Comments to “Is epileptogenesis a key to treatment of childhood epileptic encephalopathies?”

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Dear Editor

I’ve read with great interest and pleasure the letter of Sergiusz Jóźwiak about the perspectives in prophylactic treatment of epilepsy. Of cause the idea of a preventive treatment of epileptiform discharges on EEG in infants with tuberous sclerosis complex (TSC) is a revolutionary one, and Professor Jóźwiak is a pioneer in this field. During the past 2 years my group has been undertaking similar work whereby we EEG our infant patients with TSC (monthly) and subsequently prescribe antiepileptic drugs. Unfortunately it is not always with vigabatrin because it is not registered in our country. The results of this approach are good (but not as good as those published by Professor Jóźwiak and this may be due to the difficulty in sourcing vigabatrin).

In more than 20 infants that we treated there was only 1 case of West syndrome; all other children either did not have epilepsy or had a rather benign focal variant without psychomotor regression.

However, I would be very cautious to extrapolate this approach to the very wide spectrum of other epileptic encephalopathies. I know, there are many monogenic epileptic encephalopathies (more than 30 in internet database Online Mendelian Inheritance of Man – OMIM), many metabolic epilepsies (about 200 disorders with epilepsy) manifesting as encephalopathies, epileptic encephalopathies due to the different cortical dysplasias and neurodegenerative diseases. An experienced pediatric neurologist sometimes can diagnose the TSC early (before the start of seizures) – by the presence of cardiac rhabdomyomas and hypomelanotic macules; in familial cases we can diagnose the TSC in siblings with genetic testing. Is it possible to predict the development of other epileptic encephalopathies or define some to seizures in this group? I think, we cannot in the majority of cases. However, there are some exceptions to my mind: may be the infant with cerebral palsy due to grade 4 periventricular leucomalacia has a high risk of infantile spasms. If we see lissencephaly on brain MRI, it means obligatory infantile spasms in a child. But how can we predict other genetically determined epileptic encephalopathies – making the exon sequencing as neonatal screening? May be such screening can be undertaken once, but what should be done in the future? Also, I am not sure that we can find the universal biomarkers for all epileptic encephalopathies – as they are very heterogeneous in terms of their pathogenesis. We are feeling very enthusiastic about the EPISTOP project and finding the biomarkers of epilepsy in it, but they are the markers of epilepsy in certain condition – TSC. Will they be universal for other epileptic encephalopathies? Sergiusz Jóźwiak has the same concerns (see his letter).

The other consideration is that vigabatrin appears to have unique efficacy for epilepsy (and may be not only epilepsy) in TSC. It seems not to be a simple antiseizure drug, but a drug influencing the basic mechanisms of the disease. Bo Zhang et al. (2013) showed that vigaba-
trin partially inhibited mTOR pathway activity and glial proliferation in the knock-out mice in vivo, as well as reducing mTOR pathway activation in cultured astrocytes from both knock-out and control mice. For other epileptic encephalopathies, we still must find (or create) such effective drugs, and they can be specific for each epileptic encephalopathy. There are some hopes – remarkable phenytoin sensitivity was recently described in epileptic encephalopathy due to SCN8A (Boerma et al., 2015).

In conclusion I think that we have a long way ahead of us until the prophylactic treatment of epilepsy will become our everyday clinical practice. Preventive treatment of TSC is still a very successful and pleasant exclusion from the general rule.

REFERENCES