ing a reliable determination of the shape of the blood flow curve. Under conditions of acute experiment the intravascular transducer makes it possible to investigate the hemodynamics in alert animals. The duration of the operating period of intravascular transducers under these conditions has not yet been established, and depends on the quality of the materials used. However, the relative benign procedure of implantation, greatly reduces the time before postoperative studies can be begun, which is an important plus for physiological investigations.

REFERENCES

1. L. N. Belkina, D. D. Matsievskii, and F. Z. Meerson, *Byull. Eksp. Biol. Med.*, **95**, № 6, 36 (1983).
2. A. A. Vishnevskii, A. M. Chernukh, Yu. D. Volynskii, *et al., Eksp. Khir.*, № 4, 6 (1968).
3. Yu. D. Volynskii, B. B. Keilin, and D. D. Matsievskii, *Krovoobrashchenie*, № 2, 25 (1968).
4. Sh. I. Ismailov, V. S. Baranov, O. S. Medvedev, *et al., Fiziol. Zh. SSSR*, № 8, 1171 (1982).
5. D. D. Matsievskii and V. S. Sinyakov, in: *Physiological Scientific Instrumentation* [in Russian], Moscow (1971), p. 12.
6. D. D. Matsievskii, *Byull. Eksp. Biol. Med.*, **97**, № 3, 377 (1984).
7. D. D. Matsievskii, O. S. Medvedev, E. V. Oranovskaya, *et al., Ibid.*, **106**, № 12, 674 (1988).
8. D. D. Matsievskii, L. M. Belkina, and E. A. Tolmacheva, *Ibid.*, **114**, № 7, 19 (1992).
9. N. V. Sanotskaya and D. D. Matsievskii, *Ibid.*, **94**, № 12, 119 (1982)
10. G. G. Chichkanov, E. A. Tolmacheva, and D. D. Matsievskii, *Ibid.*, **107**, № 5, 588 (1989).
11. L. S. Ul'yaninskii, O. S. Medvedev, A. N. Bunatyan, *et al., Ibid.*, **100**, № 9, 282 (1985).
12. G. G. Chichkanov, D. D. Matsievskii, and E. A. Tolmacheva, *Ibid.*, **111**, № 4, 359 (1991).
13. C. J. Hartley and J. S. Cole, *Med. Instrum.*, № 8, 241 (1974).
14. K. Plass, *IEEE Trans. Biomed. Eng.*, **11**, № 4, 154 (1964).

Role of the Liver in the Regulation of Sideremia Biorhythms in Rabbits with Acute Alcoholic Intoxication

E. N. Barkova, O. V. Gurov, and O. P. Gurova

UDC 612.35+612.015.31:616.36-07:577.31

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 116, № 8, pp. 147-149, August, 1993
Original article submitted February 19, 1993

Key Words: *biorhythms; iron metabolism; alcohol; liver*

One mechanism through which alcohol exerts its hepatotoxic effect is the activation of lipid peroxidation (LPO) [12,15], which is initiated by a rise in the concentration of variable valency metals, in particular iron and copper, and their transition from the bound to a free state [2,10,11]. The liver, as a depot of iron, is involved in regulating the circadian rhythmicity of sideremia, which is dependent on the activity of free-radical LPO [1]. It is therefore important to know what role this organ plays in the regulation of diurnal variations in sideremia, LPO, and antioxidants in acute alcoholic intoxication.

The purpose of this study was to examine the impact of acute alcoholic intoxication (AAI) on the temporal organization of iron metabolism, LPO, and antioxidants by considering diurnal variations in the concentrations of serum iron, LPO products, and α-tocopherol in blood from the portal and hepatic veins.

MATERIALS AND METHODS

For the experiments, which were conducted in winter, 80 male brush rabbits (*Sylvilagus bachmani*)

Department of Pathological Physiology, Medical Institute, Tyumen. (Presented by E. D. Gol'dberg, Member of the Russian Academy of Medical Sciences)

0007-4888/93/0008-0936$12.50

weighing 2.8-3.2 kg were used. Rabbits of the test and control groups were maintained under natural lighting conditions (7 h light/17 h darkness) at an ambient temperature of 18-20°C, received the same diets, and had free access to water. AAI was produced by a single intragastric administration of 40% ethanol at 10 ml/kg body weight 90 min before the test was started. Under intrapleural Hexenal anesthesia (50 mg/kg body weight), laparotomy was performed and blood was collected for biochemical examination from the portal vein and a hepatic vein at 6:00, 12:00, 18:00, and 24:00 hours. The plasma concentration of iron was determined by the diphenylphenanthroline method with spectrophotometry at 540 nm [5]. LPO activity was assessed by measuring concentrations of malonic dialdehyde (MDA) [4] and diene conjugates (DC) [3] in plasma and in erythrocyte membranes. Concurrently, plasma concentrations of α-tocopherol were determined. The data obtained were evaluated by Student's *t* test and rhythmometric parameters calculated using *Kosinor* software.

