Recording of ictal epileptic activity using on-scalp magnetoencephalography

Odile Feys, MD[1,2], Pierre Corvilain, PhD[2], Audrey Van Hecke, MD[3], Claudine Sculier, MD[4], Estelle Rikir, MD, PhD[1], Benjamin Legros, MD[1], Nicolas Gaspard, MD, PhD[1], Gil Leurquin-Sterk, MD, PhD[2,6], Niall Holmes, PhD[5], Matthew Brookes, PhD[5], Serge Goldman, MD, PhD[2,6], Vincent Wens, PhD[2,7], Xavier De Tiège, MD, PhD[2,7]

[1] Université libre de Bruxelles (ULB), Hôpital Universitaire de Bruxelles (HUB), CUB Hôpital Erasme, Department of Neurology, Brussels, Belgium.

[2] Université libre de Bruxelles (ULB), ULB Neuroscience Institute (UNI), Laboratoire de Neuroimagerie et Neuroanatomie translationnelles (LN^{2}T), Brussels, Belgium.

[3] Université libre de Bruxelles (ULB), Hôpital Universitaire de Bruxelles (HUB), Hôpital Universitaire des Enfants Reine Fabiola (HUDERF), Department of Pediatric Neurology, Brussels, Belgium.

[4] Université libre de Bruxelles (ULB), Hôpital Universitaire de Bruxelles (HUB), CUB Hôpital Erasme, Department of Pediatric Neurology, Brussels, Belgium.

[5] University of Nottingham, School of Physics and Astronomy, Sir Peter Mansfield Imaging Centre, Nottingham, United Kingdom.

[6] Université libre de Bruxelles (ULB), Hôpital Universitaire de Bruxelles (HUB), CUB Hôpital Erasme, Department of Nuclear Medicine, Brussels, Belgium.

[7] Université libre de Bruxelles (ULB), Hôpital Universitaire de Bruxelles (HUB), CUB Hôpital Erasme, Department of Translational Neuroimaging, Brussels, Belgium.

Corresponding author: Dr Odile Feys, Laboratoire de Neuroanatomie et Neuroimagerie Translationnelles (LN^{2}T), ULB Neuroscience Institute (UNI), Université libre de Bruxelles (ULB), 808 Lennik Street, Brussels, Belgium. Telephone: +3225555588. E-mail: odile.feys@ulb.be

Key words

Ictal recording, seizure, magnetoencephalography, optically pumped magnetometers

In drug-resistant focal epilepsy (DRFE), seizures are infrequent and unpredictable, requiring prolonged recordings to identify the seizure-onset zone (SOZ).(1) Cryogenic magnetoencephalography (MEG) is thus scarcely used for ictal recordings but rather to detect interictal epileptiform discharges (IEDs) and localize the irritative zone (IZ), which may differ from the SOZ.(1) On-scalp MEG based on a new-generation, cryogenic-free magnetic sensors, "optically-pumped magnetometers" (OPM-MEG), allows successful localization of IEDs with higher amplitude and signal-to-noise ratio (SNR) than cryogenic MEG.(2) Although OPM-MEG has clear advantages (i.e., on-scalp recording, increase in SNR, free head movements (3)) over cryogenic MEG to record ictal discharges, no study has demonstrated the ability of OPM-MEG to detect ictal discharges.

We report on a 10-year-old boy suffering from DRFE (>5 seizures/day) who underwent on-scalp ictal and interictal video-OPM-MEG recording at rest (1h) and during hyperventilation as a seizure activation procedure (3min). Hôpital Erasme's Ethics Committee approved this study (P2019/426). The patient and his legal representative gave written informed consent.

Twenty-four triaxial OPMs (QZFM-G3, QuSpin; sampling frequency: 1200Hz) were used alongside video recording (LifeCam Cinema, Microsoft Corporation) within a magnetically shielded room (OPM-Compact MuRoom, Cerca Magnetics Limited; remnant field <1-2nT after degaussing and active field nulling (4)). MRI/OPM co-registration was based on 3D optical scanning (EinScan, Shining 3D; Figure A-B). See (2) for on-scalp OPM placement, signal analysis, and source localization methods. IEDs were averaged based on signal morphology and sensor topography and brain source was localized at the peak of average IED. The SOZ was localized by imaging brain sources' amplitudes (Hilbert envelope after 13-40Hz band-pass filtering) averaged over the first 500ms of each seizure. Mean amplitude of entire seizures, of preceding background activity (devoid of IEDs), and their ratio (seizure SNR) were compared

during rest and hyperventilation using Welch's unpaired t-tests at the sensor with maximal ictal amplitude.

Two types of IEDs emerged amongst >600 IEDs: ~70% of left mesio-occipital IEDs originating from the left cuneus and ~30% of left temporo-occipital IEDs from the left supramarginal gyrus (Figure C-D). Fifteen spontaneous and six hyperventilation-induced seizures appeared as transient low-voltage fast activity (LVFA) followed by 3-4 Hz spike-wave discharges originating from multiple regions (left frontal, n=3; temporal, n=1; parietal, n=9; occipital, n=5; right parietal, n=2; occipital, n=1; see Figure C-D). Ten seizures were accompanied by eye, palpebral or head movements (Supplementary video). Hyperventilation led to higher seizure and background amplitudes (seizure, 1.92 ±0.04pT; background, 0.69 ±0.02pT) than rest (seizure, 1.49 ±0.05pT; background, 0.52 ±0.03pT, $p<0.003$). SNR was similar (hyperventilation, 2.79 ±0.07; rest, 2.97 ±0.19; $p=0.43$).

