Human alpha oscillations in wakefulness, drowsiness period, and REM sleep: different electroencephalographic phenomena within the alpha band

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Summary – Cortical oscillations in the range of alpha activity (8–13 Hz) are one of the fundamental electrophysiological phenomena of the human electroencephalogram (EEG). Evidence from quantitative EEG data has shown that their electrophysiological features, cortical generation mechanisms, and therefore, their functional correlates vary along the sleep-wake continuum. Specifically, spectral microstructure and EEG coherence levels between anterior and posterior cortical regions permit to differentiate among alpha activity spontaneously appearing in relaxed wakefulness with eyes closed, drowsiness period, and REM sleep, by reflecting distinct properties of neural networks involved in its cortical generation as well as a different interplay between cortical generators, respectively. Besides, the dissimilar spatio-temporal features of brain electrical microstates within the alpha range reveals a different geometry of active neural structures underlying each alpha variant or, simply, changes in the stability level of neural networks during each brain state. Studies reviewed in this paper support the hypothesis that two different alpha variants occur during human REM sleep: ‘background responsive alpha activity’, blocked over occipital regions when rapid eye movements are present, and ‘REM-alpha bursts’, non modulated by the alternation of tonic and phasic periods. Altogether, evidence suggests that electrophysiological features of human cortical oscillations in the alpha frequency range vary across different behavioural states, as well as within state, reflecting different cerebral phenomena with probably dissimilar functional meaning. © 2002 Éditions scientifiques et médicales Elsevier SAS

alpha rhythm / alpha activity / wakefulness / drowsiness / REM / quantitative EEG techniques / spectral analysis / coherence / brain microstates / humans

Résumé – Oscillations alpha au cours de l’éveil, de la somnolence et du sommeil paradoxal : différents phénomènes EEG au sein de la bande alpha. Les oscillations corticales dans la bande alpha (8–13 Hz) sont un des phénomènes electrophysiologiques fondamentaux de l’électroencephalogramme humain (EEG). L’EEG quantifié a montré que les caractéristiques electrophysiologiques, les mécanismes de génése corticale et les corrélats fonctionnels de cette activité varient le long du continuum veille–sommeil. En particulier, la microstructure spectrale et les
INTRODUCTION

The application of signal processing techniques to the human EEG together with the increased number of derivations at which cortical activity can be simultaneously recorded has provided new insights to delimit the neocortical dynamic function at a macroscopic level [82]. Cerebral rhythms dramatically vary with changes in brain state, and a close correspondence is often established between waveforms and sleep stages [92], pathologic states such as epileptic seizures [30], sleep disorders [57, 114], and coma [10, 115]. Therefore, more than 70 years after the first report concerning the human EEG, this technique remains extraordinarily useful in evaluating brain functions both in health and disease.

Since the discovery of the alpha rhythm [12], originally named ‘waves of first order’ or ‘Berger rhythm’, it became one of the fundamental features of the human EEG, as well as one of the most studied human electro-physiological phenomena. This brain activity can be easily identified by its topographic distribution (maximum amplitude over occipital regions), frequency range (8–13 Hz), and reactivity (it suffers a dramatic amplitude attenuation with the opening of the eyes) [47]. The study of alpha oscillations has generated a vast amount of literature related with physiological, maturational, clinical, and psychophysiological aspects [e.g., 29, 78, 87, 99]. This extensive work has prompted the use of quantitative measures extracted from this brain activity in the evaluation of different clinical disorders and cognitive functions.

Rhythmic activities in the alpha range also appear in human brain states different from wakefulness, specifically during the drowsiness period at sleep onset and in the rapid eye movement (REM) sleep stage. Drowsiness-alpha activity is typically characterized by decreased amplitude over occipital areas, as compared with the wakefulness-alpha rhythm, simultaneous to the appearance of a slower alpha pattern localized over anterior cortical regions [41, 97]. Short bursts of alpha activity are also observed with the naked eye during REM sleep [17, 50]. These REM-alpha bursts are always shorter than 3 s, and no increases in muscular tone and/or other electrophysiological signals of awakening appear simultaneously (figure 1). These reasons encourage their study separately from EEG arousals, since they might be a different brain phenomenon.

