

Waves of consciousness: ongoing cortical patterns during binocular rivalry

Diego Cosmelli,* Olivier David,¹ Jean-Philippe Lachaux, Jacques Martinerie, Line Garnero, Bernard Renault,* and Francisco Varela²

Cognitive Neuroscience and Brain Imaging Laboratory, CNRS UPR 640, Hôpital de La Salpêtrière, 75651 Paris Cedex 13, France

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We present here ongoing patterns of distributed brain synchronous activity that correlate with the spontaneous flow of perceptual dominance during binocular rivalry. Specific modulation of the magnetoencephalographic (MEG) response evoked during conscious perception of a frequency-tagged stimulus was evidenced throughout rivalry. Estimation of the underlying cortical sources revealed, in addition to strong bilateral striate and extrastriate visual cortex activation, parietal, temporal pole and frontal contributions. Cortical activity was significantly modulated concomitantly to perceptual alternations in visual cortex, medial parietal and left frontal regions. Upon dominance, coactivation of occipital and frontal regions, including anterior cingulate and medial frontal areas, was established. This distributed cortical network, as measured by phase synchrony in the frequency tag band, was dynamically modulated in concert with the perceptual dominance of the tagged stimulus. While the anteroposterior pattern was recurrent through subjects, individual variations in the extension of the network were apparent.

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Introduction

What happens if you see in the same place two different objects, one with each eye? Apparently, there is no way we can interpret such location in space as having a unique meaning and our perception inevitably goes back and forth between both alternatives. This phenomenon, known as binocular rivalry, is paradigmatic among the so-called multistable perception phenomena (Blake, 1989; Leopold and Logothetis, 1999). Binocular rivalry

is particularly interesting because, as in all multistable phenomena, perception changes while the visual stimulation remains the same. This would in principle enable one to reveal the neural processes underlying specifically endogenously driven conscious perception. While the debate on the origins of rivalry is yet inconclusive (Alais and Blake, 2002), it has been suggested that the resolution of the perceptual conflict most likely depends on an interplay of low- and high-level neural processes (see Blake and Logothetis, 2002, for a review).

Several authors have stressed that perception may depend on the coactivation of specific brain regions (Damasio, 1990; Dehaene and Naccache, 2001; Freeman, 1975; Llinas et al., 1998; Singer, 1999; Varela et al., 2001). In this context, it has been proposed that phase synchronization of neural signals could be important for conscious perception by allowing the establishment of dynamical links among distributed neural populations (Engel and Singer, 2001; Rodriguez et al., 1999; Varela et al., 2001). In the particular case of visual perception, the coordinated activation of visual cortex and a parietofrontal network may be essential for conscious availability of a given percept (Crick and Koch, 2003; Dehaene and Naccache, 2001; Mesulam, 1999).

Nevertheless, a dynamical picture of the integration of actual cortical activity during ongoing perception remains to be described. Binocular rivalry offers an ideal experimental condition to assess this question as conscious perception of a given stimulus spontaneously fluctuates *in time*. Demonstrating the concomitant fluctuation of coordinated ongoing activity in distributed cortical areas upon perceptual dominance would be of significant interest to the understanding of the neural mechanisms underlying conscious perception. The magnetoencephalography (MEG) system is particularly well adapted for this type of exploration as it provides full head coverage with a time resolution in the ms range. Although its spatial resolution is limited, recent development in source reconstruction (Baillet et al., 2001; David et al., 2002; Ioannides, 2001; Jensen and Vanni, 2002) has shown that it is possible to estimate cortical activity from electromagnetic scalp data in various experimental setups, including single trials and ongoing activity.

In this paper, we have used a MEG binocular rivalry paradigm to study the neural events underlying the spontaneous emergence into consciousness of a visual stimulus in human beings. The target stimulus (a series of expanding checkerboard rings) possesses an intrinsic frequency to specifically tag MEG signals that correlate

* Corresponding authors. Cognitive Neuroscience and Brain Imaging Laboratory, CNRS UPR 640, Hôpital de La Salpêtrière, 47 Bld de l'Hôpital, 75651 Paris Cedex 13, France. Fax: +33-145862537.

E-mail addresses: diego.cosmelli@chups.jussieu.fr (D. Cosmelli), bernard.renault@chups.jussieu.fr (B. Renault).

¹ Current address: Functional Imaging Laboratory, Wellcome Department of Imaging Neuroscience, 12 Queen Square, London WC1N 3BG, UK.

² Deceased May 2001.

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with its dominance periods. The rival stimulus (a human face) has been chosen to act as a strong suppressor of the target stimulus; it has no intrinsic frequency, therefore controlling for the specificity of the modulation of the activity induced by the tagged stimulus. We have estimated the cortical sources responsive to the frequency tag using an adapted inverse problem framework without averaging MEG signals. To follow the spatiotemporal network dynamics of sources oscillating at the same frequency, we have used phase locking between reconstructed brain signals. We reveal ongoing dynamical patterns of distributed synchronous activation between visual cortex and anterior portions of the brain, particularly anterior cingulate and medial frontal gyrus, that follow the waves of conscious moments.

Materials and methods

Experimental design and MEG recordings

Seven healthy voluntary subjects (six men, one woman; mean age 29.8 years) participated in this study. Neuromagnetic recordings were done in a 151-SQUID sensor CTF MEG (CTF System Inc., Port Coquitlam, BC, Canada) in the MEG Centre, Hôpital de la Salpêtrière, Paris, France. The experimental protocol was approved by the Hôpital de la Salpêtrière ethics committee (CCPPRB). Subjects were exposed to two viewing conditions: a black screen (resting condition) and rival viewing condition. During the rival viewing, one eye saw a series of expanding black and white checkerboard rings (see Scalp MEG data section for details) while the other saw a black and white feminine face of emotionally neutral expression (Fig. 1). Rival viewing condition was obtained by projecting polarized nonfusible images onto a screen situated 85 cm in front of the subject. To separate both images, subjects used polarized MEG-compatible lenses. Stimuli were viewed foveally through a circular aperture of 4° radius. Subjects were instructed to maintain fixation on a dim spot at the center of the aperture. For each subject, luminance was adjusted for each stimulus independently until a full and comfortable perceptual

oscillation was achieved as indicated by his/her verbal report. The face was projected into the dominant eye to favor a good suppression of the expanding rings. We extensively trained all subjects (totaling a minimum of 2 h of rival viewing per subject) previous to actual MEG recording and registered the subjects' naïve verbal descriptions about the experience. Subjects reported smooth and consistent transitions from one image to the other. They were instructed to indicate by pressing one of two buttons when full dominance of each image was achieved. Subjects were instructed not to indicate mixed periods of dominance. Each viewing condition lasted 2 min and was followed by a pause of 40 s. MEG signals were acquired continuously at 1250 Hz and band passed between 0 and 200 Hz. Horizontal and vertical electrooculogram (EOG) was recorded in parallel. The two-condition block was repeated several times to obtain long segments of steady-state data. Throughout the seven subjects, an average of 89.4 s of continuous eye movement-free and artifact-free data was obtained with a maximum of 100 s and a minimum of 70 s. Following Leopold and Logothetis (1999), normalized dominance phases distributions were adjusted to a gamma distribution: $f(x) = \{1/[b\Gamma(c)]\} * \{x/b\}^{c-1} * e^{-(x/b)}$, where b is the scale parameter, c is the shape parameter and Γ is the gamma function (Statistica 6.0, StatSoft Inc, 1994–2004). The expanding rings dominated perception for an average of 2.3 s with a standard deviation of 1.3 s ($b = 0.0966$, $c = 4.193$). The face dominated an average of 2.02 s with a standard deviation of 1.46 s ($b = 0.0828$, $c = 4.282$).

