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Arousal thresholds during human tonic and phasic REM sleep

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SUMMARY The goal of the present study was to investigate arousal thresholds (ATs) in tonic and phasic episodes of rapid eye movement (REM) sleep, and to compare the frequency spectrum of these sub-states of REM to non-REM (NREM) stages of sleep. We found the two REM stages to differ with regard to behavioural responses to external acoustic stimuli. The AT in tonic REM was indifferent from that in sleep stage 2, and ATs in phasic REM were similar to those in slow-wave sleep (stage 4). NREM and REM stages of similar behavioural thresholds were distinctly different with regard to their frequency pattern. These data provide further evidence that REM sleep should not be regarded a uniform state. Regarding electroencephalogram frequency spectra, we found that the two REM stages were more similar to each other than to NREM stages with similar responsivity. Ocular activity such as ponto-geniculo-occipital-like waves and microsaccades are discussed as likely modulators of behavioural responsiveness and cortical processing of auditory information in the two REM sub-states.

KEYWORDS arousal threshold, EEG, frequency analysis, microsaccades, phasic REM, tonic REM

INTRODUCTION

Being able to wake up upon external stimulation enables an organism to react adequately to danger signals. Rapid eye movement (REM) sleep is accompanied by several phenomena that increase the vulnerability and endangerment of an organism against external threat. In REM sleep, we lose the ability for temperature control and our gravitational muscles become atonic, which, at least theoretically, lessens our ability to react quickly to danger cues and which puts the organism at a disadvantage in terms of its ability to carry out a fight or flight response (Cannon, 1929). However, published reports on behavioural arousal thresholds (ATs) in REM sleep are inconclusive. Only few studies actually find lowered responsivity in REM sleep (Bonnet *et al.*, 1978; Townsend *et al.*, 1976; Williams *et al.*, 1964). Most reports show equal (Keefe *et al.*, 1971; Okuma *et al.*, 1966; Pisano *et al.*, 1966; Watson and Rechtschaffen, 1969; Williams *et al.*, 1966) or even lower ATs in REM compared with sleep stage 2 [non-REM (NREM) stage 2; Arkin *et al.*, 1966; Cobb *et al.*, 1965; Langford *et al.*, 1974], suggesting that, in spite of atonia and poikilothermia, the organism is relatively easy to arouse from REM sleep. Because ATs in REM sleep are relevant for theoretical deliberations about its function, it is important to investigate possible mediating factors or methodological issues leading to these discrepant findings.

Common to almost all studies on ATs in REM sleep is the neglect to distinguish between tonic and phasic intervals. Tonic REM sleep refers to the state of widespread, low-voltage, fast electrocortical activity with hippocampal theta, a decrease in neck and chin electromyogram (EMG) amplitude, and brain temperature elevation (Baust *et al.*, 1964; Pessah and Roffwarg, 1972; Rechtschaffen, 1978). Phasic REM sleep characterizes those periods in which distinct oculomotor activity (REMs) as well as middle-ear muscle activity, extra-ocular phasic integrated potentials and cardiorespiratory irregularities occur (McCarley and Hobson, 1975; Sallinen *et al.*, 1996). These two REM states are mediated by separate yet interactive neuroanatomical loci (McCarley and Hobson, 1975). Moreover, phasic REM sleep periods include distinctive oculomotor activity (REMs) that is associated with ponto-geniculo-occipital (PGO) waves (Callaway *et al.*, 1987; Datta and

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Hobson, 1994; Lim *et al*., 2007). PGO waves are a feature of REM sleep, which are generated or propagated in the pontomesencephalic tegmentum. In the presence of PGO waves, higher cortical processing of external stimuli is inhibited (Lim *et al*., 2007; Miyauchi *et al*., 2009; Wehrle *et al*., 2007). PGO waves immediately precede saccadic and microsaccadic activity in REM sleep (Amzika and Steriade, 1996; Fernandez-Mendoza *et al*., 2009; Martinez-Conde *et al*., 2009), and it is quite possible that perceptual inhibition is still active during those phases in which REMs occur.

