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Motor Cortex Dynamics in Visuomotor Production of Speech and Non-speech Mouth Movements

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We investigated timing and hemispheric balance of motor cortex activation when kinetically similar speech and non-speech mouth movements and sequences of such movements were triggered by visually presented letter- and symbol-strings. As an index of motor cortex activation, we used magnetoencephalographic recording of task-related change of precentral 20 Hz (16–24 Hz) activity. Suppression of the 20 Hz rhythm revealed pre-movement activation in the face representation areas that was tied to visual instruction, not movement onset. The 20 Hz rhythm remained suppressed throughout the preparation and execution of mouth movements and was followed by post-movement rebound. Left hemisphere preceded the right at the onset and offset of the suppression, similarly for isolated and sequential speech and non-speech movements. Pattern of task-related change in 20 Hz activity was otherwise symmetrical. In the face areas, the overall modulation of 20 Hz activity increased with sequence length and motor demands. Hand representation areas showed also weak reactivity, with systematically larger modulation of 20 Hz activity for non-speech than speech movements. Our results suggest an active role for the motor cortex in cognitive control of visually triggered mouth movements, not limited to movement execution.

Keywords: 20 Hz rhythm, face area, hand area, lateralization, MEG

Introduction

Mouth movements are required in a variety of human motor behaviors, from eating to non-speech gesturing and articulation. The volitional control of lip, jaw and tongue movements is accompanied by bilateral activation of the rolandic sensorimotor cortex (SMC) lining the central sulcus (Penfield and Boldrey, 1937; Kuypers, 1958; Penfield and Roberts, 1959; Huang *et al.*, 1988, 1989; Murphy *et al.*, 1997; Corfield *et al.*, 1999). The most essential part of this region for production of mouth movements seems to be the face representation area of the primary motor cortex (M1) in the anterolateral bank of the central sulcus (Penfield and Boldrey, 1937; Huang *et al.*, 1989). Within this area, intracranial studies on monkeys have revealed complex, distributed representation of mouth movements (Huang *et al.*, 1988, 1989; Murray and Sessle, 1992; Graziano *et al.*, 2002).

M1 appears to have far more elaborate function than generation of separate muscle twitches (Georgopoulos, 2000; Sanes and Donoghue, 2000; Graziano *et al.*, 2002; Crowe *et al.*, 2004). Besides execution, M1 activation has been observed during preparation of hand and arm movements (Jasper and Penfield, 1949; Tanji and Evarts, 1976; Neshige *et al.*, 1988; Georgopoulos *et al.*, 1989; Alexander and Crutcher, 1990; Szurhaj *et al.*, 2003) and also mouth movements (Salmelin *et al.*, 2000; Yoshino *et al.*, 2000). Furthermore, it seems that

preparatory activation of the M1 is not only related to motor programming but also reflects visuomotor transformation and even stimulus specification in externally triggered movements, e.g. when a monkey maps different stimulus colors onto different arm movement directions (Zhang *et al.*, 1997). For humans, overt reading is an important example where visuomotor mapping is employed to produce mouth movements. Preparatory M1 activation during a delay between single word presentation and 'go' signal for articulation has been shown in a noninvasive magnetoencephalographic (MEG) study (Salmelin *et al.*, 2000). However, it is currently unestablished if this pre-movement activation is time-locked to the movement onset (motor programming) or if it is driven by the instruction for movement (visuomotor mapping). This question should be accessible by introducing variability in the reaction times from instruction to execution.

SMC is activated bilaterally for mouth movements. Whether the SMC activation reflects the typically observed left-hemisphere dominance for speech production in most right-handed individuals (Penfield and Roberts, 1959; Wada and Rasmussen, 1960) is currently unclear. Several studies have reported equal bilateral involvement for speech and non-speech mouth movements (Penfield and Roberts, 1959; Petersen *et al.*, 1988; Wohlert, 1993; Pfurtscheller *et al.*, 1994; Murphy *et al.*, 1997; Corfield *et al.*, 1999; Wise *et al.*, 1999; Tarkka, 2001; Blank *et al.*, 2002; Huang *et al.*, 2002), whereas other studies have shown signs of left-hemisphere dominance for speech movements (Price *et al.*, 1996; Riecker *et al.*, 2000a; Salmelin *et al.*, 2000) but not for non-speech movements (Wildgruber *et al.*, 1996; Epstein *et al.*, 1999; Riecker *et al.*, 2000b; Salmelin and Sams, 2002). It seems that these variations cannot be explained solely by differences between brain research techniques but attention must also be paid to differences in the experimental paradigms. First, the covert mode of speech production used to avoid movement artefacts in some of the functional resonance imaging (fMRI) studies (Wildgruber *et al.*, 1996) seems to intensify speech-related left-hemisphere dominance in the M1 (Riecker *et al.*, 2000a). Second, non-speech mouth movements used in functional neuroimaging studies have been understandably simpler than those needed in articulation of words and sentences. Processing of isolated phonemes or syllables and simple non-speech gestures does not seem to be lateralized at the level of SMC (Wohlert, 1993; Riecker *et al.*, 2000b; Tarkka, 2001; Salmelin and Sams, 2002). Moreover, transcranial magnetic stimulation (TMS) applied to the left motor face area disturbs production of complex speech more efficiently than that of simple speech and non-speech mouth movements (Epstein *et al.*, 1999). Thus, even if lateralization for speech existed in the SMC, it is unresolved whether it reflects purely

linguistic aspects or, rather, complexity of the movement sequence.

Intriguingly, SMC activation during mouth movements is not restricted to the lateral face area but is present also in the medially adjacent hand representation area, as demonstrated with MEG (Salmelin *et al.*, 2000; Salmelin and Sams, 2002) and TMS (Tokimura *et al.*, 1996; Meister *et al.*, 2003). Neuroimaging studies using positron emission tomography (PET) or fMRI have not explicitly reported such activation and there is only preliminary understanding of this phenomenon. The hand area seems to be the only non-face representation area in the SMC showing activation during mouth movements and its activation coincides with movement execution rather than preparation. Moreover, both MEG and TMS studies have demonstrated that this activation differentiates between speech and simple non-speech mouth movements (Salmelin *et al.*, 2000; Salmelin and Sams, 2002; Meister *et al.*, 2003).

