Modeling and Detecting Deep Brain Activity with MEG & EEG

Yohan Attal, Manik Bhattacharjee, Jérôme Yelnik, Benoit Cottereau, Julien Lefèvre, Yoshio Okada, Eric Bardinet, Marie Chupin, Sylvain Baillet

Abstract—We introduce an anatomical and electrophysiological model of deep brain structures dedicated to magnetoencephalography (MEG) and electroencephalography (EEG) source imaging. So far, most imaging inverse models considered that MEG/EEG surface signals were predominantly produced by cortical, hence superficial, neural currents. Here we question whether crucial deep brain structures such as the basal ganglia and the hippocampus may also contribute to distant, scalp MEG and EEG measurements. We first design a realistic anatomical and electrophysiological model of these structures and subsequently run Monte-Carlo experiments to evaluate the respective sensitivity of the MEG and EEG to signals from deeper origins. Results indicate that MEG/EEG may indeed localize these deeper generators, which is confirmed here from experimental MEG data reporting on the modulation of alpha brain waves.

I. INTRODUCTION

Deep brain structures such as the hippocampus and nuclei from basal ganglia are crucial to multiple brain processes and related disorders (memory, emotions, motor control, epilepsy, Parkinson, Huntington and Alzheimer diseases, etc.). They form with the cortex a dense array of interconnected functional networks that are essential to be explored using functional brain imaging. The millisecond time resolution asset of MEG and EEG source imaging is unfortunately compensated by the rapid decrease of their sensitivity as neural sources are located deeper inside the brain. Furthermore, the cellular architecture of these structures has long been considered as closed-field thereby supposedly producing very limited if any scalp electromagnetic fields. A limited number of MEG studies have however reported on thalamic and/or hippocampal activations [1], [2], [3], but such evidences would remain rather sparse or even controversial as long as no comprehensive evaluation of the sensitivity of the MEG and the EEG based on realistic source and data modeling is achieved.

Here we introduce a dedicated anatomical and electrophysiological model of a large collection of deep brain structures. We first detail the models in question and subsequently introduce dedicated numerical experiments. We also discuss preliminary results from the experimental evaluation of this model: imaging of generators of strong brain wave modulations at about 10Hz in MEG (alpha waves) was conducted in an eyes-open–eyes-closed paradigm.

II. MODELING DEEP BRAIN STRUCTURES

A. Anatomical modeling

Robust and efficient software solutions are now available for the segmentation of the cortical surface from individual T1-weighted Magnetic Resonance Image (MRI) sequences. However signal contrast and/or anatomical boundaries of deep brain structures may be ill-defined on these images where generic segmentation approaches fail. This requires specific detection and segmentation techniques that we have used in this present study and that we shall now briefly describe. Individual T1-weighted MRI axial scans (1x1x1.5mm voxel size) are processed as follows.

1) Neocortex and Hippocampus: Segmentation and triangulation of the cortical mantle was obtained from the automatic pipeline available in The Anatomist/brainVISA free software solutions (http://brainvisa.info). Automatic segmentation of the hippocampus and amygdala was achieved by a competitive region-growing approach [4] that was also operated via the brainVISA environment (see Fig. 1).

2) Basal ganglia: The basal ganglia is a set of central grey nuclei with various cell types and densities, not all being readily identifiable from basic MRI sequences. Segmentation was therefore achieved by using a recent deformable atlas...
of basal ganglia and related structures combining detailed histological slices with the post-mortem MRI of a specimen anatomy. The methodology of the atlas warping procedure to the individual anatomy of subjects to extract the elements of basal ganglia is detailed in [5]. Here we have restricted the central grey nuclei to 5 main structures: the striatum (putamen and caudate nucleus), thalamus, reticular perithalamic nucleus (RPN), lateral geniculate nucleus (LGN) and external pallidum (EGP) (Fig.1).

