Respiratory Physiology & Neurobiology 185 (2013) 249–256

Contents lists available at SciVerse ScienceDirect

Respiratory Physiology & Neurobiology

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

Sniffing-related motor cortical potential: Topography and possible generators

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ARTICLE INFO

Article history:
Accepted 5 October 2012

Keywords:
EEG
Respiration
Motor cortical potential
Bereitshaftspotential
Principal component analysis
Current source density

ABSTRACT

This study estimated the whole-scalp topography and possible generators of the cortical potential associated with volitional self-paced inspirations (sniffs). In 17 healthy subjects we recorded a 32-channel electroencephalogram (EEG) during sniffing, for comparison during finger flexions. We averaged the EEG with respect to movement onset, and performed current source density and principal component analysis on the grand averaged data. We identified an early negative sniffing-related cortical potential starting ~1.5 s before movement at the vertex, which, in its time-course and dipole orientation, closely resembled Bereitshaftspotential preceding finger flexions. Around the movement onset, its topography became unique with three negative current sources: one at the vertex, and two bilaterally over the fronto-temporal derivations. We conclude that sequential cortical activation in preparation for sniffing is similar to other volitional movements. The current sources at sniff onset at the vertex likely reflect somatotopic motor representation of the diaphragm, neck and intercostal muscles, whereas current sources over fronto-temporal derivations likely reflect the somatotopic representation of the orofacial muscles.

1. Introduction

Breathing depends on an elaborated neuronal network within the central nervous system that includes cortex, limbic system and brainstem. The motor neurons of the respiratory muscles are controlled via two major descending pathways: automatic control is exerted via bulbo-spinal pathways from the medulla, and voluntary control via cortico-spinal and possibly also via cortico-bulbo-spinal pathways (Butler, 2007). Projections from motor cortex to respiratory muscles in humans have been confirmed by transcranial electrical (Gandevia and Rothwell, 1987; Gandevia et al., 1990) and magnetic stimulation (Maskill et al., 1991; Sharshar et al., 2004). Several neuroimaging studies have revealed that the primary motor cortex (M1), premotor cortices and supplementary motor area (SMA) are more active during volitional than during spontaneous or passive breathing (Colebatch et al., 1991; Ramsay et al., 1993; Evans et al., 1999; McKay et al., 2003; Simonyan et al., 2007; Koritnik et al., 2009).

Electroencephalography (EEG) has rarely been used for studying cortical control of breathing. A few studies (Macefield Gandevia, 1991; Raux et al., 2007; Tremoureux et al., 2010) have focused on the so-called movement-related cortical potential (MRCP) which has been shown to precede different volitional movements (see Shibasaki and Hallett, 2006 for review). MRCP consists of several components. Qing Cui and Deecke (1999) distinguished three, namely early Bereitshaftspotential (BP1), late Bereitshaftspotential (BP2) and motor potential (MP). BP1 begins approximately 2 s before the onset of volitional movement, is maximal at the vertex and is symmetrically distributed over the scalp. It is followed by a steeper slope, BP2, which begins about half a second prior to movement and is larger at the central area contralateral to the moving limb. MP occurs in approximately the same area just before the movement onset. MRCP is believed to reflect electrical activation of motor cortical areas in preparation for volitional movements (Shibasaki and Hallett, 2006). Studies on breathing-related motor cortical potentials in healthy humans have shown that volitional self-paced, as well as loaded inspirations and expirations, are preceded by MRCP, while quiet breathing on a breath-by-breath basis is not (Macefield Gandevia, 1991; Raux et al., 2007; Tremoureux et al., 2010). Brief self-paced inspirations (sniffs) have been studied because they are easy to perform, have a well defined electromyographic onset in the inspiratory muscles, and produce a rapid change in nasal air pressure which is convenient when using electromyogram (EMG) and pressure changes as triggers for EEG averaging. So far, investigators have used only few recording electrodes (Macefield Gandevia, 1991; Raux et al., 2007), which enabled them to record MRCP over central scalp region, but the whole scalp topography of sniffing-related cortical potential has, to our knowledge, not been investigated. Our aim was to estimate this MRCP topography and its possible generators. The topography of the BP

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http://dx.doi.org/10.1016/j.resp.2012.10.006

was not expected to differ substantially from other volitional movements (Shibasaki and Hallett, 2006). However, we anticipated a symmetrical distribution of possibly more than one MP on the scalp, reflecting the M1 somatotopy of the inspiratory muscles, active in sniffing (Penfield and Rasmussen, 1968; Katagiri et al., 2003).

2. Methods

2.1. Subjects

Seventeen healthy subjects, aged 23–37 years (five men) participated in this study. All participants except one were right-handed. They gave written, informed consent for the protocol, which was approved by the National Research Ethics Committee in accordance with the Declaration of Helsinki.

2.2. Experiment

Participants sat comfortably in a chair with their forearms lying on a table and watched a fixation point on the computer screen. They were asked to perform two tasks: volitional self-paced sniffs and volitional self-paced right index finger flexions evaluated by pressing on a rubber bulb (diameter = 4 cm). The experimental session started with 15 min of finger flexions followed by 15 min of sniffing. The participants were asked to execute one movement per approx. 5–10 s and were instructed to consciously decide on its initiation and to execute it rapidly. The required intensity of the movements was 30% of each subject's maximal pressure developed in the nose during sniffing, and in the rubber bulb during finger flexions. The maximal pressure was determined at the beginning of each task. All subjects underwent a short familiarization session before the actual recording began. During this period, visual feedback of the movement was provided for subjects to become skilled in producing the correct intensity and frequency of movements.