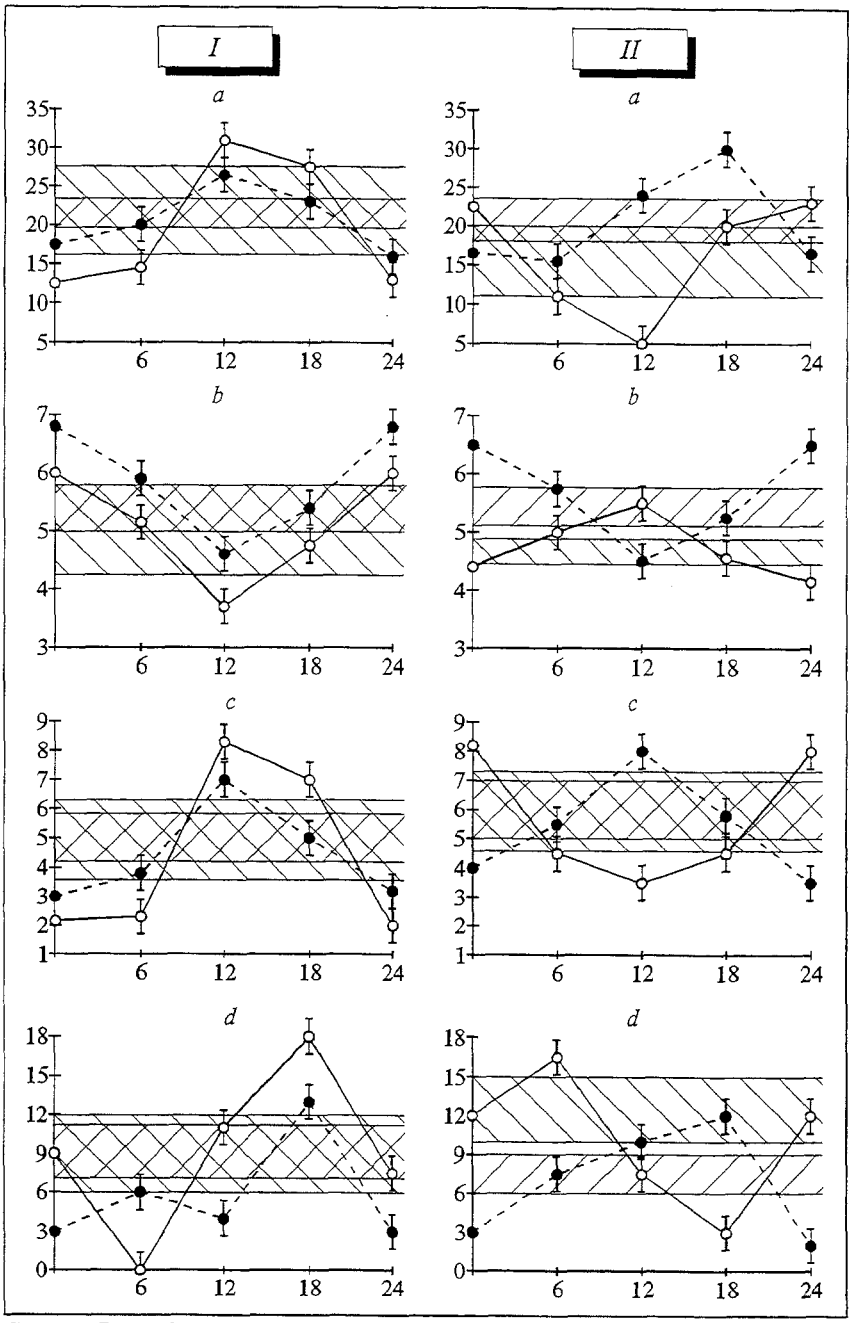

Fig. 1. Diurnal variations in the concentration of iron, α-tocopherol, diene conjugates (DC), and malonic dialdehyde (MDA) in blood plasma from portal (dashed lines) and hepatic (solid lines) veins in intact rabbits (*I*) and rabbits given a single dose of ethanol (*II*). Abscissa: time of day, hours. Ordinate: *a*) iron, μmol/liter; *b*) α-tocopherol, μmol/liter; *c*) DC, nmol/ml; *d*) MDA, nmol/ml.

