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MÜXTƏLİF VARIANTLI DEMENSİYASI OLAN XƏSTƏLƏRDƏ BAŞ BEYNİNİN FUNKSIONAL VƏZİYYƏTİ VƏ GECƏ POZUNTULARININ XÜSUSİYYƏTLƏRİ

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Xülasə. Məqalədə demensiyanın müxtəlif variantlarına (Alzheimer xəstəliyi, Parkinson xəstəliyi, Hentinqton xəstəliyi, damar mənşəli demensiya, posttravmatik demensiya) məruz qalmış 170 xəstənin neyrofizioloji müayinəsinin nəticələri təqdim edilmişdir. Tədqiqat ciddi koqnitiv pozuntuları olan xəstələrdə baş beyninin funksional vəziyyətinin qiymətləndirilməsi və gecə pozuntularının müqayisəli səciyyələndirilməsi məqsədilə aparılmışdır.

Müəyyən edilmişdir ki, demensiyanın degenerativ formaları ilə birgə damar demensiyası olan xəstə qruplarında yüksək amplitudalı-aritmik və aşağıamplitudalı-aritmik EEG tiplərinin rastgəlmə faizi xüsusilə çoxdur (müvafiq olaraq 31,6 % və 26,6 %); α - və β -ritmlərin əhəmiyyətli dərəcədə azalması və Θ -ritmin artımı ($p < 0,001$) müşahidə edilmişdir. Variantından asılı olmayaraq, bütün demensiyalı xəstələrdə aydın ifadəli yuxu pozulması olmuşdur. EEG-da yuxu millərinin artması Hentinqton xəstəliyi üçün səciyyəvidir. Damar demensiyası olan xəstələrdə gecə oyanmalarının sayı əhəmiyyətli dərəcədə artmışdır. Buna obstruktiv apnoe (52,3 %), aşağı ətrafların bükücü-açıqıcı mioklonik hərəkətləri (56,4 %), nikturiya (35,2 %), baldır əzələlərində tutmaşəkilli ağrı hissiyyəti (2,3 %) şərait yaradır. Demensiyanın damar mənşəli və degenerativ formaları olan bütün xəstələrdə yuxunun müxtəlif dərəcəli pozulmaları müşahidə edilmişdir. Xəstələrin əksəriyyəti həm də yuxunun dərinliyindən və davam etmə müddətindən razı qalmamışdır; xəstələrin 93 %-i yuxulamaqda çətinlik çəkmişdir. 83,3 % xəstədə yuxu səthi olmuş və onlar tez-tez oyanmışlar. 86,6 % xəstədə isə yuxulamadan 3-4 saat sonra erkən səhər oyanması müşahidə edilmişdir.

Açar sözlər: Alzheimer xəstəliyi, Hentinqton xəstəliyi, damar mənşəli demensiya, posttravmatik ensefalopatiya

Ключевые слова: болезнь Альцгеймера, болезнь Гентингтона, сосудистая деменция, посттравматическая энцефалопатия

Key words: Alzheimer's disease, vascular dementia, Huntington's disease, electroencephalography, post-traumatic dementia, neurophysiological diagnostics

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THE FUNCTIONAL STATE OF THE BRAIN ACCORDING TO THESE NEUROPHYSIOLOGICAL METHODS OF STUDY AND FEATURES OF NIGHT DISORDERS IN PATIENTS WITH VARIOUS VARIANTS OF DEMENTIA

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The article presents the results of a neurophysiological assessment in 170 patients with various types of dementia (Alzheimer's, Parkinson's, Huntington's disease, vascular dementia, post-traumatic dementia). The aim of the study was to assess the functional state of the brain and to give a comparative description of nocturnal disorders in patients with various clinical variants of dementia.