Stereo-electroencephalography (SEEG; 16 electrodes over posterior areas) confirmed multifocal SOZ (Figure E). Ictal patterns consisted in brief focal LVFA (50ms) with rapid propagation to several electrodes, followed by low-frequency periodic discharges.

This case study demonstrates that OPM-MEG can detect ictal discharges in a school-aged epileptic child with DRFE, with sufficient SNR to record ictal discharges from multiple neocortical areas even during seizure-related movements.

The absence of simultaneous OPM-MEG/SEEG recording or comparison with cryogenic MEG (unavailable at the time of recording due to technical issues) prevents proper estimation of OPM-MEG localization accuracy for ictal discharges. Still, posterior SOZ and IZ from OPM-MEG colocalized with those of SEEG recordings. The frontal SOZs were not observed with SEEG as no frontal electrodes were implanted (OPM-MEG results unavailable for implantation planning) nor with scalp-EEG, which is congruent with the better detectability of frontal

discharges with cryogenic MEG.(5) As a limited OPM sampling of brain activity could impede the detection of some epileptiform discharges, developing whole-scalp-covering OPM-MEG is of critical importance.

Thanks to its many advantages over cryogenic MEG, OPM-MEG allows prolonged recordings and hyperventilation procedures. This case paves the way towards the use of video-OPM-MEG for ictal recordings in epileptic patients.

Acknowledgments

O.F. is supported by the Fonds pour la formation à la recherche dans l'industrie et l'agriculture (FRIA, Fonds de la Recherche Scientifique (FRS-FNRS), Brussels, Belgium). P.C. is supported by the Fonds Erasme (Convention « Alzheimer », Brussels, Belgium). X.D.T. is Clinical Researcher at the FRS-FNRS.

The OPM-MEG project at the Hôpital Universitaire de Bruxelles and Université libre de Bruxelles is financially supported by the Fonds Erasme (Projet de Recherche Clinique et Convention « Les Voies du Savoir 2 ») and by the FRS-FNRS (Crédit de Recherche: J.0043.20F, Crédit Équipement: U.N013.21F).

The authors would also like to thank QuSpin, Magnetic Shields Limited and Cerca Magnetics Limited for their help and support.

Competing interests

N.H. and M.J.B. hold founding equity in Cerca Magnetics Limited, a spin-out company whose aim is to commercialize aspects of OPM-MEG technology. The remaining authors have no conflicts of interest.

Author Contribution

OF and XDT contributed to the conception and design of the study; OF, PC, VW and XDT contributed to the acquisition and analysis of data; OF, PC, AVH, CS, ER, BL, NG, GLS, NH, MB, SG, VW and XDT contributed to manuscript drafting or revision.

References

1. Rosenow F, Luders H. Presurgical evaluation of epilepsy. Brain. 2001;124(Pt 9):1683-700.
2. Feys O, Corvilain P, Aeby A, Sculier C, Holmes N, Brookes M, et al. On-Scalp Optically Pumped Magnetometers versus Cryogenic Magnetoencephalography for Diagnostic Evaluation of Epilepsy in School-aged Children. Radiology. 2022:212453.
3. Boto E, Hill RM, Rea M, Holmes N, Seedat ZA, Leggett J, et al. Measuring functional connectivity with wearable MEG. Neuroimage. 2021;230:117815.
4. Holmes N, Rea M, Chalmers J, Leggett J, Edwards LJ, Nell P, et al. A lightweight magnetically shielded room with active shielding. Sci Rep. 2022;12(1):13561.
5. Ossenblok P, de Munck JC, Colon A, Drolsbach W, Boon P. Magnetoencephalography is more successful for screening and localizing frontal lobe epilepsy than electroencephalography. Epilepsia. 2007;48(11):2139-49.

Figure. A. OPMs housed in homemade 3D-printed sensor mounts sewn on a EEG-like cap, with homemade 3D-printed top covers with a reflective sticker dedicated to optical digitization. **B.** Left and posterior views of OPM positions relative to the scalp and cortical surface, after co-registration with structural brain MRI. **C.** Samples of OPM-MEG signals illustrating background activity devoid of epileptiform discharges (2sec; left), two types of IEDs (1sec; middle; most common type 1 circled in blue; type 2 in yellow) and ictal activity (10sec; right; onset circled in green). **D.** Source-localized OPM-MEG maps of the averaged IEDs (type 1, blue; type 2; yellow) and of each ictal onset (green) are displayed beneath these signals on axial (left), coronal (middle), and sagittal (right) MRI slices. **E.** SEEG localization of ictal onsets zones (orange dots) displayed on axial slices of co-registered preoperative T1-weighted brain MRI and postoperative brain CT scans.