Clustering of Early Cortical Responses to Median Nerve Stimulation from Average and Single Trial MEG and EEG Signals

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Summary: Median nerve electrical stimulation (MNES) produces early and strong averaged magnetoencephalography (MEG) or electroencephalography (EEG) signals, despite considerable single trial (ST) variability, demonstrated in separate MEG and EEG studies. Here, simultaneous MEG/EEG recordings are used to assess whether same or different aspects of ST variability are influencing EEG and MEG. Clustering techniques provided groupings for the ST timeseries for cortical responses to MNES derived from one modality. These groupings were applied to the corresponding ST timeseries derived from the other modality to quantify the similarity in variability captured by MEG and EEG signals. Estimates of early cortical activity elicited by MNES derived from MEG and EEG signals were very similar, provided ongoing mu rhythm was removed. Similarity between EEG and MEG estimates included both results based on average signals and measures of ST variability. Either MEG or EEG can provide a robust measure of the early cortical activity elicited by MNES as well as of its variability. Reliable indices of early cortical responses to MNES can be derived from either MEG or EEG data. These indices can be based on average signals, as is routinely done with clinical EEG, but it could also rely on hitherto little utilized measures of ST variability.

Key words: EEG; MEG; Somatosensory evoked response; Primary somatosensory cortex; Magnetic field tomography; Single trial variability.

Introduction

The early human brain responses to median nerve electrical stimulation (MNES), recorded by EEG and MEG as Somatosensory Evoked Potentials (SEP) and Fields (SEF) respectively, are amongst the most reproducible responses to an external stimulus, making them useful tools in clinical neurophysiology for routine diagnostic purposes as well as in neuroscience research (Wood et al. 1985; Tiilinen et al. 1989; Baumgartner et al. 1991; Kakigi 1994; Buchner et al. 1994; Mauguiere et al. 1997; Hari and Foss 1999). The most common method used for the analysis of SEFs and SEP's is averaging, in which the SEP/SEF is obtained as the sample mean of a large number of single trials (STs), preserving only the signal which is time-locked to the stimulus. Any other activity that relates to the processing of the stimulus but is not time-locked to its onset will be eliminated or at least strongly attenuated. The use of just the average signal assumes that there is no coupling between mechanisms underlying the background activity and the stereotypical evoked response and therefore that it is possible to separate the stimulus-induced brain activity from the ongoing activity. The limitations of averaging have been highlighted in numerous studies, first in the auditory modality (Liu and Ioannides 1996) and most notably in the visual system where the non-linear coupling between background rhythms and the evoked response has been demonstrated both in terms of the EEG signal (Makeig et al. 2002) and in terms of the MEG signal and its generators (Laskaris et al. 2003). In earlier studies the analysis of ST responses in the somatosensory system were restricted to just one modality, either MEG (Ioannides et al. 2002; Tang et al. 2002) or EEG (Mast and Victor 1991; Haig et al. 1995; Zouridakis et al. 1997; Brandt 1997; Jung et al. 2001; Lutz et al. 2002; Rodionov et al. 2002; Jansen et al. 2003).
The identity of the generators of the early cortical response elicited by MNES has been the source of controversy for many years. The obvious candidate generators sites include the primary somatosensory cortex (SI), composed of the posterior bank of the contralateral central sulcus, Broadman area 3b (BA3b), the fundus of the central sulcus (BA3a) and the crown of the postcentral gyrus (BA1) as well as areas anterior and posterior to SI. The conclusions of different studies can be placed somewhere between the orthodoxy view that has been generally adopted in EEG and MEG studies and an alternative view that is gaining momentum recently. The orthodox view posits that the main generator of the short latency SEP/SEPs (20 – 40 ms as defined by Allison et al. 1989) is located primarily within BA3b, possibly extending a little posterior into BA1. This view is supported by studies using EEG, MEG and intracortical recordings (Hari et al. 1984; Wood et al. 1987; Allison et al. 1989; Baumbgartner et al. 1991; Buchner et al. 1994; Vanni et al. 1996; Pizzella et al. 1999; Barba et al. 2004; Balzamo et al. 2004). According to this view the main early response to the MNES is a biphasic event: the N20/N20m peak, reflecting the first cortical activation and considered to represent intracortical postsynaptic current flow in the pyramidal cells, is followed by the P30/P30m (P35m in some studies) peak, produced by current flow in the opposite direction approximately in the same cell population (Allison et al. 1989; Vanni et al. 1996) and is modelled as a tangential dipole on the anterior bank of the post-central sulcus, close to the omega-shaped hand area of the postcentral gyrus.