It was found that in the group of patients with degenerative forms of dementia and vascular dementia, the highest percentage fell on high-amplitude-arrhythmic (26.6% and 31.6%) and low-amplitude – (25% and 26.6%) arrhythmic EEG types, in particular, there was a pronounced decrease in α - and β -rhythms and a significant increase in the Θ -rhythm, in particular the δ -rhythm, statistically significant ($p < 0,001$). All

patients with dementia, regardless of its variant, had severe sleep disorders. Prolonged falling asleep, frequent waking up at dawn and at night, reduced sleep quality, superficial sleep, fear of not falling asleep, fear of bed, reduction in total duration, decrease in the fourth stage – wave sleep. A pronounced increase in sleep spindles was noted in patients with HD. In patients with vascular dementia, the number and duration of nocturnal awakenings significantly increased. This was facilitated by the phenomena of obstructive apnea (52.3%), flexion-extensor myoclonic movements of the lower extremities (56.4%), bedwetting (35.2%), cramping pain in the calf muscles (2.3%). With vascular, as well as with degenerative dementia, various sleep disorders were detected in all patients. Also, all patients were dissatisfied with the duration and depth of sleep. Difficulties with falling asleep were noted in 93.3% of patients. Superficial sleep with frequent nocturnal awakenings during sleep was found in 83.3% of patients. In 86.6% of patients, early morning awakening was recorded three to four hours after falling asleep.

Introduction. Currently, there is an increase in dementias of various genesis all over the world, which is associated with the aging of the planet's population [1]. Dementia occurs both at a young and working age, which makes the problem of dementia not only a medical, but also an important social problem [2-6].

Dementia is a complex disorder, a condition characterized by a decrease in cognitive functions (memory, attention, motor skills, intellect and other processes controlled by the brain) caused by intoxication, metabolic disorders, infectious-inflammatory or traumatic lesions of the brain, leading to everyday, social and social maladaptation [7-10].

In Alzheimer's disease (AD), dementia with Lewy bodies are independent diseases in the form of destruction of the cerebral cortex [11]. Huntington's disease (HD) has an autosomal dominant pattern of inheritance, characterized by a steadily progressive course of the disease. The reason is a mutation of the HTT gene located on the short arm of the fourth chromosome (4p16.3) [12].

Vascular dementia (VD) occurs predominantly in the elderly and develops as a result of the appearance of cerebrovascular pathology [13]. Post-traumatic dementia (PTD) is caused by traumatic brain injury. The clinical picture depends on the severity and location of the injury. The main clinical feature of post-traumatic dementia can be called a gradually increasing decrease in intelligence, while due to memory impairment, criticality to one's condition disappears [14].

Diagnosis of dementia is carried out in several stages, by a neurologist and a psychiatrist. A detailed history and comp-

laints of the patient are collected, and primary diagnostics are carried out. Also, experts examine the level of cognitive abilities and the degree of their damage, a picture of the mental state of a person is established [15]. Instrumental diagnostics is carried out using the methods of encephalography, computed tomography, MRI, radiography, and other studies of the state of the brain [16-20]. With the help of hardware research, the degree of brain damage and the causes of the disease are determined.

The most promising areas in the differential diagnosis of various variants are the developed systems for predicting the development, course, and outcome of dementia, based on the identification of a set of informative methods (clinical, electrophysiological, biochemical, and immunological), which will reveal the widest application in clinical medicine [21].

Materials and methods. We examined 170 people with various clinical variants of dementia: AD, Parkinson's disease (PD), VD, and PTD, 78 men (45.8%) and 92 women (54.2%), aged 45 to 86 years (mean age 65.87 ± 9.5 years). All patients underwent brain studies: electroencephalography (EEG), polysomnography, electrooculography (EOG), and electromyography (EMG). Based on the results of EEG recordings, all patients were grouped into three groups. The first group included 60 patients with degenerative type dementia: 25 patients with AD, 20 patients with PD, and 15 patients with HD. The second group of subjects consisted of 60 patients with VD. The third group included 50 patients with PTD. The diagnosis of AD was established according to the updated clinical practice criteria proposed for the diagnosis of Alzheimer's disease by the Alzheimer's Association of the National Institute on Aging in 2013. The significance of differences in mean values was assessed using the Fisher angle equation, the conversion method, and Student's t-test.

Results. The first group of subjects with degenerative diseases had normal or relatively normal electrical activity. The EEG was dominated by α - or β -rhythms with the preservation of zonal differences and had normal amplitude indicators (β -rhythm in the range from 30 to 50 μ V, and α -rhythm from 60 to 100 μ V). In addition, the majority of patients in this group also showed polyrhythm behind the dominant rhythm. Studies have shown that more than half of the patients had changes in bioelectrical activity by the type of diffuse disorganization, which were predominantly polymorphic in nature and also manifested in various variants of paroxysmal symptoms. The dysrhythmic type manifested itself in the form of two variants: high-amplitude and low-amplitude.

