CHANGES IN THE STAGES OF NOCTURNAL SLEEP IN PATIENTS WITH LESIONS OF THE HYPOTHALAMUS AND BRAIN STEM

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Polygraphic investigations of nocturnal sleep in 18 patients with lesions of the hypothalamus and mesencephalon revealed a shortening of stage II and lengthening of stages III and IV of slow sleep compared with the corresponding durations in patients with lesions of pontobulbar structures (9 patients) and healthy subjects (8 persons) of the control group. Analysis of qualitative indices of the EEG of slow sleep (relative number of sleep spindles per minute in stage II, the Δ index, and amplitude of the Δ waves in stages III and IV) showed a tendency toward their increase in patients with lesions of the hypothalamus and mesencephalon. In the patients of this group the frequency of spontaneous changes from deeper to more superficial stages of sleep was reduced.

KEY WORDS: *Stages of nocturnal sleep; lesions of the hypothalamus and brain stem.*

Many investigations on animals have shown the leading role of the nonspecific synchronizing and desynchronizing systems of the brain stem in the various phases of diurnal cycle of waking and sleep [9, 10]. The role of individual brain formations and, in particular, of structures of the hypothalamus and brain stem in the mechanism of human sleep has received comparatively little investigation [1-4, 7, 8].

In this investigation nocturnal sleep was analyzed in patients with chronic lesions (syringobulbia, tumors, inflammatory lesions) of the brain stem at various levels.

EXPERIMENTAL METHOD

Nocturnal sleep was analyzed in 27 patients aged between 16 and 50 years (mean age 31 years). The location of the lesion was established by clinical neurological examination and by x-ray contrast methods. In some cases it was confirmed at neurosurgical operation.

The investigations of sleep included continuous recording of the EEG (central and fronto-central leads), the electrooculogram, electromyogram of the muscles of the oral diaphragm, and the ECG. Recordings were made after adaptation of the subjects to the conditions of the investigation during the previous night. The records were analyzed in accordance with the international classification of the stages of sleep [11]. To assess qualitative differences between EEGs in the individual stages of slow sleep, the total number of sleep spindles in stage II and their number per minute of that stage were counted. In stages III and IV the index of Δ activity with an amplitude of over 57 μV and a frequency of less than 2/sec, reflecting the specific character of these stages [3], was analyzed. The results were compared with sleep indices of eight healthy subjects. Statistical analysis was carried out with the use of the Wilcoxon–Mann–Whitney nonparametric criterion [5].

EXPERIMENTAL RESULTS

Depending on the location of the lesion the following groups were distinguished: 1) pituitary-hypothalamic – 3 patients, 2) hypothalamic – 11 patients, 3) mesencephalic – 4 patients, 4) pontine – 3 patients, and 5) bulbar – 6 patients.

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TABLE 1. Structure of Nocturnal Sleep in Patients with Lesions of Hypothalamus and Brain Stem

Group	Duration of sleep, h	Stage I	Stage II	Stage III	Stage IV	Phase of fast sleep	Latent period, min				
		%					going to sleep	stage II	stage III	stage IV	phase of fast sleep
1-	6,5	10,6	26,3	16,8	21,9	21,4	24,1	6,2	13,4	19,1	87
2-	6,7	18,4	31,5	13,3	19,0	17,1	16,3	9,0	17,0	20,4	126,1
3-	6,8	15,6	34,0	13,6	20,8	16,0	19,2	20,2	32,6	38,1	123,1
4-	6,1	26,1	39,0	9,5	5,9	15,9	10,0	9,2	33,9	93	83,2
5-	6,7	14,7	43,4	13,5	7,0	20,3	9,1	14,7	23,4	45,8	75,2

TABLE 2. Characteristics of Nocturnal Sleep in Patients with Lesions of Pituitary-Hypothalamic-Mesencephalic (PHMS) and Ponto-Bulbar Structures (PBS) and in Healthy Subjects (HS)

Group	Duration of sleep, h	Stage I	Stage II	Stage III	Stage IV	Phase of fast sleep	Latent period, min					No. of sleep spindles		Δ Index, %
		%/day					going to sleep	stage II	stage III	stage IV	phase of fast sleep	total	per min of stage II	
Patients with lesion of PHMS	6,7	4,6	8,4	3,8	5,6	4,9	18,3	11,0	19,9	24,1	118,9	1231	9,6	62,9
Patients with lesion of PBS	6,5	4,7	11,6	3,3	1,7	5,2	9,4	12,9	26,9	61,5	77,9	1534	8,6	51,5
HS	7,6	4,0	15,5	2,7	2,5	5,5	14,3	4,0	19,3	35,8	109	1738	7,2	48,4

TABLE 3. Frequency of Changes from Deeper to More Superficial Stages (per conventional hour of stage) in Patients with Lesions of Pituitary-Hypothalamic-Mesencephalic (PHMS) and Ponto-Bulbar Structures (PBS)

