SESSION 6

TRACE ELEMENTS AND MINERALS IN NEUROLOGY AND PSYCHIATRY

MICROELEMENTS METABOLIC DISORDER IN PATIENTS WITH WILSON-KONOVALOV DISEASE

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The biosubstrates levels of microelements (ME) and macroelements (MaE) are important markers in the diagnostics of genetic diseases associated with ME/MaE metabolic disorders. For example, Cu^{2+} serum and urine levels have high diagnostic potential in detecting of the Wilson-Konovalov disease (WK) in patients. At the same time, the WK disease dynamics is characterized by changes in mineral metabolism. We examined 9—16 years old 66 patients with suspected WK disease. The control group included 20 healthy volunteers. ME (Cu, Zn, Mn, Fe, Se) and MaE (Mg, Ca, K) serum and urine levels were measured using the inductively coupled plasma atomic emission spectroscopy (ICP-AES) following sample acid mineralization. In WK patients, the measurement results showed opposite-direction changes in Cu and Zn levels (decreased Cu and increased Zn serum levels; increased Cu and decreased Zn urine levels) which indicates that Cu and Zn excretion mechanism was broken. However at the same time, Se and Mg serum levels and Zn, Ca and K urine levels exceeded «normal» levels at this age group and also the control group levels so indicating the imbalance of these elements. In addition, the difference in Mn, Fe and K serum and urine concentrations did not reach the confidence level which indicates that the role of these elements in WK progress is insignificant. The results of this study and other research publications confirm that genetic Cu metabolic disorder is accompanied by MaE-ME imbalance (these elements also participate in cellular differentiation, bone and cartilaginous tissues formation and other processes). Moreover, when correcting the microelement status at WK patients one should take into account MaE-ME antagonism and synergy.

COMPARISON OF NATURAL SILVER AND 64COPPER LOADING TESTS IN FIBROBLASTS FOR THE DIAGNOSIS OF MENKES DISEASE

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BACKGROUND: Menkes disease is a rare X-linked genetic disorder of copper metabolism. Copper uptake and retention assays on fibroblast cultures are used for postnatal diagnosis when the bio-molecular diagnosis is impossible. This in-vitro loading test is complicated by the use of ^{64}Cu, which is more and more difficult to get, particularly for diagnosis purpose and has a very short (12.8 hours) half-life. As silver is also a substrate for the Menkes ATPase (ATP7A), we compared the classical test to in-vitro loading test using natural silver. METHOD: Menkes fibroblasts were grown in three 75-cm^2 culture flasks in RPMI medium supplemented with 15% foetal calf serum. Fibroblast cultures just reaching confluence were loaded either with 2.5μCi ^{64}Cu (approximately 125 ng Cu) /ml culture medium or 200 ng Ag/ml culture medium for 20 h (Uptake). The cell layers were then washed twice and the medium was replaced by fresh medium without added amount of Cu or Ag and cells were further cultured for 8h (Retention). Fibroblasts were harvested before labelling (T0), after loading (T20) and after efflux (T28) and the cellular ^{64}Cu was measured using a gamma-ray counter whereas the cellular Ag was measured by ICP-MS (^{107}Ag and ^{109}Ag stable isotopes). The cellular protein concentration was also determined. Uptake was expressed as μCi ^{64}Cu or ng Ag/mg total protein whereas retention was expressed as the percentage of the incorporated dose remaining after 8 h. RESULTS indicate acceptable agreement between the two methods, both for the uptake (Controls, n = 4: 0.18—0.34 μCi ^{64}Cu vs 8—58 ng Ag/mg protein; Menkes, n = 5: 1.05—2.66 μCi ^{64}Cu vs 219—335 ng Ag/mg protein) and retention (Controls, n = 4: 38—56% for Cu vs 50—78% for Ag; Menkes, n = 5: 93—100% for Cu vs 84—94% for Ag) of the metal ion. Measurements on a larger scale should allow us to substitute natural silver to radioactive copper, which represents a noticeable advantage when ICP-MS is available.