In the present study, we used MEG for combined spatial and temporal characterization of motor cortex activation during speech and non-speech mouth movements. Simultaneous electromyogram (EMG) was recorded from mouth (the orbicularis oris muscle) and arms (the extensor digitorum communis muscle). As an index of motor cortex activation, we used movement-related change of the rolandic 20 Hz range rhythm (Jasper and Penfield, 1949; Gastaut, 1952; Chatrian *et al.*, 1959; Pfurtscheller, 1981; Hari and Salmelin, 1997; Pfurtscheller and Lopes da Silva, 1999) that is not disturbed by electric signals from orofacial muscles (Salmelin *et al.*, 2000; Salmelin and Sams, 2002). MEG studies have demonstrated that this rhythm features somatotopy (Salmelin *et al.*, 1995) and is generated predominantly by synchronous neural activity in the precentral M1 (Salmelin and Hari, 1994a; Salmelin *et al.*, 1995; Salenius *et al.*, 1997). At rest, only hand areas seem to show identifiable 20 Hz rhythm (Salmelin and Hari, 1994b). Detectable 20 Hz rhythm in other motor representation areas is related to movement (Salmelin *et al.*, 1995, 2000; Salmelin and Sams, 2002). Typically, when the SMC is involved in movement performance (activation phase), the rolandic 20 Hz rhythm is suppressed. The suppression is followed by a post-movement rise above the baseline level ('rebound'), apparently reflecting cortical inactivation or immobilization when returning to rest (Pfurtscheller, 1981; Salmelin and Hari, 1994b; Stancak and Pfurtscheller, 1995; Salmelin *et al.*, 1995; Pfurtscheller *et al.*, 1996; Chen *et al.*, 1998; Pfurtscheller and Lopes da Silva, 1999; Szurhaj *et al.*, 2003). In the present study, the change in the amount of 20 Hz rhythm from the minimum level of synchronization (suppression) to the maximum level (rebound) was taken as a measure of task-related change in activation of the motor cortex.

In order to clarify the effect of movement complexity on M1 activation, we used both isolated and sequential mouth movements. Simple (one-item) movements were isolated phonemes (P) and non-speech gestures (G), and complex (four-item) movements were sequential utterances including Finnish CVCV (Consonant, Vowel) words (WO), CVCV pseudowords (PW), four-letter consonant strings (CS) and strings of four different non-speech gestures (GS). In both speech and non-speech tasks, mouth movement were produced silently (without phonation) and they were triggered with visual instructions. For speech movements, the stimuli were letters and, for non-speech movements, novel symbols depicting specific lip, jaw or tongue movements. Special emphasis was laid on the

visual similarity of the instructions and physical similarity of the movements in the speech and non-speech conditions. We assumed that consonant strings and non-speech gesture strings would place stronger demands on movement programming than words and pseudowords or isolated movements, and that symbol-to-movement mapping in non-speech tasks would be more effortful than letter-reading in speech tasks. These contrasts were expected to introduce natural variability in the reaction times, thus facilitating separation of effects tied to visual presentation versus movement onset.

Our specific questions were: (i) Is there preparatory 20 Hz suppression in the face area for mouth movements and, if yes, is this reactivity time-locked to movement or to visual instruction? (ii) Can we observe left-hemispheric lateralization and, if yes, is it specific for complex speech movements? (iii) Do the 20 Hz modulation patterns differ for isolated versus sequential (simple versus complex) movements and for sequential movements with variable linguistic content, familiarity, and automatization? (iv) Is the hand area reactive and, if yes, does its 20 Hz modulation vary with speech-likeness or sequence complexity of the mouth movements?

Materials and Methods

Subjects

Nine healthy, right-handed, Finnish-speaking students (five females, 20–33 years, mean age 26 years; one female ambidextrous) participated in this study. All subjects gave their informed consent to participate in the study which had prior approval of the Helsinki and Uusimaa Ethics Committee.

Stimuli and Tasks

Figure 1a illustrates visual stimuli that were used to trigger speech and non-speech mouth movements, both produced without phonation. The stimuli for one-item speech movements were 11 letters (consonants K, L, M, N, P, V; vowels A, E, I, O, U). Out of these letters, we constructed 20 Finnish CVCV words (medium or high frequency) without using any letter twice within the same word. Importantly, the Finnish language has an exceptionally regular orthography (one-to-one correspondence between graphemes and phonemes) and thus the letters in a word exactly represent the phonemes that are articulated. The CVCV pseudowords (20) were formed, with few exceptions, by rearranging the letters of the real words used. Consonant strings (20) were based on the real words by replacing vowels with consonants (R, B, N, G, D) according to shared visual features with vowels and rearranging the letters to avoid visual word recognition.

The stimuli for one-item non-speech movements were 11 symbols (Fig. 1b) that were designed to have very simple letter-like features and to represent the associated movement in an easy and transparent way. The non-speech movements were chosen to be natural and easily acquired gestures, like touching the teeth with the tongue and making a kissing movement. There were seven lip/jaw and four tongue movements, and many of them resembled articulatory gestures (Fig. 1b). The four-item sequences were formed on the basis of the words by substituting letters with specific symbols and organizing them into 20 strings with relatively easy movement sequences.

To learn symbol-gesture associations, the subjects practiced them at home with a special leaflet (11 symbols and their written explanations, photographs of a female instructor making the gestures, the 20 symbol strings used). Immediately before the MEG recording another learning session was carried out with computer presentation of all the stimuli. Individual guidance was given, for example on the suitable magnitude of the movements. The subjects were instructed to specifically avoid moving their head during mouth movements.

Stimuli were presented on a projector screen at a distance of 0.9 m from the subject, with black lines on a medium gray background. The one-item and four-item stimuli spanned a visual angle of $-1 \times 1^\circ$ and $4.5 \times 1^\circ$ (width \times height), respectively. Each stimulus was presented for

(a) **One-item**

A	PHONEMES	(P)
∨	GESTURES	(G)

Four-item

VALO	WORDS ("light")	(WO)
LOVA	PSEUDOWORDS	(PW)
RVGL	CONSONANT STRINGS	(CS)
∨◇∧∇	GESTURE STRINGS	(GS)

(b)

SYMBOL	ASSOCIATED MOVEMENT	RELATED ARTICULATORY GESTURE
⊠	KISS I (mouth closed)	/ u /
◇	KISS II (mouth open)	/ o /
∨	SMILE	/ i /, / e /
⊠	LIPS TOGETHER	/ m /
∩	"SAD LIPS"	none
—	LIPS AS A LINE	none
∇	LOWERING JAW	/ a /
∧	TONGUE ON PALATE	/ l /
∩	TONGUE BEHIND TEETH	/ n /
⊠	TONGUE ON CHEEK	none
⊠	TONGUE PROTRUSION	none

Figure 1. (a) Examples of one- and four-item stimuli for speech and non-speech mouth movements. (b) Specifications of 11 symbols depicting non-speech mouth movements, and the articulatory gestures they are most closely related to.

