

Early energetic medical treatment in epilepsy syndromes



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What is « energetic » treatment ?

- Using unusually high doses of drugs
 - E. g. high-dose valproate in childhood epileptic encephalopathies (specific risks)
- Using polytherapies, often at high doses
- Using uncommon drugs/treatments
 - antiepileptic: vigabatrin (IS), felbamate...
 - Steroids, immunoglobulins
 - Ketogenic diet
 - Vagal nerve stimulation
- Considering surgery (at the right time... not too early, not too late)

There are pros and cons

PROS

1 - « Seizures beget seizures »: if seizures are energetically suppressed, epilepsy will remit (conversely, if not it will become severe)

2 - The epileptic process produces developmental delay (may be definitive if it happens at crucial stages), as well as behavioural and psychiatric problems, thus seizures and EEG changes should be suppressed at all cost !

There are pros and cons

CONS

1 - Epilepsies have a tendency to remit spontaneously (esp. certain syndromes)

2 - Epilepsies follow their own course, there is no real influence of treatment on the long-term prognosis

3 - Heavy-handed treatment is dangerous in several respects

« seizures beget seizures »

(W. Gowers, late XIXth century)

The facts behind this statement ?

- Some epilepsies may become difficult to treat if seizures have not been adequately controlled early on (« lost time » is a factor of drug resistance)
 - Because seizures provoke brain damage
 - Ample evidence from animal studies
 - Examples of progressive hippocampal sclerosis after repeated long convulsive seizures, after repeated febrile seizures
 - Because seizures provoke head trauma (hence brain lesions), social and psychological problems that create drug resistance

« seizures beget seizures »

The facts behind this statement ?

In some cases, with symptomatic epilepsies, seizures become drug-resistant (with all the complications) when there is a relapse after discontinuation of treatment

- there is no clear explanation for this
- such patients are mostly found among surgical candidates.... « *they should never have stopped my treatment* ».

« seizures beget seizures »

- In summary:
 - This is true in selected cases
 - This does not apply for most epilepsies, that appear to have their own natural history
 - Antiepileptic drugs do not appear to influence the natural history of epilepsies in most patients
 - See long-term studies in untreated patients (Africa)

Epilepsy may produce developmental delay

-In epileptic encephalopathies

- ESES syndrome (continuous spikes and waves during sleep)
- Lennox-Gastaut syndrome
- Severe myoclonic epilepsy in infancy (Dravet syndrome)
- most inborn metabolic disorders with epilepsy

-In severe focal epilepsies

-esp. with brain lesions:

cortical dysplasia

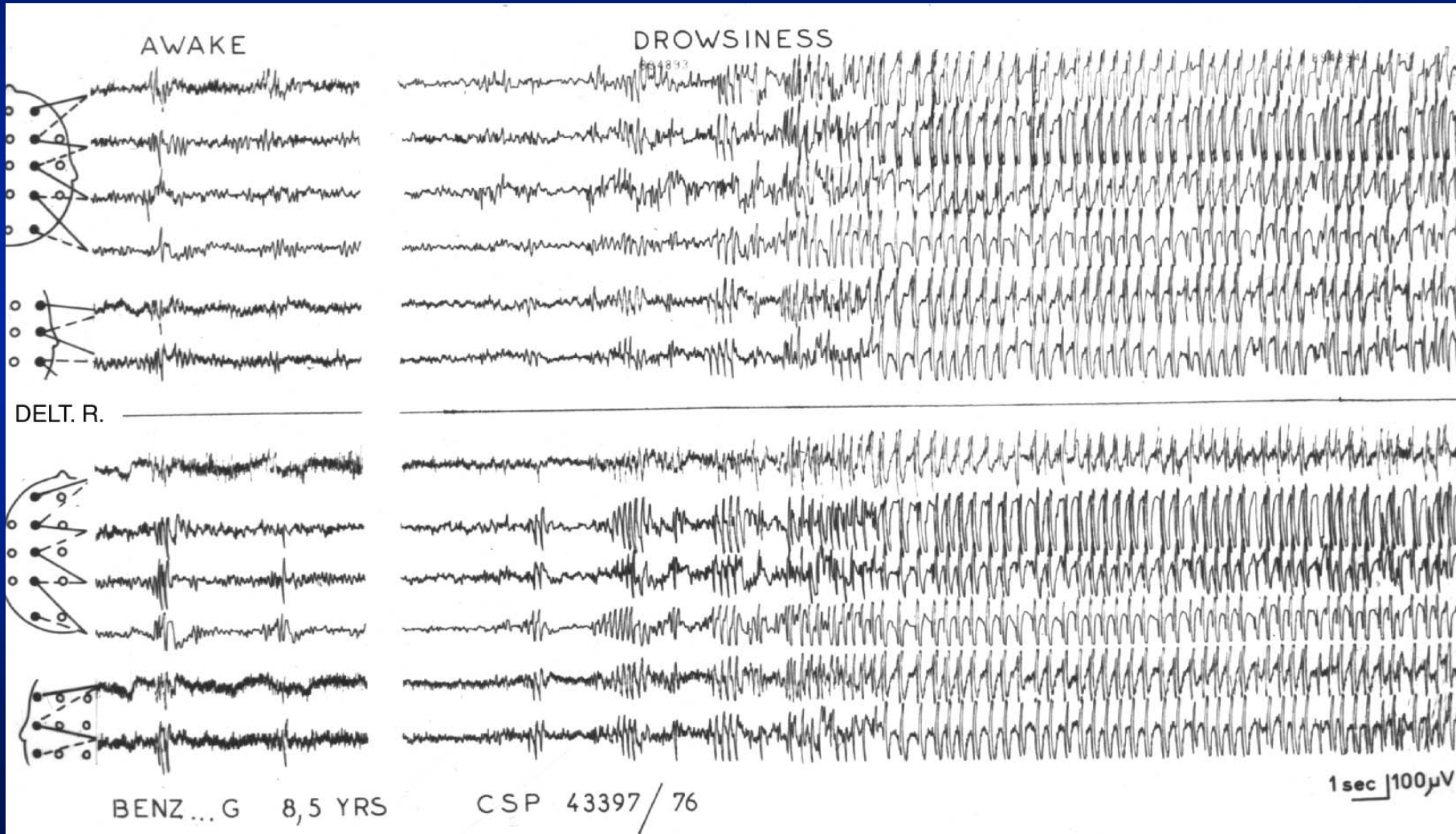
tuberous sclerosis

Sturge-Weber angiomatosis

-esp. in progressive diseases

Rasmussen's encephalitis

The ESES syndrome



Epilepsy may produce other difficulties

-Social isolation

- the consequences are very severe if this occurs at primary school age and during adolescence
- the patient may never develop normal relationships thereafter, even if epilepsy ultimately remits

-Lost opportunities (school, profession)

- chronic dependency on social help and family

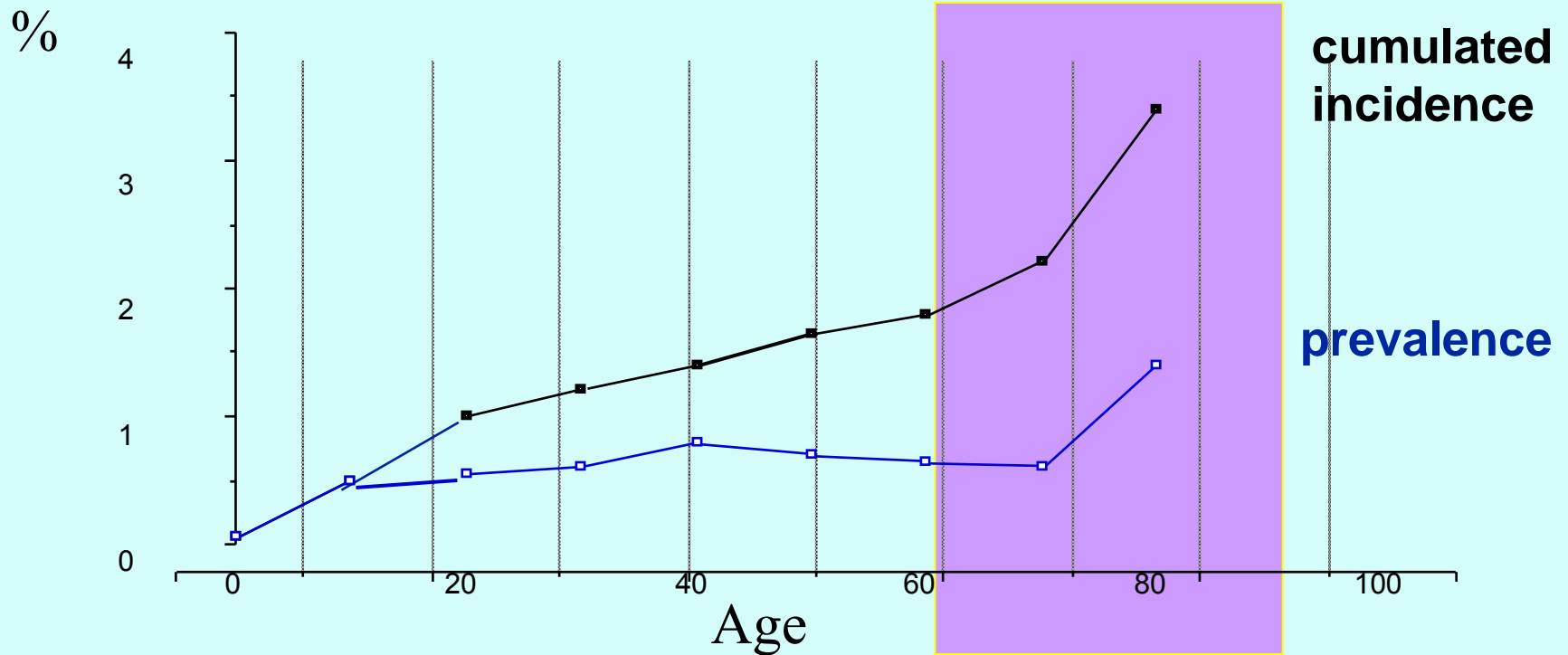
-Behavioural problems develop at adolescence in patients with uncontrolled epilepsy, and psychiatric problems at any age

