Medium-Range Oscillatory Network and the 20-Hz Sensorimotor Induced Potential

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Although synchronously oscillating neuronal assemblies have been the subject of many studies, a clear identification of the spatiotemporal characteristics of a medium-range oscillatory network is still lacking. Herein, we present a method for the extraction of a new waveform, namely the mean induced potential (IP), which allows the identification of the spatiotemporal characteristics of induced EEG responses. The IP calculation was applied to the 20-Hz component of the sensorimotor rhythm in order to obtain a 20-Hz sensorimotor induced potential (20-Hz SIP). The spatiotemporal characteristics of the 20-Hz bursts seen after median nerve stimulation and self-paced finger movements were extracted by means of current source density reconstruction and synchronization analysis. A cortical network including the contralateral primary motor cortex, the supplementary motor area, and the contralateral supramarginalis gyrus was found to generate the 20-Hz bursts, and the various activated areas were found to be highly synchronized. Our results demonstrate for the first time the existence of a medium-range cortical network in the human sensorimotor region whose constituents oscillate synchronously.

Key Words: human; EEG; 20-Hz sensorimotor rhythm; medium-range cortical network; neural assemblies; synchronization; information transfer.

INTRODUCTION

An increasing body of evidence suggests that induced EEG power increases in the gamma range (30–80 Hz) may be related to sensory integration and object representation (for review see Tallon-Baudry and Bertrand, 1999). Furthermore, phase synchronization between neural groups oscillating in the same frequency range might be the neural mechanism underlying large-scale integration within the human brain (for review see Varela et al., 2001). Synchronous oscillations should allow information transfer between neuronal groups within a cortical area or between different cortical areas, both at the same hierarchical level and across different levels of organization.

This framework of EEG interpretation has been recently extended to include cortical rhythms at other frequency bands, especially in the alpha band (8–13 Hz) (Nunez et al., 2001). Cortical rhythms are seen as a combination of local and global brain dynamic processes, and the relative contribution to the EEG dynamic can vary with brain state and frequency band. The best examples of globally dominated states are anesthesia, coma, and some epileptic phenomena. Confined gamma band power increases might be interpreted as a locally dominated state. Different brain and cognitive states are thus seen as reflecting differences between more locally dominated and more globally dominated dynamics (Nunez et al., 2001).

However, this general framework for the interpretation of EEG/MEG data still needs experimental evidence. To date only indirect evidence has been provided, such as coherence and phase synchronization analysis and mean power calculations, suggesting the presence of multiple sources synchronously oscillating within the human brain. To the knowledge of the authors, the spatial and temporal characteristics of an oscillatory network have not been described yet.

In this study, we approach this topic and try to verify the existence of synchronously oscillating neuronal networks in the sensorimotor cortex. In particular, this framework of analysis has been applied to the beta (15–30 Hz) sensorimotor rhythm which is known to show a strong rebound immediately after nerve stimulation (Salmelin and Hari, 1994), movement execution (Salmelin and Hari, 1994; Pfurtscheller et al., 1996) and imagination (Neuper and Pfurtscheller, 1999).

The beta component of the sensorimotor rhythm, also defined as the 20-Hz rhythm, might originate from discrete neuronal oscillators localized in the primary motor cortex contralateral (MIc) to the movement (Salmelin et al., 1995; Neuper and Pfurtscheller, 1996).
or from the interplay of multiple cortical areas, including the supplementary motor area (SMA) (Kaiser et al., 2000; Stancak et al., 2000) and other areas adjacent to MI (Pfurtscheller et al., 2000). Increased coherence between the primary and supplementary motor cortex in the beta range (Gerloff et al., 1998) supports the idea that multiple areas are involved in the generation of the 20-Hz rhythm, although a description of the dynamics of activation and the level of interaction of the different foci is still lacking. Therefore, the 20-Hz oscillating sensorimotor network seems a plausible and interesting candidate for a medium-range (1–3 cm) network.

The 20-Hz bursts belong to the class of induced EEG responses. According to the nomenclature suggested by Galambos (1992) and reviewed by Tallon-Baudry et al. (1999), evoked responses are EEG activities which appear at the same latency and phase in each single trial, and induced responses are oscillatory bursts whose latency jitters from trial to trial. Thus, induced responses cannot be extracted by classical trial averaging, but they can be identified as average amplitude or power variations with respect to a baseline time interval (for review see Pfurtscheller and Lopes da Silva, 1999; Tallon-Baudry and Bertrand, 1999). On the other hand, the cortical sources of induced responses cannot be modelled from power-transformed data, because the between-sensors phase relationships are lost. Consequently, a method for the extraction of the mean spatiotemporal pattern of EEG induced activity, which preserves the power and phase information is presented and a new quantity, namely the mean spatiotemporal pattern of EEG induced activity, is introduced. This method is applied to the 20-Hz rhythm and the calculation of the 20-Hz sensorimotor induced potential (20-Hz SIP) allows the localization of the neuronal generators of the 20-Hz sensorimotor network and the study of their dynamics of activation.