Despite the presence of alpha activity during normal sleep, few attempts have been made to study the electrophysiological features, cortical generation mechanisms, and functional correlates of both drowsiness and REM-alpha variants, where the term ‘alpha variants’ is equivalent to normal types of alpha activity recorded most prominently over the posterior regions of the head [47]. Whether or not a different cortical dynamic underlies the generation of each human EEG alpha variant is still an unanswered question. Evidence has demonstrated that EEG oscillations overlapping the alpha range – wakefulness-alpha rhythm and barbiturate spindles – differ in their spectral contribution, topography, thalamo-cortical coherence, and reactivity [71], suggesting that cortical oscillations within the alpha range provide a unique signature of each sleep state.
Figure 1. Examples of REM-alpha bursts (solid lines) in both phasic and tonic REM fragments. Note that this transient event is not associated to changes in muscular tone and/or followed by awakenings (Modified from 17). Electrodes displayed (frontal, central, and parietal midline, and right occipital) were referenced to averaged linked mastoids.
same spectral band are not necessarily equivalent brain phenomena.

The present review is aimed at providing electrophysiological evidence about the cortical generation mechanisms of rhythmic alpha oscillations appearing during relaxed wakefulness, drowsiness period at normal sleep onset, and REM sleep. Data derived from quantitative EEG analyses strongly suggests the activation of different brain mechanisms and, most likely, different functional roles underlie normal EEG alpha variants occurring during these behavioral states.

**BRAIN GENERATION MECHANISMS UNDERLYING THE WAKING-ALPHA RHYTHM**

Rhythmic activity within the alpha range has been described in different mammalian species (figure 2). Originally, oscillatory EEG activity such as the waking-alpha rhythm was thought to entail reverberating activity in thalamo-cortical and cortico-cortical circuits [59, 73]. Thus, the visual cortex and the lateral geniculate nucleus of the thalamus were found to generate highly coherent alpha oscillations with significant phase shifts [25, 70, 72], supporting the involvement of thalamo-cortical circuits in the generation of waking-alpha rhythm. However, electrophysiological evidence from isolated cerebral cortex determined that cortical circuits were capable of generating alpha waves quite independently of thalamic influences [56]. In addition, cortico-cortical alpha coherence values were higher than any thalamo-cortical coherence [70], and relatively independent of thalamic influences [72]. Accordingly, cortical epicentres were later found to show high coherence and consistent phase shifts within the alpha range, indicating that neuronal populations located over different cortical areas are seemingly interconnected via excitatory and inhibitory synapses during the waking-alpha rhythm generation [69].

The cortical generator sources of alpha activity are located in layer V of the occipital cortex as revealed by results from in vitro preparations [100] and in vivo recordings [68]. The latter studies found that pyramidal cells in this cortical layer generate stable synchronized oscillations between 5–12 Hz through the tonic activation of N-methyl-D-aspartate receptors by endogenous glutamate. These excitatory cells impose their rhythmic inputs onto other cortical layers and when a sufficient number of neurons in different cortical columns fire in synchrony the alpha oscillations are observed over the scalp [27, 49]. Therefore, neocortical neurons located in the layer V of the occipital cortex seem to be intrinsic alpha generators. They may receive thalamic inputs in order to maintain activation of cortical columns at an optimal level depending on the brain activation state. Considering the cortical origin of the waking-alpha rhythm, together with the fact that the EEG is due to temporal and spatial summation of postsynaptic potentials from cortical pyramidal cells [8, 98], results obtained in the above-revised studies confer a high reliability to those obtained from human scalp-recorded alpha activity by using quantitative EEG techniques.

