NeuroImage 91 (2014) 360–365

Contents lists available at ScienceDirect

NeuroImage

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

Beta oscillations reflect changes in motor cortex inhibition in healthy ageing

Holly E. Rossiter *, Emma M. Davis, Ella V. Clark, Marie-Hélène Boudrias, Nick S. Ward

Sobell Department of Motor Neuroscience and Movement Disorders, UCL Institute of Neurology, 33 Queen Square, London, WC1N 3BG, UK

ARTICLE INFO

Article history:
Accepted 5 January 2014
Available online 16 January 2014

Keywords:
Ageing
Motor
Beta
Oscillations
MEG
Plasticity

ABSTRACT

Beta oscillations are involved in movement and have previously been linked to levels of the inhibitory neurotransmitter GABA. We examined changes in beta oscillations during rest and movement in primary motor cortex (M1). Amplitude and frequency of beta power at rest and movement-related beta desynchronization (MRBD) were measured during a simple unimanual grip task and their relationship with age was explored in a group of healthy participants. We were able to show that at rest, increasing age was associated with greater baseline beta power in M1 contralateral to the active hand, with a similar (non-significant) trend in ipsilateral M1. During movement, increasing age was associated with increased MRBD amplitude in ipsilateral M1 and reduced frequency (in contralateral and ipsilateral M1). These findings would be consistent with greater GABAergic inhibitory activity within motor cortices of older subjects. These oscillatory parameters have the potential to reveal changes in the excitatory–inhibitory balance in M1 which in turn may be a useful marker of plasticity in the brain, both in healthy ageing and disease.

Introduction

The capacity for neuroplastic change is altered in the ageing brain (Chollet, 2013; Kolb and Teskey, 2012). A key determinant of the capacity for plasticity in the adult brain is the balance between GABAergic inhibition and glutamatergic excitation (Benali et al., 2008) and a shift of balance away from inhibition tends to increase plasticity (Hensch, 2005).

Age-related changes in intracortical excitation and inhibition of primary motor cortex (M1) at rest have been explored in a number of transcranial magnetic stimulation (TMS) studies. Short-interval intracortical inhibition (SICI) and long-interval intracortical inhibition (LICI) are TMS protocols designed to probe inhibitory mechanisms mediated by GABA-A and GABA-B receptors respectively. Results from these studies are contradictory. Some demonstrate decreased inhibition with age (Heise et al., 2013; Hortobágyi et al., 2006; Marneweck et al., 2011), whereas others suggest an increase in inhibition (McGinley et al., 2010; Smith et al., 2009). Furthermore, SICI and LICI are most commonly measured at rest and so may not reflect the dynamic changes during movement that are important for task-dependent plasticity.

More recently, there has been interest in investigating cortical inhibitory mechanisms using magnetoencephalography (MEG) and electroencephalography (EEG). MEG can detect the oscillatory signals generated by changes in the post-synaptic fields of glutamatergic pyramidal cells. Pyramidal cells are reciprocally connected to GABAergic interneurons and so changes in oscillatory signals are dependent on the balance between inhibition and excitation within these microcircuits (Yamawaki et al., 2008). As such, oscillatory changes could reflect the potential for both local and network plasticity (Traub et al., 2004). Oscillations in the beta frequency band (15–30 Hz) are known to be important in movement. In M1, they are present at rest and are suppressed during movement (movement-related beta desynchronization — MRBD) (Pfurtscheller and Lopes da Silva, 1999).

Evidence that the properties of beta oscillations are related to GABAergic activity comes from pharmacological manipulations of GABA prior to and during movement in both animals and humans (Hall et al., 2010, 2011; Roopun et al., 2006; Yamawaki et al., 2008). Diazepam, a GABA-A agonist, increased the amplitude of baseline beta power (Hall et al., 2010) and accentuated MRBD (Hall et al., 2011). It also increased SICI in healthy controls (Florian et al., 2008). Tiagabine, a GABA-reuptake inhibitor (Muthukumaraswamy et al., 2012), increased amplitude of baseline beta power and enhanced MRBD. Furthermore, the frequency of beta oscillations have been found to decrease with administration of benzodiazepine concurrent with an increase in baseline beta power amplitude (Jensen et al., 2005). These results suggest that higher baseline beta power, decreased beta

* Corresponding author.
E-mail address: h.rossiter@ucl.ac.uk (H.E. Rossiter).

http://dx.doi.org/10.1016/j.neuroimage.2014.01.012

frequency and greater amplitude of MRBD reflect increased levels of intracortical GABAergic inhibition. We can therefore use these findings to make inferences about changes in GABAergic inhibition from measurements of beta oscillatory power.

One key question is which brain regions we should examine for such movement related changes. FMRI studies have shown that healthy ageing is associated with more widespread activation of motor areas during movement, and specifically less 'deactivation' in the ipsilateral M1 in older subjects (Talelli et al., 2008; Ward and Frackowiak, 2006; Ward, 2006; Ward et al., 2008). We therefore examined task-related changes in beta oscillations in M1 both contralateral and ipsilateral to the moving hand. Many previous studies have suggested that there is a reduced capacity for plasticity (at rest) with increasing age (Fathi et al., 2010; Sawaki et al., 2003; Tecchio et al., 2008) most likely due to greater cortical inhibition. In this study, we were interested in investigating age-related changes in beta oscillations (as a marker of the balance between excitation and inhibition) at rest and during movement, because of their potential relevance for practice-dependent cortical plasticity.