Group	Changes connected with movement					Spontaneous changes					Total number of changes				
	stage I	stage II	stage III	stage IV	phase of fast sleep	stage I	stage II	stage III	stage IV	phase of fast sleep	stage I	stage II	stage III	stage IV	phase of fast sleep
Patients with lesion of PHMS	5,8	4,2	3,8	2,8	5,6	4,1	2,7	33,5	21,9	2,2	9,9	6,9	37,3	24,7	7,8
Patients with lesion of PBS	3,0	5,9	2,8	2,3	5,3	1,4	2,8	55,3	59,4	1,7	4,4	8,7	58,1	61,7	7,0

As the results given in Table 1 show, the main differences were found between groups including the oral (groups 1-3) and caudal (groups 4 and 5) levels of brain-stem lesion.

Comparison of the indices of the sleep structure of patients divided into two main groups on the basis of the location of the lesion (pituitary-hypothalamic-mesencephalic and ponto-bulbar) revealed the same differences: a decrease in the extent of stage II and an increase in the duration of Δ sleep (stages III and IV) in lesions of the oral region compared with lesions of the caudal structures of the brain stem ($P<0.05$). The same was true of the latent periods of going to sleep and of the individual stages of sleep. Comparison with the sleep indices for healthy subjects showed differences in the duration of sleep. For this reason, the indices for the patients and healthy subjects were compared on the basis of the durations of the individual stages of sleep expressed as a percentage of 24 h (Table 2). The main differences were found between healthy subjects and patients with lesions of the pituitary-hypothalamic-mesencephalic structures ($P<0.05$). Analysis of the qualitative features of the EEG of slow sleep showed that, despite the shorter duration of stage II and the associated decrease in the total number of sleep spindles in patients with lesions of oral structures compared with patients with lesions of the caudal zones of the brain stem, and also with healthy subjects, the relative frequency of appearance of these spindles did not differ significantly in these groups and it even showed a tendency to be higher in the first group (Table 2). The Δ index also was higher ($P<0.05$) in patients with lesions of the oral structures. A tendency also was found for the amplitude of the Δ waves to increase.

Determination of the frequency of changes from deeper to more superficial stages of sleep, reflecting to some degree the stability of processes responsible for the course of the individual stages of sleep, either associated with movement or arising spontaneously, also revealed significant differences in the value of this index in patients with lesions of the pituitary-hypothalamic-mesencephalic and ponto-bulbar structures (Table 3). In lesions of the oral structures the frequency of changes from stage I was increased whereas the number of changes of the stages in Δ sleep was significantly lower ($P<0.05$) than in patients with caudal lesions. The increase in the number of changes from stage I in patients with oral lesions of the brain stem was attributable both to an increase in the frequency of movements in that stage of sleep and also to spontaneous activation changes of the EEG, which themselves largely induced an increase in the duration of that stage. The difference in the number of changes from one stage to another took place on account of differences in the frequency of spontaneous changes in the groups of patients compared. If the frequency of spontaneous changes from deeper to more superficial stages is regarded as an inverse function of the stability of tonigenic synchronizing processes, this must correspond to an increase in the duration of Δ sleep, a shortening of its latent period, and an increase of the Δ index and it points to relative strengthening of synchronizing effects in lesions of the pituitary-hypothalamic-mesencephalic structures. The decrease in the duration of stage II although the relative frequency of generation of sleep spindles was preserved in this situation can be explained by acceleration of depression of the activating systems during going to sleep, resulting in an earlier onset of Δ sleep, during which the inhibition of activating ascending influences reaches its maximum. These changes can be regarded as indices of a subclinical lowering of the nonspecific activation level in oral lesions of the brain stem, in agreement with existing data on changes in the diurnal EEG of an analogous group of patients [6].

The absence of differences between the indices of activation connected with movements in these two groups of patients indicates preservation of the reactivity of the activating system of the brain stem and provides a basis for postulating the functional heterogeneity of nonspecific systems of phasic and tonic activation. These marked differences in the character and degree of changes in the structure of sleep and its polygraphic characteristics in patients with lesions of ponto-bulbar and mesencephalo-hypothalamic structures are in harmony with A. M. Vein's hypothesis [2] of the two contours of sleep regulation. The first includes structures participating directly in the generation of the individual phases and stages of sleep (bulbar, pontine, thalamic, cortical), whereas the second is a superstructure and is responsible for the integrative interaction of activating and inhibitory systems in the process of sleep and waking. It includes structures of the limbico-reticular complex, among which, as investigations in the writers' laboratory have shown, the mesencephalo-hypothalamic and mediobasal formations play the most important role in the regulation of waking and sleep. It is when their functional or organic integrity is impaired that the greatest degree of disorganization of sleep is observed [2].

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