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Location of brain rhythms and their modulation by preparatory attention estimated by current density

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ABSTRACT

To test the hypothesis that there is a functional modulation of conventional EEG bands associated with preparatory attention, putative changes in the spontaneous brain rhythms and their associated cerebral sources were addressed. The goals of the present report were, first, to find the brain areas with maximal rhythmic activity before warning and imperative stimuli in a classic contingent negative variation (CNV) paradigm, and, second, to study the modulation of the EEG rhythms of these areas during the preparatory attention interval which precedes the S2 (imperative) stimulus. Trial by trial LORETA analysis found similar brain rhythm generators during both pre-S1 and pre-S2 intervals. Each theta, alpha and beta traditional EEG rhythm originates in several anatomically distinct brain structures. Preparatory attention is associated with a decrease in power in alpha (right and left occipital and temporal areas) and low-beta (left frontal, bilateral occipital and middle frontal areas) EEG bands. In these structures power changes associated with preparatory attention modulated either a dominant or a non-dominant oscillatory band, suggesting that non-dominant rhythms of a cerebral area have some functional relevance. Our results imply distributed regional sources for brain rhythms and support the view that during preparatory attention there is a modulation of the brain sources generating alpha and beta brain rhythms. Moreover, the proposed combined approach makes it possible to explore the definition of a given brain area not only anatomically, but also by the frequency content and the functional reactivity of the electrical rhythms that it generates.

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1. Introduction

In the last decade, interest in the role of EEG rhythms in cortical information processing has increased (Rodríguez et al., 1999; Singer and Gray, 1995; Varela et al., 2001), particularly their function in preparatory attention, working memory and

other brain processes (Pfurtscheller and Klimesch, 1992). Although this is a major topic in cognitive neuroscience, several methodological issues complicate the performance and interpretation of these studies, for instance: (i) the ever-changing nature of the time evolution of the spontaneous EEG signal (non-stationarity); (ii) the difficulties in establishing

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stable brain functional states for analysis in rhythm terms; and (iii) the limitations of traditional analysis of rhythms based on techniques which take EEG information solely from the scalp. This study tackles these shortcomings by exploring preparatory attention, in which it has been suggested that there is functional modulation of conventional EEG frequency bands (Bastiaansen et al., 1999, 2001; Bastiaansen and Brunia, 2001; Gómez et al., 2004b), and by examining specific EEG rhythmic changes at the level of the structures responsible for generating the rhythms.

Previous studies have found that functional situations of preparatory attention, related to the analysis of the response to the next incoming stimulus, are expressed by changes in ongoing scalp EEG rhythms (Gómez et al., 1998, 2004b; Gonzalez Andino et al., 2005). This seems to extend to a broad EEG spectral band including the theta, alpha, beta and gamma bands. However, most of the classic studies of preparatory attention are based on the contingent negative variation (CNV) event-related potential (ERP). This negative wave is generated in the interval preceding an imperative stimulus (S2) that needs further processing. A necessary condition for the S1 to generate a CNV is that it acts as an advertising signal (Rockstroh et al., 1982; Walter et al., 1964). One of the most influential neurophysiological theories about the CNV is that it reflects a subthreshold activation of the cortex during the S1–S2 period, making the cortex ready for processing the next stimulus and response (Rockstroh et al., 1982). Brain generation of the CNV is due to the tonic activation of the lateral and medial frontal cortex, motor cortex and sensory cortex (Brunia, 1999; Gómez et al., 2003). Nevertheless, CNV analysis, as it is an ERP obtained by averaging of the trials synchronized relative to stimuli, is not able to capture the EEG modulations of oscillatory activity that appear at the same time as the CNV component (Pfurtscheller and Lopes da Silva, 1999). Thus, in the search for the functional modulation of the rhythms, analysis of the original EEG is required instead of averaged information.

The scalp spatial topography of brain rhythms can be roughly described as: midline fronto-central distribution for the theta rhythm, posterior distribution for the alpha rhythm, and frontal distribution for the low- and high-beta range (Asada et al., 1999; Gómez et al., 2004b; Luu and Tucker, 2001; Pfurtscheller and Lopes da Silva, 1999). However, for decades, there were no useful non-invasive methods for accessing sources of electrical brain activity and its rhythms. The advent of multichannel recordings and of non-invasive location techniques has enabled possible location of the different brain rhythms to be inferred (Lehtela et al., 1997). Several approaches, such as dipolar models (Scherg and Von Cramon, 1985) and distributed source models (Grave de Peralta Menendez et al., 2000; Hamalainen and Ilmoniemi, 1994; Pascual-Marqui et al., 1994), have been used to approximate the location of the neural generators of EEG rhythms.