**METHODS**

**Experimental Set-Up and Recordings**

Six healthy, right-handed volunteers (five men, one woman) aged from 26 to 29, participated in the experiment. All subjects signed informed consent agreements. Five subjects underwent median nerve stimulation experiments, whereas four subjects performed self-paced right index finger movement experiments. The median nerve was stimulated at the right wrist using a constant square wave pulse with a duration of 0.2 ms at an intensity corresponding to the motor threshold of the thumb. Approximately 1000 stimulations were given to each subject with an interval of 2.5 s between trials. In the index finger movement experiment, subjects were asked to perform self-paced index finger extensions every 10–15 s. EEG was recorded using a 32-channel system (Neuroscan) throughout the experimental sessions and scalp potentials (bandpass filtered 0.25–200 Hz; A/D rate 1000 Hz) were recorded from 30 electrodes distributed according to a modified 10–20 system, with a right mastoid electrode as reference. The electrooculogram (EOG) was also recorded to reject trials with contaminated eye movements. Artifact-free trials were baseline corrected and common average referenced; 700 and 350 corrected epochs per subject were stored for further analysis for median nerve stimulation and finger movement experiment, respectively. Electrode 3D coordinates were collected using a Polhemus Fastrak digitizer (Neuroscan) for subsequent integration with MRI data. In a separate session, morphological MRI scans from each subject were collected using a 1.5 T imager (Philips Gyroscan ACS II). The 3-D data set with full head coverage and 1.4 mm³ voxel was acquired using a gradient echo (GRE) sequence.

**Time-Frequency Analysis and Induced Potential Calculation**

Beta oscillations are not phase-locked to the stimulus and belong to the class of induced rhythms that cannot be detected by averaging over single EEG trials. Therefore, time-frequency (TF) representations (Tallon-Baudry et al., 1996; Bertrand et al., 1999) of the instantaneous amplitude of the signal were computed from 4 to 45 Hz and then averaged across trials. This approach provides estimates for the local energy of the signal as a function of time and frequency (see Appendix). A nonparametric sign test (Bertrand et al., 1999) was used to detect oscillatory bursts as emerging form baseline activity. This statistical method compares, for every trial, each post-stimulus TF energy value to its corresponding prestimulus baseline value in the same frequency band. The baseline activity for each trial and each frequency band is defined as the median value of the TF energy in the prestimulus interval ΔB (from −0.5 s to stimulus onset for median nerve stimulation and from −2 s to −1.5 s for self-paced finger movement). A Z score is then computed at each TF points as

\[ Z(t,f) = \frac{(N^- (t,f) - 1/2N)}{1/2N^{1/2}} \]

where \( N^- (t,f) \) is the number of poststimulus TF energy values above the baseline activity and \( N \) is the number of trials. Significant increases and decreases with respect to baseline activity show up as positive and negative Z values, respectively, and tabulated probability values indicate that, for absolute values of \( Z > 3.09 \) we have \( P < 0.001 \). Statistical analysis was performed on each recording electrode and the channels displaying significant increases in the beta range (Z value > 3.09, \( P < 0.001 \)) were selected for further analysis (Fig. 1a). The positive peak in the TF representation of the Z values for each selected channel was identified as the resonance frequency \( f \), as seen by each electrode (Fig. 1a). The
FIG. 1. Diagram showing the pre-processing steps which lead to the IP calculation. (a) Channels displaying significant increase in the frequency band of interest are selected (grey box) and the resonance frequency $f_r$ is defined as the positive peak in the TF representation of the $Z$ values for each selected channel (only two of the selected channels are shown). The most reactive frequency $f_{mr}$ is then identified as the mean resonance frequency averaged across the selected channels. (b) The global amplitude at $f_{mr}$ across the selected channels is calculated for each trial (top) and the time interval $\Delta T$ showing significant ($P < 0.001$) increase in oscillatory response at $f_{mr}$ is calculated (bottom). (c) Only those trials displaying a significant increase in mean global amplitude in $\Delta T$ with respect to the baseline interval $\Delta B$ are taken for further analysis (checked trials 2 and 3). (d) The EEG signals are filtered at $f_{mr}$ and averaged across all the selected channels (grey box); this waveform is taken as an estimate of the occurrence of the oscillatory activity at $f_{mr}$ and it is calculated for each selected trial (trial 2 and 3) (top right). The occurrence of the positive peak in the average filtered signal (red circle) is taken as the time jitter $t_j$ of the oscillatory burst for each selected trial. $t_j$ represents the time point of maximal power in each trial. The EEG in each trial is then realigned to its corresponding $t_j$, which is then set to zero time (not shown in the figure). The pre-processing procedure results in a set of EEG epochs displaying a statistically significant increase in oscillatory activity at $f_{mr}$, realigned in time with respect to the instant of maximal oscillatory response ($t_j$). The IP is then calculated according to Eq. (1).