In the second group of patients (60 people with VD), a low-amplitude dysrhythmic variant was identified. This type of EEG was manifested by polymorphic α -, β - and Θ -rhythms with amplitude activity not higher than 40, 50 μ V. Smoothing of regional differences in rhythm and a decrease in reactivity were also noted during the performance of all functional tests.

The third group (50 patients with PTD) had symmetrical bilateral paroxysmal activity, especially in the range of α -, Θ - and δ -frequencies, with rounded blunt peaks. The distribution of the main types of changes in bioelectrical activity is presented in Table 1.

Based on the results of the analysis, patients with different types of dementia were divided into two groups, which had the most informative data on the bioelectrical activity of

the brain (BAB). The first group included EEG parameters that reflected the frequency-amplitude features of the BAB and also the strength of the spectrum of the main EEG rhythms. The second group included the measure of spatio-hour organization and the coefficients of interhemispheric asymmetry. The average values of the relative strength of the spectrum of α -, β -, Θ - and δ -rhythms, and their asymmetry coefficients are described in (Table 2).

The analysis of the above tables showed that in the first group, patients with dementia of the degenerative type had the highest representation of the high-amplitude arrhythmic type (26.6%), as well as the low-amplitude arrhythmic type (25%). More than (38.3%) EEGs were of the paroxysmal type, and 50% were of the pronounced epileptiform type. Patients with HD had the most pronounced EEG disturbances. The usual EEG type was found in 11.6% of patients: in 5 patients with AD and in 3 patients with HD. Most patients had "mild" or moderate severity of dementia. There was also a pronounced decrease in α - and β -rhythms and a significant increase in the Θ -rhythm, in particular the δ -rhythm, statistically significant ($p < 0.001$). In addition, the coefficient of interhemispheric asymmetry was somewhat reduced, as well as pronounced changes in the spatio-hourly formation of the BAB, in particular, a pronounced EEG disturbance, especially in the anterior parts of the brain. In addition, in the group, there was a decrease in EEG activity in response to light stimulators, and paroxysmal activity increased significantly during hyperventilation.

Table 1. Distribution of types of EEG changes depending on the type of dementia (%)

Types of EEG changes	Dementia variant		
	Degenerative dementia (n=60)	Vascular dementia (n=60)	Post-traumatic dementia (n=50)
Conditionally normal	8.60	6.65	6.0
Low-amplitude dysrhythmic	25.0	26.6	10.0
High-amplitude dysrhythmic	25.7	27.6	8.0
Local-paroxysmal	5.75	6.65	14.0
Bilateral-paroxysmal	10.5	12.6	32.0

Table 2. Average values of EEG indicators of patients depending on the variant of dementia

EEG indicators	Dementia variant			
	Degenerative dementia (n=60)	Vascular dementia (n=60)	Post-traumatic dementia (n=50)	Normal value
Relative power of the α -rhythm spectrum	36.2±2.2	29.4±1.8	31.5±3.0	98.5 ± 4.1
Relative power of the β -rhythm spectrum	18.5±1.3	21.2±1.9	28.3±2.4	41.3± 2.8
Relative power of the Θ -rhythm spectrum	56.8±3.0	60.4±3.4	81.4±3.0	38.9 ± 3.3
Relative power of the δ -rhythm spectrum	106.3±4.8	120.5±.5	101.4±5.0	29.8 ± 2.4
Hemispheric asymmetry coefficient	0.84±0.06	0.51±0.05	0.6±0.06	0.91±0.06

In the group of patients with VD, the highest percentage also fell on high-amplitude (31.6%) and low-amplitude (26.6%) arrhythmic EEG types. The paroxysmal nature of BAB was observed in 38.3% of patients, most of them were epileptiform type. Expressed variants of BAB were in patients with multi-infarct and strategic infarct dementia. In 6 patients, a normal EEG was present. The conditional strength of the α -rhythm range is statistically significant ($p<0.01$) and lower than the strength of the β -rhythm. The strength of pathological fluctuations in δ - and Θ - also increased. Statistically significant asymmetry of BAB between hemispheres ($p<0.05$) of the brain. In particular, asymmetry was found in patients with infarct dementia. In addition, in patients with vascular dementia, smoothing of regional differences in rhythms and a decrease in resistance during functional tests were noted.