Dipole location techniques have shown the involvement of the superior medial frontal cortex in the generation of the theta rhythm (Asada et al., 1999; Luu and Tucker, 2001). For the alpha rhythm, the dipolar models show regional sources in parieto-occipital areas (Hari et al., 1997; Lu et al., 1992; Salenius et al., 1995; Salmelin and Hari, 1994), occipitoparietal sulcus (Manshanden et al., 2002) and areas around the calcarine

sulcus (Hari et al., 1997; Michel et al., 1992; Salenius et al., 1995; Salmelin and Hari, 1994; Williamson and Kaufman, 1989). Moreover, the beta rhythm has a cerebral location anterior to the alpha generators (Michel et al., 1992).

In the last 5 years low-resolution tomography, LORETA, has been used to determine the generators of the oscillatory rhythms of the EEG. This method computes a single solution for the 3D intracerebral sources, using a Laplacian operator as smoothing constraint (Pascual-Marqui et al., 1994). Evidence of the usefulness of this approach are the correlations between generators of frequency bands computed with LORETA and glucose metabolism measured through positron emission tomography (PET) (Dierks et al., 2000; Gamma et al., 2004), those found with functional magnetic resonance imaging (fMRI) (Mulert et al., 2004) and epileptic seizures measured by intracranial electrodes (Lantz et al., 1997). Other studies have shown that LORETA can be used to search for differences in sources of spectral bands after stimulant substance consumption (Frei et al., 2001), at sleep stages (Anderer et al., 2001) or in patients (Babiloni et al., 2004). This report follows a similar approach to the one proposed by Babiloni et al. (2004). The main difference is the use of a thresholding criterion to pick up the areas of greater rhythmical activity.

Preparatory attentional and intentional modulation extends to a broad spectral band including theta, alpha, beta and gamma bands (Gómez et al., 2004b; Vijn et al., 1991). Previous work sought to evaluate the preparatory attention modulations of the spectral bands based on the analysis of scalp EEG. There are no studies on the effects of preparatory attention on the rhythms studied at the brain generator level, with comparison of the pre-S1 and pre-S2 periods.

A common limitation to studies on EEG rhythms and their brain sources is that there is a conflict between two different methodological needs in the analysis of brain oscillations: long EEG intervals could reflect changing/mixed functional cerebral situations (Nunez, 1995), while short time intervals are inadequate for analyzing low-EEG frequencies due to the lack of spectral resolution. The procedure used here tries to overcome, as far as possible, these problems. In a compromise solution, we selected for analysis brief intervals of EEG (512 ms in our case), to favor the selection of a quasi-stationary interval of rhythms and to find relatively stable functional cerebral situations, long enough to analyze adequately most traditional EEG frequencies (theta, alpha and beta rhythms, excluding delta ones). In a second step, using a strategy similar to that in ERP studies, we searched for functional repeatability by obtaining a high number of intervals that shared the same experimental conditions (pre-S1 or pre-S2, respectively, in the visual S1–S2 paradigm employed). The spectral content and the LORETA brain sources of the EEG intervals were then analyzed trial-by-trial, before separate averaging of data for the pre-S1 and pre-S2 conditions.

The goals of this report were, first, to find the brain areas in which brain rhythms activity is maximal in the intervals immediately preceding S1 (warning) and S2 (imperative) stimulus of a visual S1–S2 paradigm; and second, to study the modulation of EEG rhythms during the interval immediately preceding the S2 imperative stimulus. The hypothesis is that some of the brain areas that oscillate spontaneously during prestimuli intervals could show

reduced EEG power during the preparatory attention period preceding S2. To test this hypothesis, the current density of the brain areas generating the different brain rhythms during the interval prior to the S1 stimulus, considered as a baseline period, was compared with the current density of the same areas during the expectancy period prior to S2 stimulus. Finally, the possibility that the areas defined by LORETA as the generators of reactive brain rhythms could have particular amplitude versus frequency pattern was explored. These combined approaches allow us to explore the possibility of defining a given brain area not only anatomically, but also by its frequency content and its functional reactivity.

2. Results

Fig. 1a shows the spectral band power of the pre-S1 interval; and Fig. 1b gives the corresponding spectrum for the pre-S2 interval. Their frequency spectra are very similar and show in both cases the $1/f$ decay that is characteristic in EEG spectral power, accompanied by a peak of power in the alpha range. Fig. 1c gives the subtraction of the power spectrum in pre-S2 from the pre-S1, showing an alpha peak and a low-beta peak. Scalp spatial distribution of the theta, alpha, low-beta and high-beta rhythms appears in Fig. 1d for descriptive purposes. The figure shows pre-S1 and pre-S2 intervals with a similar distribution of spectral power. As expected, theta had a fronto-central distribution, alpha was focused bilaterally at posterior sites, low beta had a frontal bilateral distribution, and high beta had a bilateral prefrontal distribution.

