Relationship between Delta, Sigma, Beta, and Gamma EEG bands at REM sleep onset and REM sleep end

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Abstract

Objective: The aim of the present study was to analyze in detail the relationship of two newly introduced measures, related to the Beta and Gamma EEG bands during REM sleep, with Delta and Sigma activity at REM sleep onset and REM sleep end, in order to understand their eventual role in the sleep modulation mechanism.

Methods: For this purpose, power spectra of 1 EEG channel (C4, referred to A1) were obtained by means of the fast Fourier transform and the power of the bands ranging 0.75–4.50 Hz (Delta), 4.75–7.75 (Theta), 8.00–12.25 (Alpha), 12.50–15.00 (Sigma), 15.25–24.75 (Beta), 25.00–34.75 (Gamma 1), and 35.00–44.75 (Gamma 2) was calculated for the whole period of analysis (7 h), in 10 healthy subjects. Additionally, two other time series were calculated: the ratio between Beta and Gamma2, and between Gamma1 and Gamma2 (Beta and Gamma ratios). For each subject, we extracted 3 epochs of 30 min corresponding to the 15 min preceding and the 15 min following the onset of the first 3 REM episodes. Data were then averaged in order to obtain group mean values and standard deviation. The same process was applied to the 30-min epochs around REM sleep end.

Results: The course of the Delta band around REM sleep onset was found to be characterized by a first phase of slow decline lasting from the beginning of our window up to a few seconds before REM onset; this phase was followed by a sudden, short decrease centered around REM onset, lasting for approximately 1.5–2 min. At the end of this phase, the Delta band reached its lowest values and remained stable up to the end of the time window. The Sigma band showed a similar course with stable values before and after REM sleep onset. The Beta and Gamma ratios also showed a 3-phase course; the first phase, in this case, was characterized by stable low values, from the beginning of our window up to approximately 5 min before REM onset. The following second phase was characterized by an increase which reached its maximum shortly after REM sleep onset (approximately 1 min). In the last phase, both Beta and Gamma ratios showed stable high values, up to the end of our time window. At REM sleep end, the Delta band only showed a very small gradual increase, the Sigma band presented a more evident gradual increase; on the contrary, both Beta and Gamma ratios showed a small gradual decrease.

Conclusions: The results of the present study show a different time synchronization of the changes in the Delta band and in Beta and Gamma ratios, at around REM sleep onset, and seem to suggest that the oscillations of these parameters might be modulated by mechanisms more complex than a simple reciprocity. All these considerations point to the fact that REM sleep can be considered as a complex phenomenon and the analysis of high-frequency EEG bands and of our Beta and Gamma ratios represent an additional important element to include in the study of this sleep stage. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Sleep; REM sleep; EEG power spectrum; High-frequency EEG bands; Beta band; Gamma band; Fast Fourier transform

1. Introduction

After the publication of the study by Llinás and Ribary (1993) who reported an important increase in 40-Hz magne-toencephalographic activity during REM sleep, interpreted as a correlate of cognitive processes taking course during this sleep stage, in recent years, the study of the scalp-recorded EEG activities as fast as 15–30 Hz (Beta and Gamma bands) has received particular attention because they show a time course opposite to that of the delta band, reaching their maxima during REM sleep, when the slow-wave activity shows its minima (Aeschbach and Borbély,

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1993; Röschke and Mann, 1994; Uchida et al., 1992, 1994; Merica and Blois, 1997).

More recently, the study of the spectral content of all-night sleep recordings obtained in healthy young subjects was extended in order to include frequencies up to 45 Hz (Ferri et al., 2000). In this way it was demonstrated that the power of the EEG frequencies between 15 and 35 Hz was positively correlated with the occurrence of REM sleep; on the contrary, the power of the EEG band between 35 and 45 Hz showed an opposite behavior being lower during REM than during non-REM sleep. In the same study, the use of the ratio between Beta (15–25 Hz) or Gamma1 (25–35 Hz) and Gamma2 (35–45 Hz) was introduced in order to approach better the analysis of REM-related scalp EEG activities.