Evidence from EEG, magnetoencephalographic (MEG) and positron emission tomography (PET) studies suggests that alpha rhythm is mainly generated over posterior brain regions [e.g., 1, 40, 93, 94, 96]. The number and exact location of occipital alpha generators remain, however, unclear. Studies using one-dipole source localization methods determined an alpha brain generator located over the midline, near the ventromedial nucleus of the thalamus [42], or more posterior and higher in the vertical plane [75]. In contrast, two equivalent dipoles symmetrically located over the occipital regions were found with a double-dipole modeling [111]. Given the lack of agreement on the existence of only one versus two homologous alpha generators, Rodin and Rodin [93] applied a two-step analysis considering both possibilities. Although results obtained by these authors supported the two-generator hypothesis, it was difficult to delimit the degree of separation of the two regional sources from the midline. Such a separation depended on the specific model used and on inter-individual variability. This latter aspect has also been recently shown by Ciulla et al. [26]. In their study, alpha MEG dipole sources over the calcarine fissure, parieto-occipital sulcus, and surrounding parieto-occipital areas were not equally present in a homogeneous sample of ten subjects. Previous MEG studies located cortical generators of the 10-Hz alpha rhythm over parieto-occipital regions [40, 96]. However, the calcarine origin of this activity was less evident than in the Ciulla et al. [26] study. Given the important role attributed to the visual cortex in alpha generation [68], possible explanations of these contradictory findings are that the calcarine fissure scarcely generates alpha activity in humans, and/or that multiple MEG alpha signals originated over the calcarine fissure may be canceled in most cases due to their specific orientations [40].
Figure 2. Waking-alpha rhythm in different mammalian species. A. Left. Raw EEG data displaying alpha oscillations in cat visual cortex (anterior part of area 18, monopolar recording) and thalamus (dorsal lateral geniculate area, bipolar recording) simultaneously. Right. Spectrogram showing a sharp 10-Hz peak resulting of analysing cat alpha rhythm recorded at visual cortex (Adapted with permission from 25). B. Left. EEG recordings of alpha rhythm (eyes closed) in dogs both in visual cortex (marginal gyrus) and lateral geniculate nucleus. Both derivations are against a common reference, and were simultaneously recorded. Right. Spectral contribution of alpha rhythm recorded in cortical and thalamic sites. Note the similar frequency peak in both spectrograms (Adapted with permission from 70). C. Left. Spontaneous EEG pattern in the range of alpha activity recorded from right parieto-occipital scalp derivations (bipolar montage) in a Rhesus monkey. Right. Spontaneous EEG frequency distribution in Rhesus monkey. Percentages of each frequency component were accumulated from recordings performed during quiet wakefulness. Note that the most prevalent frequency was 10-Hz. (Adapted with permission from 53). D. Left. Human EEG alpha rhythm recorded over the right occipital scalp region during relaxed wakefulness with eyes closed. Right. Equivalent spectrogram from the same temporal series. Note that the main spectral contribution was found in the 10 Hz frequency component, suggesting that alpha rhythm in humans and different inferior species are similar brain phenomena.
Recordings of waking-alpha rhythm over anterior scalp regions have also been extensively reported in the human EEG literature [e.g., 62, 81]. Alpha rhythm was demonstrated to peak towards slower components over the anterior than posterior cortical surface [79]. This result suggests the existence of anterior alpha generation sources with different spectral properties from those recorded over occipital regions. Lehmann [62] also proposed the existence of a fronto-central generator on the basis of the topography of alpha peak maxima in equipotential maps. An interaction between anterior and posterior cortical circuits has been consistently supported by EEG coherence studies [e.g., 20, 22, 103, 107]. This functional relationship seems to be anatomically supported by the long fronto-occipital fasciculi travelling parallel to the midline [14, 74]. It is plausible, therefore, that different cortical generators are mechanistically involved in the generation of alpha oscillations. Thus, both anterior and posterior EEG alpha patterns during relaxed wakefulness may constitute a single brain phenomenon spatially distributed over the whole scalp.

Anterior alpha patterns accomplishing to the parieto-occipital waking-alpha rhythm should be distinguished from other EEG activities appearing in the alpha frequency range with different spatial distributions, reactivity features and, most likely, different functional implications [65, 77, 86, 96, 108]. One of the most relevant activities overlapping the alpha range is the so-called mu rhythm. This rhythmic activity displays a central scalp distribution resulting from brain generators located over the somatosensory cortex, and selectively desynchronizes after somatic stimulation and/or body movements. In addition, the human mu rhythm shows a faster frequency peak than the visual-related anterior alpha pattern [e.g., 2, 85, 86, 109]. Likewise, a magnetic 8–10 Hz rhythm has also been reported over temporal regions in humans. This activity is known as tau rhythm and is only responsive to auditory stimulation. Its magnetic cortical sources are perpendicularly to the supratemporal cortical surface and dominant over the right hemisphere [65, 108]. Therefore, rhythmic oscillations overlapping the alpha frequency range are definitively present during wakefulness with different reactivity features, suggesting that alpha activity may be reflecting a common oscillatory mode of neural networks when sensory and/or higher-order processing is absent. This conclusion gives support to those studies suggesting that EEG synchronization within the alpha band may be an electrophysiological correlate of deactivated cortical areas during wakefulness state [87].

Cortical generation mechanisms of the waking-alpha rhythm have been extensively described in both animal and human literature. However, quantitative EEG studies of spontaneous alpha variants appearing during other brain states are rare and restricted to contributions extracted from spectral analysis performed to different sleep stages. Results from these studies, reviewed in the following section, indicate that alpha oscillations vary their electrophysiological features in brain states characterized by different levels of arousal.

**ELECTROPHYSIOLOGICAL FEATURES OF HUMAN EEG ALPHA OSCILLATIONS DURING WAKEFULNESS, DROWSINESS PERIOD, AND REM SLEEP**

Traditionally, quantitative EEG studies of human sleep have focused on rough descriptions of specific sleep stages [e.g., 28, 33, 34, 36, 37, 51, 95]. Considerably less effort has been devoted to the study of the electrophysiological properties of transient phenomena during normal sleep. Different EEG sleep events, overlapped in the same frequency range, may appear during the same sleep stage (delta waves versus K-complexes) or in different sleep stages (theta activity during stage 1 versus sawtooth waves during REM), pointing out the need for elaborating unambiguous quantitative description of sleep microstructure [58, 106].

