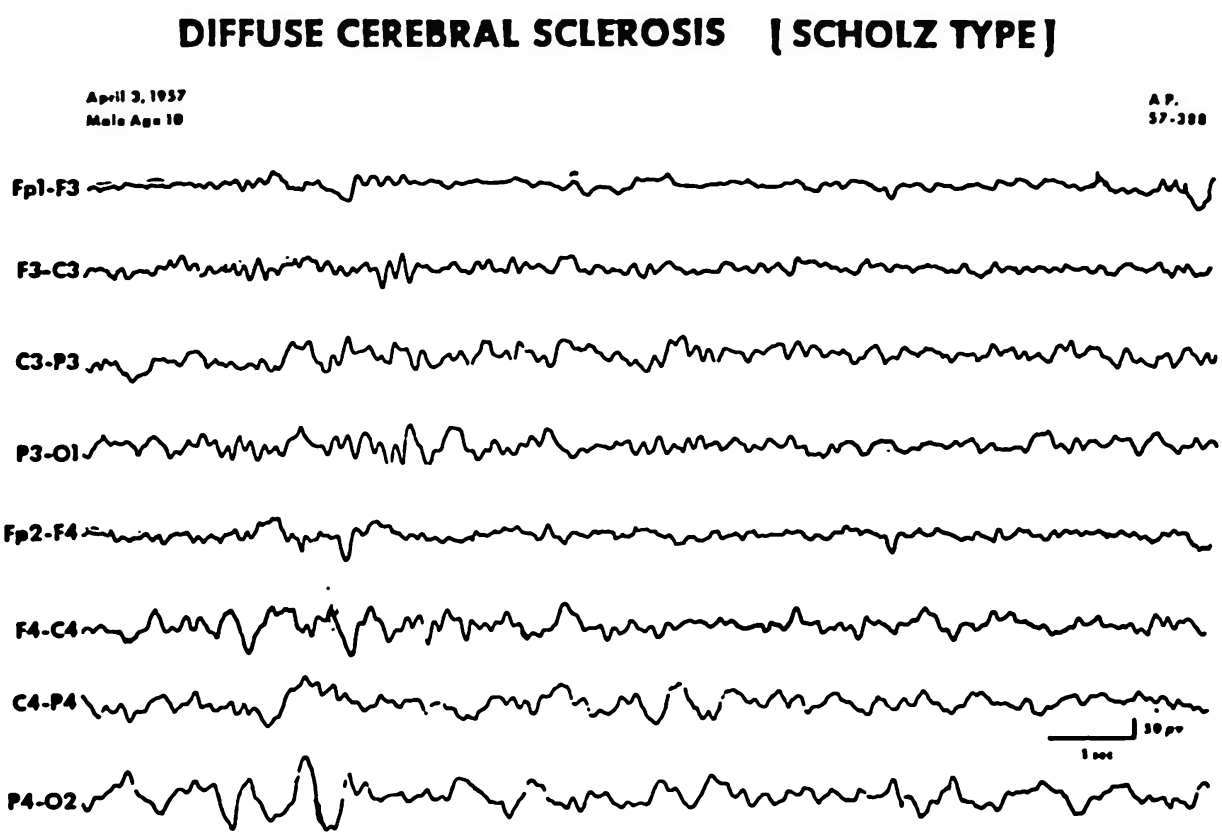


Figure 9.

Group IV is composed of seven patients with diffuse cerebral disease of predominantly white matter pathology but with some cortical and subcortical grey matter involvement (Table 9). Electroen-

TABLE 9

DIFFUSE ENCEPHALOPATHIES

GROUP IV:

Diffuse Cerebral Disease with Predominant White Matter Pathology and some Cortical and Subcortical Grey Matter Involvement

7 Patients

Subacute Sclerosing leukoencephalitis (Van Bogaert)	**4**
Niemann-Pick's disease	**1**
Krabbe's disease	**1**
Progressive encephalomyelopathy of unknown origin	**1**

cephalographic features of the patients in this group are summarized in Table 10.