In patients with PTD, bioelectric paroxysmal activity predominated (80%). High-amplitude and low-amplitude arrhythmic types of EEG were observed only represented by 20%. A relatively normal EEG was detected in 6% of patients. In addition, a statistically significant decrease in the strength of the α - and Θ -rhythm, ($p<0.05$) as well as an increase in the strength of the pathological Θ - and δ -rhythm, a disorder in the spatial-clock organization of the BAB due to hemisphere asymmetry, and the

manifestation of island-wave paroxysmal activity, especially in the anterior regions of the brain. The cerebral cortex of patients with dementia of traumatic origin responded to irritation with bioelectrical paroxysmal activity.

The analysis of the degree of BAB in patients with different types of dementia did not show significant differences between them. In all variants of dementia, low- and high-amplitude dysrhythmic EEG patterns predominated. Behind the frequency, in second place are all kinds of BAB options. Comparatively normal bioelectric activity in each group of patients with dementia occupied more than 10% of the EEG. There was also a sharp violation of the spatial-clock formation of the BAB as a result of hemisphere differences and as a result of the disorder found, in particular in the cortex of the frontal lobes of the brain. Also, the rate of functional load was reduced with the formation of bioelectric paroxysmal activity. So the EEG is a kind of scoreboard showing the functionality of the structure of the cerebral cortex. Thus, these changes in BAB can be provided as a result of the destruction of the processes of cerebral homeostasis, stem-thalamo-cortical and also its commissural mechanisms.

Summarizing the results of the studies, it should be noted that the EEG method plays an important role in the diagnosis and pathogenetic mechanisms of the development of cognitive

disorders. EEG diagnostic method allows to establish the degree of functional changes in the brain as well as the relative localization of the pathological process, to determine the paroxysmal-convulsive readiness. In the studied variants of dementia, a violation of functional intersystemic brain connections, both vertically and horizontally organized, cortical-thalamo-stem and interhemispheric-transcallosal, was revealed.

High-quality, restorative sleep is an indicator of a balanced, rhythmic brain function. With age and in various diseases, the architecture of sleep is disturbed [22]. Its intensity, quality, depth and continuity diminish. The susceptibility of sleep to adverse factors increases [23].

Sleep is organized cyclically. Each sleep cycle consists of non-REM sleep and REM sleep. The number of cycles per night in a healthy person ranges from 4 to 6, the duration of one cycle is from 60 to 100 minutes. In the first half of the night in the cycles, the phase of non-REM sleep (NREM) is more represented, in the second half of the night - the phase of REM sleep (REM). In adults, REM sleep

accounts for 25% of total sleep duration (TSD) [24].

In the elderly, bedtime increases due to prolongation of sleep latency, the period of wakefulness during dreams, the lengthening of the moment of falling asleep after spontaneous awakening, and being in bed due to early awakening. The number of awakenings increases up to 6-8 times. The entire awakening period in the elderly is much longer than in young people – 83.9 and 25.6 minutes, respectively [25].

Sleep architecture disorders are also common in patients with dementia [26] (Table 3). We used the international classification of phases and stages of sleep (ICD-10). In terms of depth, the NREM phase is divided into four successive stages, one after the other. They are characterized by a gradual replacement by slow oscillations of the α -rhythm, the formation of "sleepy spindles", K-complexes and regulatory Θ -activity. The REM phase is characterized by desynchronization of the BAGM "pollen discharges"; on the electrooculogram (EOG) – rapid movements of the eyeballs, on the electromyogram (EMG) of the oral diaphragm – a sharp decrease in muscle tone.

