"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

epilepsy from the position of predictors of status epilepticus in female epilepsy is an urgent task.

Methods: The study included 155 women of reproductive age (16-45 years). Inclusion criteria was a verified diagnosis of epilepsy according to the ILAE classification (2017), based on a combination of clinical, electroneurophysiological and neuroradiological survey data. SE present in some women's history was taken into account according to the status epilepticus new ILAE classification of SE (2015).

Results: By type of therapy, patients with epilepsy were divided into 3 groups. The first group consisted of patients receiving monotherapy AED (68 - 44%), the second group included women who are on polytherapy AEDs (67 - 43%). In the third group patients did not receive AEDs in the last six months (20 - 13%). The average age was 25.6 ± 5.5 years and accounted for the optimal reproductive period. Tonic-clonic status epilepticus was found in 6 patients in history, which amounted to 3.9%. Of the patients of the first group - SE in history there was only one case, in the second group - in 5 women, in patients of the third group of status epilepticus in the history was not. One of the predictors of the possible development of SE is the duration of the disease. In our observations in patients of the first group, the average duration of epilepsy was 10 years, in the second group 15 years, in third group 3-5 years. According to our observations, in 17%, provocation of SE was caused by changes in the concentration of AEDs and hormonal status during pregnancy.

Conclusions: The frequency of SE in women of reproductive age is higher with resistant forms of the disease. A special feature in female epilepsy is the provocation of SE by specific hormonally-induced changes. Of particular danger is the status epilepticus during pregnancy and childbirth.

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Status epilepticus; Experience in our intensive care unit since 2014

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Background: Status epilepticus (SE) is a condition secondary to a failure of the control mechanisms for seizure termination or initiation, which leads to abnormally prolonged seizures. It is a condition that can have long-term consequences including neuronal death, neuronal injury, and alteration of neuronal networks. In Europe, the incidence of SE is 9,0 – 27,2 patients per year. Different studies point to a mortality rate between 11 and 37 %, with this rate being higher in refractary SE. As such, SE is a neurological emergency with considerable mortality and morbidity rates.

Methods: We analyzed 40 cases of SE admitted in our intensive care unit (ICU) between 2014 and 2018.

Results: 62,5% of our cases were diagnosed as non-convulsive status epilepticus (NCSE) in the setting of arreactive coma and the remaining 37,5% were diagnosed after seizures. The most common cause of SE was traumatic brain injury (35%). Another cause was drugs, ischemic strokes, intracraneal masses or inadequate epilectic treatment. 4/40 (10%) of NCSE was refractary and 24/40 (60%) was superrefractary. The global mortality rate was measured to be 35%, which increased to 37,5% for patients in super refractary non convulsive status. The average stay in the Intensive Care Unit was 30 days. The most frequent complication (affecting 50% of the patients) was nosocomial pneumonia (pneumonia associated with mechanical ventilation).

Conclusions: SE is a neurologic emergency with high mortality, especially NCSE. For the diagnosis of SE, a high degree of clinical suspicions is necessary, as well as an EEG to confirm the diagnosis. The treatment of epileptic crisis and status epilepticus should be performed in an ICU with cerebral electrical activity monitoring. A multidisciplinary team with neurologist, intensivist and electrophysiologist is required to diagnosis and treat SE.

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Evaluation of our Psychogenic non-epileptic seizure status

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Psychogenic non-epileptic seizures are the most common paroxysmal medical condition misdiagnosed as epilepsy. They significantly affect quality of life and functional status of patients.

Episodes of recurrent, prolonged PNES also called "non-epileptic psychogenic status" and defined as episodes lasting more than 30 minutes and occur in one-third of patients with PNES. Prolonged PNES can mimic Status Epilepticus (SE).

Patients with prolonged PNES are incorrectly evaluated as SE by inexperienced physicians and these patients are intubated and sent to epilepsy centers.

This study included twelve patients with PNES who were admitted to the emergency service for more than 30 minutes or patients with prolonged PNES who were admitted to the emergency room in the intubated state with real SE in mind.

Then, all patients were diagnosed with PNES by monitoring in VEM unit. While 3 patients had mixed seizures (both real and psychogenic) 9 patients had only PNES or PNES status during VEM.

Psychiatric consultation and psychometric tests were applied to all patients.

Patients with psychogenic status are incorrectly admitted to the intensive care unit and undergone unnecessary parenteral antiepileptic drug treatment.

As a result, PNES status and actual SE separation are not easy. Diagnosis can only be made by monitoring the patients in VEM unit. The increase in experienced neurologists related to the subject will facilitate the diagnosis.

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