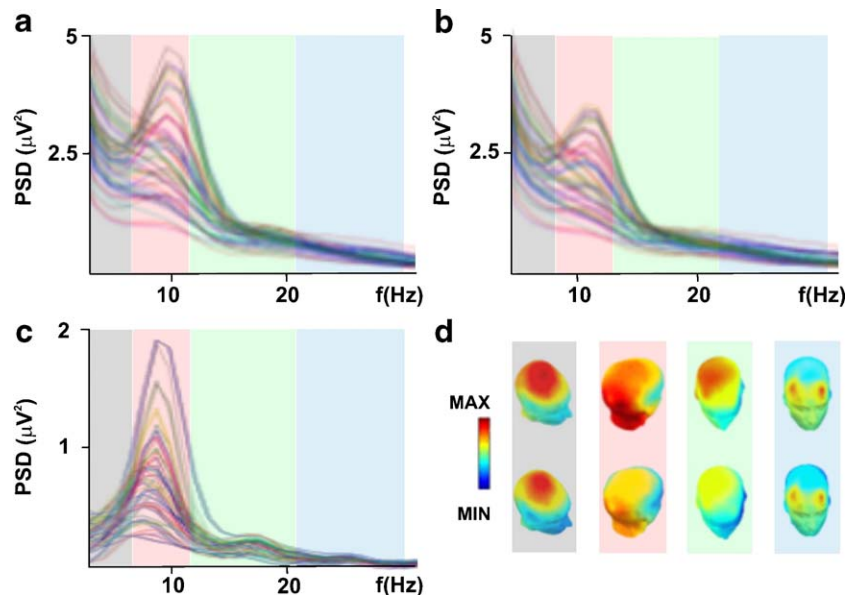


Fig. 1 – Power spectral density of the 512 ms prior to the arrival of the warning stimulus (pre-S1; a) and prior to the arrival of the imperative stimulus (pre-S2; b). Note the $1/f$ shape of the spectrum and the reburst of activity in the alpha range. Colors indicate the different frequency ranges: theta (grey, frequency range 6–8 Hz), alpha (pink, 8–12 Hz), low beta (green, 13–20 Hz) and high beta (blue, 20–30 Hz). Panel c shows the amplitude–frequency plot of the subtraction of pre-S2 from pre-S1. Panel d shows the scalp topographies for the different brain rhythms and conditions. Theta, alpha, low beta and high beta run from left to right. The top row is for the pre-S1 period and the bottom row is for the pre-S2 period. Note that negative modulation of brain oscillations occurs in the great majority of electrodes and frequencies considered. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Fig. 2 and Table 1 show the cerebral areas with current density activation, on the criteria established in Experimental procedure section (two standard deviations over the mean of overall activity), in each rhythm and LORETA analysis. There is great similarity between activated areas for pre-S1 and pre-S2 stimulus. The theta band has activations in right and left occipital and occipitotemporal regions, with an additional contribution from left precentral cortex. The main activations of the alpha band are located in occipital areas (both cortices) and in left parietal cortex. Finally, the main generators of beta bands are located in the frontal and temporal cortices, with occipital contributions to the low-beta band (see Table 1 for a detailed list of activated areas).

Comparisons between pre-S1 and pre-S2 show significant differences in the alpha band at lateral and medial occipital (BA 18, 31 $p < 0.01$; BA 17, 19 $p < 0.05$) and right occipitotemporal (BA 19, 37 $p < 0.01$) areas. For the low-beta band the differences were at left frontal (BA 6 $p < 0.01$), left middle frontal (BA 10, $p < 0.05$) and medial occipital (BA 18, $p < 0.05$). In all cases pre-S2 had less activity than pre-S1. The location of these areas is given in Fig. 2, highlighted in blue. No differences between pre-S1 and pre-S2 conditions were found at any cerebral location in the theta and high-beta ranges. Note that the Holmes non-parametric method is corrected from multiple comparison problem.

Fig. 3 shows the power amplitude–frequency plots for the areas with statistically significant differences between pre-S1 and pre-S2 in the alpha (Figs. 3a and b) and low-beta (Figs. 3c and d) bands. All the brain areas with modulation in the alpha range show the dominant spectral peak in the same band (peaking at 10 Hz), with less amplitude in pre-S2 than in pre-S1.

