iii. by eliminating some high Hz, and all lower, measurements;

With these adaptations, we devised a prospective, randomized, crossover, controlled iv 2h study using frequent measurements of the evoked Photo-paroxysmal EEG Response (PPR) as a pharmacodynamic (PD) efficacy endpoint. We conducted an *intra*-patient comparison of three PD metrics (time to effect-time to peak effect-magnitude of effect), in adult photosensitive epilepsy patients, time 0-2h, post-15-min zero-order infusion LEV 1500 mg versus equipotent BRV 100 mg, on two separate occasions, in random, crossover, double-blind fashion (n = 8 patients).

Results: We adapted 'The Model' such to be able to elicit data to compare the *rapidity* of effect of two similar AEDs given *intravenously*. The adaptation of 'The Model' has worked in the first patients being investigated (comparative AED EEG data generated).

Conclusion: Adaptation of the standard "Photosensitivity Model" should allow the determination of differences (if it exists) in time to CNS entry (effect) of i.v. infusion of two nearly identical AEDs. Data obtained in such a manner could help SE treatment algorithms.

doi:10.1016/j.yebeh.2019.08.016

Epilepsy & Behavior 101 (2019) 106742

Possible epigenetic regulatory effect of dysregulated circular RNAs in epilepsy

Woo-jin Lee, Hang-Sang Lee, Hye-Rim Shin, Eun-Young Kim, Hyoshin Son, Yong-Won Shin, Hyeyoun Chang, Soon-Tae Lee, Kyung-Il Park, Kon Chu, Sang Kun Lee
Seoul National University Hospital, Seoul, South Korea

Background: Circular RNAs (circRNAs) involve in the epigenetic regulation and its major mechanism is the sequestration of the target micro RNAs (miRNAs). We hypothesized that circRNAs might be related with the pathophysiology of chronic epilepsy and evaluated the altered circRNA expressions and their possible regulatory effects on their target miRNAs and mRNAs in a mouse epilepsy model.

Methods: The circRNA expression profile in the hippocampus of the pilocarpine mice was analyzed and compared with control. The correlation between the expression of miRNA binding sites (miRNA response elements, MRE) in the dysregulated circRNAs and the expression of their target miRNAs was evaluated. As miRNAs also inhibit their target mRNAs, circRNA–miRNA-mRNA regulatory network, comprised of dysregulated RNAs that targets one another were searched. For the identified networks, bioinformatics analyses were performed.

Result: Forty-three circRNAs were dysregulated in the hippocampus (up-regulated, 26; down-regulated, 17). The change in the expression of MRE in those circRNAs negatively correlated with the change in the relevant target miRNA expression ($r = -0.461$, $P < 0.001$), supporting that circRNAs inhibit their target miRNA. 333 dysregulated circRNA–miRNA-mRNA networks were identified. Gene ontology and pathway analyses demonstrated that the up-regulated mRNAs in those networks were closely related to the major processes in epilepsy. Among them, STRING analysis identified 37 key mRNAs with abundant (≥4) interactions with other dysregulated target mRNAs. The dysregulation of the circRNAs which had multiple interactions with key mRNAs were validated by PCR.

Conclusion: Dysregulated circRNAs might have a pathophysiologic role in chronic epilepsy by regulating multiple disease relevant mRNAs via circRNA — miRNA — mRNA interactions.

doi:10.1016/j.yebeh.2019.08.017

Epilepsy & Behavior 101 (2019) 106743

Two Russian cases of malignant migrating partial seizures of infancy due to KCNT1 mutations

Alexey Kholin[a], Inessa Fedonyuk[b], Anna Antonets[c], Ilya Komar'kov[c], Elena Il'ina[b], Nikolay Zavadenko[a]
[a]*Department of Child Neurology, Neurosurgery and Medical Genetic, Pirogov Russian National Research Medical University, Moscow, Russian Federation*
[b]*Department of Psychoneurology N2, Russian Children Clinical Hospital, Moscow, Russian Federation*
[c]*Center of Medical Genetics "Genomed", Moscow, Russian Federation*

Background: Malignant migrating partial seizures of infancy (MMPSI) or Coppola-Dulac syndrome is severe form of epileptic encephalopathy developing migrating multifocal status epileptic of polymorphic seizure types. This epileptic syndrome has heterogenic etiology including autosomal dominant mutations in gene KCNT1 encodes a sodium-activated potassium channel. OMIM genetic classification for this type of MMPSI is early infantile epileptic encephalopathy, type 14 (EIEE14; 614959).

Methods: DNA sequencing - panel "Hereditary epilepsy" (Next Generation Sequencing on platform IlluminaNextSeq 500, USA) was done for two Russian girls with MMPSI. Diagnose was verified by clinical observation with dynamical video-EEG monitoring investigation ("Encephalan-Video" RM-19/26 "Medicom MTD", Russia). 1,5 Tl MRI (Siemens, Germany) revealed no dysplastic changes.

Results: In two unrelated Russian girls with MMPSI - M.V., 3 years and 3 month old and T.V., 9 month old were newly identified de novo mutations in KCNT1 gene. Girl T.V. has renowned mutation in chromosome 9: 138651532G>A with amino acid substitution Gly288Ser (OMIM: 608167.0010). The girl M.V. has previously not described mutation in 12 exome KCNT1 gene (chr9:138656907C>T, rs752514808) with amino acid substitution Arg356Trp. Mutations were confirmed by Sanger sequencing. Girl M.V. had seizure onset at the age of 4 month with seizures of behavior arrest and tonic versive. Girl T.V. developed seizures at 4,5 months in the manner of behavior arrest and ophthalmo-clonic seizures with hyperemia of face. Both the girls had further developing typical clinical and EEG characteristics of MMPSI. T.V. was resistant to valproates and hormone therapy, aggravation on levetiracetam, oxcarbazepine and barbiturate (pagluferalum-1), but with positive effect to combination of topiramate and benzodiazepine (nitrazepamum). M.V. demonstrated resistance to valproates, lamotrigine, topiramate, levetiracetam, oxcarbazepine, ethosuximide, zonisamide, benzodiazepines and hormone therapy, with weakly positive effect to barbiturate (pagluferalum-1) and rufinamide treatment was started.

Conclusions: KCNT1 is a major disease-associated gene for the MMPSI phenotype. All the children with pharmacoresistant epileptic encephalopathy need complex investigations including dynamic video-EEG monitoring, high quality neuroimaging, but also genetic investigation. Next Generation Sequencing (NGS) methodics - panel