THE FATE OF TRACE ELEMENTS IN THE BRAIN, MUSCLES AND LIVER, AS SHOWN BY THE RESULTS OF SINUSOSTOMY AND ANGIOSTOMY DURING STIMULATION AND INHIBITION OF THE CENTRAL NERVOUS SYSTEM

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There are few reports in the literature on the metabolism of trace elements in the brain in various functional states of the central nervous system.

G. A. Babenko [1] observed a decrease in the content of copper and manganese in the brain of guinea pigs in a state of sleep induced by narcotic drugs, in camphor convulsions or in unconditioned and conditioned reflex excitation.

According to A. O. Voinar's findings [3], during excitation caused by metamphetamine and caffeine there is a fall in the content of manganese, silicon, aluminum, titanium and copper in the grey matter of the cerebral cortex and in isolated nuclei of nerve cells in the brain of dogs. A fall in the content of copper in the brain of rabbits during excitation by caffeine was observed by I. G. Priev [6], and of manganese – by R. V. Zharova [4]. The authors cited [1, 3, 6] account for the fall in the copper content of the brain during excitation by the fact that copper passes from the brain into the blood stream.

Narcotic and hypnotic drugs cause complex changes in the distribution of trace elements between the nuclei and cytoplasm of nerve cells, depending on the nature of the action of the drugs, their dose and the depth of sleep induced [3].

A. P. Kukhtina [5] showed that under the influence of bromides the content of copper, both ionized and in the form of organic complexes, in the brain of rats of all ages is increased.

R. V. Zharova observed an increase in the content of manganese in the brain tissue of rabbits under the influence of sodium bromide; an increase in the copper under the same conditions was observed by I. G. Priev, who suggested that copper enters into the composition of certain compounds of a protein nature which are synthesized during inhibition and intensively decomposed during excitation of the nervous system.

The aim of the present investigation is to study the metabolism of certain trace elements in the brain in chronic experiments on dogs after the operation of exposure of the longitudinal venous sinus, as shown by the results of analysis of the blood entering and leaving the brain and of the cerebrospinal fluid, taking into consideration the rate of the blood-flow in the brain during excitation and inhibition of the central nervous system.

EXPERIMENTAL METHOD

Experiments were carried out on 30 dogs. The longitudinal venous sinus of the dogs was exposed by E. S. London's method. The experiment was performed 6-7 days later, when the wound had healed and the tenderness at the site of operation had greatly diminished.

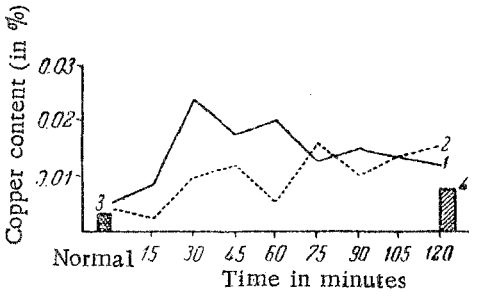

Fig. 1. Copper content of the blood entering (1) and leaving (2) the brain and of the cerebrospinal fluid under normal conditions (3) and during excitation due to caffeine (4) (calculated as a percentage of the sol).

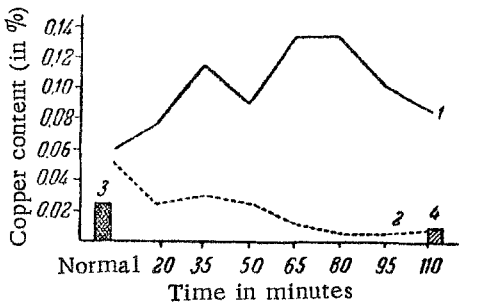

Fig. 2. Copper content of the blood entering (1) and leaving (2) the brain and of the cerebrospinal fluid under normal conditions (3) and during ether anesthesia (4) (calculated as a percentage of the sol).

in a dose of 50 mg/kg body weight of the animal, and pentothal intravenously in a dose of 4-10 ml of a 5% solution and subcutaneously at the same time in a dose of 3-7 ml.

Blood for examination was taken by means of a syringe simultaneously from the femoral artery and the longitudinal venous sinus, both under normal conditions and every 15 minutes during a period of 2 hours in narcotic sleep or in a state of excitation of the animal.