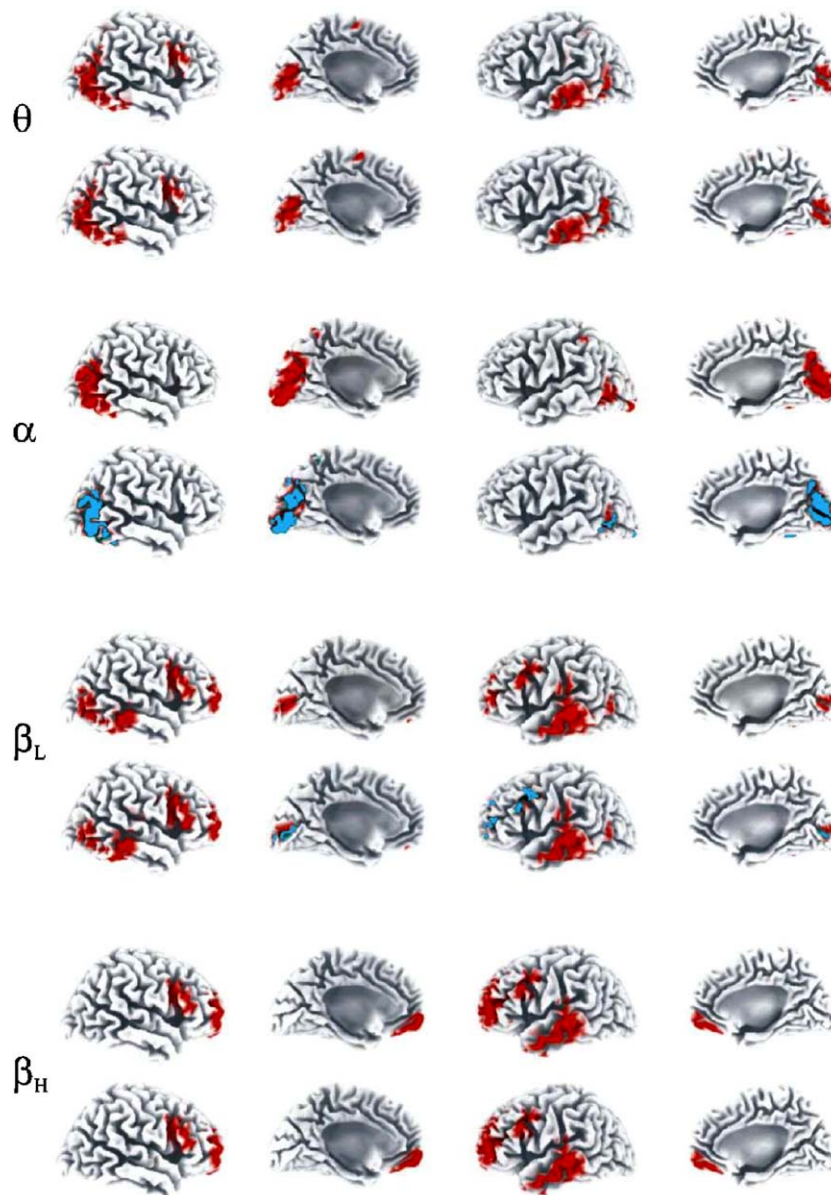


Fig. 2 – Activated areas in the theta (6–8 Hz), alpha (8–12 Hz), low-beta (13–20 Hz) and high-beta (20–30 Hz) ranges. Areas with activation greater than twice the standard deviation from the mean are colored. Only the areas marked in blue had a statistically significant negative modulation during the expectancy period, when compared with the baseline period. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

In contrast, the reactive areas at low-beta band have their maximum activity at other frequencies, high-beta band (peaking at 24 Hz) in the case of the two frontals (BA 6 and BA 9–10), and alpha band (peaking at 10 Hz) for the occipital area BA 17.

3. Discussion

The main results reported here are (1) the obtaining of the maximally activated LORETA areas for the different brain rhythms, (2) the modulation of some of the areas obtained in 1 in the alpha and beta band during expectancy periods and (3) the determination of the spectral frequencies of the areas obtained in 2. These results lead us to suggest that the

characterization of a functional brain rhythm should include not just its possible brain localization and the spectral frequency content of generators, but also the cognitive modulation of the rhythm.

3.1. Brain rhythm location

One of the main objectives of this research was to obtain the sources of brain EEG rhythms during short quasi-stable (in both functional and spectral terms) intervals during waking brain function, such as those provided by the pre-S1 and pre-S2 time windows of a CNV conventional paradigm. We found very similar brain sources for each rhythm in both pre-S1 and pre-S2 EEG, suggesting similar involvement of related structures

