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PROVOCATION OF CONVULSIVE ACTIVITY IN THE EEG BY PROMAZIN-HCl-INDUCED SLEEP IN CHILDREN

A. MÁTTYUS, Adrienne HALÁSZ

Neurological Department, Heim Pál Children's Hospital, Budapest, Hungary

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The authors report on the convulsive activity provoking effect of Promazine as shown on EEG during sleep. It has successfully been used in infants and children who do not tolerate sleep deprivation. Promazine had smaller effect on the EEG-pattern than other related compounds or barbiturates. The greatest efficacy could be reached in generalised epilepsy, but the method was also helpful in other epilepsies. It is emphasized that in cases of acute neurological symptoms of not epileptical origine the compound is helpful to exclude epilepsy since Promazine induced sleep was never associated with convulsive activity on EEG in these cases.

Inducement of convulsive activity in EEG-recording during sleep with intravenously administered barbiturates has been well known for about 40 years. Their side effect which is particularly common with the later synthetized phenothiazine-preparations is that they change basic activity, thus results might be misinterpreted. Furthermore, Phenothiazines occasionally may also evoke clinical convulsions.

A natural sleep during EEG-examination will parry any artificial changes. For this purpose sleep deprivation - also has been known for over 20 years - is an excellent method /1,2,6/ though it might be tiresome for both the children and the personnel on duty. Moreover, it can rarely be used under the age of 5 years. Convulsions also occur relatively often during or within a few days after the sleep deprivation.

Akadémiai Kiadó, Budapest

Degen et al /3/ have found that in spite of being a Phenothiazine preparation EEG-recordings in Protactile-(Promazine-HCl) induced sleep have been nearly equivalent to those registered in 48 hours after sleep deprivation.

We have also used this method in 23 hospitalized children with later proven epilepsy. Their ages varied between 23 months to 17 years, nine of them were under 5 years of age.

The ages of 18 other children with doubtful diagnoses of epilepsy were from 10 months to 15 years. Catamnestic time in both groups was 5 to 9 months.

The preparation was administered orally in a dose of 3-4 mg/kg body weight, i.e. more than Degen et al /3/ had used. If the children's age and behavior made it possible we repeated the investigation within 48 hours in sleep deprivation, too. Some of the smaller children fell asleep spontaneously during the examination.

Some 30-90 min. after the intake of the tablets, the patients became drowsy and fell asleep. We observed a transient high excitement in one child only. No convulsions could be observed either during or after the examination.

Table I shows the data of the 18 patients with doubtful epilepsy diagnosis. All of them had some acute symptoms before. The patients showed no convulsive EEG-recording awake or in P-induced sleep. The EEG of one child with sleep apneic events, showed a slightly atypical picture after sleep deprivation and P-induced sleep in stadium B, C. However, we do not consider this too important.

Table II shows the data of the 23 patients who were diagnosed as epileptics, yet the EEG recorded in awake state did not reveal any convulsive activity. Again the slight anomalies found in some cases are of no major importance.

The elapsed time between the first epileptic event and the EEG in P-sleep varied from 6 months to 9 years.

We grouped our patients into different epilepsy categories according the antecedent events, the type of the attack and the clinical course. In most but not all cases the EEG pattern was typical for the clinical picture.

Table II. Partial epilepsy: 3 patients, in the first case (E.K. 23 mo's) similarly to spontaneous sleep, Promazine induced convulsive activity.

In the second patient (Z.E.) a slow focus could be detected after sleep deprivation, it became more pronounced in P-sleep. In this case an edematous rarefiction could also be seen on CT.

Two of the 6 patients with secondary generalized epilepsy showed convulsive activity during P-sleep (cases 1 E.K. and 3 Z.K. - Fig. 1). The recording of case 4 (R.T.) was normal with Promazine, however, photostimulation triggered a convulsive activity after sleep deprivation. In case 2 (R.V.) a slight slowing in the right temporal region became more pronounced in induced sleep.

