Međunarodni simpozijum o eksperimentalnom tremoru: 1-3. april 1971. godine

Stern, Pavao

1972

Akademija nauka i umjetnosti Bosne i Hercegovine

https://bastina.anubih.ba/items/05bee08e-28ec-4b12-b10e-5c9e89b50461

AKADEMIJA NAUKA I UMJETNOSTI BOSNE I HERCEGOVINE

POSEBNA IZDANJA
KNJIGA XVII

ODJELJENJE MEDICINSKIH NAUKA
KNJIGA 4.

MEĐUNARODNI SIMPOZIJUM

O EKSPERIMENTALNOM TREMORU

1 — 3. APRIL 1971. GODINE

Urednik
PAVEL ŠTERN,
redovni član Akademije nauka i umjetnosti
Bosne i Hercegovine

SARAJEVO
1972

RISTO BOKONJIĆ

TRACE METALS PATTERNS IN SOME EXTRAPYRAMIDAL DISEASES

The content of different trace metals in normal and pathologic human brain tissue has been investigated a decades ago by different techniques (Bodansky 1922, Tingey 1937, Alexander and Myerson 1938, Butt et al. 1954, 1958 and others) but the role o these findings are not completely understood.

After the famous findings of Cumings 1948 on excessive amount of copper in brain tissue from persons died of Wilson's disease, the attention was paid to other diseases and other related and non related trace metals.

Gumings mentioned a slight increase of iron (Fe) in Wilson's disease and Butt and coowork. increase of silver (Ag) content in whole brain. Lowental 1958 only noticed the increase of aluminium (Al) in brain tissue of Wilson's disease.

Huntington's chorea, another degenerative, dominantly inherited extrapyramidal disease, characterized by choreatic jerks, was rarely object of trace metal investigations in brain tissue. The only paper dealing with brain's trace metals in this disease was published by Courville and coowork 1963. They found decrease of iron and copper in almost all investigated regions, but significant increase of Strontium (Sr) in brain.

The task of this work was to prove the content of trace metals (iron. copper, aluminium, silver) in brain tissue from persons died of Huntington's chorea and Wilson's disease by very sensitive technique-emission spectrography.

MATERIAL AND METHOD

10 brains were used from persons died from Wilson's disease and 7 from those of Huntington's chorea. The control group consisted the brain tissue from healthy people killed in accident.

All brain tissue was previously formoled, but Lowental 1958 showed that formolisation of material did not essentially change the content of trace metals in the tissue.

In Wilson's disease determinations were made in brain cortex, white matter, basal ganglia, cerebellum, brain stam and spinal cord. In Huntington's chorea only brain cortex, white matter and basal ganglia were examined on trace metals content.

Tissue was cut with plastic instruments which were chemically cleaned in order to avoid possible contamination. All laboratory vesels built of quartz, were chemically cleaned, too.

The tissue was dried during 72—90 hours and afterthat put in Kjeldahl's vessel for mineralisation by wet way, using nitric acid (D 1, 39) and perchloric acid (D 1, 61) pro analysi, and continious heating. The mineralisation was made until complete destruction of organic components i. e. complete decolorisation of vessel's content. This procedure lasted several days.

Mineralized content of vessel was mixed with sodium carbonate and germanium dioxide (relation 150:1) and homogenised pastilles were made.

Spectrographic analyses were performed on a spectrograph with quarz optic and focal distance of 60 cm. Excitation was gained from the Durr generator giving an alternative arch of 50 periods per second, at 36 micro F, 10 Ohms, 800 micro Hz. Precombustion lasted 5 seconds and combustion 30 seconds.

Analytical factor (ratio between known quantitaty of trace metal and germanium) was read on spectroprojector Zeiss and diagramme of dosage (DD) was used for interpretation of spectra and computation of trace metal expressed in mg/100 g of dried tissue matter.

RESULTS

The results of these determinations, including the quantity of wet matter (WM), dried matter (DM), as well as percentage of later with computed standard error of the mean are presented on following tables:

Table I

Region	No of determinations	WM	DM	%	Fe_d	± St. Er.
Cerebral cortex	8	3,8704	0,9451	28,2	43,6	3,20
Subcortical ganglia	10	3,3365	0,7123	20,4	54,7	2,70
White matter	10	3,8921	0,9782	24,5	33,5	2,30
Cerebellar cortex	8	5,3662	0,8127	16,5	53,0	1,90
Cerebellar white matter	7	1,9148	0,4740	24,8	49,0	2,75
Brain stem	7	1,6643	0,5169	31,3	57,0	3,25
Spinal cord	7	1,0264	0,2719	26,1	55,4	2,40

Table I showing the content of Fe in different regions of brain in Wilson's disease

Table II

Region	No of determinations	WM	DM	%	Cu	± St. Er.
Cerebral cortex	8	3,8704	0,9451	28,2	24,7	1,45
Subcortical ganglia	10	3,3365	0,7123	20,4	36,0	1,70
White matter	10	3,8921	0,9782	24,9	29,9	0,95
Cerebellar cortex	7	5,3462	0,8127	16,6	35,0	1,90
Cerebellar white matter	7	1,9148	0,4740	24,8	35,5	1,50
Brain stem	7	1,6643	0,5169	31,3	35,6	1,60
Spinal cord	7	1,0264	0,2719	34,7	14,7	1,05

Table II showing the content of Cu in different regions of brain in Wilson's disease.