Cerebrospinal fluid was obtained in a volume of 4 ml by suboccipital puncture of the cisterna magna.

For quantitative estimation of the content of trace elements in the blood and cerebrospinal fluid, the blood was dried in a drying cupboard at a temperature of 80°C, and the cerebrospinal fluid was evaporated to dryness in platinum dishes.

The dry samples of blood and cerebrospinal fluid were converted into sols in a platinum vessel in a muffle furnace at a temperature not exceeding 400°C and the sols were subjected to quantitative spectrochemical analysis on an ISP-22 quartz spectrograph.

The content of trace elements (manganese, silicon, aluminum, titanium and copper) in the spectrograms obtained was estimated quantitatively by means of a MF-2 microphotometer by comparison of the density of blackening of the spectral lines of the elements tested in the spectrograms of the test samples and standards. In the quantitative photometry of the lines of the trace elements named, we employed these wavelengths: manganese – 2801.1 A, silicon – 2881.6 A, aluminum – 3082.2 A, titanium – 3236.6 A, and copper 3274.0 A.

The rate of the blood flow in the brain was determined by means of radioactive phosphorus $Na_2HP^{32}O_4$ which was injected into the carotid artery included in the skin flap. The moment of appearance of the radioactive phosphorus in the longitudinal venous sinus gave the time for the blood to pass through the brain.

EXPERIMENTAL RESULTS

The general character of the changes in the content of copper in the blood entering and leaving the brain and in the cerebrospinal fluid during excitation induced by caffeine is shown in Fig. 1.

As may be seen from the curves illustrating the changes in the copper content of the arterial blood and the blood in the longitudinal sinus, they are of an ascending character, showing an increase in the content of this particular trace element in the blood both entering and leaving the brain, with a decrease in the arteriovenous difference.

It also follows from Fig. 1 that during excitation due to caffeine an increase is also observed in the content of copper in the cerebrospinal fluid. Evidently during excitation excretion of copper by the brain takes place not only into the outflowing blood but also into the cerebrospinal fluid.

A similar relationship was observed by us also in respect of manganese, silicon, aluminum and titanium.

TABLE 1

Content of Trace Elements in the Blood Entering and Leaving the Brain of Dogs in Normal Conditions and During Excitation due to Metamphetamine (as a % of the sol)

Experimental conditions	Manganese		Silicon		Aluminum		Titanium		Copper	
	blood entering	blood leaving	blood entering	blood leaving	blood entering	blood leaving	blood entering	blood leaving	blood entering	blood leaving
Normal	0,0032	0,0028	0,0501	0,0417	0,0179	0,0141	0,0100	0,0060	0,0024	0,0010
Excitation in minutes										
20	0,0059	0,0032	0,1202	0,1380	0,0501	0,0832	0,0794	0,0129	0,0525	0,0174
35	0,0095	0,0022	0,1000	0,1862	0,0759	0,0457	0,0457	0,0302	0,0174	0,0190
50	0,0028	0,0120	0,1259	0,1778	0,0708	0,0269	0,0692	0,0081	0,0074	0,0054
65	0,0047	0,0151	0,1820	0,1202	0,1380	0,1148	0,0501	0,0069	0,0275	0 0141
80	0,0039	0,0089	0,1000	0,0501	0,1660	0,0324	0,0339	0,0166	0,0038	0,0074
95	0,0151	0,0034	0,1660	0,1202	0,3802	0,0324	0,0302	0,0081	0,0141	0,0141
110	0,0190	0,0132	0,0930	0,0417	0,2692	0,0708	0,0501	0,0123	0,0074	0 0050
125	0,0089	0,0039	0,0710	0,2240	0,0977	0,1950	0,0501	0,0078	0,0074	0,0027
140	0,0012	0,0017	0,1000	0,1047	0,1950	0,0708	—	—	—	—

TABLE 2

Content of Trace Elements in the Blood Entering and Leaving the Brain of Dogs in Normal Conditions and During Narcotic Sleep Induced by Luminal (as a % of the sol)