Overview of MEG data analysis procedure

We present here a short overview of the procedures that will be detailed in the following paragraphs. Data analysis followed three main steps. (i) Scalp: continuous scalp data are subject to spectral analysis to determine the presence of the frequency tag. Specificity of the frequency tag amplitude for the dominance of the tagged stimulus is then assessed respect to the subjects button press. (ii) Cortical source estimation: continuous segments of scalp data filtered around the frequency tag are treated as ongoing steady-state responses of one underlying process (the perceptual

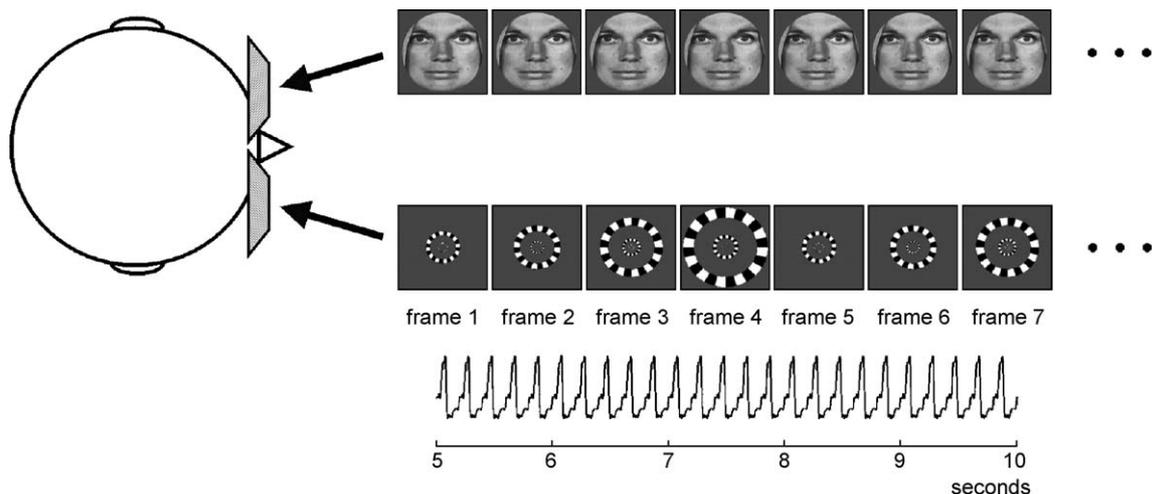


Fig. 1. Experimental setup of the binocular rivalry paradigm. Subjects viewed through MEG-compatible polarized lenses the conflicting images presented with two different orthogonally polarized projectors as indicated in the top part of the figure. The face remained unchanged through the successive video frames of the first projector. In contrast, the expanding checkerboard rings were constructed using different successive frames (see text for details). The lower panel presents 5 s of the time course of a diode placed at the output of the second projector showing the 5-Hz frequency tag.

alternation or the resting state). Successive epochs of 1 s are used to estimate via a focal solution of a distributed model the contribution of cortical sources to the scalp signal. A unique source space that is used to adjust the entire segment of continuous scalp data is then obtained by determining the recurrence of sources throughout the 1-s epochs (Fig. 2 provides a schematic description of this approach). (iii) Dynamical analysis: reconstructed cortical time courses are used for further phase synchrony analysis to determine the spatiotemporal evolution of evoked synchronous brain networks.

Frequency tagging

To guide the source estimation algorithm (see below) and reveal the cortical network correlated to conscious perception, we have used a frequency tagging approach (Brown and Norcia, 1997; Cobb et al., 1967; Lansing, 1964; Tononi et al., 1998). The principle of this approach consists in using an intrinsic frequency in a given stimulus that can be followed in the subsequent evoked brain response. In our experiment, the expanding checkerboard rings extended radially from 0 to 4° of visual eccentricity, as in an optical flow. Because of the retinotopic organization along the calcarine and primary visual cortex, the expanding checkerboard

rings will produce a concomitant posterior–anterior wave of activation. The spanning velocity can thus be used as a frequency tag (Wandell, 1999), which in our experiment was fixed at 5 Hz. To overcome the limitation imposed by the refresh rate of the projector, we used three concentric checkerboard rings (see Fig. 1). Additionally, the diameter of individual checkerboard rings followed the relation given in Wandell (1999, p. 155). This way it is possible to induce a consistent stimulation of visual cortex despite changes in receptive field properties with eccentricity. A diode placed at the output of the projector controlled the rate of presentation (Fig. 1).

Scalp MEG data

To determine the presence of the frequency tag during the binocular rivalry experience, continuous segments of scalp data filtered between 1 and 45 Hz were analyzed using a fast Fourier transform (FFT) (MATLAB 6.5, The MathWorks, Inc.). To evaluate the specificity of the frequency tag for conscious perception of the expanding checkerboard rings during rivalry, we then followed the evolution of the 5-Hz tag amplitude in time. To this extent, we first selected the MEG scalp sensor with the best sensitivity to the 5-Hz tag for each subject. It was defined as the sensor showing the

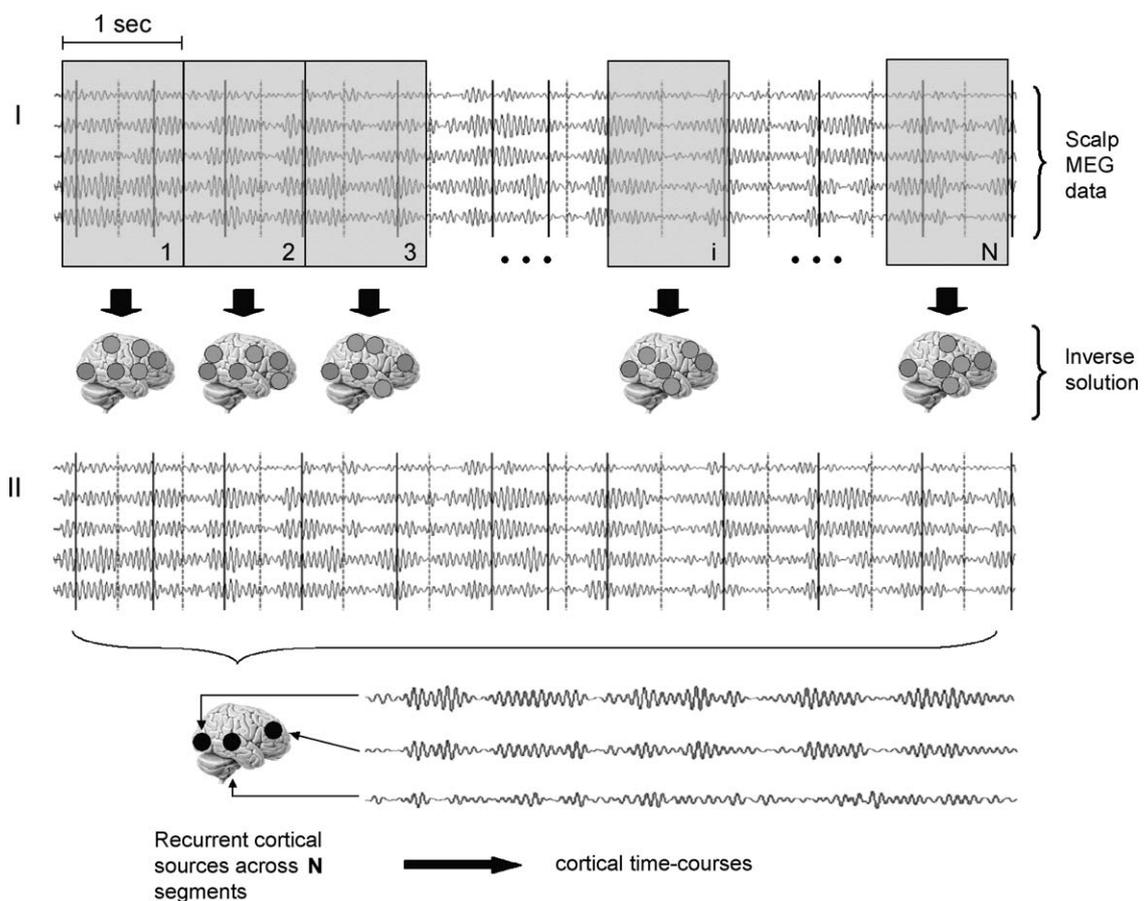


Fig. 2. Schematic presentation of the methodological approach followed in this study. (I) Continuous scalp MEG data of either viewing condition is segmented into 1-s successive epochs (1, 2, 3, . . . , N). Broken and unbroken vertical lines indicate dominance of face and rings, respectively. Each epoch is subject to the inverse estimation of cortical sources using a focal solution of a distributed model. (II) Only those sources that recur significantly throughout the N epochs (as compared to surrogate data) are kept and used to adjust the entire scalp-viewing period. The cortical time courses are then used for further dynamical analysis.

highest ratio of 5 Hz peak amplitude of the power spectra to the average amplitude around it in the 3- to 7-Hz band. We then evaluated the average amplitude of the selected sensors in 500-ms time windows centered on the button presses signaling full perceptual dominance of the rings and of the face, for each subject individually, and across subjects.

