Sensorimotor mapping with MEG: An update on the current state of clinical research and practice with considerations for clinical practice guidelines.

Xavier De Tiège[1,2], Mathieu Bourguignon[2,3,4], Harri Piitulainen[5], and Veikko Jousmäki[5,6,7]

[1]Department of Functional Neuroimaging, Service of Nuclear Medicine, ULB-Hôpital Erasme, Brussels, Belgium.

[2]Laboratoire de Cartographie fonctionnelle du Cerveau, ULB Neuroscience Institute (UNI), Université libre de Bruxelles (ULB), Brussels, Belgium.

[3]Laboratoire Cognition Langage et Développement, UNI, ULB, Brussels, Belgium.

[4]Basque Centre on Cognition, Brain and Language, Donastia-San Sebastian, Spain.

[5]Department of Neuroscience and Biomedical Engineering, School of Science, Aalto University, Espoo, Finland.

[6]NatMEG, Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden.

[7] Cognitive Neuroimaging Centre, Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore.

Disclosure of Conflicts of Interests: Xavier De Tiège benefited from some consulting fees from Elekta (Stockholm, Sweden) during the last five years. Veikko Jousmäki is a qualified Elekta MEG trainer.

Corresponding Author: Xavier De Tiège, Department of Functional Neuroimaging, Service of Nuclear Medicine, ULB-Hôpital Erasme, 808 Lennik Street, 1070 Brussels, Belgium. E-mail: xdetiege@ulb.ac.be Tel: +32.2.555.89.62.

Number of words for the Abstract: 104

Number of words for the Article: 5785

ABSTRACT

In this paper, we present the clinical indications and advances in the use of magnetoencephalography (MEG) to map the primary sensorimotor (SM1) cortex in neurosurgical patients non-invasively. We emphasize the advantages of MEG over the SM1 mapping using functional magnetic resonance imaging. Recommendations to the referring physicians and the clinical magnetoencephalographers to achieve appropriate SM1 cortex mapping using MEG are proposed. We finally provide some practical advice for the use of corticomuscular coherence, cortico-kinematic coherence, and mu-rhythm suppression in this indication. MEG should now be considered as a method of reference for presurgical functional mapping of the SM1 cortex.

1. Introduction

In 2011, the American Clinical Magnetoencephalography Society (ACMEGS) established (among others) Clinical Practice Guidelines (CPGs) for the use of magnetoencephalography (MEG) for presurgical functional brain mapping.[1] These CPGs represented "minimum standards" for the routine clinical use of MEG in this indication and covered the investigation of the somatosensory, motor, visual, auditory, and language systems.[1] They were motivated by the growth of clinical MEG centers in the United States (and worldwide) over the last two decades and aimed at providing a set of practical recommendations that should help laboratories and clinicians practice clinical MEG more uniformly and consistently.[2] In 2017, the ACMEGS has also published a position statement about the existence of sufficient credible evidence to support the routine use of MEG in the presurgical mapping of eloquent cortex of patients undergoing surgical treatment of operable lesions or medically intractable localization-related epilepsy.[3]

In the present paper, we review the current state of clinical practice in MEG and advances in the field with specific focus on the use of MEG for presurgical functional mapping of the primary sensorimotor (SM1) cortex. The three basic aims of this paper are:

(i) To present the current clinical role and indications of presurgical functional mapping of the SM1 cortex using MEG and to elaborate on the information that should be communicated by referring physicians to clinical magnetoencephalographers (and vice-versa).

(ii) To describe the research progresses made in the field since the first ACMEGS CPGs.

(iii) To provide practical advices about protocols that can be used to perform presurgical functional mapping of the SM1 cortex using MEG.

This paper should be viewed as an experts' opinion and as such, there are several considerations that will not be addressed here as they were properly covered in the seminal ACMEGS CPGs or they should be covered in future CPGs related to functional mapping of the SM1 cortex using MEG.

2. Current clinical roles of MEG in sensorimotor mapping

2.1. Roles and Clinical Indications

A non-invasive presurgical functional mapping of the SM1 cortex is recommended in neurosurgical patients with brain lesions located close to or at the central sulcus. In this context, the aim of the functional mapping procedure is to determine as precisely as possible the anatomical relationship between the primary motor (M1) and sensory (S1) cortices and the brain lesion in order to optimally tailor the surgical resection, assess related functional risk(s), and contribute to the decision-making process. In more specialized clinical centers, other possible clinical indications can be the guidance of non-invasive (e.g., transcranial magnetic stimulation[4]) and invasive (e.g., electrical epidural cortex stimulation[5]) cortical stimulation procedures in order to provide accurate stimulation target(s) in patients with or without brain lesion(s). Also, results of functional SM1 cortex mapping can be integrated into stereotactic radiosurgery planning systems in order to minimize the radiation dose applied on functionally eloquent cortices and reduce undesirable radiosurgery-related side effects.[6-8]

2.2. Why MEG ?

Functional magnetic resonance imaging (fMRI) is by far the most widely used neuroimaging technique for non-invasive presurgical functional mapping of the SM1 cortex. Still, clinicians ought to keep in mind that fMRI suffers from several limitations for presurgical functional mapping in patients with brain disorders. First, this technique relies on the integrity of the neurovascular coupling that can be altered in various brain disorders, potentially leading to false positive or negative results.[9-12] Second, its relatively poor temporal resolution (at the level of the seconds) due to hemodynamic response time hampers fine discrimination of the sensory and the motor components in fMRI activation maps.[13] Consequently, fMRI activation maps may be much more challenging to interpret in patients with brain lesions than in healthy subjects.[10,13] In this context, MEG is increasingly considered as an attractive alternative to fMRI for presurgical functional mapping in patients with brain disorders.[3] Indeed, this neurophysiological technique provides direct information about neuronal activity with a millisecond temporal resolution and does not rely on the neurovascular coupling.

Several studies have previously shown that a combination of fMRI and MEG increases the localization reliability of the SM1 cortex and that MEG may be superior to fMRI in some patients with unclear fMRI localization.[11,13-21] Also, although a uni- or bimodal approach has been proven sufficient for functional mapping of the SM1 cortex in many patients, fMRI or MEG results can be confusing or challenging to interpret in some patients.[13,22] Such situation may occur in patients with lesion-induced anatomical distortion, atypical localization of hand sensorimotor function (see, e.g. ref [23]), false negative/positive results (see, e.g. ref [24]) or discordant results when used in combination (see, e.g. ref [13,22,25]). In those particular patients, it can be

difficult to assess the benefit-risk ratio associated with resective surgery using such uni- or bimodal mapping approach without further non-invasive functional neuroimaging or intracranial mapping procedures.