It is, thus, likely that the discrepant findings concerning the behavioural ATs in REM sleep are related to the neglected discrimination between phasic and tonic periods of REM sleep. The goal of our study was to test this hypothesis by measuring responsiveness to acoustic stimuli during all stages of sleep, and partitioning REM sleep into phasic and tonic intervals. In addition to behavioural data, we compare frequency spectra of sleep stages with similar behavioural ATs.

MATERIALS AND METHODS

Participants

The study was approved by the local ethics committee of the Medical Faculty of the Goethe-University Frankfurt am Main, Germany. Written consent was obtained prior to the study and subjects were free to withdraw from participation at any time.

Twelve volunteer participants (six female, six male) between the ages of 20 and 40 years (mean age 27.25 years) were recruited from the medical student population at the Goethe-University of Frankfurt. Subjects were screened for health problems, medication use and abnormal sleep/wake schedules. They received 50 Euro as compensation for participation. Exclusion criteria included history of a psychiatric disorder, evidence of a sleep disorder, history of a chronic somatic illness (e.g. cardiovascular, pulmonary, haematologic, hepatic or renal disease), absence of an acute illness, and past or current substance abuse. Audiometry was performed on all subjects at the clinic for otorhinolaryngology at the Goethe-University of Frankfurt. All subjects were able to reliably detect 1000 Hz tones at an intensity of 30 dB. As part of the screening process, each subject filled out standardized questionnaires on depression, anxiety and sleep quality, prior to the study. Questionnaires used were the Beck-Depression-Inventory (BDI), Beck-Anxiety-Inventory (BAI), Pittsburgh Sleep Quality Index (PSQI), and Sleep Questionnaire A and B ('Schlaffragebogen A/B' SF-A, SF-B).

Two subjects were excluded from data analysis because their scores on the PSQI were suggestive of a sleep disorder (PSQI total score > 5), so that data from 10 subjects (five females, five males) were included in the analysis.

Polysomnographic procedure and stimuli

On two consecutive nights, the subjects slept in the sleep laboratory in the Department of Neurology at Goethe-University. Standard PSG was recorded on both nights, first-night PSGs were utilized to screen for sleep disorders and to compare frequency spectra of the electroencephalogram (EEG) during the different NREM sleep stages and phasic and tonic REM. Recordings were made from approximately 23:00 hours to 07:00 hours.

Polysomnography recordings were performed using Comlab 32 Digital Sleep Lab, Brainlab V 3.3 Software, Schwarzer GmbH, Munich, Germany. EEGs were recorded from two channels (C3, C4) referenced to linked mastoids. Electrooculogram was taken from the outer canthi of both eyes and supraorbitally to the left eye. EMG electrodes were placed submentally. Acoustic stimuli were presented through earphones, using commercially available software (Presentation 11.0, Presentation Software, Neurobehavioral Systems, Inc., Albany, CA, USA). Behavioural responses were recorded through a microswitch taped to the palm of the subjects' preferred hand. EEG impedances were kept below 5 kΩ. Data were sampled at 200 Hz, and the band width was set to 0.5–70 Hz for the EEG.

The PSG recordings were monitored online for classification of sleep stages according to the Rechtschaffen and Kales (1968) criteria. Acoustic stimuli were presented during sleep stages NREM 2–4, and REM sleep at several times throughout the night. As sleep scoring guidelines such as those of Rechtschaffen and Kales (1968) do not provide criteria for defining phasic and tonic sub-states within REM sleep, we chose to classify epochs as tonic REM sleep when REMs were absent for at least 15 s prior to a 30-s epoch. Likewise, REMs had to have been absent for a minimum of 15 s before stimulus presentation was initiated in this stage. During phasic REM sleep, stimulus presentation was always initiated during a REM burst. Acoustic stimulation consisted of 1000-Hz tone series, beginning at 35 dB, increasing in 5-dB steps up to 100 dB. The mean number of awakenings performed in each sleep stage is listed in Table 1. Tones were separated by 10-s intervals. Subjects were instructed to push the microswitch attached to their hand to disrupt further presentation of the tone series.

