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Lower Limb Primary Sensory and Motor Cortical Activity as Assessed by Functional Source Separation (FSS)

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Abstract. Motor and sensory counterparts of cortical lower limb representation were distinctly assessed by the new functional source separation (FSS) procedure in healthy subjects (2 females, 5 males, 29±7 years). Resting state and left and right voluntary isometric foot dorsiflexion were investigated by magnetoencephalography and simultaneous bilateral tibialis anterior (TA) electromyography (EMG). Primary sensory (FS_{S1}) and motor (FS_{M1}) area activities were discriminated by the FSS in the two hemispheres. Left and right FS_{S1} and FS_{M1} were also characterized during separate left and right common peroneal nerve stimulation. FS_{S1} was recruited during sensory stimulation only contra-laterally, as well coherence with TA muscular activity appeared only with FS_{M1} contralateraly. Beta reactivity was found for both sources during movement. Higher power of gamma rhythms was found in FS_{M1} than FS_{S1}. Right foot representation displayed higher gamma power than the left foot for FS_{S1}. FSS procedure was able to consistently identify sensory and motor counterparts of lower limb primary cortical representation, making possible to identify their different spectral and behavioural properties.

Keywords: Ankle movement; Sensorimotor; Magnetoencephalography; Functional Source Separation

1. Introduction

The present study aims at obtaining a tool to investigate the activity of the cortical region dedicated to lower limb control, focusing on the primary sensory and motor cortices via a suitable and repeatable paradigm. Our intent was to provide a useful description both for research and clinical practice, capable of characterizing the cerebral activity during different movement conditions, for example active vs. passive movement, as produced by neuromuscular electrical stimulation or the ankle mobilization by an active orthosis (Pittaccio et al., 2007).

The characterization of central correlates of movement can be done with great advantage if the contributions of primary sensory (S1) and primary motor (M1) areas are well discriminated. In a preceding paper (Porcaro et al., 2007), a novel source extraction method from magnetoencephalographic (MEG) extra-cephalic signals (Functional Source Separation, FSS, Barbati et al., 2006; Tecchio et al., 2007a) was demonstrated to be able to obtain the temporal dynamics of different primary cortical network activities devoted to hand representation. In particular, two sources were mainly involved in the sensory inflow, and the other to the motor control. FSS adds *ad hoc* functional constraints, designed on the basis of time-frequency characteristic of the cerebral source activities to be extracted, to the statistical contrast function of a standard independent component analysis algorithm (ICA), in order to bias the solution towards the searched sources. This procedure is capable to provide the activity of a given source in a variety of different experimental conditions based

on specific information about that source, which can be gained by exploiting a functional 'fingerprint' behavior arising under a limited-time experimental condition.

The aim of this study was to achieve by means of FSS an adequate description of the highly interconnected and temporally overlapping primary sensory-motor cortical network devoted to lower limb control. An easy and repeatable experimental setting to obtain cerebral activity controlling voluntary motor performance is hardly feasible, in particular when patients with limb impairment are involved. In fact, it would require repetitions of rapid and precise movements. In the last decade, the coupling between oscillations of primary motor cortex and muscular activity (Gerloff et al., 2006) in frequencies around 20 Hz during an isometric contraction has been demonstrated to characterize the motor control. Systematic cortico-muscular coherence both for the upper and lower limbs has been demonstrated to be related to the patterns of motor output and sensory input, both in healthy subjects and in patients suffering from movement disorders (Gerloff et al., 2006). For this reason, the maximal cortico-muscular coherence has been used as functional constrain to obtain the activity of M1. The stimulation of the peroneal nerve above the motor threshold evokes a robust and stable response, which originate in the primary sensory cortex (Shimojo et al. 1996). The M40 component of evoked response is the marker of the stimulus arrival in the primary sensory cortex. It is known to be mainly generated by excitatory postsynaptic potentials impinging on BA 3a pyramidal cells. The maximal power around 40 ms of the evoked response was used as the constraint for S1 activity extraction.

