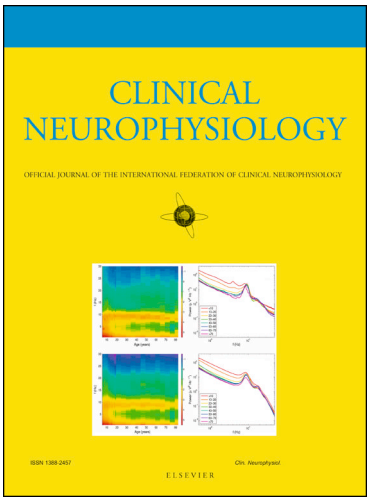

Editorial

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Arjan Hillebrand, William Gaetz, Paul L. Furlong, Alida A. Gouw, Cornelis J. Stam

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Editorial

Practical guidelines for clinical magnetoencephalography – Another step towards best practice

Arjan Hillebrand[a,*], William Gaetz[b], Paul L. Furlong[c], Alida A. Gouw[a,d], Cornelis J. Stam[a]

a) Department of Clinical Neurophysiology and Magnetoencephalography Center, VU University Medical Center, Amsterdam, The Netherlands
b) Department of Radiology, Children's Hospital of Philadelphia, Philadelphia, USA
c) Aston Brain Centre, School of Life and Health Sciences, Aston University, Birmingham, UK
d) Alzheimer Center & Department of Neurology, VU University Medical Center, Amsterdam, The Netherlands

* Corresponding author.

The first successful recordings of electrical activity from the human brain using scalp EEG were performed nearly a century ago (Berger, 1929). Its clinical relevance, particularly for epilepsy, was realized and established within a few years. Since then, scalp EEG has found many applications in neurological and neuropsychiatric disorders (Schomer et al., 2018). However, the limitations of EEG were already acknowledged in these early years, notably by one of its pioneers, Edgar Adrian, who wrote "*With present methods the skull and the scalp are too much in the way, and we need some new physical method to read through them*" (Adrian, 1944). It took another 40 years before such a technique, Magnetoencephalography (MEG), was developed (Cohen, 1968, 1972). MEG records the extracranial magnetic fields that are induced, unperturbed by the skull and scalp, by the electrical activity in the brain. Further developments in analysis approaches and hardware, particularly the availability of whole-head systems and the increases in computing power that are needed to display and analyze these spatially- and temporally-rich signals, have ensured that MEG is now a mature technique. It has an important clinical role in epilepsy, where it is used for diagnosis and for the presurgical evaluation of patients with refractory epilepsy who are candidates for neurosurgical treatment. During this presurgical workup, MEG is used to generate an hypothesis about the epileptogenic zone, i.e., the minimum area that needs to be resected in order to achieve seizure freedom (Luders et al., 2006), and to establish eloquent cortex that needs to be spared because of its involvement in sensation, motor function, or language.

A question that can justifiably be asked is: why is it that despite the obvious advantages of MEG and its close relationship with EEG, that there are not many more established clinical applications of MEG? In particular: why is MEG not used more widely in epilepsy or neurodegenerative and neuropsychiatric disorders (Stam, 2010)?

One of the reasons could be historical: the medical community was involved in EEG from the outset; Hans Berger was a psychiatrist, and Edgar Adrian an electrophysiologist. In contrast, the MEG community has for a long time been dominated by physicists and engineers, and later on also by neuroscientists, for whom identifying opportunities for, and development of, clinical applications might not have been top priority.

Another reason could be that due to the richness and complexity of MEG data, there are many factors that should be taken into account when recording and analyzing these data. As a consequence, there are few generally accepted protocols for MEG. The IFCN-endorsed practical guidelines for clinical magnetoencephalography presented in this issue of *Clinical Neurophysiology*, Hari et al. (2018), attempt to address this latter issue. The guidelines are written by an international group of prominent experts who bring with them many years of experience in the development of MEG and its application in both neuroscience and clinical care. As one would expect from such a group, the guidelines do contain, besides a comprehensive introduction to MEG, many useful practical tips that help in obtaining high quality MEG data, in performing thorough analysis, and writing clear and informative reports. These guidelines could therefore aid the establishment of standardized clinical protocols. Although we expect that these guidelines will be broadly supported, it should be noted that the authors represent a minority of the clinical MEG users, and that the guidelines are therefore potentially incomplete and biased by the experiences and expertise of its authors. Moreover, although these are the first IFCN-endorsed clinical MEG guidelines, several clinical and general MEG guidelines already exist: The American Clinical Magnetoencephalography Society has published guidelines for the recording and analysis of spontaneous activity (Bagic et al., 2011b), presurgical

