

HISTOPATHOLOGIC SUBSTRATES FOR EPILEPTOGENICITY IN CORTICAL MALFORMATIONS

Epileptogenicity of Focal Malformations due to Abnormal Cortical Development: Direct Electrocorticographic–Histopathologic Correlations

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PURPOSE: Malformations due to abnormal cortical development (MCDs) are common pathologic substrates of medically intractable epilepsy. The in situ epileptogenicity of these lesions as well as its relation to histopathologic changes remains unknown. The purpose of this study was to correlate the cellular patterns of MCDs with the expression of focal cortical epileptogenicity as assessed by direct extraoperative electrocorticographic (ECoG) recordings by using subdural grids.

METHODS: Fifteen patients with drug-resistant focal epilepsy due to pathologically confirmed MCDs who underwent subdural electrode placement for extraoperative seizure localization and cortical mapping between 1997 and 2000 were included in the study. Areas of interictal spiking and ictal-onset patterns were identified and separated during surgery for further pathologic characterization (cellular and architectural). Three pathologic groups were identified: type I, architectural disorganization with/without giant neurons; type IIA, architectural disorganization with dysmorphic neurons; and type IIB, architectural disorganization, dysmorphic neurons, and balloon cells (BCs). The focal histopathologic subtypes of MCDs in cortical tissue resected were then retrospectively correlated with in situ extraoperative ECoG patterns.

RESULTS: Cortical areas with histopathologic subtype IIA showed significantly higher numbers of slow repetitive spike pattern in comparison with histopathologic type I ($P = 0.007$) and normal pathology ($P = 0.002$). The ictal onset came mainly from cortical areas with

histopathologic type IIA (nine of 15 patients). None of the seizures originated from neocortical areas that showed BC-containing MCDs (type IIB).

CONCLUSIONS: This study shows that areas containing BCs are less epileptogenic than are closely located dysplastic regions. These results suggest a possible protective effect of BCs or a severe disruption in the neuronal networks in BCs containing dysplastic lesions. Further studies are needed to elucidate the nature and the potential role(s) of BCs in MCD-induced epileptogenicity.

COMMENTARY

Malformations due to abnormal cortical development not uncommonly constitute the pathologic substrate for pharmacoresistant epilepsy treated with surgical resection. At the histologic level, these malformations demonstrate disrupted cortical architecture, as well as various cellular abnormalities—dysmorphic neurons, giant neurons, and so-called balloon cells (cells with features of neurons and glia that possess large portions of opalescent cytoplasm and eccentric nuclei). These anomalies of cellular constituents vary from patient to patient, and within the same patient, the resected tissue shows regional differences in cellular composition within the cortical malformation itself. This study provides a detailed correlation between specific cellular abnormalities ultimately seen histologically in the resected tissue and the electrophysiologic abnormalities previously recorded by subdural grids sitting atop this tissue during pre-resection monitoring.

The authors analyze 15 cases, characterizing the pattern and location of interictal and ictal electrocorticographic discharges and the histopathologic findings that localize to the overlying contacts of the subdural grids. Interictal discharges, derived from sampled epochs, were categorized into one of four patterns: isolated spikes, repetitive spikes, paroxysmal fast activity, or runs of slow repetitive spikes. Ictal-onset patterns were cataloged as paroxysmal fast activity, repetitive spiking, or paroxysmal fast discharges intermixed with repetitive spiking. Each region of resected tissue corresponding to a contact of the subdural grid was classified into one of



three histologic patterns: architectural disorganization with or without giant neurons, architectural disorganization with dysplastic neurons, or architectural disorganization with balloon cells.

Correlation between electrocorticographic findings and histologic features showed that higher total spike counts and isolated spikes tended to occur more frequently in areas with dysmorphic neurons, and slow repetitive spikes occurred significantly more frequently in cortical areas marked by this type of histopathology. As well, ictal-onset zones were localized to areas containing dysmorphic neurons in the majority of patients (the most common patterns being paroxysmal fast activity with or without repetitive spikes) but never occurred in areas containing balloon cells. The ictal-onset zone was co-localized

with areas demonstrating the slow repetitive spike pattern interictally.

The analyses undertaken in this report provide the basis for a better understanding of the pathophysiologic basis for the differential epileptogenicity of malformed cerebral cortex and may indeed shed light on mechanisms underlying cortical epileptogenicity in general. Furthermore, careful correlation between electrophysiologic findings in the epilepsy monitoring unit and the histopathology of resected epileptogenic tissue may eventually guide surgical decision making to optimize clinical outcomes for patients with intractable epilepsy caused by malformations of cerebral development.

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