The aim of the present study was to analyze the relationship of these new measures with Delta and Sigma activity at REM sleep onset and REM sleep end, in order to understand their eventual role in the sleep modulation mechanism.

2. Subjects and methods

2.1. Subjects and sleep recording

Ten healthy females aged 18–20 years participated to this study. Polysomnography (EOG, EMG of the submentalis muscle, EEG from at least 3 derivations: F3 and/or F4, C3 and/or C4, and O1 and/or O2, all referred to the contralateral mastoid) was performed in all of them for two consecutive nights following one adaptation night; however only data from the second recording night were used for further analysis. Signals were sampled at 128 Hz and stored on hard disk; for each subject, the C4 derivation (referred to A1) was used for all the following computational steps. Sleep stages were scored following standard criteria (Rechtschaffen and Kales, 1968) on 12-second epochs, the same epochs were used for the following spectral analysis. This epoch length was chosen in order to match carefully visual and spectral analyses; visual scoring was based on the rules of the Rechtschaffen and Kales manual (1968) which admits epochs as short as 20 s. However, the basic epoch for spectral analysis, in this study, was only 4 s long (see below). We chose epochs of 12 s in order to obtain a time window wide enough to apply reliably the rules of Rechtschaffen and Kales (1968) but closer to the spectral analysis epoch length than the classical 20-s or 30-s epochs.

2.2. EEG spectral analysis

For each recording, power spectra were calculated, after Hanning windowing, by means of the fast Fourier transform for consecutive 4-s epochs, during the first 7 h of sleep and the mean values for consecutive 12-s epochs were then obtained by averaging 3 consecutive 4-s epochs. Finally, the power of the bands ranging 0.75–4.50 Hz (Delta), 4.75–7.75 (Theta), 8.00–12.25 (Alpha), 12.50–15.00 (Sigma), 15.25–24.75 (Beta), 25.00–34.75 (Gamma 1), and 35.00–44.75 (Gamma 2) was calculated for a total of 2100 data points (number of 12-s epochs in 7 h) representing the whole period of analysis. Data were then smoothed by means of a simple 3-point moving average method. Both averaging and smoothing allowed us to reduce the effects of the eventual presence of transient non-stationarities in the EEG spectral content. Finally, we also computed two additional time series: the ratio between Beta and Gamma2 (Beta ratio), and between Gamma1 and Gamma2 (Gamma ratio) (Ferri et al., 2000).

2.3. Data analysis

The software developed for the analysis of the spectral content of the whole night multichannel sleep EEG recording allowed us to visualize the results relative to the entire spectrum up to 45 Hz; however, in this study attention was focused on 4 parameters: delta and sigma band power, Beta ratio and Gamma ratio (Ferri et al., 2000).

Moreover, for each recording, we extracted 3 epochs of 30-min corresponding to the 15 min preceding and to the 15 min following the onset of the first 3 REM episodes. Data from the different subjects were then averaged in order to obtain group mean values and standard deviation. In this way, a total of 12 averages corresponding to Delta and Sigma power, Beta ratio and Gamma ratio for the first 3 REM sleep episodes were obtained.

In the same way, 12 additional averages were obtained for the 15 min preceding and the 15 min following the end of the first 3 REM episodes.

3. Results

Fig. 1 shows, as an example, the all-night time course of the Delta band power, Sigma band power, Beta ratio and Gamma ratio in one of the subjects included in this study. In this figure, it is possible to note that, as already described in our previous report (Ferri et al., 2000), there is a negative relationship between the course of Delta and that of both Beta and Gamma ratios, which appear to be opposite in phase. As expected, the time course of the Delta band shows a pseudocyclic pattern with peaks during non-REM sleep and, in particular, during slow-wave sleep, with an overall tendency to decrease in amplitude during the night (Borbély, 1982). Also the Sigma band shows a pseudocyclic pattern with peaks during non-REM sleep; however, its peaks precede those of the Delta band and do not show an overall tendency to decrease in amplitude through the night.