mapping (Burgess et al., 2011), reporting (Bagic et al., 2011c), and qualification of MEG/EEG personnel (Bagic et al., 2011a). The Japanese clinical MEG community has published guidelines regarding recording, analysis and documentation (Hashimoto et al., 2005), and many practical tips can also be found in Gross *et al.* (2013). Similarly, there is a large overlap with guidelines for clinical use of EEG and evoked potentials as endorsed by the IFCN[1] and ACNS[2]. Integration of information between these guidelines is missing: it will be difficult for novice users of clinical MEG to determine which guidelines should be adopted, which represent conventional (i.e., historical) preferences, and which were based on a consensus approach. Hence, although these new guidelines would provide novice clinical users a quick introduction to MEG, as well as many practical tips, for more detailed guidelines regarding specific applications one would be well advised to consult these alternatives as well.

Another issue that has been holding back the clinical application of MEG is the absence (in comparison with EEG) of analysis and reporting software that combines ease of use in a clinical environment with access to sophisticated analysis routines. Many MEG laboratories develop their own software tools or use open source packages (Baillet et al., 2011). These packages have many advantages, such as access to sophisticated analysis routines and flexibility to add new ones. However, clinical use also requires that the software fulfils the regulatory requirements (FDA approval/CE marking), that it enables easy access to data by clinicians, and that a clinical report can be generated quickly. These latter aspects often mean that the data should be moved from a Unix environment, in which data are acquired, to a Microsoft Windows environment, that the software contains a database through which the data are accessible, and that data can be processed quickly and (semi-)automatically. The former aspect means that developing such software is prohibitively expensive in a relatively small marketplace. This has led to a chicken-and-egg situation, where it is difficult to establish the clinical utility of MEG due to the absence of clinical software, and where clinical software is not developed because there are not enough clinical applications that warrant the investment. One strategy to break this deadlock is to take existing clinical EEG applications and convert them to MEG. By doing so, patients benefit from a more comfortable and faster recording, and researchers benefit from the build-up of large datasets that can be utilized for more advanced analyses than what would be possible with EEG. Analysis of oscillatory activity and evoked activity with regards to brain anatomy, functional interactions and topology of functional networks, all benefit from MEG's simpler forward solutions, absence of the choice of reference, and increased number of sensors in comparison to clinical EEG. Importantly, by building up databases of sizes that are rarely achieved in research-based projects, one can start to utilize 'big data' approaches in order to discover biomarkers for diagnosis and prognosis, which may lead to novel clinical applications of MEG. For example, Bosl *et al.* (2018) have applied machine learning methods to resting-state EEG data and can now predict autism in infants as young as 3 months old – a demonstration with obvious implications for early-intervention treatment strategies.

Initially, one could start with conversion of relatively straightforward EEG protocols, such that analysis can be carried out using software that has not yet been optimized for clinical use (at the expense of an extra time-investment by MEG technicians and clinicians for analysis and interpretation). As an example, our group

[1] http://www.ifcn.info
[2] https://www.acns.org/practice/guidelines

has taken a clinical EEG protocol for diagnosis of patients in the memory clinic (Gouw et al., 2016) and converted that to MEG. That is, the EEG recording/reporting protocols and outcome measures are used, but for MEG the analysis is performed on source-reconstructed data, alongside the sensor-level analysis that would have been done with EEG. By doing so, a cohort consisting of more than 240 patients has been built in 3 years' time. One envisages that this strategy could readily be adopted to some of the clinical applications that the guidelines describe as being on the horizon: mild traumatic brain injury, stroke, chronic pain, hepatic encephalopathy, psychiatric disorders, brain maturation, autism, and Parkinson's disease (e.g. Klassen et al., 2011, Olde Dubbelink et al., 2014). Conversion to common clinical practice may be further accelerated by the sharing of large datasets for healthy controls that were recorded in accordance with the guidelines (Niso et al., 2016), so that age- and gender-matched population means and standard deviations can be derived against which the clinical data can be assessed.

More advanced protocols could be tackled when new technologies become available that address potential stumbling blocks for wider uptake of MEG as a clinical technique, such as installation and running costs, as well as access to some patient populations (e.g. neonates, comatose patients, and patients on intensive and medium care). The guidelines describe a few exciting new techniques that include high-temperature SQUIDS, hybrid quantum interference devices, and optically pumped magnetometers.