FIG. 2. (a) Representative 20-Hz SIP from electrode C3, left sensorimotor cortex, in Subject 1 after median nerve stimulation. Zero time corresponds to the time point of maximum increase in 20-Hz bursts $t_j$. The stimulus onset occurs at different latencies before the maximum of the beta burst. (b) Probability distribution of stimulus occurrence. (c and d) TF representations of mean amplitude and PLF, respectively, at the same electrode. Values were calculated across the selected and shifted epochs with significant increase in beta activity (see Methods). (e) Contour map of the instantaneous mean amplitude $A(t)$ at the most reactive frequency $f_{mr}$ at $-6$ ms; the colored patch is data clipped at 80% of the maximum amplitude. (f) Contour map of the 20-Hz SIP at $-6$ ms. Note the “radial” pattern probably produced by a central and a sensorimotor source.

FIG. 3. Individual sources displayed on cortical surfaces obtained from MRI data. Color codes: active sources in the contralateral primary motor cortex (MIc), in red; dorsal precentral region, blue; anterior parietal cortex, green; ipsilateral somatosensory cortex, yellow; superior parietal cortex, purple. (a) Cortical sources for each subject in the stimulation condition. (b) Cortical sources for each subject in the movement condition.
most reactive frequency \( f_{mr} \) in the beta band was then identified as the mean resonance frequency averaged across the selected channels. In order to assess whether the selected channels showed different resonance frequencies, the standard deviation was taken as a measure of the amount of frequency spreading. A large variability (i.e., high standard deviation values) in the peak resonance frequency across the selected channels might imply the presence of multiple oscillatory networks. Once the most reactive frequency \( f_{mr} \) of the oscillatory network was calculated, the next step was to detect the time interval \( \Delta T \), which displayed a significant increase in beta activity. The global amplitude for each trial was defined as the instantaneous amplitude at the most reactive frequency \( f_{mr} \) averaged across the selected channels (Fig. 1b). The sign test previously described was performed on the global amplitude of each trial to calculate the Z values. All time points with Z values greater than 3.09 (\( P < 0.001 \)) defined the time interval \( \Delta T \) with a significant increase in beta band activity (Fig. 1b).

The pattern of the 20-Hz induced activity is not constant across trials, but varies both in maximum amplitude and jitter. In order to restrict our analysis to only those trials displaying clear signs of beta rebound, the global amplitude of each trial was taken as a measure of the presence of a beta band rebound pattern. We then performed a sign test on the single trial global amplitude and only those epochs displaying a significant increase in amplitude (Z > 1.59, \( P < 0.05 \)) in the time range \( \Delta T \) previously calculated with respect to the baseline period \( \Delta B \) were considered for further analysis (Fig. 1c). Once the epochs displaying large beta bursts were selected, we had to cope with the temporal variability in beta activity across trials. We realigned the selected epochs with respect to the instant of maximal beta band response in each selected trial. Since the choice of a fixed channel across trials for the calculation of the maximum beta activity would have biased the phase relationships between sources, we took the EEG signals filtered at \( f_{mr} \) and averaged across all the selected channels as an estimate of the occurrence of the beta activity in each selected trial (Fig. 1d). The positive peak in the average filtered signal was taken as the time jitter \( t_j \) of the beta burst, representing the time point of maximal power in each trial (Fig. 1d). Finally, the selected epochs were realigned with respect to \( t_j \), which was set to zero time. The estimate of \( t_j \) does not depend on a particular recording channel and the phase relationships between channels are not disrupted after realignment. This method assumes that the spatiotemporal pattern of the oscillatory activity under investigation (i.e., the 20-Hz sensorimotor rhythm in this study) is stable across trials, but varies only in amplitude and latency.

