THE ELECTROENCEPHALOGRAM IN HEPATO-LENTICULAR DEGENERATION (WILSON'S DISEASE)[1]

GRANT L. HELLER, M.D.[2] AND KENNETH A. KOOI, M.D.

The Department of Neurology and the Neuropsychiatric Institute, University of Michigan, Ann Arbor, Mich. (U.S.A.)

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Most textbooks of neurology and of electroencephalography offer little or no information about the EEG in hepato-lenticular degeneration (HLD). This fact is not surprising, because HLD is an uncommon disease and so the opportunity to study a group of patients is limited. However, a search of the available world literature reveals 29 studies reporting 80 cases in which EEG interpretations are available. This report attempts to evaluate these cases as a group and to relate the findings in an additional five cases to trends evident from the prior studies. EEG's were abnormal in 43, questionably normal in six and normal in 31 cases (see Table I). A patient with more than one EEG has been tabulated as "abnormal" if at least one tracing was abnormal, even though he may also have had one or more normal records.

The types of abnormalities reported varied; the most common were continuous generalized slow activity, bursts of slow waves, and asymmetries. Focal abnormalities have also been noted. Hollister *et al.* (1960) reported a patient with seizures, presumed to be unrelated to previous shock therapy; the main feature of the EEG was a left frontal slow wave focus. Although there had been no definite clinical sign corresponding to this focus, at post mortem examination the left frontal subcortical white matter showed spongy softening. No other such definite EEG-pathological correlation was found.

Konovalov *et al.* (1957) cited 28 cases; three were described in detail, two more were illustrated, and the rest noted as "normal" or "abnormal". These authors stated that paroxysmal EEG's occur frequently in HLD with or without clinical epilepsy; they reported one case with clinical seizures and spike-and-wave patterns on the EEG. Zhirmunskaya and Chukhrova (1959) also commented upon the occurrence of paroxysmal "sharp and slow waves" without clinical convulsive disorder.

EEG findings during dimercaprol (BAL) therapy have been reported. Streifler and Feldman (1953) presented a patient with a slow, paroxysmal EEG before treatment; this patient showed parallel clinical and EEG improvement during therapy. Multiple clinical and EEG examinations were done. Giordano (1956) reported a patient whose initial EEG was questionably abnormal and whose tracings showed minimal changes toward normal on BAL therapy.

No correlations could be established statistically by *t*-test between EEG abnormality and either the age at onset of the disease or the duration of the disease from data in the literature (Table I). A trend toward greater EEG abnormality with more severe clinical involvement appeared to exist. There was a possible tendency toward relationship between EEG abnormality and degree of tremor and incoordination. No other clinical factor (mental state, motor power, tone, sensory changes, etc.) seemed to correlate with EEG findings.

Our present series consists of nine EEG's done on seven different patients (Table II). The first EEG of patient R.P. was also reported by Scharenberg and Drew (1954) and patient

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[2] Present address: Mount Sinai Hospital, Cleveland 6, Ohio (U.S.A.).

A. M. was reported also by Bihl (1959). Every patient had Kayser-Fleischer rings. There were three definitely abnormal (A) records, three borderline (B), and three normal (N) tracings. In all cases, even in those with normal records, the basic frequency was abnormally slow or at the slow end of the normal spectrum (see Fig. 1).

