



Published in final edited form as:

J Clin Neurophysiol. 2011 August ; 28(4): 355–361. doi:10.1097/WNP.0b013e3182272ffe.

American Clinical Magnetoencephalography Society Clinical Practice Guideline 2: Presurgical Functional Brain Mapping Using Magnetic Evoked Fields*

Richard C. Burgess[†], Michael E. Funke[‡], Susan M. Bowyer[§], Jeffrey D. Lewine^{||}, Heidi E. Kirsch[¶], Anto I. Bagi[#], and for the ACMEGS Clinical Practice Guideline (CPG) Committee^{****}

[†]Epilepsy Center, Department of Neurology, The Cleveland Clinic Foundation, Cleveland, Ohio, U.S.A.

[‡]Magnetic Source Imaging, Department of Neurology, Clinical Neurosciences Center, The University of Utah, Salt Lake City, Utah, U.S.A.

[§]Neuromagnetism Laboratory, Henry Ford Hospital, Detroit, Michigan, U.S.A.

^{||}MIND Research Network, Albuquerque, New Mexico, U.S.A.

[¶]UCSF Epilepsy Center, UCSF, San Francisco, California, U.S.A.

[#]University of Pittsburgh Comprehensive Epilepsy Center (UPCEC), Department of Neurology, University of Pittsburgh, Pittsburgh, Pennsylvania, U.S.A.

Abstract

The following are “minimum standards” for the routine clinical recording of magnetic evoked fields (MEFs) in all age-groups.

Practicing at minimum standards should not be the goal of a magnetoencephalography (MEG) center but rather a starting level for continued improvement. Minimum standards meet only the most basic responsibilities to the patient and the referring physician.

These minimum standards have been put forth to improve standardization of procedures, to facilitate interchange of recordings and reports among laboratories in the United States, and to confirm the expectations of referring physicians.

Recommendations regarding Laboratory (Center) Environment and Preparation for MEG Recordings are detailed in the American Clinical Magnetoencephalography Society Clinical Practice Guideline (CPG) 1 : Recording and Analysis of Spontaneous Cerebral Activity, except for its EEG aspect that is not considered necessary (although may be helpful in trained hands) for MEFs (presurgical functional brain mapping).

*Revisions of the document authored by the task force were made and the final version was approved unanimously by the ACMEGS Board (Anto I. Bagi , Gregory L. Barkley, Richard C. Burgess, Michael E. Funke, Robert C. Knowlton, Jeffrey D. Lewine) on December 18, 2010.

A. I. Bagi chaired the ACMEGS Clinical Practice Guideline (CPG) Committee.

**Task Force for somatosensory, movement/motor, auditory, and visual MEFs: R. C. Burgess, M.I E. Funke, H. E. Kirsch.

***Task Force for language evoked fields (LEFs): S. M. Bowyer, J. D. Lewine.

Copyright © 2011 by the American Clinical Neurophysiology Society

Address correspondence and reprint requests to Richard C. Burgess, MD, PhD, Epilepsy Center, Department of Neurology, The Cleveland Clinic Foundation, Mail Code S51, 9500 Euclid Avenue, Cleveland, OH 44195; BUR-GESR@ccf.org.

GENERAL INDICATIONS FOR MEG EVOKED FIELDS IN PRESURGICAL FUNCTIONAL BRAIN MAPPING

Magnetoencephalography shares with EEG high temporal resolution, but its chief advantage in presurgical functional brain mapping is in its high *spatial* resolution. Magnetic evoked fields are therefore done for *localization*; unlike electrical evoked potentials (EPs), MEF latencies and latency asymmetries are not typically used to detect abnormalities.

Like other laboratory tests, it is important that clinicians involved in MEG acquisition and interpretation be informed of the indications for the various modalities of testing and of the clinical question to be answered. In return, the results of the MEG should answer the questions that prompted the referral. Both proper referrals and useful answers depend on timely and complete communication between the referring physician and the clinical magnetoencephalographer. Such communication may necessitate follow-up conversations to clarify indications or provide some education.