THE POSSIBLE CONNECTION BETWEEN INTELLECT, VIOLENCE AND MINERAL METABOLISM

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BACKGROUND: There are some data concerning the influence of toxic metals accumulation on the deviant behaviour, aggressiveness and violence. AIM: To investigate elemental and psychological status of prisoners (P) and personnel of prisons (PP). METHODS: Totally 98 male prisoners, 56 male prison stuff persons and 74 healthy local controls (LC), aged from 30—37 y.o., living in the Orenburg region, were clinically and laboratory investigated. The elemental content of daily food consumption, hair (H) and whole blood (WB) samples were determined by ICP-AES/ICP-MS methods. RESULTS: Chemical analysis of daily food intake of P group revealed elevated consumption of Na, I, Se, Cr, and suboptimal intake of Ca, Mg, P, Fe, Zn, Mn. The multielement analysis detected the increased hair Na, K, P, Fe, I, Si, Cr, Mn, Ni, Cd, Pb, Be, Al, Ti in the P group in comparison with PP and LC groups. But hair Zn, Cu, Se levels in prisoners were relatively lower. The H and WB elemental contents positively and significantly correlated in case of Ca (r = 0.75), Mg (r = 0,88), Cr (r = 0.62), Sr (r = 0,58), Zn (r = 0,55), As (r = 0,59), Hg (r = 0,64), Pb (r = 0,73) and negative interrelationships for hair and whole blood in cases of Na (r = -0,54), K (r = -0,56), Fe (r = 0,75). Among the P there were mainly peoples with low or medium IQ score, contrary to LC and PP (prevalence of medium and high IQ score). Lower IQ correlated with the hair accumulation of toxic metals (As, Pb, Sn, Al, Be) and Fe, Co, Cr, Ni, Se, Mn and decreasing of macro elements. The similar picture was obtained in P, divided in 3 groups depending on severity of their crimes: the severe violence correlated with elevated hair Na, Ni, Ti, Be, Cd, I and decreased Mg, Cr, Cu. CONCLUSION: Low intellect and severity of violence have the similar hair elemental content peculiarities (elevated toxic metals and decreased macro elements and some trace elements). Thus, it is possible to influence the intelligence and behaviour through correction of mineral status.

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MOLECULAR DIAGNOSIS OF WILSON DISEASE BY DIRECT SEQUENCING AND MULTIPLEX LIGATION-DEPENDENT PROBE AMPLIFICATION (MLPA) ANALYSIS IN ATP7B GENE

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INTRODUCTION: Wilson disease (WD), an autosomal recessive disorder of copper (Cu) transport shows wide genotypic and phenotypic variability. The WD gene, ATP7B, encodes a Cu transporting ATPase that is involved in the transport of Cu into the plasma protein ceruloplasmin and in the excretion of Cu from the hepatocyte. ATP7B mutations result in Cu storage in liver and brain. OBJECTIVE: Most of the over 350 mutations identified to date in ATP7B gene are point mutations or small deletions/insertions detectable by conventional sequencing. This study was undertaken to determine whether testing for large gene rearrangements could improve the mutation detection rate. METHOD: Total genomic DNA was isolated from peripheral blood and mutation analysis was carried out on 66 WD unrelated patients presenting hepatic and/or neurological form of illness. Direct sequencing of the 21 exons and their flanking introns were performed on an AB 3730 Genetic Analyser equipped with Seqscape software.The cases with only one mutation were tested using a MLPA assay. RESULTS: In our 66 WD unrelated patients, two mutations were identified by direct sequencing in 53 WD cases and one mutation in 13 cases. The distribution of mutation type is 74% missense, 16% frameshift, 7% nonsense and 3% splice site. The 13 WD cases with only one mutation have been screened with MLPA technique for large gene rearrangement study. In one WD patient, we identified the deletion of exon 4 of the ATP7B gene. CONCLUSION: Direct sequencing for ATP7B mutations analysis is feasible and leads to the detection of about 90% of the mutated chromosomes. The MLPA assay for detection of exon deletions may be valuable in individuals with clinical WD diagnosis where one or no mutations have been identified by sequencing. WD is a rare affection but an important one to remember because it is eminently treatable. So molecular diagnosis is very useful in clinical practice to confirm or support clinical and/or biochemical suspicion.