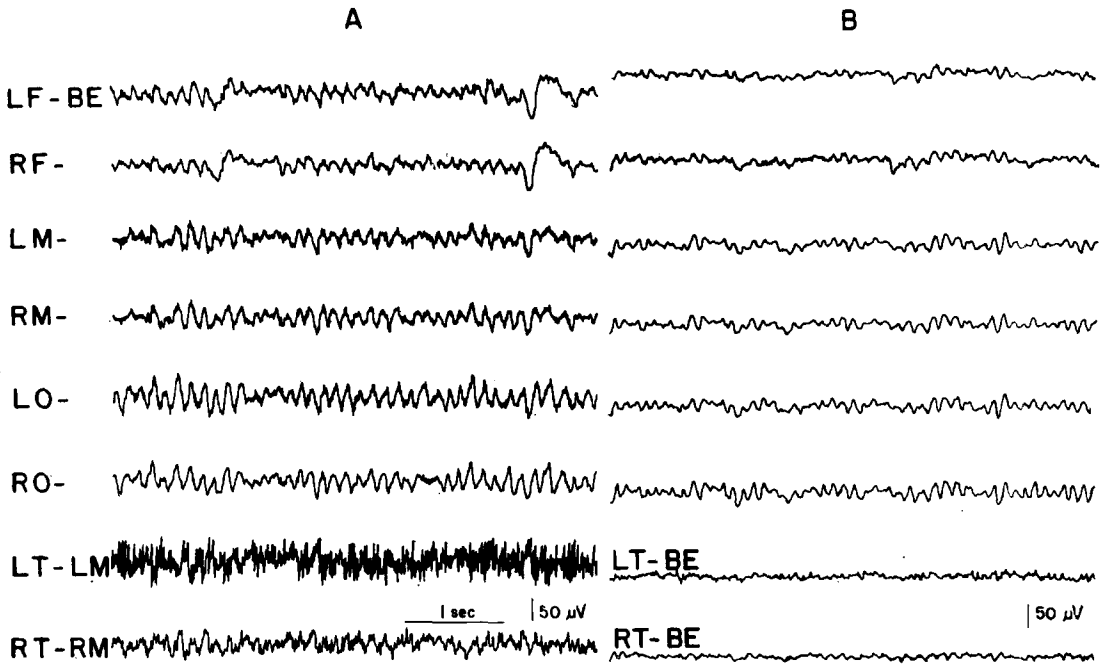

Fig. 1

R.P., male, age 20. *A*: tracing obtained 5/17/51. Duration of illness 2 years. Basic pattern slightly slow (7.5–8 c/sec). *B*: recorded 1/19/53. Three courses of BAL followed first EEG. EEG appears improved with faster basic frequency and lower amplitude. Questionable improvement in neurological status.

Other trends included occasional sharp diphasic forms bicentrally, continuous slow activity (usually 4–8 c/sec, occasionally slower), and bursts. As in other reports, no abnormality specific for this disease was found.

Two patients had two EEG's each. R. P. showed slight background improvement in his second tracing, about 1½ years after the first (Fig. 1); whether this change was due to the three courses of BAL therapy he received or to spontaneous remission is open to speculation. B.M. had an increase of 1 c/sec in background frequency in his second record compared with the first; it is impossible to state whether or not this minor change was caused by penicillamine therapy.

A.M. had a normal record in 1955, reported by Bihl in 1959; a tracing done in 1960 showed some minimal borderline changes. She also had several courses of therapy (usually BAL; penicillamine once briefly) between the two EEG's.

Inspection of Table II indicates that no close relationship existed between clinical and EEG abnormality. Age at onset and duration of illness did not seem to be correlated with EEG abnormality; one of the patients with an abnormal record had only a 7 month history of illness. Degree of tremor and incoordination roughly parallelled the degree of EEG abnormality; however, in one case, rigidity and bradykinesia of severe degree were present in the face of a normal EEG (W.O., Table II); the literature seems to agree with this point. It should be pointed out in this regard that the effect of therapy complicates the evaluation of liver disease.