The above considerations emphasize that MEG presents an additional key strength over fMRI, which is the ability to investigate in one single MEG session different neurophysiological processes (i.e., evoked magnetic responses, induced magnetic responses, coupling between peripheral and cortical signals, and cortico-cortical coupling) that can be altered or affected differently by brain disorders or patients' clinical status. Thus, MEG provides the unique opportunity to acquire several MEG "*functional localizers*" in a reasonable time for the patients. Here, a "functional localizer" is defined as a given validated MEG method to localize the SM1 cortex regardless of the source reconstruction methods used (i.e., equivalent current dipole modeling, minimum norm estimate, spatial filtering approaches); i.e., electrical peripheral nerve stimulation[13,17,25-31], tactile stimulation[20,32], readiness and motor evoked fields[16,17,28,33,34], rolandic mu rhythm desynchronization/suppression (alpha or beta band)[25,28,35,36] or cortico-muscular coherence (CMC)[25,26]. The anatomical convergence of the different MEG functional localizers at the central sulcus has been demonstrated in healthy subjects and contributes to the assessment of the confidence level in functional mapping results (compared with a uni- or bimodal approach) and to determine the clinical need to undergo further intracranial mapping procedures.[25] Such approach also increases the yield of MEG in case of failure, inaccurate or atypical localization of one MEG functional localizer or fMRI mapping.[25] Associating multiple MEG functional localizers represents an elegant approach to overcome (i) the difficulty of MEG to reliably discern the anterior (M1 cortex) and the posterior (S1 cortex) banks of the central sulcus due to its limited

spatial resolution (about 5 mm), (ii) the issue of somatosensory or motor specificity of some of these MEG functional localizers, and (iii) the certain degree of inaccuracy of each MEG functional localizer related to various methodological issues. As an example, one study failed using equivalent current dipole modeling to identify spatially distinct distribution between motor and tactile evoked fields in a large group of patients with lesions close to the central suclus.[34] Also, this approach provides a compromise to the absence of consensus in the clinical MEG literature about which MEG functional localizers and source reconstruction methods should be used in a specific clinical situation. Finally, it is a way to indicate functional reorganization associated with the brain lesion as it will induce an increase in the spread of the different sensorimotor functional localizers.

Therefore, when available, MEG should be considered in the clinical indications described in 2.1. alone or in combination with fMRI. MEG is mandatory when fMRI shows atypical sensorimotor maps in patients with brain lesions. Also, several MEG functional localizers of the SM1 cortex should be considered for presurgical functional mapping, especially in patients with atypical mapping of the SM1 cortex when using one single MEG functional localizer.

Of note, the ACMEGS survey of the prevailing clinical MEG practices in the USA published in 2011 revealed that MEG is much less often used for presurgical functional mapping of the SM1 cortex than for epilepsy mapping (>800 MEG investigations done for epilepsy in 2007 and 2008 in 15 clinical MEG centers compared with >450 investigations of motor-related or somatosensory evoked fields). Furthermore, most recordings of somatosensory evoked fields were actually done to provide a “biological reference” validating the source reconstructions obtained for epilepsy mapping rather than to identify surgical landmarks *per se*. Similar results

where found in the European survey published in 2017 (542 MEG investigations done for epilepsy in 2014 in 12 clinical MEG centers compared with 244 investigations done for functional brain mapping in 10 of those 12 clinical MEG centers).[37] These data highlight that, despite its worldwide increased availability, MEG is actually underexploited for presurgical functional mapping in neurosurgical patients. This appears quite surprising considering the advantages of MEG over fMRI described above for this indication. Therefore, efforts need to be done to promote at national and international levels the major interests of MEG in this clinical indication among neurologists and neurosurgeons. In that respect, the position statement of the ACMEGS on "the value of magnetoencephalography (MEG)/magnetic source imaging (MSI) in non-invasive presurgical mapping of eloquent cortices of patients preparing for surgical interventions" represents a major achievement.[3]

3. Update of the clinically pertinent research progresses

Since the formulation of the first ACMEGS CPGs, three main research progresses have been made in the field of functional SM1 cortex mapping using MEG: (i) the validation of the spatiotemporal signal space separation method (tSSS) for the subtraction of high-amplitude MEG artifacts caused by nearby or internal sources of interference, (ii) the development and validation of the cortico-kinematic coherence (CKC) method to pinpoint the SM1 cortex, and (iii) the identification of the sensorimotor resting state network (RSN) using source-space beta-band-envelope correlation. tSSS and CKC are now considered as robust and validated clinical MEG tools, while the mapping of SM1 cortex using MEG RSNs is, by analogy with resting state functional magnetic resonance imaging (fMRI), at the stage of being recognized as a method with future potential clinical usefulness.

3.1. Spatiotemporal signal space separation

One of the limitations of MEG is its high sensitivity to magnetic interferences. Effective passive (e.g., magnetically shielded room) and active (e.g., active interference cancellation system, internal or external) shielding systems are used to drastically attenuate environmental magnetic artifacts (e.g., power line interference, moving metallic objects, etc.). By contrast, nearby or subject-related sources of interference (e.g., heart beats, implanted stimulator, dental braces, neurosurgical implants, CranioFix, etc.) are more difficult to abate. Unfortunately, these latter magnetic interferences are often encountered in neurosurgical patients in need of non-invasive presurgical functional mapping, and especially in patients requiring a second surgery.[25,38,39]

Apart from spatial filtering approaches that improve SM1 cortex source localization in subjects with metallic implants[27], the tSSS method has been specifically designed to overcome this issue. First, the conventional signal space separation (SSS) method—based on sensor geometry and Maxwell's equations—separates measured MEG signals into brain-related signals, external interference signals, and remaining intermediate components.[40-42] Second, artifacts generated by nearby or internal sources of interference are identified based on the high correlation they generate between brain-related signals and intermediate components.[41] Finally, identified intermediate components are regressed out of the brain-related MEG signals.[41]

The tSSS method has been shown to substantially reduce the high-amplitude magnetic artifacts associated with implanted vagal nerve stimulator, which typically hampered proper interpretation of MEG data obtained in epileptic patients with such stimulator.[43-47] Also, some studies have validated that this approach makes it possible

to obtain reliable MEG functional mapping of the SM1 cortex using either somatosensory and movement evoked fields or CKC (see 2.2.) in subjects with dental braces[39] or ferromagnetic material located on the scalp.[38,39] These findings therefore extend the clinical applicability of MEG in this clinical indication, making it feasible to investigate SM1 processing in patients hitherto not eligible for MEG recording. Although tSSS is originally available for one type of MEG system (i.e., Elekta Oy, Helsinki, Finland), it has been adapted to another commonly available MEG system (i.e., CTF Inc., Vancouver, Canada).[48] Finally, other methods have been developed and tested to remove magnetic interferences from MEG signals such as, e.g., the blind source separation method, which has the advantage of being system independent.[49,50] Future progresses in this field of MEG signal processing will also increase the applicability of MEG for clinical indication.