PLASMA SELENIUM LEVELS IN PKU PATIENTS WITH RESTRICTIVE DIET AT MIGUEL SERVET UNIVERSITARY HOSPITAL FROM SARAGOSSE (SPAIN) SINCE 2005 TO 2010

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INTRODUCTION: Phenylketonuria (PKU) is an autosomal recessive inborn error of phenylalanine metabolism resulting from deficiency of phenylalanine hydroxylase. The inherited inability to convert the amino acid phenylalanine into tyrosine results in an accumulation of phenylalanine Left untreated, the condition results in severe mental retardation and other serious health problems. However, since the introduction of newborn screening programs and with early dietary intervention, children born with PKU can now expect to lead relatively normal lives. OBJECTIVE: To analyze if the PKU-restricted diet may result in a dietary deficiency of selenium (Se), nutrient needed by the human body in small amounts. MATERIALS AND METHODS: A descriptive retrospective cross-sectional study was designed. Se was measured from plasma samples of 23 PKU patients, aged between 1 to 30 years, all of whom were following the low phenylalanine diet. The results were compared with those obtained from 20 samples of presumably healthy patients of same age range, by using SPSS software. Plasma Se levels were analyzed by Graphite Furnace Atomic Absorption Spectroscopy using a ZEEnit 600 Spectrophotometer from Analitik Jena, based on the Zeeman-background correction, palladium nitrate and Triton X-100 as matrix modifiers and calibration by the addition standard method. Our laboratory is accredited to UNE-EN ISO 15189. RESULTS: Plasma Se concentrations were 96.6 ± 11.42 (SD) μg/l for the healthy control group, whereas it was 73.35 ± 24.76 (SD) μg/l for the PKU patients group. It was observed a significant difference between both groups ($p < 0.001$), indicating that Se concentration was significantly lower in the subjects with PKU than in the healthy group. CONCLUSIONS: Se concentration seems to be influenced by the restrictive diet of PKU patients, so it may be worth monitoring Se levels in PKU patients.

CONCENTRATION OF MINERAL CHEMICAL ELEMENTS (Ca, Mg) AND TRACE ELEMENTS (Cu, Fe, Zn, Mn) IN CEPHALORAQUIDEAL LIQUID: PHYSIOPATHOLOGICAL EVALUATION

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INTRODUCTION AND AIMS: The composition of cerebrospinal fluid (CSF) is similar to a plasma infiltrate. Nevertheless, differences indicate that the CSF formed in the choroid plexi is produced both by filtration and active secretion. CSF and the cerebral interstice are separated from blood circulation by the haematoencephalic and haematocephaloraquideal barriers. The aim of this study is to obtain the reference values of elements Ca, Mg, Cu, Fe, Zn and Mn in normal CSF and observe their variations for cell and protein increase. PATIENTS AND METHODS: The observation study was performed in CSF of 37 people with normal results of glucose, protein, globulin (Pandy), aspect (colour and transparency, and in pathological CSF of 136 patients from Neurology and Neurosurgery. CSF was extracted by puncture in the lumbar cistern. The analysis of cations was performed by atomic absorption spectrophotometry. RESULTS: Mean values, standard deviation and range, obtained for each cation analysed were as follows: Ca: 4.95 mg/dL, 0.70, 4.4—5.8; Mg: 2.74 mg/dL, 0.10, 2.5—2.9; Cu: 15.7 μg/dL, 13.5, 1.9—61.0; Fe: 13.1 μg/dL, 3.6, 4.4—23.3; Zn: 17.4 μg/dL, 9.5, 3.3—52.4; Mn: 2.5 μg/dL, 0.7, 1.2—3.9. In the pathological CSFs, grouped according to cell and protein content, significant increases were seen ($p < 0.05$) with respect to the normal group for Ca, Cu, Fe and Zn, in both cell and protein increases. A significant decrease of Mg ($p < 0.05$) was seen in the groups with sell and protein increase. No significant differences were noted in Mn. CONCLUSIONS: The results of the cations analysed in the normal CSF group correspond to those of other authors. The significant differences seen in these cations in pathological CSF are caused by encephalic barrier alterations.