On the contrary, the time course of Beta and Gamma ratios appears clearly correlated with the occurrence of REM sleep periods in the hypnogram with minima during non-REM sleep. The first peak in Beta and Gamma ratios is synchronous with the occurrence of the first REM sleep period in 7 subjects; in the remaining 3 – as already reported in the above mentioned previous study carried out by our
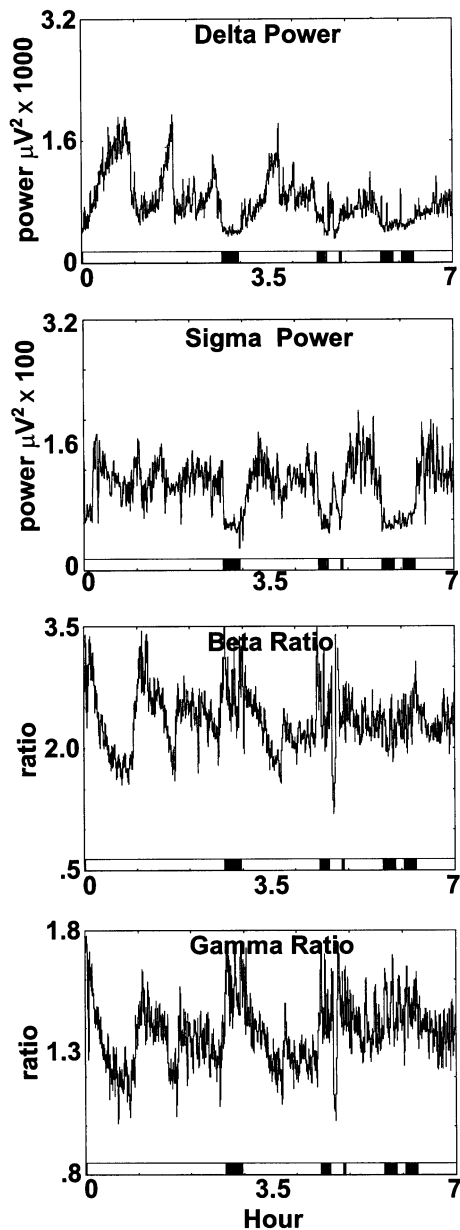
Fig. 1. All-night time course of the Delta band power, Sigma band power, Beta ratio and Gamma ratio in one of the subjects included in this study. At the bottom of each diagram a bar indicates the occurrence of REM sleep (black).

group – in whom the first REM period, expected at around 90–100 min from sleep onset, was not seen in the sleep polygraphic recording, the peak in Beta and Gamma ratios was nevertheless present. The subject in Fig. 1 is one of them.

Fig. 2 shows, in detail, the group average changes (and standard deviation) in the Delta and Sigma bands power around the onset of the first 3 REM sleep episodes; in this figure, and in the following ones, also ± standard deviation values are displayed. It is possible to note that the power of the pre-REM Delta band declines from the first to the third episode; on the contrary, the pre-REM average power of the

Sigma band does not decline in subsequent periods. The course of the Delta band around REM sleep onset is characterized by a first phase of slow decline lasting from the beginning of our time window (−15 min) up to a few seconds before REM onset; this phase is followed by a sudden, short decrease centered at REM onset, lasting for approximately 1.5–2 min. At the end of this phase, the Delta band reaches its lowest values and remains stable up to the end of the time window (+15 min). The behavior of the Sigma band seems to be simpler with a stable level during the pre-REM period followed by a sudden, short decrease centered around REM onset, lasting for approximately 2–3 min. Also the Sigma band shows its lowest values during the REM phase and remains stable up to the end of our time window.

Fig. 3 shows that, on the contrary, the REM values of both Beta and Gamma ratios do not change in the different episodes. However, Beta and Gamma ratios show a 3-phase course different from that of the Delta and Sigma bands. The first phase, in this case, is characterized by stable low values, from the beginning of our window up to approximately 5 min before REM onset. The following second phase is characterized by a clear increase which reaches its maximum shortly after REM sleep onset (approximately 1 min). In the last phase, both Beta and Gamma ratios show stable high values, up to the end of our time window.

