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Short Communication

Phenotypic spectrum in families with mesial temporal lobe epilepsy probands

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ABSTRACT

Purpose: The traditional perception of mesial temporal lobe epilepsy (MTLE) as a predominantly acquired disorder is challenged due to emerging evidence of familial aggregation. In this study, we ascertained the extent of familial occurrence of epilepsy in MTLE patients, as well as phenotypic heterogeneity in affected relatives.
Methods: We identified and reevaluated patients with MTLE, treated at Epilepsy Department for a period of two years. All eligible putatively affected relatives were asked to participate in the study. In addition to comprehensive epilepsy interview, they underwent EEG and MRI studies.
Results: 52 patients with MTLE were included; nine of them (17%) had at least one family member with epilepsy. Subsequently, we analyzed nine probands with MTLE and a total of 15 relatives with seizures. Among affected relatives, spectrums of clinical manifestations were observed. Typical MTL seizures were described in five individuals, while other types of focal or generalized tonic-clonic seizures were reported in other ten relatives. A total of seven individuals had febrile seizures. Hippocampal sclerosis was found in three probands and none of the relatives. Two of affected family members had a traumatic brain injury in addition to febrile seizures, prior to the occurrence of their epilepsy.
Conclusion: We demonstrate that familiar occurrence of epilepsy and subsequently putative genetic background, accounts for a substantial proportion MTLE patients. In addition, we foreground the remarkable intra- and interfamilial phenotypic heterogeneity than usually described, displaying the complexity of the genotype-phenotype correlations.

1. Introduction

The etiology of mesial temporal lobe epilepsy (MTLE) remains unknown and traditionally is perceived as an acquired disorder. Lately, this notion is challenged due to emerging evidence of familial aggregation.

Originally, familial mesial temporal lobe epilepsy (FMTLE) was characterized as a benign syndrome with prominent psychic and autonomic seizures and no association with hippocampal sclerosis (HS) or febrile seizures (FS) [1]. The same group subsequently presented clinical and family history data on 20 new families with the uniform benign course [2]. More heterogeneous phenotypes, with mild to severe MTLE, and a variable association with HS and FS, has also been described [3,4]. Currently, a few different subtypes are recognized: benign FMTLE without HS or FS and FMTLE associated with HS and/or FS [5]. A recent study has found that FMTLE accounts for almost one-fifth of newly diagnosed non-lesional MTLE [6].

Several loci have been implicated in the genetic architecture of the FMTLE; main being DEPDC5 [7,8], and SCN1A [9,10].

In our study, we ascertained the extent of familial occurrence in MTLE patients. By describing electroclinical, imaging and family history data on families with MTLE probands, we further highlight phenotypic heterogeneity in affected relatives.

2. Materials and methods

We identified patients with MTLE treated at Epilepsy Department, Clinic of Neurology in Skopje, from January 1, 2014 to December 31, 2015. Selection was made by following criteria for diagnosis of MTLE [11,12]:

(1) Typical auras that consisted of epigastric, autonomic, and/or psychic sensations followed by an arrest of motor activity,

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progressive loss of consciousness, and automatisms of the mouth and hands, with or without secondary generalisation; (2) Interictal or ictal EEG epileptiform abnormalities over temporal or frontotemporal regions; Epileptiform EEG abnormality was not required for diagnosis where there was a clear and typical clinical description of seizures. Possible candidates were identified by reviewing clinical records from the databases of the hospital and were invited for reevaluation visit. Then, they were assessed by two epileptologists who were participating in the study (E.C. and G.K.T) and candidates that fulfilled aforementioned criteria were included. A meticulous family pedigrees were made and all eligible putatively affected relatives were asked to participate in the study. All MTLE patients and accessible relatives underwent 20-min standard EEG recording during wakefulness and when possible, 2-h EEG during diurnal sleep induced by sleep deprivation. Prolonged video-EEG monitoring with a recording of typical seizures was obtained in five individuals. MRI images using 1, 5 T scans were acquired in all proband and available affected relatives. Scans were evaluated by visual inspection for evidence of hippocampal sclerosis, as well as other abnormalities.

Written informed consent was obtained from all participants or their guardians in the case of minors. The study was approved by the Ethics Committee of Faculty of Medicine, Skopje, R. Macedonia.