We expected to find that older subjects would demonstrate increased baseline beta power and MRBD amplitude along with a decrease in beta frequency as a reflection of a reduced potential for plasticity in the motor cortices.

Materials and methods

Subjects

Thirty-two healthy participants (mean age 51 ± 21 years, range 22–82 years; 11 female, 2 left-handed) took part in this study. 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.

Behavioural testing

All participants were scored on the Nine Hole Peg Test (NHPT), Box and Blocks test and Grip strength in order to cover a range of upper limb motor abilities, from dexterity to power.

Motor task

Participants performed visually cued isometric hand grips with their dominant hand using a manipulandum during MEG recording. Prior to scanning, maximum voluntary contraction (MVC) was obtained for each participant. Sixty trials were performed. The cue to perform a hand grip was the appearance of a 'force thermometer' on the screen which provided continuous visual feedback about the force exerted. The target force was set at 30% of their MVC and displayed visually. Each grip was sustained for 3 s with an interstimulus interval that jittered between 3 and 7 s.

MEG recording

MEG signals were measured continuously at 600 Hz during the task using a whole-head CTF Omega 275 MEG system (CTF, Vancouver, Canada). Head localization was monitored continuously during the recordings in order to check for excessive movement. The MEG data were pre-processed offline using SPM8 (Wellcome Trust Centre for Neuroimaging, www.fil.ion.ucl.ac.uk/spm) (Litvak et al., 2011). Data were down-sampled to 300 Hz and were filtered from 5 to 100 Hz. Data were epoched from −3 s to +3 s where time 0 indicated onset of the visual cue for analysis. Data with large eye blinks or other artefacts were excluded.

Structural MRI recording

A 3 T Siemens Trio scanner (Siemens, Erlangen, Germany) was used to acquire high resolution T1-weighted anatomical images (1.3 × 1.3 × 1.3 mm voxels); 176 partitions, FoV = 256 × 240, TE = 2.48 ms, TR = 7.92 ms, FA = 16°). Structural MRIs could not be obtained in four of the participants due to MRI contraindications.

Data processing and analysis

Lead fields were computed using a single-shell head model (Nolte, 2003) based on an inner skull mesh derived by inverse-normalizing a canonical mesh to the subject's individual MRI image (Mattout et al., 2007). For subjects without an individual MRI the canonical mesh was affine-transformed to fit their MEG fiducials. Coregistration between the MRI and MEG coordinate systems used three fiducial points: nasion, left and right pre-auricular. Whilst acquiring the structural MRI, fiducial points were marked with vitamin-E capsules in order to coregister with the MEG fiducials.

Oscillatory changes in the beta band (15–30 Hz) between rest and grip were localised using the Linearly Constrained Maximal Variance (LCMV) beamformer (Hillebrand and Barnes, 2005; Vrba and Robinson, 2001) as part of the SPM8 software. The beamforming method is based on the linear projection of sensor data using a spatial filter computed from the lead field of the source of interest and the data covariance (Van Veen et al., 1997). We computed the data covariance matrix using two time windows (passive and active). The passive time window was taken from −2.5 s to 0 s with 0 as the onset of the visual cue to move. The active time window was from 0.5 s to 3 s following the visual cue onset. We then made volumetric t-statistic images per 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 (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 both contralateral and ipsilateral 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 mean percentage decrease in beta power (MRBD) was then extracted from the 3 s movement period for each participant. The absolute baseline beta power (−1 s to 0 s) was also obtained. These beta parameters were then correlated with age.

Results

All subjects were able to perform the grip task adequately. The average and range for the behavioural tests were as follows: NHPT average = 0.74 pegs per second, range = 0.53–0.96, Box and Blocks test average = 61 blocks per minute, range = 44–91, Grip strength average = 75 kg, range = 46–117 kg.

A change in beta power was seen between rest and grip in all participants in M1 both contralateral and ipsilateral to the moving hand. The location of these peaks can be seen in Fig. 1A. Fig. 1B shows a group average spectrogram spanning from 5 to 80 Hz across a trial with 1 s baseline, 3 s of grip and 2 s post-grip. MRBD during grip can be seen clearly and appears stronger in contralateral M1 than ipsilateral M1.

At rest, baseline beta amplitude in contralateral M1 correlated positively with age (R = 0.63, p = 0.0001, 95% CI = 0.49–0.77) (Fig. 2A). There was a similar yet non-significant trend in ipsilateral M1 (R = 0.33, p = 0.07, 95% CI = 0.05–0.56) (Fig. 2B). Peak beta frequency did not alter significantly with age in either contralateral or ipsilateral M1, although there was a non-significant trend (R = −0.36, p = 0.06, 95% CI = −0.66– −0.05) towards a decrease in frequency with increasing age in contralateral M1 (Fig. 2C).