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Research Article

Association between Hemispheric Asymmetry and Horizontal Rapid Eye Movements during Rapid Eye Movement Sleep

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Summary

Objective: The origin and functional importance of rapid eye movements (REMs) during REM sleep in humans has not been completely understood. It is interesting that REMs occur simultaneously with dreaming during REM sleep and central nervous system activation. In the present study, we aimed to measure the directional properties (amplitude and angular values) of horizontal REMs (hREMs), determine their relationship with age, explain the anatomical and physiological basis of REMs, and contribute to the concept of hemispheric asymmetry.
Method: Using standard procedures, 25 subjects (age range, 19-70 years) were recorded during one night of spontaneous sleep. hREM distribution analysis to the right and left, hREM angular values, and hREM amplitude means were compared during an REM period of one night.
Result: Statistical analysis revealed no significant results that would indicate a hemispheric asymmetry.
Conclusion: The findings suggested that no hemispheric dominance can be demonstrated for REM sleep, REMs, or dream. Although some studies have demonstrated the dominance of one hemisphere over the other, others have advocated (also supported by our study) that both hemispheres function in coordination.

Key words: REM sleep, horizontal rapid eye movement, hemispheric asymmetry

REM Uykusundaki Horizontal Hızlı Göz Hareketlerinin Hemisferik Asimetri İle İlişkisi

Özet

Amaç: İnsanlarda REM uykusunda oluşan hızlı göz hareketlerinin (HGH) fonksiyonel önemi ve orijini tam anlaşılamamıştır. HGH'nin, REM uykusunda rüya görme ve merkezi sinir sistemi aktivasyonuyla eşzamanlı görülmesi ilginçtir. Bu çalışma; REM uykusunda oluşan horizontal hızlı göz hareketlerinin (HHGH) yöneliş-amplitüt-açısal değerlerini ölçmeyi, yaşla ilişkilerini, hızlı göz hareketlerinin temelindeki anatomik, fizyolojik mekanizmaları açıklamayı ve hemisferik asimetri kavramına katkı sağlamayı amaçlamaktadır.
Yöntem: Yaşları 19-70 arasında değişen 25 denek bir gecelik spontan uyku esnasında standart prosedürler uygulanarak kayıtlandı. Bir gecelik REM periyodunda sağa ve sola HHGH dağılım analizi, HHGH açısal değerleri ve HHGH amplitüt ortalamaları karşılaştırıldı.
Bulgular: Yapılan istatistiki değerlendirmeyle hemisferik bir asimetriyi gösterecek anlamlı bir sonuç elde edilmedi.
Sonuç: REM uykusu, HGH ve rüya için dominant bir hemisfer göstermek mümkün gözükmemektedir. Çalışmaların bir kısmı sağ hemisfer bir kısmı sol hemisfer üstünlüğünü ortaya koymaya çalışırken diğer kısım ki (bizim çalışmamızda bunu desteklemekte) iki hemisferin koordineli çalıştığını savunmaktadır.

Anahtar kelimeler: REM uykusu, horizontal hızlı göz hareketleri, hemisferik asimetri

INTRODUCTION

Sleep is a reversible state of behavior and consciousness in which the organism becomes detached from the environment, with reduced perception and reaction. Sleep has been the subject of many studies both in terms of its mechanisms and its functions. Sleep is still not understood completely since the time electrical activity of the brain during sleep was recorded by a galvanometer eight decades ago (1,2). Especially, studies in the 20th century have demonstrated that sleep is a dynamic, active state under the control of complicated mechanisms.

Functional importance and origin of rapid eye movements (REMs) that occur during REM sleep in humans has not been completely understood. It is interesting that REMs occur simultaneously with dreaming during REM sleep and central nervous system activation (3). Measurement and comparison of orientation-amplitude-angular values of horizontal REMs (hREMs) may provide important information for understanding the oculomotor system during sleep and cerebral dominance. On the other hand, it may also elucidate the pathological mechanisms of cortical-subcortical structures that modulate the oculomotor activity, especially the pontine premotor areas that produce REMs during REM sleep.

MATERIAL AND METHODS

SUBJECTS

Twenty-five subjects (age range, 19-70 years), most of who were hospital personnel and people accompanying patients, were included in this study. The subjects had no history of neurological disease, and their neurological examinations were normal.

SLEEP STUDY RESULTS

The subjects were recorded in the EEG laboratory of our clinic during one night of spontaneous sleep. Recording was started at 00.00 and was continued for 8 h. Recording was terminated early in subjects who woke up and wanted to get up before the end of recording process.