SPECIFIC INDICATIONS, METHODS OF ACQUISITION, AND ANALYSIS TECHNIQUES FOR MEG EVOKED FIELDS

Satisfactory localization of a magnetic evoked response depends on obtaining a satisfactory signal. All the MEFs depend on averaging to achieve an adequate signal in comparison with the background activity that is not related to the response, that is, an adequate signal to noise ratio (SNR). What constitutes an adequate SNR is not fixed but rather depends on the individual patient and the modality being tested. In general, an adequate SNR is determined by the appearance of a robust response based on the magnetoencephalographer's experience. Ensembles containing too many trials can also be problematic. As noted in the "analysis" segments below, the SNR of the average can be improved by some or all of the following: noise cancellation applied to the raw signals, discarding noisy or otherwise corrupted trials, judicious use of time-domain or spatial filters. All these techniques rely on post hoc averaging from the continuously recorded raw data. While the number of trials that must be recorded to obtain a sufficient number of good ones is highly variable, the suggestions below provide ranges that are typical in clinical patients. Real-time averaging is used only as a rough indication that responses are being satisfactorily obtained but should not substitute for off-line (post hoc) averaging. These important points are reiterated in each of the acquisition and analysis segments below.

Somatosensory Evoked Fields

Indications

- Localization of somatosensory cortex (often in situations where there are large central lesions or other abnormalities in the vicinity of the expected central region).
- Localization of the central sulcus (in conjunction with motor evoked fields).
- Biologic quality check of coordinate transformation (spatial biocalibration).

Stimulation

- Sites of electrical stimulation frequently used in clinical somatosensory evoked fields (SEFs) examination include the median nerve and tibial nerve, and mechanical stimuli can be used for fingers, lips, tongue, and other regions of the body.
- Electrical stimulation

- Stimulus parameters: a constant current, monophasic rectangular pulse of 100 to 300 μ s should be used.
- Somatosensory stimulus amplitude should be adjusted for the individual patient to exceed motor threshold (i.e., to cause a clearly visible twitch). Although sensory responses are produced at lower stimulation levels, setting the stimulation at 0.5 to 1 mA above the motor threshold ensures that sensory fibers are being stimulated. This procedure also provides an objective means to obtain reproducible sensory stimulation levels. Typical stimulus amplitudes required to achieve a twitch range from 5 to 10 mA.
- Stimulation electrode impedance should be 5 k Ω or less.
- The aggregate stimulus frequency should not be higher than 5 per second even if distributed to multiple stimulation sites.
- Electrode placements for stimulation of a particular nerve should follow accepted guidelines established in the field of EPs, as described in the corresponding American Clinical Neurophysiology Society Guidelines.
- Mechanical stimulation
 - Devices include air puffs, pressurized bellows (sometimes incorporated into specialized gloves), handheld brushes consisting of an optic fiber bundle, and other electrically triggered devices.
 - Tactile stimulation may not produce results that are as reliable as electrical stimulation, but some centers have well-established routines using this type of stimulation, and they may be advantageous in infants and toddlers or in patients with impaired cognition.

Recording (Data Acquisition Based on Electrical Stimulation)

- Band pass of 0.03 to 300 Hz with a digitization rate of at least 1,000 Hz is preferred to facilitate postprocessing of the raw data.
- Recording the raw data is mandatory to permit discarding undesirable trials or channels post hoc.
- Real-time averaging is optional and may help to determine the number of necessary trials; 200 to 500 trials may be required to yield an adequate number of acceptable trials. Averaging offline after data collection permits noise reduction processing and manual or automatic artifact rejection.
- Epoch duration of –50 ms to 250 milliseconds. Additional prestimulus baseline (e.g., back to –100 ms) may be useful for offset correction.
- Inter-stimulus interval (ISI) of 500 to 2,000 milliseconds (similar for mechanical stimulation).
- Stimulus channel indicators should be present and clearly labeled in the raw data to indicate stimulation triggers.
- Jitter less than 100 μ s.
- Head position measurement should be carried out before each ensemble or data block. Use of continuous head position tracking is preferred if available.
- The testing paradigm should be repeated to assess reproducibility and ensure consistent results.

Data Analysis

Averaging (based on electrical stimulation)

- Optional real-time averaging (i.e., during recording) can be helpful to obtain an estimate of the SNR.
- Recording of the raw data is mandatory, and the analysis system must permit post hoc averaging.
- The analysis system must permit inspection of raw data.
- 100 to 300 trials per stimulus location may be required to acquire an adequate number of acceptable repetitions.
- Off-line averaging after data acquisition permits
 - noise reduction processing,
 - elimination of artifact-containing traces, and
 - judicious selection of band-pass filtering (typical high-pass cutoff from 1 to 20 Hz and low-pass cutoff from 40 to 100 Hz).

Source localization

- During source analysis computations, the location of the N20m and or P35m peaks should be fitted and their quality assessed by the localization difference between replications (usually in the range of 4–5 mm).
- Ensemble replications should differ from each other by less than 5 mm for N20m and P35m localizations.

