ENKEPHALIN LEVEL IN BRAIN REGIONS OF RATS PRENATALLY EXPOSED TO ETHANOL

M. Ya. Maizelis and A. L. Zabludovskii

UDC 612.822.1:[547.95:547.943]-06:612.647.014.46:547.262

KEY WORDS: brain; enkephalins; ethanol; intrauterine pathology

The role of endogenous opioids in the pathogenesis of alcoholism has been discussed in the literature in recent years [2, 3]. It has been shown that under the influence of acute and chronic alcoholic intoxication changes take place in concentrations of enkephalins and endorphins in the brain regions of animals with different degrees of alcohol motivation [3, 5] and in binding of enkephalins with receptors [1, 8]. In view of data on interaction of ethanol with endogenous opioids, it appears interesting to study enkephalin levels in the CNS under the influence of ethanol on the developing brain. Recent studies have demonstrated changes in endogenous opioid concentrations in the brain of newborn animals [9] and in the pituitary gland and individual brain structures (globus pallidus) of adult animals exposed prenatally to ethanol [7].

The aim of this investigation was to determine concentrations of Leu- and Met-enkephalins in other parts of the brain, namely the cerebral cortex, hippocampus, and hypothalamus, of animals exposed prenatally to ethanol.

EXPERIMENTAL METHOD

From the 4th through the 21st days of pregnancy (the day of conception was identified by means of vaginal films) rats were given 2.5-3 ml of 40% ethanol daily by gastric tube (4-5 g/kg). The progeny of the experimental and control animals was kept under identical animal house conditions. At the age of 4 weeks the young rats were put on a standard diet. Concentrations of Leu- and Met-enkephalins in brain structures of the experimental and control animals, at the age of 32-35 days, by radioimmunoassay using standard kits from Immuno Nuclear Corporation (USA). Altogether 20 experimental and control rats were used.

EXPERIMENTAL RESULTS

Regional differences were noted in concentrations of Leu- and Met-enkephalins in parts of the brain studied in control and experimental rats: the lowest level in the hippocampus and cortex, the highest in the hypothalamus.

Sex differences were discovered in the enkephalin levels in brain regions. The concentration of Met-enkephalin was higher in male rats than in females in all structures and, in particular, in the cerebral cortex and hippocampus. These differences for Leu-enkephalin were observed in the hypothalamus, where in male rats the peptide concentration was 30% higher on average than the characteristic level in females. Allowing for the differences noted above, levels of the neuropeptides were compared in brain regions of experimental and control animals of the same sex.

The experimental results showed (Table 1) that the Met-enkephalin concentration in the brain structures studied in rats (both males and females) exposed prenatally to ethanol did not differ significantly from the concentration in control animals. Only in the hypothalamus of male rats was a tendency observed for the peptide concentration to fall. Investigation of the Leu-enkephalin concentration in the cerebral cortex and hippocampus of the experi-

Laboratory of Brain Pathology, Moscow Research Institute of Psychiatry, Ministry of Health of the RSFSR. [Presented by Academician of the Academy of Medical Sciences of the USSR V. V. Zakusov (deceased).] Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 101, No. 3, pp. 311-312, March, 1986. Original article submitted March 6, 1985.

0007-4888/86/0003-0315$12.50

TABLE 1. Concentrations of Enkephalins (in pg/mg tissue) in Regions of Rat Brain (M ± m)

Sex of animals	Experimental conditions	Met-enkephalin			Leu-enkephalin		
		cortex	hippocampus	hypothalamus	cortex	hippocampus	hypothalamus
Males	Control	33,9±5,9	26,4±1,8	121,0±13,1	14,5±1,8	8,6±2,3	89,5±8,9
	Experiment	33,6±6,6	22,7±1,2	98,0±10,9	13,2±1,3	9,3±1,7	56,0±7,8*
Females	Control	21,3±1,5	24,1±5,5	85,2±10,4	13,9±1,8	10,2±2,6	60,6±7,0
	Experiment	20,3±5,3	26,1±4,5	83,7±6,4	10,8±0,8	8,8±0,9	40,2±5,5*

Legend. *P < 0.05.

mental rats revealed hardly any change in its level compared with the control. Meanwhile in the hypothalamus of experimental rats of both sexes, the Leu-enkephalin concentration was significantly depressed by 34-37%.

The results confirm data in the literature on the distribution of enkephalins in parts of the brain, showing highest concentrations to be present in the basal ganglia (globus pallidus) and also in the hypothalamus. Meanwhile the results of the present experiments differ from those obtained by some workers [7] who found no sex differences in the concentration of enkephalins in the globus pallidus and pituitary gland of rats.

The results indicate that changes in enkephalin levels in different parts of the brain in animals (both males and females) exposed prenatally to alcohol differ: the concentrations of Met- and Leu-enkephalins in the cerebral cortex and hippocampus did not differ from the control, whereas in the hypothalamus they were greatly reduced. Selective regional changes in the enkephalin concentrations in brain structures under the influence of ethanol have also been demonstrated in other investigations. For instance, during the formation of alcohol dependence in rats preferring ethanol, the Met-enkephalin level rose predominantly in the basal ganglia, whereas in animals preferring water, it rose mainly in the hypothalamus. In sexually mature rats exposed to ethanol during embryonic development, the Leu- and Met-enkephalin concentrations in the pituitary remained unchanged, but were increased in the globus pallidus [7]. These changes in the enkephalin levels in the brain evidently developed durin postnatal ontogeny. This is shown by the fact that the enkephalin levels in the mid- and hind brain of day-old rats exposed prenatally to alcohol were unchanged [9]. It can be concluded from these data that changes in enkephalin levels observed in the present experiments in individual brain structures of rats are not due to the direct effect of ethanol on the endogenous opioid system, but develop as a result of indirect reactions. Possible confirmation of this conclusion is given by data on the dynamics of development of opioid mechanisms in the brain, evidence of a gradual increase in binding of Met-enkephalin and naloxone in brain structures and the development of receptors in the postnatal period [6, 10].

LITERATURE CITED

1. I. P. Anokhina, L. F. Panchenko, and O. S. Brusov, in: Alcoholism [in Russian], Moscow (1981), pp. 52-56.
2. Yu. V. Burov, Vest. Akad. Med. Nauk SSSR, No. 5, 72 (1982).
3. Yu. V. Burov, R. Yu. Yukhananov, and A. I. Maiskii, Byull. Éksp. Biol. Med., No. 7, 48 (1983).
4. S. V. Petrenko, in: Abstracts of Proceedings of the 4th Congress of Pharmacists, Pharmacologists, and Toxicologists [in Russian], Minsk (1983), pp. 168-169.
5. R. Yu. Yukhananov, in: The Pharmacology of Experimental Alcoholism [in Russian], Moscow (1982), pp. 54-59.
6. A. Bayon, W. Shoemaker, and F. E. Bloom, Brain Res., 179, 93 (1979).
7. R. F. McGivern, A. N. Glancy, S. Mousa, et al., Life Sci., 34, 585 (1984).
8. I. M. Hiller, L. M. Angel, and E. I. Simon, Science, 214, 468 (1981).
9. W. I. Shoemaker, Alcoholism, 6, 153 (1982).
10. D. Tsang, in: Advances in Endogenous and Exogenous Opioids, Tokyo (1981), pp. 60-62.