500 ms in the one-item condition and for 2000 ms in the four-item condition. The inter-stimulus interval varied randomly between 2000 and 3000 ms. The subjects were requested to respond to the stimulus as quickly and accurately as possible. It was emphasized that letters should be articulated as phonemes, not named. In the four-item condition, subjects were instructed to fill the stimulus presentation time with movements, that is, they had to articulate the words and pseudowords in slow motion. The subjects were instructed to stop the movement when the stimulus disappeared, irrespective of whether they had completed the speech/non-speech sequence or not. The order of the different stimulus categories within each condition was pseudorandomized.

In addition to the mouth movements, subjects made self-paced index finger lifts (every ~2 s) with the left and right hand, in separate recordings. This task was included to allow localization of the hand areas independently of the mouth movement data. Also, MEG data was recorded when the subject was at rest, with eyes open (2 min) and eyes closed (2 min). These data were used for evaluating the base level at rest for the 20 Hz rhythm in the M1 face and hand areas. A fixation point was presented during finger movements and collection of the resting activity.

MEG and EMG Recording

Cortical magnetic signals were recorded with a whole-head 306-channel MEG system (Vectorview™, Neuromag Ltd, Helsinki, Finland).

MEG signals reflect synchronous postsynaptic potentials in neuronal populations mainly in the fissural cortex. Two orthogonally oriented planar gradiometers and one magnetometer are located in each of the 102 different locations of the helmet-shaped MEG sensor array. In this study, we used the planar gradiometers that record maximum signal directly above an active cortical area (for detailed description of the MEG method, see Hämäläinen *et al.*, 1993). The signals were acquired with a 0.03–200 Hz filter and digitized at 600 Hz. During all the measurements, EMG activity was recorded with bipolar electrodes from the diametrically opposite corners of the mouth (the orbicularis oris muscle) and from the left and right arm (the extensor digitorum communis muscle). Blinks and eye movements were monitored with bipolar EOG (electro-oculography) electrodes placed diametrically at the peripheral corners of the eyes.

The measurement started with recording of resting activity (when necessary; for four subjects recent recordings were available). Finger lifts then followed, with the movement onsets measured optically. After this, one-item and four-item mouth movements were produced in separate blocks, and the order of these blocks was randomized across subjects. Within these blocks, there were 88 trials per each one-item category (P, G) and 80 trials per each four-item category (WO, PW, CS, GS). The one-item block lasted ~10 min and the four-item block ~25 min.

To present the MEG data on anatomical magnetic resonance images (MRIs), available for all subjects, two coordinate systems were aligned with the help of four small coils placed on the subjects' head before the MEG measurement. Using a 3-D digitizer (Isotrak 3S1002, Polhemus Navigation Sciences, Colchester, VT), the positions of these coils were determined with respect to three landmarks on the head, i.e. nasion and points just anterior to the ear canals, readily identified on the MRIs. The locations of the coils with respect to the MEG helmet were determined by briefly energizing the coils and calculating their locations from the generated magnetic field.

Data Analysis

For determining movement onset trial by trial, the EMG signal was high-pass filtered at 7 Hz and rectified. Movement onset was individually defined as the time point where the signal first exceeded the baseline noise level after stimulus. The rectified EMG was averaged with respect to stimulus and movement onsets, smoothed (low-pass filter at 20 Hz), and normalized with respect to the pre-stimulus level for calculation of the mean amplitude and estimated duration (full width at half maximum) from movement onset averages.

Fast Fourier Transform (FFT) was used to calculate amplitude spectra of the MEG signals for each subject in the different experimental conditions (one-item and four-item mouth movements, left and right index finger lift, resting with eyes open, resting with eyes closed). By comparing these individual spectra it was possible to identify distinct frequency ranges around 10 and 20 Hz, where the amount of rhythmic activity varied by task. Around 20 Hz, we identified generally two reactive frequency ranges (low and high 20 Hz) per subject, and evaluated the mean level of activation in low and high 20 Hz ranges as a function of time with the Temporal Spectral Evolution (TSE) approach (Salmelin and Hari, 1994b). TSE consists of bandpass filtering, rectification (absolute value) and averaging of the signals with respect to a trigger. On the basis of these data, a fixed 16–24 Hz range was considered appropriate for quantification of the task-related change of 20 Hz activity in all the subjects. We computed the 20 Hz TSEs with respect to both stimulus onset and movement onset, from -1800 to +3500 ms in the one-item and from -1800 to +5000 ms in the four-item condition. The pre-stimulus level was determined from a 1 s interval, from -1300 to -300 ms with respect to stimulus onset and from -1800 to -800 ms with respect to movement onset, corresponding approximately to the same time interval. In the finger-lift data, TSEs were also calculated in the 16–24 Hz range, in the time window -1800 to +4000 ms with respect to movement onset.

The finger-lift tasks showed the typical concentration of 20 Hz modulation medially over the central sulcus, whereas in the mouth movement task the 20 Hz modulation extended clearly more laterally in both hemispheres. We determined the individual sources of the 20 Hz activity separately in the data recorded during finger lifts and mouth movements. The source areas were modeled as equivalent current

dipoles (ECD), which represent the center of an active cortical patch and the direction and mean strength of current flow therein. These sources were searched every 5 ms from three 30 s blocks cut from the beginning, middle, and end of the non-averaged MEG data sets. An individually determined spherical head conductor model was employed in the dipole modeling process (Tarkiainen *et al.*, 2003). To search for sources from mouth movement data we included a subset of 22–24 gradiometers around the lateral maximum of the TSE modulation, separately for each hemisphere. To search sources from finger lift data we used 20–28 gradiometers above the more medial maximum of TSE modulation, again separately for each hemisphere. As a result of this search, we obtained clusters of dipoles with good fit to the data (g -value > 85%) in the lateral and medial parts of the central sulcus. One ECD was selected from each cluster. To select these ECDs, anatomical *a priori* assumptions and the level at which the dipole represented the entire cluster were considered but the criterion for final selection was its ability to account for the observed 20 Hz modulations (TSE curves). Finally, we constructed individual 4-dipole models from the selected ECDs representing the M1 face and hand area in both hemispheres. In each subject, the dipoles differed sufficiently in location and orientation to allow independent mapping of activation in the left and right face and hand area (space angle at least 47°; typically >60°). For mouth movement data, these dipoles were used to calculate 20 Hz TSEs in the hand and face areas with respect to both stimulus and movement onsets (source TSE waveforms). The individual 4-dipole model was also applied to the MEG data recorded during rest, with eyes open, in order to obtain an estimate of the resting level 20 Hz activity in the face and hand areas (average of 100 epochs of 1 s). For comparison of source areas across subjects, an elastic transformation method (Schormann *et al.*, 1996; Woods *et al.*, 1998a,b) was used to convert the dipoles to a standard brain coordinate system (Roland and Zilles, 1996).