Interpretation and Reporting of Somatosensory Evoked Fields—Addressed jointly for SEFs, motor evoked fields, auditory evoked fields (AEFs), and visual evoked fields (VEFs) in the section Interpretation and Reporting of MEG Evoked Fields.

Movement-Related Magnetic Fields and Motor Evoked Fields

Indications

- Localization of primary motor cortex in situations with rather large abnormalities (cystic encephalomalacia, polymicrogyria, etc. or smaller caliber abnormalities, space demanding processes in vicinity of the expected central region) before neurosurgical intervention or radiosurgical procedures.

Activity

- Motor functions evaluated and timing fiducial
 - finger tapping, self-paced
 - finger tapping, cued (visually, auditory)
 - light-beam interruption, switch closure, or another available time fiducial may be used as a timing indicator for averaging
 - repeated contractions with electromyogram (EMG) onset as a timing indicator for averaging, with or without tactile cuing
 - isometric contraction, simultaneous EMG.

- Note that the subject's level of consciousness must permit co-operation and task execution. Habituation and boredom often limit repetitions.
- Silent counting is not permitted, as this attenuates the movement-related magnetic field potential.

Recording (Data Acquisition)

- Band pass of 0.03 to 300 Hz with a digitization rate of at least 1,000 Hz is preferred to facilitate post-processing of the raw data.
- Recording the raw data is mandatory to permit discarding undesirable trials or channels post hoc.
- Real-time averaging is optional and may help to determine the number of necessary trials. 100 to 500 trials may be required to yield an adequate number of acceptable trials. Averaging off-line after data collection permits noise reduction processing and manual or automatic artifact rejection.
- Epoch duration and intermovement interval
 - finger tapping, self-paced, –500 to 200 milliseconds, intermovement interval 1 to 2 s
 - finger tapping, cued (visual, auditory), –500 to 200 ms, intermovement interval 2 to 3 seconds
 - repeated contractions with EMG, –500 to 200 ms, intermovement interval 2 to 3 seconds
 - isometric contraction, 240 s of isometric contraction (with short interruptions permitted)
- Stimulus channel indicators should be present and clearly labeled in the raw data to indicate stimulation triggers.
- Head position measurement should be carried out before each ensemble or data block. Use of continuous head position tracking is preferred if available.
- The testing paradigm should be repeated to assess reproducibility and ensure consistent results.

Data Analysis

Averaging

- Optional real-time averaging (i.e., during recording) can be helpful to obtain an estimate of the SNR.
- Recording the raw data should be mandatory, and the analysis system must permit post hoc averaging.
- The analysis system must permit inspection of raw data.
- Averaging with respect to the appropriate trigger (e.g., light beam interruption, EMG burst) must be selectable post hoc at the magnetoencephalographer's discretion.
- Off-line averaging after data acquisition permits
 - noise reduction processing,
 - elimination of artifact-containing traces, and

- judicious selection of band-pass filtering (typical band pass of 1–25 Hz for finger tapping).
- Typical number of averages required to ensure adequate SNR are
 - finger tapping, self-paced, 70 to 100 each left and right
 - finger tapping, cued, 50 each left and right
 - repeated contractions with EMG, 70 to 100 each left and right
 - isometric contraction, calculating corticomuscular coherence.

Source localization

- Source analysis computations
- finger tapping, movement-related field approximately 30 to 40 milliseconds before movement onset.
- repeated contractions with EMG, movement-related field approximately 30 to 40 milliseconds before movement onset.
- isometric contraction, coherence peak at 20 Hz.

Interpretation and Reporting of Motor Evoked Fields—Addressed jointly for SEFs, motor evoked fields, AEFs and VEFs in the section Interpretation and Reporting of MEG Evoked Fields.

Auditory Evoked Fields

Indications

- Localization of primary auditory cortex on the superior temporal gyrus.
- Assessment of hearing in children.
- In contrast to electrical auditory EPs, the early latency signals (brainstem auditory evoked potential) are not well recorded by the MEG.

Stimulation

- Tones, typically 1,000 Hz, presented monaurally.
- Individual stimulus parameters, 80 to 90 dB sound pressure level (~60 dB above hearing threshold), 50- to 200-millisecond duration.
- Interstimulus interval, typically 1 to 2 second ISI, jitter less than 100 μ s.
 - A longer ISI, up to 3 seconds may be required in children to obtain an adequate response.
 - In adults, the use of long ISIs may lead to a dual peak in the N100m response.
- Contralateral white noise masking at 40 to 50 db hearing level will prevent unintended cross-stimulation of the contralateral ear.

Recording (Data Acquisition)

- Band pass of 0.03 to 300 Hz with a digitization rate of at least 1,000 Hz is preferred to facilitate postprocessing of the raw data.