TABLE I

Summary of cases from the literature

Authors	Number of cases	Age of onset	Duration (years)	Side of clinical involvement	Liver	EEG class	EEG abnormality	Remarks
Weatherly 1941	1	22	3	R>L	?N	A	"Outbursts", R>L	One illustration
Babcock and Brosin 1941	1	19	2/12	L	A–L	A	Slow	
Bertrand *et al.* 1942	1	NC	NC	NC	NC	A	Slow, poor alpha blocking	
Bridgman and Smyth 1944	1	11	3	R>L	A–P	A	"Paroxysmal", L>R	One illustration; febrile convulsions in childhood
Carter 1948	2	14	4	1 L>R	A–L	?A	Slow, slight HV build-up	Neither had Kayser-Fleischer rings by slit lamp
		15	10	1 L=R	A–L	A	Slow	
Herz and Drew 1950	5	29	5	3 L=R	N	5N		
		29	2	2 R>L	A–B			
		32	1		A–C			
		26	8/12		N			
		19	20		N			
Denny-Brown and Porter 1951	2	30	7	1 head to L	A–L	N		
		29	13	1 L=R	N	N		
Nayrac *et al.* 1951, 1952	1	10	6/12	L=R	A–B	?N	"Dysrythmie épisodique"; "une activité lente"	Same case reported twice, apparently
Stephens 1952	9	NC	NC	NC	NC	5A		
						2?A	Slow	
						2A	Slow; 1 L>R	
Boudin *et al.* 1952	1	?26	?3	L>R	A–B	N		
Heuyer *et al.* 1952	1	12	9/12	L>R	A–B	A	Slow; "rythmes rapides en bouffées"	
Strauss *et al.* 1952	4	NC	NC	NC	NC	4N		
Schechter and Jones 1953	1	24	1 1/2	R>L; fainting	A–B	A	"Non-specific"	Sleep EEG
Streifler and Feldman 1953	1	25	4	L>R; fainting	A–C	A	Diffuse slow; bursts	Several illustrations; multiple EEG's and clinical exams improving on BAL
						N		
Sullivan *et al.* 1953	2	13	21	1 L>R	N–B	2A	"Non-specific"	
		13	19	1 L=R	N–B			
Scharenberg and Drew 1954	1	18	2	L=R	A–C	A	Slow (7.5–8)	Same case included in present series (R.P.)
Gilsanz *et al.* 1954	2	19	1	1 R>L	A–B	2N		
		18	8/12	1 R=L	A–C			
Hornbostel 1954	2	32	1	1 L>R	A–B	N	"Allgemeine Dysrhythmie"	
		31	13	1 L=R	A–C	A		

Lamy *et al.* 1955	1	13	5/12	L>R	A–C (3 yrs.)	N		
Larmande and Margaillan 1955	1	22	1	R>L	A–B	N		Several EEG's
Lichtenstein and Gore 1955	1	?38	?5	R 6 yrs. ago R=L now	A–P	A	"Reduced amplitude in the left hemisphere"	
Alajouanine *et al.* 1955	1	?23	?3	R sided fits and grand mal then L>R	A–B	N ↓ A	Left central paroxysmal activity during seizure; varying changes with time	Several illustrations; course and EEG's vary but generally worse despite BAL
Giordano 1956	1	14	5	R>L	?N	?N	Very minimal changes	Two illustrations; slight changes toward normal on BAL
Faure and Loiseau 1957	4	24	1	3 R>L	A–L	N ↓ A	Slow; sharp waves	Several illustrations; serial EEG's worse as disease progresses
		30	6/12		A–L	A	Slow	
		17	2/12		N	A		
		23	4	1 L>R	A–L	N		
Konovalov *et al.* 1957	3	9	6	2 L=R	A–C	1A	Slow	Illustrations and text descriptions of these three
		21	6		NC	1?N	Slow	
		?15	?17	1 epilepsy	A–B	1A	Spikes, slow	
	2	20		2 L=R	NC	2A	Paroxysmal, slow	Illustrations but no text on these two
		28			NC			
	23			23 NC		17A 6N		No further comment on these
Zhirmunskaya and Chukhrova 1959	(39)	–	–	–	–	–	–	No case reports; patients studied in connection with investigations of Konovalov
Beard 1959	1	18	6	R>L	A–C	N		HLD and schizophrenia
Bihl 1959	1	17	10	L=R	A–L	N		Pregnancy; later EEG in present series (A.M.)
Hollister *et al.* 1960	1	20	3	L>R; seizures	A–P	A	Left frontal slow wave focus	One illustration; left subcortical white matter necrosis at autopsy
Berard-Badier *et al.* 1960	2	? since birth (had CD) or age 13	?5/12	L>R	N	N ↓ A	Slow basic frequency, fusiform bursts, R>L	
		8	6/12	R>L	A	A	Normal background, fusiform bursts, 6/sec bifrontal-bicentral	

NC — No comment on this subject; N — Normal; B — Borderline; A — Abnormal; (under Liver: C — Clinical; L — Laboratory; P — Post mortem examination; B — Biopsy); HV — Hyperventilation; R>L — in clinical column: right side of body more involved than left (usually only slight difference); R>L — in EEG column: right hemisphere more abnormal then left.