B. Electrophysiological modeling

1) Modeling mass neural electrophysiology: In classical MEG and EEG source modeling, the cortical grey matter is supposed to support the primary neural currents generating the external signals. The current flow resulting from postsynaptic potentials (PSP) is classically modeled by an equivalent current dipole (ECD). The ECD is oriented along the direction originating from the cell soma and pointing toward the principal axis of the dendritic tree [6].

Proper additivity of elementary neural currents is not shared equally everywhere in the brain as we shall see in II-B.2 and depends greatly on the types of neural cells that make the detailed architecture of each anatomical structure. Two main types of neural cells were considered as possible elementary MEG/EEG generators. Pyramidal cells are typically large and ‘open-field’ neurons. Because their global cell morphology is essentially longitudinal, the vector sum of the PSPs along their dendritic tree is strong. Conversely, dendrites of stellate cells form a radial arborisation about the cell body. The resulting net vector sum of PSPs within the dendritic tree is much weaker than that of pyramidal cells. This explains why brain structures hosting this type of cells have been considered so far as closed-field, hence undetectable by MEG and EEG.

Recent results from basic electrophysiological and micro MEG recordings from preparations however indicate that these structures may produce magnetic fields at some distance with stronger amplitudes than initially expected [7]. The global source model introduced here builds on these findings by introducing electrophysiological indices that we shall now detail (see Table I).

2) Neocortex: Layers III and V of the neocortical mantle (which will be called cortex thereafter) host macrocolumns of pyramidal neurons which are oriented perpendicularly to the cortical surface. An ECD model of local/regional activity will therefore follow the circumvolutions of the cortical surface accordingly. Hence imaging approaches to the MEG/EEG inverse problem consider a distributed model of normally-oriented elementary equivalent dipoles over the entire cortical sheet.

Neural current density greatly varies across anatomical structures as it depends on cell types and organization. For cortex and all other structures considered here, current density values were obtained from micro-MEG recordings in animals models [7] and converted to current dipole moment density. In the case of cortex, the average dipole moment density was estimated as $\sigma_c = 0.4$ nAm.mm$^{-2}$.

3) Hippocampus: The hippocampus is a folded cortical structure with quite a distinctive intimate cellular architecture from the rest of the cortex. Several crucial functional subregions of the hippocampus however contain pyramidal neurons, also oriented along the local surface normals of the hippocampal envelope. Here we have reduced the distributed current model to the entire external envelope of the hippocampus, in a similar manner as with the cortex (see Section II-B.2). More detailed modeling would require considering substructures of the hippocampus e.g. the granular neural cells in the dentate gyrus.

Surfacic current dipole moment density for hippocampus was found considerably larger than that of the cortex ($\sigma_h = 1$ nAm.mm$^{-2}$). Therefore, though being located deeper into the brain, we speculate that a greater current density might help detect MEG/EEG signals originating from the hippocampus.

4) Basal ganglia and related structures: We have considered 4 types of neuronal architecture for these structures. While the thalamus and striatum contain mainly closed-field neural cells, dendrites in the pallidum and perithalamic nucleus are essentially layered, open-field and oriented longitudinally along the nucleus body (i.e. the anteroposterior axis) [8]. Cell architecture of the LGN is also longitudinal, but with neurons organized along 6 concentric semi-circles directed towards the temporal lobe.

These elements are volumic nuclei of grey matter. Therefore their large-scale electrophysiology cannot be approximated with a surfacic distribution of current dipoles. Thus regular volumic grids were fitted within their surface envelopes to support a volumic distribution of elementary current dipoles. For nuclei with oriented sources (pallidum, perithalamic nucleus and LGN), dipoles were oriented along the principal axis of their respective surface envelope.

Thalamus and putamen are essentially made of closed-field cells – i.e. with no preferred source orientation – hence a current dipole was placed at each node of the inner volumetric grid with a random orientation.