TSEs averaged with respect to stimulus onset were used for measuring the suppression onset, and TSEs averaged with respect to movement onset for measuring the suppression duration and offset and the change from suppressed to rebound level of 20 Hz rhythm. A relatively standard procedure in analyzing task-related modulation of cortical rhythms is to estimate level of suppression and rebound separately and relate them to the pre-task 'baseline' level (e.g. Pfurtscheller and Lopes da Silva, 1999; Salmelin and Sams, 2002). In the present task, all subjects showed both suppression and subsequent rebound but the relative emphasis between these phases varied across individuals. A composite measure, rebound maximum minus suppression minimum, proved optimal for quantifying the amount of change in the motor cortical 20 Hz activity associated with different mouth movements. This measure was further normalized (%) with respect to spontaneous activity at rest (eyes open) in order to render different subjects and tasks comparable.

In the face areas, the suppression onset was determined as the time point at which suppression had reached half of the minimum value (with respect to the pre-stimulus level). Similarly, the suppression offset was determined as the time point when suppression returned to half of the minimum value, and the duration as the difference between these offset and onset values.

In the hand area, reactivity was mostly rather weak. Because of that, fixed time windows were used for collecting the suppression minimum (one-item: -800 to +700 ms; four-item: -800 to 1700 ms) and rebound maximum (one-item: 700 to 3500 ms; four-item: 1700 to 5000 ms). Onset and offset latencies were not collected because of insufficient signal level.

Statistical analyses were performed with repeated-measures analysis of variance (ANOVA), and planned contrasts with *t*-tests. In the ANOVA analyses, the Greenhouse–Geisser correction was applied when necessary. Pearson's correlations were used to evaluate relationships between cortical activity in the two hemispheres and cortical activity and EMG signals. To include both speech and non-speech movements (Task) and different sequence length conditions (Length) to the ANOVA analyses, we selected only the extreme tasks, WO and GS, to represent the four-item condition, allowing fully factorial analyses. The following independent factors were used in the different ANOVA analyses: Length (sequence length: one or four), Task (speech or non-speech), Hemi (hemisphere: left or right), Area (representation area:

face or hand), Site (recording site: left face area, right face area, mouth EMG) and Level (level of 20 Hz activity: rest, one-item pre-stimulus interval, four-item pre-stimulus interval).

Results

Mouth Movements Recorded with EMG

Figure 2 depicts EMG signals recorded from the mouth and arm in one-item and four-item mouth movements. Comparison of real phonemes/words versus gestures/gesture strings (P, G, WO, GS) showed that speech movements started earlier than non-speech mouth movements [2 (Length) × 2 (Task) ANOVA: Task, $F(1,8) = 88.2$, $P < 0.001$], and that this difference was more pronounced for four-item than for one-item movements [Length-by-Task interaction, $F(1,8) = 49.9$, $P < 0.001$]. Planned contrasts showed that P, WO and PW movement onsets did not differ from each other, but G (*t*-test, $P < 0.001$) was significantly delayed with respect to P, and CS ($P < 0.01$) and especially GS ($P < 0.001$) were delayed with respect to WO. The reaction times thus showed the expected variability to enable separation of cortical effects tied to visual presentation versus movement onset.

Non-speech mouth movements showed higher mean amplitude of EMG activity than speech movements [2 (Length) × 2 (Task) ANOVA: Task, $F(1,8) = 16.2$, $P < 0.005$] with larger difference for sustained four-item than for transient one-item movements [Length-by-Task interaction, $F(1,8) = 5.5$, $P < 0.05$]. We instructed the subjects to finish the articulation of sequential movements within the duration of stimulus. The salient second peak in EMG activity for GS movements (Fig. 2) is likely to be related to this time constraint as some subjects may have compensated for the difficulties in less automatized sequence completion with increased muscular activity. The left and right arms showed no EMG activity during mouth movements.

Reactivity of 20 Hz Rhythm

Figure 3 illustrates modulation of 20 Hz activity in one subject, recorded by MEG sensors during GS movements. The 20 Hz rhythm was clearly reactive to the mouth movement in both hemispheres. Sensors above the lateral and medial rolandic areas showed distinct time courses of modulation.

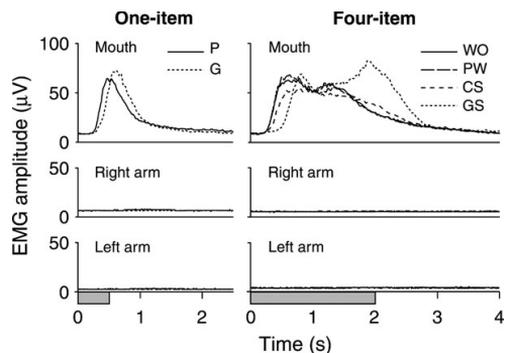


Figure 2. Mean EMG time courses recorded from the mouth and the right and left arm during the one-item (P, G) and four-item (WO, PW, CS, GS) mouth movements, averaged with respect to stimulus onset, across all subjects. The gray rectangles indicate the stimulus duration.

