

BIOPHYSICS AND BIOCHEMISTRY

Metabolism of Neurotransmitters in Cortical and Subcortical Brain Structures in Rats with Different Behavioral Characteristics

E. L. Dovedova and M. Yu. Monakov

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 130, No. 9, pp. 289-291, September, 2000
Original article submitted April 20, 2000

Experiments were performed on Wistar rats with high and low locomotor activities. In rats with high locomotor activity, activities of acetylcholine transferase, acetylcholine esterase, and monoamine oxidase A increased in the subcellular fractions of the sensorimotor cortex and arcuate nucleus, while monoamine oxidase B activity decreased compared to those in rats with low locomotor activity. The peculiarities of neurotransmitter systems in brain structures of rats with different behavioral patterns were related to genetic and functional organization of the central nervous system.

Key Words: *enzyme activity; neurotransmitter systems; brain subfractions; rat locomotor activity*

It was reported that peculiarities of neurotransmitter metabolism in the brain of genetically different animals are related to their structural and functional reactivity and manifest in various behavioral patterns [3,9].

Individual peculiarities in emotional reactivity and locomotor activity were revealed within the same animal population (e.g., in rats) [1,4].

Here we studied neurochemical peculiarities of interaction between neurotransmitter systems in rats with various locomotor activities in an open field (OF).

We compared activities of enzymes involved in neurotransmitter metabolism, monoamine oxidases (MAO) A and B, acetylcholine transferase, and acetylcholine esterase, in cortical and subcortical brain structures in rats with different behavioral characteristics.

MATERIALS AND METHODS

Experiments were performed on adult male Wistar rats weighing 180-200 g. The rats were divided into 2 groups with high (HLA) and low (LLA) locomotor activities in OF. Behavioral tests were performed daily for 2 weeks (5 min a day) in a square dark chamber. Rats with HLA and LLA crossed 178.9 ± 15.0 and 69.3 ± 7.7 squares, respectively.

After OF test, the animals were decapitated under light ether anesthesia. The sensorimotor cortex and arcuate nucleus were isolated in a cold chamber. Synaptosomal and mitochondrial membranes were isolated from brain tissue homogenates by consecutive differential and gradient centrifugation. Protein concentration was estimated spectrophotometrically at 750 nm by the method of Lowry. MAO A, MAO B, and acetylcholine esterase activities were measured at 250 [13], 540 [6], and 450 nm [11], respectively. Acetylcholine transferase activity was estimated radiometrically [10].

Specific enzyme activities were expressed in optical density units per mg protein, and the HLA/LLA

Laboratory of Cytochemistry, Institute of Brain Research, Russian Academy of Medical Sciences, Moscow

ratio was calculated in percents. The results were analyzed by Student's *t* test.

RESULTS

The rats were assigned to LLA and HLA groups, if the total number of crossed squares during the test was 140-200 and below 70, respectively. Daily OF testing was described previously [5]. Specific activity of MAO A (serotonin is the substrate) in synaptosomes and mitochondria of the cortex and arcuate nucleus from rats with HLA 1.5-2.0-fold surpassed that in rats with LLA and was maximum in the mitochondrial subfraction (Table 1). Specific activity of MAO B (p-nitrophenyl ethylamine is the substrate) in the brain of rats with HLA was 28-30% lower than in rats with LLA. The maximum inhibition of enzyme activity was revealed in cortical mitochondrial subfraction (Table 1).

Activities of both enzymes involved in acetylcholine metabolism in the cortex and arcuate nucleus in rats with HLA increased compared to those in rats with LLA (Table 2). Acetylcholine esterase activity in all subfractions also increased (Table 2), which indicated activation of the brain cholinergic system in rats with HLA.

There were also reciprocal changes in the serotonin- and catecholaminergic systems estimated by the enzymes of neurotransmitter utilization (specific activities of MAO A and B). Similar results were obtained previously [12,14].

Our results confirm that the locomotor activity inversely correlates with emotionality. This manifests in various relationships between neurotransmitter systems in the brain of rats displaying different behavioral patterns during locomotor overload [2,7,8].

