These observations can explain the disappearance of hypercapnic responses in the cerebral circulation observed previously in response to administration of acetazolamide to animals [2, 9].

LITERATURE CITED

1. V. P. Akopyan, Krovoobrashchenie, 10, 12 (1977).
2. É. S. Gabrielyan, Some Aspects of the Physiology and Pharmacology of the Cerebral Circulation [in Russian], Erevan (1976).
3. V. A. Glazkova and I. N. Chernyakov, Kosmich, Biol., No. 2, 20 (1975).
4. Yu. E. Moskalenko, G. B. Vainshtein, I. T. Demchenko, et al., The Intracranial Hemodynamics; Biophysical Aspects [in Russian], Leningrad (1975).
5. G.I. Mehedlishvili, Function of the Vascular Mechanisms of the Brain [in Russian], Leningrad (1963).
6. G. E. Shpak, Usp. Sovrem. Biol., 89, 18 (1980).
7. E. Betz, Physiol. Rev., 52, 525 (1972).
8. A. M. Harper, in: Scientific Foundations of Neurology, London (1972), p. 235.
9. S. S. Kety, in: Handbook of Physiology, Section 1, Neurophysiology, Vol. 3, Washington (1960), p. 1751.
10. J. S. Meyer and F. Gotoh, Neurology (Minneapolis), 11, 46 (1961).
11. J. D. Pickard et al., in: Ionic Action on Vascular Smooth Muscle, Berlin (1976), p. 101.
12. J. W. Severinghaus and G. Cotew, Scand. J. Lab. Clin. Invest., Suppl. 102 (1968).

ROLE OF SEROTONIN OF NEURONS AND NEUROPIL IN THE VISUAL SYSTEM

M. G. Uzbekov, S. Murphy, S. P. R. Rose, and Z. D. Pigareva

UDC 612.843.7:612.822.1:577.175.823

There have been many studies of the principles governing serotonin (5-HT) metabolism [8]. However, problems concerned with the 5-HT content and its turnover in different types of cells of the CNS have not hitherto been studied, despite the fact that methods of isolating fractions enriched with neurons and neuroglial cells from brain tissue have recently been developed [14].

One of us (M.G.U.) suggested previously that 5-HT plays a specific role in the activity of the visual system [3]. Accordingly, in the present investigation the 5-HT content was studied in fractions enriched with neurons and neuropil (neuroglial cells and axodendritic fragments taken together) of the visual and motor areas of the rat cortex, using early visual deprivation as the model.

EXPERIMENTAL METHOD

Male Wistar rats were used. The animals of group 1 served as the control, the rats of group 2 were visually deprived (kept for 50 days after birth in darkness), and group 3 consisted of rats exposed to light for 3 h after 50 days of visual deprivation. Altogether six experiments were carried out on each group. The animals of all three groups were decapitated, the brain was removed, and the visual and motor areas of the cortex were isolated. All operations of the brain were performed at 0°C. The tissue of the corresponding regions from 5-7 rats in each group was pooled and used to obtain the cell fractions. Fractions enriched with neurons and neuropil (neuroglial cells + axodendritic fragments) were isolated by the method in [13, 14]. The 5-HT content in these fractions was determined by a spectrofluorometric method [12], in the modification of [4, 5], and the protein content by the method in [11].

KEY WORDS: serotonin; visual system; deprivation; visual cortex.

Laboratory of Biochemistry of the Brain, Brain Institute, Academy of Medical Sciences of the USSR, Moscow. Department of Brain Studies, Open University, Milton Keynes, England.

(Presented by Academician of the Academy of Medical Sciences of the USSR S. S. Debov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 91, No. 4, pp. 389-390, April, 1981. Original article submitted May 28, 1980.

TABLE 1. 5-HT Content in Neurons and Neuropil of Visual and Motor Areas of Cortex (in ng/mg protein) of Normal, Visually Deprived Rats, and Rats Exposed to Light for 3 h (M ± m)

Experimental condition	Visual cortex		Motor cortex	
	neuropil	neurons	neuropil	neurons
Normal	182,66±21,19	67,96±7,70	164,10±27,70	74,34±5,84
Visual deprivation	97,29±27,63	100,23±22,58	81,03±14,90	83,42±26,42
Exposure to light	260,06±43,94	99,04±13,40	131,13±32,76	98,19±20,32

EXPERIMENTAL RESULTS

The 5-HT content in the fraction of neuropil from the visual and motor areas of the cortex of normal rats were practically identical and was greater than its content ($P < 0.05$) in the neuron fraction: 2.7 times in the visual cortex and 2.2 times in the motor cortex, respectively (Table 1).

The 5-HT in the neuropil fraction could belong, on the one hand, to neuroglial cells, which contain this monoamine, assimilate it, and inactivate its excess, which is liberated during the nervous impulse. According to the previous reports [2, 10], active systems for uptake and inactivation of 5-HT are present in glial cells. Meanwhile, in the neuropil fraction axonal fragments of serotoninergic neurons of the mesencephalic nuclei raphe are present and send their processes into the cortical zones of the brain and contain 5-HT. However, it was then necessary to determine what part of the total 5-HT content of the neuropil fraction belonged to neuroglial cells.