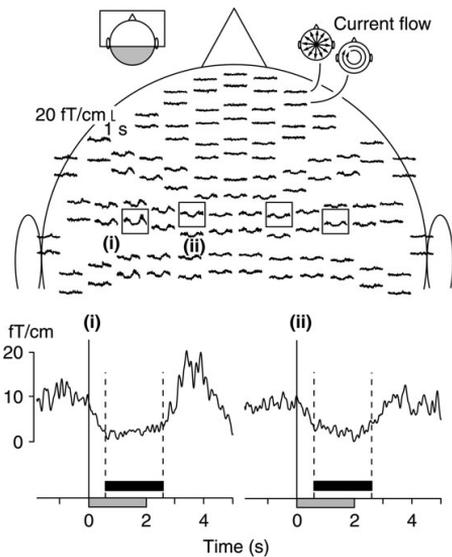


Figure 3. Top: Frontocentral 20 Hz modulation measured with MEG planar gradiometers during production of gesture strings (GS). At each recording site, there are two gradiometers that are most sensitive to orthogonally oriented source currents (see schematic heads in the upper right corner). Boxes indicate sensors picking up distinct responses from lateral (i) and more medial (ii) rolandic regions. Bottom: Enlarged views of the lateral (i) and medial (ii) 20 Hz modulation in the left hemisphere. The black rectangles indicate the mean duration of the mouth movement and the gray rectangles presentation of the visual instruction.

The local modulation of 20 Hz activity was accounted for by task-related changes of activation in four different areas along the central sulcus, which were adequately represented by equivalent current dipoles (ECDs). Figure 4 illustrates the mean source locations and directions of current flow in axial planes (Fig. 4a) and on lateral surface renditions (Fig. 4b). The individual 4-dipole models were in good agreement with the previously described anatomical arrangement of the hand and face areas in the SMC (Woolsey *et al.*, 1979; Hari *et al.*, 1993; Salmelin *et al.*, 1995; Nakamura *et al.*, 1998). The medial sources were located in the so-called hand knob (Yousry *et al.*, 1997) and the lateral sources about 2 cm inferior and 1 cm anterior to this site.

Figure 5 shows grand averaged (\pm SEM) 20 Hz modulations at the source level, in the left and right face and hand areas (rows), for the one- and four-item conditions (columns). The level of 20 Hz activity was averaged with respect to the stimulus onset and normalized with respect to the resting level of 20 Hz rhythm. The face area appears to be more responsive than the hand area, and the modulation stronger and more sustained in the four-item than in the one-item condition.

Timing of 20 Hz Suppression in the Face Areas

Within each face area, the suppression onset was essentially constant for all movement tasks (Fig. 6). The apparently earlier onset latencies in the one-item than in the four-item condition in Figure 6a are attributable to the present quantification of the onset latency, i.e. the latency at which the suppression reached half of the maximum suppression, and to the overall stronger

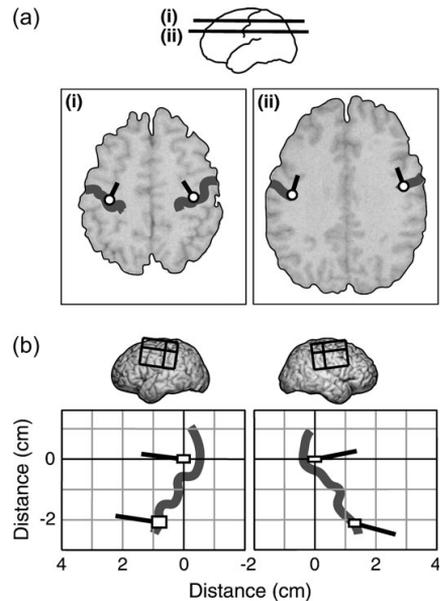


Figure 4. (a) Mean locations (circles) and orientations (tails) of the four equivalent current dipoles (ECDs) used in modeling the data, presented on a standard brain. Two axial planes are shown, one at the level of the hand areas (i), the other at the level of the face areas (ii). (b) The mean \pm SEM locations (rectangles) and directions of the face and hand area ECDs in left and right lateral views. The thick dark lines indicate the course of the central sulcus.

suppression in the four-item than in the one-item condition. As illustrated in Figure 6b, the one-item and four-item conditions showed comparable kinetics at the beginning of the suppression. Most importantly, Figure 6 demonstrates that the suppression started on average 90 ± 57 ms earlier in the left than in the right hemisphere [2 (Length) \times 2 (Task) \times 2 (Hemi) ANOVA: Hemi, $F(1,8) = 7.6$, $P < 0.05$], suggesting brief left-hemisphere lateralization for the initial stage of face area activation.

The onset of the 20 Hz suppression preceded the muscle activity recorded with mouth EMG [2 (Length) \times 2 (Task) \times 3 (Site) ANOVA: Site, $F(1,8) = 35.5$, $P < 0.001$; planned contrasts between EMG and the left ($P < 0.001$) and right face area ($P < 0.001$)]. This effect was strongly accentuated for the non-speech movements with longer reaction times [Task-by-Site interaction, $F(1,8) = 38.4$, $P < 0.001$]. Accordingly, suppression onset was more strongly tied to the onset of visual instruction than to the movement onset.

The duration of the 20 Hz suppression in the face area (cf. Fig. 5) was significantly shorter in the one-item than in the four-item condition [2 (Length) \times 2 (Task) \times 2 (Hemi) ANOVA: Length, $F(1,8) = 306.1$, $P < 0.001$], but did not differ for speech and non-speech movements or for the left and right hemisphere. Like the onset, the suppression offset was on average 172 ± 118 ms earlier in the left than in the right hemisphere [2 (Length) \times 2 (Task) \times 2 (Hemi) ANOVA: Hemi, $F(1,8) = 6.4$, $P < 0.05$]. In all tasks, the cortical 20 Hz suppression outlasted the muscle activity for 313 ± 126 ms in the left and 485 ± 138 ms in the right hemisphere [2 (Length) \times 2 (Task) \times 3 (Site) ANOVA: Site, $F(1,8) = 16.5$, $P < 0.001$; planned contrast between EMG and the left ($P < 0.05$) and right face area ($P < 0.001$)].