The volumic current density must then be evaluated for each of these structures. It was defined as being linearly dependent on the ratio between the approximate average density of neuronal population within each nucleus and that within the neocortex (see Table I). Indeed, the typical frequency spectrum of electrophysiological signals is typically below 1KHz. Consequently, the physics of MEG and EEG can be described by the quasi-static approximation of Maxwell’s equations. The charge-conservation equation yields a divergence-free current flow $J$ where:

$$J = \sigma.S = \gamma.V;$$  \hspace{1cm} (1)

$S$ and $V$ are the surface and volume currents of the neuronal population under consideration, and $\sigma$ and $\gamma$ are the surface and volumic current densities, respectively. To move from surfacic to volumic current density estimation within the cortex – and subsequently express the volume current density in other nuclei as ratios to this reference value – we considered the average cortical thickness as $e_c = 4$mm. Therefore, from Eq.1, the volumic current density of the cortex writes $\gamma_c = \frac{\sigma_c}{e_c}$.  

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A. MEG and EEG forward modeling

The MEG and EEG gain matrices relating the surfacic and volumic source grids of the source model were computed on the 151-channel sensor array from the CTF/VSM Omega whole-head system and a conventional 128-EEG channel montage, respectively. The analytical MEG and EEG forward models in spherical geometry was used as implemented in BrainStorm (http://neuroimage.usc.edu/brainstorm). We anticipated that very minor qualitative changes in the results could be expected from realistic solutions to the MEG/EEG forward problems; the crucial point being here the distance between sources and surface sensors. Extensive source simulations consisted in virtually and sequentially activating surfaces or volumic patches of increasing size at every source locations (cortex, hippocampus and basal ganglia). For each structure, the number of simulations was set to the number of nodes of the respective source grid (see Table I).

1) Cortex and hippocampus surface activations: All surfacic source patches defined on the cortical and hippocampal envelopes consisted of a subset of connected vertices of the surface tessellation. The size of surface areas was controlled by a growing process accumulating vertex neighbors from a preselected seed point. The simulations were conducted for patch sizes ranging from 0.5 to 10.5 cm² by steps of 1 cm², and were limited to the left hemisphere of the brain. Using Eq.1 and 2, the strength $J_i$ of the $i^{th}$ dipole of the surface (resp. volume) was computed following: $J_i = \sigma_i S_i$ (resp. $J_i = \gamma_i V_i$) where $S_i$ (resp. $V_i$) is the elementary surface area (resp. volume) associated to the $i^{th}$ dipole in the region under consideration, and $\sigma_i$ (resp. $\gamma_i$) the corresponding surface (resp. volume) current density.

2) Basal ganglia: The inner volumes of all nuclei were first computed from their surfacic envelope. Like in the surface model, an elementary volume was attributed to each source of the regular volumic grid sampling each nucleus, and was defined as the ratio between the nucleus volume and the number of sources within the volumic grid. Simulated source volumes of various sizes were generated within each nucleus and ranged between [0.05, 5.5] cm³ for the putamen and thalamus, [0.05, 1] cm³ for the pallidum and reticular nucleus and [0.01, 0.15] cm³ for the LGN.

IV. Results

A. Descriptive statistics

For a given size of surfacic or volumic patch, the mean, maximum and standard deviation of the magnetic fields and electric potentials obtained from the global source model were computed. All structures from the model but the pallidum and reticular nucleus were found to generate scalp data at levels significantly above the intrinsic MEG instrumental noise (∼10fT at 10Hz); see Table I for a comprehensive summary.

<table>
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<tr>
<th>Cortex</th>
<th>Hippocampus</th>
<th>EGP</th>
<th>Putamen</th>
<th>LGN</th>
<th>Thalamus</th>
<th>RPN</th>
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</tr>
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<td>120 ± 70</td>
<td>90 ± 40</td>
<td>0.61 ± 0.03</td>
<td>90 ± 30</td>
<td>25 ± 0.8</td>
<td>2.9 ± 1</td>
<td>0.40 ± 0.03</td>
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<td>8 ± 12</td>
<td>6.5 ± 1.8</td>
<td>0.22 ± 0.003</td>
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</tbody>
</table>

**TABLE I**

Characteristics of the brain structures in the global source model. Left to the double vertical bar (resp. right) are surfacic (resp. volumic) source structures of the left hemisphere. P stands for pyramidal cells and S for stellate cells. Average scalp electric potentials and magnetic fields are displayed with evaluations of the maximum subspace correlation between the MEG fields or EEG potentials generated by each structure and any neocortical patch. The estimation of the minimum number of trials necessary to detection within ongoing brain activity is also reported.