TABLE 10

DIFFUSE ENCEPHALOPATHIES

GROUP IV Diffuse Cerebral Disease with predominant White Matter pathology and some Cortical and Subcortical Grey Matter involvement

CASE	PATHOLOGY	ALPHA	PAROXYSMAL BILATERAL SYNCHRONY	PAROXYSMAL UNILATERAL SYNCHRONY	PERIODICITY	DIFFUSE ASYNCHRONOUS SLOW WAVES	FOCAL ABNORMALITIES
P.G.	S.S.L.E.	0	+ (less. cont. in late rec.)	+ (in last record intermittent)	+	+	0
M.P.	S.S.L.E.	0 (late records)	+	0	+ (1st exam.)	+ (intermittent)	0
M.C.	S.S.L.E.	0 (late records)	+ (except last record)	+ (2nd record)	0	+	0
G.L.	S.S.L.E.	0 (late records)	+	0	+ (in some exam.)	+	0
B.G.	N.P.D.	R	+	+ (rare)	0	+	0
P.S.	K.D.	+	+ (during sleep)	0	0	+	0
J.T.	D.E.M.P.	0	+ (intermittent)	0	0	+	0
TOTAL: 7		5:0 (3 with early alpha) 1 (R) 1:N	7: + (2 with breakup of synchrony in late rec.) (1 intermittent) (1 sleep only) (0:0)	4:0 3: + (2 only in late records) 1 rare	3: + (transient in 2) 4:0	7: + (1 intermittent) (0:0)	7:0

Five of these patients had no signs of alpha rhythm, in one case alpha rhythm was present but reduced, and in another it was normal. All patients had some degree of paroxysmal bilateral synchrony which became less pronounced as the disease process progressed. This sometimes led to the complete disappearance of this electroencephalographic sign. In the course of the breaking up of bilateral paroxysmal synchrony the synchronization between the two hemispheres (Figure 10) seemed to be lost, first with a change from bilateral to unilateral synchrony (Figure 11). Periodicity of discharge was present in three of the seven patients. Diffuse asynchronous slow waves were evident in all of these patients although only intermittently in one patient.

This fourth group seems to combine some of the features of the three other groups. Paroxysmal bilateral synchrony was present in all cases at least at some stage of the disease, and diffuse asynchronous