MEG source estimation

The inverse problem approach used in this study is composed of two main steps (see Fig. 2 for a schematic presentation). Data was filtered between 3 and 7 Hz before inverse estimation. Successive 1-s epochs of continuous scalp data, recorded during the different viewing conditions, are considered individually and the corresponding active cortical source space for each epoch is estimated using a focalization of a cortically distributed inverse solution (David et al., 2002). A unique source space is defined as the ensemble of sources that show significant recurrence across the successive epochs (David et al., 2003). A null distribution of source recurrence is constructed using surrogate data as described in detail elsewhere (David et al., 2003). The unique source space is then used to compute the time course of the entire data segment using a minimum norm source estimate. To obtain realistic extensions of locally coherent brain activity (Nunez and Silberstein, 2000) and to regroup clusters of correlated sources we apply an expansion algorithm using the recurrent source space as seeds (David and Garnero, 2002). We thus explain the scalp energy of the steady-state condition (the ongoing perceptual alternation or the ongoing rest state) by a source space composed of those brain sources that are recurrent in cortical location *with no restrictions on the temporal sequence of their activation*. This approach explicitly takes into consideration the variable dynamics of the perceptual transitions in binocular rivalry and avoids any averaging procedures. Sources are then labeled according to standard morphological landmarks (Duvernoy, 1999).

Dynamical analysis

As a measure of dynamical interaction among sources oscillating in the same frequency band, we have quantified phase locking between reconstructed brain signals. To obtain the instantaneous phases ϕ of the neural signals, we have used the Hilbert transform approach (Le Van Quyen et al., 2001; Tass et al., 1998). An index of phase synchrony (Lachaux et al., 2000) ρ quantifying the dispersion of the difference of instantaneous phases is then computed every 50 ms for each source pair on a sliding time window (1-s duration, i.e., five oscillations at 5 Hz). ρ values are comprised between 0 and 1, and increase with the strength of the phase locking. The square of the envelope obtained from the absolute value of the Hilbert transform provides us also with the instantaneous power emission P , which reflects the strength of local synchronization.

We are interested, a priori, in synchronous activity that shows a certain stability in time. Furthermore, our experimental protocol does not provide a high number of independent events (trials) that can be used to estimate the stability of phase relations across them as in traditional visual presentation protocols. We have therefore proceeded in a different way by taking into account the temporal extension of the signals. We define a first threshold (th_1) for a $P < 0.01$ by generating $K = 99$ surrogate ρ (ρ^s) time courses from independent Gaussian noises with the same length and filtering as

the original signal: $th_1 = \max[\rho^s_1, \dots, \rho^s_K]$. Over these K realizations, the maximum percentage of time that surrogate ρ^s reaches th_1 defines a temporal threshold (th_2). If the synchrony value of a given pair of brain signals is above th_1 longer than th_2 , it is considered significant.

To reveal the cortical evoked synchronous networks that correlate with the perceptual dominance of the expanding rings, we calculated the normalized cross-correlation (CC) at lag = 0 between all ρ time courses and the 5-Hz envelope of the MEG scalp sensor with the best tag sensitivity. CC was then thresholded for each source pair at a value of CC^s which was determined using surrogate data of type FT1 (Palus and Hoyer, 1998) that realize the null hypothesis of two linear stochastic processes asynchronously oscillating with the same frequencies (power spectra) as the original time series under study. We set the threshold to $P < 0.05$ by generating 19 FT1 surrogate ρ time courses for each source pair and estimating the CC^s with the corresponding 5-Hz envelope. Only those ρ time courses with higher CC to the 5-Hz envelope than the maximum of their surrogate distribution are considered.

Results

Scalp MEG and frequency tagging

Fig. 3A shows the average spectra over all subjects and all scalp sensors for both resting and rival viewing conditions. Apart from the nonspecific α component, a clear peak at the tag's frequency is evident only in the rival viewing condition. Likewise, the rival condition shows small harmonics at 15 and 20 Hz. We then studied the amplitude time series of the 5-Hz tag to evaluate its specificity for conscious perception of the expanding checkerboard rings during rivalry. As described in Materials and methods, we first selected the MEG scalp sensor with the best sensitivity to the 5-Hz tag as the sensor showing the highest ratio of 5 Hz peak amplitude of the power spectra to the average amplitude around it, in the 3- to 7-Hz band. For the seven subjects (S1–S7), ratios were S1: 34.1; S2: 14.9; S3: 16.1; S4: 14.7; S5: 14.1; S6: 9.0; S7: 22.9; mean = 17.97, and the selected sensors were consistently occipital. Average amplitude of these sensors upon rings and face dominance is presented in Fig. 3B for each subject and across subjects. All subjects presented higher amplitude during rings perception than during face perception (Mann–Whitney U test for independent samples: $P < 0.025$). The mean difference across subjects was also significant (Wilcoxon test for paired samples: $P < 0.025$). Nevertheless, the difference in the ratios presented above and the average amplitudes seen in Fig. 3B suggest a differential sensitivity to the frequency tag among subjects. Fig. 3C shows the ongoing modulation of the frequency tag for one subject during binocular rivalry. It can be seen that the modulation of the frequency tag shows a strong correlation to the subject's response to the perceptual dominance of expanding rings. These results are in accordance with previous work (Brown and Norcia, 1997; Cobb et al., 1967; Lansing, 1964; Tononi et al., 1998), which show that during binocular rivalry, the evoked brain response to a frequency tag is consistently modulated throughout perceptual alternations.

Anatomical localization

The strong ongoing modulation of the MEG scalp response suggests that estimating the underlying cortical sources in the