NEUROTROPIC EFFECTS OF THE TITANIUM DIOXIDE NANOSIZE

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The titanium dioxide (TiO_2) now is one of the most widespread nanoparticles. In experiment rats-males of Wistar line have been used contained on a standard diet. By means of the test «open field» has been allocated 30 individuals with identical type of nervous system. From these animals have been generated control and 2 skilled groups, receiving within 7 days in the morning TiO_2 in dose 250 mg/kg as a part of an attractive forage or nanodisperse (δ_{50}~ 9 nm, S_{rel} 119 m^2/g) or micro disperses (δ_{50} ~ 350 nm, S_{rel} 4.5 m^2/g) forms. During experiment the round-the-clock video shooting of animals was spent. After the termination of experiences defined the maintenance of the titanium, sodium and potassium in blood, brain, liver, kidneys by method of mass spectrometry with is inductive coupled argon plasma («Plasma», Tomsk). Results were processed by means of nonparametric statistics. It is established that at the rats receiving TiO_2, in comparison with control animals the maintenance of titanium has not changed. The parity of concentration Na/K in blood has increased after introduction TiO_2 of 350 nm. In liver this factor has increased but in brain has decreased after introduction TiO_2 of 5 nm. In the test «open field» at control animals horizontal activity did not change, a mink component and grooming raised and vertical activity and an emotionality decreased in comparison with the initial data. At the rats receiving TiO_2 studied indicators of behaviour changed similarly, but is more considerable ($P < 0.05$), especially at the rats receiving micro disperses of TiO_2. Video observations have shown that throughout 7 days in the afternoon activity of rats in all three groups was equally low and did not differ between groups. In a night-time it is established that activity, aggression and sensitivity to stress of the rats receiving nanodisperse TiO_2, was above, than in the control ($P < 0.05$), and activity, aggression of the rats receiving a micro disperse TiO_2, was more low, than in the control ($P < 0.05$). Work is executed under the State contract № П1260 «Research of features of influence on an organism nanosize substances» (code number «НК-30П») from August, 27th, 2009 in a direction «Fundamental medicine and physiology».