Table 1 – Most activated areas for each frequency range

	Pre-S1	Pre-S2
Theta (6 Hz)	Occipital (BA 17–18) Right/Left occipito-temporal (BA 37–19) Right supratemporal (BA 39) Right inferior frontal (BA 44) Left middle/inferior temporal (BA 20–21) Left precentral (BA6)	Right middle/inferior temporal (BA 20–21)
Alpha (10–12 Hz)	Occipital (BA 17–18)* Right/left occipito-temporal (BA 37–19)* Occipito-parietal cissure (BA 31–7) Left parietal (BA 7)	
Low Beta (14–18 Hz)	Left middle/inferior temporal (BA 20–21) Right inferior frontal (BA 44) Right/left * middle frontal (BA 9–10) Left parietal (BA 40) Left frontal (BA6)* Right/left occipito-temporal (BA 37) Occipital (BA 17–18)*	
High Beta (24–28 Hz)	Left/Right middle frontal (BA10) Orbital (BA11) Right inferior frontal (BA 44) Left middle/inferior temporal (BA 21) Left inferior frontal (BA 45) Left frontal (BA6)	Left middle frontal (BA9)

Structures whose activity was more negatively modulated during the pre-S2 than the pre-S1 period are marked by an asterisk. For details, see main text. The areas that are under the criteria only in one of the two considered periods are indicated under the labels, pre-S1 and pre-S2.

and similar oscillatory behavior in supporting the underlying specific brain function states. This similarity between pre-S1 and pre-S2 oscillatory behavior could be partly explained by the fixed 2-s intertrial interval used (period S2–S1), that would allow to subjects entering in an expectancy to visual and temporal cues in the S2–S1 period, and entering in an expectancy to visual and temporal cues, but also to motor responses, in the S1–S2 period. As mentioned in the Introduction and the Experimental procedure section, the LORETA technique only allows an estimation of the current sources under the assumption that sources are smooth. Thus, some caution is required if present results are to be interpreted correctly. In this section, we try to confront the sources of brain rhythms obtained by the LORETA technique with other methods.

In the EEG *theta* range (6–8 Hz), the LORETA algorithm obtained activation in posterior, temporal and frontal areas. Related to occipital (BA 17–18) and right/left occipitotemporal theta activations (BA 37–19), these areas are also active in the alpha range, and might be explained as the low frequency extreme of the posterior alpha range (see Fig. 3b). Such a topographically widespread near-alpha lower range (7–10 Hz) occurs during a great variety of tasks, and has been related to attentional task demands (Klimesch et al., 1990). The present study also shows a theta activity source in the middle/inferior temporal lobe (BA 20–21). One possible explanation for the origin of this activity could be hippocampal participation, whose depth is underestimated by the LORETA algorithm. As the hippocampus is one of the sources for theta activity in

the mammalian brain (Buzsaki, 2002), it cannot be ruled out that a substantial part of the temporal activation obtained in the theta range could in fact have a deeper origin, at the level of the hippocampus and parahippocampal gyrus. However, a recent study of theta origin, based on intracranial recordings, shows that during relaxed wakefulness there is no theta burst activity in the human hippocampus, and that theta activity is prominent in the basal temporal lobe (Cantero et al., 1999). In addition, during arousals following awakenings from sleep, prominent theta activity was described in the inferior and middle temporal lobes (Cantero et al., 1999). Thus, part of our theta temporal lobe activity may be accounted for by the basal temporal lobe and the inferior and middle temporal gyri, which previous studies identified as structures that are active at different periods of wakefulness. However, there are big differences between the recording situations in our study and in that of Cantero et al., 1999. The Cantero study is based on identified theta bursts instead of total EEG activity analysis, and information is given by implanted electrodes. Another contribution to theta activity might come from what is known as the tau rhythm (6–9.5 Hz), described in MEG recordings (Lehtela et al., 1997) and which has its origin in the superior temporal plane. The LORETA algorithm may also pick up this activation but locates it 1–2 cm ventral to the tau sources described, contributing to the activations located in the middle temporal cortex. We also encountered two sources of the theta rhythm in the frontal cortex. One is in the right inferior frontal cortex (BA 44), as reported by Cantero et al., 1999, during resting wakefulness. The other is in the left precentral cortex (BA 6). Involvement of the superior medial frontal cortex in the generation of the theta rhythm was described previously with dipole location techniques (Asada et al., 1999; Gevins et al., 1997; Luu and Tucker, 2001). However, given that LORETA finds it difficult to locate deep sources (Grave de Peralta and González Andino, 2000), as mentioned above, part of the theta activity located in the supplementary motor area could originate in a deeper source in the anterior cingulate cortex (Feenstra and Holsheimer, 1979).