Table 3. Structure of night sleep in patients with different types of dementia (minutes)

Indicators	Dementia variant				
	Degenerative dementia (n=60)	Vascular dementia (n=60)	Post-traumatic dementia (n=50)	Normal value	
				Middle age	Old age
Sleep duration	370.2±35.4	302.1±28.2	379.2±43.2	425.8±51.7	398.4±59.8
The 1-st stage of sleep	62.4±12.2	53.3±13.2	55.6±17.1	72.1±23.4	66.4±24.0
The 2-d stage of sleep	173.5±35.5	149.1±31.5	172.0±38.0	189.6±53.0	180.6±44.1
The 3-d stage of sleep	56.4±10.2	43.2±12.1	58.4±16.2	53.1±16.9	57.8±15.3
The 4-th stage of sleep	15.8±3.0	13.4±3.1	22.4±4.0	32.8±8.0	16.0±4.3
Delta sleep	72.2±12.2	56.8±11.2	80.6±15.4	85.9±23.4	73.8±16.7
REM sleep phase	63.4±13.4	41.8±13.2	70.2±14.5	78.2±21.0	77.7±19.1
Number of completed cycles	3.5±0.5	2.0±0.6	2.8±0.6	4.0±1.1	3.5±1.1

As the results of the study showed, all patients with degenerative dementia made various complaints about sleep disorders. 88.3% of patients experienced difficulty falling asleep. In 80% of patients, superficial shallow sleep was noted. Morning raising was observed in 76.6% of patients. Frequent nocturnal waking during sleep and difficulty falling asleep were found in 90% of the subjects. All patients complained about the violation of the duration and depth of sleep. "Fear of not falling asleep", "fear of bed" and unpleasant dreams were observed in 56.6% of patients. The main factors worsening sleep in this group were obstructive sleep apnea (60%) and nocturnal myoclonus (11.6%). The increase in the number and duration of nocturnal awakenings, which disturbed nocturnal sleep, led to increasingly superficial awakenings. Daytime sleepiness was observed in more than half of the patients.

In the study of night sleep in patients with degenerative variants of dementia, a decrease in the total duration of sleep was noted not only in relation to the middle-aged control group, but also to the elderly control group. Θ -activity decreased not only in time, but also in amplitude. Statistically significant ($p < 0.05$) decreased the fourth stage of slow-wave sleep. A trend towards a decrease in the number of completed sleep cycles was found. During the comparative characteristics of sleep in patients with various types of degenerative dementias, it was found that their TSD did not differ significantly, but was somewhat shorter in the group of patients with AD. Also, in these patients, the percentage of paradoxical sleep was higher than in other diseases. Despite the absence of reliable signs in the quantitative characteristics of the stages, some features were found in the qualitative organization of the sleep stage in various types of degenerative dementia. Patients with AD had more pronounced fragmentation of nocturnal sleep and the incidence of "sunset" syndrome, which was characterized by nocturnal arousal, aimless wandering and, in severe cases, delirium. With HD, a slight increase in sleep spindles was registered. With vascular, as well as with degenerative dementia, various sleep disorders were detected in all patients. Also, all patients were dissatisfied with the duration and depth of sleep. Difficulties with falling asleep were noted

in 93.3% of patients. Superficial sleep with frequent nocturnal awakenings during sleep was found in 83.3% of patients. In 86.6% of patients, early morning awakening was recorded three to four hours after falling asleep. Fear of not falling asleep, fear of bed, chronic anxiety, and unpleasant negative content of the dream were noted in 70% of the examined. More than half of them (66.6%) had daytime sleepiness.

In patients with VD, the number and duration of nocturnal awakenings significantly increased. This was facilitated by the phenomena of obstructive apnea (52.3%), flexion-extensor myoclonic movements of the lower extremities (56.4%), bedwetting (35.2%), cramping pain in the calf muscles (2.3%). In patients with VD, there was also a decrease in total sleep duration not only in relation to the middle-aged control group, but also in relation to the elderly control group. The duration of the 4-th stage of slow-wave sleep also significantly decreased ($p < 0.05$). In addition, it was found that δ -activity was observed lower than in the control group. The period of REM sleep duration was statistically shorter than in the control group ($p < 0.05$). When comparing the nature of sleep in patients with various forms of vascular dementia, despite the absence of significant differences in the quantitative characteristics of the stages, some features of the qualitative organization of sleep were identified. Consequently, respiratory disorders in the form of an increase in the frequency of apnea were most pronounced in patients with multi-infarct dementia. In patients with strategic infarct dementia – behavioral disorders, chronic anxiety, restlessness in paradoxical sleep. In patients with subcortical dementia, flexion-extensor polyclonic movements of the lower extremities were observed more often than in other forms of VD.