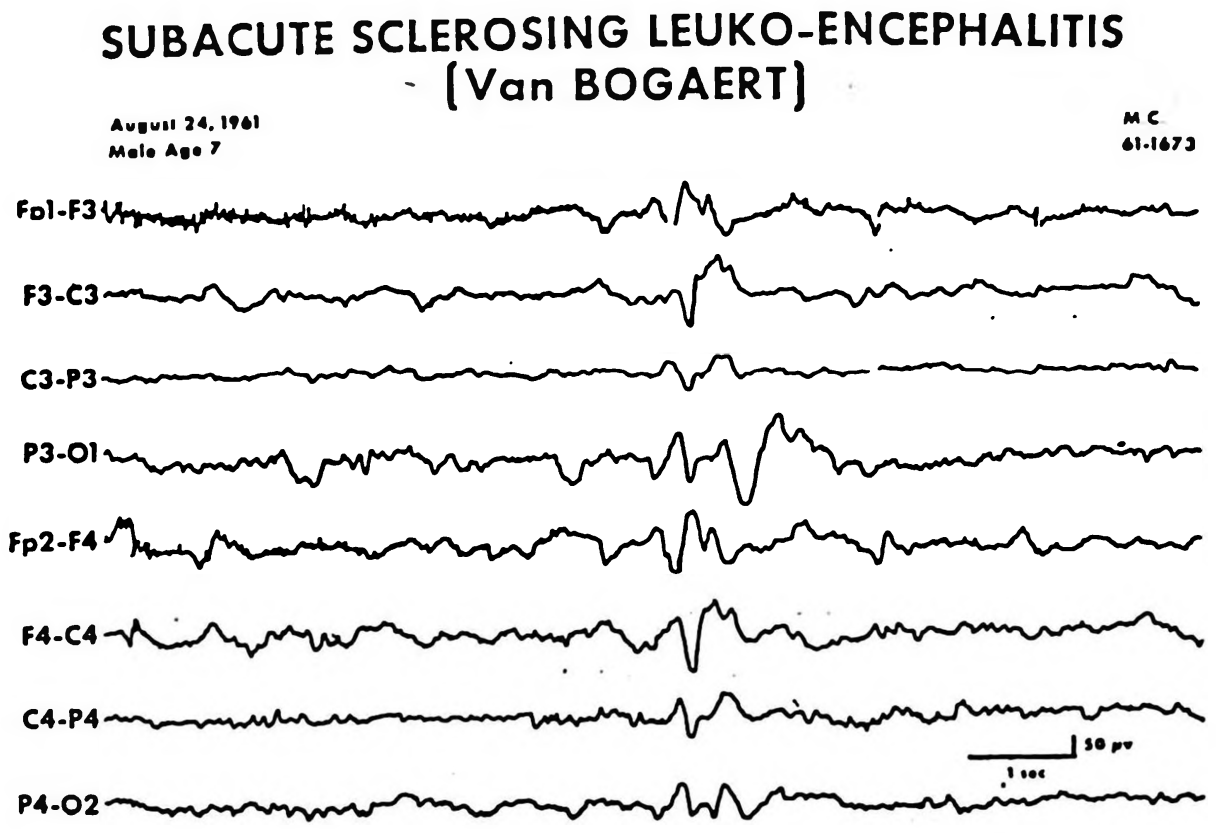


Figure 10.

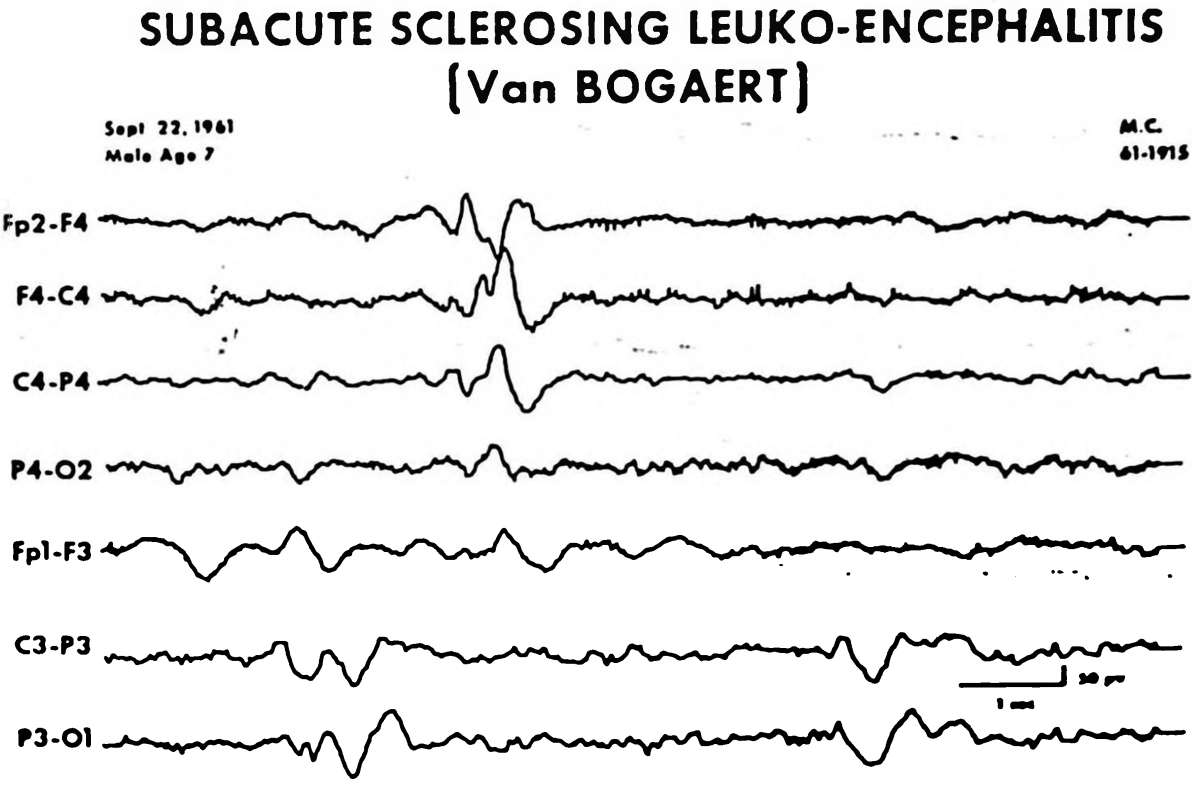


Figure 11.

slow waves were also present in all of these cases. It is probable that the paroxysmal bilateral synchrony is dependent upon involvement of grey matter, especially subcortical grey matter. The breakdown of synchrony may be due to gradual destruction of the connecting fibers between the subcortical grey matter and the cortex due to the white matter disease.

Samples of the electroencephalographic records from patients in this group are seen in Figures 10, 11, 12 and 13.

