NeuroImage 133 (2016) 224–232

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Computational modelling of movement-related beta-oscillatory dynamics in human motor cortex☆

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ARTICLE INFO

Article history:
Received 19 November 2015
Accepted 29 February 2016
Available online 5 March 2016

Keywords:
Beta
Oscillations
Movement-related beta desynchronisation
DCM
MEG
Primary motor cortex
M1

ABSTRACT

Oscillatory activity in the beta range, in human primary motor cortex (M1), shows interesting dynamics that are tied to behaviour and change systematically in disease. To investigate the pathophysiology underlying these changes, we must first understand how changes in beta activity are caused in healthy subjects. We therefore adapted a canonical (repeatable) microcircuit model used in dynamic causal modelling (DCM) previously used to model induced responses in visual cortex. We adapted this model to accommodate cytoarchitectural differences between visual and motor cortex. Using biologically plausible connections, we used Bayesian model selection to identify the best model of measured MEG data from 11 young healthy participants, performing a simple handgrip task. We found that the canonical M1 model had substantially more model evidence than the generic canonical microcircuit model when explaining measured MEG data. The canonical M1 model reproduced measured dynamics in humans at rest, in a manner consistent with equivalent studies performed in mice. Furthermore, the changes in excitability (self-inhibition) necessary to explain beta suppression during handgrip were consistent with the attenuation of sensory precision implied by predictive coding. These results establish the face validity of a model that can be used to explore the laminar interactions that underlie beta-oscillatory dynamics in humans *in vivo*. Our canonical M1 model may be useful for characterising the synaptic mechanisms that mediate pathophysiological beta dynamics associated with movement disorders, such as stroke or Parkinson's disease.

Introduction

There is increasing interest in studying oscillations as a marker of brain function. Neuronal oscillations in the beta frequency range (15–30 Hz) in primary motor cortex (M1) are fundamental for motor control (Engel and Fries, 2010) and are a putative biomarker of pathophysiology in conditions like Parkinson's disease.

Magnetoencephalography (MEG) studies have shown that voluntary movement is associated with a systematic reduction in power of beta oscillations (movement-related betadesynchronisation, MRBD) in M1, which rebounds following movement cessation (post-movement beta rebound, PMBR) (Salmelin and Hari, 1994). The characteristics of beta oscillations change with healthy ageing (Rossiter et al., 2014a) and in disease states such as stroke (Rossiter et al., 2014b) and Parkinson's disease (Brown, 2006). An understanding of the mechanisms underlying these changes may therefore provide novel therapeutic opportunities (Ward, 2015a,b).

In this paper, we show how a biophysical (neuronal mass) model facilitates the investigation of the laminar interactions underlying non-invasive measurements of neuronal oscillations from primary motor cortex (M1) in humans. Insights into cortical microcircuit dynamics in M1 to date have come from in vitro intra- and extracellular recordings in animals. From this work, the dominant (interlaminar) pathway in the cortical column appears to be from superficial to deep pyramidal cell layers (Weiler et al., 2008). Excitation of the deep pyramidal layer (Yamawaki et al., 2008) or possibly synchronous hyperpolarisation of superficial and deep pyramidal layers (Lacey et al., 2014) gives rise to beta oscillations. In both cases, recurrent interactions with inhibitory interneurons are important, as is the case for gamma oscillations (Traub et al., 2001).

We applied dynamic causal modelling (DCM) to MEG data acquired from humans. We focused on the spectral characteristics of a single source within M1 in order to model underlying neuronal activity in terms of specific cell populations within a typical motor cortical column.

☆ **Software note:** The analyses presented in this paper use algorithms that are available as part of the SPM academic freeware.

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http://dx.doi.org/10.1016/j.neuroimage.2016.02.078

DCM then allows one to infer (i.e., estimate) synaptic and connectivity parameters associated with neuronal these sources (Moran et al., 2008, 2011, 2013).

Recently, advances have been made in DCM towards developing a canonical (repeatable) microcircuit model. This model has been developed under the dual constraints of complying with known intrinsic architecture within microcircuits and, at a functional level, is consistent with the computational anatomy of hierarchical Bayesian filtering (e.g., predictive coding) (Bastos et al., 2012). The nature of this model means it can explain cortical dynamics over a wide range of sensory brain areas (Bastos et al., 2012). However, the canonical microcircuit (CMC) model may not be appropriate for M1, given the cytoarchitectonic differences between such areas and M1 (Shipp, 2005). Our primary goal was to construct a canonical model taking account of known M1-specific microstructural characteristics and then, through Bayesian model comparison, determine the specific model architecture most likely to account for movement-related alterations in measured beta-band oscillations from M1. We used the ensuing model to examine laminar connectivity in human M1 (in comparison to known findings from rodent M1) and, in particular, test for a dominant descending excitatory drive through the connection from superficial to deep pyramidal layers at rest, empirically observed in previous animal studies (Weiler et al., 2008). Finally, we explored alterations in laminar connectivity during movement-related changes in beta oscillations. This series of analyses establish the face and construct validity of a canonical model for M1 activity that we hope will be useful in future DCM studies of pathophysiology, particularly in conditions that are associated with abnormal beta dynamics.