3.2. Corticokinematic coherence

During repetitive limb movements, electroencephalographic (EEG) and MEG cortical activity is coherent with movement kinematics.[51-54] This coupling phenomenon was termed CKC. Up to now, CKC has been mainly used for MEG functional mapping of the SM1 hand area in healthy subjects and patients with brain lesions but data are also available for foot mapping in healthy subjects.[55] The main advantages of CKC in the clinical context rely on its simplicity, robustness, and reliability at the individual level compared with other validated MEG functional localizers such as, e.g., CMC. CKC sources can be localized at the individual level with conventional dipole modeling in the time-domain using the cross-correlogram[25,51] or using more advanced source reconstruction methods such as dynamic imaging of coherent sources (DICS).[56]

In a typical CKC setting, participants perform repetitive flexion-extensions of the fingers or of the index finger at ~3-Hz for ~3 min, while their cortical signals are recorded with MEG and their finger kinematics is recorded with an accelerometer.[51,57] Coherence is then computed between MEG and acceleration signals. CKC typically peaks at finger movement frequency and its first harmonic, with its main cortical source located in the SM1 hand area contralateral to finger movements.[51,57] CKC can also be estimated based on other kinetic, kinematics or EMG signals.[58] Indeed, apart from acceleration or velocity signals, CKC has been reported based on (i) pressure signals, (ii) force signals, and (iii) rectified EMG signals.[58] CKC can therefore be investigated with typical surface EMG (sEMG) electrodes that are available in most of the clinical MEG settings. Of notice, CKC has also been demonstrated during goal-directed hand action tasks[52,59] and slower finger movement rates (at 1~ Hz and 2 Hz).[60] Importantly, the movement rate had no influence on CKC level and source location.[60] This finding is of particular interest in the clinical context because patients with motor deficit or movement disorder might struggle to perform fast repetitive movements and moving at a slower rate would undoubtedly ease their task and reduce potential movement-related artifacts. Still, the only disadvantage associated with decreasing the movement rate is that recording length has to be increased to maintain the amount of movement cycles.[60]

CKC is also observed during passive movements (i.e., when participants' limb is moved by an experimenter or a device), with similar coherence level and source location compared with active tasks.[55,61] This finding is also of high interest for the clinical application of CKC since it does not require any additional cooperation from the participants than staying still in the MEG scanner. Passive movements should therefore be considered in young children, in patients who struggle to perform

repetitive movements, and in patients with implanted ferromagnetic material (e.g., CranioFix®) located close to the MEG sensors to avoid as much as possible any head movement artifact synchronized with active movements of the limbs. Still, in this latter situation, specific signal preprocessing approaches (e.g., tSSS) might help uncover proper CKC (see 3.1.).[38] If needed, patient's cooperation can be increased by presenting a movie during the passive movement task, which is highly relevant in young children. Passive movements can be elicited either by an investigator moving the distal part of the limbs (see, e.g., ref [61]) or by a stimulator such as, e.g., the pneumatic artificial muscle stimulator.[55] This latter stimulator is of particular interest in the clinical setting since it makes possible to investigate CKC in a robust and reliable manner at various fixed frequencies, which is ideal for within (e.g., longitudinal studies) and between patients' comparisons. Also, such a movement actuator provides brain responses robust enough to identify the index and hallux SM1 cortex based on only 1 min of MEG recording.[55]

The neurophysiological basis of the CKC phenomenon has been investigated by comparing active and passive index finger movements with various tactile input levels as well as by assessing coupling directionality (with renormalized partial directed coherence; rPDC).[61,62] These investigations showed that CKC is mainly driven by proprioceptive inputs to the SM1 cortex. Indeed, CKC and rPDC levels were independent of the motor output, while rPDC levels were influenced by the amount of tactile afferences (i.e., increased afferent coupling with increasing tactile input) but not CKC levels. These findings are in agreement with the fact that both S1 (Brodmann areas 3a and 2) and M1 cortices receive proprioceptive feedback during both active and passive hand movements.[63] These data also suggest that, apart from presurgical functional mapping of the SM1 cortex, CKC is an interesting method to

investigate the pathophysiology of nervous system disorders that affect proprioceptive pathways.

To sum up, active and passive CKC should now be considered as valid and robust MEG functional localizers of the SM1 cortex. Considering its simplicity, robustness, and reliability, CKC should be considered in future CPGs about MEG functional mapping of the SM1 cortex and integrated in the list of available and validated MEG functional localizers of the SM1 cortex.

3.3. Resting state functional connectivity

Evidence suggests that presurgical functional mapping of the SM1 cortex could rely on resting-state brain dynamics. Indeed, brain activity at rest is spatially and temporally structured into large-scale neural networks known as resting state networks (RSNs; for a review, see ref [64]). Nodes of these networks (such as bilateral SM1 cortices for the motor network) can be uncovered with functional connectivity measures. Such approach would be of particular clinical interest in young children, patients with strong motor deficits, and patients inducing movement-related artifacts.

RSNs share some close topological properties with functional brain networks.[64] A particular RSN that has been robustly identified using fMRI[65] is the SM1 network. This RSN (among other classical fMRI RSNs) has also been disclosed using MEG and source-space beta-band power envelope correlation.[66-68] It displays a typical inter-hemispheric resting-state functional connectivity (rsFC) between left and right SM1 cortices, so that SM1 cortex in one hemisphere can be identified using seed-based rsFC from the homologous SM1 cortex. This result established for healthy subjects suggests that SM1 cortex could be mapped in the affected hemisphere of neurosurgical patients using rsFC from the homologous area in the non-affected

hemisphere, as demonstrated by several fMRI studies.[69-72] Indeed, such resting-state fMRI mapping approach has been validated in neurosurgical patients against task-based motor fMRI and intracranial stimulations; the results showing that it might even be more reliable than task-based fMRI.[70,73,74] Considering the limitations of fMRI in patients with brain disorders (see 2.2.), it would be of particular clinical interest to determine if rsFC-based functional mapping of the SM1 cortex could be accurately performed using a neurophysiological technique with a good spatial resolution such as MEG. Interestingly, among the RSNs disclosed by MEG rsFC using envelope correlation and a seed-based approach, the SM1 network has been shown to be the most robust at the individual level.[75] Accordingly, rsFC-based mapping might indeed be of high clinical interest. A pilot MEG study[76] performed in ten patients with focal brain lesions located close to the central sulcus has illustrated the feasibility and the potential clinical interest (mapping in agreement with some classical MEG functional localizer(s) in 8 patients) of this rsFC MEG approach (Figure 1). Still, further dedicated studies are clearly needed before introducing it in the clinical armamentarium of MEG methods to map the SM1 cortex. This approach should indeed be validated (as done for resting state fMRI) against task-based sensorimotor MEG and intracranial stimulations before using it in clinics.