The result of these operations was a set of epochs displaying a statistically significant beta band increase realigned in time with respect to \( t_j \) which was then set to the new zero time. These shifted sweeps were then used for the calculation of the induced potential IP. The IP is defined as

\[
IP_k(t, f_{mr}) = \text{Re}(A_k(t, f_{mr}) - b_k(f_{mr})) \cdot e^{i \phi_k(t, f_{mr})},
\]

where \( k \) is the number of channels, \( A_k(t, f_{mr}) \) is the mean instantaneous amplitude, \( b_k(f_{mr}) \) is \( A_k(t, f_{mr}) \) averaged in the baseline time interval \( \Delta B \), and \( \phi_k(t, f_{mr}) \) is the instantaneous phase at the most reactive frequency \( f_{mr} \) (see Appendix). The 20-Hz SIP is then defined as the IP obtained from the selected and shifted epochs at the most reactive frequency \( f_{mr} \) in the beta band. These new waveforms represent the mean spatiotemporal pattern of the 20-Hz bursts (i.e., both their mean instantaneous amplitude and phase are maintained) and were used for further analysis.

In order to quantify the level of interaction between the 20-Hz rhythm with other frequency bands, we computed the TF representations of the instantaneous amplitude and of the phase-locking factor (PLF) (Tallon-Baudry et al., 1996) of the selected and aligned epochs. Statistically significant variations of the mean amplitude with respect to the baseline interval were detected as previously described. Phase ordering was assessed using a Rayleigh test of uniformity of angle (Mardia, 1972). Increases in local energy and/or high PLF values at other frequency bands might indicate coupling between frequencies or might indicate the presence of other global/local oscillatory networks. Moreover, as one of our main objectives was to identify the neuronal network producing the 20-Hz bursts, we performed source reconstruction from the 20-Hz SIP. The IP calculations were performed using Matlab software (The Math Works, Inc.) and the code needed to perform the IP calculation is freely available on request from the corresponding author.

Cortical Current Density Reconstruction

Among the different approaches to the biocurrent inverse problem, the current density reconstruction methods (CDR) provide the most general solutions. Source reconstruction was performed using current density analysis using a minimum norm least square (MNSL) approach (Ilmoniemi, 1991). We preferred a MNSL algorithm to nonlinear methods (Fuchs et al., 1999), because large and multiple cortical areas were expected to be significantly active. Sources were constrained and normally oriented to a surface of about 20000 nodes representing the gray matter, which was segmented from MRI data. An extended source model (Wagner, 2000) with radius of 10 mm was used to model cortical connectivity and suppress focal artifact sources. Realistic three compartment boundary element models (BEM) each consisting of approximately
1000 nodes were used for each subject as the volume conductor model. All steps of current density analysis were performed using Curry software (Curry 4.5, Philips research, Hamburg, Germany).

Regions of interest (ROI) showing high current density strengths were determined by dipping the strength of the sources to a threshold value of 50% of the maximum strength. The coordinates of the center of mass of each cluster were calculated and the time courses of the cortical current density sources within each cluster were averaged to give a mean time course for each activated area. Finally, the coordinates of the center of mass of each cluster were transformed to standard stereotactic space (Talairach and Tournoux, 1988) using Statistical Parametric Mapping software (SPM99, Wellcome Department of Cognitive Neurology, London, UK) to allow comparison across subjects (Friston, 1995). Moreover, in order to characterize the oscillating network, we calculated the instantaneous phase difference and the strength of synchronization S between the mean time courses of all the foci pairs by means of the Hilbert transform (see Appendix).

### RESULTS

#### 20-Hz SIP and TF Analysis

In accordance with published data on EEG and MEG studies (Pfurtscheller, 1981; Salmelin and Hari, 1994), the mean jitter in latency of the beta burst after median nerve stimulation was smaller than after self-paced finger movement: 0.735 ± 0.1 s and 1.451 ± 0.7 s, respectively (mean ± SD, N = 5 and 4, respectively). The most reactive frequency $f_{mr}$ in the stimulation condition was 19 ± 0.4 Hz, 25.2 ± 0.4 Hz, 26.4 ± 0.6 Hz, 20.2 ± 0.5 Hz, and 20.8 ± 0.7 Hz (mean ± SD), for subjects 1, 2, 3, 4, and 6, respectively. In the movement condition, the most reactive frequency $f_{mr}$ was 20.1 ± 0.8 Hz, 17 ± 0.9 Hz, 17.5 ± 0.4 Hz, 19.3 ± 0.3 Hz (mean ± SD), for subjects 1, 2, 4, and 6, respectively. Averaged across subjects, the most reactive frequency $f_{mr}$ was 22.3 ± 3.3 Hz and 18.5 ± 1.5 Hz (mean ± SD) for stimulation and movement experiments, respectively. The number of epochs showing significant increases in beta activity was 20 ± 6% and 70 ± 6% (mean ± SD) for stimulation and movement experiments, respectively. The beta band reacts stronger after movement than after stimulation and this is reflected in the difference in the number of selected epochs for the two experimental conditions. These results (i.e., t, $f_{mr}$, and the selected trials) were then used for the calculation of the mean 20-Hz SIP according to Eq. (1).