- Recording the raw data is mandatory to permit discarding undesirable trials or channels post hoc.
- Real-time averaging is optional and may help to determine the number of necessary trials; 200 to 500 trials may be required to yield an adequate number of acceptable trials. Averaging offline after data collection permits noise reduction processing and manual or automatic artifact rejection.
- Epoch duration of –200 to 500 milliseconds.
- Stimulus channel indicators should be present and clearly labeled in the raw data to indicate stimulation triggers.
- Head position measurement should be carried out before each ensemble or data block. Use of continuous head position tracking is preferred if available.
- Patient must be awake. Therefore, adequate sleep of the patient before AEF testing is essential.
- The testing paradigm should be repeated to assess reproducibility and ensure consistent results.

Data Analysis

Averaging

- Optional real-time averaging (i.e., during recording) can be helpful to obtain an estimate of the SNR.
- Recording of the raw data should be mandatory, and the analysis system must permit post hoc averaging.
- The analysis system must permit inspection of raw data.
- Off-line averaging after data acquisition permits
 - noise reduction processing,
 - elimination of artifact-containing traces, and
 - judicious selection of band-pass filtering (as narrow as 1–30 Hz).
- Include sufficient trials to obtain a robust response, typically 100 artifact-free epochs.

Source localization

- Localize the N100m component of the AEF.

Visual Evoked Fields

Indications

- Localization of primary visual cortex before neurosurgical resections.
- Assessment of abnormal visual function.

Stimulation

- Typically generated using specialized presentation computer with image shown on a back-projection screen.
- To eliminate partial visual field effects, computer graphics output cards, and projectors must be specially chosen for fast response.

- To eliminate timing errors or jitter (because of uncertainty of timing from computer, raster refresh rate, etc), a timing synch pulse (either from the stimulus computer or from an independent indicator such as a photocell) that is accurate to within 1 millisecond must be recorded by the MEG system.
- To assess the visual system, full-field, hemifield, and/or quadrant steady-state stimuli may be used; contrast, luminance, screen placement, check size, and field size to produce the appropriate subtended visual angle should follow the parameters used for conventional scalp visual evoked potential guidelines.
- Half-field checkerboard reversal pattern with 1-second ISI is the most common procedure.
- A fixation point should be provided. If patient cannot fixate well, full-field stimulation should be used.
- Adequate sleep of the patient before VEF testing is essential.

Recording (Data Acquisition)

- Band pass of 0.03 to 300 Hz with a digitization rate of at least 1,000 Hz is preferred to facilitate postprocessing of the raw data.
- Recording the raw data is mandatory to permit discarding undesirable trials or channels post hoc.
- Real-time averaging is optional and may help to determine the number of necessary trials; 200 to 500 trials may be required to yield an adequate number of acceptable trials. Averaging offline after data collection permits noise reduction processing and manual or automatic artifact rejection.
- Epoch duration of –100 to 300 milliseconds.
- Stimulus channel indicators should be present and clearly labeled in the raw data to indicate stimulation triggers.
- Jitter less than 50 μ s.
- Head position measurement should be carried out before each ensemble or data block. Use of continuous head position tracking is preferred if available.
- The testing paradigm should be repeated to assess reproducibility and ensure consistent results.

Data Analysis

Averaging

- Optional real-time averaging (i.e., during recording) can be helpful to obtain an estimate of the SNR.
- Recording of the raw data should be mandatory, and the analysis system must permit post hoc averaging.
- The analysis system must permit inspection of raw data.
- Off-line averaging after data acquisition permits
 - noise reduction processing,
 - elimination of artifact-containing traces, and

- judicious selection of band-pass filtering (typical high-pass cutoff from 1 to 9 Hz and low-pass cutoff from 50 to 100 Hz).
- Include sufficient trials to obtain a robust response, typically 100 to 200 artifact-free epochs.

Source localization

- During source analysis computations, the location of the P100m should be identified.
- Ensemble replications should differ from each other by less than 5 mm for the localization of the P100m.

Interpretation and Reporting of Auditory Evoked Fields—Addressed jointly for SEFs, motor evoked fields, AEFs and VEFs in the section Interpretation and Reporting of MEG Evoked Fields.

Interpretation and Reporting of MEG Evoked Fields

Common aspects of reporting MEG–EEG studies are addressed in the American Clinical Magnetoencephalography Society Clinical Practice Guideline 3 (ACMEGS CPG#3): MEG–EEG Reporting.