Data analysis

Behavioural ATs

Data were analysed with a repeated-measures analysis of variance (ANOVA), with sleep stage as factor (NREM stages 2–4,

Table 1 Mean number of arousals in each sleep stage during night 2

	n	*Mean*	*SE*
Sleep stage 2	10	5	0.67
Sleep stage 3	10	7	0.89
Sleep stage 4	10	8	0.80
Phasic REM	10	7	0.86
Tonic REM	10	4	0.49

REM, rapid eye movement.

REM phasic, REM tonic) and mean dB-level as dependent variable. *Post hoc* comparisons were conducted with repeated-measures *t*-tests (statistical software: SPSS version 17.0, SPSS Inc., Chicago, Illinois, USA).

Evoked micro-arousals and alpha activity

Presentation of auditory stimuli during sleep has been shown to be accompanied by state-dependent changes in EMG and PGO-like activity in the cat (Wu *et al*., 1989). Moderate acoustic stimulation evokes PGO-like activity in all states, but suppresses EMG activity during phasic REM and enhances it during NREM sleep and waking (Wu *et al*., 1989). To test if the differences in the observed behavioural motor responses in tonic versus phasic REM sleep may be related to a confounding enhancement of EMG atonia during REM sleep, we analysed background alpha power and the frequency of micro-arousals in the 10-s interval between tone presentations during night 2. Alpha power is independent of EMG activation and has been reported to be suppressed in phasic compared with tonic REM sleep (Cantero *et al*., 2000). By contrast, micro-arousals in REM sleep per definition (ASDA criteria, Bonnet *et al*., 1992) go along with an EMG enhancement. Sleep stage-specific differences in the occurrence of micro-arousals would, thus, be suggestive of a modulatory effect of EMG inhibition on the behavioural response. Specifically, we would expect phasic REM sleep to have the lowest number of arousals because PGO activity is at a maximum in this stage. Micro-arousals in phasic REM sleep had to be significantly lower than in sleep stage 4 and also than in tonic REM sleep.

Frequency analysis

In order to investigate whether the difference in responding between tonic and phasic REM sleep was related to selective activation in specific frequency bands, we analysed the scalp activity (power) in frequency bands δ (1–4 Hz), θ (4–8 Hz), α (8–12 Hz), β (12-20 Hz) and γ (36–45 Hz).

Power analyses based on the Fast Fourier Transform (FFT, Hanning windowing) inform about state-specific variations in activity within a given frequency band of the EEG. For data analyses, EEG records (no tone presentations) were partitioned into 1-min epochs with 30 s overlap. All data were corrected for ocular artefacts using the Gratton *et al*. (1983) algorithm before statistical analysis. If, following this correction procedure, eye movements were still detectable upon visual inspection, these epochs were excluded from further analysis. A bandpass filter was applied (0.5–70 Hz) and a notch filter set at 50 Hz. The filtered signal was baseline corrected (range for mean value calculation = 0–60 s) and subjected to an automatic artefact rejection procedure (maximum allowed voltage step = 50 μV, maximum and minimum amplitude = 400 μV, maximum allowed absolute difference of values in the segment = 600 μV, lowest allowed activity = 0.5 μV). Frequency analyses of bands δ, θ, α, β and γ are based on first-night EEG recordings. Additional analyses were performed for α power during the 10-s interval between stimulus presentations during night 2.

Statistical analyses were performed for mean standardized FFTs (dependent variable) to facilitate between-subject comparisons. Standardization was achieved through normalization of power over the 0.5–45-Hz range, yielding the relative distribution of activity on the individual spectral lines. Hence, for each epoch of the EEG, the sum of power values from all frequency bins equals 100%.

RESULTS

Standard sleep measures, such as total sleep time, time spent in stage 2 and slow-wave sleep, were inconspicuous in all subjects during the first night in the laboratory. BDI and BAI scores were also normal. Analysis of first-night recordings gave no indication of a sleep disorder in either participant (Table 2).