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4. Recommendations for clinical practice

4.1. Recommendations for the referring physicians

MEG can be used to map the hand, foot, and face SM1 cortical areas using various functional MEG localizers (see Table 1). The referring physicians should

therefore clearly indicate to the magnetoencephalographer at the time of referral which area(s) of the SM1 cortex need(s) to be located and what is the clinical indication of the functional mapping procedure (see 2.1.). Information about patient's clinical status that could influence the MEG data acquisition should also be provided upon referral. This information should comprise patient's neurological (and especially sensorimotor), cognitive or behavioral status, as well as the location and the type of brain lesion. Referring physicians should also bear in mind that MEG is highly sensitive to implanted ferromagnetic materials (e.g., braces, dental works, CranioFix®, neurosurgical clips, vagal nerve stimulator, ventricular shunt, etc.) and that such materials generate high-amplitude magnetic artifacts that can hamper proper MEG investigation. They should therefore ask patients whether they carry such implanted materials to identify those that will be at risk of inducing such magnetic artifacts. Special care should also be taken when it comes to patients who already underwent intracranial surgical procedures as they might produce magnetic artifacts due to implanted ferromagnetic material. The magnetoencephalographer should therefore be warned at referral about any potential implanted ferromagnetic material and, in any case, referring physicians should clearly indicate if the patient already underwent neurosurgical procedures. Of notice, this does not mean that MEG cannot be performed in such patients but special care needs to be taken during MEG data acquisition (e.g., type of MEG functional localizer used) and data processing (see 3.1.).

4.2. Recommendations for the clinical magnetoencephalographer

As stressed in 4.1., it is mandatory that clinicians involved in MEG acquisition, analysis, and interpretation be informed of the patients' clinical status and

of the clinical indication of the functional mapping procedure. Clinical magnetoencephalographers should make available to referring clinicians a structured and comprehensive medical examination request form for such MEG investigation to maximize the chance of getting all the mandatory information. Such form could also be established at the clinical MEG societies level to harmonize clinical MEG referrals across MEG centers. Also, based on the considerations developed in 2.2, clinical MEG centers should make available to their patients referred for functional SM1 cortex mapping several validated functional localizers that have been properly and formally tested in-house in a sufficiently large group of healthy subjects prior to clinical use. Magnetoencephalographers should master the advantages, limits, and neurophysiological bases of each functional localizer under use for this application at their center. Some of the validated MEG functional localizers that can be used in this clinical indication have been described in details in the first ACMEGS CPGs.[1] Others will be detailed below.

5. Practical advices

Based on the above considerations, several MEG functional localizers are recognized for functional mapping of the SM1 cortex (see 2.2. for a list of references):

i. Somatosensory evoked fields following electrical peripheral nerve stimulation,
ii. Somatosensory evoked fields following mechanical (i.e., tactile) passive stimulation,
iii. Readiness and motor evoked fields,
iv. CMC, i.e., the coupling between cortical and sEMG signals during isometric contraction,

v. CKC of active or passive continuous movements,

vi. Rolandic mu (alpha or beta band) rhythm desynchronization/suppression to volitional movements.

Depending on the area of the SM1 cortex (i.e., face, hand, and foot representation) that needs to be located, different MEG functional localizers can be used (Table 1). Practical recommendations for i-iii have been developed in details in the ACMEGS CPGs. These methods are indeed classically used to obtain MEG functional localizers for presurgical SM1 cortex mapping. Here, we will further develop the practical advices for iv-vi, which are either methods requiring special practical considerations (iv and vi) or newly developed SM1 cortex MEG functional localizer (v). Of notice, the general considerations for interpretation of iv-vi do not differ substantially from those described in the seminal ACMEGS CPGs.[1] Advices will be developed for the functional mapping of the hand area but they can easily be extrapolated to the face or foot areas.

5.1. Corticomuscular coherence

5.1.1. Neurophysiological bases

- During sustained isometric contraction, sEMG signals, representing algebraic sum of motor unit action potentials, are coherent with MEG signals recorded from the SM1 cortex. This coupling between muscle and cortical activities, referred to as CMC, typically occurs at 15–40 Hz over the SM1 cortex contralateral to muscle contraction.
- When studied with MEG, CMC mainly reflects corticospinal communication from the M1 cortex, with minimal influence of peripheral afferents.

- CMC studies have mainly focused on the upper limbs but there are studies that have investigated other body parts (lower limbs or face muscles) and that have shown that CMC occurs in a somatotopic manner along the M1 cortex.
- For unknown reasons, CMC is too weak to be detected in 5 min in ~10–30 % of healthy individuals.[64] Increasing the recording time may help recovering significant CMC at the expense of participants' cooperation.

5.1.2. Motor task

- Steady isometric contraction for ~5 min.
- If available and depending on the muscles under investigation, contraction should be performed against a force transducer to provide feedback (visual or auditory) of the desired force level to the participant.
- Force level should be ~8–15% of the maximal voluntary contraction force. Low contraction force is recommended to avoid muscle fatigue.
- Set target force based on patients' maximal voluntary contraction test: 2–3 maximum contractions, each lasting for 3–4 s, with 2-min rest periods in-between. Use the highest force value.
- In absence of force signal, free-weights (steady work against gravity) or isometric co-contraction of both agonist and antagonist muscles (e.g., contracting wrist flexors and extensors simultaneously) can be used.
- For mapping of the hand area of the M1 cortex, pinch (thumb-index finger opposition) is typically used.
- Allow few training trials before actual recording.
- Participants should avoid eye movements and excessive blinking, and focus on maintaining the isometric contraction as steady as possible.

5.1.3. Recording

- Band pass of 0.03 to 300 Hz with 1000 Hz sampling rate or higher.
- Record raw data. All signal processing is done post hoc.
- Use continuous head position tracking if available.
- Record sEMG from the superficial agonist muscles and, preferably, from all accessible synergist muscles to yield multiple cortical source estimates (one for each sEMG signal).
- Use monopolar sEMG recording with one common reference on inactive area (e.g., over bony area) and electrode(s) over the target muscles. Compared to bipolar recordings, monopolar recordings are less sensitive to variations in electrode placement, and provide ~20% stronger CMC level.
- When available, record force signal to provide real-time feedback, but also to discard unsuccessful segments of the data post hoc.