Fig. 4 shows the changes in the Delta and Sigma bands power around the end of the first 3 REM sleep episodes. The Delta band shows only small changes, mostly represented by a small increase starting at REM end, preceded by stable low values during REM. The Sigma band power shows a similar behavior but its increase is more pronounced than that of the Delta band.

Fig. 5 shows the values of both Beta and Gamma ratios around the end of the first 3 REM sleep episodes. The changes shown by these two parameters near the end of the REM episodes are less pronounced than those observed at REM sleep onset and are represented by a slow decrease throughout the entire time window.

4. Discussion

REM sleep is generated by a complex mechanism in which brainstem structures play a key role (Siegel, 1985); in particular, lesion studies have shown that REM sleep is suppressed by the destruction of the nucleus reticularis pontis oralis (Sastre et al., 1981; Friedman and Jones, 1984). Moreover, pontine REM sleep-on and REM sleep-off cells have been reported by unit recording studies (Sakai, 1980; Shiromani et al., 1987). On the contrary, the more subtle role that non-brainstem structures might have in the generation of REM sleep has certainly received less attention, although REM sleep in brainstem isolated animals carries some significant differences from REM sleep of
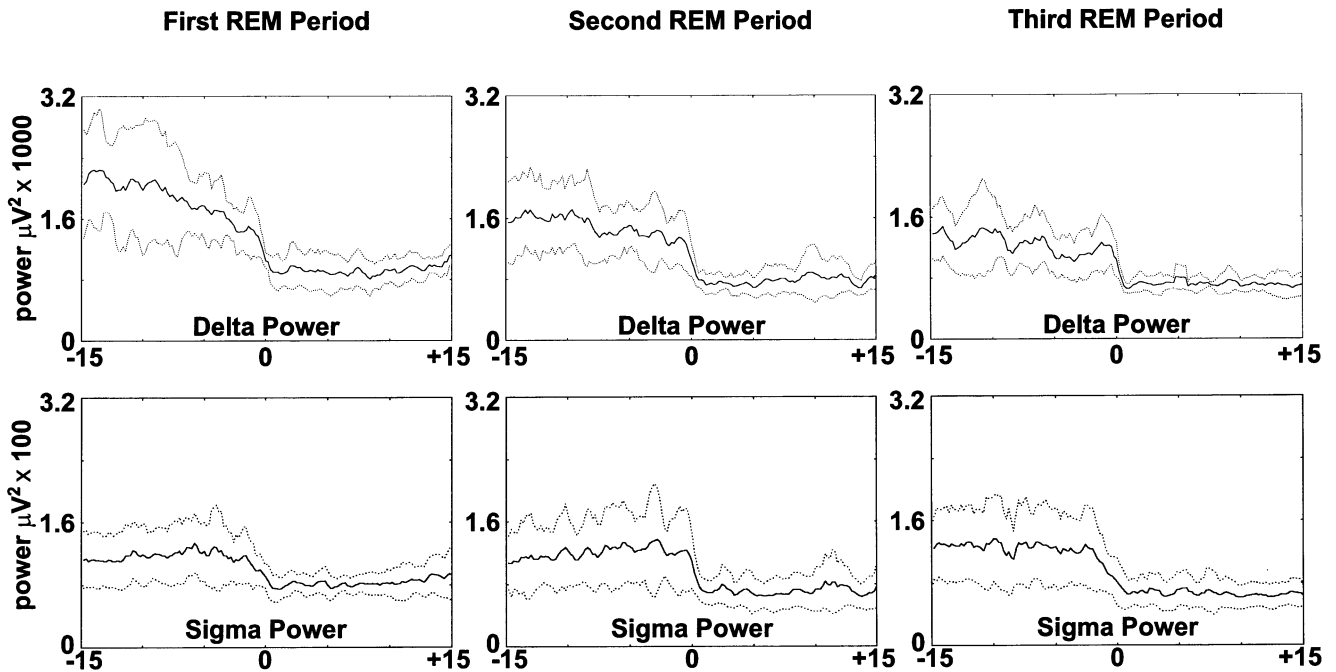
First REM Period   **Second REM Period**   **Third REM Period**