Figure 2a shows a representative 20-Hz SIP after nerve stimulation. It is clear that the evoked component phase-locked to the stimulus is absent, as each epoch is realigned with respect to the beta burst time jitter $t$. Since we set zero time at $t$, stimuli occurring at different latencies before the beta band rebound as shown in Fig. 2b. In order to characterize the selected epochs displaying considerably high beta rebounds, we calculated the TF representations of the instantaneous amplitude and of the phase-locking factor (PLF). The
TF representations of the amplitude showed a single peak in the beta band in all subjects and in both conditions. Moreover, TF of the PLF showed significant increases (Rayleigh test, PLF > 0.26, P < 0.001) in all selected channels and did not show peaks other than the one at approximately 20 Hz. The fact that the PLF was high in all the selected channels means that the aligned signals were phase-locked to the new zero time. Therefore, the phase relations between channels were maintained, which also indicates that no further analysis of coherence or synchronization between channels is needed, and source analysis will reveal the 20-Hz network. Figures 2c and 2d show representative TF representation of the amplitude and of the PLF, respectively. These results indicate that the mean amplitude increases were due to oscillations phase-locked to the new zero time. Consequently, no other networks oscillating at different frequencies (e.g., in the alpha band) produced detectable increases in energy on the scalp that were either phase-locked or non-phase-locked to the 20 Hz rhythm.

Figure 2e shows the contour map of the instantaneous amplitude with a peak located over the contralateral sensorimotor cortex which is similar to published results (Pfurtscheller, 1981). In contrast, the contour map of the 20-HZ SIP (Fig. 2f) shows a significantly different spatiotemporal pattern that is most likely produced by radially oriented dipole layers. This oscillatory pattern is not visible if mean amplitude or power calculations are performed and an estimate of the neuronal generators from mean power analysis might be misleading. Thus, in order to localize the cortical generators of the beta bursts it is essential to perform source analysis on the 20-Hz SIP, because it conveys information about both the mean amplitude and phase of the oscillatory activity under investigation at each recording electrode.

**Source Analysis**

Cortically constrained current density reconstruction was performed and regions-of-interest (ROI) were identified by setting a threshold value to 50% of the maximum source strength. The analysis of the beta response after median nerve stimulation indicates that the ROIs cluster in three different cortical regions (Fig. 3a): the controlateral motor strip, the dorsal pre-rolandic region and the anterior parietal cortex. In subject 3 the ipsilateral somatosensory cortex (SII) was also active. The analysis of the beta bursts after index finger movement (Fig. 3b) showed significant sources located in all subjects in the controlateral motor area (MIc) and in the dorsal precentral region. Moreover, the anterior parietal cortex was active in subject 2 and 3. In subject 6, another active area was located in the superior parietal lobule.

The coordinates of the sources of mass of each cluster were transformed to standard stereotaxic space (Talairach and Tournoux, 1988) to allow comparison across subjects. Table 1 shows the stereotaxic coordinates (Talairach and Tournoux, 1988) of the center of mass of the ROI for each subject in the two experimental conditions together with their mean location and mean standard deviations (MSD). The mean locations indicate that the 20 Hz activity after median nerve stimulation and finger movement originate from MIc, SMA, and SMGc (Brodmann area 40). We need to note that a MSD of approximately one cm (Table 1) does not allow the distinction between controlateral, ipsilateral and/or bilateral activation of SMA.

Figure 4a shows a schematic view of the mean locations of the neuronal generators of the 20-Hz rhythm after nerve stimulation superimposed on a cortical surface segmented from MRI scans spatially normalized to Talairach space. The mean time courses of each cluster are comparable in amplitude (Fig. 4b) and the high level of synchronization is shown as the presence of a narrow distribution in the phase difference histogram (Fig. 4c). Figure 5a shows the average locations of the sources of the 20 Hz rhythm after finger movement. Also shown are the mean time courses for each ROI (Fig. 5b) and the histograms of the phase difference and level of synchronization (Fig. 5c). Again, the different average ROIs appear to oscillate synchronously (i.e., narrow distribution in the phase difference histogram) with comparable amplitudes.