5.1.4. Data Analysis and preprosessing

5.1.4.1. Preprocessing

- When available, use appropriate methods to suppress external interferences and to compensate for head movements (e.g., signal-space separation).
- Band-pass filter MEG signals between 1–195 Hz.
- Inspect visually all MEG, sEMG and force signals, and discard all unsuccessful channels.

5.1.4.2. CMC analysis

- Split data into 1000-ms epochs with 800-ms epoch overlap (frequency resolution of 1 Hz).
- Discard MEG epochs contaminated by eye movements, muscle activity, head movement, and system artifacts.

- Normalize individual sEMG epochs by their root mean square (RMS) value. This normalization ensures that CMC estimation is minimally affected by changes in contraction strategy.
- Compute power- and cross-spectra, as well as cross-correlograms, between all MEG and RMS-normalized sEMG signals.
- Apply a ±2.5 Hz spectral smoothing. A multitapering approach with 5 tapers can be used to that effect.
- Rectification of the sEMG signal(s) is not recommended.
- Compute coherence spectra as in ref [775].
- Inspect the coherence spectra. CMC should peak at ~20 Hz.

5.1.4.3. Source localization

- Use the cross-correlograms or the cross-spectrum for source analysis.
- Band-pass filter the cross-correlograms at 10–45 Hz, and fit an equivalent current dipole (ECD) at the timing of the most prominent peak among a fixed selection of ~40 sensors over the SM1 cortex contralateral to muscle contraction.
- Alternatively, fit an ECD at the ~20-Hz peak of the cross-spectrum. The cross-spectrum is complex; both real and imaginary parts can be used.
- A spherical head model fitted to individual MRI can be used for ECD estimation.
- ECDs can be visualized on the coregistered individual MRIs.

5.2. Corticokinematic coherence

5.2.1. Neurophysiological bases

See 3.2.

5.2.2. Motor task

- Self-paced active flexion-extensions of the finger(s) or the toe(s) at 3 Hz.

- Passive flexion-extensions of the index finger or the big toe by an experimenter at 1–3 Hz or a stimulator at 1–12 Hz.
- Movement frequency has to be as constant as possible.
- Passive movement amplitude can be limited to few millimeters.
- For active movements, experiment duration needs to be adapted to movement frequency (1 Hz, 6–10 min; 2 Hz, 4–8 min; ≥ 3 Hz, 2–3 min).
- For passive movements generated by a precise movement actuator, the movement frequency can be set to 1–12 Hz with a minimum of 1-min recording duration, but ~3-min is recommended.
- Earplugs should be used to block auditory noise synchronized with the movements.
- The moving limb should not be visible to the subject to avoid any visual contact with the moving limb.
- During passive movements, participants can watch a movie to maximize the cooperation and keep their vigilance high.

5.2.3. Recording

- Band pass of 0.03 to 300 Hz with 1000 Hz sampling rate or higher.
- Record raw data. All signal processing is done post hoc.
- Use continuous head position tracking if available.
- Record movement kinematics synchronously with MEG signals with either a MEG-compatible accelerometer placed on the index finger, or sEMG with electrodes placed so that they capture the movement frequency from EMG amplitude modulation (see CMC part for more information about how to place the sEMG electrodes).
- The testing paradigm should be repeated to assess reproducibility and ensure consistent results.

5.2.4. Data analysis

5.2.4.1. Preprocessing

- When available, use appropriate methods to suppress external interferences and to correct for head movements (e.g., signal space separation).
- In case of motion artifacts in the sEMG signals, band-pass the sEMG signals at 10–195 Hz, otherwise use same filter as for the MEG/EEG signals.

5.2.4.2. Data analysis

- Split data into epochs long of ~6 movements cycles and 80 % overlap. i.e. for 3-Hz movements, epochs are 2000-ms-long with 1600-ms overlap, leading to a frequency resolution of 0.5 Hz.
- Discard epochs contaminated by eye movements, muscle activity, head movement and system artifacts.
- Compute power- and cross-spectra, as well as cross-correlogram between all MEG and movement kinematics signals.
- Compute coherence spectra as in ref [775].
- Inspect the coherence spectra. CKC should peak at movement frequency and twice movement frequency.

5.2.4.3. Source localization

- Use the cross-correlograms or the cross-spectrum for source analysis
- Filter the cross-correlogram using a band-pass filter that encompasses the coherent frequencies (usually, from half the movement frequency to > 5 times movement frequency; if movement artifacts are too strong, rise the lower cut off to 1.5 times movement frequency).
- Fit an ECD at the main peak of the filtered cross-correlogram function.

- Alternatively, fit an ECD at the peaks of the cross-spectrum. The cross-spectrum is complex; both real and imaginary parts can be used.
- If required, use a subselection of (>40) MEG sensors centered over the SM1 cortex contralateral to the moving limb.
- ECDs can be visualized on the coregistered individual MRIs.

5.3. Rolandic mu rhythm desynchronization/suppression to volitional movements

5.3.1. Neurophysiological bases

- The rolandic mu rhythm is characterized by two main frequency components peaking at ~10 Hz (alpha component) and ~20 Hz (beta component) that appear to be related to different functional processes: the alpha component mainly (but not exclusively) reflects somatosensory cortical processes, while the beta component appears predominantly involved in motor cortex function.
- The two components of the mu rhythm are transiently suppressed during movements and subsequently enhanced shortly after movements offset.
- The 20-Hz-movement-related modulation is organized in a somatotopic manner along the precentral gyrus while this is less clear for the 10 Hz modulation, which has been shown to mainly occur close to the hand region of the postcentral gyrus regardless of the body part moved.
- Movement-related suppression seems to represent an active state of the sensorimotor network while, movement-related enhancement is thought to reflect cortical inhibition, active cortical stabilization or suppression, or an active motor process keeping responsiveness to future movements (the "*status quo*" hypothesis).

5.3.2. Motor task

- Single self-paced or auditorily-/visually-cued brisk movements of the fingers (e.g.,

fingers extensions), toes (e.g., toes extensions) or lips (e.g., lips pouting).

- 100–200 movements should be performed at an interval of about 3 s (2.5–3.5 s random inter-movement interval when cued).
- When cued, participants should react as quickly as possible while avoiding any anticipation or counting.
- Participants should keep their eyes opened and avoid looking at the moving limb.

5.3.3. Recording

- Band pass of 0.03 to 300 Hz with 1000 Hz sampling rate or higher.
- Record raw data. All signal processing is done post hoc. On-line averages are recommended to check the responses during the recording.
- Use continuous head position tracking if available.
- Optimally, sEMG should be used to capture movement onsets. This is necessary for self-paced movements.

