Journal of Neuroscience Methods 260 (2016) 283–291

Contents lists available at ScienceDirect

Journal of Neuroscience Methods

journal homepage: www.elsevier.com/locate/jneumeth

Clinical neuroscience

Non-invasive brain mapping in epilepsy: Applications from magnetoencephalography

Khalid Hamandi[b,*], Bethany C. Routley[a], Loes Koelewijn[a], Krish D. Singh[a]

[a] Cardiff University Brain Research Imaging Centre, School of Psychology, Cardiff University, Cardiff CF10 3AT, United Kingdom
[b] The Alan Richens Welsh Epilepsy Centre, University Hospital of Wales, Cardiff CF5 6LR, United Kingdom

HIGHLIGHTS

- MEG is ideally suited to study epilepsy at the network level.
- New analysis strategies include spatial filters, time–frequency analysis for cortical dynamics and graph theory applications for connectivity.
- Novel MEG analyses approaches show altered cortical dynamics and widespread network alterations in focal and generalised epilepsies.
- Identification of regional network abnormalities may have a role in epilepsy surgery evaluation.

ARTICLE INFO

Article history:
Received 29 June 2015
Received in revised form
17 November 2015
Accepted 18 November 2015
Available online 28 November 2015

Keywords:
Magnetoencepahlography
Epilepsy
Cortical osciilations
Connectivity
Graph theory

ABSTRACT

Background: Non-invasive in vivo neurophysiological recordings with EEG/MEG are key to the diagnosis, classification, and further understanding of epilepsy. Historically the emphasis of these recordings has been the localisation of the putative sources of epileptic discharges. More recent developments see new techniques studying oscillatory dynamics, connectivity and network properties.
New method: New analysis strategies for whole head MEG include the development of spatial filters or beamformers for source localisation, time–frequency analysis for cortical dynamics and graph theory applications for connectivity.
Results: The idea of epilepsy as a network disorder is not new, and new applications of structural and functional brain imaging show differences in cortical and subcortical networks in patients with epilepsy compared to controls. Concepts of 'focal' and 'generalised' are challenged by evidence of focal onsets in generalised epileptic discharges, and widespread network changes in focal epilepsy. Spectral analyses can show differences in induced cortical response profiles, particularly in photosensitive epilepsy.
Comparison with existing method: This review focuses on the application of MEG in the study of epilepsy, starting with a brief historical perspective, followed by novel applications of source localisation, time–frequency and connectivity analyses.
Conclusion: Novel MEG analyses approaches show altered cortical dynamics and widespread network alterations in focal and generalised epilepsies, and identification of regional network abnormalities may have a role in epilepsy surgery evaluation.

Contents

* Corresponding author. Tel.: +44 2920743807.
E-mail address: hamandik@cf.ac.uk (K. Hamandi).

http://dx.doi.org/10.1016/j.jneumeth.2015.11.012
0165-0270/

1. Introduction

Neurophysiological EEG recordings have defined our understanding of seizure and epilepsy classification (International League Against Epilepsy (ILAE), 1989, 1981). The key electrophysiological features of interictal (between seizure) and ictal (seizure) discharges remain the paramount clinical tool in supporting and classifying an epilepsy diagnosis. Advances in computational processing and the fine temporal resolution of both EEG and magnetoencephalography (MEG) have engendered an increase in fundamental research probing the mechanisms underlying these epileptic features, as well as novel epilepsy markers.

New analysis methods and revised concepts in epileptology have seen a shift from studies of localisation of EEG/MEG epileptic phenomena towards studies of oscillatory dynamics, neuronal coupling and connectivity. These studies are challenging some of the assumptions around epileptic seizure classification, particularly the distinction between focal and generalised seizures, and support the notion of epilepsy as a network disorder measurable as an abnormal interplay in large scale brain dynamics (Engel et al., 2013; Richardson, 2012). These new techniques have potential for development of novel diagnostic and prognostic disease biomarkers, and better pre-surgical localisation methods and predictions of surgical outcome.