**Using an estimation of the cell density $d_i$ within each nucleus $i$, the corresponding estimation of volumic current density eventually writes:**

$$\gamma_i = \frac{\sigma_i}{d_i} = \frac{\sigma_i V_i}{\epsilon_i d_i}$$

(2)

III. Detection of MEG and EEG signals from deep brain regions: a simulation study

A. MEG and EEG forward modeling

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B. Correlation of field and potential topographies between deep structures and cortex

The similarity (hence ambiguity) between the scalp patterns of fields and potentials generated across the structures within the global source model was subsequently evaluated. The patterns of forward fields are discriminant factors between brain regions at fixed SNR levels that might impede the resolution of the associate inverse problem. Hence subspace correlations between forward fields from multiple brain structures in the model were evaluated [6].

The average cross-correlation between forward fields generated from the cortex and other volumic sources are shown in Table I. Fields generated within the hippocampus, thalamus and putamen were found to correlate moderately (66%) on average. Fields from other structures had strong subspace correlation scores, hence may lead to considerable ambiguity in the elucidation of the origins of the signals.

C. Detection of deep brain sources within cortical ongoing activity

We further questioned whether the structures within the global source model would be detected from ongoing brain activity assumed to be generated from the cortex. Cortical signals were therefore considered as a nuisance, non-stimulus locked term \( b \). The energy of \( b \) is therefore modulated by the number of experimental trials \( N_T \) as: \( \| b \| / \sqrt{N_T} \). Receiver Operating Characteristics (ROC) analysis was achieved by considering that deep brains signals were detected from MEG/EEG traces when the corresponding largest scalp measure exceeded that of the ongoing cortical activity. Ongoing MEG fields and EEG potentials were simulated from 500 cortical source patches of various sizes. The theoretical minimum number of experimental trials for each structure in the global source model is defined as the one making the area under the ROC curve (AUC) index reach 0.7. Results in Table I show that a standard small amount of repeated trials are required to detect signals generated in the hippocampus and putamen. Other structures may require non-evoked procedures such as steady-state paradigms to ensure detection (see Section V).

V. EXPERIMENTAL STUDY

A single subject volunteered to participate in a demonstrative MEG experiment consisting of a block-designed eyes-open/eyes-closed paradigm consisting of five 30 s runs during which the subject was resting with his eyes alternatively opened or closed. The power spectrum density of scalp traces was computed using the Welch’s periodogram to identify the subject’s main alpha oscillatory activity. Data were subsequently band-pass filtered between 10 and 12 Hz with a zero-lag filter before sources were estimated from the weighted minimum norm image model of BrainStorm. Significant variations of source amplitudes were identified from the contrast between the close vs. open eyes conditions using non-parametric permutation tests \( (p < 0.01) \) [9]. These were found in posterior cortical and thalamic regions, which are densely interconnected and generally assumed to be involved in the generation and modulation of alpha brain waves (Fig.2).

VI. CONCLUSION

Realistic geometrical modeling of the cortical and deep brain regions was introduced. A first approach to the realistic modeling of deep brain activations from prior knowledge on neuronal architecture and expected current density was also completed. Systematic investigations show that the main deep brain structures may be detected from MEG and EEG external data. This result was confirmed by occipital and thalamic activations in the alpha band revealed in an MEG eyes open/eyes closed experiment. These encouraging results need to be extended to further experimental validations.

REFERENCES

[3] K. Jerbi et al., Coherent Neural Representation of Hand Speed in Humans Revealed by MEG Imaging , in press, Proc Natl Acad Sci USA