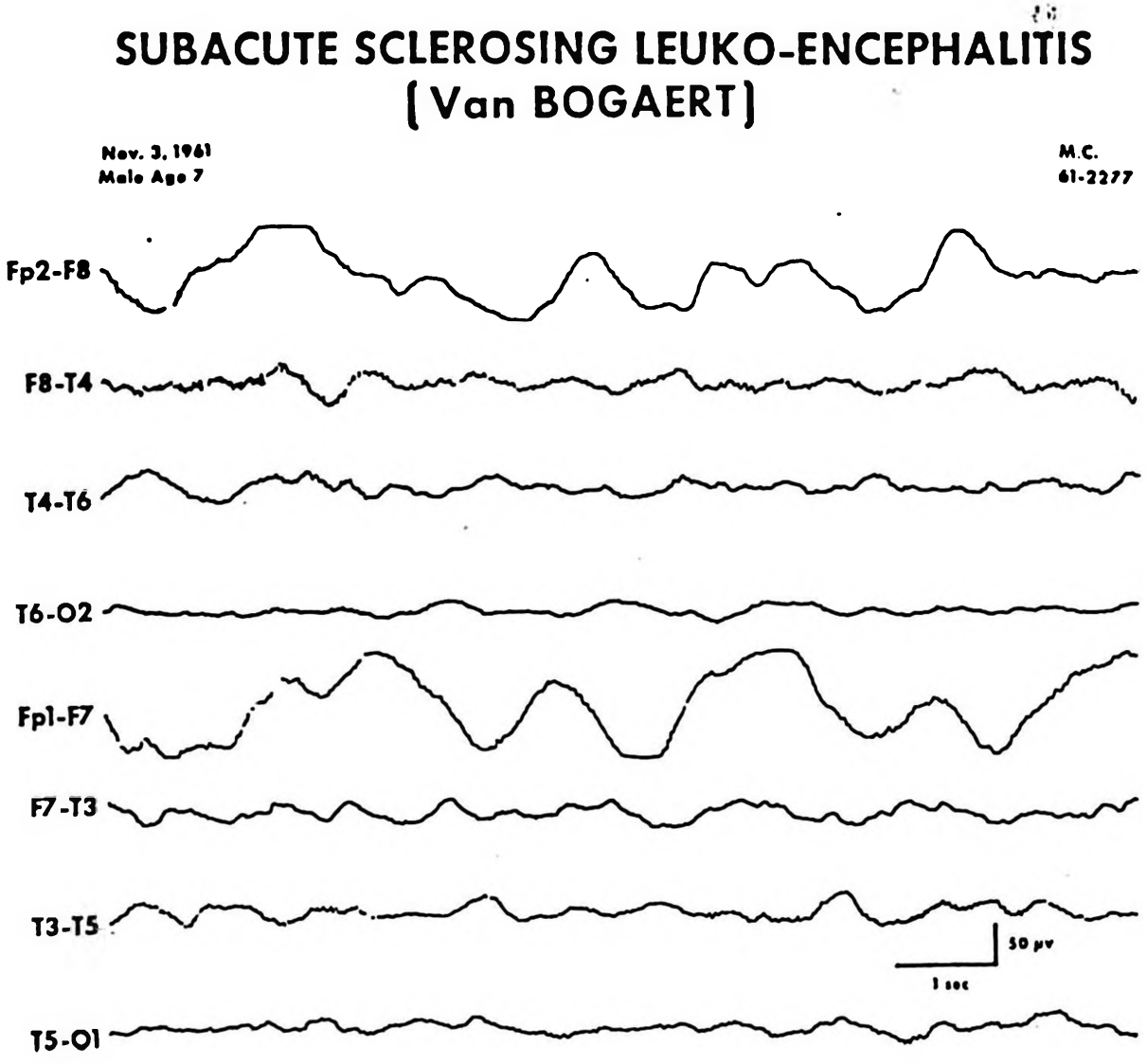


Figure 12.