Experimental conditions	Manganese		Silicon		Aluminum		Titanium		Copper	
	blood entering	blood leaving	blood entering	blood leaving	blood entering	blood leaving	blood entering	blood leaving	blood entering	blood leaving
Normal	0,0024	0,0024	0,1200	0,1050	0,0490	0 0417	0,0107	0,0100	0,0110	0,0085
Narcosis, 15 minutes	0,0014	0,0008	0,1700	0,0720	0,0282	0,0240	0,0085	0,0018	0,0110	0 ,C03
» 30 »	0,0008	0,0014	0,0407	0,0316	0,0331	0,0190	0,0263	0,0029	0,0175	0,0071
» 45 »	0,0033	0,0005	0,1150	0,0339	0,245	0,0174	0,0091	0,0021	0,0129	0,0021
» 60 »	0,0035	0,0010	0,2140	0,0081	0,1047	0,0151	0,0148	0,0022	0,0214	0,0060
» 75 »	0,0019	0,0009	0,4070	0,0195	0,0977	0,0263	0,0245	0,0036	0,0178	0,0027
« 90 »	0,0024	0,0008	0,1050	0,0095	0,0525	0,0240	0,0371	0,0024	0,0178	0,0030
» 105 »	0,0021	0,0006	0,4480	0,0055	0,0490	0,0129	0,0309	0,0032	0,0117	0,0021
» 120 »	0,0039	0,0005	0,2510	0,0209	0,1698	0,0138	0,0288	0,0022	0,0162	0,0012

TABLE 3

Content of Trace Elements in Blood from the Hepatic Vein in Normal Conditions and During Excitation due to Caffeine (as a % of the sol)

Element	Experiment	Normal	Excitation							
			15 minutes	30 minutes	45 minutes	60 minutes	75 minutes	90 minutes	105 minutes	120 minutes
Manganese	1	0,0010	0,0020	0,0023	0,0008	0,0040	0,0040	0,0054	0,0016	0,0037
Silicon	1	0,0051	0,0060	0,0060	0,0200	0,0347	0,0132	0,0240	0,0288	0,0479
Aluminum	1	0,0044	0,0078	0,0132	0,0537	0,0589	0,0132	0,0389	0,0302	0,0389
Titanium	1	0,0138	0,0335	0,0174	0,0174	0,0269	0,0107	0,0316	0,0166	0,0490
Copper	1	0,0048	0,0240	0,0912	0,0182	0,0427	0,0162	0,0214	0,0162	0,0513

TABLE 4

Content of Trace Elements in Blood from the Hepatic Vein in Normal Conditions and During Ether Anesthesia (as a % of the sol)

Element	Experiment	Normal	Anesthesia						
			30 minutes	45 minutes	60 minutes	75 minutes	90 minutes	105 minutes	120 minutes
Manganese	1	0,0010	0,0013	0,0039	0,0017	0,0020	0,0025	0,0025	0,0029
Silicon	1	0,0095	0,0257	0,0617	0,0076	0,0407	0,0257	0,0240	0,0117
Aluminum	1	0,0093	0,0275	0,0240	0,0891	0,0331	0,0229	0,0309	0,0158
Titanium	1	0,0016	0,0079	0,0087	0,0295	0,0056	0,0056	0,0144	0,0079
Copper	1	0,0076	0,0309	0,0011	0,0708	0,0490	0,0708	0,0182	0,0339

The increased content of the trace elements studied in the blood both entering and leaving the brain, with the decreased arteriovenous difference demonstrate the excretion of the trace elements by the brain during excitation.

The rate of the blood flow through the brain in the experiments with administration of caffeine was quickened from a normal 8-9 seconds to 6-7 seconds at the time of excitation.

In the state of excitation by metamphetamine an increase was also observed in the content of the trace elements studied, in the blood both entering and leaving the brain (Table 1).

The curves of the changes in the content of manganese, silicon, aluminum, titanium and copper in the arterial blood and in the blood from the sinus during excitation by metamphetamine are also of an ascending character, with periodic alternation of retention and excretion of the elements by the brain. It must be pointed out that in the experiments with metamphetamine the periods of alternation, of retention, and excretion of the trace elements by the brain into the outflowing blood were more prolonged than in the experiments with caffeine.

Evidently the trend of the changes in the content of the trace elements in the blood depends on the nature of the analeptic used.