THE HAIR ELEMENTOME IMAGE OF THE HUMAN DEPRESSION REVEALS THE SYNDROME OF MAJOR BODY INACTIVITY

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OBJECTIVE. Depression (D) is the most prevalent human mental health impairment in the world of unknown origin. The aim of this prospective, observational, cross-sectional, clinical, epidemiological, and analytical study was to analyze the changes of the human hair elementome in the D subjects. By elementome we consider the contextual space frame of the multielement profile where all the aspects of element interactions are viewed simultaneously. METHODS. The depression was diagnosed by the DSM-IV criteria; the study adhered to the Declaration of Helsinki principles on human subject research. Forty elements were analyzed in the hair samples of 96 subjects (D: 15 Men and 33 Women vs. Control (C): 23 Men and 25 Women) by the ICP-MS at the CBM, Moscow, Russia. The difference of ≥15% between the median of an element in the C and D subjects was considered to be significant. RESULTS. The results showed a distinct pattern of elementome change in D subjects and revealed the syndrome of the physical and/or metabolic inactivity of the body. Thus, hair Ca and Mg were increased in D subjects, presumably by their mobilization from the bone. Similarly, Na (La), and K (Rb) were increased by the lost of the inactive muscle cell mass (sarcopenia), and Fe (Mn) was increased due to the reduced oxygen needs of the sarcopenic muscles («use it or loose it» principle). In contrast, the essential trace elements I, Se, Zn, and Cu were decreased in the depressed subjects, indicating the deficiency induced slowdown of metabolism due to the impairment of the mutual interrelationships among the members of the elementome (Liebig's Law of minimum). The invariant concentrations of Cr, Co, Ni, and Mo, indicate that hair growth velocity is not changed in D subjects. CONCLUSION. Elementome showed depression to be the multifactorial syndrome of decreased overall body activity where the respective deficit of essential nutrients may be either the initial trigger or a secondary consequence.

STUDY ON TRACE ELEMENTS IN HUMAN BRAIN SAMPLES

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Analyses of human brain tissues are becoming of great interest in the medical field since trace elements may influence in the cognitive functions as they are involved in metabolic processes and redox reactions. Besides, essential elements are required in the brain for development and maintenance of the central nervous system, and to play an important role in neurodegenerative disorders. The aim of this study was to investigate on trace elements in two regions (hippocampus and medium frontal cortex) of human brains from normal individuals, selected according to Clinical Dementia Rating score. This research was approved by the Ethic Committee and brain samples from 32 normal individuals (17 females and 15 males) aged 51—95 years were provided from the Brain Bank of the Brazilian Aging Study Group of São Paulo University, Medical School. The brain tissues were cut using a titanium knife, ground, freeze-dried and then analyzed by neutron activation analysis. Samples and element standards were irradiated at the IEA-R1 nuclear reactor under a thermal neutron flux for Br, Fe, K, Na, Rb, Se and Zn determinations. Student's t test ($p = 0.05$) was applied for comparison of results. Results indicated higher concentrations of Fe, Se and Zn in frontal cortexthan those found in hippocampus. No significant difference was found between the genders for frontal cortex tissues. However, the males presented higher Zn concentrations (69 ± 8 mg/kg) in hippocampus than those presented by females (62 ± 6 mg/kg). Comparative study based on two different age groups of individuals indicated that the element concentrations of hippocampus region from group aged 51 to 75 years showed significant difference for Fe from those for the group of 76 to 95 years. Most of our results agreed with the literature ones. It is our intention to extend the study to Alzheimer disease human brains. Biological certified reference materials were also analyzed for quality of the analytical results.

ZINC, A NOVEL IONIC MEDIATOR OF NEURONAL INJURY

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Glutamate is the most widespread neurotransmitter in the brain and when released in excessive amounts like during ischemia, epilepsy or Alzheimer's disease is potently neurotoxic. In the last thirty years many molecular mechanisms linked to glutamate dependent neurotoxicity, also called excitotoxicity, have been clarified. Key factors involved in the excitotoxic cascade are loss of intracellular homeostasis for ions such as Ca^{2+}, Na^{+}, and K^{+}, alterations in mitochondrial function, and generation of reactive oxygen species (ROS). However, recent findings indicate a more complex scenario. In recent years, a new ionic mediator of excitotoxicity has been proposed: Zn^{2+}. Zn^{2+} is present at synapses of many glutamatergic neurons and released during ischemia, brain trauma and epilepsy. Zn^{2+} enters neurons through three different routes (NMDA receptors, voltage sensitive $Ca2^{+}$ channels and Ca^{2+}-permeable AMPA receptors (Ca-ARs) in response to glutamate receptor activation. Among all the entry routes, Zn^{2+} preferentially fluxes through «Ca-ARs», and rapid (micromolar) Zn^{2+} accumulation causes mitochondria to undergo prolonged and irreversible alterations in their function with consequent increases in ROS production. Interestingly, even lower $[Zn^{2+}]_i$ rises potently activate mitochondrial cell death signaling pathways, triggering, with far greater potency than Ca^{2+}, induction of the mitochondrial permeability transition (mPT), mitochondrial swelling, and release of the mitochondrially sequestered pro-apoptotic factors, cytochrome C and apoptosis inducing factor. Moreover, recent findings indicate that Zn^{2+} is also a potent activator of autophagy. Finally, a major pathogenic role for Zn^{2+} has been suggested in the neurodegeneration associated with Alzheimer's disease (AD) as the cation is a key component of amyloid plaques and the cerebral amyloid angiopathy observed in AD. This lecture will describe a novel blueprint of Zn^{2+}-dependent death signaling pathways involved in the neuronal loss associated with major neurological conditions.