Table III

Region	No of determinations	WM	DM	%	Al	± St. Er.
Cerebral cortex	8	4,0848	1,4277	32,1	52,0	4,07
White matter	10	4,5152	1,0282	25,1	20,9	3,7
Subcortical ganglia	10	3,3156	0,7002	19,0	14,3	1,2
Corebellar cortex	6	5,0065	0,8306	17,6	10,5	0,67
Cerebellar white matter	6	1,0750	0,4472	25,1	8,7	1,0
Brain stem	6	1,6643	0,5169	31,3	27,3	1,9
Spinal cord	6	1,0364	0,2719	26,1	40,3	0,95

Table III showing the content of Al in different regions of brain in Wilson's disease.

Table IV

Region	No of determinations	WM	DM	%	Ag	± St. Er.
Cerebral cortex	8	4,0848	1,4277	32,1	1,1	0,2
White matter	10	4,5152	1,0282	25,1	0,52	0,1
Subcortical ganglia	10	3,3156	0,7002	19,0	0,41	0,05
Cerebellar cortex	6	5,0065	0,8306	17,6	2,1	0,3
Cerebellar white matter	6	1,0750	0,4472	25,1	0,65	0,1
Brain stem	6	1,6643	0,5169	31,3	2,1	0,9
Spinal cord	6	1,0364	0,2719	26,1	2,1	0,07

Table IV showing the content of Ag in different regions of brain in Wilson's disease.

Table V

Region	No of determinations	WM	DM	%	Fe	± St. Er.
Grey matter	7	1,7744	0,2948	16,3	17,95	2,39
White matter	7	1,9768	0,5519	27,4	10,78	0,97
Basal Ganglia	7	1,2627	0,2496	17,9	16,85	2,07

Table V showing the content of Fe in different regions of brain in Huntington's chorea.

Table VI

Region	No of determinations	WM	DM	%	Cu	± St. Er.
Grey matter	7	1,7744	0,2948	16,3	2,35	0,36
White matter	7	1,9768	0,5519	27,4	1,61	0,11
Basal Ganglia	7	1,2627	0,2496	17,9	2,18	0,18

Table VI showing the content of Cu in different regions of brain in Huntington's chorea.

Table VII

Region	No of determinations	WM	DM	%	Al	± St. Er.
Grey matter	7	1,7744	0,2948	16,3	16,07	2,50
White matter	7	1,9768	0,5519	27,4	11,7	1,09
Basal Ganglia	7	1,2627	0,2496	17,9	12,80	2,17

Table VII showing the content of Al in different regions of brain in Huntington's chorea.

Table VIII

Region	No of determinations	WM	DM	%	Ag	± St. Er.
Grey matter	6	1,7744	0,2948	16,6	7,81	3,06
White matter	7	1,9768	0,5519	27,4	2,52	0,50
Basal Ganglia	7	1,2627	0,2496	17,9	4,77	1,04

Table VIII showing the content of Ag in different regions of brain in Huntington's chorea.

COMMENT

The content of iron in all examined regions of brain in Wilson's disease confirms the results of Cumings (1948) but the increase of this trace metal is not significant except in spinal cord.

Well known fact of significant, about 10 fold increase of copper content of whole brain, revealed by Cumings (1948), is confirmed by this method of determination (see Table III).

Aluminium, trace metal, so far little examined is significantly increased in all examined regions in Wilson's disease, paralel with those of copper. This fact was only mentioned by Lowental (1958) but not completely elaborated.

We could not confirme the findings of Butt and coowork. (1958) concerning increase of silver content of brain tissue in Wilson's disease. On the contrary, the content of silver is significantly decreased in regions of pronounced pathologic process, i. e. gray matter, white matter, and basal ganglia.

As far as Huntington's chorea is concerned, the profil of trace metals content show some difference. The data of Courville and coowork. (1963) regarding moderate decrease of iron and copper content in brain cortex, white matter and basal ganglia were confirmed by this technique. These decreases are highly significant. ($p<0,0001$). We tried to prove the findings of same investigators concerning the increase of Strontium (Sr) in brain, but the content of this metal in brain tissue of Huntington's chorea, as well as in control group, was so small that could not be determined by this technique.

The principal finding is a highly significant ($p<0,001$) increase of Aluminium (Al) in all examined regions, the fact not revealed so far.

Possible implications of these findings are numerous the changes in trace metals content might be related to proliferation of blood vessels or glia cells, changes of blood brain barrier system, changes in nerve cell components, enzyme systems and others. The aim of these investigations is solely to be a contribution to chemical pathology of the nervous system.