Electrodes were inserted in accordance with the International 10-20 Montage system in polysomnography (PSG). Two-channel EEG (C4-A1 and C3-A2); 1-channel EOG, where the right and left eyes were referred to each other, and 1-channel chin EMG were used. The recordings were made using Nihon Kohden-5208 EEG device, which operates with alternative current. EEG and chin EMG were recorded via Ag-AgCl disc electrodes. An earth electrode was placed on the glabella. In all recordings, a band pass filter of 35 Hz was used at a paper speed of 10 mm/s.

The subjects were advised to not use sedative or stimulating medications or liquids at least 1 week before PSG. It was ensured that such medications and liquids were not used during the night of recording as well. The subjects were also advised to avoid daytime sleep on the day of recording.

EYE MOVEMENT RECORDINGS

hREMs during wakefulness and REM sleep were recorded via monopolar Ag-AgCl electrodes attached next to the outer epicanthi of each subject in one channel of EEG device (Image 1). Records were made with a sensitivity setting of 50 μv and a time constant of 5.0 s.

A proximal vision analysis (calibration) was performed before sleep, with each subject informed beforehand about what to do. T-square with a line (visual target-initial position) at a distance of 35 cm from the subject's pupillae and with side targets at 30° to the right and left of the line was used. T-square was placed with a leg perpendicular to each subject's philtrum. The subject was told to look at 30° to the right of the target in the initial position with eyes open, then at the target in the initial position, and then again at the target on the right successively till measurable EOG deflections were obtained (Image 2). The same procedure was repeated for the left side (Image 3). It was ensured that the targets were within the plane of horizontal vision in proximal vision analysis.

SCORING AND CALCULATIONS

Beginning and end of REM periods were determined according to standardized scoring of sleep stages. hREMs were measured for each subject in each REM period, and the number of eye movements to the right and left were calculated. hREMs in REM periods that were recorded throughout a single recording were summed up, and the number of eye movements to the right and left were calculated. The value obtained was divided by the number of REM periods, and the mean numbers of eye movements to the right and left were calculated.

Appropriate saccades in the proximal vision study during wakefulness and all amplitudes of hREM to the right and left were measured with a ruler and summed up. Both total amplitude value of rightward and leftward saccades in the proximal vision analysis, and total amplitude of hREMs to the right and left obtained during a single recording were divided by the number of rightward and leftward saccades and the number of hREMs to the right and left, and the mean amplitude value was calculated. In addition, angular values of both hREMs to the right and left were calculated by a simple equation created based on the mean angular value and amplitude in the proximal vision analysis.

STATISTICAL EVALUATION

Values obtained from subjects were initially divided into groups regardless of age and subsequently into groups based on age: group A, 19-42 years and group B, 47-70 years; the values were then compared between the groups. For the statistical analysis of the values, t-test was performed using SPSS 10.0 program.