Patients with PTD complained of various disorders of the sleep-wake period. 78% of patients had difficulty falling asleep. Early awakening was noted in 58% of the examined. In 82% of patients, superficial sleep was observed. 76% of patients had frequent nocturnal awakenings during sleep and difficulty falling asleep after waking up. More than half of the patients (56%) had a lack of rest after sleep. Daytime sleepiness was observed in

48% of the subjects. In 40% of patients, night sleep was interrupted by nocturnal urge to urinate, restless legs syndrome. There was also a slight decrease in the total duration of sleep, in comparison with the control group, to the lengthening of the period of falling asleep and the latent periods of all stages of the stages of slow sleep, as well as the period of the stage of REM sleep. As a result, patients with traumatic dementia had both qualitative and quantitative transformations in the organization of nocturnal sleep and the sleep-wake period.

All patients with dementia, regardless of its variant, had severe sleep disorders. Prolonged falling asleep, frequent waking at dawn and at night, reduced sleep quality, superficial sleep, fear of not falling asleep, fear of bed, reduction in total duration, decrease in the fourth stage – wave sleep. Along with this, each variant of dementia had its own specific sleep disorders. Thus, in HD patients, the fragmentation of nocturnal sleep and the increase in the "sunset" syndrome were more pronounced. A pronounced increase in sleep spindles was noted

in patients with HD. Patients with diabetes significantly increase the number and duration of nocturnal awakenings, obstructive sleep apnea, nocturnal myoclonus, and spasmodic pain in the calf muscles. With PTD, there was a tendency to lengthen the latent periods of all stages of non-REM sleep, increase the time of awakening in the middle of the night, and increase the number of movements per hour. Sleep disorders are more pronounced in patients with various types of dementia than in the control group of the same age.

Conclusions. Comparison of clinical, anamnestic and polygraphic characteristics of the sleep-wake period in patients with various types of dementia suggested that the subjective feeling of quality and completeness of sleep is associated with the cyclical organization and structure of sleep. Processes that give the full functioning of the sleep-wake period, structural and functional relationships with systems that contain the optimal degree of intellectual-mnemonic activity and emotional reaction.

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ФУНКЦИОНАЛЬНОЕ СОСТОЯНИЕ ГОЛОВНОГО МОЗГА ПО ДАННЫМ НЕЙРОФИЗИОЛОГИЧЕСКИМ МЕТОДАМ ИССЛЕДОВАНИЯ И ОСОБЕННОСТИ НОЧНЫХ РАССТРОЙСТВ У БОЛЬНЫХ С РАЗЛИЧНЫМИ ВАРИАНТАМИ ДЕМЕНЦИЙ

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В статье представлены результаты нейрофизиологического обследования 170 больных с различными вариантами деменций (болезнь Альцгеймера, болезнь Паркинсона, болезнь Гентингтона, сосудистая деменция, посттравматическая деменция). Целью исследования было провести оценку функционального состояния головного мозга и дать сравнительную характеристику ночных расстройств у больных с грубыми когнитивными нарушениями.

Было установлено, что в группах пациентов с дегенеративными формами деменций и сосудистой деменцией наибольший процент приходился на высокоамплитудно-аритмический (31,6%) и низкоамплитудно-аритмический (26,6%) ЭЭГ типы. Отмечено выраженное снижение α - и β -ритмов и достоверное увеличение Θ -ритма ($p < 0,001$). Все больные деменцией, независимо от ее варианта, имели выраженные расстройства сна. Увеличение сонных веретен отмечено при болезни Гентингтона. У пациентов с сосудистой деменцией значительно увеличивалось количество и

продолжительность ночных пробуждений. Этому способствовали явления обструктивного апноэ (52,3%), сгибательно-разгибательные миоклонические движения нижних конечностей (56,4%), ночное недержание мочи (35,2%), схваткообразные болезненные ощущения в икроножных мышцах (2,3%). При сосудистой, а также при дегенеративных формах деменций у всех больных выявлялись различные нарушения сна. Большинство также были не удовлетворены его продолжительностью и глубиной. Трудности с засыпанием отмечены у 93,3% больных. Поверхностный сон с частыми ночными пробуждениями наблюдался у 83,3% больных. У 86,6% больных зафиксировано ранний утренний подъем через три-четыре часа после засыпания.

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