**DISCUSSION**

One of the major outcomes of the present study concerns the development of a method for the extraction of
a new quantity, namely the mean induced potential IP. The IP represents the mean spatiotemporal pattern of the brain process under investigation, since it is obtained from the mean instantaneous amplitude and phase in each channel. Therefore, the oscillatory network can be immediately characterized by source reconstruction where both the dynamics of activation and spatial extents of the foci are calculated. No further analysis of coherence or synchronization is needed, as source analysis will reveal all the spatiotemporal features. In this study, we tried to emphasize the importance of direct analysis on the cortical sources rather than on recording channels. Contrary to mean power calculations or coherence analysis, this method allows the localization of the cortical areas generating the induced activity and the extraction of the connectivity patterns between multiple sources. This approach can also be applied to the study of brain responses induced by other sensory stimuli, motor acts, and cognitive tasks such as the human 40-Hz EEG activity induced by coherent visual stimuli (Tallon-Baudry et al., 1996). We expect that the calculation of the IP, the precise localization of the generators of the cortical rhythms, and the characterization of the dynamic of interaction between the different foci should help to better understand the macroscopic EEG oscillations. The application to spontaneous brain rhythms still appears problematic due to the fact that no “virtual” trigger (i.e., \( t \), in our study) can be identified.

In our study, the IP calculation method has been applied to the beta band of the sensorimotor rhythm to obtain the 20-Hz SIP. We demonstrate that the 20-Hz bursts seen after median nerve stimulation and movement execution are generated by multiple cortical areas (Figs. 3–5). The medium-range cortical circuits responsible for 20 Hz oscillatory bursts are very similar across subjects and conditions, mainly comprising three sources located on the motor strip, the dorsal precentral region, and the anterior parietal cortex, respectively. It is worth noting the intersubject variability in source localization which is most pronounced in the motor cortex in the stimulation condition (Fig. 3a and MSD in Table 1). The human motor cortex has been proposed to be divided into cytoarchitecturally and neurochemically distinct anterior and posterior regions within BA 4 (area 4A and 4P, respectively; Geyer et al., 1996) where two distinct representations of the fingers might exist. There is also some evidence suggesting that MI itself might be segregated functionally, so that any attentional modulation may differentially affect distinct subregions and still be strongly subject dependent (Johansen-Berg and Matthews, 2002). EEG recordings might be sensitive to this functional differences and this might account for the large variability occurring especially in the MI sources (i.e., MSD 12.3 mm across subjects). As a matter of fact, MI location in subject 2 and possibly subject 3 might correspond in area 4a, while MI locations in subjects 1, 4, 5, and 6 might correspond to the superficial projection of the activity from area 4p. Furthermore, anatomo-functional variabilities could be enhanced by mislocalizations inherent to source modelling procedures, but the presence of similar source reconstructions in the same subjects (MI source in Fig. 3, subjects 1, 2, and 4) suggests that most of the variability in source localization is due to true differences rather than to mislocalizations in the source modelling procedure. On the other hand, the contribution and relevance of these effect cannot be estimated from our data, but the inter-subject variability can be minimized by averaging corresponding source locations across subjects. Therefore, interpretation of results can be performed only on grand average data. According to the mean locations of the ROIs (Table 1), the generator of the 20-Hz SIP is not restricted to the motor area, as previously suggested on the basis of MEG (Salmelin and Hari, 1994) and EEG (Pfurtscheller et al., 1996) studies, but is rather a complex network composed of MIc, SMA and, in most subjects, SMGc. The discrepant results might be attributed to the different recording techniques and/or to different methods for source estimation. IP contour maps produced by radially oriented cortical patches (e.g., Fig. 1f) were evident in our data. MEG sensors clearly pick up the 20-Hz oscillatory signal generated by the primary motor area within the central sulcus (Salmelin and Hari, 1994), but they would not detect the oscillatory activity produced by areas such as the SMA and SMGc, which mainly produce “radial” patterns. Moreover, equivalent current dipole methods would obscure the presence of simultaneously active multiple foci or alternatively may result in misleading source configuration, and mean power methods would not allow source fitting. Such a cortical network has never been described in either EEG or MEG studies. However, recent fMRI studies showed the activation of multiple cortical areas after median nerve stimulation (Boakye et al., 2000) and self-paced finger movements (Joliot et al., 1999), including also the primary sensorimotor cortex, SMA, and the posterior parietal cortices such as SMG. Comparing studies performed with different experimental techniques may lead to misleading interpretations, but we suggest that the relation between neuronal electrical activity and metabolic requirements could also be tackled by considering the macroscopic induced activity. The integration between both the evoked and induced EEG/MEG activity with fMRI data might shed some light on the brain processes behind complex oscillatory cortical networks.