RESULTS

In intact rabbits (Table 1 and Fig. 1), the level of sideremia in the hepatic vein was significantly higher than in the portal vein during the period when it was highest and significantly lower when it was lowest, which indicates that deposition of iron in and its release from the liver occurred with rhythmic oscillation. The observed synchronization of serum iron, DC, and MDA concentrations and also the finding that the level of LPO products in the blood issuing from the liver was elevated when sideremia was at its maximum support the conclusion, reached by us previously, that there is a relationship between the parameters of LPO activity and the iron level in the liver [1]. The observation that the concentration of α-tocopherol also showed a circadian rhythmicity and was in counterphase with those of DC and MDA makes it evident that the modulating effect of LPO and the antioxidant system (AOS) serves as an oscillator of the processes by which iron is deposited in and released from the liver, which regulates, in the final analysis, the circadian rhythm of sideremia.

In rabbits with AAI (Table 1 and Fig. 1), the rhythmometric parameters of sideremia in the hepatic veins varied to a much greater extent than they did in intact animals. As the only apparent

Table 1. Rhythmometric Parameters of Iron Metabolism, Lipid Peroxidation, and Antioxidants in Intact Rabbits and Rabbits Administered a Single Dose of Ethanol (Values are Means±SEM)

Concentrations	Blood plasma from portal vein				Blood plasma from hepatic vein			
	period	mesor	amplitude	acrophase	period	mesor	amplitude	acrophase
Intact Rabbits								
Iron, μmol/liter	24.3±0.5	20.83±0.8	6.10±0.21	14.18 (11.16–17.12)	24.1±0.3	21.41±0.24	11.42±0.27	14.07 (9.55–18.54)
α–Tocopherol, μmol/liter	23.9±0.2	5.35±0.12	1.11±0.18	1.04 (23.03–3.04)	24.1±0.1	4.99±0.4	1.47±0.14	1.05 (0.08–2.02)
DC, nmol/ml	23.6±0.3	4.89±0.39	2.25±0.22	13.18 (11.23–15.33)	23.5±0.6	5.18±0.48	3.89±0.26	14.21 (11.06–18.36)
MDA, nmol/ml	24.14±0.6	8.87±0.25	3.21±0.15	16.08 (13.35–19.21)	24.2±0.3	10.76±0.56	5.33±0.37	17.13 (14.08–20.18)
Rabbits Given Ethanol								
Iron, μmol/liter	24.2±0.3	20.46±0.44	8.01±0.73	16.44 (13.55–19.25)	24.1±0.6	16.09±0.63*	8.24±0.6	21.36* (18.16–24.56)
α–Tocopherol, μmol/liter	24.2±0.2	5.23±0.16	0.47±0.19	2.25 (0.10–4.35)	23.9±0.3	5.02±0.38	0.57±0.27	10.31* (8.31–12.23)
DC, nmol/ml	23.9±0.4	5.81±0.51	2.17±0.29	12.40 (11.36–13.44)	23.8±0.5	5.35±0.63	2.25±0.21*	0.43* (23.34–1.52)
MDA, nmol/ml	23.8±0.3	12.12±1.06	4.89±0.32*	14.31 (10.38–18.24)	23.9±0.4	13.9±1.21*	4.97±0.28	5.11* (3.50–6.31)

Note. The asterisk indicates a significant difference from control rabbits at $p<0.05$.

change in the rhythmic oscillation of sideremia from the portal vein was a shift of the acrophase from 12.00 h to 18.00 h, the observed fall of the iron level in the hepatic veins during the daytime without any alteration in the rhythm of its supply from the portal vein could only be due to its fixation in the liver. During the night hours, in contrast, iron was removed from the liver in excess, thereby altering the oscillatory circuit of sideremia. The LPO-AOS system was reorganizing in synchrony with this inversion of the circadian rhythm of sideremia: when DC were at their height, the portocaval difference in terms of plasma α-tocopherol concentration was diminished and the concentration of serum iron was very high. It is most likely, therefore, that the inversion of diurnal LPO and AOS rhythms plays the major role in altering the circadian organization of sideremia in alcohol-induced liver damage.

Oxidation of primary alcohols causes cytochrome P-450 to initiate the formation of free radicals [8] which then release iron from its bound state [2,11]. By catalyzing chain reactions, the free iron accelerates the development of a peroxidation syndrome if antioxidants are deficient [10]. Under such circumstances, the function of α-tocopherol, a major radical scavenger, is considerably activated.

That LPO and AOS play leading roles in the mechanisms via which the temporal organization of iron metabolism is impaired in AAI is also evidenced by the direct correlation found between the rate of LPO and DC concentrations ($r=+0.91$; $p<0.05$) and the inverse correlation between the α-tocopherol and DC concentrations ($r=-0.89$; $p<0.05$).