2. Material and Methods

Seven healthy right-handed subjects (mean age 29±7 years, 5 men), participated in the study. Brain magnetic fields were recorded by means of a 28-channel MEG system over sensory-motor regions devoted to leg control (CZ position of the 10-20 International System). MEG signals was sampled at 1 kHz (band-pass filtering 0.25-250 Hz).

MEG activitiy and the tibialis anterior (TA) electromyogram (EMG) were collected during different conditions, namely: rest (2 minutes, open eyes, Rest); somatosensory electrical stimulation to the common peroneal nerve (631 ms inter-stimulus interval, stimulus intensity just inducing a painless foot twitch, Sensory); 3 minutes of periods of 20 seconds of voluntary isometric dorsiflexion at 5% of the maximal voluntary contraction (Motor), intermingled by 20 seconds of rest.

FSS was applied to identify the cortical neural networks devoted to the ankle muscle representation in primary motor (FS_{M1}) and primary sensory (FS_{S1}) areas. In our application, supplementary information was added to the kurtosis, used as cost function by FastICA algorithm (Hyvärinen et al., 2001):

$$C = K + \lambda F_R$$

where K is the kurtosis, λ weighs the two parts of the contrast function, F_R accounts for the prior information to extract single sources. C was optimized for each extraction R (M1 and S1), starting each time from the original MEG data.

To extract FS_{M1} maximal coherence with TA rectified electromyographic signal was required. The corresponding functional constraint was:

$$F_{M1} = \sum_{f_M-\Delta_1 f}^{f_M-\Delta_2 f} \mathrm{Coh}(FS_{M1}, f)$$

where Coh is a the coherency function (Gross et al., 2000). For each frequency f, Coh is the amplitude of the cross-spectrum between the source FS_{M1} and the rectified EMG, normalized by the root mean square of the power spectral densities of these two signals. The Bartlett procedure was used to estimate the power spectra (frequency resolution of 1.95 Hz, Hamming window, no overlap). The frequency interval $[f_M - \Delta_1 f, f_M - \Delta_2 f]$ corresponded to a coherence amplitude higher than 50% of the maximal value, individuated in the beta band (13.5-33 Hz).

To extract FS_{S1} maximal responsiveness to common peroneal nerve stimulation at around 40 ms was required. The functional constraint taking into account the ''reactivity'' to the sensory stimulus was defined as:

$$F_{S1} = \sum_{t_{40}-\Delta_1 t_{40}}^{t_{40}-\Delta_2 t_{40}} \left|\mathrm{EA}(FS,t)\right| - \sum_{10}^{20} \left|\mathrm{EA}(FS,t)\right|$$

with the evoked activity EA computed by averaging FS_{S1} epochs triggered on the pereonal nerve stimulus; t_{40} is the time point with the maximum magnetic-field value on the maximal original MEG channel around 40 ms after the stimulus arrival; the time interval $[t_{40} - \Delta_1 t_{40}, t_{40} - \Delta_2 t_{40}]$ corresponds to a field amplitude of 50% of the maximal value. The baseline was computed in the time interval from 10 to 20 ms.

Once the sources that optimize *C* have been obtained, the estimated solutions were multiplied by the Euclidean norm of its corresponding weights, in order to allow amplitude comparisons among different sources.

To control the position of the extracted sources, FS_{S1} and FS_{M1} were separately retro-projected so as to obtain their field distribution. The positions of the sources were estimated by a moving Equivalent Dipole Source (ECD) model inside a homogeneous sphere. The coordinates were expressed in a Cartesian coordinate system defined on the basis of the anatomical landmarks: the xy plane passing through the two preauricular points and the nasion; the y axis passing through the nasion and the midpoint between the two preauricular points and directed towards the nasion; the x-axis directed rightward.

Involvement of the sources during each experimental condition was estimated through their power band distributions (Hanning window, 512 ms duration, 60% overlap) in the classical frequency bands (alpha: 8-13 Hz, beta: 14- 32 Hz, gamma1: 33-60 Hz, gamma2: 61-90 Hz). The estimate was obtained separately for the Rest and Motor conditions.

Repeated-measure ANOVA was applied to each power band of the source activities with *Source* (FS_{S1}, FS_{M1}), *Hemisphere* (Left, Right), *Condition* (Rest , Motor) and *Movement* (Left ankle, Right ankle) as within-subject factors.