2. Magnetoencephalography (MEG)

MEG is an established non-invasive brain imaging technique that has very much come of age over the past two decades with commercial systems that allow whole head neurophysiological recordings. The first MEG measurements in 1972, included the measurement of abnormal waveforms in a patient with epilepsy (Cohen, 1972), and showed potential for study in this area. Until the 1990s a single sensor, or arrays with few sensors covering only part of the head, were available. This was a limit to the utility of MEG, increasing recording times and limiting inferences and localisation methods. Current MEG systems with a high number of sensors (~300), arranged in a helmet-like dewar, allow whole-head recordings of rest or task related activities and projection into source space. It is this advance in MEG scanners and associated ease with which recordings can be made that have driven many new applications and studies (Braeutigam, 2013; Gross et al., 2013).

MEG measures weak perturbations in the magnetic fields generated at the scalp surface by underlying electrical activity in the brain. As signals in EEG and MEG arise from the synchronous firing of large numbers of neurons, these techniques by their nature emphasize synchronous activity across several centimetres of the cortex. The millisecond temporal resolution of both EEG and MEG make them ideal for the study of spontaneous, evoked and induced oscillatory processes at different frequency bands. In EEG, source localisation accuracy is limited due to the unknown individual conductivity profile of the head and the problem of volume conduction. Connectivity analysis is confounded by interference between neighbouring or distant sensors, and contamination from neural activity detected by the chosen reference electrode. This can create spurious synchrony between electrodes that does not reflect the organisation of underlying brain sources (Schoffelen and Gross, 2009). Furthermore underlying muscle or eye movement artefact can confound EEG, particularly in higher frequencies (Yuval-Greenberg et al., 2008). MEG is less susceptible to these issues (van den Broek et al., 1998). Furthermore MEG is reference free, giving distinct advantages over EEG in the connectivity analyses. The relative insensitivity of MEG to radial sources in a spherical volume conductor is sometimes put forward as a drawback of MEG. However only a very small percentage of cortex (~5) in thin strips (~2 mm wide) at the crests of gyri present a purely radial source (Hillebrand and Barnes, 2002); and source depth is a greater liming factor than orientation (Hillebrand and Barnes, 2002).

3. Localisation of seizure-related activity

3.1. Dipole source models

The source localisation of epileptiform activity has been the main clinical application of MEG, and it is established in many clinical epilepsy surgery centres (Ebersole, 1997). Source localisation methods can be divided broadly into three methodological categories (Leijten and Huiskamp, 2008). The simplest involves modelling single or multiple dipolar sources at varying positions and strengths in the brain. The second category evokes distributed current models in which the varying model parameter is the strength of a series of dipoles of fixed orientation and location within the cortical mesh. Third, spatial scanning methods use a filter to search for dipoles over all possible source points in the brain, maximising the signal at a given position and minimising noise or cross-talk from other locations.

The equivalent current dipole (ECD), or discrete source analysis remains one of the most popular source localisation methods for interictal spikes in clinical usage (Knowlton, 2006; Ochi and Otsubo, 2008) mainly due to its availability in clinically approved commercial analysis packages. Each ECD represents a single extended brain region, comprising position and moment, and is considered valid when this explains the majority of the signal recorded at sensors. Single or multiple dipoles are fitted to the EEG/MEG data these can vary in position and strength. Concordance of MEG ECD with intracranial EEG recordings has been shown (Oishi et al., 2002; Rose et al., 1987) and surgical outcome (Genow et al., 2004); and MEG ECD can resolve the likely focal origin in cases with secondary bilateral synchrony (Chang et al., 2009). Disadvantages of ECD include an element of subjectivity in selecting plausible sources based on differing criteria for 'goodness of fit', poor estimates if signal to noise is low and a failure to capture temporal dynamics or network properties of epileptic spikes.

In the distributed source model EEG/MEG channel level data is projected to the "source" space (intracranial space) by placing an equivalent current dipole (ECD) in each node (vertex) of a calculated surface mesh, and estimating a distributed solution for the inverse problem constrained to these dipole positions. The surface mesh having been calculated from the MRI brain scan using a realistic head model (Dale and Sereno, 1993). Current dipoles are considered at all candidate locations within the surface mesh in order to find the optimal solution to fit the observed data. The minimum norm estimate (MNE) is one of the most well-known distributed source models (Hamalainen and Ilmoniemi, 1994). In