The transient or so-called phasic events have been hypothesized, at least during non-REM sleep stages, to play an essential role in both sleep regulation and facilitation of a flexible contact between the sleeper and the surrounding environment [for a review, 39]. This suggests that quantitative studies of the sleep microstructure may provide a better understanding on how the brain achieves transitory arousal changes without awakenings in different brain states. Based on the assumption that a shift from a random pattern of neural activity to an oscillatory mode may be the most adequate way to accomplish a change of state [67], alpha synchronization in different cerebral states may be reflecting changes between brain macrostates or within state. Thus, both the waking-alpha rhythm and fronto-central alpha pattern typical of the drowsiness state may be electrophysiological responses associated to the change from wakefulness to sleep and to sleep-maintaining processes [90], respectively. On the other hand, we hypothesized that short bursts of alpha activity observed during REM sleep are reflecting transient
fluctuations of the arousal level without an abrupt interruption of the brain state.

Electrophysiological evidence from quantitative EEG studies indicates that the waking-alpha rhythm, drowsiness-alpha activity and REM-alpha bursts are different electrophysiological phenomena. Behavioural states are controlled by the reticular activating system, whose inputs are relayed in the basal forebrain, thalamic nuclei, and hypothalamus en route to the cerebral cortex. Since thalamo-cortical networks are under indirect control of the brainstem, cortical oscillations are expected to suffer selective modulations during different brain states [43, 104]. This neurophysiological model will guide part of our hypotheses about the cortical generation mechanisms of the different alpha variants across the sleep-wake continuum.

Spectral composition and topographic distribution of alpha oscillations in different brain states

Brain mapping techniques provide a preliminary outlook to detect broad changes in the topography of EEG activities. Using this technique, Cantero et al. [18] found that three alpha variants (wakefulness, drowsiness, and REM sleep) displayed a highly similar scalp distribution (figure 3, top). All these alpha variants peaked over occipital regions and showed a progressive decrease of spectral power towards anterior cortical areas. However, the spectral composition of the alpha band was found to be state-dependent (figure 3, bottom). Thus, spectral energy within the middle alpha range (9.5–11 Hz) significantly decreased from wakefulness to REM sleep and the fast alpha band (11.5–13 Hz) made differences between the waking-alpha rhythm and the sleep alpha variants clear. On the contrary, the spectral contribution contained in the slow alpha range (7.5–9 Hz) seemed to be independent of the brain state, suggesting common neuronal synchronization mechanisms in the cortical generation of the slowest portion of the alpha band [18].

Earlier studies dealing with the waking-alpha rhythm showed that lower (8.5 Hz) and upper (10 Hz) peaks generally have different scalp distributions [79]. Similar findings were reported with regard to the drowsiness-alpha activity. Thus, Hasan and Broughton [41] observed that the alpha pattern over anterior cortical regions reaches its maximum power at about 7–8 Hz, whereas the occipital rhythm peaks between 9.5–10 Hz. The possibility that the anterior alpha pattern was due to a passive spreading of the activity from posterior to anterior cortical sites was ruled out by using source dipole analysis. In that study, posterior alpha rhythm showed an equivalent dipole located deep in the occipital regions and horizontally oriented, whereas the dipole of slow alpha in drowsiness was more anterior, deep in the centre of the brain, and antero-superiorly oriented [41]. These results indicate the existence of two different cortical generators of drowsiness-alpha activity, which might be also active during the waking-alpha rhythm. Whether or not the inter-dependency between anterior and posterior alpha cortical sources is state-dependent will be discussed later in the light of coherence studies performed on the different EEG alpha variants.

The decrease in alpha power from wakefulness to sleep (see figure 3, bottom) has been previously reported [11, 34]. However, these studies showed controversial results about the power contribution of the alpha band across sleep stages. For instance, Dumermuth et al. [34] found that alpha power at 8–10 Hz over parieto-occipital leads was remarkably constant during sleep, suggesting that alpha activity is independent of the sleep stage. On the contrary, Benca et al. [11] reported a higher alpha power during NREM sleep when compared to REM. According to the latter authors, their results could be explained by the higher cortical activation level intrinsic to REM sleep stage. However, it is also possible that the slower frequency components of sleep spindles were masking the genuine alpha contribution during NREM. Furthermore, spectral analysis of sleep stages does not allow one to study separately contributions of EEG background and transient sleep events, making the interpretation of these studies difficult.