In the *alpha* range (8–12 Hz), LORETA analysis suggests an exclusive contribution of posterior neural sources: the calcarine sulcus (BA 17 and 18), the parieto-occipital sulcus (BA 7–31) and occipitotemporal areas (BA 19 and 37). Intracranial recordings of the human brain have shown alpha activity in the whole occipital lobe (Pérez-Borja et al., 1962) and dipolar models have found parieto-occipital sources (Hari et al., 1997; Lu et al., 1992; Manshanden et al., 2002; Salenius et al., 1995; Salmelin and Hari, 1994). Moreover, using LORETA, Babiloni et al. (2004) found posterior sites for the alpha generators. Specifically, calcarine sulcus has been extensively described as one of the neural generators of the alpha rhythm (Hari et al., 1997; Parra et al., 2000; Salenius et al., 1995; Salmelin and Hari, 1994; Williamson and Kaufman, 1989). A functional support to the idea that the calcarine sulcus is an area contributing to generation of the alpha rhythm is the blocking of the alpha rhythm by retinotopically focused mental imagery (Kaufman and Williamson, 1991). Therefore, present results with LORETA confirm all previously proposed sources for the alpha rhythm, supporting the simultaneous contribution of several occipitotemporal compact neighboring areas to its generation, with the addition of parietal contributions.

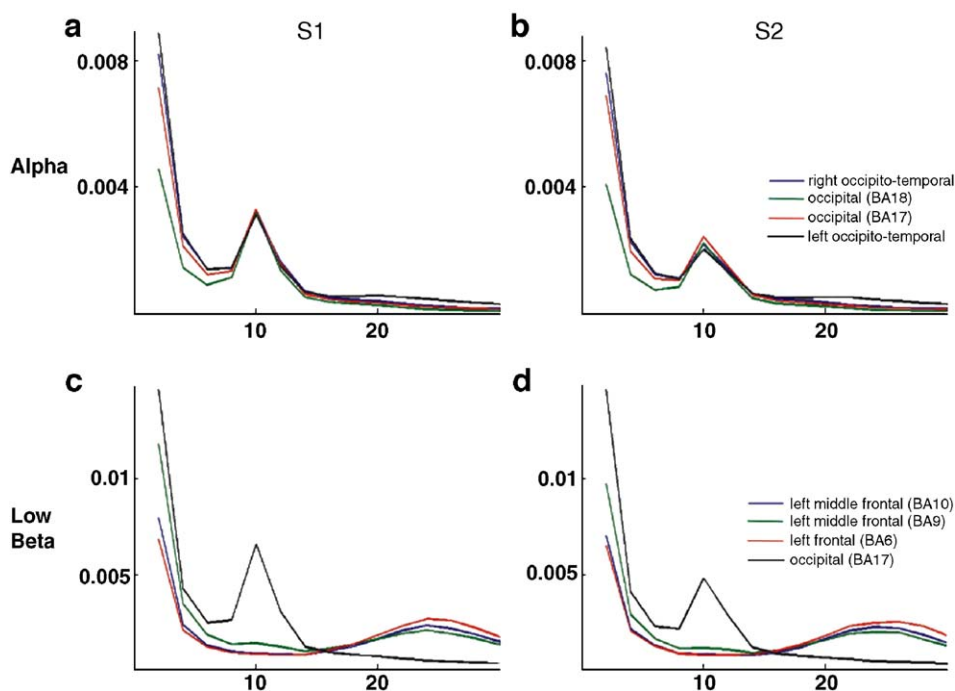


Fig. 3 – Amplitude–frequency plots during the pre-S1 (a and c) and pre-S2 (b and d) periods for the areas showing modulation during the expectancy period. The structures with differences in the alpha range (a and b) are the lateral and medial occipital (BA 18; BA 17) and the right and left occipitotemporal (BA 19, 37) areas. Note the enhanced activity between 6 and 14 Hz, and the peaking at around 10 Hz. For the modulated areas in the beta range (c and d) the areas shown are: BA 6 and BA 9 and 10 in the frontal lobes, and BA 17 in the occipital lobe. Note the broad increase from 15 Hz to 30 Hz, peaking around 25 Hz. Area 17, which was modulated in the low-beta band, has the characteristic features of an alpha peak and then slowly decay in the beta range.

For the beta rhythm (14–28 Hz), the LORETA algorithm showed several sparse sources and highlighted some structural differences in the origin of low and high beta. The main differences between high (24–28 Hz) and low beta (14–18 Hz) lie in the posterior structure's participation in low beta (BA 37, BA 17, BA18) and more anterior activations in high beta (BA11 and BA45).

Low beta from the posterior sites, occipital (BA 17 and 18) and right/left occipitotemporal (BA 37), could be interpreted as the high tail of the frequency range traditionally classified as alpha rhythm. This proposal is reinforced by the amplitude–frequency plot for occipital structures, which shows that the alpha range extends to the lower beta band (see Fig. 3). Moreover, the occipital contribution vanishes completely in the high-beta range. Rhythmical activity in the occipital cortex spreads from 6 to 14 Hz, surpassing the low (9 Hz) and high (12 Hz) values attributed to the alpha range, which suggests that the traditional idea of the limits of EEG rhythms should be enlarged by shifting our focus from a frequency definition to a spatial-frequency definition.