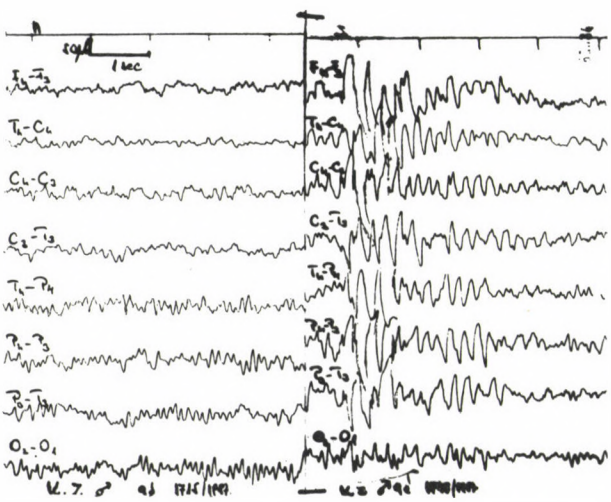

Fig 1. Z.K. 9 Y Secondary generalized GM epilepsy
A: normal
B: in sleep state BC asymmetrical irregular spike-wavws I>R

From the 12 primary generalized epilepsies (6 GM ep., 3 infantile myoclonic ep., 3 juvenile myoclonic ep.) the EEG-s of 10 turned to convulsive form during P-sleep: 5 from the 6 GM ep.-s, (shown in Fig. 2), 2 from the 3 infantile forms and all juvenile myoclonic ep.-s (R.N. Fig. 3).

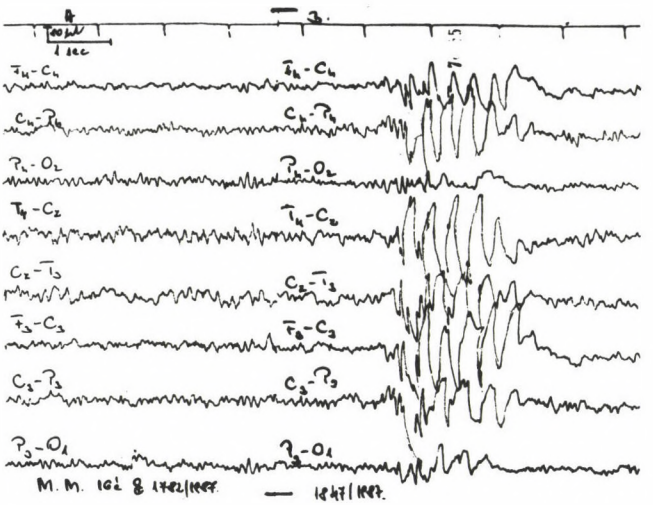

Fig 2. M.M. 17 Y Primary generalized GM epilepsy
A: normal
B: bilat. spike-theta bursts with frontal accentuation

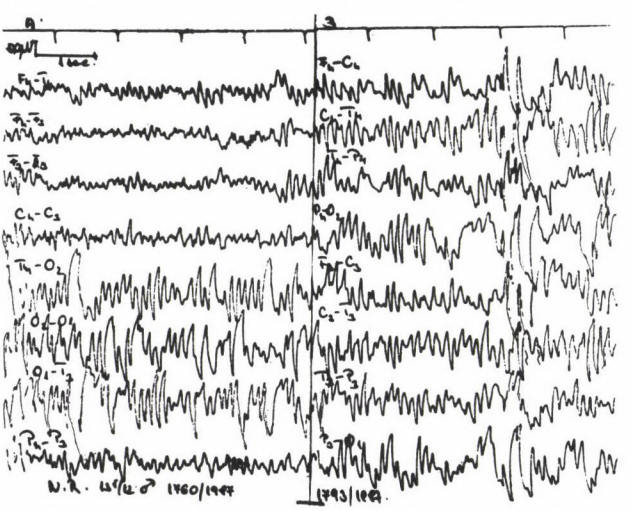

Fig 3. R.N. 13 Y Juvenile myoclonic epilepsy
A: bioccipitally high theta waves with rudimentary spikes
B: in arousal generalized polyspike and wave bursts

In case 5 (O.O.) of the generalized GM-group the EEG in P-induced sleep produced only generalized sharp waves, while a convulsive activity could be detected after sleep deprivation.

In both the "burned out" Lennox-Gastatut-syndrome (I.T.) and in the one unclassifiable case (Z.U.) with clinical signs of temporal lobe epilepsy a generalized epileptic activity in the P-induced sleep-EEG could be detected (Z.U. Fig. 4).