Determining spectral differences between cortical activities overlapping the same frequency range requires examining the EEG spectral microstructure, substituting the spectral broad band models for their high-resolution counterparts. High-resolution spectral procedures have already shown a greater sensitivity than broad band spectral models to detect abnormal oscillations in epilepsy [105], to characterize brain changes during the normal transition from wakefulness to sleep [7], or to discriminate between different types of sleep spindles [48, 113, 116]. The same strategy of analysis was recently used to differentiate between drowsiness-alpha activity and REM-alpha bursts [16]. Figure 4 shows results obtained in that study for each frequency bin (0.39 Hz) of the alpha band over different scalp regions. Frequency components between 9.7 and
Figure 3. Top frame. Topographic representation of scalp-recorded alpha activity during relaxed wakefulness, drowsiness period, and REM sleep (each map was computed using a linear interpolation algorithm with twenty-eight EEG electrodes and considering the averaged absolute power across 10 subjects). Note the same spatial distribution in all alpha variants. Bottom frame. Spectral contribution of each human alpha variant considering three alpha subdivisions (slow: 7.5–9 Hz; middle: 9.5–11 Hz; fast: 11.5–13 Hz) and different scalp areas (prefrontal, frontal, parietal, occipital, anterior and posterior temporal). (Modified from 18).
10.9 Hz showed a higher energy in drowsiness than in REM sleep, while the opposite was observed for the slowest alpha spectral bins (7.8–8.6 Hz). Accordingly, the maximum energy within the alpha band over occipital areas was circumscribed to the 10.1 Hz component during drowsiness and to the 8.6 Hz component during the REM-alpha bursts [16].

These electrophysiological differences in the spectral microstructure between sleep-alpha variants might be reflecting changes in the intrinsic properties of the cortical neuronal networks involved in the alpha activity generation during different sleep states. This hypothesis receives support from Johannisson and Nilsson’s model about the cortical generation of brain rhythms [49]. These authors hypothesized that the frequency of different cortical activities is determined by the number of cortical columns simultaneously showing the same activation level and by the period of time that each column maintains a high activation level. Both factors seem to be regulated by thalamic structures, which, in turn, receive inputs from the brainstem.

Findings reported here in relation with the different spectral contributions of alpha variants might have some practical implications in developing more reliable algorithms for automatic classification of human sleep. Automatic discrimination between stage 1 and REM sleep is one of the main obstacles to improve the reliability of these algorithms [76, 101] particularly due to the presence of ocular movements and alpha activity in both brain states. Typically, when occipital alpha activity appears during REM sleep with amplitude of 15–20 µV, the computer-based system often scores this EEG epoch as stage 1 or even as waking [60]. Therefore, results derived from studying the spectral microstructure of alpha variants in both wakefulness and REM sleep should provide some practical advantages in the automatic discrimination between these brain states provided that occipital derivations are included in the recording montage. On the other hand, clinical studies are clearly needed to confirm that REM-alpha bursts are a stable sleep event that can be electrophysiologically differentiated from normal and abnormal EEG arousals during this brain state.

Cortico-cortical interactions underlying alpha oscillations in different brain states

Cortical oscillations in the alpha frequency range showed a maximum spectral power over occipital areas.
that progressively decreased towards anterior areas independently of the brain state [18]. This topographic distribution might well be due to passive spreading of the activity through the cortical tissue from posterior to anterior locations. However, this argument has been successfully rejected by applying different quantitative techniques to the EEG alpha activity. Furthermore, anterior alpha of considerable amplitude is easily observed in normal subjects, which can transitorily show higher amplitude than posterior alpha, especially during the wake-to-sleep transition. Finally, a different frequency structure and dipole source localization of posterior and anterior alpha patterns has been reported [41].

EEG coherence technique provides an indirect and non-invasive measurement of both the strength of short-range collaterals between neocortical columns and long-range interactions through long cortico-cortical fibre tracts [80, 82, 83]. High coherence values obtained between EEG signals recorded from distant cortical areas suggest that these regions are functionally coupled with the aim of generating and/or maintaining a specific brain activity [35]. Antero-posterior coherences in the alpha range were considerably high when common [20, 22, 107] and Laplacian references were used in different studies. The latter highly eliminates the influence of volume conduction on coherence measures [103]. In addition, these long-range alpha coherences showed to be dependent on the age [103], mental activity [82], and brain state [22]. Taken together, evidence reviewed allows hypothesizing that physiological processes other than passive spreading may be determining antero-posterior interactions during the human EEG alpha generation in different normal conditions. In agreement with this assumption, the longitudinal fronto-occipital fascicle has been suggested to mediate the inter-play between anterior and posterior alpha sources during relaxed wakefulness [107].