Epilepsies remit spontaneously

- This is true statistically for most epilepsies (see epidemiological studies)
- This is true clinically in many syndromes
 - benign focal epilepsies in infancy, in childhood
 - Even after « a stormy onset »
 - Landau-Kleffner syndrome, ESES syndrome
 - childhood absence epilepsy

Epilepsy: epidemiology

Cumulated incidence and prevalence vs age



Treatment has no influence on the long-term outcome

- This is true in many cases
 - Most idiopathic generalized epilepsies
- But there are exceptions
 - In ESES and LKS, special treatment (using steroids) does clearly minimize the long-term consequences
 - In Lennox-Gastaut syndrome, the same has been stated
 - In many instances, in symptomatic focal epilepsies

Juvenile myoclonic epilepsy

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Treatment is very effective
but does not change the long-
term prognosis (seizures persist
at any age)

No « energetic » treatment
is justified, and lifestyle issues
may play an important part

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Lafora's disease evolution within 3 years

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A fatal disorder, there is no clear effect of « intensive » therapy.
New treatment procedures may be developed following the
elucidation of the genetic mechanisms

The ring chromosome 20 syndrome

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- No response to any drug
- Side-effects will accumulate without clear benefit
- Seizures may respond to other approaches (including psychosocial)

Myoclonic-astatic epilepsy

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- Idiopathic
- Variable prognosis, from very severe to self-limited`
- Intensive treatment may be useful in order to influence the long-term course

Lennox-Gastaut syndrome

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Intensive treatment has been shown to be associated with
better long-term prognosis

Energetic treatment may be dangerous

- May be true in many cases
 - Addition of side-effects of drugs
 - Idiosyncratic, severe effects
 - Drugs like felbamate (LGS, SME), vigabatrin (Infantile spasms) have their specific risks
 - Steroids may cause permanent growth deficit (among other complications)
 - Cave: paradoxical aggravation of epilepsy due to certain drugs, often used in combination, with difficult-to-manage polytherapies

Paradoxical aggravation: a patient on carbamazepine and vigabatrin for severe focal epilepsy

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In summary:

- Energetic treatment at onset ? **Justified**
 - When cognitive functions are at stake, even if epilepsy is benign or self-limited
 - ESES, LKS
 - When epilepsy is clearly the main factor of cognitive, social, psychological impairment
 - Lennox-Gastaut syndrome
 - Myoclonic-astatic epilepsy (Doose syndrome)
 - Some symptomatic focal epilepsies
 - Think of surgical possibilities as early as possible
 - When epilepsy is due to a treatable medical condition (treat the medical condition !)

In summary:

- Energetic treatment at onset ? **Not justified** (because intensive treatment has its own risks)
 - When there is no clear cognitive impairment
 - E. g. in the presence of impressive EEG changes only
 - When epilepsy is not the main factor of cognitive, social, psychological impairment
 - Epilepsies associated with progressive conditions
 - Epilepsies associated with major brain lesions
 - Whenever treatment does not clearly influence the course of the epilepsy

In conclusion

- A thorough evaluation and syndromic approach is necessary before energetic treatment can be chosen
- Treatment strategies will change in the coming years, due to new possibilities of treatment in the most severe epilepsies