As traditionally described frontal areas were sources of beta rhythm in both low- and high-beta bands in the present study (see Fig. 2). One of the contributions for the low-beta range, almost overlapping with the upper alpha range, is an oscillation related to the functional state of the somatosensory and motor cortex, sometimes referred to as the mu rhythm (Hari et al., 1997; Pfurtscheller and Klimesch, 1992). Motor-related activity in the beta range is located close to

sensory motor areas (Stancak and Pfurtscheller, 1996). The activation obtained in the left premotor area 6 and parietal area 40 (see Fig. 2) could reflect the activation of these somatosensory and motor areas, as inferior parts of motor area 4 and premotor area 6 extend over the precentral gyrus in a thin strip of cortex, which makes it hard to distinguish between activity arising from areas 6 or 4. The reason why the beta rhythm in sensorimotor areas was more prominent on the left side could be because right-hand movements were required. This movement and their sensory re-afference produces a post-movement beta rebound only in the left hemisphere during the intertrial period (baseline period) (Pfurtscheller and Lopes da Silva, 1999). Other activated areas in the beta range were: the middle temporal sulcus (BA 20–21), the inferior and middle frontal cortex (BA 44, 9 and 10) and the orbito-frontal cortex (BA 11). Given that all these cortical areas are related to higher order functions this anatomical pattern reinforces the idea of a relationship of the beta rhythm to higher order cognitive processes (Fuster, 2003).

3.2. Modulation of brain sources during preparatory attention/expectancy periods

Another objective of our research was to test the modulation of the EEG rhythms of the areas activated during the preparatory attention/expectancy preceding the imperative S2 stimulus.

In a previous report, a broader negative modulation of scalp power spectra activity was described (Gómez et al., 2004b). Other studies showed a modulation in alpha and beta bands in a variety of tasks relating to the attentional and intentional preparation for the stimulus, with the use of the event-related desynchronization/event-related synchronization (ERD/ERS) technique (Fu et al., 2001; Gómez et al., 2004a; Klimesch et al., 1993; Pfurtscheller and Lopes da Silva, 1999; Worden et al., 2000). For instance, ERD in the alpha range is found in the motor cortex during preparation for movement (Bender et al., 2005; Pfurtscheller and Lopes da Silva, 1999) and during expectancy of a visual feedback stimulus (Bastiaansen et al., 1999; Bastiaansen and Brunia, 2001). The opposite – alpha increase – has also been obtained during preparatory periods, in areas that should be deactivated for a correct performance of the task (Fu et al., 2001; Worden et al., 2000) and prior to imperative stimulus in a category judgement task (Kaufman and Williamson, 1991). In these cases, alpha enhancement was explained as the selective inactivation of some brain areas (Pfurtscheller and Lopes da Silva, 1999). The negative correlation of alpha band power with reaction time has also been described (Gonzalez Andino et al., 2005). In the experiment reported here, a bilateral negative modulation of alpha rhythm appears in posterior locations (Figs. 1 and 2). Bilateral modulation can be explained by the fact that the subject has no directional cue that indicates where the imperative stimuli S2 will appear. LORETA analysis gave several posterior visual areas as the neural sources for negative modulation, including the calcarine sulcus in which functional V1 area is located. One possible function of alpha modulation could be the reduction of neural noise to allow for effective neural transmission along the visual pathways (Gómez et al., 2004b). Decreased alpha activity has already been reported during various visual cognitive tasks, such as attention (Goldman et al., 2002; Vazquez Marrufo et al., 2001), imagination (Michel et al., 1993) and phasic REM period (Cantero et al., 2003). Moreover, reduction of alpha rhythm could be related to increased metabolic rate in the calcarine sulcus during attentional demands (Di Russo et al., 2003), given that alpha power correlates negatively with metabolic blood flow in posterior sites (Goldman et al., 2002).

In the low-beta range, we found negative modulation in the cortex contralateral to the required response hand in left dorsolateral prefrontal cortex (BA area 9) and left premotor cortex (BA 6). These findings can be related to the motor-related ERD described in the literature that occurs in the upper alpha and in the lower beta bands, and is located close to sensorial-motor areas (Pfurtscheller and Lopes da Silva, 1999; Stancak and Pfurtscheller, 1996). Motor-related ERD represents a reduction of activity in these frequency ranges that could help the adequate performance of the intended movement. It is possible that some modulation of alpha sources previously described in motor areas are lost in the present report (Bender et al., 2005; Pfurtscheller and Lopes da Silva, 1999), given that we only considered for comparative analysis the areas that were maximally activated in each frequency band. However, some of the previously described motor-related high-alpha and/or low-beta

ERD could in fact have a premotor source (area 6, Fig. 2, Table 1).