The sensorimotor network oscillating at approximately 20-Hz resonates whenever a nerve stimulation, motor act or imagination is terminated and the cortical generators comprising this complex medium-range network form short-lasting synchronously oscillating neuronal assemblies. Power increases in the beta band
indicates that neurons in the distinct foci are engaged in common overall activity. The presence of a single reactive frequency in the EEG also suggests that the beta band network is partly independent from other oscillatory networks. On the other hand, results from literature (Pfurtscheller et al., 2000; Stancak et al., 2000) indicate that distinct cortical areas can display increased oscillatory activity in different resonance frequencies after finger movements, but showing different levels of power increase. The discrepant results might be attributed to the selection of the most resonance frequency \( f_{rr} \) in each selected channel. \( f_{rr} \) is calculated from the resonance frequency \( f \), seen by each selected channel, which corresponds to the positive peak in the TF representation of the Z values (please refer to Methods and Fig. 1a). The presence of additional oscillatory responses occurring at different frequencies, but displaying lower power increases would be overshadowed by the most prominent oscillatory network. However, the SD of the resonance frequencies \( f \), across the selected channels is less that 1 Hz in all subjects and conditions, and no additional peaks are present in the TF representations of the mean amplitude and PLF (Figs. 2c and 2d). These two results suggest that the beta band network here described is partly independent from other oscillatory networks, but further work is needed to clearly assess the independence of this rhythm with respect to other frequency bands. In addition to power increase in distinct cortical areas, frequency and phase locking between the multiple cortical generators might also subserve information transfer. High synchronization strengths were shown to occur between the activated areas and this might indicate that neurons in the distinct foci are engaged in common oscillatory activity and that dynamic connections are formed between the network components. On the other hand, the basic mechanisms behind synchronized oscillations cannot, to the knowledge of the authors, be extracted from phase lags. Several models for synchronized networks can be proposed: for example, a single subcortical pacing region might entrain the cortical sources to oscillate with different phase lags corresponding to conduction delays between the pacing and the entrained cortical structures. Alternatively, we could claim that the network could arise from the dynamical coupling between the different cortical areas and that the phase lags could be related to dynamic relationships between the cortical areas comprising the network. Many hypothetical landscapes can be imagined, but information about location and phase lags between sources will not bias the choice of a model for synchronized networks. On the other hand, this is one of the first studies in which phase synchrony (and possibly information transfer) is demonstrated to occur between localized cortical areas in man. Whether power increase in oscillatory activity and phase synchronization between cortical areas are independent or are just two aspects of the same phenomenon is still unclear, as are the mechanisms behind large scale cortical synchronization.

Whether synchronous oscillations are just a by-product of cortical processing or they actually subserve cortical integration (e.g., in the medium-range scale) is still under debate. However, the present work should provide a better understanding of cortical rhythms and in particular of the 20-Hz sensorimotor bursts. As far as functional interpretations are concerned, the 20-Hz rebound may reflect inhibition and a resting or "idling" state of the motor cortex (Salmelin et al., 1995; Pfurtscheller et al., 1996). Alternatively, it might play an active role in movement control, possibly integrating distributed activity between the cortex and the muscle (Feige et al., 2000). The first interpretation is supported by transcranial magnetic stimulation experiments, which showed a decrease in the motor cortex excitability after median nerve stimulation and self-paced finger movements in time instants corresponding to the beta bursts (Chen et al., 1998, 1999). Studies showing a reduction of the 20-Hz rebound after median nerve stimulation during exploratory finger movements (Salenius et al., 1997), object manipulation, and movement imagination tasks (Schnitzler et al., 1997) also support the former hypothesis. The second possibility results from studies showing high coherence in the beta band between cortical neuronal sources located both in M1c and in the premotor area (PMA) synchronized to the electromyogram (EMG) after phasic movements (Feige et al., 2000). While our study does not confirm either of these hypothesis, the fact that Feige et al. found no neuronal sources significantly synchronized to the EMG in SMA and SMGc would suggest that the cortical network presented in this report has a different origin. It might also be possible that only some components of the 20-Hz rhythm, in particular those generated in M1c and PMAc, mediate corticomotor integration. The remaining might set up the network herein described. The 20-Hz oscillatory activity is common to both motor acts and somatosensory stimulations and the cortical circuitry involved spans different hierarchical levels that comprise primary (M1), secondary (SMA), and tertiary (SMG) areas. This would suggest that the 20-Hz sensorimotor rhythm is not related to the first stages of information processing within the brain, but rather to higher-order brain functions. The large variability in amplitude and time jitters during the experimental sessions also supports the hypothesis that this process is influenced by higher-order brain functions such as varying levels of attention, as it would be expected during several repetitive stimulations and motor acts. Moreover, if we interpret synchronously oscillating neuronal assemblies as representing cognitive states (Varela et al., 2001; Nunez et al., 2001), we can reasonably argue that this phenomenon might reflect experi-
ence of movement termination, whether produced by stimulation, by actual execution, or just imagination.