SUMMARY

The author presents the results of determination of some trace metals in different regions of human brain from persons died of Wilson's disease and Huntington's chorea. Determinations were made by emission spectrography after drying the tissue and destroying organic components. Iron (Fe), Copper (Cu), Aluminium (Al) and Silver (Ag) were determined in brain cortex, white matter basal ganglia and some other regions of brain.

Beside of very well known fact of extreme increase of copper content in brain tissue from patients died of Wilson's disease, significant increase of Aluminium and decrease of Silver has been found. Previous

findings of significant increase of Strontium in brain tissue in Huntington's chorea were not confirmed, but highly significant decrease of Iron and Copper as well as increase of Aluminium was found.

RISTO BOKONJIĆ

SADRŽAJ NEKIH METALA U MOŽDANOM TKIVU PRILIKOM EKSTRAPIRAMIDALNIH OBOLJENJA

KRATAK SADRŽAJ

Izloženi su rezultati određivanja oligoelemenata u moždanom tkivu kod pacijenata umrlih od Wilsonove bolesti i Huntingtonove horeje. Determinacije su vršene u formolisanom tkivu poslije prethodnog sušenja metodom emisione spektrografije. Redovno su determinacije vršene u moždanoj kori (CC), supkortikalnim ganglijama (BG) i u bijeloj masi (SA).

Prilikom Wilsonove bolesti, pored dobro poznatog povećanog sadržaja bakra (Cu) u svim regijama, nađeno je i signifikantno povišenje sadržaja aluminijuma (Al) u svim ispitivanim regijama. Pored toga, nađeno je i signifikantno sniženje sadržaja srebra (Ag).

Prilikom Huntingtonove horeje je nađeno signifikantno sniženje sadržaja gvožđa (Fe) i bakra (Cu) u svim ispitivanim regijama. Sadržaj aluminijuma (Al) visoko je signifikantno povišen u svim ispitivanim regijama. Ranije nađeni povećan sadržaj stroncijuma (Sr) prilikom ovog oboljenja nije mogao biti potvrđen.

REFERENCES

1. Alexander, L., Myerson, A.: Minerals in Normal and in Pathological Brain Tissue Studied by Microincineration and Spectroscopy. Arch. Neurol. Psychiat. 39: 131 (1938).
2. Bodansky, M.: The Zinc and Copper Storage of the Human Brain J. Biol. Chem., 48: 361 (1921).
3. Butt, E. M., Nusbaum, R. E., Gilmour, T. C., Didio, S. L.: Use of Emission Spectrograph for study of inorganic Elements in Human Tissue. The Am. J. of Clin. Path., 24: 385 (1954).
4. Butt, E. M., Nusbaum, R. E., Gilmour, T. C., Didio, S. L.: Trace Metal Patterns in Disease States; Haemochromatosis and Refractery Anaemia. The Am. J. of Clin. Pathol., 26: 225 (1956).
5. Butt, E. M., Nusbaum, R. E., Gilmour, T. C., Didio, D. L.: Trace Metal Patterns in Disease States. Copper Storage Diseases with Consideration of Juvenile Cirrhosis, Wilson's Disease and Hepatic Copper in the Newborn. The Am. J. of Clin. Pathol., 30: 479 (1958).

6. Courville, C. B., Nusbaum, R. E., Butt, E. M.: Changes in trace Metals in Brain in Huntington's Chorea. Arch. Neurol., 8: 481 (1963).

7. Cumings, J. N.: Copper and Iron Content of Brain and Liver in Normal and Hepato-lenticular Degeneration Brain, 71: 410 (1948).

8. Gumings, J. N.: Heavy Metals and the Brain. Blackwell Sci. Publ Oxford, 1959.

9. Lowental, A.: Teneur du cerveau normal et pathologique en quelque elements simples. Psychiat. Neurol., Neurochir., 63: 192 (1960).

10. Tingey, A. H.: The Iron, Copper and Manganese Content of the Human Brain. J. of. Ment. Sci., 83: 452 (1937).

DISCUSSION

Dimitrijević: One synic comment. What you call by normal human brain in neurochemistry.

Bokonjić: Brain tissue of normal man which did not show any abnormality, and taken from healthy people killed in accident.

Schnieden: Could I have some information on the physiological role of aluminium?

Bokonjić: The physiological role of aluminium is little examined. I suspect Al is important trace metal in metalo-enzimes complex of LDH. In somewhere, especially in liver, that is very well known. LDH activity in brain has been examined by Dr Richard and some paralelism has been found.

Barbeau: I may not agree that using formaline treated brains is safe when studying trace metals. Using fresh materials is preferable because our experience is that formalin does contain contaminans. This may not explain the large changes in Cu or Al that you found, but would be expected in Parkinson's disease.

Bokonjić: Formalisation of material does not change so much the content of trace metals in gross neurochemistry. Comparison of trace metal content from fresh brain and formalised brain showed little, not significant differences.