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Review

Look back to leap forward: The emerging new role of magnetoencephalography (MEG) in nonlesional epilepsy

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HIGHLIGHTS

- MEG in the form of Magnetic Source Imaging (MSI) can increase the diagnostic yield of MRIs.
- MSI-guided re-review of supposedly negative MRIs may reveal significant pathology including focal cortical dysplasia (FCD).
- Clinical magnetoencephalographers ("MEG practitioners") and the referring epilepsy teams ("MEG users") should change their evaluation protocols accordingly.

ABSTRACT

This review considers accumulating evidence for a new role of MEG/MSI in increasing the diagnostic yield of supposedly negative MRIs, and suggests changes in the use of MEG/MSI in presurgical epilepsy evaluations. Specific alterations in practice protocols for both the MEG practitioner (i.e. physician magnetoencephalographer) and MEG user (i.e. referring physician) are proposed that should further enhance the overall value of MEG/MSI. Although advances in MEG analysis methods will likely become increasingly assisted by computers, interpretive competency and prudent clinical judgment remain irreplaceable.

Contents

1. Introduction

Resective epilepsy surgery (Wiebe et al., 2001; Engel et al., 2003, 2012) is the best therapeutic option (and the only potential cure) for many persons with pharmacoresistant focal epilepsy (Engel, 2008; Haneef et al., 2010; Wiebe and Jetté, 2012; Englot

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et al., 2012). Resultant seizure freedom or even "worthwhile improvement" (Engel et al., 1993) leads to meaningful improvements in the quality of life (Fiest et al., 2014). However, even among the small minority of potential surgical candidates who do get referred for presurgical evaluation (Engel et al., 1993; Luoni et al., 2011; Kerr, 2012), up to 25% of those evaluated invasively ultimately do not have a resection (National Association of Epilepsy Centers, 2012 self-reported data). Furthermore, surgical outcomes vary considerably (Ansari et al., 2010a,b; Englot et al., 2013; Najm et al., 2013), and are least favorable in patients with nonlesional extratemporal epilepsy (NLETE) (Bien et al., 2009; Noe et al., 2013; Schneider et al., 2013). In fact, in this most challenging group, only 11% of those initially evaluated for surgery may have ultimately an operation with "an excellent" long-term outcome (Noe et al., 2013). More resections in all evaluated (non-invasively and invasively) and better overall outcomes require a more successful identification and accurate delineation of epileptogenic zones (Rosenow and Luders, 2001; Najm et al., 2013). This necessitates further improvements in presurgical evaluations (Velez-Ruiz and Klein, 2012; So and Lee, 2014), particularly in truly MRI-negative cases, as illustrated in Fig. 1.

One of the more recent attempts to improve surgical outcomes in MRI-negative epilepsy includes the sophisticated diagnostics of single photon emission tomography (SPECT) (Sulc et al., 2014). However, "improved statistical parametric SPECT mapping of the ictogenic zone" was not associated with better surgical outcomes in this group (Sulc et al., 2014; Henry, 2014). Previous attempts with MR spectroscopy (Suhy et al., 2002), EEG-fMRI (Moeller et al., 2009) or even 7T MRI (Pan et al., 2013) mostly added to the understanding of the problem, but not necessarily to its practical alleviation. In practice, focal cortical dysplasia (FCD) (Taylor et al., 1971; Blumcke et al., 2011) is the most frequently identified