Behavioural ATs

A repeated-measures ANOVA with sleep stage as factor (NREM 2–4, REM phasic, REM tonic) and mean dB level as dependent variable yielded a significant effect for sleep stage ($F = 5.9$, df = 4, 5, $P < 0.05$), with a strong effect size ($\eta_p^2 = 0.83$). Inner subject contrasts (polynomials) showed a significant quadratic trend ($F = 24.60$, $P < 0.001$, $\eta_p^2 = 0.76$), indicating a linear increase in thresholds across NREM stages 2–4 and phasic REM sleep, and an attenuated threshold in tonic REM sleep. This distribution is shown in Fig. 1. Concerning contrasts (repeated-measures *t*-tests) between single sleep stages, phasic REM sleep and stage 4 sleep are both elevated over stage 2 and tonic REM sleep. Sleep stage 2 ATs are statistically indifferent from tonic REM sleep ATs (Table 3). Behavioural threshold in phasic REM sleep is higher than in stage 4 sleep, on a descriptive level only.

Table 2 Mean sleep measures during night 1

	n	*Mean*	*SE*
Sleep stage 2 (% SPT)	10	55.10	1.82
SWS (% SPT)	10	22.75	2.60
REM (% SPT)	10	15.13	2.16
WASO (% SPT)	10	7.02	1.40
SOL SS2 (min)	10	18.00	1.76
TIB (min)		418.64	9.93
SPT (min)		391.35	17.76
TST (min)		363.95	17.53
Sleep efficiency (TST/TIB)		86.84	1.24

REM, rapid eye movement; SOL SS2, sleep onset latency sleep stage 2; SPT, sleep period time (time from sleep onset to morning awakening); SWS, slow-wave sleep; TIB, time in bed from lights out to lights on; TST, total sleep time (NREM + REM sleep); WASO, wake after sleep onset.

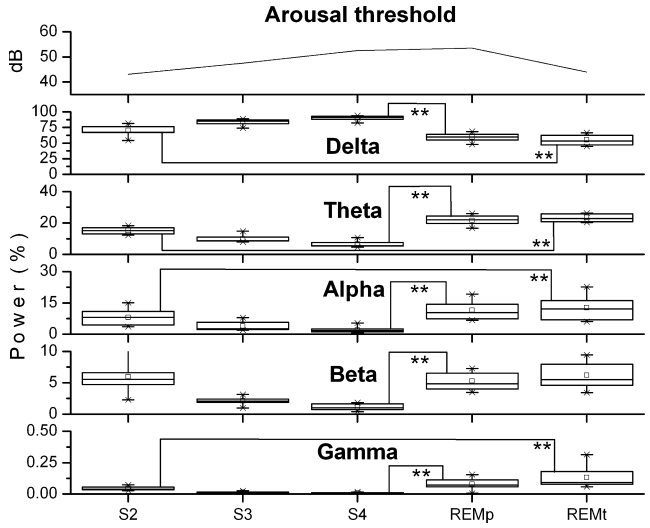

Figure 1. Top row: mean behavioural ATs across sleep stage 2, NREM 3 and 4, and phasic and tonic REM sleep. $n = 10$. Rows 2–6: box plots of mean standardized power in frequency bands δ, θ, α, β and γ in each sleep stage. REM, rapid eye movement. $^{**}P < 0.01$; $^{*}P < 0.05$.

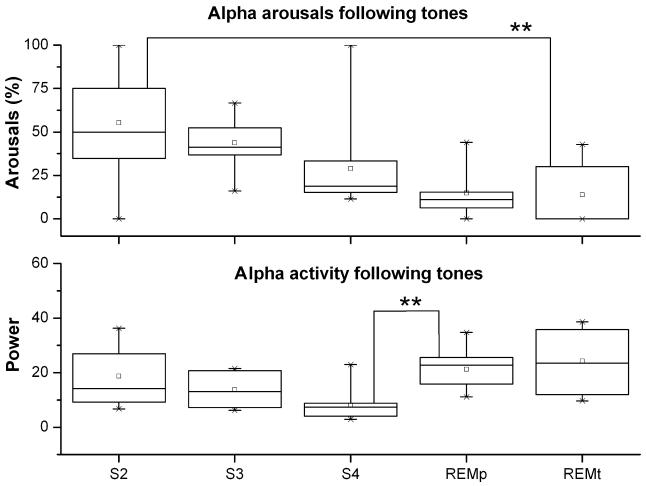

Figure 2. Top row: box plots of mean micro-arousals following tone presentation in each sleep stage. Bottom row: box plots of mean absolute power in the α frequency band following tone presentation in each sleep stage. $^{**}P < 0.01$; $^{*}P < 0.05$.

