

Distal transport of sodium ions, mkmol/2 hours	I	453,82±54,921	361,75±20,441	448,07±45,831	432,77±48,501	238,86±31,421	377,28±19,671
	II	314,16±28,822 p=0,048	333,62±39,572 p=0,542	256,61±25,871 p=0,005	363,33±16,612 p=0,805	392,80±33,411 p=0,009	346,95±39,351 p=0,504
Proximal transport of sodium ions, mkmol/100 mkl of glomerular filtrate	I	11,55±0,262	12,04±0,212	11,81±0,432	11,85±0,522	10,92±0,461	12,40±0,462
	II	11,96±0,261 p=0,291	11,74±0,165 p=0,266	11,64±0,081 p=0,706	11,70±0,242 p=0,799	11,88±0,181 p=0,081	11,56±0,122 p=0,100
Distal transport of sodium ions, mkmol/100 mkl of glomerular filtrate	I	0,60±0,041	0,73±0,112	0,80±0,051	0,68±0,103	0,28±0,041	0,46±0,051
	II	1,03±0,021 p=0,000	0,76±0,031 p=0,796	1,10±0,081 p=0,010	0,91±0,073 p=0,069	1,07±0,061 p=0,000	0,85±0,051 p=0,000

**Note:** n – number of animals; p – reliable difference as compared with previous time interval.

### Conclusions.

1. Daily rhythm of sodium ions excretion was of an inversion character relatively to the control chronograms with decreasing mesor three times that of the indices of intact animals
2. In spite of a low filtration loading of nephrons with sodium ions, absolute re-absorption of ions remained lowered in all the examined periods of time.
3. The rhythm amplitude of proximal transport of sodium ions was reliably decreased against the ground of changed architectonics of the rhythm.

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**Table 2 NO blockade influence upon ion regulation renal function in albino rats under physiologic PB conditions ( $\bar{x} \pm S_x$ )**

Index		Hour					
		08.00	12.00	16.00	20.00	24.00	04.00
		(n=6)	(n=6)	(n=6)	(n=6)	(n=6)	(n=6)
Concentration of sodium ions in urine, mmol/L	I	4,50±1,083	3,75±0,292	3,17±0,167	2,75±0,125	3,42±0,306	5,92±0,875
	II	1,46±0,119 p=0,019	1,38±0,119 p=0,000	1,57±0,067 p=0,000	1,83±0,067 p=0,000	1,63±0,144 p=0,000	1,48±0,075 p=0,000
Excretion of sodium ions, mkmol/2 hours	I	15,66±3,145	10,77±0,576	11,79±1,437	9,52±1,029	7,46±0,761	18,12±2,750
	II	3,46±0,233 p=0,003	3,63±0,420 p=0,000	3,20±0,347 p=0,000	5,35±0,225 p=0,008	5,05±0,709 p=0,048	4,10±2,462 p=0,008
Excretion of sodium ions, mkmol/100 mkl of glomerular filtrate	I	2,54±0,535	2,60±0,362	2,51±0,255	1,87±0,287	1,14±0,250	2,61±0,397
	II	1,42±0,136 p=0,926	1,01±0,081 p=0,008	1,64±0,149 p=0,015	1,60±0,088 p=0,390	1,62±0,097 p=0,104	1,21±0,067 p=0,006
Concentration of sodium ions in blood plasma, mmol/L	I	121,67±2,511	127,92±2,292	126,25±3,751	125,42±5,208	112,08±4,375	128,75±4,792
	II	130±2,511 p=0,040	125,00±1,671 p=0,327	127,51±1,251 p=0,758	126,25±2,501 p=0,889	129,58±1,528 p=0,004	124,17±1,667 p=0,366
Filtration fraction of sodium ions, mkmol/min	I	78,58±7,871	57,64±7,631	61,41±8,701	81,81±19,211	90,01±17,311	93,16±8,391
	II	33,33±3,452 p=0,000	46,16±5,081 p=0,239	25,26±2,961 p=0,003	43,02±3,371 p=0,075	40,47±4,721 p=0,020	42,65±5,021 p=0,000
Absolute re-absorption of sodium ions, mkmol/min	I	78,45±7,871	57,55±7,621	61,31±8,701	81,73±19,201	89,94±17,301	93,01±8,381
	II	33,30±3,451 p=0,000	46,13±5,081 p=0,241	25,23±2,951 p=0,000	42,98±3,371 p=0,003	40,42±4,721 p=0,020	42,62±5,011 p=0,000
Relative re-absorption of sodium ions, %	I	99,82±0,040	99,83±0,023	99,83±0,021	99,87±0,022	99,91±0,019	99,84±0,018
	II	99,91±0,010 p=0,054	99,93±0,005 p=0,002	99,89±0,009 p=0,025	99,89±0,005 p=0,000	99,90±0,006 p=0,627	99,92±0,004 p=0,001
Concentration index of sodium ions, UN	I	0,04±0,009	0,03±0,003	0,03±0,001	0,02±0,002	0,03±0,004	0,045±0,005
	II	0,01±0,001 p=0,008	0,01±0,001 p=0,000	0,01±0,001 p=0,000	0,02±0,001 p=1,000	0,01±0,001 p=0,001	0,01±0,001 p=0,000
Sodium/potassium coefficient	I	0,51±0,136	0,27±0,035	0,15±0,027	0,40±0,068	0,22±0,044	0,38±0,089
	II	0,13±0,009 p=0,019	0,10±0,010 p=0,140	0,13±0,011 p=0,508	0,12±0,008 p=0,002	0,11±0,006 p=0,033	0,12±0,009 p=0,024
Clearance of sodium ions, ml/2 hours	I	0,13±0,028	0,09±0,006	0,09±0,011	0,08±0,009	0,07±0,008	0,14±0,017
	II	0,03±0,002 p=0,193	0,03±0,003 p=0,000	0,03±0,003 p=0,000	0,04±0,002 p=0,001	0,04±0,005 p=0,010	0,03±0,004 p=0,000
Clearance of sodium-free water, ml/2 hours	I	3,72±0,431	2,83±0,151	3,55±0,312	3,41±0,341	2,14±0,242	2,95±0,211
	II	2,41±0,211 p=0,021	2,66±0,301 p=0,623	2,01±0,191 p=0,002	2,88±0,101 p=0,166	3,03±0,272 p=0,033	2,78±0,301 p=0,652
Proximal transport of sodium ions, mmol/2 hours	I	8,96±0,891	6,54±0,911	6,91±1,021	9,38±2,271	10,55±2,052	10,78±0,991
	II	3,68±0,391 p=0,000	5,20±0,571 p=0,240	2,77±0,331 p=0,003	4,79±0,401 p=0,074	4,46±0,532 p=0,016	4,77±0,571 p=0,000