As may be seen from Fig. 2, ether anesthesia, which causes a state of profound inhibition of the central nervous system, leads to an obvious fall in the copper content of the blood leaving the brain and a rise in the content in the blood entering.

As a result a considerable increase is noted in the arteriovenous difference, which is evidence of increased retention of copper by the brain.

The fall in the copper content of the cerebrospinal fluid at the time of ether anesthesia (Fig. 2) demonstrates that retention of this particular trace element takes place not only on account of a decrease in its elimination in the outflowing blood but also its excretion in the cerebrospinal fluid.

We observed a similar relationship in respect of manganese, silicon, aluminum and titanium.

The rate of the blood flow through the brain during ether anesthesia is slowed to 10-11 seconds.

The state of anesthesia due to luminal like that caused by ether, also causes an obvious fall in the content of the studied trace elements in the blood leaving the brain, with an increase in the content in the blood entering (Table 2).

The other hypnotic drugs which we used (sodium amytal, pentothal) cause a less marked change than do ether or luminal narcosis.

During excitation of the central nervous system the content of trace elements in the blood entering the brain rises rapidly than in the blood in the sinus – leaving the brain, and during the action of ether and hypnotic drugs, with an obvious fall in the content of the studied trace elements in the blood from the sinus, their content in the arterial blood is also increased.

Evidently the more intensive rise in the content of the trace elements in the arterial blood, by comparison with the blood from the sinus, during excitation, and their increased content in the arterial blood during inhibition are connected with the fact that the content of trace elements in the arterial blood is an overall index of the biochemical dynamics of many organs.

In this connection we decided to study the part played by certain other organs – the muscles and liver – in the changes in the content of trace elements in the arterial blood.

In experiments in which blood was repeatedly taken from the femoral artery and vein, and caffeine was administered as a drug causing excitation of the central nervous system, we observed a clear increase in the content of manganese, silicon, aluminum, titanium and copper in the blood both entering and leaving the muscles.

During the frequent removal of blood from the femoral artery and vein of an animal under ether anesthesia we observed an obvious fall in the content of the studied trace elements in the blood leaving the muscles and an increase in their content in the blood entering them.

It should be mentioned that a similar phenomenon was also found by G. A. Belykh [2].

Our investigations, in agreement with the findings of this author, thus demonstrate that the muscles take part in the increase of the content of manganese, silicon, aluminum, titanium and copper in the arterial blood only during excitation of the central nervous system; during inhibition the muscles retain these trace elements from the blood.

In a study of the content of trace elements in blood from the hepatic vein of dogs subjected to angiostomy by E. S. London's method, we showed that during excitation of the central nervous system with caffeine and during ether anesthesia the liver excretes manganese, silicon, aluminum, titanium and copper into the outflowing blood (Tables 3 and 4), which shows that the liver takes part in the increase of the content of these trace elements in the arterial blood during both excitation of the central nervous system and ether anesthesia.

The latter phenomenon is possibly due to a direct action of ether on the liver tissue [7].

SUMMARY

Experiments were performed on sinuso- and angiostomized animals by E. S. London's method.

It was established by the method of spectrochemical analysis that during the excitation of the central nervous system the content of manganese, silicone, aluminum, titanium and copper is increased in the inflowing and outflowing brain blood. There is a decrease in the difference of concentration in the arterial and venous blood and an increased content of these microelements in the cerebrospinal fluid. This shows that these elements are given of by the brain not only into the outflowing blood, but also into the cerebrospinal fluid.

Inhibition of the central nervous system is connected with a distinct drop of manganese, silicone, aluminum, titanium and copper in the blood flowing from the brain and in the cerebrospinal fluid. At the same time the content of these microelements rises in the blood flowing to the brain and there is an increased difference in the concentration of these elements in the arterial and venous blood. This points to increased retention of the above mentioned microelements by the brain not only as a result of diminished release by the brain into the outflowing blood, but also into the cerebrospinal fluid.

In studying the participation of other organs in increaseing the content of the above-mentioned microelements in the arterial blood it was demonstrated that during excitation the microelements are given off into the systemic circulation not only by the brain, but also by other organs (liver, muscles). Liver also releases microelements into the outflowing blood during ether anesthesia.

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