3. Results

FS_{S1} and FS_{M1} were suitably identified in both hemispheres for all subjects. The FS_{S1} and FS_{M1} positions were spatially distinct in both hemispheres [*Source* factor [F(3,4) = 13.692; p=0.014], with FS_{M1} more medial and anterior than FS_{M1} (figure 1).

The two sources reacted differently to common peroneal nerve stimulation and displayed different coherence levels with muscular activity (Figure 2).

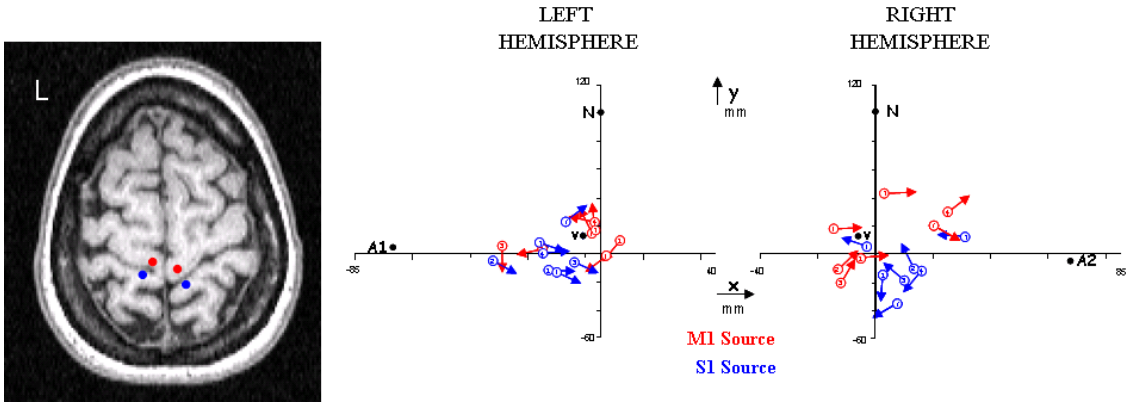

Figure 1. *Left: Mean position across subjects of FS_{S1} (blu) and FS_{M1} (red), projected on an axial slide of a template MRI image. Right: for each subject, position and orientation of ECD corresponding to FS_{S1} (blu) and FS_{M1} (red), in the xy plane of coordinate system defined in the text. The mean across subjects of anatomical points are displayed (N: nasion; A1, A2: preauricular points; V: vertex).*

ANOVA results showed that FS_{S1} and FS_{M1} had different spectral behavior, with higher gamma power in FS_{M1} than FS_{S1} at rest [*Source* effect F(1,6) = 8.312, p = 0.028: FS_{S1}: 3.34 ± 0.02 vs FS_{M1}: 3.47 ± 0.04 log(fT^2)]. Moreover, higher power at high frequencies (gamma) were found in FS_{S1} in the left hemisphere with respect to the right one [*Soruce* * *Hemisphere* effect, F(1,6) = 12.570, p = 0.012 for gamma-1, F(1,6) = 22.653, p = 0.003 for gamma-2, figure 3].

Beta reactivity in beta band was found for both sources in both hemispheres during movement [*Condition* effect, F(1,6) = 9,668; p = 0.021, figure 3].