Table 3 Contrasts in behavioural ATs (repeated-measures *t*-tests) between selected sleep stages

Sleep stage	*t*	*df*	*P*
Sleep stage 2 versus stage 4	5.05	9	< 0.01**
Sleep stage 2 versus stage 3	2.73	9	< 0.05*
Sleep stage 2 versus REM phasic	3.60	9	< 0.01**
Sleep stage 2 versus REM tonic	0.37	9	n.s.
Sleep stage 4 versus REM phasic	0.34	9	n.s.
Sleep stage 4 versus REM tonic	3.47	9	< 0.01**
REM phasic versus REM tonic	3.77	9	< 0.01**

REM, rapid eye movement.

Background alpha activity and micro-arousals in response to tone presentations

A repeated-measures ANOVA showed a significant sleep stage effect for alpha band power ($F = 6.74$, $P = 0.05$, df = 4, 5, absolute power). In agreement with the literature (Nishida *et al.*, 2005), alpha band power was significantly elevated in phasic REM sleep compared with sleep stage 4 ($t = 5.47$, df = 9, $P < 0.01$). Phasic and tonic REM sleep had similar levels of alpha frequency band activity (Fig. 2, bottom row).

Regarding micro-arousal frequency, a repeated-measures ANOVA was calculated with the relative frequency of arousals (%) as the dependent variable and sleep stage as the independent variable.

The effect for micro-arousals was not significant. As can be seen from Fig. 2 (top row), micro-arousals occurred in response to tone presentations in all sleep stages. Descriptively, the mean number of arousals decreased linearly across NREM sleep stages 1–4 and REM sleep (phasic and tonic). Contrary to expectations, micro-arousals were lowest in tonic REM, not in phasic REM, sleep. Further, an explorative analysis (repeated-measures *t*-tests) of between-stage contrasts did not confirm the hypothesis of higher arousal frequency in sleep stage 4 compared with phasic REM sleep.

Of course, micro-arousals and background alpha activity represent only indirect measures of EMG suppression. However, our findings suggest that, at least in this sample, selective enhancement of atonia during REM sleep was not the major factor determining behavioural responsiveness to tones.

Frequency analysis of night 1 (no tone presentation)

Repeated-measures ANOVA yielded significant effects for each frequency band, with $P < 0.01$ (Pillai Spur) in all multivariate analyses (delta: $F = 593.55$, $\eta_p^2 = 0.99$; theta: $F = 105.60$, $\eta_p^2 = 0.99$; alpha: $F = 13.78$, $\eta_p^2 = 0.90$; beta: $F = 25.23$, $\eta_p^2 = 0.94$; gamma band: $F = 19.24$, $\eta_p^2 = 0.93$; df = 4, 6). Repeated-measures *t*-tests were calculated for the contrasts of phasic and tonic REM sleep to test if the frequency pattern in these two stages may account for the observed differences in ATs. For the same reason, we looked at contrasts between stages of similar ATS, i.e. tonic REM versus stage 2 sleep, and phasic REM versus stage 4 sleep.

The frequency spectra of stage 4 and phasic REM sleep show a significantly different activation in all frequency bands, in spite of similarly elevated ATs in both stages (Table 4). Regarding the differences between the two REM stages, tonic REM sleep has higher activity in frequency bands theta, beta and gamma, and lower activation in the delta frequency band.

Because the amount of low-frequency band activity is a marker of sleep depth and high-frequency activation indicates cognitive processing of external events (Fries *et al.*, 2007; Voss

Table 4 Repeated-measures *t*-statistics on frequency band-specific power in selected sleep stages (df = 9)

Frequency band	*δ*	*θ*	*α*	*β*	*γ*
Sleep stage	*t*	*t*	*t*	*t*	*t*
Sleep stage 2 versus tonic REM	11.09**	11.81**	4.70**	0.39	3.46
Sleep stage 4 versus phasic REM	27.76**	15.04**	8.43**	9.33**	5.33**
Phasic versus tonic REM	2.59*	2.13	1.43	2.40*	2.80*

REM, rapid eye movement.
*$P < 0.05$, **$P < 0.01$.

et al., 2009), this pattern of activation is suggestive of deeper sleep in phasic REM compared with tonic REM sleep.

