

within a team consisting of two clinical research fellows, a Professor of molecular genetics, a pediatric neurologist and a genetic counsellor. Analysis of the first eighty families recruited by WERN identified four broad familial endophenotypes: classical GEFS+; borderline GEFS+; unclassified seizures are rare events but were specific (97.5%, but not sensitive) for identifying GEFS+ or GEFS+ borderline families, where they accounted for 24 and 19% of febrile seizures respectively.

Results: Borderline GEFS+ families have many of the characteristics of GEFS+ families—such as prominent atypical febrile seizures and early-onset febrile seizures. However, borderline families have more adults with focal epilepsies (as opposed to idiopathic generalized epilepsies predominating in GEFS+) and double the prevalence of migraine. Atypical febrile seizures are rare events but were specific (97.5%, but not sensitive) for identifying GEFS+ or GEFS+ borderline families, where they accounted for 24 and 19% of febrile seizures respectively.

Discussion: Subcategorizing families with epilepsy is important as it helps target both clinical and research resources. As most families with GEFS+ have no identified causal mutation – the process of endophenotyping (both individuals and families) becomes more important to identify genetic homogeneity.

p301

UNVERRICHT-LUNDBORG DISEASE: REPORT OF A NEW MUTATION

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Introduction: Unverricht-Lundborg disease is the most frequent cause of progressive myoclonic epilepsy. *CSTB* mutations, with cystatin B loss of function, have been described as the major cause of this disease.

Case Report: We present a 33-year-old man with the first epileptic seizure at age 14. He started seeing bright lights followed by a myoclonic seizure. Afterwards he had similar seizures, some with longer duration and consciousness impairment. Occasionally, while walking/running, he had sudden falls, caused by loss of tone in his legs. By the age of 18, upper limb bilateral, irregular myoclonus appeared, worsened by unexpected sounds or bright light. At the age 20 he developed progressive dysarthria, bilateral dismetria and axial ataxia. Currently, he maintains reflexive and negative myoclonic seizures; he has normal cognitive functions, moderate dysarthria, generalized myoclonus, apendicular and truncal ataxia, and an independent gait. Interictal EEG disclosed bilateral synchronous polyspike-and-wave activity, with photosensitivity.

Genetic testing identified a mutation Q22Q in homozygosity that leads to abnormal splicing and partial inclusion of intronic sequence. Potential interference with a splicing consensus region led to the study of the cDNA and subsequent bioinformatics analysis. The data obtained at the RNA level substantiates the causal nature of the *CSTB* genetic lesion and corroborates the existing clinical suspicion. Concordant results showed activation of an alternative splice site with partial inclusion of an intronic sequence.

Conclusions: We describe a patient with a classic clinical Unverricht-Lundborg disease secondary to a new splicing mutation in homozygosity of cystatin B gene.

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p302

FIRST REPORT AND DESCRIPTION OF PATIENTS WITH DRAVET SYNDROME AND GENETIC CONFIRMATION OF MUTATION ON NEURONAL VOLTAGE-GATED SODIUM CHANNEL ALPHA SUBUNIT TYPE 1 GENE IN CHILE

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Purpose: Description of phenotypic and genotypic characteristics of patients with genetic confirmation of neuronal voltage-gated sodium channel alpha subunit type 1 (*SCN1A*) gene mutations and Dravet syndrome (DS) in our country.

Method: Retrospective descriptive analysis of first seizure, clinical evolution, electroencephalographic (EEG), neuroimaging findings and mutation analysis in six patients with DS.

Results: Six unrelated patients had normal psychomotor development prior to seizure onset and moderate to severe development compromise was recorded at last visit. Epilepsy family history was found in 1/6 patients. Subjects first seizure was between 2 and 6 months, 5/6 of them with fever and duration of 15 min or more. All but one had normal neuroimaging. EEG findings were normal in all patients during first year of life. No same mutations were found; two intron mutations and four exon mutations.

Conclusion: First national report of genetic confirmation of *SCN1A* mutations in six patients with classic DS manifestations. Six different point mutations were found in all unrelated patients.

p303

SPECTRUM AND FREQUENCY OF *SCN1A* MUTATIONS IN DRAVET SYNDROME PATIENTS: THE FIRST ATTEMPT OF MOLECULAR DIAGNOSTIC IN POLAND

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Purpose: Dravet syndrome (DS) is a severe epilepsy syndrome characterized by prolonged febrile hemiconvulsions starting in the first year of life with myoclonic, absence and complex partial seizures appearing later accompanied with psychomotor delay resulting in mental retardation.

About 80–90% cases of DS are caused by dominant mutations of the *SCN1A* gene coding for the sodium channel α -1 subunit (Na_v1.1). Because missing knowledge about the frequency of DS and the molecular background of this disorder in Poland we performed the *SCN1A* gene mutations analysis for the group of patients diagnosed as DS. The result of this research—frequency and the type of identified mutations are shown.

Method: The molecular tests of the *SCN1A* gene were performed for 53 patients from different neurological centres in Poland and included sequence analysis and screening for intragenic deletions. DNA sequencing was performed for all, for patients without point mutations, gene deletion/duplication was analyzed by MLPA. The range of identified deletion in *locus* 2q24.3 was established by array CGH.

Results: The *SCN1A* mutations were confirmed in 20 out of 53 DS patients. Nineteen (95%) had point mutations (11 missense, six nonsense, one splice); in one case the deletion of the all *SCN1A* exons was identified. The deletion spans to 1.5 Mb and covers not only *SCN1A* but also adjacent genes (*GSRNP*, *GALNT3*, *TTC212B*, *SCN9A*, *SCN7A* and *XIRP*). For seven patients we were able to perform analysis of parents DNA and confirmed de novo mutations in all cases (point mutations and gene deletion).

Conclusion: The frequency of the *SCN1A* mutations in the analyzed group of DS patients was estimated as 38%. This data were obtained for