Fig. 2. Group average changes in the Delta and Sigma bands power around the onset of the first 3 REM sleep episodes. Also ± standard deviation values are displayed.

the intact animal (Hoshino et al., 1976; Jouvet, 1962) and a role for cerebellum and frontal cortex in REM sleep mechanisms has been demonstrated (Gadea-Ciria, 1976; Morrison and Bowker, 1975). More recently, Steriade (1997) showed that fast spontaneous oscillations depend on the depolarization of thalamic and cortical cells which

appear in a sustained manner during waking and REM sleep. In this author's view, corticothalamic neurons, discharging high-frequency spike-bursts at 30–40 Hz, can be considered as good candidates to synchronize fast oscillations in reentrant thalamocortical loops.

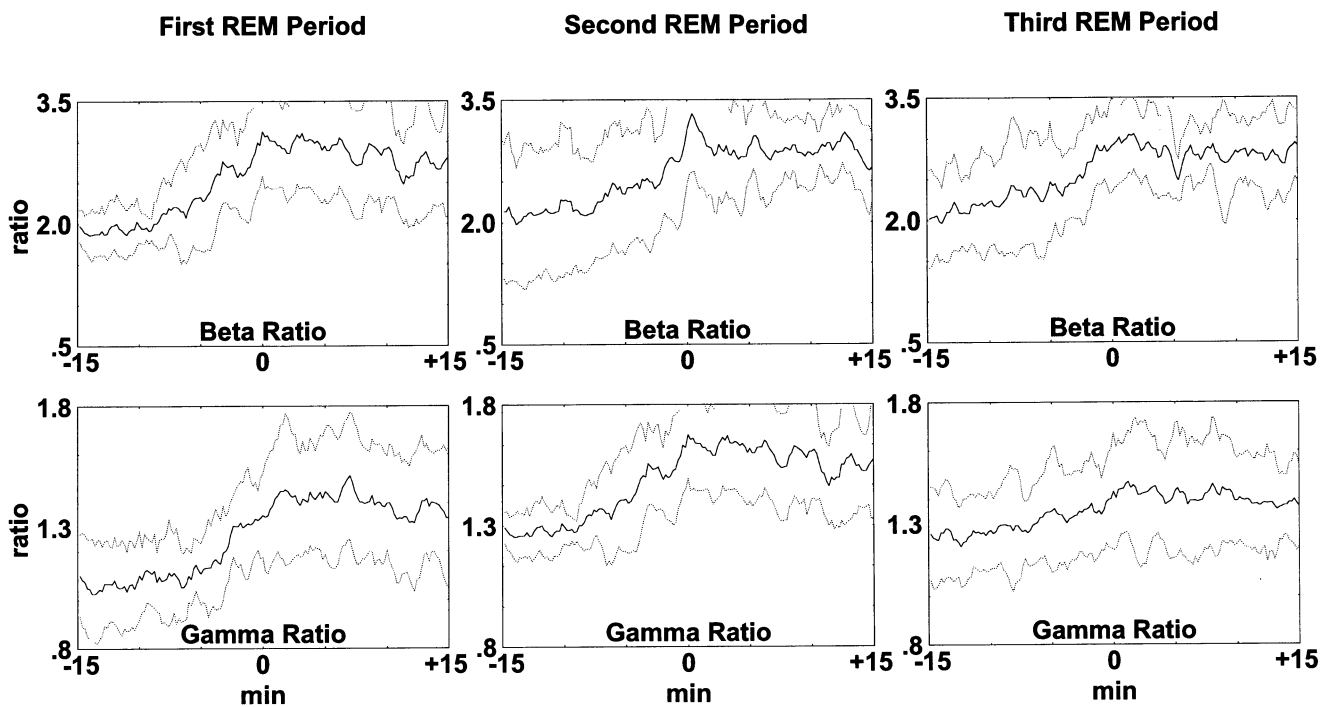Scalp-recorded fast EEG activities during sleep (15–30

First REM Period   **Second REM Period**   **Third REM Period**

Fig. 3. Group average Beta and Gamma ratios around the onset of the first 3 REM sleep episodes. Also ± standard deviation values are displayed.

