SEROTONIN CONCENTRATION IN VARIOUS PARTS OF THE BRAIN DURING HIBERNATION AND WAKING

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The beginning of hibernation in Sousliks (Citellus major erythrogenys) is accompanied by an increase in the serotonin level in the hind brain and hippocampus. During hibernation the serotonin concentration remains high in the hippocampus. Awakening from hibernation is characterized by a decrease in the serotonin level in the hippocampus and in the rhombencephalon, diencephalon, and mesencephalon.

Serotonin has attracted the attention of research workers as a possible factor in the mechanisms of sleep production [1, 6, 7, 11]. It is therefore interesting to study this biogenic amine in a natural model of prolonged, deep sleep such as arises periodically in hibernating animals. Data in the literature on changes in the serotonin concentration during hibernation relate only to its mean level in the brain of the hedgehog [10] and American souslik [9]. However, the activity of the brain is known to vary in its different parts during hibernation [3, 4], so that their role in the development of hibernation must undoubtedly vary.

The object of the investigation described below was therefore to study the distribution of serotonin in the brain of the red-cheeked souslik, one of the most convenient objects in which to study hibernation.

EXPERIMENTAL METHOD

The experiments were carried out on male sousliks (Citellus major erythrogenys Brandt), caught in Novosibirsk Region. Each animal was kept in a separate cage in the laboratory and was given food and water ad lib. In the fall the sousliks were transferred to a special room with a constant temperature of 3-4°C, in which the animals fell into hibernation. The serotonin concentration was studied in seven parts of the brain – the hemispheres, hippocampus, hypothalamus, diencephalon (without hypothalamus), mesencephalon, and rhombencephalon – in the waking animals, during the onset of hibernation, and during deep hibernation. Changes in the serotonin level in these same parts of the brain were also studied during the first few hours and days of awakening of the sousliks and their emergence from hibernation. The animals were decapitated under the same conditions as they were kept. The brain was quickly removed and divided into its parts, which were weighed and placed in polyethylene tubes chilled in ice. The serotonin concentration was determined by a fluorimetric method [8] in the modification described in [2].

EXPERIMENTAL RESULTS

The serotonin level estimated in summer in actively waking sousliks lies between the same limits as are characteristic of other mammals [5], and its distribution in the different parts of the brain follows the same general pattern. The highest serotonin concentrations were found in the hypothalamus and the lowest in the cerebellum.

The serotonin concentration in most parts of the animals' brain during hibernation showed no significant difference from its level in the waking sousliks. However, the process of falling asleep into hibernation

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TABLE 1. Serotonin Level in Different Parts of the Brain of the Red-Cheeked Souslik in a Waking State, When Falling into Hibernation, and during Hibernation (M ± m)

Part of brain	Serotonin (in μg/g)		
	waking (n = 18)	falling asleep (n = 4)	hibernation (n = 10)
Hippocampus	0,430±0,029	0,738±0,072*	0,605±0,037*
Rhombencephalon	0,736±0,036	1,229±0,157*	0,766±0,055
Hypothalamus	0,751±0,093	1,250±0,225	0,889±0,067
Diencephalon (without hypothalamus)	0,499±0,022	0,647±0,085	0,569±0,040
Mesencephalon	0,710±0,028	0,957±0,126	0,724±0,056
Cerebellum	0,209±0,024	0,268±0,057	0,179±0,017
Cerebral hemisphere	0,429±0,029	0,333±0,069	0,483±0,040

*P < 0.05 compared with values for waking animals

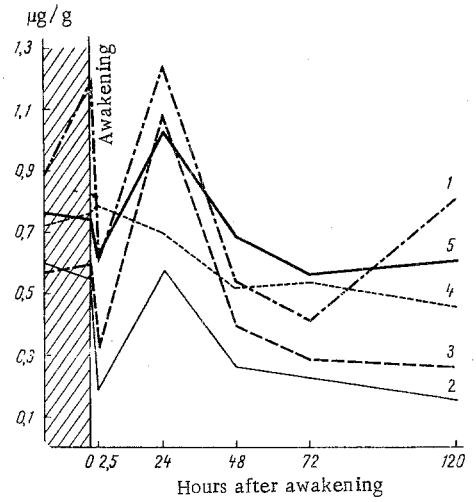

Fig. 1. Changes in serotonin concentration in the brain of red-cheeked sousliks during awakening from hibernation. Initial level of serotonin concentration taken to be that during deep hibernation in November to January (shaded part). 1) Hypothalamus; 2) hippocampus; 3) diencephalon; 4) mesencephalon; 5) rhombencephalon.

and reawakening from it was accompanied by definite changes in the serotonin level in certain parts of the brain.