The alternative view allows for a near simultaneous activation of a very extended cortical area which includes all subdivisions of SI and extends both anterior to the precentral gyrus (BA4) and posterior in the parietal lobe (BA5 and 7). Evidence for this view was provided by intracranial recordings in monkey (Arezzo et al. 1981) and man (Papakostopoulos and Crow 1980) and evidence for differential effect on SEPs from precentral and parietal cortices depending upon the location of lesions in the internal capsule (Mauguire and Desmedt 1991). The recent dense epidural and intracortical mapping in monkey provided the most convincing evidence yet for widespread activation that begins in area BA3b but spreads within a few milliseconds widely to the adjacent sulci and gyri (Peterson et al. 1995). The authors have also identified reasons why earlier studies only identified activity in a more restricted area around BA3b. Even for the case of intracranial recording, the contribution from different generators on either side of the central sulcus is difficult to disentangle unless dense electrode recording and current source density analysis are used (Peterson et al. 1995).

Simple visual inspection of raw ST MEG and EEG signals shows no obvious similarities between them. Mathematically, the MEG and EEG signals are generated by complementary physical properties of the generators (Tripp 1983), but the biological generators producing the observed signal have macroscopic dimensions where the two mechanisms are acting together as part of the same biological process. It is not therefore likely that these differences are entirely due to different mechanisms for the generation of the signal. It is rather more likely that the observed dissimilarity between the MEG and EEG single trial signals simply reflects the complexity of the factors affecting the contribution of different generators in the signal recorded at each MEG coil and especially at each EEG electrode. Even if the same generators are responsible for the generation of the components that dominate the MEG and EEG signal, recovering these generators would vary in difficulty for each modality. Errors in modelling the conducting medium (e.g. the sphere model in our case) would lead to bigger localization error for EEG components. In this paper we set aside the quest of accurate localization for both modalities. We ask instead whether similar timecourses for the early generators of MNES response can be derived in MEG and EEG data, guided by the experience gained in our earlier studies. In one of our previous studies we have used magnetic field tomography (MFT, Ioannides et al. 1990) to identify strong generator activity elicited by MNES from either the average or ST MEG signal (Ioannides et al. 2002). In addition a spatial filter was constructed as a weighted sum of MEG channels, with weights defined by the spatial pattern of the earliest peak of the average MEG signal. The same spatial filter was applied to the ST MEG signal to estimate the ST timecourse of the early MNES generators.

This analysis showed that the variability in the MFT tomographic solutions was consistent with data-driven and model-independent measures derived directly from the MEG signal. This result was easy to understand, given that the dominant contributions to the early MNES responses were expected to be from superficial generators in SI, primarily from its BA3b sub-division with current density orientation tangential to the cortical surface. It is not however obvious that a similar result can be derived for EEG where generators with radial current density direction (e.g. from the BA1 and BA3a sub-divisions of SI) could produce the strongest signal. In this work we extend the spatial filter analysis of ST MNES responses to EEG data recorded simultaneously with MEG. The EEG was recorded with a fairly standard electrode arrangement, but with a denser coverage of electrodes around the central sulcus. We derived the single trial responses using spatial filters optimized separately for MEG and EEG. In each case we use as a guide the peak response and corresponding source localization at the peak of the average MEG signal. Each spatial filter is then applied to the corresponding ST MEG and EEG signals. The resulting set of timecourses is analyzed using pattern analysis leading to