5.3.4. Data analysis

5.3.4.1. Preprocessing

- When available, use appropriate methods to suppress external interferences and to correct for head movements (e.g., signal space separation).

5.3.4.2. Data analysis

- Split data into 3500-ms epochs extracted from -1500 to 2000 ms relative to movement onsets if available or sensory cues otherwise.
- Discard epochs contaminated by eye movements, muscle activity, head movement and system artifacts.
- Apply a Morlet wavelet-based time-frequency decomposition to the remaining epochs with a standard time-frequency compromise (7-cycle wavelets).
- Compute the evolution of the average power of the wavelet coefficients.

- Identify the timing of minimal power, relative to a reference interval (chosen from –1000 to –500 ms with respect to movement onset), separately at ~10 Hz and ~20 Hz.

5.3.4.3. Source localization

- For both frequency components, use a distributed source model (e.g., minimum norm estimate) or a spatial filter approach (e.g., minimum variance beamformer) to estimate the mean power at the identified timing and in the baseline.
- Use a whole-brain-covering source space.
- For both frequency components, visualize the ratio between the power at the identified timing and that in the baseline on individual anatomical MRI. Local power minima should localize at the SM1 cortex, usually bilaterally.
- ECDs can be visualized on the coregistered individual MRIs.

6. Conclusions

MEG is a neurophysiological technique that, when combined with structural MRI, makes it possible to map noninvasively the functionally eloquent cortices by investigating different features of human cortical activity. Considering the available literature and the clear advantages of MEG over fMRI, MEG should now be considered as a method of reference for presurgical functional brain mapping. Recent advances generalize the use of MEG functional mapping of the SM1 cortex to patients who could hitherto not be considered candidates for such MEG mapping procedure. Efforts should be made to promote and disseminate the knowledge about the manifest interests and strengths of MEG for this clinical indication.

7. Acknowledgments

Xavier De Tiège is Post-doctorate Clinical Master Specialist at the Fonds de la Recherche Scientifique (FRS-FNRS, Brussels, Belgium).

Mathieu Bourguignon has been supported by the program Attract of Innoviris (grant 2015-BB2B-10), by the Spanish Ministry of Economy and Competitiveness (grant PSI2016-77175-P), and by the Marie Skłodowska-Curie Action of the European Commission (grant 743562).

Harri Piitulainen has been supported by the Academy of Finland (grants #266133 and #296240), Jane and Aatos Erkko Foundation, and Emil Aaltonen Foundation.

The authors would like to thank Professor Riitta Hari for her support in most of the research works published by the authors and presented in this paper.

The MEG project at the CUB Hôpital Erasme is financially supported by the Fonds Erasme (Research convention “Les Voies du Savoir”, Fonds Erasme, Brussels, Belgium).

8. References

1 Burgess RC, Funke ME, Bowyer SM et al. American Clinical Magnetoencephalography Society Clinical Practice Guideline 2: presurgical functional brain mapping using magnetic evoked fields*. J Clin Neurophysiol 2011;28:355-361.

2 Burgess RC, Barkley GL, Bagic AI. Turning a new page in clinical magnetoencephalography: practicing according to the first clinical practice guidelines. J Clin Neurophysiol 2011;28:336-340.

3 Bagic AI, Bowyer SM, Kirsch HE et al. American Clinical MEG Society (ACMEGS) Position Statement #2: The Value of Magnetoencephalography (MEG)/Magnetic Source Imaging (MSI) in Noninvasive Presurgical Mapping of Eloquent Cortices of Patients Preparing for Surgical Interventions. J Clin Neurophysiol 2017;

4 Neggers SF, Langerak TR, Schutter DJ et al. A stereotactic method for image-guided transcranial magnetic stimulation validated with fMRI and motor-evoked potentials. Neuroimage 2004;21:1805-1817.

5 Pirotte B, Voordecker P, Neugroschl C et al. Combination of functional magnetic resonance imaging-guided neuronavigation and intraoperative cortical brain mapping improves targeting of motor cortex stimulation in neuropathic pain. Neurosurgery 2005;56:344-359; discussion 344-359.

6 Stancanello J, Cavedon C, Francescon P et al. BOLD fMRI integration into radiosurgery treatment planning of cerebral vascular malformations. Medical physics 2007;34:1176-1184.

7 Pantelis E, Papadakis N, Verigos K et al. Integration of functional MRI and white matter tractography in stereotactic radiosurgery clinical practice.

International journal of radiation oncology, biology, physics 2010;78:257-267.

8 Conti A, Pontoriero A, Ricciardi GK et al. Integration of functional neuroimaging in CyberKnife radiosurgery: feasibility and dosimetric results. Neurosurgical focus 2013;34:E5.

9 Bartsch AJ, Homola G, Biller A, Solymosi L, Bendszus M. Diagnostic functional MRI: illustrated clinical applications and decision-making. J Magn Reson Imaging 2006;23:921-932.

10 D'Esposito M, Deouell LY, Gazzaley A. Alterations in the BOLD fMRI signal with ageing and disease: a challenge for neuroimaging. Nat Rev Neurosci 2003;4:863-872.

11 Inoue T, Shimizu H, Nakasato N, Kumabe T, Yoshimoto T. Accuracy and limitation of functional magnetic resonance imaging for identification of the central sulcus: comparison with magnetoencephalography in patients with brain tumors. Neuroimage 1999;10:738-748.

12 Rossini PM, Altamura C, Ferretti A et al. Does cerebrovascular disease affect the coupling between neuronal activity and local haemodynamics? Brain 2004;127:99-110.

13 Korvenoja A, Kirveskari E, Aronen HJ et al. Sensorimotor cortex localization: comparison of magnetoencephalography, functional MR imaging, and intraoperative cortical mapping. Radiology 2006;241:213-222.

14 Beisteiner R, Erdler M, Teichtmeister C et al. Magnetoencephalography may help to improve functional MRI brain mapping. Eur J Neurosci 1997;9:1072-1077.

15 Beisteiner R, Gomiscek G, Erdler M et al. Comparing localization of conventional functional magnetic resonance imaging and magnetoencephalography. Eur J Neurosci 1995;7:1121-1124.

16 Kamada K, Houkin K, Takeuchi F et al. Visualization of the eloquent motor system by integration of MEG, functional, and anisotropic diffusion-weighted MRI in functional neuronavigation. Surg Neurol 2003;59:352-361; discussion 361-352.