TABLE II

Summary of cases from the present series

Patient	Age	Sex	EEG overall	Basic freq.	Atypical or abnormal EEG features	Duration of illness	Clinical status	I.Q.	K.-F. ring	Remarks
R.F.	43	F	A	8.5	Low voltage, poor form and modulation. Low voltage slow waves central and occipital regions.	6 yrs.	Anxious, emotionally labile, severe intention tremor, tone normal, severe incoordination.	102	Definite	Uterine fibroid. Minimal liver dysfunction.
R.G.	13	M	B	9	Infrequent sharp waves asymmetrically in temporals.	1 yr.	Somnolent; organic and emotional changes, some athetoid movements, rigidity, moderate ataxia, bilateral plantar responses.	91	Definite	Prior to EEG: penicillamine, potassium sulfide, Pagitane, Diuril, low copper diet. Penicillin allergy. Liver disease-ascites.
B.M.	13	M	N	8.5–9	Some sharp forms, monophasic and diphasic, bicentrally.	6 mos.	Neurologically normal except minimal left-sided ataxia.	126	Definite	Liver disease-ascites. Prior to EEG: low copper diet, Diuril, Aldactone, penicillamine. Serum ceruloplasmin, 0.6.*
	14	M	N	9.5	Basic pattern faster, better organized. Occasional diphasic sharp waves bicentrally.		No significant change.	—	Same	Still on low copper diet, Diuril, Aldactone, penicillamine. Also on potassium sulfide.
A.M.	27	F	B	9–9.5	Occasional bimotor slow bursts.	10 yrs.	Emotional lability: resting and intention tremors, L>R, mild ataxia.	Average	Definite	Prior to EEG: Marplan, previous courses of BAL and penicillamine. Ceruloplasmin 0*. Liver not abnormal.
R.P.	20	M	A	7.5–8.5	Mildly slow, stereotyped. Few constricted alpha bursts.	2 yrs.	Guilt feelings, severe intention tremor, some wing-beating, ataxia, diminished associated movements.	—	Definite	After EEG: 3 courses of BAL over 8 months, Reported by Scharenberg and Drew, 1954.
	22	M	B	8.5–9.5	Rare right temporoparietal slowing. Background improved.		Mentally intact, generalized tremor, some wing-beating, ataxia. Several grand mal seizures 2 days prior to EEG.	Average	Same	Died 13 days after EEG of bleeding esophageal varices.
W.O.	16	M	N	9.0	None	3 yrs.	No evidence of organic deterioration. Slight perioral tremors, rigidity, hypokinesia.	83	Definite	Before EEG: high protein diet, methionine. Cirrhosis, esophageal varices. Liver tests abnormal in spite of Rx.
R.S.	20	F	A	7–7.5	Slow rhythm, central and occipital regions. Bicentral diphasic sharp thetas and occasional abortive bursts.	7 mos.	Mentally intact, severe head tremor, tone normal, ataxic speech.	Average	Definite	Liver normal.

* Serum ceruloplasmin determinations by Wallace W. Tourtellotte, M.D., Ph.D.; normal range 10.9–31.6 mg/100 ml, average 21.7.

It is interesting that all our patients except one (W.O.) had "average" or higher I.Q. ratings. I.Q. did not appear to correlate with the EEG. It is impossible to state whether the mental retardation of W.O. was life-long or secondary to HLD.

Extremely low serum ceruloplasmin values occurred without significant EEG abnormality (B.M. and A.M., Table II). At the present time we cannot make any attempt at neurochemical-EEG correlations in HLD.

SUMMARY

The literature on EEG's in hepato-lenticular degeneration has been reviewed; over half of 80 reported patients had abnormal tracings. Eight additional EEG's on seven patients are presented; two definitely abnormal, three borderline and three normal. Trends include continuous slowing of background frequency and sharp diphasic forms bicentrally and elsewhere. There is no specific EEG abnormality in this disease.

Although there are many exceptions, in general the degree of EEG abnormality parallels the severity of clinical involvement. No individual clinical finding consistently relates to EEG abnormality, although there is a suggestion both from our cases and those previously reported that tremor and incoordination may show such a relationship.

Some patients have EEG improvement during or after treatment; it is uncertain whether this change is cause-and-effect or coincidence. More studies of pre- and post-treatment EEG's would be of interest.

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