THE INFLUENCE OF THE FUNCTIONAL STATE OF THE CENTRAL NERVOUS SYSTEM ON THE DISTRIBUTION OF BROMIDES IN SOME TISSUES AND ORGANS OF THE ALBINO RAT

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The present investigation was concerned with the elucidation of the dependence of bromide metabolism in the animal body, and particularly in various compartments of the brain, on the functional state of the central nervous system.

We were interested in the effect of stimulation and inhibition on the distribution of bromides in the body.

A number of published communications have dealt with this problem. Their authors generally reported changes in bromide concentrations in blood as well as in some of the compartments of the central nervous systems in animals in which the state of the central nervous system was altered by a variety of means. However, a careful analysis of the experimental results showed them to be statistically unreliable, or based on the use of unsatisfactory experimental procedures [1-6, 8-11].

TABLE 1

The Effect of Physical Exhaustion on the Distribution of Bromides (Tagged with Br^{82}) in Some Tissues and Organs of the Albino Rat

Tissue	Control (2 rats)	Physical exhaustion (3 rats)	Percent of control
Blood	1	1	100
Thyroid	0.76	0.96 ± 0.03	124.7
Pituitary	0.45	0.44 ± 0.15	97.5
Large hemispheres	0.19	0.18 ± 0.01	94.7
Midbrain	0.19	0.21 ± 0.01	110.6
Cerebellum	0.21	0.21 ± 0	100.0
Medulla oblongata	0.21	0.22 ± 0.001	104.8
Muscle	0.19	0.16 ± 0.04	84.2

Experimental Methods

Albino rats were used throughout. The changes in the state of the nervous system were accomplished by both physical action on the system, as well as by chemical agents. Bromide distribution was followed by tagging with radioactive bromide (Br^{82}), which was introduced as sodium bromide subcutaneously, in doses ranging from

TABLE 2

The Effect of Sleep Deprivation Over Various Periods of Duration on the Distribution of Bromides (Tagged with Br^{82}) in Some Organs and Tissues of the Albino Rat

Material tested	Expt. 1			Expt. 2					Expt. 3		
	control (3 rats)	17 hr sleepless (7 rats)	% of control	control (1 rat)	61 hr sleepless (1 rat)	% of control	amytal-induced sleep (1 rat)	% of control	control (1 rat)	72 hr sleepless (1 rat)	% of control
Blood	1	1	100	1	1	100	1	100	1	1	100
Thyroid	1,45	1,46	100,7	1,05	1,79	170	1,68	160	2,24	1,64	73,2
Pituitary	0,60	0,69	115,0	0,50	0,38	76	0,50	98	0,56	0,56	100
Nerves	0,51	0,50	98,0	0,59	0,71	120	0,68	121	0,57	0,59	103,5
Cerebral hemispheres	0,19	0,18	94,7	0,17	0,16	94	0,18	95	0,17	0,17	100
Midbrain	0,24	0,24	100,0	0,22	0,22	100	0,22	100	0,23	0,24	104,3
Cerebellum	0,23	0,24	104,3	0,25	0,20	80	0,25	100	0,23	0,21	91,3
Medulla oblongata	0,30	0,31	103,3	0,25	0,20	80	0,31	124	0,25	0,24	96,0
Suprarenals (adrenals)	—	—	—	0,35	0,37	106	0,27	77	0,31	0,30	96,6

TABLE 3

The Effect of Certain Pharmacological Agents on the Distribution of Bromide (Tagged with Br^{82}) in Some of the Tissues and Organs of the Albino Rat

Material tested	Expt. 1			Expt. 2			Expt. 3				
	control (3 rats)	ether anaesthesia (2 rats)	% of control	control (2 rats)	phenamine stimulation (4 rats)	% of control	control (4 rats)	phenamine stimulation (3 rats)	% of control	inhibition by amytal sleep (3 rats)	% of control
Blood	1	1	100	1	1	100	1	1	100	1	100
Thyroid	0,95	1,01	106,3	1,26	1,09±0,04	86,5	2,60±0,10	2,48±0,07	95,4	2,42±0,20	93,1
Pituitary	0,64	0,53	82,8	0,64	0,57±0,06	89,0	0,51±0,03	0,56±0,01	109,3	0,48±0,05	94,1
Nerves	—	—	—	—	—	—	0,58±0,05	0,68±0,04	117,2	0,55±0,11	94,8
Cerebral hemispheres	0,21	0,20	95,2	0,24	0,22±0,02	91,7	0,22±0,02	0,19±0,01	86,4	0,20±0,02	90,9
Midbrain	0,25	0,24	96,0	0,28	0,24±0,02	85,7	0,28±0,01	0,26±0,01	92,9	0,25±0,01	89,3
Cerebellum	0,27	0,26	96,3	0,30	0,28±0,04	93,3	0,28±0,01	0,27±0,01	96,4	0,27±0,02	96,4
Medulla oblongata	0,26	0,26	100,0	0,28	0,26±0,03	92,8	0,31±0,03	0,29±0,01	93,5	0,32±0,01	103,2
Suprarenals (adrenals)	0,31	0,36	116,1	—	—	—	0,38±0,20	0,40±0,01	105,3	0,39±0,06	102,6
Muscle	0,18	0,16	88,8	0,26	0,19±0,03	73,1	—	—	—	—	—