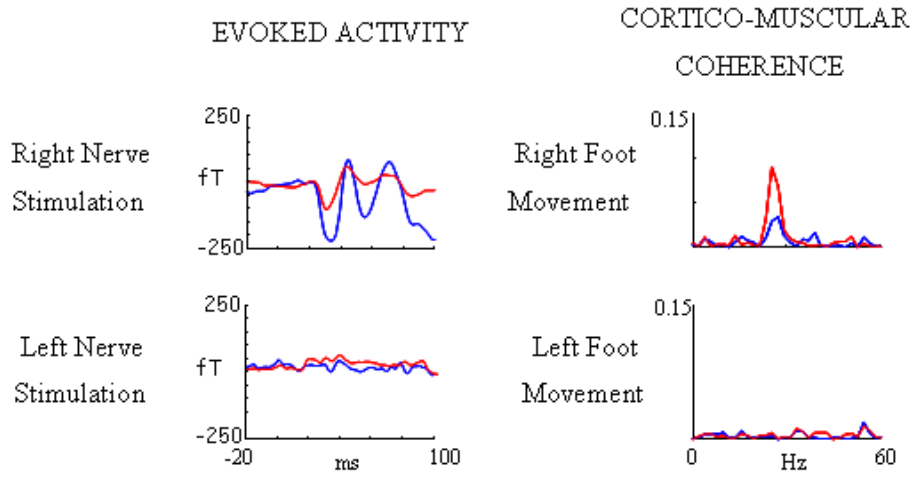

Figure 2. *For one representative subject (left hemisphere): Left: the reactivity of bilateral FS_{S1} (blu) and FS_{M1} (red) to sensory stimulation as evaluated by the evoked activity in a time interval of 120 ms (with 20 ms of pretrigger, 0 corresponding to the stimulus onset). To be noted that only the FS_{S1} contralateral to the stimulation is maximally responsive to galvanic stimulation. Right: Coherence between FS_{S1} and FS_{M1} with rectified electromyographic activity during isometric contraction. The cortico-muscular coherence is maximal for FS_{M1} during the controlateral muscle movement*

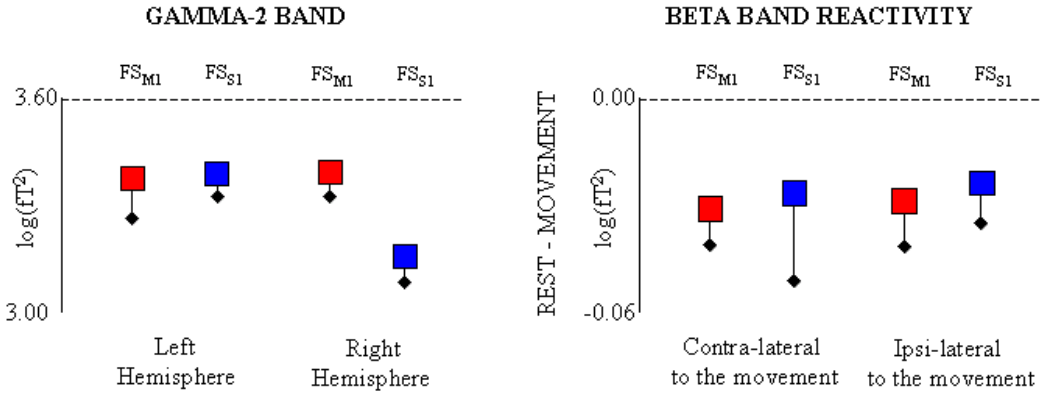

Figure 3. *Left: marginal mean (standard error) across condition of gamma-2 in left and right hemisphere for FS_{S1} (blu) and FS_{M1} (red). Right: mean (standard error) of reactivity in beta band, evaluated as difference between rest and movement condition, for the movement of both contra-lateral and ipsi-lateral foot.*

4. Discussion

The FSS procedure suitably discriminated the sensory and motor source activity devoted to the ankle cortical representation in healthy volunteers. The extracted positions are consistent with the activation of primary sensory cortex for FS_{S1} and of primary motor area for FS_{M1}. The two sensory sources responded correctly to the stimulation of the contralateral nerve more than the corresponding motor ones. On the other hand, FS_{M1} displayed a stronger cortico-muscular coherence with contralateral muscular activity than FS_{S1}. Interestingly, we were able to document that primary sensory areas in the left hemisphere had more gamma activity than the areas controlling the right one, in agreement with a more specialized organization of these regions in a dominant left rather than right hemisphere (Tecchio et al., 2007b).

The active movement was clearly differentiated from the rest condition by power spectral analysis in both sensory and motor regions. In particular, in agreement with previous results (Müller et al., 2003), we found bilaterally a decrease of beta power during movement with respect to rest.

In conclusion, FSS reveals a suitable method to differentiate the activity of primary motor from primary sensory areas devoted to lower limb control. The experimental protocol used is suitable for recording activity of patients with lower limb sensory-motor impairment.

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