BLOOD LEAD AND CADMIUM LEVELS IN BIPOLAR DISORDER

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BACKGROUND: Bipolar disorder (BD) is associated with increased and premature mortality due to cardiovascular disease (CVD) and hypertension. However, in spite of the evidence of multiple sources of CVD risk among BD, including higher prevalence of tobacco smoking behaviour compared with the general population, there is limited evidence regarding the association between BD and CVD. Recent studies have shown an association between low blood lead and cadmium levels with an increased risk of cardiovascular disease and hypertension. The objective of this study is to determine blood lead and cadmium concentrations in patients diagnosed with bipolar disorders and to compare these levels with those of a control group. MATERIAL AND METHODS: The study was carried out on 25 patients (mean age: 49.4 years) and 24 healthy controls (mean age: 45.3 years). Blood lead (μg/dL) and cadmium (μg/L) concentrations were determined by electrothermal atomic absorption spectrometry with Zeeman background correction. Statistical package SPSS 15.0 was used for data analysis. RESULTS: Median blood lead (3.0 IQR: 1.4—4.2) and cadmium (0.39 IQR: 0.1—1.15) in patients were higher ($p = 0.040$, $p < 0.001$ respectively) than in controls (Lead: 2.20 IQR: 0.9—3; Cadmium: 0.1 IQR: 0.05—0.3). Median blood cadmium in manic phase was higher (0.5) than in depressive phase (0.1) in relation to smoking behaviour ($p = 0.034$). CONCLUSIONS: There seems to be higher blood lead and cadmium levels in patients with bipolar disorder. Further studies are needed to clarify the role that these trace elements can play in the increased risk of CVD in bipolar disorders.

HAIR TRACE ELEMENTS PROFILES IN AUTISTIC CHILDREN AND CHILDREN WITH PSYCHOVERBAL RETARDATION

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BACKGROUND: During last decades it was found, that essential TE (Zn, Cu, Se, J, etc.) deficiencies and some toxic metals (Pb, Hg, Cd) accumulation can play an important role in the pathogenesis of psychoverbal retardation (PR) and autism (AU) in children. The aim of present study was to use the occipital hair samples multielement analysis as non-invasive screening test for evaluation of elemental status of children, suffering from AU and PR. METHODS: The 29 of 3—9 y.o. AU and 88 of 5—10 y.o. PR children were clinically observed and their hair samples were investigated for multielemental content by ICP-AES/ICP-MS in laboratory of Centre for Biotic Medicine (Moscow). Date of 220 5—10 y.o. relatively healthy children as controls were used in each group there were 1:1 both sexes children. According to literature date, the most of analyzed macro- and TE contents in hair not differ significantly between prepubertal boys and girls. RESULTS: There are decreased hair Ca, Mg ($p < 0.001$), Zn ($p < 0.01$) and the tendency ($p < 0.1$) to decreased Se and elevated Pb levels in PR children elevated. AU children had the decreased hair Mg ($p < 0.01$), Se ($p < 0.01$) and elevated Pb, Cd ($p < 0.05$), Al ($p < 0.1$) levels. The hair Ca, Cu, Cd levels were higher and J lower in Au children in comparison to PR ones. It is important to decline the elevated levels of hair Pb (6% in PR, 7% in AU), Hg (5.7% in PR, 3.6% in AU), Cd (5.7% in PR) in patients in comparison to controls (1.4%, 0.9%, 1.4% respectively). The frequency of decreased Se level and increased Mn level were maximal in AU children and higher in PR children as compare to controls. PR children were often deficient in Cu hair level. CONCLUSION: Hair multielement test the possible involvement of macro- and TE metabolism disorders in the pathogenesis of psychoverbal retardation and autism demonstrated.