the intact animals. The rhythm acrophase was detected at 12 p.m., and bathyphase shifted from 12 p.m. to 4 p.m. An average daily level of cation distal transport was reliably higher against the ground of reduced amplitude of circadian fluctuations concerning the index of the control group (table 1). The phase structure of the rhythm was similar to the chronogram of intact rats, except at 12 p.m. (fig.4).

**Table 1 NO blockade influence upon ion regulation renal function of albino rats under PB physiologic conditions ( $\bar{x} \pm S_{\bar{x}}$ )**

Index	Intact animals		Intact + No blockade	
	Mesor	Amplitude %	Mesor	Amplitude %
Concentration of sodium ions in urine mmol/L	3,9±0,47	29,2±1,61	1,6±0,11 p=0,000	10,2±1,01 p=0,000
Excretion of sodium ions, mkmol/2 hour	12,2±1,62	32,5±2,61	4,1±0,73 p=0,001	21,4±1,61 p=0,005
Excretion of sodium ions, mkmol/100 mkl of glomerular filtration	2,2±0,35	26,9±1,91	1,4±0,12 p=0,056	18,2±1,41 p=0,004
Concentration of sodium ions in blood plasma, mmol/L	123,7±1,08	5,0±1,21	127,1±1,85 p=0,144	1,9±0,32 p=0,033
Sodium/potassium coefficient	0,3±0,07	41,3±1,51	0,1±0,01 p=0,018	9,7±1,21 p=0,000
Filtration fraction of sodium ions mkmol/min	77,1±1,52	19,0±2,71	38,5±2,11 p=0,000	20,2±1,12 p=0,691
Absolute re-absorption of sodium ions, mkmol/min	76,9±1,51	9,0±1,82	38,5±2,12 p=0,000	20,2±1,11 p=0,000
Relative re-absorption of sodium ions, %	99,9±0,02	0,1±0,01	99,9±0,01 p=1,000	0,1±0,01 p=1,000
Clearance of sodium ions, ml/2 hours	0,1±0,01	28,3±2,41	0,1±0,11 p=1,000	17,2±0,01 p=0,000
Clearance of sodium-free water, ml/2 hours	3,1±0,28	18,8±0,42	2,6±0,23 p=0,198	14,1±0,01 p=0,000
Proximal transport of sodium ions, mmol/2 hours	8,9±1,36	20,2±0,41	4,3±0,47 p=0,010	20,9±0,39 p=0,791
Distal transport of sodium ions, mkmol/2 hours	385,4±2,81	21,1±0,41	334,6±2,61 p=0,000	13,9±0,39 p=0,000
Proximal transport of sodium ions, mkmol/100 mkl of glomerular filtrate	11,8±0,39	4,2±0,41	11,8±0,17 p=1,000	1,3±0,76 p=0,007
Distal transport of sodium ions, mkmol/100 mkl of glomerular filtrate	0,6±0,07	32,6±0,41	0,9±0,05 p=0,004	14,2±0,17 p=0,000
Concentration index of sodium ions, UN	0,1±0,01	28,2±0,41	0,1±0,01 p=1,000	15,1±0,26 p=0,000