To begin with, considerable changes in its concentration were found in October, when the sousliks were starting to hibernate. The animals were sacrificed when their body temperature had fallen to 15-16°C but their sleep was still not very deep. Comparison of these animals with sousliks in an active state in the same period showed that the onset of hibernation is characterized by elevation of the serotonin level in the hippocampus and medulla, while a tendency for its level to rise was observed in the hypothalamus, mesencephalon, and diencephalon (Table 1). Considerable individual variations in the serotonin level in the hypothalamus were characteristic of the animals falling into hibernation. These differences may be connected with differences in the depth of the developing sleep, although the body temperature was the same in all sousliks of this group. Meanwhile the onset of sleep had no significant effect on the serotonin level in the cerebral hemispheres and cerebellum.

With the onset of deep sleep the serotonin level fell slightly in nearly all parts of the brain, and remained definitely above the level in the waking state only in the hippocampus.

Characteristic changes, but now in the opposite direction, were observed when the animals awoke from hibernation in April. Comparison of the serotonin concentration in the different parts of the brain before awakening and 2.5 h after its beginning showed a sharp decrease in its concentration in the hippocampus, rhombencephalon, hypothalamus, and diencephalon during awakening of the animals (Fig. 1). On the day after awakening the serotonin concentration in these parts rose sharply, but on the 2nd-5th day it again was considerably lowered. The decrease in the serotonin concentration compared with that in the hibernating animals was significant in the hippocampus, diencephalon, and mesencephalon. The change in the serotonin level in the cerebral hemispheres and cerebellum was not significant.

The "pendulum" effect observed 24 h after awakening, when the sharp initial decrease in the serotonin concentration in the hippocampus, hypothalamus, rhombencephalon, and diencephalon was followed by a marked increase (which disappeared the following day), is evidently attributable to a compensatory increase in serotonin formation as a reaction to the preceding sharp decrease in its level.

The dynamics of the serotonin level in the mesencephalon was somewhat uncharacteristic. The sharp decline in the serotonin level on awakening did not take place as it did in the hippocampus, hypothalamus, diencephalon, and rhombencephalon. The subsequent sharp rise in the serotonin concentration likewise was

not observed in the mesencephalon. Nevertheless, during the first days after awakening the serotonin concentration in the mesencephalon fell gradually, so that after 3-5 days it was significantly lower than during hibernation.

The clear changes in the serotonin concentration in the hippocampus at all stages of hibernation – at its beginning, during deep sleep, and on awakening – are noteworthy. Together with information on the preservation of the electrophysiological activity of hippocampal neurons during deep hibernation [4], these results suggest a possible role of serotonin in the mechanisms of onset and maintenance of hibernation.

The rapid increase in the serotonin level in the hippocampus and rhombencephalon in animals falling into hibernation in October compared with sousliks remaining in an active state at the same period is evidence that these are not merely seasonal changes but characteristic manifestations of hibernation. This is further shown by the sharp decrease in the serotonin concentration taking place during the 2.5 h after the beginning of awakening in the hippocampus, hypothalamus, rhombencephalon, and diencephalon in the spring. On the other hand, the fact that the serotonin level did not undergo identical changes in all the organs studied as the animals fell into hibernation suggests that the changes observed are not only the result of the lowered metabolism in hibernation, but also a reflection of differences in the functional activity of the various parts of the brain and also, perhaps, differences in their role in the production of hibernation and in reawakening from it.

The marked increase in the serotonin level observed in certain parts of the brain of sousliks falling into hibernation and its characteristic dynamics during awakening are in full agreement with the data for sousliks awakening from hibernation after blocking of serotonin synthesis by parachlorophenylalanine or when its level is lowered after destruction of the nuclei of the raphe in the mesencephalon [9]. Serotonin can be presumed to play an essential role in the mechanisms of onset of hibernation, but the character of this role requires further elucidation.

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