6. G. Gandolfo, C. Gottesmann, J.-N. Bidard, et al., Eur. J. Pharmacol., **160**, 173 (1987).
7. J. J. Habbitz and U. Heinemann, Develop. Brain Res., **36**, 229 (1987).
8. U. Heinemann and B. Hamon, Exp. Brain Res., **65**, 1 (1986).
9. F. B. Meyer, R. E. Anderson, T. M. Sundt, et al., Mayo Clin. Proc., **61**, 239 (1986).
10. F. B. Meyer, P. W. Tally, R. E. Anderson, et al., Brain Res., **384**, 180 (1986).
11. J. Overweg, C. D. Binnie, J. W. A. Meyer, et al., Epilepsia, **25**, 217 (1989).
12. G. Paxinos and C. Watson, The Rat Brain in Stereotaxic Coordinates (1986).
13. R. Puman, J. Louvel, and I. Kurcewitz, Calcium Electrogenesis and Neuronal Function, Berlin (1986), pp. 345-359.
14. D. Rample and D.J. Triggle, Trends Pharmacol. Sci., **7**, 461 (1986).
15. D. M. Woodbury, Antiepileptic Drugs, New York (1980), pp. 447-471.

Zn^{2+}-, Cu^{2+}-CONTAINING SUPEROXIDE DISMUTASE IN BRAIN TISSUE OF RAT OFFSPRING EXPOSED ANTENATALLY TO ALCOHOL

M. G. Uzbekov and I. K. Karpachevskaya

UDC 618.33-06:616.89-008.441.13]-092.9-07:
[616.831-008.931:577.152.1]-053.31

KEY WORDS: superoxide dismutase, antenatal exposure to alcohol, rat brain

Exposure to alcohol and its metabolites in the antenatal period of development leads to various neurochemical disturbances in the brain tissue of the offspring in postnatal ontogeny [1, 4, 6]. We have suggested that one possible pathogenetic mechanism of the metabolic disturbances developing in the brain tissue of the offspring after antenatal exposure to alcohol may be increased production of free radicals, which exert a teratogenic action on the developing brain [3, 5]. An increase in free radical production in adult animals under the influence of alcohol has been demonstrated [7, 12]. Manifestation of the damaging effect of free radicals may be facilitated by exhaustion of the antioxidant protection reserves following exposure to alcohol [7, 13].

Zn^{2+}-, Cu^{2+}-containing (cytoplasmic) and Mn^{2+}-containing (mitochondrial) isozymes of superoxide dismutase (SOD) have been discovered in mammalian tissues. It has been shown [10, 14] that the greatest specific activity of SOD in brain tissue is due to the Zn^{2+}-, Cu^{2+}-containing isozyme. Changes in SOD activity in the brain tissue of the offspring, in cases of antenatal pathology, have been studied extremely inadequately. However, such research would be very promising in connection with the establishment of the pathogenetic mechanisms of development of inborn disturbances of the CNS and the development of corrective methods.

The aim of this investigation was to study activity of Zn^{2+}, Cu^{2+}-containing SOD in the brain tissue of the offspring of rats exposed antenatally to alcohol, during postnatal development.

EXPERIMENTAL METHOD

Experiments were carried out on 32 young Wistar rats aged 14 and 30 days. The mothers of the experimental animals consumed 12% ethanol (on average 8 g/kg body weight/day) as the sole source of fluid throughout pregnancy. Control and experimental animals were kept on the standard animal house diet. The rats were decapitated at the appropriate age, the brain was removed, and the cerebral cortex, hippocampus, and brain stem (mesencephalon plus diencephalon together) were separated. All operations with the brain were carried out at 0°C.

Laboratory of Brain Pathology, Research Institute of Psychiatry, Ministry of Health of the RSFSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR S. S. Debov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 111, No. 4, pp. 354-355, April, 1991. Original article submitted April 26, 1990.

TABLE 1. Zn^{2+}-, Cu^{2+}-Containing SOD Activity (in conventional units/mg protein) in Different Parts of the Brain of Rat Offspring Exposed Antenatally to Alcohol (M ± m)

Age of animals, days	Experimental conditions	Exposure to alcohol	Hippocampus	Brain stem
14	Control	35,07±1,75(9)	32,66±2,02(14)	40,1±3,81(9)
	Exposure to alcohol	25,56±2,89*(9)	22,5±1,69*(8)	26,72±2,97*(9)
30	Control	38,5±4,67(10)	28,4±2,72(10)	35,9±3,91(10)
	Exposure to alcohol	32,55±2,81(8)	25,33±2,39(8)	27,5±2,03(8)

Legend. *$p < 0.05$ compared with control. Number of animals given in parentheses.

Brain tissue homogenate (1:10) was prepared with medium of the following composition (in mM): sucrose 250, Tris-HCl 10, EDTA 10; pH 7.4. SOD activity was determined in the supernatant obtained after centrifugation of the homogenate at 20,000*g* for 30 min, by the method in [11], based on the ability of SOD to inhibit autooxidatlon of adrenalin in an alkaline medium. Activity of the enzyme was expressed in conventional units per milligram protein. The unit of activity was taken to be the quantity of enzyme required to inhibit autooxidation of adrenalin by 50% under experimental conditions. Protein was determined by Lowry's method.

EXPERIMENTAL RESULTS

No significant differences in enzymic activity were found in 14- and 30-day-old control animals in any of the brain formations studied (Table 1). It can be postulated that during this period activity of the enzyme was formed, in agreement with results in [9], indicating a sharp increase in SOD activity in different parts of the rat brain at the later stages of postnatal development (2-3 months).