3.3. Frequency content of reactivity to preparatory attention/expectancy areas

The areas that showed reactivity to the expectancy conditions were situated in posterior sites (for the alpha range) and in frontal and occipital sites (for the beta range). At posterior sites the alpha burst, peaking at 10 Hz, exceeded the classic 8–12 Hz and overlaid the high theta range and the lower beta band. At frontal sites, the areas showed clearly peak at around 24 Hz, while differences between pre-S1 and pre-S2 periods were in the low-beta range (14–20 Hz). In these structures, power changes associated with preparatory attention modulated either a dominant or a non-dominant oscillatory band, that is, there is a modulation not only in the frequency bands that present a peak in the spectral content reflected by the FFT, but also in those that do not present it, suggesting that non-dominant rhythms of a cerebral area have some functional relevance. Present results suggest that definition of a frequency rhythm would be more precise if anatomical location was added to frequency range criteria. In addition, the functional reactivity of a given area is a distinguishing factor to be taken in account, given that not all the areas oscillating at the same frequency have the same functional modulation. Therefore, the proposed method of amplitude–frequency plots enables preferred oscillatory frequencies of any brain area to be defined, and contributes to identification of functional brain areas based on their basic oscillatory behavior and rhythmical reactivity.

4. Experimental procedures

Twelve right-handed subjects (7 women) between 18 and 27 years old gave written consent to their participation in the study. Subjects were seated in a comfortable chair, in front of a computer screen. The warning (S1) stimulus consisted of a green square that appeared for 1 s in the center of the screen (0.91° of visual angle). The imperative stimulus (S2) appeared for 1 s after the central stimulus was switched off, and consisted of another green square that appeared randomly to the left or right of the first one (eccentricity 11.4°). Left and right targets had a probability of 0.5. Subjects were instructed to fix their eyes on the first central square and to show, by pressing the left or the right button of a mouse with the right hand index and middle fingers respectively, the position of the second stimulus. The subjects were instructed to promptly respond when they had enough confidence of the presence of the target. 500 pairs of S1–S2 stimuli were presented to each subject by means of a Stim system. The intertrial interval was 2 s. EEG was recorded at 500-Hz sampling rate, using 58 electrodes on the scalp, following an extended version of the 10–20 system, with Neuroscan® equipment. All the electrodes were referred to the left mastoid and re-referenced off-line to the linked mastoid. Impedance was maintained below 5000 Ω . Data were filtered using a band-pass of 0.01–100 Hz (1/2 amplitude low- and high-frequency cut-offs); the amplification gain was 30,000.

EOG was recorded using four electrodes placed at the external canthi of both eyes for horizontal movements, and on the inferior and superior areas of the ocular orbit for vertical eye movements.

Data were analyzed by EEGLAB v4.4 (Delorme and Makeig, 2004) under Matlab 7.0. Epochs were selected from 512 ms before the onset of the S1 and S2. Epochs exceeding $\pm 100 \mu\text{V}$ in EEG or in electro-oculogram were automatically rejected. Trial-by-trial spectral frequency content was computed with the Welch method (Hamming windowed) and separately averaged for each condition. The current density scalp spectral topographies and intracerebral neural generators of the EEG rhythms were trial-by-trial determined for theta (6–8 Hz), alpha (8–12 Hz), low-beta (14–18 Hz) and high-beta (24–28 Hz) EEG bands, and independently averaged for pre-S1 and pre-S2 conditions. Given the length of the trials (512 ms), we did not include the delta band (0.5–4 Hz) in the analysis.

To search for sources of selected bands, the data was analyzed by LORETA (Pascual-Marqui et al., 1994), as explained in Frei et al., 2001, using LORETA-KEY software. In this implementation the LORETA algorithm searches within 2394 voxels located in the cortex and hippocampus of a Talairach human brain model. Using a thresholding approach, the areas whose activities were two standard deviations over the mean of overall activity, for each band (theta, alpha, low beta, high beta) and condition (pre-S1 and pre-S2), were considered the main neural generators of these bands. This method defines the most important contributors to EEG scalp topography and has been used before to avoid the fact that, in the LORETA method, all studied voxels have a certain current density (Marco Pallarés et al., 2005).

To search for significant differences between pre-S1 and pre-S2, Holmes non-parametric method comparison, which is corrected from multiple comparison problem, was used between conditions (Holmes et al., 1996). Voxels activated in pre-S1 and/or pre-S2 following the two standard deviation criteria and showing $p < 0.05$ in the Holmes non-parametric analysis were accepted as present differences between conditions in a given spectral band. Finally, in order to study areas that present differences between pre-S1 and pre-S2 conditions, power amplitude of these areas computed using LORETA as a function of frequency (from 1 to 30 Hz) was plotted in both conditions. These graphics enabled to establish whether or not the bands modulated by preparatory attention were or not dominant ones in the studied structures.

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