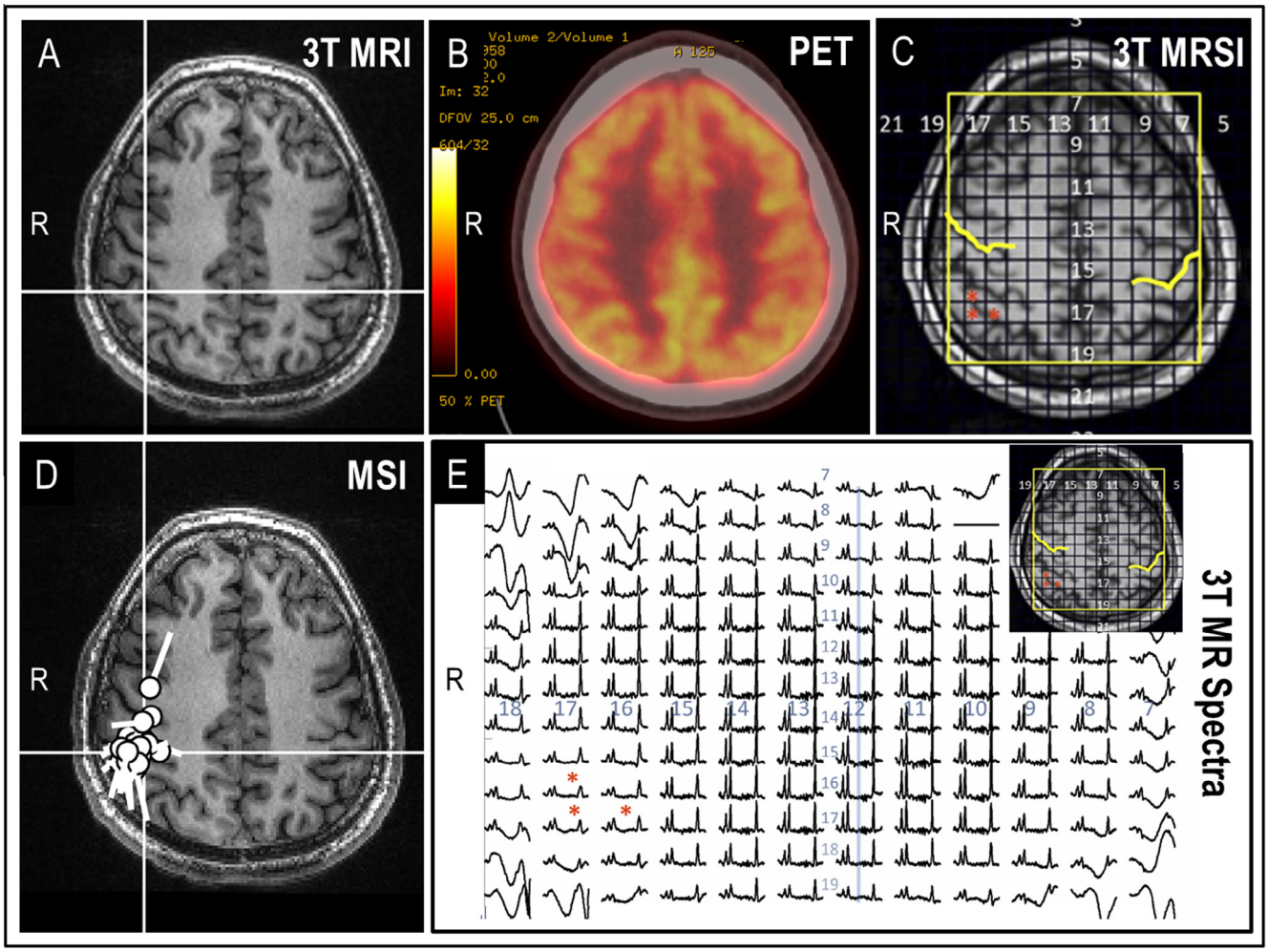

Fig. 1. An illustrative patient with a truly NLETE (i.e. no structural abnormalities on a 1.5 and 3.0 T brain MRI with epilepsy protocol, including their MSI-guided re-review), but with a positive congruent MSI and MRS. *Clinical History: A* 29-year-old male with a history of a fall in childhood (his only known seizure risk factor!), headaches, hypertension, depression, burns on his chest (a result of the gang violence), lumbar spine surgery (2012), prolonged PR interval and epileptic seizures since the age of 5 years. He had failed two (lamotrigine, carbamazepine) and continues to experience seizures on his current three (divalproex, levetiracetam, topiramate) antiepileptic medications. In consideration of epilepsy surgery, he underwent a standard presurgical evaluation that included a 1.5T and 3.0T brain MRI with epilepsy protocols, routine EEG, video-EEG, Neuropsychological Testing (NPT), FDG-PET and MEG-EEG. He also kindly participated in a research MRS study (PI: Julie W. Pan, MD, PhD) comparing a 3T (was able to remain still only for this part of the scanning!) and 7T magnet's sensitivity to detect cerebral metabolic abnormalities and his MRSIs were available for a *post hoc* consideration at multidisciplinary epilepsy patient management conference (MEPMC). *Pertinent diagnostic investigations*: An example of a normal 3T brain MRI with epilepsy protocol (A), normal FDG-PET (B), but positive findings from an MSI (D) indicative of significant cerebral dysfunction and epileptic potential expressed through the right inferior parietal lobule and a congruent 3T MRS (C; E) indicative of significant metabolic abnormality in the *right inferior parietal lobule*. Yellow lines on the scout image of panel E and panel C outline estimated position of the central sulcus (CS). (*MRS images on panels C and E were kindly provided by Julie W. Pan, MD, PhD; University of Pittsburgh Comprehensive Epilepsy Center, Pittsburgh, PA; methods used were previously published in* Pan et al., 2013). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)