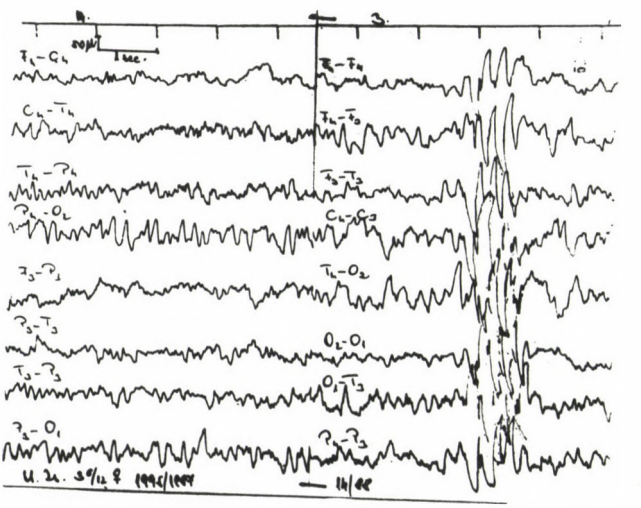

Fig. 4. Z.U. 4 1/2 Y Unclassifiable
A: normal
B: bilat, spike-theta bursts in somnolent state
R: right
L: left
A: awake
B: in Promazine sleep
Y: years

Fortunately, clinical epileptic attack and/or respiratory disturbance had never developed among the 41 (18+23) patients either during P-induced sleep, or after awakening.

Degen et al /3/ found convulsive EEG activity in the awake state in 25.7 % of 136 patients suffering from generalized GM ep. (92 of them with other forms of attacks). We only studied patients with normal or slightly altered EEG in alert state.

Their patients' age also differed from ours: in Degen's group 4.4 % ranged from 0 to 10 years, 29.4 % was between 11-20 years, and all the others were older. Our patients were all infants, children or adolescents.

Based on our experience, the described method gives the best results in generalized epilepsies and this is in agreement with Degen's findings /3/. It might also be useful in partial and secondary generalized epilepsies, for convulsive EEG during or after P-sleep could develop, as in one third of our cases. Besides the non generalized epilepsies /4/, the method could also be applied in other cases (please see our last 2 patients).

It should be emphasized that it is an excellent method also to exclude epilepsy in cases where such possibility had arisen. In this regard, it is important to note that none of our 18 patients - later proven as non epileptics - showed a convulsive EEG in P-induced sleep.

Last but not least we have found that with Promazine the EEG-investigation can safely be done in agitated and confused persons, both children (and also adults).

We used sleep deprivation only in 4 of the 23 epileptics, other 2 had fallen into natural sleep during the examination. So we could not really compare the EEG-recordings of the P-sleep with those without Promazine. At any rate, in one case of the secondary and primary generalised group (4 resp. 5) convulsive activity existed only after sleep deprivation. The opposite could be seen in the third case of the primary generalised GM-epilepsies. So there might exist some difference between the EEG-recordings in sleeping states reached in different ways.

In our observations with Promazine we saw convulsive activity when patients fell asleep, then in their various sleep phases or immediately after awakening. This is in contrast with the findings of most authors who registered convulsive EEG-s in sleep stadium B and C /1,3,4,5,8/.

The detailed analysis of the EEG-s was not the aim of this paper. We only wanted to provide evidence that the Promazine induced, EEG-activating method can be safely and reliably used in the examination of infants and children.

TABLE I

Not epileptic cases

Diagnosis	No of Pat.	EEG			
		In awake state	In spontaneous sleep	After sleep deprivation	In Promazine sleep
Collapse	5	3 asymm. sharp wav.		1 slightly asymm.	1 slightly asymm.
		2 normal	did not sleep	4 normal	4 normal
Dizziness of card. origine	1	right sharp waves	did not sleep	not done	normal
Affective apn.	2	normal	normal	not done	normal
Sleep apnea	1	normal	did not sleep	in state B C slightly atypical activity	no difference
Nocturnal pav.	1	normal	normal	not done	normal
Functional attack	4	normal	did not sleep	2 normal 2 not done	normal
Migraine accompagnée	2	normal	did not sleep	not done	1 normal 1 asymm.
Tremor familiale	1	slightly asymm.	did not sleep	not done	slightly asymm.
Tic	1	slightly asymm.	sleep spindles spike-wave suspect forms	not done	slightly asymm.