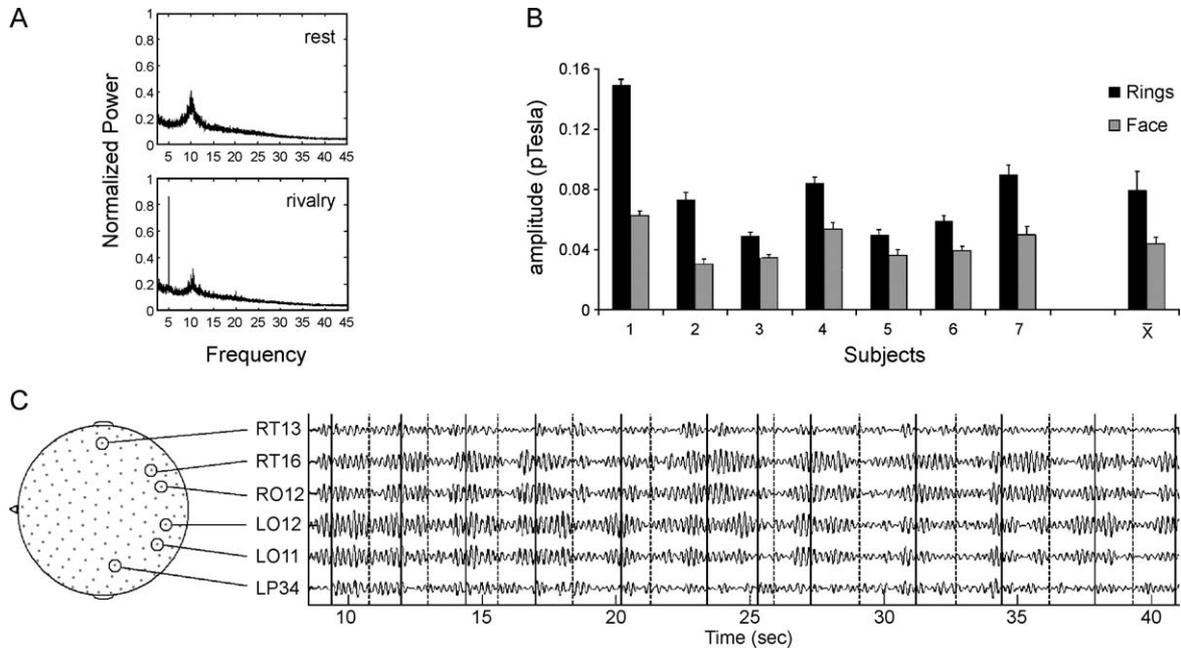


Fig. 3. Specificity of the frequency tag for the perceptual state. (A) Average scalp spectra for both resting and rival viewing conditions showing the sharp peak at 5 Hz. Frequency is plotted against normalized power. (B) Mean amplitude during rings (black bars) and face (gray bars) perception of the MEG sensor with the best sensitivity to the tag, for each subject (S1–S7), and across subjects (X). Error bars indicate 1 SEM. (C) Time course of six MEG sensors filtered in the 3- to 7-Hz band for S1. Position of the sensors is indicated on the left diagram. Dotted lines indicate subject's answer to face perception; continuous lines indicate expanding rings perception.

frequency tag band could reveal brain regions whose activity is specifically modulated during conscious perception of the expanding rings. To do so, we localized active brain regions in the tagging frequency band (3–7 Hz), as described in Materials and methods. Table 1A presents the localization results obtained throughout the entire rival viewing period with respect to the resting condition across all subjects. In accordance with the visual nature of the task, the strongest activation was systematically observed in medial occipital cortex, particularly the calcarine sulcus and lingual gyrus. Moreover, strong activity in the lateral occipitotemporal junction (MT) was also evidenced. Activity in bilateral superior parietal gyrus and left precuneus was likewise detected as well as in the temporal pole. Interestingly, several frontal areas were revealed: posterior parts of the left superior and inferior frontal gyri, bilateral anterior cingulate cortex and adjacent medial aspect of the superior frontal gyrus, and orbitofrontal cortex.

We then evaluated which sources among those detected showed significantly stronger activation during the subject's perception of the tagged stimulus. To do so, we followed a similar procedure to that used on the scalp MEG sensors (Frequency tagging section) by evaluating for all sources the amplitude upon the subjects' indication of alternative percepts. This analysis revealed an ensemble of regions suggesting a coordinated activation of occipital, parietal and frontal regions upon perceptual dominance (Table 1B). Bilateral medial occipital cortex, lateral occipitotemporal junction, precuneus and the posterior part of the left superior and inferior frontal gyri were significantly more active (Mann–Whitney U test for independent samples, $P < 0.01$) during periods of conscious perception of the frequency tagged stimulus. No regions showed stronger activation during suppression periods.

Brain synchrony and perception

It has been extensively argued that perceptual integration may rely on a coordinated network of temporally coherent brain activity (Edelman and Tononi, 2000; Engel and Singer, 2001; Rodriguez et al., 1999; Singer, 1999; Varela et al., 2001). Accordingly, the results presented in Table 1B show that the modulation of brain activity during perceptual dominance may implicate distributed brain regions. We therefore hypothesized that during conscious perception of the 5-Hz rings, synchronous activation in this frequency band should rise and fall in concert with perceptual dominance. Fig. 4 shows the time course of significant phase synchronous activity between brain sources (see Materials and methods for definition) centered on the response for rings perception, averaged across subjects and dominance periods. A consistent correlation between the time course of the synchronization of the cortical network and alternations in conscious perception is evident. As expected, the time course of the evoked synchronous activation tightly correlates with the envelope of the 5-Hz scalp response. Thus, the frequency tag revealed a specific coactivated cortical network that was endogenously modulated throughout the successive waves of conscious perception during binocular rivalry.

To analyze the spatiotemporal dynamics of the specific cortical networks evoked by the tagged stimulus during conscious perception, we followed the ongoing pattern of synchronous brain activity throughout a series of perceptual transitions. Fig. 5 shows this evolution for one subject (S2). It is possible to see how the average cortical synchrony in the tag's frequency band follows tightly the perceptual alternation throughout the rival viewing. When a series of individual dominance periods are analyzed, a dynamical buildup of the evoked synchronous brain network is

Table 1

Cortical landmark	z score	
	LH	RH
<i>(A)</i>		
Calcarine sulcus/lingual gyrus	7.2	11.6
Anterior fusiform gyrus	2.7	–
Lateral occipitotemporal junction	5.3	3.7
Temporal pole	2.3	–
Superior parietal gyrus lateral aspect/intraparietal sulcus	2.0	2.8
Superior parietal gyrus medial aspect (precuneus)	2.4	–
Subparietal sulcus/precuneus/marginal cingulate	2.3	–
Anterior cingulate gyrus/cingulate sulcus/superior frontal gyrus medial aspect	2.6	4.5
Superior and inferior frontal gyrus posterior part/precentral sulcus and gyrus inferior part	3.2	–
Orbitofrontal cortex	3.2	2.7
<i>(B)</i>		
Calcarine sulcus/lingual gyrus	7.2	11.6
Lateral occipitotemporal junction	5.3	3.7
Superior parietal gyrus medial aspect (precuneus)	2.4	–
Superior and inferior frontal gyrus posterior part/precentral sulcus and gyrus inferior part	3.2	–

(A) Anatomical localization: average results over all subjects is shown for visual rivalry for all cortical landmarks detected. Data are represented in standard deviations from the mean energy in the resting condition (*z* score). Only regions that present a *z* score above 2 are shown. (B) Brain regions that show significantly stronger amplitude ($P < 0.01$) during expanding rings perception than during face perception are kept.

apparent. At the beginning of each transition, very few synchronous pairs are evident (first column of snapshots). As dominance develops, the occipital pole shows an increase in local synchrony involving primary visual cortex and more dorsal occipital areas. Long-range synchronous activation is then established between the occipital regions and more frontal areas, including mainly medial frontal regions. This pattern of occipitofrontal coactivation is maintained for several moments (1–2 s) and coincides with the full dominance of the tagged expanding checkerboard rings. As suppression begins, long-range synchronous activation falls apart leaving coactive areas in the occipital pole, and in some cases, infero-temporal regions up to the temporal pole. During full suppression, very few synchronous regions are left and brain patterns returns to the pre-transition situation.

To better describe the evoked brain network that is coactive during the conscious perception of the expanding rings, it is necessary to be able to select specifically the synchronous sources that correlate with dominance throughout the whole rival viewing. Since the scalp 5-Hz envelope amplitude shows a tight correlation with the subjective state (Figs. 3B, C and 4), we chose to use it as a ‘perception function’. Fig. 6 presents the resulting cortical networks for all seven subjects, whose synchronous activation correlates with the 5-Hz envelope of the MEG scalp sensor with the best sensitivity to the frequency tag ($H_0 = FT1: P < 0.05$, see Materials and methods).