17 Kober H, Nimsky C, Moller M et al. Correlation of sensorimotor activation with functional magnetic resonance imaging and magnetoencephalography in presurgical functional imaging: a spatial analysis. Neuroimage 2001;14:1214-1228.

18 Morioka T, Mizushima A, Yamamoto T et al. Functional mapping of the sensorimotor cortex: combined use of magnetoencephalography, functional MRI, and motor evoked potentials. Neuroradiology 1995;37:526-530.

19 Morioka T, Yamamoto T, Mizushima A et al. Comparison of magnetoencephalography, functional MRI, and motor evoked potentials in the localization of the sensory-motor cortex. Neurol Res 1995;17:361-367.

20 Roberts TP, Rowley HA. Mapping of the sensorimotor cortex: functional MR and magnetic source imaging. AJNR Am J Neuroradiol 1997;18:871-880.

21 Shimizu H, Nakasato N, Mizoi K, Yoshimoto T. Localizing the central sulcus by functional magnetic resonance imaging and magnetoencephalography. Clin Neurol Neurosurg 1997;99:235-238.

22 Juenger H, Ressel V, Braun C et al. Misleading functional magnetic resonance imaging mapping of the cortical hand representation in a 4-year-old boy with an arteriovenous malformation of the central region. J Neurosurg Pediatr 2009;4:333-338.

23 Makela JP, Vitikainen AM, Lioumis P et al. Functional plasticity of the motor cortical structures demonstrated by navigated TMS in two patients with epilepsy. Brain stimulation 2013;6:286-291.

24 De Tiège X, Connelly A, Liegeois F et al. Influence of motor functional magnetic resonance imaging on the surgical management of children and adolescents with symptomatic focal epilepsy. Neurosurgery 2009;64:856-864; discussion 864.

25 Bourguignon M, Jousmäki V, Marty B et al. Comprehensive functional mapping scheme for non-invasive primary sensorimotor cortex mapping. Brain Topogr 2013;26:511-523.

26 Makela JP, Kirveskari E, Seppa M et al. Three-dimensional integration of brain anatomy and function to facilitate intraoperative navigation around the sensorimotor strip. Hum Brain Mapp 2001;12:180-192.

27 Cheyne D, Bostan AC, Gaetz W, Pang EW. Event-related beamforming: a robust method for presurgical functional mapping using MEG. Clin Neurophysiol 2007;118:1691-1704.

28 Willemse RB, Hillebrand A, Ronner HE, Vandertop WP, Stam CJ. Magnetoencephalographic study of hand and foot sensorimotor organization in 325 consecutive patients evaluated for tumor or epilepsy surgery. Neuroimage Clin 2016;10:46-53.

29 Solomon J, Boe S, Bardouille T. Reliability for non-invasive somatosensory cortex localization: Implications for pre-surgical mapping. Clin Neurol Neurosurg 2015;139:224-229.

30 Vitikainen AM, Lioumis P, Paetau R et al. Combined use of non-invasive techniques for improved functional localization for a selected group of epilepsy surgery candidates. Neuroimage 2009;45:342-348.

31 Willemse RB, de Munck JC, van't Ent D et al. Magnetoencephalographic study of posterior tibial nerve stimulation in patients with intracranial lesions around the central sulcus. Neurosurgery 2007;61:1209-1217; discussion 1217-1208.

32 Schiffbauer H, Berger MS, Ferrari P et al. Preoperative magnetic source imaging for brain tumor surgery: a quantitative comparison with intraoperative sensory and motor mapping. J Neurosurg 2002;97:1333-1342.

33 Gaetz W, Cheyne D, Rutka JT et al. Presurgical localization of primary motor cortex in pediatric patients with brain lesions by the use of spatially filtered magnetoencephalography. Neurosurgery 2009;64:ons177-185; discussion ons186.

34 Lin PT, Berger MS, Nagarajan SS. Motor field sensitivity for preoperative localization of motor cortex. J Neurosurg 2006;105:588-594.

35 Nagarajan S, Kirsch H, Lin P et al. Preoperative localization of hand motor cortex by adaptive spatial filtering of magnetoencephalography data. J Neurosurg 2008;109:228-237.

36 Willemse RB, de Munck JC, Verbunt JP et al. Topographical organization of mu and Beta band activity associated with hand and foot movements in

patients with perirolandic lesions. The open neuroimaging journal 2010;4:93-99.

37 De Tiège X, Lundqvist D, Beniczky S, Seri S, Paetau R. Current clinical magnetoencephalography practice across Europe: Are we closer to use MEG as an established clinical tool? Seizure 2017;50:53-59.

38 Bourguignon M, Whitmarsh S, Piitulainen H et al. Reliable recording and analysis of MEG-based corticokinematic coherence in the presence of strong magnetic artifacts. Clin Neurophysiol 2016;127:1460-1469.

39 Hillebrand A, Fazio P, de Munck JC, van Dijk BW. Feasibility of clinical magnetoencephalography (MEG) functional mapping in the presence of dental artefacts. Clin Neurophysiol 2013;124:107-113.

40 Taulu S, Kajola M, Simola J. Suppression of interference and artifacts by the Signal Space Separation Method. Brain Topogr 2004;16:269-275.

41 Taulu S, Simola J. Spatiotemporal signal space separation method for rejecting nearby interference in MEG measurements. Phys Med Biol 2006;51:1759-1768.

42 Taulu S, Simola J, Kajola M. Applications of the Signal Space Separation Method. IEEE Trans Sign Proc 2005;53:3359-3372.

43 Carrette E, De Tiège X, Op De Beeck M et al. Magnetoencephalography in epilepsy patients carrying a vagus nerve stimulator. Epilepsy Res 2011;93:44-52.

44 De Tiège X, Legros B, Op de Beeck M, Goldman S, Van Bogaert P. Vagus nerve stimulation. J Neurosurg Pediatrics 2008;2:375-377; author reply 377.

45 Song T, Cui L, Gaa K et al. Signal space separation algorithm and its application on suppressing artifacts caused by vagus nerve stimulation for magnetoencephalography recordings. J Clin Neurophysiol 2009;26:392-400.

46 Tanaka N, Thiele EA, Madsen JR, Bourgeois BF, Stufflebeam SM. Magnetoencephalographic analysis in patients with vagus nerve stimulator. Pediatric neurology 2009;41:383-387.

47 Kakisaka Y, Mosher JC, Wang ZI et al. Utility of temporally-extended signal space separation algorithm for magnetic noise from vagal nerve stimulators. Clin Neurophysiol 2013;124:1277-1282.

48 Kern K, Naros G, Braun C, Weiss D, Gharabaghi A. Detecting a Cortical Fingerprint of Parkinson's Disease for Closed-Loop Neuromodulation. Frontiers in neuroscience 2016;10:110.