Partial coherence analysis eliminates from each of the two signals of a pair that part that can be determined or predicted by the remaining recorded signals, which has obvious advantages as compared with the classical coherence technique [110]. Recent results using this technique further support the state-dependent interaction between anterior and posterior cortical regions in the human alpha generation [20]. In this study, the decrease of the fronto-occipital correlation during drowsiness-alpha activity was mainly observed in the posterior-to-anterior direction, suggesting that the activation of the frontal circuits involved in the generation of this sleep-alpha pattern is largely independent of the occipital populations (figure 5). Hypothetically, the activation of fronto-central alpha generators may be part of the cascade of brain mechanisms necessary for entering into sleep or maintain it. In such a case, the anterior pattern of alpha activity would be functionally related to the drowsiness process and thus independent of the waking-alpha rhythm [41, 97]. This hypothesis is consistent with the notion that anterior alpha activity is associated with sleep-maintaining processes, whereas occipital alpha activity seems to be functionally related to the waking state and, for this reason, its appearance during sleep is interpreted as an arousal response [90].

Despite the compelling argument that anterior and posterior drowsiness-alpha patterns are independent phenomena reflecting different functional correlates, it is also feasible that the activation of both fronto-central and occipital regions be a necessary brain mechanism for the alpha generation. Thus, the activation of anterior and posterior alpha sources would support the same brain functionality, the essential difference between waking and sleep alpha variants being the interplay between both cortical generators, possibly mediated by the long fronto-occipital fascicle.

Unlike the drowsiness-alpha variant, the fronto-occipital correlation during the presence of REM-alpha bursts was much higher in the posterior-to-anterior than in the opposite direction (figure 5). Presumably, occipital generators may drive the frontal genesis of this sleep event, whereas frontal circuits are unable to return information in order to complete the bi-directional fronto-occipital feedback characterizing the waking-alpha rhythm generation. A possible explanation for this phenomenon is that the cortico-cortical interactions underlying the REM-alpha bursts represent a preliminary step before reaching the connectivity pattern typical of the waking-alpha rhythm. From this perspective, REM-alpha bursts may be considered as a microarousal without awakening which may eventually facilitate sensory contact with the external environment [17].

Brain functional microstates during the generation of alpha oscillations in different brain states

In general, brain electrical activity is highly discontinuous. These discontinuities have been revealed by sequences of momentary maps of voltage distribution.
This approach consists of mapping maximum and minimum voltage peaks during moments of optimal signal/noise ratio. These extreme voltage values, which maintain a stable spatial distribution during a variable number of milliseconds, define a functional brain microstate [64]. The temporal concatenation of these electric landscapes is discontinuous, with sudden transitions from one to the next. Several consecutive landscapes with similar shape are considered as an interval of quasi-stability, or a ‘microstate’ [84]. Therefore, each brain microstate is thought to index a specific spatial configuration of neural assemblies underlying the cortical generation of a specific EEG activity [63].

The spatio-temporal characteristics of these cerebral microstates depend on factors such as the vigilance level, the nature of the external input, the ongoing brain state, the stage of cerebral development, previous experience, drug status, and mental or physical illness [55]. Recent evidence showed that features of brain microstates underlying different alpha variants were largely different, suggesting that different neural modes are involved in alpha activity generation depending on

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**Figure 5.** Topographic representation of the correlation strength between inter- and intra-hemispheric local alpha coherence during alpha rhythm in relaxed wakefulness, alpha activity at sleep onset, and REM-alpha bursts. Note the high bi-directional antero-posterior correlation during waking alpha rhythm, suggesting an active feedback between these areas, whereas an uni-directional decrease of this association level took place during the sleep alpha variants. (Modified from 20). Levels of functional association between cortical regions were obtained using a bivariate partial correlation analysis. Solid black lines represent different correlation values ($R^2$).
the brain state (waking, drowsiness or REM sleep) [21]. In this study, drowsiness-alpha activity showed the shortest mean duration of brain microstates as well as the largest amount of different microstates per second (figure 6). This result makes clear the complex geometry of the momentarily active neural elements during the alpha oscillations present in the transition to sleep, although it is also feasible that it is simply a consequence of neural instability inherent to the transitional nature of this brain state. It is also worthwhile pointing out that hypnagogic imagery of different sensory modalities appears simultaneously with drowsiness-alpha activity during the sleep onset period [46], which may affect to the different features of brain microstates as compared with wakefulness and REM sleep.

In summary, each normal variant of human EEG alpha activity reviewed here shows a different frequency composition as revealed by their spectral properties, suggesting that those physiological properties of neural networks involved in their cortical generation are state-dependent. Furthermore, different neural mechanisms seem to be involved in the generation of alpha activity in different brain states. This is supported by two sets of results: i) coherence data exhibited a functional interplay between antero-posterior cortical populations that was different for each alpha variant, and ii) the amount and duration of momentary brain microstates was also different depending on the brain state. Taken together, these results suggest that spontaneous alpha oscillations generated in relaxed wakefulness with eyes closed, drowsiness period, and REM sleep reflect different underlying physiological processes, each one presumably serving different brain functions.