General Considerations for Interpretation and Reporting of All MEFs

- When careful elimination of individual artifact-containing traces (either automatically or manually) does not produce an adequate average, off-line noise-reduction techniques or more restrictive band-pass filtering can often improve localization.
- MEFs are not indicated for diagnosis using measurement of absolute latencies or precise calculation of interhemispheric latency asymmetries. Response time measurements are only needed to properly identify the peaks that are to be localized.
- The primary sensory responses, with latencies similar to scalp EPs, should be identified. Latencies should approximate those for scalp EPs (if simultaneous EEG has been acquired, the electrical EP peaks can be used directly to help identify the magnetic responses within a given subject).
- These major components should be localized and coregistered with the patient's own MRI. Several source localization techniques exist and may be applied, as with other MEG signals. The single equivalent current dipole is an adequate model for MEG evoked fields.
- MRI image volumes with a 1-mm-slice thickness (e.g., MPRAGE, multiecho, or similar) are optimal for adequate localization. Skin to skin MRI head coverage is necessary for proper coregistration.
- Determination of head position, necessary for coregistration, requires digitization of the position of head coils, landmarks, and at least 100 additional points distributed over the head.

Special Considerations for Interpretation and Reporting of Specialized Evoked Fields

Movement-related fields

- Movement-related magnetic field responses are more difficult to reliably elicit than somatosensory responses (such as electrical median nerve stimulation). Therefore, for clinical testing using two different paradigms per patient may be needed to increase the yield.
- Weakness of distal hand muscles (because of perinatal stroke and the like) presents an additional challenge for successful movement related field localization.

Auditory evoked magnetic field

- Providing adequate auditory stimulation in older patients may be difficult. Obtaining a stimulus above an individual hearing level might be limited in this population as presbycusis may increase the hearing threshold level, and the auditory stimulation systems available for MEG laboratories may have a limited dynamic range.
- In addition, different ear inserts (foam plugs vs. open ear inserts) for monaural stimulation may produce different loudness levels. Documenting the dynamic range of the auditory stimulation system across attenuation levels should be part of the standard procedure manual of the MEG laboratory.

It is important that these considerations be kept in mind so that the report reflects the stimulation difficulty, if encountered, and is not misconstrued as an abnormality.

Data to be Included in the Report

Patient identification

- Facility name, laboratory name, address.
- Test date, test identification number, procedure name.
- Requesting physician's name, interpreting physician's name.
- Patient name, age, gender.
- Clinical information.
- Clinical question.
- Patient information that could influence results of the study, including behavior, medications, level of consciousness.

Technical data

- Standard stimulation and recording settings.
- Volume conductor model, source model, coordinate transformation.

Results

- Number of averages, reproducibility.
- Numerical descriptors.
- Pictorial/graphical representation of results.

- Magnetic sources for responses that appear to be normal may be shown alone or in combination with other relevant sources (e.g., a motor response shown along with perirolandic spike dipoles).
- For nonprimary sensory responses (motor, language), and very abnormal looking signals of primary sensory responses, the graphical presentation of waveform should be considered part of the clinical documentation/report.

Description

- Deviation from normal location, as well as unusual waveforms and the like.

Interpretation

- Impression normal versus abnormal.
- Clinical correlation.

Language Evoked Magnetic Fields From Speech Comprehension and/or Production

Background—Linguistic stimuli presented acoustically or visually result in language-related responses (late responses) in addition to primary auditory and visual responses (early responses). Language-evoked magnetic fields (LEFs) appear after the primary sensory components and are generated in language-related areas of the brain regardless of the modality of stimulus presentation. Language-evoked magnetic fields are repeatable. Laterality of the language areas, as measured by MEG, has been found to correlate between 80% and 95% with results from the Wada procedure and mapping during intracranial recordings. Language-evoked magnetic field studies of receptive language (comprehension) localize sources to the posterior aspects of the superior and middle temporal lobe and the temporoparietal junction, whereas LEF studies of expressive language (speech production) localize activity in frontal and basal temporal areas.

The primary clinical application of LEFs is to determine the language-dominant hemisphere, which is particularly important because significant changes can result from anatomic and functional disorders. The results from these studies show that MEG LEF studies are able to replace the language portion of the invasive Wada procedure.

Indications

- Determining the language-dominant hemisphere in patients with either organic or functional brain diseases before surgical interventions, such as craniotomy, stereotactic or radiosurgical procedures; and/or
- Objective functional evaluation of language processing (i.e., identification of location and latencies).