As can be seen from Fig. 2, tonic REM sleep closely resembles phasic REM but not sleep stage 2, although behavioural thresholds in tonic REM are more similar to sleep stage 2. Only in the beta band do we see a correspondence between sleep stage 2 and tonic REM sleep.

DISCUSSION

Our data show that tonic REM sleep has a similar threshold to NREM stage 2 sleep, replicating previous results (Price and Kremen, 1980). Phasic REM sleep has the highest behavioural AT, followed by stage 4 sleep. The behavioural data are not reflected in frequency band-specific activity, however, in that NREM and REM phases of similar ATs differ substantially in their frequency spectra. The two REM stages diverge strongly with regard to behavioural ATs and are very similar in their frequency spectra. This result shows that there is a clear distinction between behavioural responsiveness and EEG-measured brain activity. As evoked alpha activity and micro-arousals are similar in the two stages, selective EMG suppression during phasic REM sleep is not a likely explanation of this dissociation.

We, therefore, argue that REM sleep must be differentiated into tonic and phasic epochs. Further, we consider it likely that other factors such as stimulus-evoked ocular activity modulate the behavioural response.

Arousal thresholds

Phasic REM sleep represents a state with maximal environmental shielding (disconnection from the external world), hence a most vulnerable phase of sleep.

Our AT data illustrate the high threshold for awakenings during phasic REM sleep using a behavioural approach. A previous functional magnetic resonance imaging (fMRI) study showed for the first time that within human REM sleep, widespread thalamocortical synchronized activity occurs selectively enhanced during phasic REM sleep when compared with predominantly tonic REM sleep background (Wehrle *et al*., 2007). Llinas and Paré (1991) proposed that the brain works as a closed thalamocortical loop during REM sleep. Our data as well as fMRI data showing reduced processing of external stimuli during phasic REM sleep may specifically confine this model to phasic REM sleep periods. From an evolutionary point of view this transition appears beneficial, as phasic REM sleep constitutes an extremely vulnerable state lacking both sensory input and executive control of reactions due to general muscle atonia. Phasic REM sleep activations usually appear in short bursts, avoiding prolonged periods of time in this isolated state, whereas tonic periods may be beneficial to detect potential danger cues.

If phasic REM sleep constitutes such an isolated state in which external stimuli are not processed cortically, the question arises why we were still able to awake our subjects, even though awakening required more intense stimulation than in other sleep stages. We speculate that even the differentiation of phasic and tonic REM sleep is only a vague approximation of the true differences within REM sleep. Assuming that the initiation of PGO waves is the controlling factor in arousability during REM sleep, blocking stimulus processing during its execution, the relative long-stimulus duration used in our study (1 s) must have outlasted this inhibitory effect (Datta and Hobson, 1994). Although during phasic REM sleep our stimuli were initiated during REM bursts, this method can only be considered a rough approximation of underlying ocular activity. We hope that an improved methodology to measure not only saccadic but also microsaccadic activity in sleep will allow us to test this hypothesis in the future.

Frequency-specific activity in phasic and tonic REM sleep

Regarding EEG pattern in the different stages of NREM and REM sleep, we find that ATs cannot be matched with activity in specific frequency bands. Although, for example, stage 4 and phasic REM sleep have similarly elevated ATs compared with all other sleep stages, we found significant differences in all frequency bands analysed. Except for delta power, which was elevated in stage 4 sleep, all frequency bands were significantly more activated in phasic REM sleep. Regarding the pattern of frequency-specific activation in sleep stages with similarly low ATs, tonic REM sleep and sleep stage 2, we also find differing activity in all bands except beta. The highest gamma activity was observed for tonic REM sleep. This could be interpreted as evidence of higher awareness of the external world in tonic REM sleep compared with all other sleep stages, with atonia preventing this awareness to be fully translated into a behavioural response. However, as recent studies suggest, gamma band activity may be confounded by microsaccades and cortical muscle activity (Trujillo *et al*., 2005; Whitham *et al*., 2007; Yuval-Greenberg *et al*., 2008), both of which were not assessed in the current study or any other published study that we have knowledge of. We consider it likely, given the strong oculomotor activity present in REM sleep, that the increase in gamma band activity in tonic REM

sleep may indeed be related to stronger microsaccadic activity in this sleep stage compared with sleep stage 2 (Wu *et al*., 1989).