**ALPHA VARIANTS DURING REM SLEEP: ELECTROPHYSIOLOGICAL PROPERTIES AND FUNCTIONAL HYPOTHESIS**

REM sleep is an inhomogeneous cerebral state characterized by the alternation of periods with oculomotor activity – phasic fragments – and without eye movements – tonic fragment –, muscular atonia, and intermixed EEG frequencies. The relation of oculomotor activity to the cognitive aspects of dreaming has been a source of speculation since late 19th century [61], and nowadays remains an open question in cognitive neuroscience. Earlier studies suggested that phasic periods are more susceptible for cognitive processing to occur, on the basis of more active [13, 89] and emotionally intense dreaming reports [31, 54] after awakenings simultaneously with the presence of rapid oculomotor activity as compared with tonic REM periods. Besides, a positive correlation between the density of oculomotor activity and visual imagery during REM sleep has also been recently reported [45]. Altogether, these findings lead to the hypothesis that background alpha activity over the visual cortex might be electrophysiologically modulated by the presence of rapid eye movements typical of phasic-REM periods, which contain a higher density and quality of visual mentation.

In agreement with this hypothesis, a blockage of REM-background alpha activity over occipital regions...
was observed during phasic periods when compared with those without oculomotor activity [23, see also 52] (figure 7, top). This effect was observed in all subjects participating in the study (see figure 3 in [19]). EEG alpha modulations during REM sleep have also been reported by Hong et al. [44], who found an attenuation of the alpha power over Broca’s or Wernicke’s area depending on the linguistic contents of dreams, being expressive or receptive, respectively. The spectral power attenuation of alpha activity during phasic REM fragments can be interpreted as an electrophysiological index of the visual features of mentation (vividness, clarity, colour saturation, and number of visual features) generated by the dreaming brain, in spite of the absence of significant positive correlation between oculomotor activity and visual imagery previously reported in the literature [88]. Unfortunately, the absence of dreaming reports in the Cantero et al.’s study [23] precludes the possibility of concluding about the relationships between the presence of rapid eye movements and mentation features during REM sleep. On the other hand, it is also feasible that the decrease of alpha power simultaneously with REM-phasic periods found in several studies [23, 52] is a mere manifestation of a higher level of arousal associated to oculomotor fragments as compared with tonic periods. Supporting this hypothesis are those studies demonstrated a positive correlation between autonomic variables and bursts of rapid eye movements [32, 102], and a significant decrease of cardiac activity simultaneously with REM-tonic periods [112]. Both hypotheses would become complementary if a close association between bursts of oculomotor activity and dream intensity was experimentally confirmed.

Alpha power attenuation during phasic REM fragments was selective for the alpha activity extracted from the REM-background EEG activity. In fact, REM-alpha bursts showed neither electrophysiological or topographical modulations when tonic and phasic REM fragments were compared [19] (figure 7, bottom).

REM-alpha bursts have a shorter duration than alpha associated with arousals, and are not accompanied by any polygraphic signs of arousal reactions and/or brain state shifts (figure 1). Spontaneous bursts of alpha activity during human REM sleep without indication of arousal or awakening were firstly reported by Johnson [50]. These authors also determined that alpha responses to auditory stimuli were clearly different depending on the brain state. Thus, sensory stimulation during REM state evoked an increase in alpha activity to the naked eye, whereas the opposite happened during relaxed wakefulness (see figure 2 in [50]). Therefore, this alpha pattern is more similar to a micro-arousal (without awakening) during REM sleep, which has been hypothesized to facilitate the momentary contact with the external environment without alterations in the REM continuity [17].

This electrophysiological phenomenon might be achieved by momentary changes in the activation level of the reticular activating system, which, in turn, would transiently alter the ongoing dynamic of both corticothalamic and cortico-cortical circuits directly responsible for the generation of alpha oscillations. The main difference between waking-alpha rhythm and REM-alpha bursts may be the completion of the fronto-occipital feedback loop, which would probably lead to an awakening during REM sleep [20]. REM-alpha bursts may index short temporal windows during which the brain is highly susceptible for processing external sensory information, and is capable of reaching the wakefulness state in a faster and more adaptive manner. This hypothesis is supported by those studies in which the activation of an enhanced response in the neocortex was initiated by pyramidal cells in layer V – where alpha oscillations are generated and dynamically modulated by the behavioral state [24]. Hypothetically, the same explanation might be valid for the REM-alpha bursts, although it needs to be experimentally tested. In agreement with this explanation, the intrusion of short bursts of alpha activity during REM sleep may contribute, at least partially, to the improved information processing observed during this brain state in comparison with slow wave sleep [3-6, 9, 66, 91], as well as to the incorporation of external stimuli into the dream contents [15, 31].