Image 1: *hREMs recorded during REM sleep*

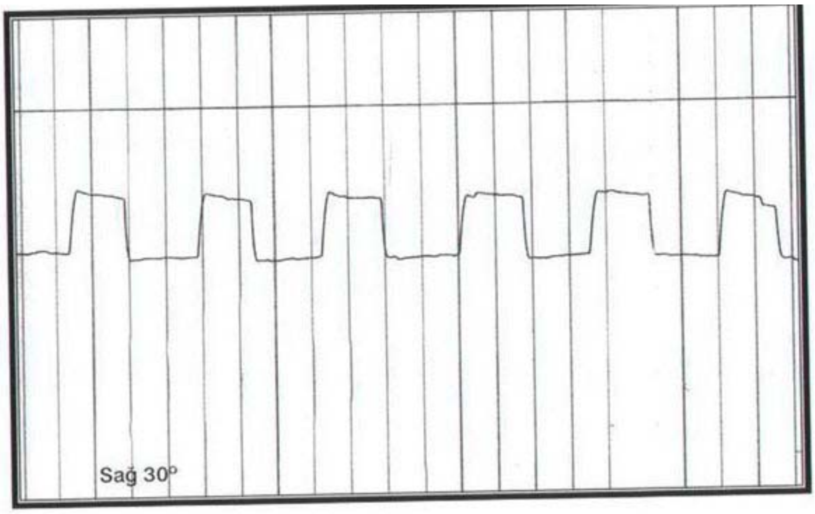

Image 2: *EOG deflections obtained by viewing the target at 30° to the right*

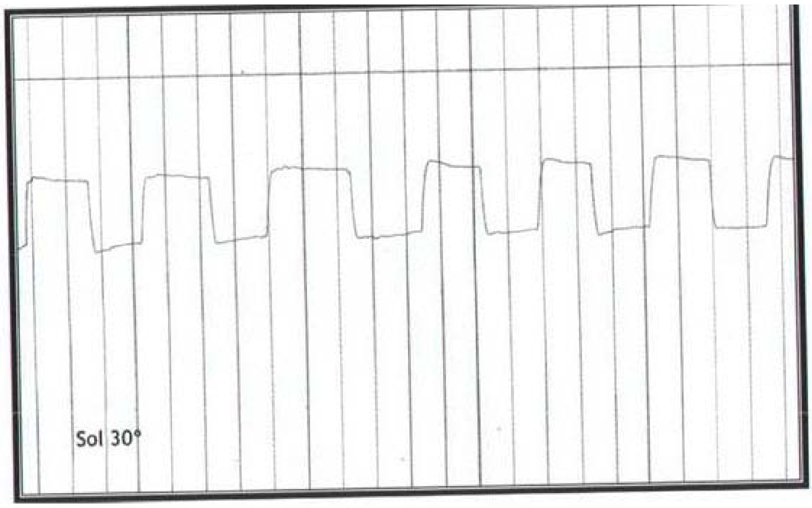

Image 3: *EOG deflections obtained by viewing the target at 30° to the left*

RESULTS

Of the 25 subjects, 22 (88%) were males and three (12%) were females. Mean age of the subjects was 41.2 ± 15.76 years. Mean age in group A was 30.4 ± 7.86 years, whereas mean age in group B was 57.4 ± 8.95 years. Group A comprised 15 male subjects (100%), and group B comprised seven male (70%) and three female (30%) subjects. No effort was made to equally distribute genders between the groups because control mechanisms and physiological characteristics do not vary between the genders in terms of both sleep and eye movements.

COMPARISON OF hREM CHARACTERISTICS REGARDLESS OF AGE

1-Comparison of numbers of hREMs to the right and left during REM sleep is given in Table 1. The findings showed that the mean number of leftward hREMs was higher than the mean number of hREMs to the right. However, standard deviation of the values was high because hREMs showed a wide distribution; therefore, the difference was not statistically significant (p = 0.519).

2-Comparison of amplitude values of hREMs to the right and left during REM sleep is given in Table 2. No statistical significance was observed between amplitude values (p = 0.854).

3-Comparison of angular values of hREMs to the right and left during REM sleep is given in Table 3. The difference between the angular values was not statistically significant (p=0.509).

4-Mean angular values of both hREMs to the right and left during REM sleep were found to be below 15° in 23 subjects (92%) and above 15° in two subjects (8%).

COMPARISON OF hREM CHARACTERISTICS IN GROUPS A AND B

1-Comparison of numbers of hREMs to the right and left in groups A and B during REM sleep are given in Table 4. The difference between the numbers of hREMs to the right (p = 0.362) and numbers of hREMs to the left (p = 0.209) in groups A and B was not statistically significant.

2-Comparison of amplitude values of hREMs to the right and left in groups A and B during REM sleep are given in Table 5. The difference between the amplitude values of hREMs to the right (p

= 0.625) and of hREMs to the left (p = 0.873) in groups A and B was not statistically significant.

3-Comparison of angular values of hREMs to the right and left in groups A and B during REM sleep are given in Table 6. The difference between the angular values of hREMs to the right (p = 0.750) and of hREMs to the left (p = 0.851) in groups A and B was not statistically significant.

Table 1. Comparison of numbers of hREMs to the right and left

	N	Mean number of hREMs	Standard deviation	P value
Number of hREMs to the right	25	59.93	37.97	0.519
Number of hREMs to the left	25	67.52	44.40	

Table 2. Comparison of amplitude values of hREMs to the right and left

	N	Mean of amplitude values (mm)	Standard deviation	P value
Amplitude value of hREM to the right during REM sleep	25	3.99	1.13	0.854
Amplitude value of hREM to the left during REM sleep	25	3.93	1.06	

Table 3. Comparison of angular values of hREMs to the right and left

	N	Mean of angular values (°)	Standard deviation	P value
Angular values of hREMs to the right dıring REM sleep	25	10.72	3.28	0.509
Angular values of hREMs to the left during REM sleep	25	10.12	3.03	