Different network distributions are evident throughout the seven subjects. S1 presents the most dense network, strongly concentrated in the occipital pole with coactive regions lying mostly dorsal (inferior parietal, lateral occipital and middle temporal) and frontal to the visual cortex. The network is bilaterally distributed and shows consistent anteroposterior coactive regions. S2 presents a sparser network yet bilateral striate and extrastriate coactivation is evidenced as well as occipitofrontal links. A similar pattern is presented by S4 although anteroposterior synchronous links tend to be lateralized towards the left hemisphere. The bilateral pattern of synchronous activation in visual striate and extrastriate regions is preserved. S3 and S5 show the sparsest networks with little occipital pole local coactivation. Nevertheless, the anteroposterior pattern seems preserved involving mostly posterior infero-temporal and inferior medial frontal regions. S6 shows a less well-organized network, distributed bilaterally but without a consistent organization. S7 shows a clear occipital network reaching into the inferior parietal regions and inferior and middle temporal cortices with a strong right hemisphere lateralization. The synchronous activation of medial frontal cortex and posterior regions is preserved. These results show that, despite individual differences, a network that comprises distributed brain regions is established during conscious perception. In particular, the occipitofrontal (mostly medial frontal) interactions are recurrent throughout subjects.

It is interesting to note that subjects that present a stronger signal during the perceptual dominance of the frequency-tagged stimulus (as indicated by the height of the black bars in Fig. 3) show a more dense network. Thus, S1 and S7 show a denser occipitoparietal and dorsolateral network that reaches into inferior temporal zones and extends into central and frontal regions. Conversely, S3 and S5 show sparse networks of cortical synchronous activation, mainly occipitofrontal, with little dorso-parietal contribution.

Discussion and conclusions

The present work inscribes itself in the line of preceding studies that have made use of a frequency tagging approach to explore brain responses during conscious perception in a binocular rivalry paradigm (Brown and Norcia, 1997; Cobb et al., 1967; Lansing, 1964; Srinivasan et al., 1999; Tononi et al., 1998). We have presented here two main extensions to previous reports by working at the cortical level with high temporal resolution and by revealing the evolution of the underlying cortical networks under non-averaged conditions. In the following sections, we discuss some methodological issues raised by this approach as well as the main results of this study.

Source localization framework

To estimate the underlying cortical sources, we have used the inverse problem method described in David and Garnero (2002) and David et al. (2002, 2003) because it provides a convenient approach when averaging is not possible. Indeed, given the ongoing, variable nature of perceptual alternations in binocular rivalry, such procedure could destroy potentially relevant information. On the other hand, considering this perceptual phenomenon as simply recurrent is only acknowledging the most basic observable structure of the experience of visual rivalry: perception

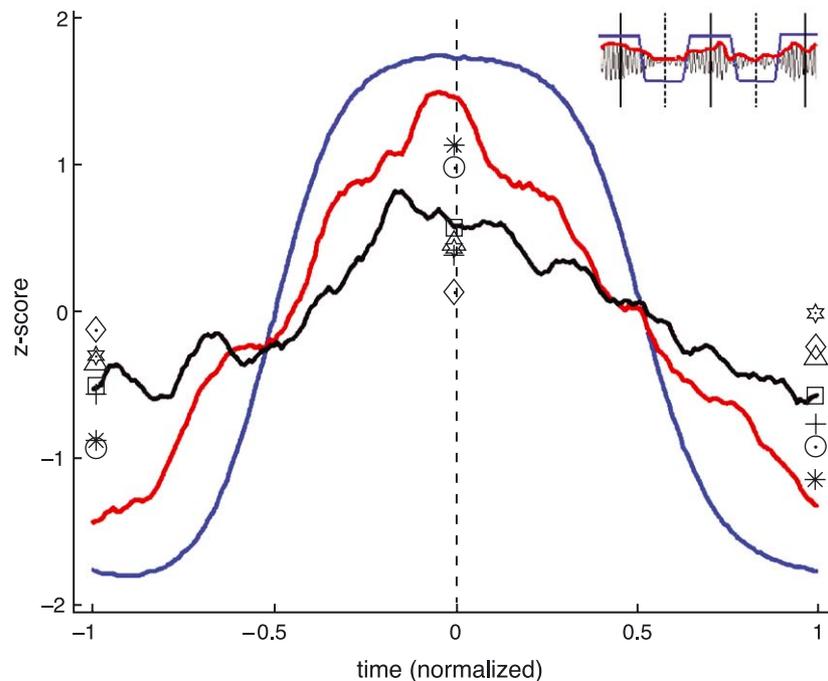


Fig. 4. Overall cortical synchrony and conscious perception: average around the answer ($t = 0$) indicating full dominance of the expanding checkerboard rings of the response function (blue line), scalp sensor with the best tag sensitivity 5 Hz envelope (red line) and synchrony (black line) over all seven subjects. Inset shows detail on the construction of the response function and 5-Hz envelope. Average z score values are shown. Individual values for synchrony are indicated by the different symbols lined onto the subjects' indication for face perception and onto $t = 0$. Time is normalized respect to the previous (-1) and subsequent ($+1$) indication of face dominance.

alternates back and forth, albeit unpredictably. If one considers that relevant activity will be recurrent through time, without restricting its occurrence to a given temporal delay, it is possible to define significant activity in a more natural way. We have applied this criterion by estimating from successive time windows a focal inverse solution on a single trial basis (David et al., 2002). A unique source space, recurrent throughout the successive time windows (see Fig. 2), is then recovered by comparison with adapted surrogate data (David et al., 2003).

The use of a cortical mesh to model the source space presents nevertheless an important shortcoming. It neglects the contribution of noncortical brain nuclei that are bound to play an important role in visual perception. It has been reported, for instance, that the pulvinar shows deactivation during perceptual reversion in multistable perception (Kleinschmidt et al., 1998). Nevertheless, given the nature of the signal to which the MEG is sensitive (Hämäläinen et al., 1993), we believe the distributed cortical model provides an adequate estimation of the brain contribution to the scalp neuro-magnetic signal.

However sophisticated the approach to determining cortical contributions from scalp MEG or EEG signals, the inverse problem in electromagnetism is inevitably ill posed and solutions are always estimations given a set of priors (Hämäläinen et al., 1993). It is important therefore to take the obtained anatomical localizations with caution. In this work, we have used a series of expanding checkerboard rings that produce a concomitant evoked brain response at the spanning frequency (see Scalp MEG data section and Fig. 1). The rationale for the choice of this stimulus is twofold: on the one hand, the frequency tag provides a specific frequency band therefore constraining the inverse estimation; on the other, the expanding checkerboard rings produce brain activation patterns

that have been explored in fMRI protocols thus providing a source of comparison and possible validation (Tootell et al., 1995, 1997; Wandell, 1999). Given the moving nature of this visual stimulus, we expected to find activation in the lateral occipitotemporal junction (putative MT), in addition to striate cortex. Indeed, the strongest activation was observed in these two cortical regions (see Table 1). More dorsal contributions along the parietal cortex including the precuneus, expected given the optical flow-type stimulus (Culham et al., 1998; de Jong et al., 1994), were also detected in our approach (Table 1). Medial frontal regions have likewise been shown active during movement perception (Zeki et al., 1993). We believe therefore that the regional specificity of our method is in good accordance with previous reports revealing a plausible distribution of brain areas. We discuss in more detail the anatomical structures in Cortical contributions and binocular rivalry section.