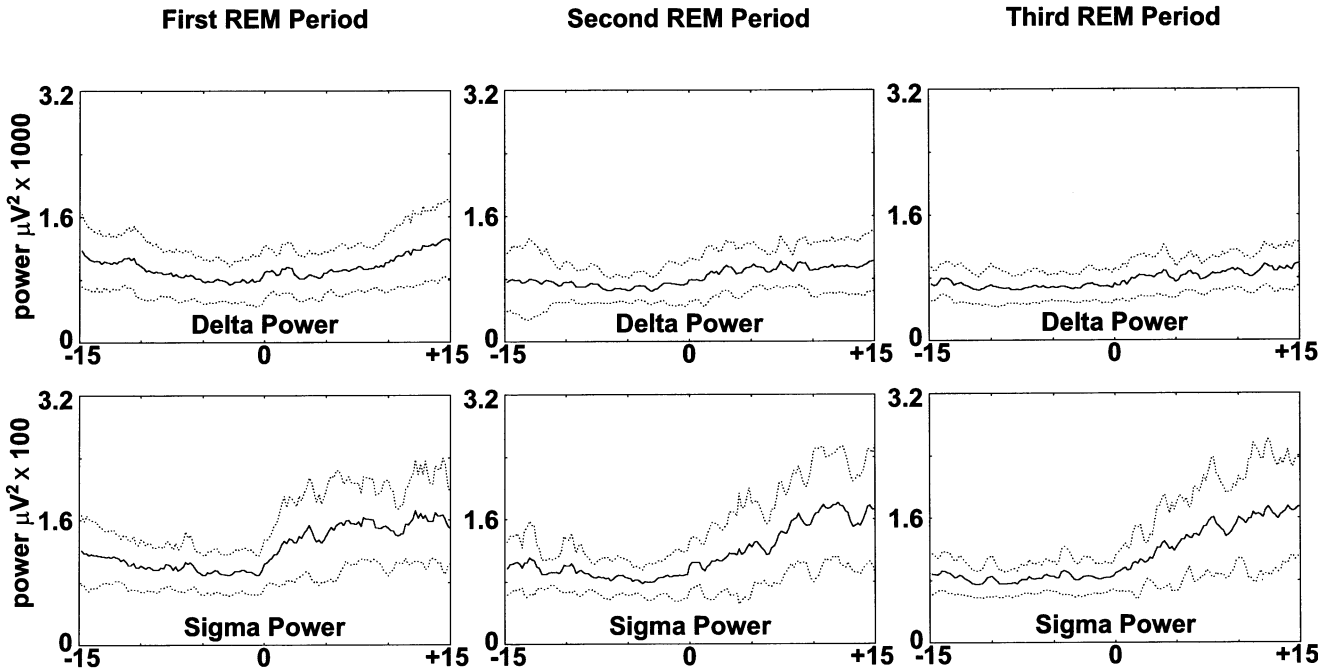**First REM Period**　　　**Second REM Period**　　　**Third REM Period**

Fig. 4. Group average changes in the Delta and Sigma bands power around the end of the first 3 REM sleep episodes. Also ± standard deviation values are displayed.