TABLE II

Epilepsy cases

Diagnosis	No of pat.	Name, sex age	EEG			
			In vigilant state	In spontaneous sleep	After sleep depriv.	In Promazin sleep
Partial e.	3	E.K. ♀ 23 M	Agitated, cannot be evaluated	Spike-waves during falling asleep L > R	Not done	Spike-waves during falling asleep L > R
		Z.E. ♂ 10 Y	L temporo-pariet slight funct. dist.	Did not sleep	L slow focus*	This focus more accentuated
		T.U. ♂ 11 Y	Normal	Did not sleep	Signs of somnolence	Normal
Part.sec. gener.	6	E.K. ♀ 4 Y	Normal	Slight asymm.	Not done	L conv. focus sec. gener.
GM e.		R.V. ♂ 41/2 Y	Slight funct. disturb. R>L	Did not sleep	Not done	R temp. slow focus
		Z.K. ♂ 9 Y	L irregular alpha activity	Did not sleep	Not done	In state BC irregular spike-waves L > R
		T.R. ♂ 12 Y	Normal	Did not sleep	Physiol.sleep. After awakening bilat. spike-waves by photost.	Physiol.sleep. No provocation by photostim.
		S.G. ♀ 12 Y	L occip. sharp waves	Did not sleep	Not done	L temp. slow sharp waves
		A.P. ♂ 15 Y	Normal	Did not sleep	Not done	R funct. disturb.

GENERALISED E. 12						
Primary gener GM e. 6	G.C. ♂ 4 Y	Bilat.temp. sharp waves	Did not sleep	Not done	Bilat. spike-wave bursts	
	A.H. ♀ 41/2Y	Bilat. parieto-occip. theta-delta w.	Did not sleep	Not done	Bilat.spike waves in somnolent state	
	F.M. ♂5 1/2Y	Slight funct. disturb.	In somnolent state theta bursts	Not done	L middle, R high theta bursts with rudimentary spikes	
	L.A. ♂6 1/2Y	Medium grade funct. disturb.	Did not sleep	Not done	Bilat. spike-waves by falling asleep or by change of the vigilance lev.	
	O.O. ♀ 15 Y	Normal	Did not sleep	In state BC bilat. fronto-precentro-temp. spikes-slow spikes L>R	Sharp waves, no convulsive activity	
	M.M. ♀ 17 Y	Slight irritative signs	Did not sleep	Not done	Bilat.spike-wave bursts	
Infantile myoclonic e. 3	I.P. ♂ 23/4Y	Theta-beta activity	Did not sleep	Not done	Bilat.spike-wave bursts	
	V.M. ♀ 33/4Y	Normal	Did not sleep	Not done	Physiol.sleep	
	A.B. ♂ 33/4Y	High polymorphic theta, gener., beta waves R sharp waves	Did not sleep	not done	Irregular spike-wave bursts during falling asleep	

Juvenile myoclonic e. 3	G.N. ♀ 7 Y	Normal	Did not sleep	Not done	Gener. 4 c/s spike-waves L>R
	Z.S. ♀ 12 Y	Sharp waves by HV R > L	Did not sleep	Not done	In state BC spike-wave bursts
	R.N. ♂ 13 Y	Bioccip.high theta waves, rudimentary spikes	Did not sleep	Not done	Repeated awakenings, bilat. poly-spike-wave bursts
Burned out Lennox-Gastaut sy. GM and myoclon. attacks	I.T. ♂ 12 Y	Irregular slowing	Did not sleep	Not done	Gener. 4 c/s spike wave bursts
Unclassifiable	Z.U. ♀ 41/2Y	Normal	Did not sleep	Not done	Bilat. spike-wave bursts in somnolent state

R: right
L: left

* L oedematous rarefiction
HV: hyperventilation

ADDENDUM

In the 18 months since the reception of the manuscript we made more than one hundred EEG-recordings in P-sleep. By two patients the preparation provoked epileptic attacks like sleep deprivation. Nevertheless, this complication seems to occur more rarely with Promazine than by sleep deprivation.

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A. MÁTTYUS MD

Heim Pál Children's Hospital
Üllői út 86.
Budapest
H-1089