APPENDIX

Continuous Wavelet Transform Using Morlet’s Wavelet

The continuous wavelet transform as described by Tallon-Baudry et al. (1996) and Bertrand et al. (1999) produces a complex function $W(t,f_c)$ that depends both on the central frequency $f_c$ of the Morlet’s wavelet and on time $t$. $W(t,f_c)$ is defined as the convolution of the raw EEG signal with complex Morlet’s wavelets $w_m(t,f_c)$. $w_m(t,f_c)$ have a gaussian shape both in the time domain (standard deviation $\sigma_t$) and in the frequency domain (standard deviation $\sigma_f$) around their central frequency $f_c$ and are defined as $w_m(t,f_c) = a \cdot \exp(t^2/2\sigma_t^2) \cdot \exp(2\pi if_c t)$, with $\sigma_f = 1/2\pi\sigma_t$, and $a = 1/(\pi\sigma_t^2)$. The real and imaginary components of $W(t,f_c)$ are the Hilbert transform of each other (Grossmann et al., 1989) so that the instantaneous amplitude $A(t,f_c)$ and phase $\phi(t,f_c)$ can be unambiguously calculated (Gabor, 1949),

$$W(t,f_c) = s(t,f_c) + i \cdot s_H(t,f_c) = A(t,f_c) \cdot e^{i \cdot \phi(t,f_c)}, \quad (2)$$

where $s(t,f_c)$ is the EEG signal filtered using a Morlet’s wavelet with central frequency $f_c$, and $s_H(t,f_c)$ is the Hilbert transform of $s(t,f_c)$. Thus, the TF representation of the instantaneous amplitude of the signal as used in this study is

$$A(t,f_c) = \frac{1}{N} \sum_{n=1}^{N} |W_n(t,f_c)|, \quad (3)$$

whereas the TF representations of instantaneous power (Tallon-Baudry et al., 1996) is

$$P(t,f_c) = \frac{1}{N} \sum_{n=1}^{N} |W_n(t,f_c)|^2, \quad (4)$$

where $n = 1, \ldots, N$, and $N$ is the number of trials.

These include instantaneous amplitude or power changes due to both EEG activity phase-locked (evoked) and non-phase locked (induced) to the stimulus. The TF representation of the evoked potential (EP) corresponds to amplitude or power changes of the phase locked EEG activity only. The TF representation of the phase-locking factor (Tallon-Baudry et al., 1996) is

$$\text{PLF}(t,f_c) = \left| \frac{1}{N} \sum_{n=1}^{N} W_n(t,f_c) \right|, \quad (5)$$

The phase-locking factor PLF$(t,f)$ ranges from 0 (purely nonphase activity) to 1 (strictly phase-locked activity). Finally, the “phasogram” or TF representations of the instantaneous phase of the signal is

$$\phi(t,f_c) = \tan^{-1} \left[ \frac{1}{N} \sum_{n=1}^{N} W_n(t,f_c) \right]. \quad (6)$$

$A(t,f_{mr})$ and $\phi(t,f_{mr})$ in Eq.(1) (cfr. Methods) are the mean instantaneous amplitude and phase at the most reactive frequency $f_{mr}$.

Phase Difference By Means of the Hilbert Transform

Although formally $A(t)$ and $\phi(t)$ can be obtained by means of the Hilbert transform for an arbitrary signal $s(t)$, they have clear physical meaning only if $s(t)$ is a narrow-band signal, (Boashash, 1992). For example, this is the case, for EEG signals transformed using a continuous wavelet transform with Morlet’s wavelet as mentioned above. Given two narrow-band signal $s_1(t)$ and $s_2(t)$, we can calculate the instantaneous phase difference $\phi_1(t) - \phi_2(t)$ as,

$$\psi_{2,1}(t) = \phi_1(t) - \phi_2(t) = \tan^{-1} \left[ \frac{s_{H,1}(t)s_2(t) - s_1(t)s_{H,2}(t)}{s_1(t)s_2(t) + s_{H,1}(t)s_{H,2}(t)} \right], \quad (7)$$

where $s_{H,1}(t)$ and $s_{H,2}(t)$ are the Hilbert transform of $s_1(t)$ and $s_2(t)$. In this paper, we assessed the strength of synchronization by calculating the first Fourier mode of the distribution,

$$S_{2,1}(t) = \langle \cos(\psi_{1,2}(t)) \rangle^2 + \langle \sin(\psi_{1,2}(t)) \rangle^2, \quad (8)$$

where the brackets denote the average over time; this value varies from 0 to 1. This method was presented by Rosenblum et al. (1996). An alternative method for the calculation of the strength of synchronization and phase difference, which was applied to EEG data analysis, has been presented by Lachaux et al. (1999).

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REFERENCES

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