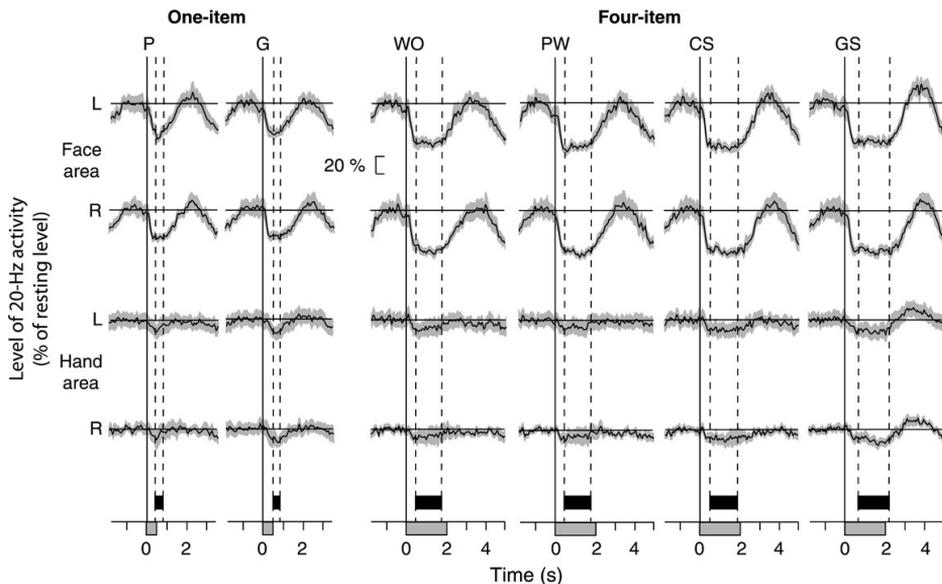


Figure 5. Mean (\pm SEM) time course of 20 Hz modulation in the face and hand areas for the one-item (P, G) and four-item (WO, PW, CS, GS) mouth movements, averaged with respect to the stimulus onset. The horizontal lines indicate pre-stimulus level of 20 Hz activity, the black rectangles mean movement durations, and the gray rectangles presentation of the visual instruction.

Task-related Modulation of 20 Hz Activity in the Face and Hand Areas

Figure 7 illustrates that the 20 Hz modulation (suppression minimum-to-rebound maximum) was overall stronger in the face than in the hand area [2 (Length) \times 2 (Task) \times 2 (Area) \times 2 (Hemi) ANOVA: Area, $F(1,8) = 16.7$, $P < 0.005$]. In the face area, the modulation was stronger in the four-item than in the one-item tasks but in the hand area the item length had no effect [Length-by-Area interaction, $F(1,8) = 29.1$, $P < 0.005$]. The 20 Hz modulation increased with decreasing linguistic content of the movements [Task, $F(1,8) = 31.9$, $P < 0.001$], with the important exception that in the one-item condition the face area showed equal change in activity for speech and non-speech movements (planned contrast, t -test, $P > 0.05$, n.s.). In the four-item condition, significant differences in the face area only emerged between WO and GS tasks (planned contrast WO $<$ GS, $P < 0.05$); PW and CS tasks did not differ from each other or from WO and GS. The hand area showed a more stepwise behavior, with all speech tasks differing significantly from the non-speech task (planned contrasts WO $<$ GS, $P < 0.005$; PW $<$ GS, $P < 0.005$; CS $<$ GS, $P < 0.01$). The pattern was the same in the left and right hemisphere. In the face areas, the amount of 20 Hz modulation and the duration of 20 Hz suppression did not covary.

Interhemispheric Correlations

All measures of timing and amount of 20 Hz modulation tended to be positively correlated between the hemispheres in all tasks. Importantly, the suppression onsets in the left and right face area were significantly correlated in the four-item WO ($r = 0.870$, $P < 0.005$) and GS ($r = 0.882$, $P < 0.005$) tasks, indicating a similar interhemispheric relationship of suppression onsets in speech and non-speech tasks.

Correlations between Cortical Activity and EMG

The onset of 20 Hz suppression in the face area was not significantly correlated with EMG onset. In contrast, for some tasks the duration and offset of the face area suppression showed significant positive correlation with EMG duration and offset, respectively. For example, the offset latencies in the PW task were correlated between cortex and EMG (left hemisphere, $r = 0.848$, $P < 0.005$; right hemisphere, $r = 0.725$, $P < 0.05$). Importantly, the amount of task-related 20 Hz modulation (suppression minimum-to-rebound maximum) in the face or hand areas did not covary with the mean amplitude or duration of EMG activity.

Task-related Modulation versus Resting Level of 20 Hz Activity

Figure 8 depicts, in each of the four source areas, the absolute level of 20 Hz activity during rest, with eyes open and no task (black bar) and during the different stages of the P (Fig. 8a) and WO (Fig. 8b) tasks: the 1 s pre-stimulus interval (dark gray), suppression minimum (white) and rebound maximum (light gray). In the face areas, the level of 20 Hz activity was significantly higher during the pre-stimulus interval of P and WO tasks than in the resting state [2 (Area) \times 2 (Hemi) \times 3 (Level) ANOVA: Area-by-Level interaction, $F(1,8) = 13.4$, $P < 0.01$; planned contrasts one-item $>$ rest ($P < 0.05$); four-item $>$ rest ($P < 0.005$)]. Also, the pre-stimulus level was higher in the four-item (WO) than in the one-item (P) condition (planned contrast one-item $<$ four-item, $P < 0.05$), while within conditions there were no differences between tasks [separate one-item (P, G) and four-item (WO, PW, CS, GS) ANOVA analyses]. In the hand areas, the pre-stimulus level was not affected by the task performance.

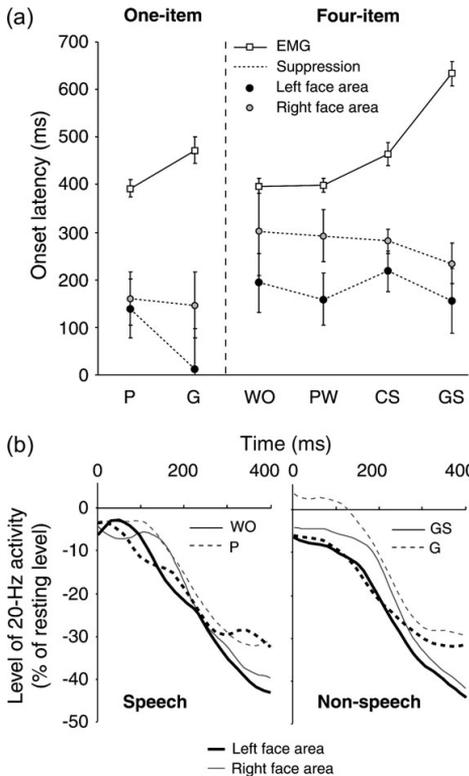


Figure 6. (a) Mean reaction time from the mouth EMG onset and the mean (\pm SEM) onset latency of the 20 Hz suppression in the left (L) and right (R) face area in the one-item (P, G) and four-item (WO, PW, CS, GS) conditions. The timing was determined with respect to the stimulus onset. (b) The mean time course of suppression onset in one- and four-item speech (P, WO) and non-speech (G, GS) tasks, illustrating the similar kinetics in the one- and four-item tasks and the earlier onset in the left than right hemisphere in both speech and non-speech tasks.