The experiment was conducted with 4 hour interval within 24 hours. The concentration and excretion of potassium ions, creatinine, and protein, glomerular filtration rate, relative water absorption and endogenous creatinine were studied. The results were calculated statistically by «Cosinor-analysis» method as well as variation statistics parameter methods. The diagnostics of functional peculiarities was based on the analysis of characteristic changes of mesor, amplitude, acrophase and shape of circadian rhythm curve. Obtained individual chronograms for every animal were grouped by the principle of maximal acrophase identity, and the traversable mesor, amplitude and phase structure (by the time interval between acro- and bathyphase) for every chronogram group was calculated by «Cosinor-analysis» method.

Examinations in the control and experimental groups of animals at night were conducted at faint red light (2 lux) which practically does not influence upon epiphyseal melatonin biosynthesis. All the stages of the experiment were conducted according to the requirements of the European Convention for the Protection of Animals.

Obtained experimental data were processed on personal computers by the program package EXCEL-2003 (Microsoft Corp., USA). The value of an average arithmetical sampling ( $\bar{x}$ ), its dispersion and average error ( $S_x$ ) was calculated for all the indices. To find reliable difference of the results in the experimental and control groups Student coefficient ( $t$ ) was detected, after that the probability of sampling differences ( $p$ ) and confidence average interval by Student distribution tables were defined. The indices with  $p < 0,05$  were considered to be reliable.

### Results and discussion.

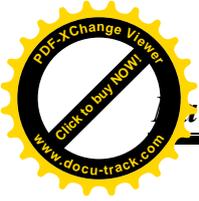
Circadian transformations of sodium ions renal transport were associated with a considerable decrease of natriuresis. The daily rhythm of sodium ions excretion was of an inversion character as compared with the control chronograms, and the mesor was three times less that of the indices of the intact animals (table 1). The rhythm acrophase was registered at 8 p.m. In spite of a low filtration loading of the nephrons by sodium ions, the absolute re-absorption of sodium cations remained decreased during all the examined periods of time (table 2), the phase rhythm structure concerning chronograms of the intact animals was changed as well.

An average daily level of this index was much lower in comparison with the same one in the control group.

As a result, sodium ions concentration in urine reliably decreased, and practically it did not change in the blood plasma (table 2).

Reliable re-absorption of sodium ions underwent reversible changes. The index increased almost at all time intervals. Maximal values were found at 12 a.m. and 4 a.m., at the same time bathyphase was registered from 4 p.m. to 8 p.m. (fig.3).

In re-calculation per 100 mkl of glomerular filtrate, an average daily level of the proximal transport of sodium ions did not differ greatly from the control values, while the rhythm amplitude was three times less that of the control one (table 1). Architectonics of the rhythm was of an inversion character concerning the same one in



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## **CHRONOMETRIC CHARACTERISTICS OF ION REGULATION RENAL FUNCTION AFFECTED BY NITRIC MONOXIDE BLOCKADE UNDER PHYSIOLOGICAL CONDITIONS OF PINEAL BODY**

**Summary.** *The work presents chronometric characteristics of ion regulation renal function under physiologic conditions of the pineal body affected by nitric monoxide (NO) blockade during 24 hours. The blockade of NO synthesis caused circadian transformation of sodium ions renal transport. The obtained results are indicative of a considerable decrease of natriuresis as compared with the indices of the intact animals.*

**Key words:** *chronorhythms, kidneys, nitrogen monoxide.*

### **Introduction.**

For recent years the study of biological rhythms as essential components of the vital systems has become more topical [1, 2]. Synchronization of the body biological rhythms is considered to be achieved by means of an integrated relations of the pineal body (PB) and hypothalamic suprachiasmatic nuclei (HSN) assuming as the main biorhythm generator of the majority of the body functions [2, 3]. The kidneys playing an important role in ensuring dynamic internal balance of the body are characterized by an accurate timely organization of its functions [4]. NO plays an important role in clinical and experimental pathophysiology of the kidneys as it regulates dilation of the blood vessels, glomerular blood circulation and releases tension from the lower urinary tract [5].

### **Objectives:**

to clarify peculiarities of chronometric characteristics of ion regulation renal function under physiologic conditions of the pineal body affected by NO blockade in rats.

Experiments were conducted on 72 mature nonlinear albino male rats with the body weight of 0,15-0,18 kg. The animals were kept in vivarium under constant temperature and air humidity on the standard dietary intake. The control group (n=36) was kept under conditions of usual light regime (12.00C:12.00T) for 7 days. The examined group included animals (n=36) kept under conditions of continuous light regime (12.00C:00T) for 7 days. On the 8<sup>th</sup> day the animals were subjected to 5% water loading heated to room temperature and excretory renal function under conditions of forced diuresis was examined.