Combined Chronic Impacts of Heavy Metals and Low Dose Irradiation Induced Metabolic Changes in Rat Brain

T.V.Ananieva, E.A.Lykholat

Ukrainian State Institute of Medical and Social Problems of Disability
Radyansky Bystr., 49027 Dniepropetrovsk, Ukraine

Abstract

In homogenates of hemispheres, cerebellum and brain stem of Wistar rats consumed during 25 days drink water with addition of Cu^{2+} (68,8 mg/l) or Co^{2+} (11,9 mg/l) in combination with fractionated irradiation (0,01 Gy per day) the malone dialdehyde (MDA) concentration, the superoxide dismutase (SOD) activity, level of the antioxidizing activity (AOA), contents of the medium molecular peptides (MMP), and succinatdehydrogenase (SDH) activity were measured. Under the chronic influence of heavy metal ions MMP level increased by 2-3 times in brain stem and hemispheres means nerve tissue intoxication. Cu^{2+} ions caused more intensive MDA accumulation in all brain compartments in comparison to Co^{2+}, with equal SOD activation (on 40%) in hemispheres and weaker one in brain stem and cerebellum. At last, prevailing AOA reduction satisfied to the deeper oxidative stress in a case of Cu^{2+} application. The whole-body 0,25Gy irradiation (R) induced intensive processes of free-radical oxidation in brain tissue and essentially reduced AOA index. Combination of the radiation and chemical factors caused a growth of the MMP level, further MDA accumulation, and falling AOA index in comparison to their single action. At the same time the additive effects upon the SOD activity were observed in brain stem at both impacts of $R+Co^{2+}$, $R+Cu^{2+}$, and in hemispheres at the action of $R+Co^{2+}$. It is possible to conclude that detected changes reflect adaptive responses of the cell-tissue level. Exhausting biochemical adaptation mechanisms occurs in process of damaging action increases and depends on metabolic stability and plasticity of brain structures.

Introduction

Radiation influence maintains a serious problem in connection with extension of atomic energy, radioisotope and roentgen investigation methods using by industry, science, and medicine. Under the real conditions human is influenced with complex environmental factors, including harmful ones, which have chemical and physical origin. Their combinations caused new unexpected biological effects. Observed increase of radioactive background by doses in tens and hundred times exceeding natural one, and also technogenic contamination of main sources of fresh water with chemical pollutants including heavy metals lead to increased radiation-chemical loading upon residents of large industrial regions. Such harmful influence is table, and progressive in numerous cases, that caused irreversible changes in main functions of intercellular enzymatic systems and structures, and as a result decreased total

resistance of organism, visible chemical disorders. That is why early elucidation of prepathologic functional and chemical changes of molecular-cellular level is exceptionally significant.

Examination of metabolic reactions in brain has a special interest, because exclusive sensitivity of central nervous system to low-dose irradiation is well-known [1-3]. At the present work it had been investigated primary reactions of rat brain compartments (hemispheres, cerebellum and brain stem) tissues under the conditions of low-dose irradiation and chronic consumption of heavy metal ions. The parameters of prooxidant and antioxidant systems and redox-processes were used as evaluation criteria, because they were known to be involved in universal biochemical adaptation mechanisms in living systems at the external dominance.

Results and discussion

Obtained experimental data showed that chronic low-dose irradiation as well as heavy metals influence caused intensification of free-radical processes (FRP) in examined brain compartments (table 1). The malon dialdehyd (MDA) levels were incresed from 18–20% in cerebellum and brain stem to 42% in hemispheres under the irradiation influence. Cu^{2+} ions increased MDA concentration in tissue from all tested brain compartments, but effects of Co^{2+} ions were obvious in homogenates of brain hemispheres only. Combined effects of radiation and chemical factors showed progressive MDA accumulation. Thus, MDA level in hemispheres exceed in 2,0 and 1,6 times control ones under the influence Cu^{2+} ions and Co^{2+} ions respectively.

To estimate antioxidizing defense potential of nervous tissue the superoxiddismutase (SOD) activity and ceruloplasmin (CP) contents were measured taking into consideration their reciprocal interaction between these systems. Under the low-dose irradiation influence it had been found increased SOD activity and CP concentration (in 2–3 times) in hemisphere and cerebellum, whereas in brain stem increased SOD activity was accompanied with reduced CP level. Chronic penetration of Cu^{2+} and Co^{2+} ions into organism caused SOD activity increase in all tested brain compartments, but CP concentrations were near the control values. CP level was significantly reduced (to 34%) by Co^{2+} ions influence in brain stem, and it was increased to 142% by Cu^{2+} ions influence in cerebellum. Another images were observed, when combined impacts of radiation and chemical toxicants were used. In brain hemispheres SOD activity was enhanced, and CP concentrations were not changed by Cu^{2+} ions and considerably reduced by Co^{2+} ions. In brain stem combined radiation-chemical effects showed SOD activation and increased CP levels in the both cases. In cerebellum combined effects of low-dose irradiation with Cu^{2+} and Co^{2+} ions were various: combination with Cu^{2+} ions induced CP content loss, combination with Co^{2+} ions induced its growth; Sod was activated in the both cases. At the same times time the additive effects upon the SOD activity were observed in brain stem at both impacts of irraiation and heavy metals, and in hemispheres at the combined action of irradiation and Co^{2+}-ions. It could be proposed that non-equal pattern of changes in SOD–CP system indicated specific adaptive triggers in various

compartment of brain, which are depend on origin and ability of impact factors. Obviously, primary reaction of tissual antioxidant system of SOD–CP is increased CP concentration with following exhausting under the permanent action of toxicants. Thus, weaker effects of Co^{2+}-ions may be explained its lower impact in proposed experimental model