TABLE 4

The Effect of Convulsive Shock on the Distribution of Bromide (Tagged with Br^{82}) in Some Tissues and Organs of the Rat

Material studied	Expt. 1		Expt. 2			Expt. 3		
	tonic convulsions (1 rat)	supraliminal inhibition (1 rat)	control (3 rats)	convulsions (3 rats)		supraliminal inhibition (3 rats)		control (3 rats)	tonic convulsions (3 rats)	
				relative radioactivity	% of control	relative radioactivity	% of control			% of control
Blood	1	1	1	1	100	1	100	1	1	100
Thyroid	1,67	1,42	1,07±0,06	1,09±0,17	101,9	0,84±0,06	78,5	1,45±0,20	1,24±0,20	85,5
Pituitary	0,63	0,53	0,58±0,11	0,49±0,08	84,5	0,70±0,05	120,7	0,55±0,07	0,67±0,05	121,8
Nerves	0,46	0,57	0,56±0,05	0,58±0,06	103,6	0,56±0,02	100	0,64±0,08	0,60±0,05	93,7
Cerebral hemispheres	0,19	0,21	0,19±0,02	0,19±0,02	100	0,20±0,02	105,2	0,20±0,01	0,20±0,00	100
Midbrain	0,26	0,26	0,25±0,01	0,28±0,05	112,0	0,23±0,01	92,0	0,29±0,03	0,26±0,00	89,6
Cerebellum	0,26	0,32	0,26±0,04	0,25±0,03	96,1	0,28±0,02	107,0	0,29±0,03	0,28±0,00	96,5
Medulla oblongata	0,29	0,27	0,38±0,02	0,29±0,03	76,3	0,30±0,02	79,0	0,28±0,02	0,30±0,00	107,1
Muscle	—	—	—	—	—	—	—	0,19±0,03	0,25±0,01	131,5

16 to 26.5 μC per kg body weight. Activities in tissues were measured with an end-window counter, the counting accuracy being kept within a 10% error. Data were subjected to statistical analysis whenever the number of measurements available permitted.*

Experimental Results

In the first experimental series, the change in bromide distribution was investigated as a function of physical exhaustion.

The rats were given $NaBr^{82}$, and two hours later were placed in a rotating drum (race), in which they were made to exercise for two hours to extreme exhaustion. Four hours after the injection of the radioactive bromide, the animals were killed, together with a batch of control animals, by rapid immersion into liquid nitrogen.

The results of this series, expressed as relative specific radioactivities with respect to blood, are shown in Table 1.

It will be seen from Table 1 that bromide distribution in various compartments of the brain and in muscle was not affected by physical exhaustion: the deviations from control values were within the limits of experimental error. The difference recorded in the thyroid tissue was a significant change.

The second experimental series was concerned with the effect of sleep deprivation of various durations on the distribution of bromides in the albino rat.

The experimental animals were denied sleep over periods ranging from 17 to 72 hr, either by severe shaking in a moving trolley, or by continuous stimulation with a direct current, interrupted with a Warren motor.

The results obtained are presented in Table 2.

Table 2 shows that the deprivation of sleep over 17 hours, or for more prolonged periods (up to 72 hr) did not elicit any appreciable change in the distribution of Br^{82} in all the tissues investigated, with the exception of the thyroid (the scatter of the analytical data was within the limits of experimental error).

In the third experimental series, we have tested the effect of various pharmacological agents on the distribution of bromides in the organs and tissues of the albino rat. The agents used were ether (light anesthesia), phenamine, and amytal (Table 3).

*The determination of the mean square deviation for small groups of animals ($n \leq 5$) was done according to the Urbach equation [7]: $\sigma_n = \pm\sqrt{\frac{E\alpha_i^2}{n-2}}$

In the first experiment, the animals, after receiving $NaBr^{82}$ solution, were placed under a glass bell, where an atmosphere of ether vapor was provided by a piece of cotton wool soaked in ether. The condition of the animals was continuously observed, and they were prevented from passing from the state of narcotic sleep into one of deep anesthesia. The animals were kept in the ether vapors for three hours.