Methods

Participants

Eleven healthy participants took part (mean age 24.7 ± 1.6 years, 7 female, 2 left handed). Full written consent was obtained from all participants in accordance with the Declaration of Helsinki. The study was approved by the Joint Ethics Committee of the Institute of Neurology, UCL and National Hospital for Neurology and Neurosurgery, UCL Hospitals NHS Foundation Trust, London.

Motor task

Participants performed visually cued dominant hand isometric handgrips using a force sensitive manipulandum during simultaneous MEG and electromyography (EMG) recording. Maximal voluntary contraction was recorded prior to scanning and subjects were then asked to perform visually cued handgrips at 30% MVC. Subjects performed 60 handgrips lasting 4 s each with an interstimulus interval ranging between 4 and 7 s.

MEG recording

MEG signals were recorded during the handgrip task from a whole-head CTF Omega 275 MEG system (CTF, Vancouver, Canada), at a sampling rate of 600 Hz. Pre-processing of the data were performed offline in SPM12 (Wellcome Trust Centre for Neuroimaging, www.fil.ion.ucl.ac.uk/spm) (Litvak et al., 2011). Data were filtered from 2 to 100 Hz and epoched from −1 s to +5 s, where time 0 indicated the onset of visual cue. Artefacts from eye blinks and muscle contractions were identified by visual inspection, and corrupted trials were excluded from analysis. Power-line artefacts at 50 Hz were estimated and subtracted from the data, and epochs containing artefacts were removed with a semi-automatic artefact rejection protocol, based on a variance threshold.

Data processing and analysis

To extract the spectral activity of M1 for subsequent dynamic causal modelling, we first estimated source activity in M1 using standard beamforming procedures: lead fields were computed using a single shell model, with a template inner skull canonical mesh being affine-transformed to fit MEG fiducials (nasion, left, and right pre-auricular).

Beta-band (15–30 Hz) power changes were localised using the linearly constrained maximal variance (LCMV) beamformer (Hillebrand and Barnes, 2005). This method projects sensor data using a linearly spatial filter derived from the lead-field of the source of interest and data covariance. The data covariance matrix was computed using three conditions (Rest, Mid-Grip and Post-Grip). The Rest time window was taken from −1 s to 0 s with 0 as the onset of the visual cue to move. The Mid-Grip time window was from 1.0 s to 2.0 s following the visual cue onset. The Post-Grip time window was from 4 s to 5 s following the visual cue onset. In short, we used the same (global) filter (Brookes et al., 2008) to estimate the induced responses in three distinct time windows.

Volumetric statistical parametric maps (SPMs) of the t-statistic were computed for each subject using a grid spacing of 10 mm. At each location, the source orientation was taken to be in the direction yielding maximal signal variance. The source signal was then extracted from the location of peak change in beta power (15–30 Hz) within the primary motor cortex contralateral to the moving (dominant) hand (Sekihara et al., 2004). From these t-statistic images, we extracted the source signal from the location of peak change in beta power (15–30 Hz) within the primary motor cortices contralateral to the moving hand. Morlet-wavelet time–frequency analysis was used to explore the changes in beta across a trial from these locations, data were epoched again in order to visualise changes before and after the movement using the time window −1 s to +5 s. The spectrograms were rescaled in order to show percentage change from baseline (− 1 to 0 s) and averaged across trials.

The extracted data were then treated as a 'virtual electrode', from which data could be modelled in 5–45 Hz frequency range. The data were re-epoched from −1 s to 0 s (rest), 1 s to 2 s (grip), 4 s to 5 s (post-grip), and concatenated (Barnes et al., 2004). Data were truncated between 5 and 45 Hz after inspection showed the majority of behaviourally tied spectral changes occurred within this range.

Dynamic causal modelling (DCM)

Biophysical DCMs of canonical cortical microcircuits are used to infer synaptic mechanisms that underlie event or induced responses—or changes in the spectral characteristics of neural oscillations (Moran et al., 2009, Moran et al., 2011). Dynamic causal models of this sort allow empirical data from invasive (e.g., LFP/ECoG) or noninvasive (M/EEG, fMRI, NIRS) recordings to be used to characterise the neuronal interactions and architectures that generated them. This approach has been validated using local field potentials recorded in animal preparations where independent pharmacological/microdialysis assays have served to corroborate the modelling results (Moran et al., 2011). To date, the canonical microcircuit used in this type of DCM has been based largely on the known laminar architecture and intrinsic connectivity of sensory cortex and has been used in studies of primary visual cortex (V1) (Fig. 1A), (Moran et al., 2009; Bastos et al., 2012).

Here, we wish to study synaptic mechanisms in primary motor cortex (M1). The laminar architecture of M1 differs substantially from that of V1. M1 is mostly described as agranular, containing cell types with differing electrophysiological characteristics (Brodmann and Garey, 1999); however, recent evidence has emerged of a functional layer 4 in mice at the layer 3/5 A border (Yamawaki et al., 2014). M1 also has different inputs (Shepherd, 2009) and different interlaminar connectivity to V1, with dominant superficial to deep interlaminar pathways (Anderson et al., 2010; Weiler et al., 2008; Yu et al., 2008). These