“Benign” childhood epilepsies with rolandic spikes

to treat or not to treat

and how?
Benign childhood epilepsy with rolandic spikes (BCERS)

- first described in 1952 (Y. Gastaut)
- well-defined concept in the years 70 and 80
- rolandic seizures + rolandic discharges
- classic picture with invariably good prognosis
- treatment usually not indicated

- rolandic discharges without seizures

1. Tzitiridou, Epil Behav 2005;7:458
This uniform picture was confirmed by a meta-analysis

- 13 studies on 794 patients included in the analysis
- aggregate remission 0.977
- no predictive variables could be identified

However:

- all studies were retrospective and concerned biased cohorts
- uniformity of the syndrome may have been an illusion and due to selection bias
- prospective studies are needed to identify outcome in an unbiased sample

1. Tzitiridou, Epil Behav 2005;7:458
DSEC: mean interval between 1st and last seizure (with 95% CI) at median follow-up of 15 years

1. Tzitiridou, Epil Behav 2005;7:458
DSEC: course of various syndromes comparison of outcomes at 2 and at 5 years of follow-up

at 2 years: TR > (fine) or < 6 months (poor)
at 5 years: TR > (fine) or < 12 months (poor)

1. Tzitiridou, Epil Behav 2005;7:458
Other manifestations described in the years 90 and 00

- autosomal dominant or X-linked rolandic epilepsy with speech dyspraxia
- rolandic discharges with other seizure types (atonic, myoclonic, absence): atypical benign partial epilepsy or pseudo-Lennox syndrome
- rolandic discharges with autonomic seizures or shifting focus
- rolandic discharges and seizures with temporary intellectual impairment or
- evolving to CSWS / Landau-Kleffner syndrome, learning disabilities and/or speech and language regression
Example: Jeanine L., 24 March 1995

- Seizures started at age 4 yrs, sometimes 2 within a few weeks, otherwise months in-between, always between 3.00 and 6.30 a.m.
- Semeiology and EEG at first typical for rolandic epilepsy; normal development
- R/ sodium valproate
- Learning and behavioral problems at school
- Neuropsychological test: low level of functioning, deterioration likely
- School performance improved with remedial support and coaching
- After 2 years of seizure-freedom: withdrawal of valproate

1. Tzitiridou, Epil Behav 2005;7:458
Jeanine L., 24 March 1995

- recurrences at age 9
- seizures with retained consciousness, left-sided hemiparesis, jerks, headache, nausea and vomiting, resembling Panaiyotopoulos syndrome
- school performance deteriorated again
- EEG: very frequent epileptiform discharges, notably in R centroparietal region, resembling “focal” CSWS during sleep
- R/ sodium valproate
- MRI normal; EEG improved rapidly after treatment
- despite a few short seizures, development resumed again and elementary school was finished at an adequate level
Jeanine L., 24 March 1995

Was this:

- Rolandic epilepsy (BCERS)?
- CSWS?
- Panaiyotopoulos syndrome?
- a continuum?

1. Tzitiridou, Epil Behav 2005;7:458
BCERS, CSWS and other benign focal epilepsies: a continuum!

- expanding and ever more convincing body of literature
- data from genetics, clinical neurophysiology, imaging and clinical neurology
- BCERS and LKS / CSWS are different syndromes at both ends of a spectrum of disorders of language and cognition
- occurring during specific stages of development and maturation of the CNS
- extending the spectrum even further, other idiopathic partial epilepsies (Gastaut, Panaiyotopoulos) are joint with the above in the concept of a benign childhood seizure susceptibility syndrome (BCSSS)

1. Tzitiridou, Epil Behav 2005;7:458
Conclusions so far

- BCERS is indeed one of the most benign epilepsy syndromes
- This justifies a restrictive attitude when faced with the decision to treat children with the classic picture

Next question

- Is it possible to recognize those cases needing AED treatment?
- Is it possible to recognize them *in time*?

No prospective studies have been done to find prognostic variables that would identify pre-symptomatic cases and so enable preventive treatment

1. Tzitiridou, Epil Behav 2005;7:458
Indications for starting therapy in BCERS

1. many and/or severe secondarily generalized seizures (clinical urgency)

2. early onset of seizures (You et al, Epil Disord 2006): the younger at onset, the greater the chance of medical refractoriness

3. more seizures prior to start of medication and the need to use more than one AED for seizure control (Al-Twajiri & Shevell, J Child Neuro 2002)

4. frequent subclinical discharges during sleep: threat to cognitive development (a.o. Nicolai et al, Epilepsia 2007)

- recognizing these indications requires careful and vigilant follow-up!
If treatment is indicated, which AED?

First choice according to expert opinion
- Europe: sodium valproate
- USA: carbamazepine or oxcarbazepine

None of these has been proven to be superior

Trials have only been done with:
- sulthiame vs. placebo
- oxcarbazepine vs. levetiracetam
Summary of results so far: Sulthiame

- 6-month placebo-controlled, double-blind trial
- outcome: rate of failure events (seizure, intolerable AE, development of another epilepsy syndrome, withdrawal by parents)
- 31 on sulthiame, 35 on placebo
- retention of drug at 6 months:
  - 81% for sulthiame
  - 29% for placebo (P < 00002)

1. Tzitiridou, Epil Behav 2005;7:458
Summary of results so far: Sulthiame

- a later open study on 6 children with BCERS studied cognition before and after 6 months of sulthiame treatment
- it suggested that sulthiame did indeed control seizures and reduce spike activity,
- but was also associated with a deterioration of cognitive function (reading ability, memory, attention and mathematics skills)

1. Tzitiridou, Epil Behav 2005;7:458
Summary of results so far: LEV vs OXC

- randomised, open-label, parallel group trial (equivalence design)
- 39 patients: 21 on LEV, 18 on OXC
- at 18 months: 19/21 on LEV and 13/18 on OXC seizure-free (N.S.)

question: is this better than the expected spontaneous course?
Summary of results so far: LEV

- LEV dosage 15-60 mg/kg/day, mean 39 mg/kg/day
- > 50% seizure reduction was obtained in 12 of 24 children
- EEG improvement correlated with cognitive and behavioral outcome, but correlation was not perfect
- LKS: 2/4 improved
- BCERS: 1/6 seizure-free, others no response
- atypical BPE: 7/10 improved, but role LEV uncertain
Summary of results so far: OXC

- One study in typical BCERS found seizure-freedom in 74% and >50% improvement of seizure frequency in 21%.
- EEG normalized in 58% and improved in 35%.

- In another study on 3 patients with BCERS with atypical features, OXC was associated with electroclinical deterioration.

1. Tzitiridou, Epil Behav 2005;7:458
Summary of results so far: other AED’s

- Lamotrigine: no series reported; one case report on a paradoxical reaction with transient cognitive deterioration
  Catania, Epilepsia 1999

- Gabapentin: only very modest positive result in one series
  Bourgeois, Epilepsia 1998, S6

- Acetazolamide: anecdotal reports of effect in LKS and atypical BCERS
  Pisani, Neuropediatrics 1999

1. Tzitiridou, Epil Behav 2005;7:458
Conclusions

- the extent and variation of the concept of benign partial epilepsies in childhood are as yet insufficiently defined

- careful follow-up of individual patients is always justified

- in the purely benign form of BCERS, treatment is usually not indicated

- in other related syndromes developing toward the more severe end of the spectrum, treatment is mandatory, but it is as yet not clear with which AED

- nor is it possible to identify children at risk before they become symptomatic