Discussion

Making use of the 20 Hz oscillatory activity of the neuronal populations in the motor cortex, we found that pre-movement face area activation, i.e. suppression of the face area 20 Hz rhythm, was time-locked to the visual instruction, not to movement onset, when mouth movements were produced according to visual stimuli. The 20 Hz suppression started about 90 ms earlier in the left than in the right face area, similarly for isolated and sequential speech and non-speech mouth movements. Consistently, the suppression also ended earlier in the left than in the right face area in all tasks, but outlasted the mouth movements in both hemispheres. Apart from the temporal asynchrony between the left and right face area activation, the duration of suppression and modulation of 20 Hz activity (suppression minimum-to-rebound maximum) indicated a bilateral and symmetrical pattern. In the face areas, the 20 Hz modulation was equal for isolated phonemes and non-speech gestures but was increased for sequences composed of these movements. Moreover, the modulation was larger for gesture strings than words, while articulation of pseudowords and consonant strings resulted in an intermediate effect. In addition, the M1 hand areas showed weak 20 Hz

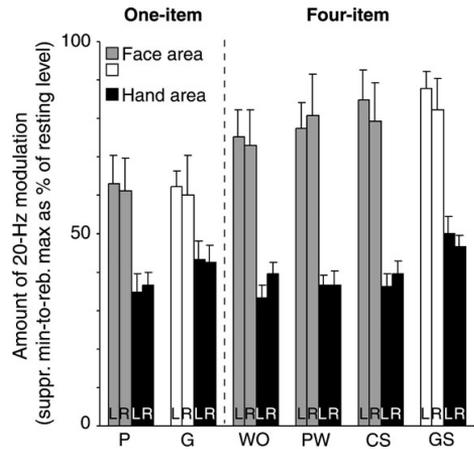


Figure 7. Mean (\pm SEM) strength of the modulation of 20 Hz activity (from suppression minimum to rebound maximum) as percent of resting level in the left (L) and right (R) face and hand areas for the one-item (P, G) and four-item (WO, PW, CS, GS) mouth movements. Modulation in the face areas is plotted in gray for speech movements and in white for non-speech movements. Modulation in the hand areas is plotted in black.

reactivity that was not affected by sequence length but was systematically stronger for non-speech than speech tasks. In the face areas, the overall level of 20 Hz rhythm was enhanced during task performance, especially in the four-item condition, as compared with the resting condition with no task, thus suggesting that a mouth movement task is required to make the face area 20 Hz rhythm identifiable.

20 Hz Suppression Tied to Stimulus Onset in the Face Area

The preparatory 20 Hz suppression in the face motor cortex that was tied to stimulus onset probably reflects visuomotor transformation followed by motor programming and execution. This view is in line with monkey data showing that activation of M1 neurons reflects various processing stages of the visuomotor task including stimulus specification and sensorimotor transformation (Zhang *et al.*, 1997). Thus, the M1 seems to be part of a distributed and parallel brain network coordinating motor and visuomotor tasks (Georgopoulos *et al.*, 1989; Alexander and Crutcher, 1990; Zhang *et al.*, 1997; Morecraft *et al.*, 2001; Dum and Strick, 2002). In this network, M1 may contribute as a motor interface for stimulus-to-response mapping (Penfield and Boldrey, 1937; Huang *et al.*, 1988, 1989; Graziano *et al.*, 2002). In the present data set, the pre-movement M1 activation of the face area was similar for isolated and sequential speech (letter-to-articulation) and non-speech (symbol-to-gesture) movements, thus indicating a basic mechanism common to all these tasks.

Interhemispheric Asynchrony in Timing of 20 Hz Suppression in the Face Area

Previously reported only for overt reading of real words (Salmelin *et al.*, 2000), a lateralized onset of 20 Hz suppression was found here for letter and gesture stimuli and for isolated and sequential movements alike, suggesting an important role for the left M1 in visuomotor production of all mouth

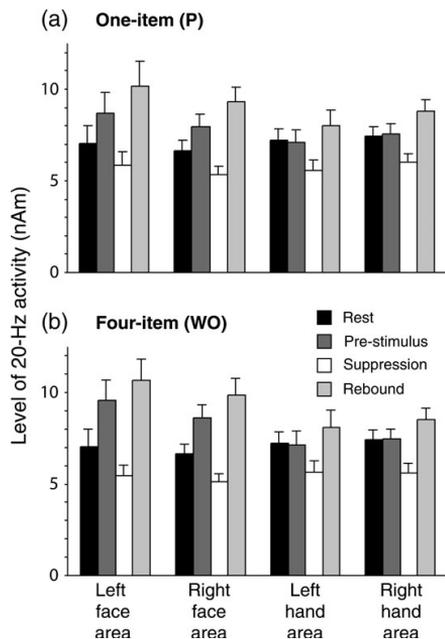


Figure 8. Absolute (mean \pm SEM) level of 20 Hz activity in the left and right face and hand areas during the resting condition (black bars) and during the different stages of (a) phoneme (P) and (b) word (WO) production: pre-stimulus interval (dark gray), suppression minimum (white) and rebound maximum (light gray).

movements. In principle, this lateralization could be linked to language dominance of the left hemisphere because the non-lingual symbol-to-gesture transformations might employ the same resources as overt reading. However, it seems more reasonable to relate this effect to general visuomotor or motor control rather than language processing *per se*. For instance, faster reactivity of the right side of the face (controlled predominantly by the left hemisphere) has been reported for both speech and non-speech mouth movements in a behavioral paradigm with no need for symbol-to-movement transformation (Wolf and Goodale, 1987). The present interhemispheric difference of about 90 ms at the suppression onset parallels a TMS result obtained in a simple vocalization task. The optimal timing of pre-movement TMS that caused the longest delay in movement onset was 50–100 ms earlier for the left than for the right motor cortex (Terao *et al.*, 2001).