Obviously, the dual functional role of alpha activity during REM sleep hypothesized here generated conceptual problems. The cortical deactivation interpretation associated to an increase in alpha synchronization might be restricted to wakefulness, since the presence of alpha activity during human sleep has been classically interpreted as an increase in the arousal level. However, REM-alpha bursts do not lead to an awakening, although they might be reflecting an increase in the arousal level without sleep disruption which simultaneously could facilitate a full awakening if the stimulus was relevant enough for the organism. Interestingly, alpha activity contained in the EEG background showed a power attenuation associated
with prominent bursts of rapid eye movements as compared with REM periods without oculomotor activity, suggesting that the cortical EEG dynamics (synchronization versus desynchronization) inherent to this alpha variant is modulated by different internal or external inputs, although in this case it is easier to think that internal rather than external commands are guiding these electrophysiological changes over the occipital cortex. But still, the possibility that spectral modulations of background alpha activity have nothing to do with dreaming features associated with the REM phasic periods should not be disregarded. One alternative explanation for these results is provided by the same rule that is applied to the microarousals during NREM sleep [38]. Thus, higher arousal levels evoke microarousals with desynchronization, while lower ones are associated with EEG synchronization. From this point of view, the ‘background alpha blocking’ phenomenon observed during REM-phasic periods would be indicative of a higher arousal than that evoked by the

![Figure 7. Scalp distribution of REM-background alpha activity (upper frame) and REM-alpha bursts (bottom frame) selected from tonic (left maps) and phasic (right maps) REM EEG segments. A similar scalp distribution of REM-alpha bursts in both fragments contrasts with the power suppression over occipital regions of the background alpha simultaneously with the appearance of prominent rapid eye movements (Adapted with permission from [19]).](image-url)
presence of the REM-alpha bursts in both tonic and phasic periods.

In summary, two variants of alpha activity seem to coexist during human REM sleep: 'background responsive alpha activity', blocked over occipital regions when rapid eye movements are present, and 'REM-alpha bursts', showing the same spectral and topographic features both in tonic and phasic fragments. Although this categorization of REM alpha activities generates some conceptual problems, because of increases and decreases of alpha power denote quantitative and qualitative different brain modes (sleep versus wakefulness, respectively) or even different levels in the hierarchy of micro- arousals not yet determined in REM sleep, also provides a quantitative description of different EEG alpha patterns in human REM sleep not available in the literature to date.

CONCLUSIONS

The study of microstructural aspects of human sleep provides insights not only about how the brain works in each state, but also about the dynamic pattern of cerebral activities supporting that functioning.

Evidence indicates that electrophysiological properties of waking and sleep-alpha variants are markedly different, suggesting that alpha oscillations do not reflect a unique brain phenomenon. Although quantitative findings reported here come from human scalp recordings, mainly reflecting cortical dynamics at a macroscopic level, additional modulation is probably occurring at the thalamic level, mediated by the reticular activating system in the brainstem. In fact, this latter influence is essential to alter the degree of cellular membrane polarization in thalamic nuclei, which, in turn, modulates the dynamic of thalamo-cortical networks involved in the generation of cerebral rhythms, depending on the behavioral state.

The different spectral composition of waking and sleep-alpha variants suggests that some properties of the neuronal circuits responsible for generation of the alpha oscillations are modulated by the behavioral state. Furthermore, long-range cortico-cortical dependence relationships contributing to the alpha generation are also state-dependent, as revealed by EEG coherence findings. The antero-posterior cortical dynamic during the spontaneous alpha oscillations provides an illustrative demonstration of how the brain state can alter the functional relationship between cortical generators within the same frequency range. In addition, a distinctive geometry of active neural structures, or simply, different levels of neural stability also characterizes each alpha variant here considered, as reflected by spatio-temporal features of brain microstates.

Although the presence of alpha activity during REM sleep has been observed since the earliest studies, the origin of this contribution has been traditionally attributed to EEG arousals. Systematic studies of short bursts of alpha activity, not associated with awakenings, clearly demonstrated that they may be mainly responsible for the alpha contribution observed in quantitative EEG studies of human REM sleep. Differential spectral modulation of REM-alpha bursts versus background-alpha activity during tonic and phasic fragments of REM sleep feeds the hypothesis that both alpha variants should have independent roles, encouraging their functional differentiation in further studies.

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