Hz) seem to show a behavior opposite to that of the delta band, reaching their maxima during REM sleep, when the slow-wave activity shows its minima (Aeschbach and Borbély, 1993; Röschke and Mann, 1994; Uchida et al., 1992, 1994; Merica and Blois, 1997). In a previous study (Ferri et al., 2000), we extended this analysis up to 45 Hz in order to detect also eventual changes at around 40 Hz in the scalp-recorded EEG, similar to the 40 Hz oscillations seen by magnetic field recording (Llinás and Ribary, 1993) and demonstrated that the power of the scalp-recorded EEG in the band between 35 and 45 Hz shows only small oscillations which we interpreted as being essentially correlated
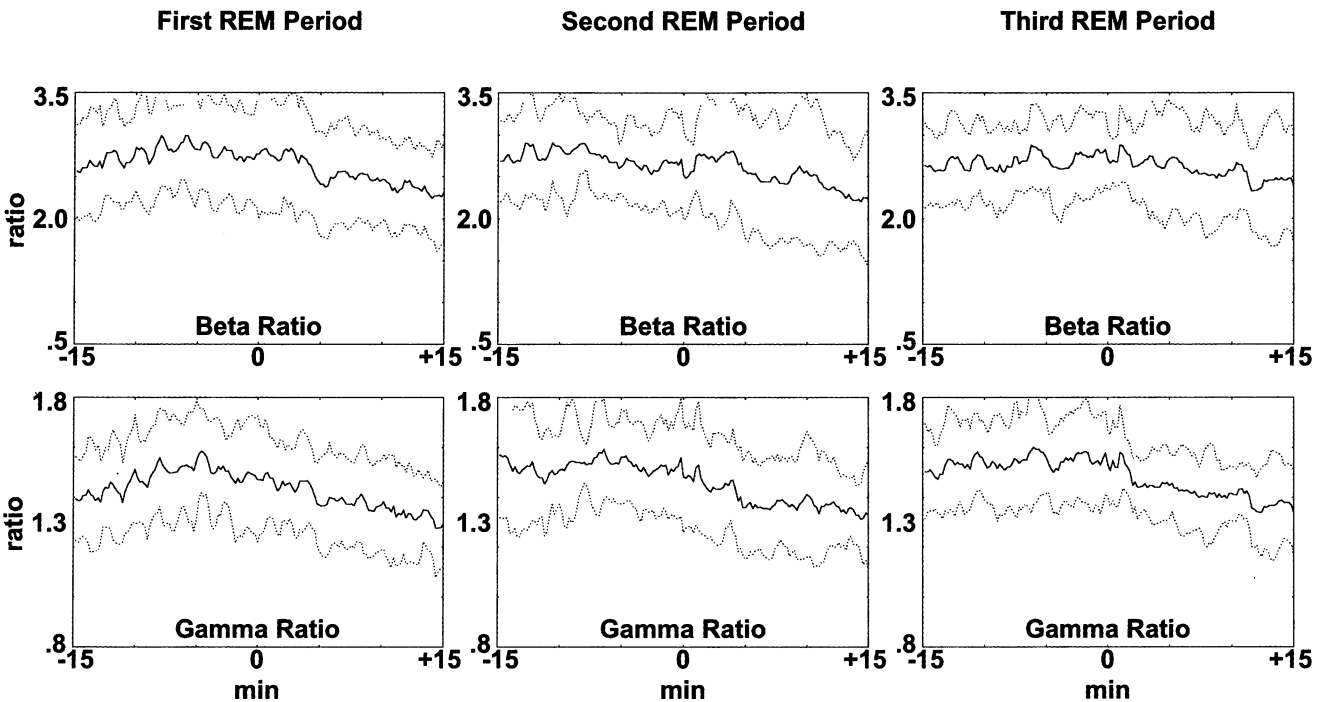
First REM Period　　　**Second REM Period**　　　**Third REM Period**

Fig. 5. Group average Beta and Gamma ratios around the end of the first 3 REM sleep episodes. Also ± standard deviation values are displayed.

with the muscle tone artifact, which is lower during REM sleep and higher during non-REM sleep. This allowed us to use the same band in order to increase the signal-to-noise ratio in the other two high-frequency bands (Beta and Gamma1) – which, on the contrary, tended to show their maxima during REM sleep – by calculating the ratio between them. Thus, we emphasized in an effective way the small changes shown by the EEG power in these bands and proposed this new measure as a tool to be used in the analysis of high-frequency sleep potentials. The results of the present report clearly confirm those obtained in the previous study (Ferri et al., 2000) in a larger group of normal subjects.