SOD activity in 14-day-old rats exposed prenatally to alcohol was found to be lower than the control level in all parts of the brain studied: by 27% in the cerebral cortex, by 31% in the hippocampus, and by 33% in the brain stem (Table 1). SOD activity in the 30-day-old experimental animals did not differ from the control values, although in the brain stem a tendency for its activity to fall was maintained.

The results indicate a disturbance of antioxidant protection in the tissues of the developing brain after antenatal exposure to alcohol in the 14-day-old offspring. One cause of the weakening of SOD activity may be a deficiency of zinc, which is essential to stabilize the enzyme molecule. It has been shown experimentally [2] that chronic alcohol intoxication leads to Zn deficiency in adult animals and their offspring. The enzyme molecule may also be damaged by free radicals and H_2O_2 formed in excess when the functional activity of other antioxidant systems is depressed. The direct damaging effect of acetaldehyde on the SOD molecule likewise cannot be ruled out.

The writers previously described a possible mechanism of neurochemical disturbances following antenatal exposure to alcohol, which was based on activation of free radical production [3, 5]. One of the main producers of free radicals is the respiratory chain [8]. Tissue hypoxia, by leading to an increase in the degree of reduction of certain carriers of the respiratory chain, leads to excessive production of free radicals [8]. Antenatal exposure to alcohol, accompanied by tissue hypoxia, causes marked changes in oxidative phosphorylation in the brain of the 14-day-old offspring [5]. All this probably leads to a considerable increase in the level of free radicals, which is accompanied (Table 1) by weakening of SOD activity in different parts of the brain. Normalization of SOD activity by the 30th day of postnatal development in the experimental offspring, in our opinion, reflects metabolic compensation in the offspring, exposed antenatally to alcohol, during maturation of the brain.

Analysis of the results of this and our previous studies [3, 5] suggest that there is a definite relationship between SOD activity and the state of terminal oxidation processes in the brain of the offspring exposed antenatally to alcohol. However, there are other sources of increased free radical and peroxide formation under pathological conditions than the respiratory chain, such as catecholamines (especially dopamine), the microsomal oxidation system, monoamine oxidase, xanthine oxidase, etc. [8]. A further study of the state of other enzyme components of antioxidant protection is therefore required.

LITERATURE CITED

1. I. P. Anokhina, S. O. Varfolomeev, B. M. Kogan, et al., Alcoholism and Heredity [in Russian], Moscow (1987), pp. 20-26.
2. A. M. Skosyreva, L. F. Kurilo, A. V. Skal'nyi, and E. V. Tatarinskaya, Alcoholism and Heredity [in Russian], Moscow (1987), pp. 134-138.
3. M. G. Uzbekov, M. A. Moshanskaya, and I. K. Karpachevskaya, Fundamental Achievements in Neurochemistry Relative to Medicine [in Russian], Gor'kii (1987), p. 60.
4. M. G. Uzbekov and M. A. Moshanskaya, Byull. Éksp. Biol. Med., No. 4, 436 (1988).
5. M. G. Uzbekov, M. A. Moshanskaya, and I. K. Karpachevskaya, Medicobiological Problems of Alcoholism [in Russian], Moscow (1988), pp. 109-113.
6. E. L. Abel, Fed. Proc., **44**, 2318 (1985).
7. M. Dianzani, Alcohol and Alcoholism, **20**, No. 2, 167 (1985).
8. B. A. Freeman and J. D. Crapo, Adv. Biol. Dis., **1**, 26 (1984).
9. M. Ledig, R. Fried, M. Ziessel, and P. Mandel, Develop. Brain Res., **4**, No. 3, 333 (1982).
10. T. C. Loomis, G. Yee, and W. L. Stahl, Experientia, **32**, No. 11, 1374 (1976).
11. H. P. Misra and I. Pridovich, J. Biol. Chem., **297**, No. 10, 3170 (1972).
12. R. Nordmann, C. Ribiere, H. Rouach, et al., Ann. Gastroent. Hepatol., **22**, No. 7, 913 (1986).
13. H. Speisky, Y. Kera, K. Pentillä, et al., Alcoholism: Clin. Exp. Res., **12**, No. 2, 229 (1988).
14. T. N. Thomas, D. G. Priest, and J. W. Zemp, J. Neurochem., **27**, 309 (1976).

EXPERIMENTAL ANALYSIS OF MACROREENTRY FORMATION IN THE RABBIT RIGHT ATRIUM

F. Bukauskas, V. Valiunas, V. Mizeras, and A. Tamoševičius

UDC 616.12-008.318-02:616.124.7-008.1-092.9-07

KEY WORDS: atrioventricular node, reentry, tachycardia, mapping

The commonest cardiac arrhythmias found in clinical practice are supraventricular disturbances of the cardiac rhythm, a large proportion of which consists of arrhythmias connected with the atrioventricular (AV) node [3, 8]. The hypothesis has been put forward that reentry formation within the AV node can be explained by assuming the existence of several pathways for the conduction of excitation in the AV node [12, 15]. On the other hand, the accumulation of clinical experience with the surgical treatment of cardiac arrhythmias has shown that several supraventricular arryhthmias can be effectively abolished by cryodestruction of the perinodal regions of the AV node [6, 11, 16]. This realistically describes the situation, for example, when macroreentry, intersecting the region of the AV node, is formed in the atria.

In the present study we concentrated our attention on arrythmias due to the formation of macroreentry in the atria, with a loop including the region of the AV node.

Kaunas Medical Academy. (Presented by Academician of the Academy of Medical Sciences of the USSR J. J. Bredikis.)

Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 111, No. 4, pp. 355-359, April, 1991. Original article submitted May 23, 1990.