Table 4. Comparison of numbers of hREMs to the right and left in groups A and B

	N	Mean number of hREMs	Standard deviation	P value
Number of hREMs to the right (Group A)	15	51.15	30.98	0.362
Number of hREMs to the right (Group B)	10	68.60	47.02	
Number of hREMs to the left (Group A)	15	58.27	25.10	0.209
Number of hREMs to the left (Group B)	10	81.38	62.62	

Table 5. Comparison of amplitude values of hREMs to the right and left in groups A and B

	N	Mean of amplitude values(mm)	Standard deviation	P value
Amplitude value of hREM to the right during REM sleep (Group A)	15	4.08	1.20	0.625
Amplitude value of hREM to the right during REM sleep (Group B)	10	3.85	1.05	
Amplitude value of hREM to the left during REM sleep (Group A)	15	3.96	1.04	0.873
Amplitude value of hREM to the left during REM sleep (Group B)	10	3.89	1.15	

Table 6. Comparison of angular values of hREMs to the right and left in groups A and B

	N	Mean of angular values (°)	Standard deviation	P value
Angular values of hREMs to the right during REM sleep (Group A)	15	10.89	3.33	0.750
Angular values of hREMs to the right during REM sleep (Group B)	10	10.45	3.36	
Angular values of hREMs to the left during REM sleep (Group A)	15	10.03	3.27	0.851
Angular values of hREMs to the left during REM sleep (Group B)	10	10.27	2.78	

DISCUSSION

Dynamic characteristics of REM sleep suggest the involvement of the processes consuming active energy for normal brain activities and that the central nervous system is actively controlled by these characteristics. The argument that REM is correlated with visual images in the dream has increased the interest of researchers in the question of which hemisphere is active during REM and dreaming (4,5,6).

Penfield and Perot conducted the first indirect study for cerebral dominance on dream-like situations (1). In their study, stimulation of sensory areas in the cerebral hemispheres in 53 epileptic patients under local anesthesia caused paresthesia, whereas stimulation of the temporal lobe of the right hemisphere led to the state referred to by researches as the "dream-like state." These observations led to a hypothesis that the cortex responds to the dreams that occur naturally and dream-like states artificially created by external electrical stimulus using the same mechanism (1).

Greenwood et al. recorded all night sleeps of patients with partial or complete section of the corpus callosum and anterior commissures in order to exclude the left hemisphere and investigated the involvement of the right hemisphere in the visuoimaginal aspects of dream (6). Data obtained from three patients failed to show the involvement of right hemisphere in dreaming; however, it was suggested that the left hemisphere was associated with the visual aspect of dreaming in patients who underwent commissurotomy. Similarly, McCormick et al. investigated cerebral lateralization of dreaming in four patients who underwent right functional or anatomical hemispherectomy and claimed that the left hemisphere plays a critical role in the generation of dreams (7). It is argued that people with left parietal cortex lesion do not dream, and in one study, no images defined as dreams were created because the connection between the occipital lobe and temporal cortex was distorted in cortex lesions; thus, visual records could not be integrated (8).

Meyer et al. investigated the presence of a hemispheric lateralization by cerebral blood flow technique during dreaming and REM sleep following inhalation of xenon-133 in four narcoleptic patients (9). Cerebral blood flow was measured during PSG, and an increase in hemispheric grey matter blood flow was detected in the right hemisphere compared with that in the left hemisphere. The investigators found that the blood flow increased maximally in the right parietal and posterotemporal areas. Conversely, Maquet et al. investigated the regional cerebral blood flow in subjects who maintained steady REM sleep and recalled their dreams upon awakening by positron emission tomography (PET) and found that the blood flow in the middle brain was positively correlated with REM sleep in the pontine tegmentum, left thalamus, both amygdaloid complexes, anterior cingulate cortex, and right parietal operculum (10).

Goldstein et al. determined the ratios between the amplitudes in the left and right cerebral hemispheres via integrative EEG analysis during spontaneous sleep (5). Data obtained from seven male subjects demonstrated higher amplitude changes in the left hemisphere compared with that in the right hemisphere during REM sleep. In EEG analysis, low amplitudes are usually found when large activations occur. Accordingly, the authors stated that the right hemisphere was more activate during REM sleep. Hirshkowitz et al. obtained higher coefficients in right and left EEG examinations of 12 male subjects during sleep, based on amplitude evaluation with respect to non-REM (11). The results of this study, in which activation of the right side was relatively higher than that of the left side, supported the hypothesis that REM sleep and right temporal lobe activation are associated (11).