In the present data, the face area 20 Hz suppression was also terminated earlier in the left than in the right hemisphere after mouth movements were completed. Nevertheless, the duration of suppression and the suppression-to-rebound change in 20 Hz activity showed a symmetrical pattern between the hemispheres, which is in line with the usual bilateral control of mouth movements. The present data thus agree with earlier reports of symmetrical SMC activation during mouth movements using PET and fMRI (Petersen *et al.*, 1988; Murphy *et al.*, 1997; Corfield *et al.*, 1999; Wise *et al.*, 1999; Blank *et al.*, 2002; Huang *et al.*, 2002) and intracranial electrical stimulation and EEG (Penfield and Roberts, 1959; Wohlert, 1993; Tarkka, 2001). Earlier hemodynamic and TMS studies indicating left-hemisphere dominance

selectively for complex speech (Price *et al.*, 1996; Wildgruber *et al.*, 1996; Epstein *et al.*, 1999; Riecker *et al.*, 2000a,b) were not supported by the present data. One reason for this may be that the present lingual task was not complicated enough (cf. Epstein *et al.*, 1999), or even that the native language (English, German versus Finnish) influences the results, as has been shown for basic auditory processing (Salmelin *et al.*, 1999). Nevertheless, it seems that left-hemisphere dominance during speech production is a more consistent finding in areas outside the SMC (e.g. Penfield and Roberts, 1959; Wise *et al.*, 1999; Blank *et al.*, 2002). The symmetrical activation pattern is obviously not in conflict with possible functional specialization of the left and right M1. For example, the left M1 may be more involved in basic articulatory aspects and the right M1 with prosodic aspects of lingual mouth movements (Alexander *et al.*, 1989).

Modulation of 20 Hz Activity in the Face Area: Item Length and Sequence Content

In the face area, the modulation of 20 Hz activity was affected by the item length (isolated versus sequential) and, for sequences, by the content of the mouth movements. The item-length effect may be partly related to a higher pre-stimulus level of 20 Hz activity in the four-item than in the one-item condition that facilitates larger modulation; on the other hand, larger task-induced modulation may also result in an apparent increase of pre-stimulus level at these relatively short interstimulus intervals. Either way, the overall modulation was larger for four-item than for one-item movements.

Both item-length and content effects could be explained by differences in generation of muscular activity via the descending innervation of the face area upper motoneurons (Kuypers, 1958; Huang *et al.*, 1988, 1989; Morecraft *et al.*, 2001). However, while the present EMG setup was limited, the amount of change in 20 Hz activity did not covary with the mean amplitude or duration of mouth EMG, nor was the amount of 20 Hz modulation determined by the duration of the 20 Hz suppression.

Another potentially important factor to consider is the mode of motor control, i.e. the balance between pre-planning and using sensory feedback to correct movement pattern (e.g. Desmurget and Grafton, 2000). Fast and easily producible one-item movements can be regarded as highly pre-determined, whereas four-item movement sequences were produced slowly and, therefore, sensory feedback was likely to play an important role. An overlearned sequence of mouth movements, like a familiar word, can apparently be produced as if it were a simple, pre-determined movement, as suggested by the similarity of 20 Hz modulation when articulating words and isolated mouth movements (Salmelin and Sams, 2002). This notion approaches the idea of 'stress groups' as motor units for normal, rapid articulation (Sternberg *et al.*, 1988). However, in our study words and pseudowords were produced more slowly than normal to keep them as similar as possible to effortful consonant and gesture strings. The relatively more prominent use of sensory feedback in face motor control could thus account for item-length effect but may not suffice to explain the variation within the set of four-item movements.

In order to understand the effect of sequence content, let us consider the cognitive effort related to organizing movement elements to a movement sequence (sequencing). Isolated mouth movements do not need sequencing and, thus, the

increased modulation of 20 Hz activity for sequential mouth movements may be linked to this additional requirement. This interpretation is in line with earlier reports of stronger SMC activation for sequential versus isolated finger movements measured with EEG (Kitamura *et al.*, 1993) and PET (Catalan *et al.*, 1998). From this standpoint, the earlier MEG finding (Salmelin and Sams, 2002) of equal 20 Hz modulation for words and isolated movements can be accounted for by the paradigm where the word was planned before the 'go' signal that served as the marker for signal analysis, thus efficiently dissociating sequencing from execution. Automatization of the sequencing process, i.e. how trained the subjects are in organizing a particular sequence, may account for the variation between the different types of four-item sequences observed in the present study: the 20 Hz modulation increased from overlearned, genuinely lingual words to underautomatized, arbitrary gesture strings, with unfamiliar pseudowords and consonant strings lacking syllabic structure between these extremes. This idea is compatible with EEG data showing that explicit training of a finger movement sequence was accompanied by decreasing modulation in the 10 Hz range (Zhuang *et al.*, 1997). The lack of a simple relationship between muscular activity or duration of 20 Hz suppression with the amount of 20 Hz modulation does not exclude them as explanatory factors but underscores the idea that the modulation of motor cortical 20 Hz rhythm is determined by multiple factors ranging from basic-level to high-level contributions, like cognitive effort related to movement sequencing.

Modulation of 20 Hz Activity in the Hand Area: Speech versus Non-speech Mouth Movements

In the present data set, the 20 Hz reactivity in the hand area during mouth movements was weaker than in earlier reports (Salmelin *et al.*, 2000; Salmelin and Sams, 2002). Nevertheless, the suppression-to-rebound change of 20 Hz activity in the hand area was stronger for non-speech than speech mouth movements regardless of string length. There was a stepwise difference between non-speech gesture strings and all sequential speech tasks. In principle, general effort associated with newly learned symbol-to-gesture mapping could explain this pattern but no dissociation was detected in the face area between isolated speech and non-speech movement tasks. Furthermore, a similar differentiation in the hand area between speech and non-speech mouth movements was detected in an earlier MEG study where no visuomotor transformation was required (Salmelin and Sams, 2002). Indeed, there seems to be a more focal representation for speech than non-speech mouth movements in the human M1 (present data; Salmelin *et al.*, 2000; Salmelin and Sams, 2002) which may be related to specialized neural architecture of the speech production system. However, this effect could also reflect essential association between non-speech mouth movements and hand movements in everyday primate behavior, like eating. A combined representation for mouth and hand movements near the M1 hand area has been demonstrated in monkeys (Graziano *et al.*, 2002).

Conclusions

The present data suggest involvement of the face motor cortex not only in control of orofacial muscle activity but also in cognitive processes, such as visuomotor mapping and movement sequencing. We found that activation of the left face area,

indexed by 20 Hz suppression, preceded that in the right face area at the onset (visuomotor mapping) and offset, similarly for speech and non-speech movements. Otherwise, the pattern of 20 Hz modulation was bilateral and symmetrical. In the face areas, we found no language-specific effect. However, the hand areas showed systematically stronger modulation of 20 Hz activity for non-speech mouth movements, which may reflect either more focal M1 activation specifically for language or importance of mouth and hand coordination in non-speech mouth movements.

Notes

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