Stimulation

- Computer systems for presenting language stimulation are the same as those used for eliciting AEFs and VEFs.
- Identification of the language-dominant hemisphere is accomplished by comparing results from language stimulation with those from nonlanguage stimulation.
- Enhancement of LEFs can be obtained in a task requiring the subject to recognize or categorize linguistic stimuli.

- Word comprehension and picture or action naming are tasks frequently used to evoke language processing. Most language stimuli are concrete nouns that can be presented visually or acoustically.
- *Auditory presentation.* Single word auditory stimuli are most commonly used, with fixed or random interstimulus intervals, typically greater than 2 seconds. Stimuli are typically presented at normal listening levels (~60 dB above normal hearing levels) and subjects may be asked to either listen passively to the words or to covertly (silently) think of an action word that goes with the word. Examples of the auditory stimuli can be found in Papanicolaou et al. (2004).
- *Visual presentation.* Visually presented words may also be used. Subjects can be asked to either read the words or they can be asked to read the word and think of an action word that goes with the word. Examples of the visual stimuli can be found in Bowyer et al. (2004).
- *State variables.* Before initiating the study of LEFs, it is necessary to confirm that the subject is in a state of wakefulness. This is critical for collecting data with a good SNR. The occipital alpha rhythm in spontaneous on-going MEG recordings can be used to monitor wakefulness during the study. The use of behavioral target stimuli interspersed in the task stimuli (e.g., push a button when you see a solid circle) can be used to determine if the subject is awake and participating in the task. The technologist running the study can watch the response channel to determine if the subject pushes the button. Data segments associated with target stimuli and lateralized motor responses should not be averaged in the final MEG evoked responses.

Recording (Data Acquisition)

- Band pass of 0.03 to 300 Hz with a digitization rate of 1,000 Hz is preferred to facilitate postprocessing of the raw data.
- MEG recording for language should be continuous.
- Triggers must be simultaneously recorded for segmenting data and averaging the evoked waveforms in postprocessing analysis.
- The data processing is similar to that used for all evoked responses.
- Online averaging runs the risk of including trials with large movement artifacts and/or eye blinks and should generally be avoided, or employed in real-time only to assess proper system operation.
- Head position measurement should be carried out before each ensemble or data block. Use of continuous head position tracking is preferred if available.
- Performance of the same task should be replicated during the same session. Independent analysis of the two data sets can help to minimize sources of error (i.e., head movement, changes in performance, attention level, variations in background activity, coregistration errors).

Data Analysis

Averaging

- When magnetic signals are small, continuously recorded data can be averaged off-line to improve the SNR.
- Averaging over the multiple time epochs is valid only when intracranial events are assumed to be identical.

- Adequate SNR for LEFs can be typically achieved with 50 to 100 artifact-free trials.
- Early evoked fields can be used for quality control (latency, topography). For example, if stimuli are presented acoustically, the auditory N100m responses should be symmetrical in topography, peaking around 100 milliseconds and with similar amplitude.
- Data should be typically band-pass filtered 1 to 50 Hz.

Initial inspection of data

- Before considering the analysis of long-latency language-related activity, it is important to evaluate the integrity of basic auditory/visual responses at ~100 milliseconds.
- Tumors and other lesions can cause lateralized compromise of basic sensory (auditory/visual) processing if located in primary or secondary sensory (auditory/visual) areas. If core sensory processing (auditory/visual) is compromised, special caution is needed in the interpretation of long-latency activity.
- Raw data used to generate averages should also be inspected. Lateralized paroxysmal spikes, sharp waves, and slow waves can have a dramatic effect on evoked responses and lead to misinterpretation of laterality profiles. Epochs with such activity must be discarded from the averaging process. In some cases, continuous lateralized slow wave activity may be present. Unless this can be selectively removed via signal processing strategies (e.g. the Signal Space Projection, Independent Component Analysis), one should not attempt to interpret language evoked fields.

Language evoked activity

- Long-latency responses (greater than 200 milliseconds in latency) evoked by language stimulation contain activity arising from multiple language areas, independent of the method of stimulation, auditory or visual. Such responses are enhanced when attention to the task is displayed. The signals reflect varying contributions from multiple language areas, including Wernicke's language area (superior temporal gyrus), Brodmann area (BA 22), the angular gyrus (BA 39), the supramarginal gyrus (BA 40), and Broca's language area (pars opercularis and pars triangularis of the inferior frontal gyrus [BA 44 and 45]). Different tasks appear to change the source regions that dominate the evoked responses.
- In general, the evoked LEF waveform will have several peaks. The initial peaks (<150 milliseconds) are generally associated with basic sensory processing in the modality of stimulation. Activity between 150 and 250 milliseconds is believed to be associated with feature processing and integration, with later activity reflecting high-order processing, including language. Regardless of the modality of stimulation and subtle details of the stimulation paradigms, linguistic stimuli evoke a large, typically lateralized, response that normally peaks between 400 and 500 milliseconds. The activity may begin as early as 250 milliseconds and may extend to 750 milliseconds or beyond.