49 Migliorelli C, Alonso JF, Romero S et al. Influence of metallic artifact filtering on MEG signals for source localization during interictal epileptiform activity. Journal of neural engineering 2016;13:026029.

50 Migliorelli C, Alonso JF, Romero S et al. Automatic BSS-based filtering of metallic interference in MEG recordings: definition and validation using simulated signals. Journal of neural engineering 2015;12:046001.

51 Bourguignon M, De Tiège X, Op de Beeck M et al. Functional motor-cortex mapping using corticokinematic coherence. Neuroimage 2011;55:1475-1479.

52 Jerbi K, Lachaux JP, N'Diaye K et al. Coherent neural representation of hand speed in humans revealed by MEG imaging. Proc Natl Acad Sci U S A 2007;104:7676-7681.

53 Kelso JA, Fuchs A, Lancaster R et al. Dynamic cortical activity in the human brain reveals motor equivalence. Nature 1998;392:814-818.

54 O'Suilleabhain PE, Lagerlund TD, Matsumoto JY. Cortical potentials at the frequency of absolute wrist velocity become phase-locked during slow sinusoidal tracking movements. Exp Brain Res 1999;126:529-535.

55 Piitulainen H, Bourguignon M, Hari R, Jousmäki V. MEG-compatible pneumatic stimulator to elicit passive finger and toe movements. Neuroimage 2015;112:310-317.

56 Gross J, Kujala J, Hämäläinen M et al. Dynamic imaging of coherent sources: Studying neural interactions in the human brain. Proc Natl Acad Sci U S A 2001;98:694-699.

57 Bourguignon M, Jousmäki V, Op de Beeck M et al. Neuronal network coherent with hand kinematics during fast repetitive hand movements. Neuroimage 2012;59:1684-1691.

58 Piitulainen H, Bourguignon M, De Tiège X, Hari R, Jousmäki V. Coherence between magnetoencephalography and hand-action-related acceleration, force, pressure, and electromyogram. Neuroimage 2013;72:83-90.

59 Marty B, Bourguignon M, Jousmäki V et al. Cortical kinematic processing of executed and observed goal-directed hand actions. Neuroimage 2015;119:221-228.

60 Marty B, Bourguignon M, Op de Beeck M et al. Effect of movement rate on corticokinematic coherence. Neurophysiol Clin 2015;45:469-474.

61 Piitulainen H, Bourguignon M, De Tiège X, Hari R, Jousmäki V. Corticokinematic coherence during active and passive finger movements. Neuroscience 2013;238:361-370.

62 Bourguignon M, Piitulainen H, De Tiège X, Jousmäki V, Hari R. Corticokinematic coherence mainly reflects movement-induced proprioceptive feedback. Neuroimage 2015;106:382-390.

63 Goldring S, Ratcheson R. Human motor cortex: sensory input data from single neuron recordings. Science 1972;175:1493-1495.

64 Fox MD, Raichle ME. Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. Nat Rev Neurosci 2007;8:700-711.

65 Biswal B, Yetkin FZ, Haughton VM, Hyde JS. Functional connectivity in the motor cortex of resting human brain using echo-planar MRI. Magn Reson Med 1995;34:537-541.

66 Brookes MJ, Woolrich M, Luckhoo H et al. Investigating the electrophysiological basis of resting state networks using magnetoencephalography. Proc Natl Acad Sci U S A 2011;108:16783-16788.

67 Hipp JF, Hawellek DJ, Corbetta M, Siegel M, Engel AK. Large-scale cortical correlation structure of spontaneous oscillatory activity. Nat Neurosci 2012;15:884-890.

68 Wens V, Mary A, Bourguignon M et al. About the electrophysiological basis of resting state networks. Clin Neurophysiol 2014;125:1711-1713.

69 Mitchell TJ, Hacker CD, Breshears JD et al. A novel data-driven approach to preoperative mapping of functional cortex using resting-state functional magnetic resonance imaging. Neurosurgery 2013;73:969-982; discussion 982-963.

70 Rosazza C, Aquino D, D'Incerti L et al. Preoperative mapping of the sensorimotor cortex: comparative assessment of task-based and resting-state FMRI. PLoS One 2014;9:e98860.

71 Shimony JS, Zhang D, Johnston JM et al. Resting-state spontaneous fluctuations in brain activity: a new paradigm for presurgical planning using fMRI. Acad Radiol 2009;16:578-583.

72 Vadivelu S, Wolf VL, Bollo RJ, Wilfong A, Curry DJ. Resting-State Functional MRI in Pediatric Epilepsy Surgery. Pediatr Neurosurg 2014;

73 Zhang D, Johnston JM, Fox MD et al. Preoperative sensorimotor mapping in brain tumor patients using spontaneous fluctuations in neuronal activity imaged with functional magnetic resonance imaging: initial experience. Neurosurgery 2009;65:226-236.

74 Qiu TM, Yan CG, Tang WJ et al. Localizing hand motor area using resting-state fMRI: validated with direct cortical stimulation. Acta Neurochir (Wien) 2014;

75 Wens V, Bourguignon M, Goldman S et al. Inter- and intra-subject variability of neuromagnetic resting state networks. Brain Topogr 2014;27:620-634.

76 Coquelet N, Wens V, Bourguignon M et al. Primary motor cortex mapping in brain-lesoined patients using MEG resting-state functional connectivity. Front Hum Neurosci 2014, C*onference Abstract: Belgian Brain Council 2014 MODULATING THE BRAIN: FACTS, FICTION, FUTURE*. doi: 10.3389/conf.fnhum.2014.214.00007

77 Halliday DM, Rosenberg JR, Amjad AM et al. A framework for the analysis of mixed time series/point process data--theory and application to the

study of physiological tremor, single motor unit discharges and electromyograms. Prog Biophys Mol Biol 1995;64:237-278.

9. Legend of the figure

9.1. Figure 1.

Functional mapping of the SM1 cortex obtained in one patient with a hypersignal MRI lesion at the level of the SM1 hand area. Location of classical MEG functional localizers (left axial slice and insert zoom; MNES: median nerve electrical stimulation, CMC: corticomuscular coherence, CKC: cortico-kinematic coherence) is compared with those of the resting state functional connectivity (rsFC) localizer (right axial slice and insert zoon) relying on beta-band envelope correlation. The seed (white round) used to compute rsFC was located at the SM1 hand area in the non-affected hemisphere. Good anatomical correspondence was observed between classical MEG functional localizers and MEG rsFC maximum in the affected hemisphere. This figure is provided by courtesy of Nicolas Coquelet et Evelien Carrette.