Frequency tagging

Frequency tagging is an experimental manipulation that enables one to reveal the extension of a certain cortical network and can thus prove very powerful in the functional exploration of the brain. In particular, its use in the study of human binocular rivalry goes back some time. In 1964, Lansing showed a flickering pattern to one eye and a static nonfusible pattern to the other. The flickering pattern produced a rhythmic response of the same frequency on the EEG recorded from two midline occipitoparietal electrodes. In this way, the effect of the rival non-flickering stimulus on the cerebral response could be studied. He observed that upon the onset of the rival non-flickering stimulus, the amplitude of the oscillatory response (as seen through an online filter) decreased dramatically

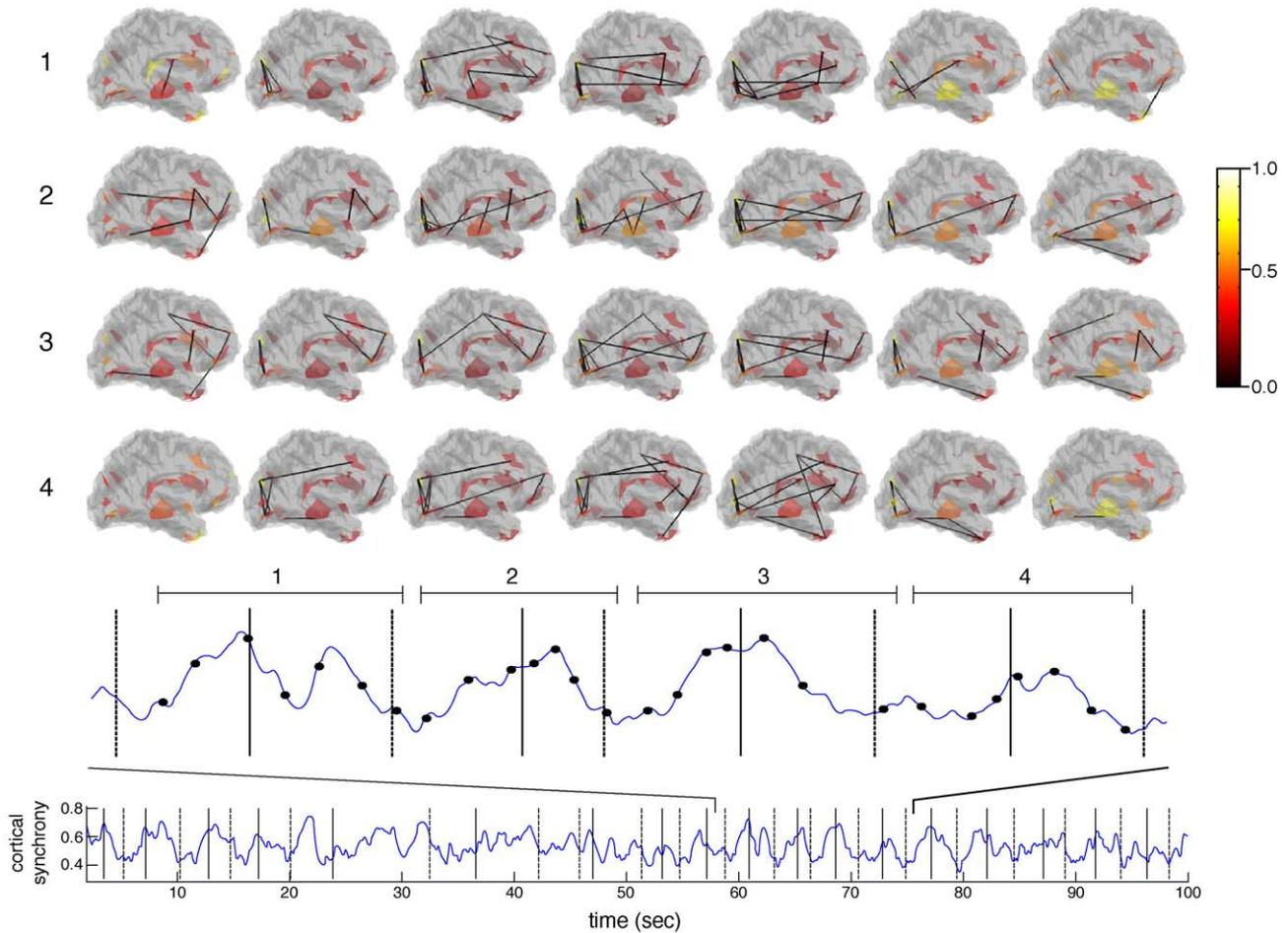


Fig. 5. Dynamic cortical patterns during conscious perception in binocular rivalry: the figure shows a series of four perceptual moments (labeled 1 through 4) during binocular rivalry in subject 2. The upper part of the figure shows the sagittal view of the evolving cortical network in successive snapshots. Color codes for sources' energy (normalized to the maximum) according to the color scale on the left. Black lines link brain regions that reach significance at the moments indicated by the black dots on the blue curve just below. The latter is a detail of the time course of average synchrony shown in the lower part. Vertical black continuous and gray dotted lines are the subject's indication of full perceptual dominance of the expanding rings or the face, respectively.

during the period of suppression that followed (as indicated by the subject's response) and only returned to the pre-rivalry baseline when suppression was over. In 1967, Cobb et al. reported the decrease of cerebral potentials evoked by the pattern reversal of a square grating during suppression phases in rivalry. More recently, Brown and Norcia (1997) described real-time following of visual evoked potentials using an adaptive filter during rivalry. They were able to sort periods of dominance and suppression based on the EEG response to two reversing patterns with two different reversal frequencies. Finally, using an approach based on orthogonal gratings with different flickering frequencies, Tononi et al. (1998) and Srinivasan et al. (1999) studied coherence of neuro-magnetic signals during rivalry. They found that both power emission and coherence between distant electrodes, at the flickering frequency of the corresponding pattern, were enhanced during the periods in which it was dominant. Our work is in the line of these studies but extends the use of this approach in two main aspects. First, we have used the frequency tag to guide the inverse estimation of underlying cortical sources, thus providing access to actual brain structures that are driven by the tagged stimulus. This way the modulation of brain activity can be related to cortical regions with distinct functional properties. Furthermore, this esti-

mation is done while respecting the inherent temporal variability of the experience of binocular rivalry. Secondly, we have performed a phase synchrony analysis between the non-averaged time courses of the estimated cortical sources. This provides insight into the ongoing temporality of the modulation of distributed brain activity throughout successive dominance and suppression periods. As can be seen in Fig. 4 and specially in Fig. 5, the development of a dominance period appears as an extended dynamical process involving the propagation of the evoked activity throughout a distributed brain network beginning in the occipital pole and extending into more frontal regions.

An important distinction is due regarding the above discussion. Because one is interested in the evolution of activity evoked by a tagged stimulus, a feed-forward network is more likely to be detected. It has been proposed that recurrent (reentrant) activation may be fundamental for the actual perceptual conscious experience (Damasio, 1990; Edelman and Tononi, 2000; Lamme, 2003; Varela, 1995). Following the evolution of the evoked network does not provide direct evidence of such reentrant activity. Nevertheless, previous studies using a similar approach (Srinivasan et al., 1999) have suggested that at least part of distant coactivation is due to active processes and cannot be accounted for uniquely on the