Hemispheric dominance for language

- The determination of hemispheric dominance for language is based on an assessment of how much language activity is evoked in each hemisphere, as assessed by the language evoked field.

- Several strategies are available for source assessment, including single and multiple dipole based strategies, and current reconstructions such as L1 norm, L2 norm, or MR-FOCUSS, and beamformers. Different laboratories have used different methods, but the most commonly used methods are based on dipoles and minimum norm estimates.
- One of the most commonly used methods is to use single moving dipoles to account for the activity beyond 150 milliseconds. In this method, at each time point, a restricted sensor array is identified encompassing the long-latency response(s). A single equivalent current dipole is calculated and if the goodness of fit exceeds a prespecified criteria (e.g., 90%), then the fits are considered valid and the dipole is retained. After all time points are fit (typically in 1-millisecond steps), a laterality index is calculated based on the number of valid dipole fits in each hemisphere. Here, laterality index is defined by $100 \cdot (R - L)/(R + L)$, where L and R are the number of accepted dipoles fit in the left and right hemispheres, respectively. Laterality index values from -100 to -20 indicate strong left hemisphere language dominance. Laterality index values from -19 to +19 indicate bilateral language activation. Laterality index values from +20 to +100 indicate right hemisphere language dominance.
- The task should be repeated to ensure replicability of the derived waveforms, localizations, and laterality indexes. In the same recording session, the use of similar tasks in visual and auditory modalities is recommended helping to dissociate modality-specific activity from language-specific activity.
- A common alternative method is to use a distributed source model (e.g., MR-FOCUSS) and compare the integrated amount of current in left and right hemispheres over the LEF time window. This can be done across all activated regions, or specified regions (e.g., basal temporal areas). Here too, it is common to derive a laterality index, based on source signal strength as opposed to number of dipole fits.
- Alternative analyses, including beamforming strategies and multiple dipole strategies, may also be viable. The key is to integrate information over the long-latency time window and to examine data within the context of a source model that accounts for the subject's physical position relative to the sensors.

Interpretation and Reporting of LEFs

- Common aspects of reporting MEG–EEG studies are addressed in the American Clinical Magnetoencephalography Society Clinical Practice Guideline 3 (ACMEGS CPG#3): MEG–EEG Reporting.
- General interpretation and reporting principles for evoked fields are outlined in the section Interpretation and Reporting of MEG Evoked Fields and should be followed.
- At a minimum, the stimulus conditions and method of data analysis should be described. When calculated, the laterality index should be stated, along with a clear statement of which hemisphere is language dominant (left dominant, right dominant, bilateral, and inconclusive).
- Plotting of language-related data on spatially aligned MRI is at the discretion of each site and should be based on their experience concerning the reliability of localization information. Such plots may give the impression to neurosurgeons that areas without plotted activity are safe to resect. This type of error (false-negative) cannot be excluded systematically, so qualifying statements may be appropriate.

Somatosensory MEG Evoked Fields

- Bast T, Wright T, Boor R, et al. Combined EEG and MEG analysis of early somatosensory evoked activity in children and adolescents with focal epilepsies. *Clin Neurophysiol.* 2007; 118:1721–1735. [PubMed: 17572142]
- Kawamura T, Nakasato N, Seki K, et al. Neuromagnetic evidence of pre- and post-central cortical sources of somatosensory evoked responses. *Electroencephalogr Clin Neurophysiol.* 1996; 100:44–50. [PubMed: 8964262]

Movement/Motor MEG Evoked Fields

- Castillo EM, Simos PG, Wheless JW, et al. Integrating sensory and motor mapping in a comprehensive MEG protocol: clinical validity and replicability. *Neuroimage.* 2004; 21:973–983. [PubMed: 15006664]
- Hoshiyama M, Kakigi R, Berg P, et al. Identification of motor and sensory brain activities during unilateral finger movement: spatiotemporal source analysis of movement-associated magnetic fields. *Exp Brain Res.* 1997; 115:6–14. [PubMed: 9224829]
- Kirsch HE, Zhu Z, Honma S, et al. Predicting the location of mouth motor cortex in patients with brain tumors by using somatosensory evoked field measurements. *J Neurosurg.* 2007; 107:481–487. [PubMed: 17886544]
- Mima T, Hallett M. Corticomuscular coherence: a review. *J Clin Neurophysiol.* 1999; 16:501–511. [PubMed: 10600018]
- Pohja M, Salenius S, Hari R. Reproducibility of cortex-muscle coherence. *Neuroimage.* 2005; 26:764–770. [PubMed: 15955485]