Although antioxidant system in brain showed functional tension, integral index of antioxidizing activity (AOA) was reduced in all experimental variants. At last, prevailing AOA reduction satisfied to the deeper oxidative stress in a case of Cu^{2+} application.. Effects of Co^{2+}-ions were liked to Cu^{2+}-effects/ that satisfied to higher biological toxicity of Co^{2+}-ions as reactive agent.

Intensification of FRP and simultaneous exhausting antioxidizing potential of tissue lead to endogenous intoxication of organism. That is supported with essential accumulation of medium mass peptides (MMP). Maximal growth of MMP concentration was marked in hemispheres and cerebellum under the combined radiation-chemical influence.

Mitochondrial succinatdehydrogenase (SDH) – the key enzyme of Krebs cycle – was equally activated in all experimental variants. Increasing of SDH activity satisfied to activation of both NADH- and NADPH-dependent redox-processes, which are connected with rapid and significant activation of catecholamines in sympatic nervous system.

Conclusion

Analysis of obtained experimental data showed that combined chronic impacts of low-dose irradiation and penetration heavy metals ions lead to considerable intensification of free-radical processes, exhausting of antioxidizing and redox-potential, endogenous intoxication of brain tissue. Levels of observed disorders depends on origin and efficiency of harmful factors, and also, on metabolic stability and plasticity of brain structures. Under the prolonged unfavorable influence the biochemical changes observed become sustainable and progressing, that satisfied to transformation of protective-adaptive reactions into prepathology stage.

References

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Table 1. Metabolic changes in hemispheres, brain stem and cerebellum of rats under combined chronic impacts of and low dose irradiation and heavy metals ions (M±m, in per cent to the control values)

Experimental conditoons	MDA concentration	SOD activity	Ceruloplasmin concentration	AOA index	MMP content	SDH activity	Brain compartment
R	142,23±4,62*	146,95±1,89*	213,23±4,66*	66,42±4,81*	147,06±9,11*	120,21±0,52*	Hemisperes
Cu^{2+}	137,05±9,97*	137,47±2,03*	103,38±5,73	75,50±2,30*	98,28±6,64	121,78±1,74*	
$R+Cu^{2+}$	218,70±5,94*	120,16±2,47*	108,58±3,29	56,23±1,29*	339,92±4,07*	120,03±1,92*	
Co^{2+}	137,22±3,02*	149,61±2,35*	105,65±8,32	76,92±1,33*	108,91±5,13	121,95±0,70*	
$R+Co^{2+}$	163,86±7,12*	138,16±1,38*	44,00±6,67*	60,34±4,62*	308,83±9,13*	118,12±9,93*	
R	120,57±5,26*	115,93±5,25	52,34±2,21*	64,55±5,49*	184,68±7,23*	121,49±0,45*	Brain stem
Cu^{2+}	134,28±5,63*	105,48±3,33	93,14±1,13	78,68±3,77*	237,42±7,23*	123,73±1,19*	
$R+Cu^{2+}$	133,97±3,27*	138,81±4,57*	177,51±1,84*	43,71±1,95*	260,50±9,17*	121,79±1,79*	
Co^{2+}	92,75±4,96	135,04±5,93*	34,29±3,94*	79,98±1,97*	258,97±7,73*	121,04±0,59*	
$R+Co^{2+}$	126,32±4,02*	157,85±6,45*	131,26±1,20*	65,42±4,70*	290,53±6,38*	109,85±3,28	
R	118,80±5,14	119,98±3,78	331,94±5,60*	62,50±1,54*	167,51±4,68*	127,98±0,73*	Cerebellum
Cu^{2+}	113,68±1,71*	111,01±2,69	141,86±6,09*	77,30±3,24*	169,35±6,54*	132,12±2,19*	
$R+Cu^{2+}$	152,99±6,51*	113,84±1,16	54,81±5,59*	55,41±4,80*	328,16±5,21*	120,92±1,95*	
Co^{2+}	102,56±1,71	122,44±3,06*	103,98±8,91	96,28±5,07	149,72±7,21*	129,68±1,22*	
$R+Co^{2+}$	133,33±4,27*	115,26±2,20	125,64±6,86*	64,32±4,05*	319,92±7,81*	122,63±3,41*	

* Significant to the control values