A fall in the rate of uptake of Br^{82} by the tissues was observed in this group in comparison with controls, but the general distribution of bromide in the tissue was not affected. The only effect of ether narcosis was therefore one of a lowered adsorption rate by the tissues.

In the second experiment of this series, the stimulant phenamine was administered to the rats (0.5 mg per kg body weight), and the Br^{82}-labeled NaBr was given 6.5 hr later. The rats were killed by immersion in liquid nitrogen 17 hr after the administration of the drug, and the radioactivity of the various tissues was examined as usual.

In the third experiments, ten rats were given radiobromide, and after 17 hr the animals were divided into three groups. The animals of the first group (three rats) received phenamine (50 mg/kg), those of the second (three rats) were given amytal (0.2 g/kg), while the remaining four rats served as controls. The phenamine-treated rats were in a highly excited state throughout the experiment, were continually mobile, and completely wet with perspiration. Those given amytal were asleep throughout the period, while the control animals behaved normally. All animals were killed two hours later by decapitation.

The analysis of the results presented in Table 3 showed the complete lack of any effect whatever of the pharmacological agents tested on the shift of bromides in the organs and tissues investigated.

In the last experimental series, the distribution of bromides was studied in animals subjected to convulsive shock. In the first two experiments of this series, the animals were shocked with alternating current from the mains, with a frequency of 50 hertz and potential of 100 V (through an LATP-2). The two electrode needles were placed in the occipital region and the upper lip, respectively. The animals passed into convulsions as soon as the current was switched on. In the further stages, the animals passed into supraliminal inhibition. The length of the stimulation period varied with experiments, and some of the animals were killed while convulsing, while others were killed in the inhibited state. The results of this experimental series are presented in Table 4.

It will be seen from Table 4 that neither strong stimulation, nor supraliminal inhibition had any effect on the distribution of bromide in the tissues of the cerebral hemispheres, midbrain, cerebellum, or nerves. Attention is drawn to the slight changes in radioactivity in the medulla, in the direction of a lower activity, which were observed both in the case of stimulation and supraliminal inhibition (Expt. 2). These data require further confirmation.

It may thus be concluded from the present experiments that the distribution of bromide between the various compartments of the brain is not affected by the functional state of the central nervous system.

The problem of a possible redistribution of bromide between the extracellular and intracellular spaces of the tissues in question during changes in the functional state of the central nervous system deserves separate study.

SUMMARY

The effect of various functional states of the central nervous system on the distribution of bromide in rats was studied with the aid of Br^{82}. The various conditions studied were fatigue, period of sleep deprivation from 17 to 72 hr, intoxication with various agents (ether, phenamine, amytal), as well as convulsive shock and supraliminal inhibition caused by the passage of alternating current through the animals' heads. Radioactivity due to Br^{82} was determined in the blood, thyroid, pituitary, nerves, large hemispheres, mesencephalon, cerebellum, medulla oblongata, adrenals, and muscles.

None of the treatments employed caused any appreciable changes in bromide distribution in brain, but some significant, though slight, changes were observed in the thyroid in some of the experiments.

LITERATURE CITED

1. M. F. Vasil'ev, Proceedings of the I. P. Pavlov Physiology Laboratory [in Russian] (Moscow-Leningrad, 1948) Vol. 14, p. 83.
2. A. A. Danilov, Collection: New Data on the Physiology of the Hypophysis [in Russian] (Moscow-Leningrad, 1941) p. 162.
3. O. S. Krivosheev, Abstracts of the Annual Conference of the Psychiatric Research Institute [in Russian] (Moscow, 1956) p. 129.
4. O. A. Krylov, Zhur. Vysshei Nerv. Deyat. 8, 3, 358 (1958).
5. F. I. Rivosh, Vestnik Rentgenol. i Radiol. 20, 83 (1938).
6. Yu. S. Tatarinov, Abstracts of the Eleventh Conference of the All-Union Federation of Physiology, Biochemistry, and Pharmacology (South RSFSR Division) [in Russian] (Stavropol-on-Kuban, 1956) p. 253.
7. V. Yu. Urbakh, Doklady Akad. Nauk SSSR 130, 1, 214 (1960).
8. H. Zondek and A. Bier, Biochem. Z. 241, 491 (1931).
9. H. Zondek and A. Bier, Klin. Wschr. 11, 759 (1932).
10. H. Zondek and A. Bier, Klin. Wschr. 12, 633 (1932).
11. H. Zondek and A. Bier, Klin. Wschr. 12, 55 (1932).