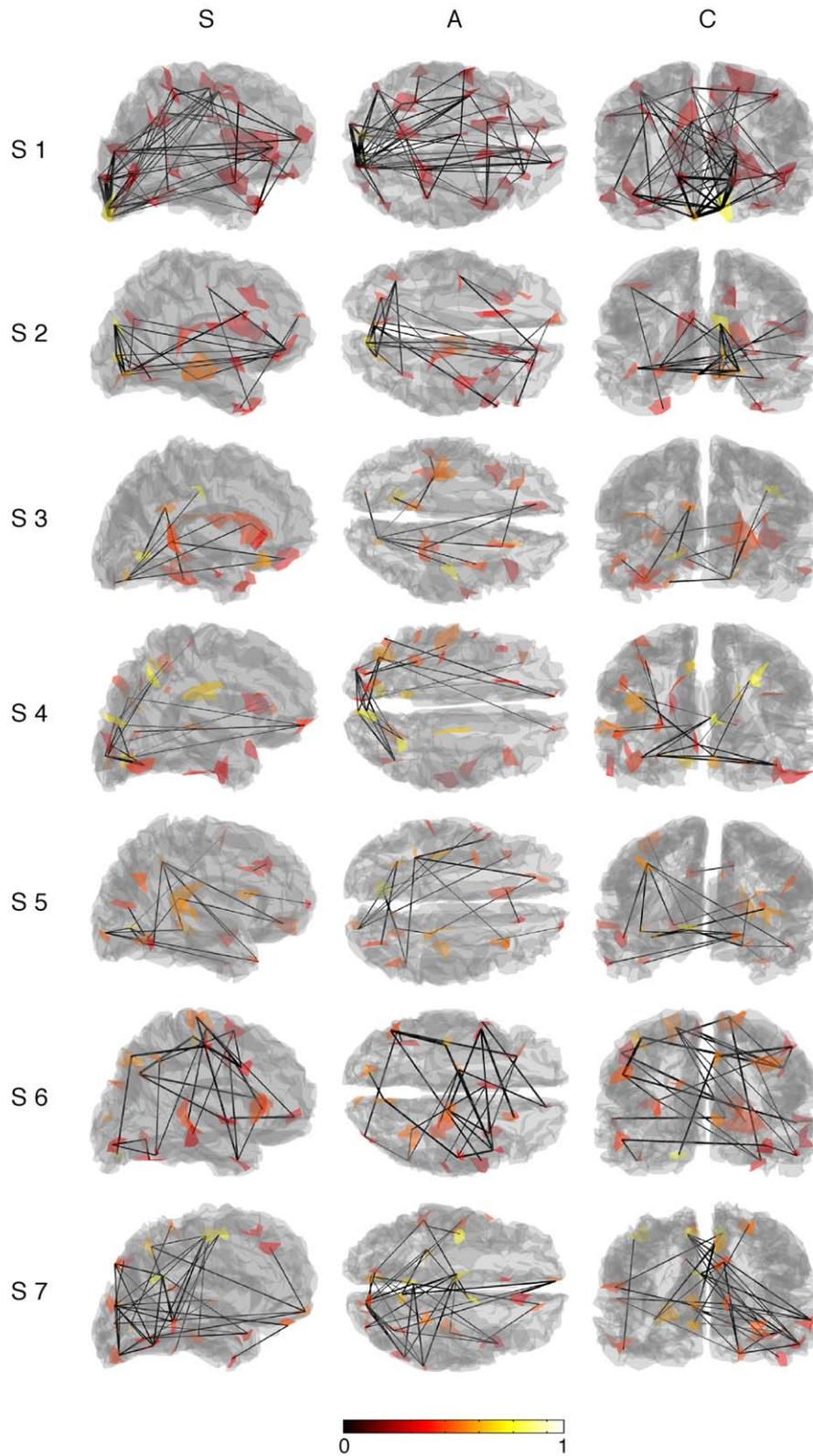


Fig. 6. Cortical networks of synchronous brain activation correlated to conscious perception. (A) Sagittal (S), axial (A) and coronal (C) semitransparent views of all seven subjects are shown. The front of the brain is on the right for the S and A views; the left is on the top for the A view and on the left for the C view. Black lines link brain regions that show synchronous activation significantly ($P < 0.05$) correlated to the 5-Hz envelope of the scalp sensor with best sensitivity to the tag. Cortical color codes for normalized average energy emission according to the color scale on the bottom.

basis of propagation (Srinivasan et al., 1999). In our study, although medial frontal regions show strong activation throughout the rival condition (Table 1A), they fail to show specific modulation in terms of signal strength when comparing dominance vs. the suppression of the tagged stimulus (Table 1B). Yet, as can be seen in Figs. 5 and 6, medial frontal regions do appear to participate in the cortical network that correlates with perceptual dominance. This suggests that frontal regions could actively establish coherent activity with posterior, sensory-driven areas by changing the temporal pattern of activation without changes in overall rate (Engel et al., 1999).

One could argue that the modulations of brain response are a reflection of attentional rather than perceptual phenomena. This is a nontrivial possibility that seems to pervade all binocular rivalry paradigms where the subjects are instructed to attend to the experience. Moreover, as attention seems a prerequisite for reported conscious perception (Posner, 1994; Lamme, 2003), unequivocally separating them is not straightforward and subtraction-based paradigms present known limitations (Newman et al., 2001; Price and Friston, 1997). Although we cannot fully discard the influence of attention on the modulation of cortical activity observed here, working with a non-frequency-tagged competing stimulus as the face provides an internal control. Changes in cortical synchrony are specific only during moments of conscious perception of the tagged rings although the driving stimulus is always present. Subjects are instructed to indicate both dominant alternatives so it is expected that attention will be, if not constant, similar for both situations. This suggests that the gating of the evoked activity, and therefore of the neural patterns observed, is rather related to the suppression mechanisms proper to rivalry than to purely attentional factors. A similar point can be made for the influence of the motor preparation and response.

The frequency tagging approach, when used under ongoing non-averaged conditions can reveal the temporal evolution of both dominance and suppression in the rising and falling of the evoked synchronous activation, respectively. This wave-type figure (see Fig. 4, red and black curves, and Fig. 5 time course of cortical synchrony) could be of interest in determining those endogenous (in contrast to stimulus-evoked) brain processes that can account for such dynamics of appearance and disappearance of a conscious moment. Certainly, although the tagged stimulus bears a simple dominant frequency, the neural response does not necessarily have to be restricted to the frequency tag. Given the highly nonlinear complex nature of the brain (Friston, 2000), it will most likely show a multifrequential response. As mentioned above, in this study, we have chosen to follow a monofrequential network and we cannot exclude that other frequencies (and therefore other networks) participate in the establishment of the conscious visual percept. It has been reported that during multistable perception, frontal gamma band (30–80 Hz) activity shows enhancement (Basar-Eroglu et al., 1996) while alpha band activity (8–12 Hz) decreases upon perceptual changes (Struber and Herrmann, 2002). Nevertheless, as can be seen in Figs. 3 and 4, not only is the frequency tagging effective but also its modulation is tightly correlated with the subjective experience of perceptual dominance. Thus, the labeling of the evoked brain activity, although restricted, is correlative to the conscious state of the subject and enables us to explore an important part of the underlying cortical dynamics in a well-defined frequency band.

While a specific modulation of the frequency tag throughout dominance and suppression periods is evident, it can be observed

that significant signal is detected in the 3- to 7-Hz band during suppression (Fig. 3B). Although this is probably in part because endogenous rhythms in that frequency band are still present thus yielding a non-zero signal (see Fig. 3A), the results are in accordance with previous studies that show that during suppression, visual-evoked potentials are reduced but not completely eliminated (Cobb et al., 1967; Tononi et al., 1998). Although a recent fMRI study has suggested that the nondominant stimulus could be fully suppressed as early as V1 (Tong and Engel, 2001), the debate on the degree of suppression is still unresolved (Blake and Logothetis, 2002). Indeed, motion aftereffects and tilt aftereffects can be produced by the suppressed stimulus (Lehmkuhle and Fox, 1976; Wade and Wenderoth, 1978), therefore suggesting a certain degree of cortical penetration of the nondominant image.

In our study, we have used a common frequency tag for all subjects to facilitate comparisons. Yet, it is well known that sensitivity to photic stimulation (of which frequency tagging as presented here is a particular case) can vary depending on the frequency of stimulation and does so in a quite specific manner depending on the subject (Fisch, 1999; Jarvis et al., 2003; Kastner et al., 2004). Results presented in Figs. 3B and 6 suggest that not all subjects presented the same sensitivity to the frequency and that differences in the extension of the revealed network may be related to this fact. One possible extension of the present work would be to maximize the individual responses by working with adapted frequencies for each subject.

Dynamical analysis

In this study, we have analyzed phase relations between cortical sources driven by a frequency-tagged stimulus during the ongoing succession of dominance and suppression periods in binocular rivalry. Yet, to be able to set a threshold of significance of such synchronous activation, it is necessary to define a certain criterion of stability. One possibility would be to arbitrarily define independent trials on the basis of individual transitions and analyze the stability of phase relations across such events. This approach assumes that transitions will develop always in a similar way, which is rarely the case in visual rivalry for stimuli that subtend more than one degree of the visual field (Blake, 1989). We have chosen, alternatively, to follow synchronous activation stable in time *throughout* a given trial (a viewing condition). Recent development in phase synchrony analysis shows that it is possible to estimate the stability of phase relations on a single trial basis with a slight compromise in temporal resolution (Lachaux et al., 2000). This approach estimates the phase difference between two signals during an integration window and then establishes statistical significance based on comparison with surrogate data. A crucial choice is therefore the size of the integration window. Small values provide better temporal resolution but sacrifice statistical resolution because in contrast to long-lasting periods, short periods of phase locking are more likely to arise by chance. High values provide better statistical resolution but result in smearing and therefore worse temporal discrimination. While no definite solution is available for this problem (Le Van Quyen et al., 2001), we have chosen to set the length to 1 s, corresponding to five cycles at the frequency tag. Dominance periods in visual rivalry are not clear cut transients but rather extended moments that develop dynamically (Blake, 1989; Wilson et al., 2001) and can last several seconds (2.3 in average in our study). Our choice thus

provides a sufficient number of phase-locking values per dominance cycle (an average of 40 points for 2-s dominance periods using 1-s windows in 50-ms steps) while keeping a reasonable temporal resolution. Furthermore, as can be seen in Fig. 4, synchrony follows closely the evolution of the both the scalp 5-Hz envelope and the behavioral response. This suggests that the resulting time course is reflecting the actual dynamics of modulation of the underlying brain response.