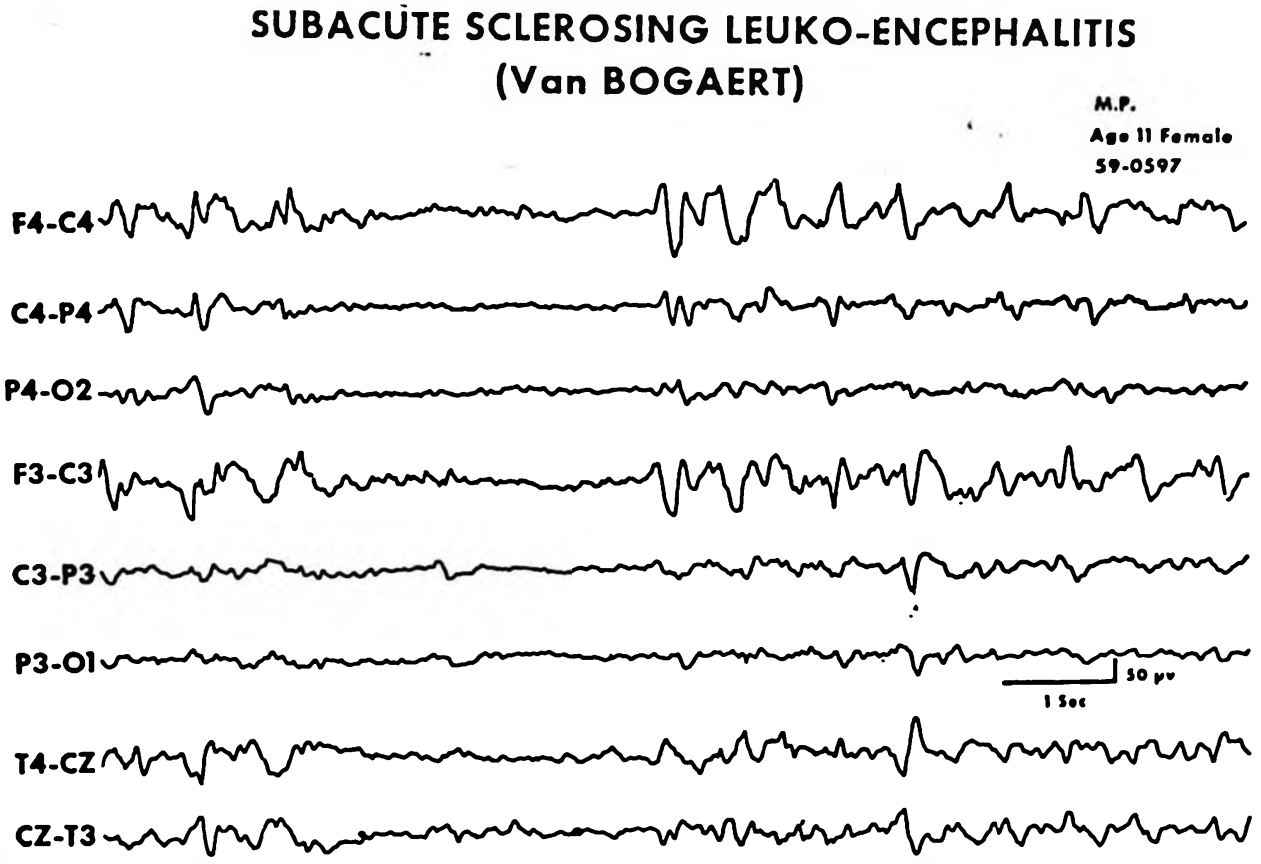


Figure 13.

Conclusions

Contrary to our impressions before analyzing these cases, the presence of diffuse paroxysmal bilateral synchrony seems to require some involvement of subcortical grey matter. We encountered only one exception to this rule in a patient of the diffuse cortical group whose E.E.G. indicated a fair amount of intermittent bilateral synchrony. The presence of unilateral synchronization of cortical activity in some of the diffuse cortical cases and the preservation of unilateral synchronization in cases where presumably bilateral synchrony is broken up by progressive destruction of white matter, as suggested by some observations in the last group indicates that some transcortical synchronization mechanisms exist.

It seems likely, therefore, that to produce paroxysmal bilateral synchrony some subcortical abnormality has to be present, but the tendency to synchronization over widespread areas bilaterally is facilitated if there is at the same time some diffuse cortical disease.

Furthermore it seems that the presence of diffuse asynchronous slow waves of the irregular delta type are closely correlated with pathology of the white matter and can be surprisingly absent in rather diffuse and severe involvement of the cortical grey matter alone. This raises an interesting problem about the underlying pathophysiology of this type of slow wave and one should not reject out of hand the possibility that these slow waves do not primarily represent potential changes across neuronal membranes but may perhaps reflect changes of electrical potential of glial elements. It is of interest in this respect that this type of slow wave abnormality is known to be quite prominent in brain lesions associated with a high degree of cerebral edema, a pathological process known from experimental studies to involve almost exclusively the white matter with surprising sparing of the cortical grey matter.