Among the studies on REM sleep and dream, those on REM characteristics with respect to the hypotheses about the concept of hemispheric asymmetry have been rarely published. Hong et al. analyzed PET findings obtained from six normal subjects to study the neural substrate of eye movements during REM sleep (12). The number of eye movements during REM sleep showed positive correlation with the glucose metabolic rate; corresponded with the (a) saccadic eye movement system (frontal eye field and dorsolateral prefrontal cortex, statistically significant only on the right side), (b) midline attentional system (cingulate and medial frontal cortex, precuneus), and (c) parietal visual spatial attentional system (bilateral superior parietal lobules, right inferior parietal lobule); and negatively correlated with left inferior parietal lobule (12). The investigators observed positive correlations between waking eye movements and metabolic rate in the same areas (except for inferior parietal lobule), and accordingly, they stated that the same cortical areas are involved in the eye movements both in REM sleep and wakefulness and that the eye movements during REM sleep are saccadic scans of targets in the dream scene (12). They also suggested that the saccadic eye movement control is specialized in the right hemisphere and that there is reciprocal inhibition in the contralateral homologous area during higher cortical functioning (12).

A general decrease in REMs in the contralateral of the lesion in cases of brain damage suggests that there is a regulatory effect of various cortex and subcortex areas in the generation of REMs in the brain stem (13). The case was first published by Greenberg during an investigation of the morphology of sleep spindles upon a coincidental finding that REM was considerably reduced toward the opposite side of the lesion in two patients with "attentive hemanopia" (the author did not report quantitative data) (14).

Patients with unilateral spatial neglect cannot examine, respond to, or orient toward stimuli, which occur in the contralateral to the lesion. Doricchi et al. found that there was reduced frequency of REMs during REM sleep in stroke patients suffering from chronic and severe unilateral spatial neglect and that the reduction occurred contralateral to the lesion (at the left side) (15,16). This defect seems to be resulting from the damage in the attention systems. This is because REMs contralateral to the lesion were reduced by a lower amount in the control group with brain-damaged patients who did not suffer from attentional neglect.

De Gennaro et al. analyzed the distribution of vertical and hREMs to the right and left during the first and last REM periods and tried to test the hypotheses that there is an increase in activity in the left (4). In this study, neither any variations nor superiority of REMs to the left were found during REM periods. It was suggested that upward movements were superior, and this was considered to be a function of the right hemisphere.

Our study is similar to the studies conducted by De Gennaro et al. in terms of the findings and different in terms of the values except for determination of distribution hREMs to the right and left. In all subjects in this study, the number of hREMs to the right (mean: 59.93 ± 37.97) was lower than the number of hREMs to the left (mean: 67.52 ± 44.40). It is observed that the standard deviation of the values was high because hREMs showed a wide distribution; therefore, the difference was not statistically significant ($p = 0.519$). This result is consistent with the findings of De Gennaro et al. In addition, when both amplitudes and angular values of hREMs to the right and left are considered, no statistical asymmetry was observed.

Bahill et al. reported that 85% of usual saccades during waking were $\leq 15°$, and Aserinsky et al. reported that 90% of REMs during the REM period were $\leq 11.5°$ (17,18). In the present study, we found that 92% of hREMs both to the right and left during REM sleep were $\leq 15°$. The result suggested that REMs during REM sleep share the same angular properties with the saccades during waking.

In addition, values were compared between groups A and B (created based on age). The number of hREMs to the right and left during REM sleep, amplitude of hREMs to the right and left, and angular values of hREMs to the right and left were analyzed. It was found that the differences between the values were not statistically significant. The results suggested that age had no effect on these values. It is interesting that although the amplitude and frequency of sleep spindles during phase 2 sleep decreased with age, mean quantitative amplitude values of hREMs were maintained. This finding may indicate the importance of REM sleep for humans throughout their lifespan.

The findings suggested that it is not possible to show a dominant hemisphere for REM sleep, REMs, and dreaming. Some studies presented above attempted to demonstrate the superiority of the right hemisphere, others attempted to demonstrate the superiority of the left hemisphere, and few others advocated that the two hemispheres work in coordination (the present study also supports this view). To confirm the results, studies with a large sample size should conducted using improved electrophysiological and imaging methods.

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