These differences between HLA and LLA rats were most pronounced in the sensorimotor cortex,

TABLE 1. Specific Activities of MAO A and B (Optical Density Units/mg protein/h) in Brain Structures of Rats with Different Locomotor Activity ($M \pm m$)

Mitochondrial fraction		Cortex			Arcuate nucleus		
		LLA	HLA	LLA/HLA, %	LLA	HLA	LLA/HLA, %
Initial							
	MAO A	0.17±0.01	0.30±0.02	176.47	0.21±0.01	0.33±0.03	15.14
	MAO B	0.22±0.02	0.15±0.01	68.18	0.36±0.04	0.25±0.02	69.44
Synaptosomal subfraction							
	MAO A	0.11±0.06	0.23±0.01	143.6	0.22±0.03	0.32±0.02	144.7
	MAO B	0.22±0.03	0.15±0.01	69.1	0.36±0.02	0.26±0.03	72.7
Mitochondrial subfraction							
	MAO A	0.24±0.01	0.49±0.04	204.16	0.20±0.01	0.35±0.03	175
	MAO B	0.42±0.03	0.17±0.01	40.47	0.37±0.02	0.24±0.01	64.86

Note. Here and in Table 2: $p < 0.01$ compared to rats with LLA.

TABLE 2. Specific Activities of Acetylcholine Esterase and Acetylcholine Transferase (ACE and ACT, $\mu\text{mol/mg protein/h}$ and nmol/mg protein/h , respectively) in Brain Structures of Rats with Different Locomotor Activity ($M \pm m$)

Mitochondrial fraction		Cortex			Arcuate nucleus		
		LLA	HLA	LLA/HLA, %	LLA	HLA	LLA/HLA, %
Initial							
	ACE	15.4±1.2	18.4±1.0	119.4	14.9±1.0	17.3±1.4	116.1
	ACT	126.8±2.7	208.0±7.5	164	502.1±16.0	498.0±22.0	99.2
Synaptosomal subfraction							
	ACE	12.0±0.9	16.5±1.0	137.7	24.8±1.8	31.00±2.02	125
	ACT	507.8±8.5	817.2±10.2	160.9	984.5±28.0	993.2±44.0	101
Mitochondrial subfraction							
	ACE	11.3±1.61	15.80±2.04	140.4	21.5±2.0	22.0±2.2	110
	ACT	330.2±12.5	480.1±23.0	148.2	634.0±33.0	710.0±40.0	114

which indicated high morphofunctional plasticity of cortical structures in the central nervous system associated with individual behavioral characteristics.

The neurochemical peculiarities related to behavioral characteristics of animals refine the molecular mechanisms of regulation of congenital and acquired behavioral characteristics.

This work was supported by the Russian Foundation for Basic Research (grant No. 00-04-48484).

REFERENCES

1. T. I. Belova, M. I. Dobrakova, T. M. Ivanova, *et al.*, *Fiziol. Zh. SSSR*, **71**, No. 7, 813-821 (1985).
 2. E. V. Buzinova, Zh. I. Slesareva, M. F. Obukhova, and I. P. Ashmarin, *Ros. Fiziol. Zh.*, **83**, No. 7, 19-21 (1997).
 3. N. M. Voitenko, N. N. Barykina, and V. G. Kolpakov, *Zh. Vyssh. Nervn. Deyat.*, **48**, No. 2, 322-330 (1998).
 4. L. M. Gershtein, A. S. Kamysheva, T. A. Chebotareva, *et al.*, *Ibid.*, **41**, No. 2, 300-305 (1991).
 5. L. M. Gershtein and E. L. Dovedova, *Vestn. Ros. Akad. Med. Nauk*, No. 1, 30-34 (1996).
 6. V. Z. Gorkin, A. V. Verevkin, L. I. Gridneva, *et al.*, *Current Biochemical Methods* [in Russian], Moscow (1968), Vol. 2, pp. 158-173.
 7. E. A. Gromova, *Catecholaminergic Neurons* [in Russian], Moscow (1979), pp. 97-105.
 8. D. A. Kulagin and D. A. Blondinskii, *Usp. Fiziol. Nauk*, **17**, No. 1, 92-109 (1986).
 9. N. K. Popova, A. V. Kulikov, V. G. Kolpakov, *et al.*, *Zh. Vyssh. Nervn. Deyat.*, **35**, No. 4, 742-746 (1985).
 10. F. Fonnum, *Biochem. J.*, **115**, No. 6, 465-472 (1969).
 11. S. Hestrin, *J. Biol. Chem.*, **180**, No. 1, 249-255 (1949).
 12. B. Jacobs, *Am. Sci.*, **82**, No. 5, 456-463 (1994).
 13. V. Popov, V. Rosler, C. Thiemann, *et al.*, *Acta Biol. Med. Germ.*, **26**, 239-245 (1971).
 14. H. Sudak and J. Maas, *Science*, **146**, 48-420 (1964).
-