2.3. EEG, EMG and pressure recordings

EEG was recorded using a cap with 32 Ag/AgCl surface electrodes in a standard montage (BrainCap, Brain Products, Germany). Electrode impedance was kept below 20 kΩ. To control for artefacts, electrocardiogram and electrooculogram were recorded as well. Simultaneously, the EMG of scalene or sternocleidomastoid muscles and of finger-flexor muscles was also recorded (Brain Vision Recorder program, Brain Products, Germany). Sampling frequency was 500 Hz, EEG and EMG signals were amplified and filtered 0.01–250 Hz with BrainAmpDC (Brain Products, Germany) and stored on the computer. Air pressure changes in one of the nostrils and in the rubber bulb (pressure sensor EST 2230, Hyb, Slovenia) were recorded simultaneously to control for the accuracy of movement execution.

2.4. EEG analysis

Off-line EEG analysis was done with Brain Vision Analyser (Brain Products, Germany). The average reference from all EEG channels was calculated and used in further analyses. Blinking and eye movement artefacts were removed using independent component analysis algorithm (Infomax Restricted Biased). Other artefacts were removed manually after the EEG recording was segmented into 3.5 s epochs (2.5 s before and 1.0 s after the EMG onset). Movement onset was automatically determined as the deflection of rectified EMG signal from baseline. From 50 to 150 EEG epochs (the number depended on EMG signal quality, artefacts and frequency of sniffing and finger flexions) in each subject were averaged. The baseline (zero potential) was determined as 2.5–2.0 s before the movement onset. The EEG data of all subjects were averaged to obtain a grand averaged EEG for each movement.

2.5. Analysis of BP1, BP2 and MP amplitudes

Amplitudes of MRCP components were measured automatically at −700 ms for BP1, −300 ms for BP2 and 0 ms for MP at five frontal (F7, F3, Fz, F4, F8), five central (T7, C3, Cz, C4, T8) and five parietal electrodes (P7, P3, Pz, P4, P8) for each subject separately.

The scalp topography of sniffing and finger-flexion related BP1, BP2 and MP was first analyzed by comparing amplitudes on these 15 electrodes. For this, one-way analysis of variance (ANOVA) and Tukey post hoc test were performed for each task and time frame separately. Left-to-right MRCP symmetry in each task was evaluated by comparing the amplitudes on each pair of homologous electrodes, i.e. F7 and F8, F3 and F4, etc. using *t*-test for paired samples for each task and each MRCP component separately. Additional testing of left-to-right MRCP symmetry in individual subjects was performed as follows. First, absolute differences between averaged MRCP on left and right electrodes (i.e. F8–F7, F4–F3, T8–T7, C4–C3, P8–P7, P4–P3) were calculated in BrainVision Analyser (Brain Products, Germany) for each subject and plotted as a curve. Then the times (relative to movement onset) when these differences exceeded zero and when they reached maximal value were visually determined.

Amplitudes of MRCP components in sniffing and finger flexions were compared statistically with independent samples *t*-test performed for each of selected 15 electrodes (for BP1, BP2 and MP separately). A significance level of $p < 0.05$ was adopted in all statistical tests, which were performed in SPSS (PASW statistics 18).

2.6. Current source density (CSD)

The CSD transform (Perrin et al., 1989) was used for summarizing surface potential topographies. It was calculated in Brain Vision Analyser (Brain Products, Germany) on the grand averaged EEG. Three 50 ms long intervals were chosen to represent current source densities during BP1 (-700 ± 25) ms, BP2 (-300 ± 25) ms and MP (0 ± 25) ms. The interpolation of four spherical splines was used, the maximum degree of the Legendre polynomial was 10 and the Lambda approximation parameter was (1e−5).

2.7. Principal component analysis (PCA)

PCA (Jackson, 1991) was used for the extraction of linearly uncorrelated signal sources (i.e. PCA components), whose topographical maps represent the location and orientation of the underlying cortical sources (i.e. dipoles) and whose time courses indicate the sources' time-varying magnitude (Schomer, 2011). Each PCA component consists of an eigenvalue, an eigenvector and a time-course. PCA eigevalues indicate the importance of the PCA component, i.e. the percentage of the explained total signal variability in the chosen time interval. PCA eigenvectors define the principal component topography by representing the contributions of EEG signals from different electrodes to the principal component. Their absolute values are generally larger for the electrodes located closer to the associated source. The projection of the eigenvector values on the head thus shows the topographical map of the underlying cortical sources associated with the principal component. The PCA time courses are calculated as a linear combination of the EEG signals and indicate the time-varying magnitude of the underlying dipoles.

PCA was performed on grand averaged EEG, separately for sniffing and finger flexions in three different time intervals, matching BP1 (−1.5 s to −0.5 s), BP2 (−0.5 s to −0.1 s) and MP (−0.1 s to +0.1 s). Matlab R2007a software (Mathworks, USA) was used for the