The finding that the rhythmic parameters of α-tocopherol in plasma from the portal vein remained unaltered indicates that the principal pathway of its entry into the liver was preserved. More than half of all reserves of this antioxidant are known to be accumulated in the liver [6], mainly in the mitochondrial and microsomal fractions of hepatocytes [7]. Its secretion only occurs after its conjugation with very high density lipoproteins synthesized by the endoplasmic reticulum of these cells [13]. Since decreased amounts of α-tocopherol were shown to enter the bloodstream when the biosynthesis and secretion of very low density lipoproteins was inhibited [9], the observed inversion of the circadian rhythm of α-tocopherol with a reduction of its mean diurnal level in the hepatic veins could be a consequence of the impairment of biosynthetic processes caused by the membranotoxic effect of LPO.

It may be concluded from this study that the circadian rhythm of sideremia is impaired in AAI as a result of an intrasystemic desynchronization occurring in the space-time organization of iron metabolism consequent to an inversion of the diurnal LPO and AOS dynamics in the hepatic microsomal system.

REFERENCES

1. E. N. Barkova, E. V. Chesnokov, and A. L. Korkin, *Byull. Eksp. Biol. Med.*, **111**, № 7, 96 (1991).
2. Yu. A. Vladimirov, *Priroda*, № 3, 36 (1987).
3. V. B. Gavrilov and M. I. Meshkorudnaya, *Lab. Delo*, № 3, 33 (1983).
4. I. D. Stal'naya and T. G. Garishvili, *Modern Methods in Biochemistry* [in Russian], Moscow (1977), p. 66.
5. Yu. S. Sukhanov, *Lab. Delo*, № 6, 17 (1982).
6. G. Bjorneboe, A. Bjorneboe, B. Hagen, *et al.*, *Biochim. Biophys. Acta*, **918**, 236 (1987).
7. J. Buttriss and A. Diploch, *Biochim. Biophys. Acta*, **962**, 81 (1988).
8. A. Cederbaum, E. Dicker, E. Rubin, and G. Cohen, *Biochem. Biophys. Res. Commun.*, **78**, 1254 (1977).
9. W. Cohn, F. Loechleiter, and F. Weber, *J. Lipid Res.*, **29**, 1359 (1988).
10. J. Gutteridge, D. Rowley, and E. Griffiths, *Clin. Sci.*, **68**, № 4, 463 (1985).
11. B. Halliwell and J. Gutteridge, *TIBS*, **11**, 372 (1986).
12. R. Litov, D. Irwing, G. Downey, and A. Tappel, *Lipids*, **13**, 305 (1978).
13. S. Rall, K. Weisgraber, R. Maley, and T. Innerarity, *J. Lipid Res.*, **25**, 1277 (1984).
14. B. Martinec, *Clin. Chem.*, **10**, 1078 (1964).
15. E. Toranzo, A. Marzi, and G. Castro, *Toxicology*, **19**, 77 (1981).

Effect of Blood Serum of Patients Undergoing Intravenous Laser Therapy on the Parameters of Synaptic Transmission

D. I. Azbel', N. V. Egorushkina, I. Yu. Kuznetsova, A. S. Ratushnyak, S. M. Shergin, A. M. Shurgaya, and M. B. Shtark

UDC 615.849.19.015.4:616.153

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 116, № 8, pp. 149-151, August, 1993
Original article submitted February 23, 1993

Key Words: *blood serum; intravenous laser therapy; hippocampus; p-spike*

Currently, biological objects (systems) able to respond to an array of external factors are being widely used in order to study the combined effect of different enzymes and biologically active substances (BAS) [1]. Surviving hippocampal sections may be counted among such systems. They are highly sensitive to BAS and demonstrate comparatively simple reactions which are easily registered [3]. These properties make it possible to use this model for testing the blood serum of patients who have undergone intravenous laser therapy (IVLT). The mechanisms of the therapeutic effect of laser are still to be elucidated, but it has been established that the effects of laser on the blood are many and varied [2], their individual analysis involving very costly and very complicated procedures. Therefore, hippocampal sections used for testing the activity of such a complex system as the blood serum are one of the most appropriate models for experiment.

In the present study we investigated the effect of blood serum of patients with ischemic heart disease, exposed to low-energy laser radiation, on the parameters of synaptic transmission in neurons of the rat hippocampus.

MATERIALS AND METHODS

Fourteen patients (living in Yakutia) aged 36 to 57 years with different types of ischemic heart disease were examined. Six patients had suffered myocardial infarction in the past. The course of laser therapy comprised 6 sessions, each of 30 min

Laboratory of Clinical Diagnostics and Treatment, Institute of General Human Pathology and Ecology; Laboratory of Central Regulation and Control Mechanisms, Institute of Medical and Biological Cybernetics, Siberian Department of the Russian Academy of Medical Sciences, Novosibirsk

0007-4888/93/0008-0939$12.50