The presence of 5-HT in the enriched fraction of neurons is interesting, for it is considered that neurons containing 5-HT are almost completely absent from the mammalian cerebral cortex [15]. This fact is difficult to explain at the present time. However, it can be tentatively suggested that 5-HT is taken up by neurons from the medium in which it may be present as a result of leakage during isolation of the cell fractions. Althaus et al. [6] mentioned leakage of various compounds from nerve cells when isolated by various methods [6]. At the same time, the possibility cannot be completely ruled out that a small quantity of 5-HT is present in native cerebral cortical neurons but cannot be detected by histofluorescence methods on which modern knowledge of the distribution of 5-HT in brain cells is based.

As a result of the early visual deprivation changes in the 5-HT content were observed only in the neuropil fraction. The level of the monoamine in these fractions of the visual and motor cortex was reduced by 46.7 and 51.6%, respectively ($P < 0.05$) compared with normal (Table 1). Meanwhile, the 5-HT content was not significantly different from normal in the neuron fraction from these two areas of the cortex. These results throw a clearer light on data obtained previously showing a decrease in the 5-HT level in tissues of the visual and motor cortex of visually deprived rats [7].

Exposure of visually deprived rats to light for 3 h was accompanied by a sharp rise in the 5-HT content selectively in the neuropil fraction of the visual cortex (Table 1). It was 2.7 times higher than its content in the corresponding fraction from visually deprived rats and 42% greater ($P > 0.05$) than in normal rats. Under these same conditions, the 5-HT content in the neuropil fraction of the motor cortex increased only a little. It did not reach the normal level, although it did not differ from it significantly. The 5-HT content in the neuropil fraction of the visual cortex at that time was almost twice as high ($P < 0.05$) as in the neuropil of the motor cortex.

The 5-HT content in the neuron fraction from both areas of the cortex after exposure of the experimental animals to light remained at the same level as in the normal and visual deprived rats. The absence of any significant change in the 5-HT content in this fraction under the experimental conditions used suggests that 5-HT does not play an evident functional role in the bodies of the cortical neurons. The reason may probably be the different character of 5-HT metabolism in the neuron bodies and neuropil at the cortical level.

Having discovered activation of 5-HT metabolism in the superior colliculus during intensive photic stimulation of the rabbit retina, Fukui and Vogt [9] suggested that the serotoninergic system in the superior colliculus may act as a defensive mechanism, protecting the visual cortex against an excessive flow of impulses. It can be concluded on the basis of this

hypothesis that the sharp rise in the 5-HT content in the neuropil (neuroglial cells and axonal fragments) discovered by the present writers in the visual cortex after exposure of the visually deprived animals to light for 3 h probably reflects activation of the liberation of 5-HT by serotoninergic endings and its uptake by neuroglial cells, and it can be regarded as a specific response of the serotoninergic system to activation of the flow of impulses induced by photic stimulation. The results now obtained show that exposure of the deprived animals to light also was accompanied by intensification of 5-HT binding with serotoninergic receptors of the visual cortex [3]. The closer connection of the serotoninergic components of the visual system with visual impulsation is confirmed by the less marked change in the 5-HT content in the motor cortex during exposure of the animals to light. This suggests that the functionally determined character of 5-HT metabolism in components of the visual cortical neuropil differs from that in the motor cortical neuropil.

At the same time the synchronization and unidirectional nature of the changes in 5-HT metabolism in these areas of the cortex during visual deprivation, as this study and the writers' previous investigations have shown [3, 7], undoubtedly reflect the close functional connection of the visual analyzer with the motor cortex, as part of an integrative triggering system [1]. This synchronization is evidence of participation of the serotoninergic system in the combination of biochemical processes that lie at the basis of functional connection between the visual system and the motor cortex in the reception and processing of visual information.

LITERATURE CITED

1. O. S. Andrianov, The Principles of Organization of Integrative Activity of the Brain [in Russian], Moscow (1976).
2. N. G. Aleksidze, in: Proceedings of the 13th Congress of the All-Union Physiological Society [in Russian], Vol. 1, Leningrad (1979), p. 24.
3. M. G. Uzbekov, Zh. Vyssh. Nerv. Deyat., 24, 1291 (1976).
4. M. G. Uzbekov, Ontogenez, 12, 58 (1981).
5. M. G. Uzbekov, D. Biesold, and Z. D. Pigareva, in: Proceedings of the 7th Scientific Conference on Evolutionary Physiology [in Russian], Leningrad (1978), p. 230.
6. H.-H. Althaus, W. B. Huttner, and H. Neuhoff, Hoppe-Seylers Z. Physiol. Chem., 358, 1155 (1977).
7. D. Biesold, V. Bigl, and M. Uzbekov, Active Nerv. Super. (Prague), 19, 154 (1977).
8. E. Costa, G. L. Gessa, and M. Sandler (editors), Serotonin, New Vistas, Vols. 1-2, New York (1974).
9. K. Fukui and M. Vogt, J. Physiol. (London), 254, 519 (1976).
10. F. A. Henn and A. Hamberger, Proc. Natl. Acad. Sci. USA, 68, 2686 (1971).
11. O. H. Lowry, N. J. Rosebrough, A. L. Farr, et al., J. Biol. Chem., 195, 165 (1951).
12. R. P. Maickel, R. H. Cox, J. Saillant, et al., Int. J. Neuropharmacol., 7, 275 (1968).
13. S. P. R. Rose and A. K. Sinha, J. Neurochem., 27, 963 (1976).
14. A. K. Sinha and S. P. R. Rose, Brain Res., 33, 205 (1971).
15. U. Ungerstedt, Acta Physiol. Scand., 367, Suppl. 10, 1 (1971).