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PRECONCEPTION ALCOHOL INTOXICATION DISTURBS THE OFFSPRING'S BRAIN METAL DISTRIBUTION

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INTRODUCTION: Formerly the significant influence of alcoholic intoxication during pregnancy and lactation in trace elements' metabolism in offsprings and their mothers was demonstrated. The aim of recent study was to compare the elemental profiles of brain structure of pubescent offsprings which were born from preconception alcoholic exposed and unexposed female rats. Alcohol intoxication was provided before conception till inbred white rats. Exposure by 15% ethanol water solution as single source of liquid was continued 20 days. METHODS: The brain cortex (n = 20), white substance (n = 20), cerebellum (n = 20) and hippocampus (n = 19) of 90 days old male offsprings by ICP-AES/ICP-MS in laboratory of Centre for Biotic Medicine (Moscow) were analyzed. RESULTS: Short term alcohol consumption by female rats before pregnancy exerts influence on distribution of macro- and trace elements in the brain structures. The most considerable changes are noted in brain cortex. It was shown the significant decrease of K, Na, Mg, Fe and Zn ($p < 0.05$) in comparison with control group. Changes in white substance were detected as significant decrease of Ca and P, Fe, Mn ($p < 0.05$). In cerebellum and hippocampus multidirectional changes were detected. Significant lack of Mn was detected in cerebellum and hippocampus and increase of zinc was detected in cerebellum ($p < 0.05$). CONCLUSION: Alcohol consumption before pregnancy by female rats disturbs offspring's brain metal distribution. The effect of alcohol can explain the minor psycho neurological deviations observed in lot of children from different countries including Russia and other CIS with tolerable point of view on moderate alcohol consumption by young females.

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PREVENTIVE ROLE OF STRONTIUM RANELATE AGAINST TO OXIDATIVE STRESS IN BRAIN

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Strontium ranelate is a new agent developed for the management of postmenopausal osteoporosis. It has been shown to prevent bone loss by maintaining bone formation at a high level and inhibiting bone absorption. Strontium ranelate is composed of an organic moiety (ranelic acid) and two atoms of strontium. It was recently demonstrated to significantly reduce vertebral and hip fracture risk in women with postmenopausal osteoporosis, and to have a good tolerability profile. There is a lot of data regarding the effects of strontium on bone but no information available related with strontium and oxidative stress. In our study, we investigated the influence of strontium therapy on oxidative stress in brain of ovariectomized rats as a postmenopausal model. Twenty-one adult albino female Wistar rats (n=7 per group) were divided into three groups as sham operated, ovariectomized, and treatment groups. Animals in treatment group were treated with strontium ranelate (500 mg/kg/day p.o.) for 120 days, starting immediately after ovariectomy. End of the experiments, all rats were sacrificed and their brain tissues removed for the measurement of superoxide dismutase (SOD), catalase (CAT), and malondialdehyde (MDA) levels. The SOD and CAT activities were decreased and MDA level was increased in ovariectomized group. In treatment group, concentration of MDA was raised and SOD and CAT levels were declined according to control group. As a result, findings may demonstrate that strontium has protective role against oxidative stress in brain of ovariectomized rats.