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.

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Possible epigenetic regulatory effect of dysregulated circular RNAs in epilepsy

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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.

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

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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

"Hereditary epilepsy" and whole exome sequencing are more preferable.

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Characterisation of an infantile rat model of de novo status epilepticus: long-term outcomes

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Background: Paediatric status epilepticus (SE) may result from acquired, metabolic, immune, genetic or unknown causes. We characterized an infantile rat model of *de novo* SE to study the pathologic sequelae ignited by unremitting seizures in the immature brain that include atrophy, cognitive deficits and epilepsy.

Methods: SE was induced by unilateral intra-amygdala injection of 2 μg kainic acid (KA) in cortical electrode-implanted postnatal day (P)13 male rat pups. Controls were injected with saline. Astrocytes and microglia activation and Fluoro-Jade-positive degenerating neurons were analyzed by immunohistochemistry and confocal microscopy; neuroinflammation and oxidative stress markers were measured by RTqPCR. Different cohorts of SE-exposed P13 rats were longitudinally video-EEG monitored, exposed to the Morris Water Maze to test learning and memory, and to T2-weighted MRI sequence to determine brain atrophy.

Results: EEG monitored convulsive SE was defined by the appearance of continuous spikes with a frequency >1.0 Hz and an amplitude at least 2.5-fold higher than the standard deviation of the baseline tracing. SE occurred 31.0 ± 2.3 min after KA injection and lasted for 3.5 ± 0.5 h (mean ± SEM, n = 9). Epileptiform events of higher amplitude were recorded in the cortex ipsilateral to injected amygdala vs the contralateral homotypic area. During SE pups displayed masticatory movements, salivation, forelimb myoclonus, loss of posture. Glia activation, induction of the ictogenic cytokines IL-1β and TNF-α and HMGB1, oxidative stress markers were measured in rats (n = 6-7 rats each group) from 2 h to 1 week post-SE. Degenerating neurons were detected in cortex, hippocampus, amydgala, striatum and reticular thalamic nucleus. Spontaneous recurrent seizures (3-5/week) developed around 1 month after SE in about 60% of rats as assessed by video-EEG recording for at least 5 months (n = 19). SE was similar in onset, severity and duration in all animals. MRI showed progressive atrophy in cortical and subcortical regions starting before epilepsy onset. Rats displayed cognitive impairment after epilepsy onset denoting an encephalopathic effect of spontaneous seizures.

Conclusions: This infantile SE rat model can be exploited for mechanistic studies, to test novel drugs and for developing biomarkers of disease onset and progression.

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Paediatric Status Epilepticus: identification of prognostic factors using the new ILAE classification

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Background: Status Epilepticus (SE) is the commonest neurological emergency in childhood. Aim of this study is to report the characteristics of paediatric patients suffering from Status Epilepticus (SE) and their outcome with some considerations to the new classification issued by ILAE.

Methods: We included 173 children treated at "Bambino Gesù" Children's Hospital in Rome (4.35 ± 4.85 years old; follow up 2.74 ± 1.9 years). Multivariate model was constructed to predict neurocognitive outcome, recurrence of SE, development of epilepsy and mortality. Adjusted ORs were calculated with 95% Confidence interval (OR[95%CI]).

Results: We observed a different prevalence of aetiologies for the different semiologies ($p < 0.05$) and for each age-group ($p < 0.05$), overlapping only in part with the recent ILAE classification. After SE, patients developed: 70% epilepsy (drug-resistant in half of them); 20% worsening of neurological exam; 16% cognitive deficit; 16% recurrent SE. At multivariate analysis: SE lasting more than 24 hours have increased risk to develop cognitive (OR = 6.00[2.0-17.1]) or neurologic sequelae (OR = 8.58[2.7-27.1]); the same finding was observed for patient younger than 1 months (cognitive OR = 4.84[1.13-17.3] and neurologic sequelae OR 6.7[1.17-27.1]). The recurrence of SE was associated with genetic (OR = 8.87[2.46-42.63]) and cryptogenic aetiology (OR = 11.5 [2.2-61.8]), as like myoclonic semiology (OR = 6.1[1.1-29.4]). Febrile SE (OR = 0.06[0.008-0.40]) and acute symptomatic aetiology (OR = 0.12 [0.04-0.40]) have a diminished risk to develop epilepsy. Drug-resistant epilepsy post SE was less frequent in focal non-convulsive SE (OR = 0.18 [0.32-0.97]) and acute symptomatic SE (OR = 0.04[0.007-0.26]).

Conclusion: Age at onset and duration of SE are critical independent variables associated to worst neurocognitive outcome. The risk to develop epilepsy is lower after acute symptomatic and febrile SE. Semiology and age of onset are useful to predict aetiology of SE. For this reason, ILAE classification respect the 4 axes seems to be a good step forward.

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Some epidemiological aspects of status epilepticus in the female epilepsy

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Background: Status epilepticus (SE) is a formidable manifestation of epilepsy. The study of the clinical features of polymorphism of