EDITORIAL

Nonlesional Focal Epilepsy: A Challenge from Genes to Surgery

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This month Nguyen and colleagues[1] present the results of a retrospective study on the prevalence of nonlesional epilepsy in a tertiary epilepsy center.

The study's findings bring to light an especially difficult group of patients, from diagnosis to management. These authors show that one third of patients in a tertiary epilepsy center do not have any visible structural abnormalities on magnetic resonance imaging (MRI), and that half of these have pharmacoresistant epilepsy.

In this retrospective study many of the images were obtained with 1.5 Tesla MRI, which is associated with a lower sensitivity to detect small lesions. Strandberg and colleagues reported that in up to 20% of cases small lesions not visible with 1.5 Tesla MRI may be demonstrated with 3 Tesla MRI images[2]. But even if all patients had 3 Tesla MRI, which is currently clinically available in some epilepsy centers, approximately one quarter of adults with epilepsy would not have a clear structural epileptogenic lesion. This is a significant problem for patients with pharmacoresistant epilepsy, in whom epilepsy surgery may be the only way to manage seizures. Since no structural abnormalities are seen, many of these patients, especially those with extra-temporal lobe epilepsy, need further investigation in the form of intracranial electroencephalogram recordings in order to determine with precision the epileptogenic focus and to guide surgical planning.

Nonlesional epilepsy may be genetically determined, and most familial cases are not associated with any specific structural abnormalities. This is the case in autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE). Luckily, most of these patients have seizures that can be easily controlled on carbamazepine. Different genes have been linked to ADNFLE[3-9], but no specific gene or mutation is associated with structural abnormalities, nor can the genetic alterations predict which part of the frontal lobes will bear the epileptogenic focus. Therefore in the rare case of pharmacoresistant ADNFLE[10], investigation with intracranial recording may be necessary.

On the other hand findings of structural abnormalities in familial mesial temporal lobe epilepsy are controversial. For instance one group found no abnormalities in 34 patients from 20 different families[11] while another group found hippocampal atrophy in 57% of 84 patients (22 families) and 34% of unaffected family members[12,13]. In both studies visual MRI inspection was done, however, quantitative hippocampal volumetry was also used in the Kobayashi studies. Although patients in the latter studies appear to have had more severe epilepsy, use of quantitative image analysis may, at least in part, explain the different results.

Quantitative measurements of volume and signal intensity can reveal abnormal epileptogenic tissue not previously detected on simple visual analysis. For instance, hippocampal or entorhinal cortex volumetry can point to the abnormal side in up to 25% of "image negative" temporal lobe cases[14]. Furthermore, when total volume quantification is not helpful, advanced quantitative methods based on surface shape models may point to the abnormal structure[15,16].

In cases of focal cortical dysplasia, the abnormal lesion may not be seen on clinical MRI exams, even when obtained with higher field strengths. In such cases, identification of histologically proven focal cortical dysplasia may be increased by 30% if computer-based models of cortical thickness, blurring and tissue intensity derived from 3D T1 weighted sequences and combined into a single composite map are used[17].

The study by Nguyen and colleagues demonstrates well the current limitations of MRI in focal epilepsy. As the authors point out, this knowledge alone should be of help to some nonlesional patients in their attempts to fully understand their condition.[1]

The findings also highlight the need to continue efforts to move special imaging techniques out of the labs and into the clinical setting. Imaging processing can reveal subtle abnormalities not previously identified by routine visual inspection and may ultimately lower the proportion of "image negative" cases of focal epilepsy. However, the various forms of imaging processing are highly specialized and time-consuming investigations, which are not routinely used and are performed mainly under investigation protocols paid for with research funds. It is not yet clear how much added benefit imaging processing will bring to the clinical setting, but this is a path that will certainly need to be followed in the coming years.

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