3. Results and discussion

Of 52 patients with MTLE, nine (17%) had at least one family member with epilepsy. Subsequently, in nine unrelated families, in

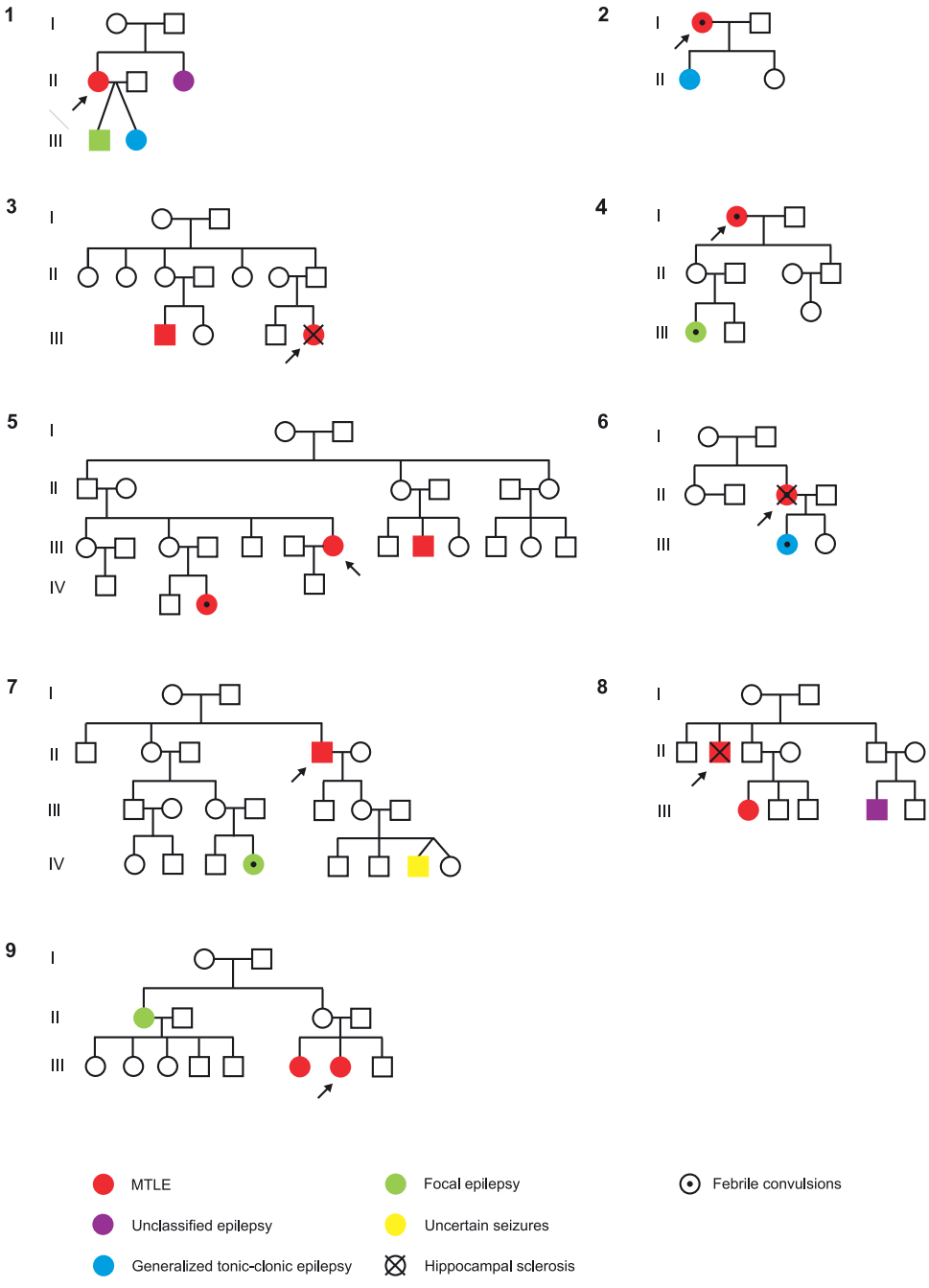

Fig. 1. Pedigrees of families of probands with mesial temporal lobe epilepsy.