Auditory MEG Evoked Fields

- Jacobson GP. Magnetoencephalographic studies of auditory system function. *J Clin Neurophysiol.* 1994; 11:343–364. [PubMed: 8089205]
- Parkkonen L, Fujiki N, Mäkelä J. Sources of auditory brainstem responses revisited: contribution by magnetoencephalography. *Hum Brain Mapp.* 2009; 30:1772–1782. [PubMed: 19378273]

Visual MEG Evoked Fields

- American EEG Society. Guidelines on Evoked Potentials. *J Clin Neurophysiol.* 1994; 84:40–73.
- Chen WT, Ko YC, Liao KK, et al. Optimal check size and reversal rate to elicit pattern-reversal MEG responses. *Can J Neurol Sci.* 2005; 32:218–224. [PubMed: 16018158]
- Harding GF, Armstrong RA, Janday B. Visual evoked electrical and magnetic response to half-field stimulation using pattern reversal stimulation. *Ophthalmic Physiol Opt.* 1992; 12:171–174. [PubMed: 1408167]
- Liu H, Tanaka N, Stufflebeam S, et al. Functional mapping with simultaneous MEG and EEG. *J Vis Exp.* 2010; 40:1668. [PubMed: 20567210]

Language Evoked Fields

- Bowyer SM, Moran JE, Mason KM, et al. MEG localization of language specific cortex utilizing MR-FOCUSS. *Neurology.* 2004; 62:2247–2255. [PubMed: 15210890]
- Bowyer SM, Fleming T, Greenwald ML, et al. MEG localization of the basal temporal language area. *Epilepsy Behav.* 2005a; 6:229–234. [PubMed: 15710309]
- Bowyer SM, Moran JE, Weiland BJ, et al. Language laterality determined by MEG mapping with MR-FOCUSS. *Epilepsy Behav.* 2005b; 6:235–241. [PubMed: 15710310]
- Breier JI, Simos PG, Zouridakis G, et al. Language dominance determined by magnetic source imaging: a comparison with the Wada procedure. *Neurology.* 1999; 53:938–945. [PubMed: 10496250]

- Breier JI, Simos PG, Zouridakis G, Papanicolaou AC. Lateralization of activity associated with language function using magnetoencephalography: a reliability study. *J Clin Neurophysiol.* 2000; 17:503–510. [PubMed: 11085554]
- Breier JI, Castillo EM, Simos PG, et al. Atypical language representation in patients with chronic seizure disorder and achievement deficits with magnetoencephalography. *Epilepsia.* 2005; 46:540–548. [PubMed: 15816948]
- Castillo EM, Simos PG, Venkataraman V, et al. Mapping of expressive language cortex using magnetic source imaging. *Neurocase.* 2001; 7:419–422. [PubMed: 11744783]
- Hirata M, Kato A, Taniguchi M, Saitoh Y, et al. Determination of language dominance with synthetic aperture magnetometry: comparison with the Wada test. *Neuroimage.* 2004; 23:46–53. [PubMed: 15325351]
- Maestu F, Saldana C, Amo C, et al. Can small lesions induce language reorganization as large lesions do? *Brain Lang.* 2004; 89:433–438. [PubMed: 15120535]
- Moran JE, Bowyer S, Tepley N. Multi-Resolution FOCUSS: a source imaging technique applied to MEG data. *Brain Topogr.* 2005; 18:1–17. [PubMed: 16193262]
- Papanicolaou AC, Simos PG, Breier JI, et al. Magnetoencephalographic mapping of the language-specific cortex. *J Neurosurg.* 1999; 90:85–93. [PubMed: 10413160]
- Papanicolaou AC, Simos PG, Castillo EM, et al. Magnetoencephalography: a noninvasive alternative to the Wada procedure. *J Neurosurg.* 2004; 100:867–876. [PubMed: 15137606]
- Patariaia E, Simos PG, Castillo EM, et al. Reorganization of language-specific cortex in patients with lesions or mesial temporal epilepsy. *Neurology.* 2004; 63:1825–1832. [PubMed: 15557497]
- Simos PG, Papanicolaou AC, Breier JI, et al. Localization of language-specific cortex by using magnetic source imaging and electrical stimulation mapping. *J Neurosurg.* 1999; 91:787–796. [PubMed: 10541236]