In conclusion, these IFCN-endorsed general guidelines for clinical MEG will be a valuable resource for novice clinical users of MEG and represents another important step to support and encourage expert clinical groups to transfer their skills in clinical EEG to clinical MEG. Hopefully, new guidelines for specific clinical MEG applications will be needed soon.

Conflict of Interest

None of the authors have potential conflicts of interest to be disclosed.

References

Adrian ED. Brain rhythms. Nature. 1944;153:360-2.

Bagic AI, Barkley GL, Rose DF, Ebersole JS, Committee ACPG. American Clinical Magnetoencephalography Society Clinical Practice Guideline 4: qualifications of MEG-EEG personnel. J Clin Neurophysiol. 2011a;28:364-5.

Bagic AI, Knowlton RC, Rose DF, Ebersole JS, Committee ACPG. American Clinical Magnetoencephalography Society Clinical Practice Guideline 1: recording and analysis of spontaneous cerebral activity. J Clin Neurophysiol. 2011b;28:348-54.

Bagic AI, Knowlton RC, Rose DF, Ebersole JS, Committee ACPG. American Clinical Magnetoencephalography Society Clinical Practice Guideline 3: MEG-EEG reporting. J Clin Neurophysiol. 2011c;28:362-3.

Baillet S, Friston K, Oostenveld R. Academic software applications for electromagnetic brain mapping using MEG and EEG. Comput Intell Neurosci. 2011;2011:972050.

Berger H. Über das Elektrenkephalogramm des Menschen. Archiv für Psychiatrie und Nervenkrankheiten. 1929;87:527-70.

Bosl WJ, Tager-Flusberg H, Nelson CA. EEG Analytics for Early Detection of Autism Spectrum Disorder: A data-driven approach. Sci Rep. 2018;8:6828.

Burgess RC, Funke ME, Bowyer SM, Lewine JD, Kirsch HE, Bagic AI, et al. American Clinical Magnetoencephalography Society Clinical Practice Guideline 2: presurgical functional brain mapping using magnetic evoked fields. J Clin Neurophysiol. 2011;28:355-61.
Cohen D. Magnetoencephalography: Evidence of Magnetic Fields Produced by Alpha-Rhythm Currents. Science. 1968;161:784-6.
Cohen D. Magnetoencephalography: Detection of the Brain's Electrical Activity with a Superconducting Magnetometer. Science. 1972;175:664-6.
Gouw AA, Stam CJ. Electroencephalography in the Differential Diagnosis of Dementia. Epileptologie. 2016;33:173-82.
Gross J, Baillet S, Barnes GR, Henson RN, Hillebrand A, Jensen O, et al. Good practice for conducting and reporting MEG research. NeuroImage. 2013;65:349-63.
Hari R, Baillet S, Barnes G, Burgess R, Forss N, Gross J, et al. IFCN-endorsed practical guidelines for clinical magnetoencephalography (MEG). Clin Neurophysiol. 2018, This Issue.
Hashimoto I, Kakigi R, Nagamine T, Nakasato N, Shiraishi H, Watanabe Y. Guideline for Clinical Application of Magnetoencephalography. Jpn J Clin Neurophysiol. 2005;33:231-52.
Klassen BT, Hentz JG, Shill HA, Driver-Dunckley E, Evidente VG, Sabbagh MN, et al. Quantitative EEG as a predictive biomarker for Parkinson disease dementia. Neurology. 2011;77:118-24.
Luders HO, Najm I, Nair D, Widdess-Walsh P, Bingman W. The epileptogenic zone: general principles. Epileptic Disord. 2006;8 Suppl 2:S1-S9.
Niso G, Rogers C, Moreau JT, Chen LY, Madjar C, Das S, et al. OMEGA: The Open MEG Archive. Neuroimage. 2016;124:1182-7.
Olde Dubbelink KT, Hillebrand A, Twisk JW, Deijen JB, Stoffers D, Schmand BA, et al. Predicting dementia in Parkinson disease by combining neurophysiologic and cognitive markers. Neurology. 2014;82:263-70.
Schomer DL, da Silva FHL. Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields: Oxford University Press; 2018.
Stam CJ. Use of magnetoencephalography (MEG) to study functional brain networks in neurodegenerative disorders. J Neurol Sci. 2010;289:128-34.