Behavioral measures and mixed dominance

In order for the subject to signal the evolution of rivalrous alternations, we have used simple button presses to indicate full dominance. Alternatively, one could ask the subject to depress a button during the dominance of one percept and release it during its suppression. We have favored the first alternative to keep transitions as clean as possible from motor components and sustained attention to a task different from the alternation itself. Thus, subjects viewed the alternation process and indicated only when maximum dominance/suppression was reached. However, this approach, as well as the alternative press/release method, neglects the spreading of mixed dominance which tends to show wave-like patterns when the stimuli are larger than one degree of visual field (Blake, 1989; Wilson et al., 2001). As it is, our paradigm does not enable us to precisely pinpoint the moment when the frequency-tagged stimulus begins to dominate. It would be interesting to provide the subjects with a more continuous measure of their perceptual experience such as a graded knob to better distinguish the appearance and disappearance of the competing percepts. Subjects did, however, describe smooth transitions from one percept to the other in accordance with the mountain-valley distribution of ongoing synchrony patterns (Figs. 4 and 5). Furthermore, the strength of the evoked response most likely depends on the dominance of the tagged stimulus, as this and previous studies suggest (Brown and Norcia, 1997; Srinivasan et al., 1999). Therefore, if long-lasting mixed periods were pervasive in our paradigm, they would tend to reduce the difference between both extrema in Fig. 4 rather than enhance it.

Cortical contributions and binocular rivalry

We have used a binocular rivalry protocol as a paradigm to study cortical patterns that are established during the ongoing flow of conscious moments. The participation of different brain areas in the binocular rivalry phenomenon is a matter of extensive discussion (Blake and Logothetis, 2002). Here, we were able to identify several regions of interest that appear active during such experience. Bilateral visual cortex, mainly the calcarine sulcus and adjacent lingual gyrus, and MT in the lateral occipitotemporal junction (Bundo et al., 2000), appeared strongly activated. Left parietal and frontal cortex, bilateral orbitofrontal cortex and right temporal pole showed a similar behavior. We also detected activation in bilateral anterior cingulate and medial frontal cortex, and right superior parietal gyrus. Among these regions, bilateral visual cortex (V1/V2), MT and the left parietofrontal regions were consistently modulated in amplitude during dominance–suppression cycles. In an fMRI study, Lumer et al. (1998) showed strong activation of the medial frontal region during rivalry. Likewise, they showed that right prefrontal cortex was specifically engaged during spontaneous transitions of perceptual dominance. In a subsequent study, Lumer and Rees (1999) presented evidence of

co-variation of parietal and lateral frontal regions in a similar paradigm. Our results are coincident regarding the participation of parietal and medial frontal regions, although obtained in a different imaging modality, during the dominance of the stimulus. We did not find significant activation, however, of right prefrontal cortices. On the other hand, while we did not find a significant modulation in local amplitude of the more medial frontal regions and the right parietal during dominance and suppression periods, phase-synchronized activity was detected between the occipital and such frontal regions during dominance (Figs. 5 and 6). As suggested above (Frequency tagging section), this could be accomplished by a temporal modulation of the firing pattern of the frontal regions without significant change in local amplitude (Engel and Singer, 2001; Engel et al., 1999). Here, again, it is important to stress the complementary nature of the different approaches. The approach used in this work will reveal stimulus-driven feed-forward networks and their spatiotemporal evolution throughout periods of dominance. On the other hand, fMRI studies as the ones discussed above will reveal regions that play important roles in driving the endogenously generated alternations. It appears that conscious perception is most likely the result of a complex interplay of (at least) these two phenomena (Lamme and Roelfsema, 2000; Rees et al., 2002).

The main results of this study are presented in Figs. 4, 5 and 6. As seen in Fig. 4, a consistent active modulation of the overall cortical synchrony upon conscious perception of the tagged stimulus is evident. The individual distribution of such coactive brain regions showed some important regularities in brain patterns during the perceptual dominance of the expanding rings. Given the ill-posed nature of the inverse problem, and despite individual differences, it is revealing to find for six out of seven subjects that interaction (as measured by phase synchrony of the evoked response) could be effectively established between occipital visual areas and more integrative regions including inferior parietal, inferior-temporal and, interestingly, medial frontal cortices. On the other hand, as supported by the results presented in Fig. 6, the extension of the network could be dependent on the individual sensitivity to the frequency tag. In Fig. 5, we have presented ongoing patterns of cortical synchronous activation that correlate with the spontaneous stream of conscious moments. The role of striate and extrastriate occipital cortex in visual awareness has been extensively studied and discussed (for a recent review, see Tong, 2003). In particular, the issue of whether primary visual cortex plays a role during dominance in binocular rivalry is still a matter of debate (Blake and Logothetis, 2002). Single cell recording in monkeys experiencing binocular rivalry shows little modification of neural activity in V1 and V2 (Leopold and Logothetis, 1996). In contrast, recent brain imaging studies suggest that modulation of activity is evident as early as V1 during visual rivalry (Polonsky et al., 2000; Tong and Engel, 2001). Our results suggest that activity in primary and secondary visual cortices (which are not distinguishable by the inverse solution we have used) undergoes significant modulation, during rivalry, not only in terms of signal strength but also in local synchronization (Fries et al., 1997), and that such modulation extends into more middle-temporal and dorsal areas bilaterally. But what appears as the most salient feature of the dynamical brain patterns is the synchronous coactivation of visual cortex and medial frontal regions during visual dominance of the tagged stimulus. This suggests that upon conscious perception, interaction between striate, extrastriate visual cortex and medial frontal regions could be dynamically established in a sort

of anteroposterior or “back-front” (Crick and Koch, 2003) dialogue. In addition to parietal and frontal cortex, the cingulate cortex appears to be involved in a network subserving the direction and maintenance of attention (Mesulam, 1999; Posner, 1994) and could thus play a critical role in the global availability of distributed brain activity and consequently in conscious perception (Crick and Koch, 2003; Dehaene and Naccache, 2001). In this study, we consistently found activation in orbitofrontal regions (Table 1). We cannot provide a definite interpretation of these results, but in a previous work under nonrival conditions with the same tagged stimulus (David et al., 2003), we also detected this cortical area. In a recent meta-analysis of functional connectivity, Stephan et al. (2000) distinguished three major connectivity clusters in primate cortex. Apart from the somato-motor and the visual clusters, a third orbito-temporo-insular cluster was evidenced. Given the feed-forward propagation of the evoked response that we have followed here, it seems plausible that the signal may have reached the temporo-polar and orbitofrontal cortices through this cluster and the ventral visual pathway.

Finally, our results underscore the importance of studying perceptual experience under non-averaged conditions (David et al., 2003; Ioannides, 2001). The ongoing establishment of the cortical networks does not follow at each transition the exact same dynamics. Nevertheless, the subject reports a subjective experience of dominance at each time. Although it is probable that part of the observed variability is dependent on the bad conditioning of the MEG source reconstruction, regularities are evident suggesting a balance between stability and variability in brain processes (Edelman and Tononi, 2000). This highlights the problem of understanding how the brain deals effectively with single trials and how such variability could be critical to the uniqueness of each conscious experience.

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