The only reliable effect of frequency-specific activation that was evident in all stages of sleep concerned delta activity. The comparison of phasic REM versus tonic REM sleep, and stage 4 versus stage 2 sleep showed significantly elevated delta band power in stages of elevated ATs, i.e. stages 4 and phasic REM sleep. This indicates that these two stages represent the deepest of sleep stages, accompanied by the highest inhibitory strength towards external stimulation.

Behavioural responsiveness and brain activation

The strong difference between responding in the two sub-states of REM sleep cannot be sufficiently explained by dissimilarities in their respective frequency spectra. Likewise, the similarity in behavioural responsiveness during stage 2 and tonic REM sleep, or stage 4 and phasic REM sleep is not reflected in the respective frequency spectra. This suggests that other – state-related – factors must modulate the behavioural and/or brain response. A possible candidate exhibiting such a confounding effect is stimulus-evoked ocular activity, such as microsaccadic ocular activity and PGO waves. Several authors have shown that microsaccades and PGO-like waves are related and that they vary as a function of sleep phase, i.e. NREM and REM sleep (Callaway *et al*., 1987; Chase and Morales, 1990; Miyauchi *et al*., 2009; Stuart and Conduit, 2009; Trujillo *et al*., 2005). It is currently not known, however, whether these ocular events constitute a mere artefact that influences levels of EMG inhibition (Chase and Morales, 1990; Wu *et al*., 1989) or whether they are related to differential inhibition of higher order information processing (Martinez-Conde *et al*., 2009; Voss *et al*., 2009; Wehrle *et al*., 2007).

The lower fast-frequency band activity during phasic REM sleep observed in our study suggests that a heightened AT in phasic REM sleep is related to reduced attentiveness to the external environment. However, the behavioural effect might also be modulated by different levels of EMG inhibition in the two REM stages (Chase and Morales, 1990; Wu *et al*., 1989), preventing a behavioural responding but not information processing. We tried to investigate this possibility indirectly by analysing alpha arousals in the absence of concurrent EMG changes, and by comparing alpha power following tone presentations in the two REM stages. We found no evidence of a selective EMG inhibition during the two REM stages in our data. We, therefore, assume that microsaccadic activity and PGO waves exert their primary inhibitory influence on inhibition of higher order information processing of external sensorial information. This interpretation is supported by imaging (Wehrle *et al*., 2007) and evoked potential data (Sallinen *et al*., 1996) showing a lowered REM-P3 response to auditory stimuli presented in phasic versus tonic REM sleep. However, the final resolution of this issue awaits the availability of an exact measurement device for microsaccadic activity in human sleep.

The results of our study are limited by the fact that we analysed broad EEG frequency bands from one derivation across a whole night. Future studies should use a multi-channel EEG that allows for better spatial and temporal information (see Montgomery *et al*., 2008 for regional frequency band differences in rats; see Nishida *et al*., 2005 for spatial differences in REM stage activity in humans).

In summary, our results show that studies on REM sleep should partition REM into tonic and phasic episodes because both strongly diverge with respect to their interaction with the external world. Phasic REM sleep responding is similar to stage 4 responsivity, and tonic REM sleep ATs approximate those in sleep stage 2. We further show that, except for delta activity, the behavioural response is not reliably characterized by frequency-specific activation in the EEG, suggesting that the NREM–REM distinction clearly marks the existence of two separate states, unrelated to behavioural responsiveness to external stimulation. The two REM stages have a very similar pattern in spite of diverging behavioural responsiveness to external stimuli, and stages of similar responsivity do not reliably share frequency-specific increases or decreases in activation. We assume that inhibitory and excitatory activation is related to oculomotor activity, and that this oculomotor activity is a better predictor of reactivity to the external world than specific frequency band activity. We are currently working on an improved method to examine saccadic and microsaccadic activity in sleep, and look forward to putting our hypotheses about inhibition of information processing as a function of ocular activity to the test.

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