In the present paper we report 3 subjects in whom the first REM period, expected at around 90–100 min from sleep onset, was not seen in the sleep polygraphic recording, the peak in Beta and Gamma ratios was nevertheless present. This phenomenon was also reported in our previous study on the same topic (Ferri et al., 2000). In intracranial EEG in humans (Gross and Gotman, 1999), gamma activity was reported to be higher during REM sleep with eye movements than during REM sleep without eye movements. Even if we did not correlate our results with the presence or absence of eye movements, our results seem to be different because we could observe a clear increase in Beta and Gamma ratios also in the absence of polygraphic REM sleep.

This finding is also interesting because it is possible to speculate that some of the dream-like mentation occurring during non-REM sleep (Cicogna et al., 2000), in some subjects and during the first part of night sleep, might be correlated to the increase in Beta and Gamma ratios.

The beta band and Beta and Gamma ratios show a clear reciprocity of oscillation with the Delta band (Uchida et al., 1992; Ferri et al., 2000) and this has been interpreted as an indication that all these bands are strictly correlated and regulated by a common mechanism. There is experimental evidence that thalamocortical neurons may oscillate either in the delta or sigma frequency range depending on their membrane potential (Steriade et al., 1993c; Contreras and Steriade, 1995) during non-REM sleep. The results of the present study showing a different time synchronization of the changes in the Delta band and in Beta and Gamma ratios, around REM sleep onset, seem to suggest that the oscillations of these parameters might be modulated by mechanisms more complex than a simple reciprocity, with REM sleep onset being preceded by an increase in Beta and Gamma ratios longer (5–6 min) than the sudden drop in the Delta band. Also the results of the analysis centered at REM sleep end support this idea and show clearly different, non-reciprocal changes in the band studied.

It should be mentioned, at this point, that the Delta band considered as a whole in our study has been shown to comprise two different oscillatory types – slow (<1 Hz) and delta (1–4.5 Hz) – at a cellular level (Steriade et al., 1993a,b,c) and in the human sleep EEG (Achermann and

Borbély, 1997). Also these two types of activity were reported to show different evolution: power of the delta waves declined from the first to the second non-REM sleep episode; on the contrary, power below 1 Hz remained unchanged (Achermann and Borbély, 1997).

Recently, it was suggested that the periodic occurrence of arousal complexes known as 'Cyclic Alternating Pattern' (CAP) is involved in the genesis and modulation of the Delta EEG activity (Terzano and Parrino, 2000). In this view, the increase in cortical synchronization during the first part of non-REM sleep might be the result of the slow oscillations induced by the CAP phases A1 (K-complex sequences and delta bursts) (Ferrillo et al., 1997). On the contrary, the transition from non-REM to REM sleep, corresponding to the period of progressive increase in rapid rhythms and of decrease in slow-wave activity observed in the present study, seems to be associated with a repetitive low-amplitude rapid EEG pattern (i.e. the CAP phases A2 and A3) (Terzano et al., 2000). Following this hypothesis, our findings might be considered as a demonstration of how the neurophysiological mechanisms determining the occurrence of REM sleep periods start during the last part of NREM sleep; on the contrary, the mechanisms responsible for non-REM sleep show a sudden fall at REM sleep onset. At a cellular level, it has already been shown that ponto-geniculo-occipital waves and activation in thalamocortical neurons occur before REM sleep, when EEG still shows slow waves (Steriade et al., 1989).

On the contrary, the process by which REM sleep is substituted by non-REM seems to be subserved by a different pattern of changes in EEG bands power. In this case there is no sudden modification of the parameters considered but a slow return of the Sigma band, mainly, with the Delta band showing only a small progressive increase, almost parallel to the slow decrease in Beta and Gamma ratios. Also in this case, our findings seem to be in agreement with the fact that CAP and, in particular, its A1 phases – responsible for the build-up of slow-wave activity – are at their lowest level during the first minutes following REM sleep (Terzano et al., 2000).

In conclusion, the results of this study clearly show that further research is needed in order to construct a reliable model for understanding the complexity of sleep regulation and that the models based only on its low-frequency components (Borbély, 1982) can be considered as being incomplete (Ferri et al., 1996, 1998). The analysis of high-frequency EEG bands and of our Beta and Gamma ratios represent an additional important element to include in such a study.

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