Chapter 2. EXPERIMENTAL RESEARCH

2.1. Introduction

Debatable mode of ionising radiation neuropsychiatric effects remains for more that a century. Some authors deny even the fact of the problem settlement if exposure doses are less than 20–60 Gy. Problem is not solved even at present time: one researchers present decisive data for nervous system radiation damage after doses under 1 Gy and others — not less reasonably insist on the effects absence in case of 2–4 Gy and more. At that objections consist not exactly in just psycho-neurological disorders registration but in ionising radiation role determination in their genesis: «It happens people name the same with different words. Words are different but meaning — the same...» (Say-Senagon, transl. Old-Japanese, X–XI century).

Up to the present time the wide amount of scientific literature is available concerning to radiocerebral effects. There is no ability and need to cover all the sources as there are monographs summarising results in the problem field [Nemenov M.I., 1950; Grigorjev U.G., 1958, 1963; Livshits N.N., 1956, 1961; Lebedinsky A.V., Nahilnitskaya Z.N., 1960; Livanov M.N., 1962; Minayev P.F., 1962; Cleave V., Durward Ch., 1963; Kimeldorf D., Hunt E., 1965; Gilbert H., Kagan A., 1980; Mettler F.A., Moseley R.D., 1985; Davidov B.I., Ushakov I.B., 1987; Davidov B.I. et al., 1991; Gutin P.H. et al., 1991; Romodanov A.P. et al., 1993; Mettler F.A., Upton A.C., 1995 etc.] both with scientific conferences proceedings [«Nervous system reaction on ionising radiation», Chicago, 1960; «Ionising radiation effects on nervous system», Vienna, IAEA, 1961; «Nervous system reaction on ionising radiation», Los-Angeles, 1962; «Ionising radiation impact on nervous system», Leningrad, 1973; «Radiation risk for developing nervous system», Nuremberg, 1985; «Human nervous system alterations under ionising radiation impact», Moscow, 1989; «Actual and prognosed mental health disorders after nuclear disaster in Chernobyl», Kiev, 1995 etc.] study of which we surely recommend.

In the preface for Russian edition of «Ionising radiation impact on nervous system function» monograph by D. Kimeldorf & E. Hunt (1969) A.B. Tsipin wrote: «To the 50th interest towards radiation impact on nervous system problem decreased sharply. Foreign radiobiologists considering nervous system low sensitive to radiation paied nearly no attention to the problem regarding it to be traditionally Russian one». At the same time the most well-known American neuroradiologists D. Kimeldorf & E. Hunt noted that phrase of E.I. Komarov in 2nd International Congress for Radiation Research in 1962 serves the best preface for their monograph: *«Inconceivable that organism* [*and brain*, according to B.I. Davidov, I.B. Ushakov (1987)] *can be simply the passive observer of its own disintegration».*

Nervous system experimental research results under acute and chronic radiation exposure are summarized in this chapter. Studies were conducted after Hiroshima and Nagasaki A-bombing i.e. within «Radioecological Period» of radiation medicine and radiation neuropsychiatry.

2.2. Acute Irradiation Effects

2.2.1. Radiation Neuro- and Psychophysiological Effects

2.2.1.1. Afferentation Systems and Neural System Radiosensitivity Problem

Ionising radiation effect the nervous system functional state and behaviour as the results of both *direct impact* on nervous system and *indirect* one due to the nervous system reactivity towards radiation injury induced in other organism systems. At that nervous reactivity considered by D. Kimeldorf & E. Hunt (1969) may have more high integrative physiological role than direct injury of nervous system from superlethal doses.

Nervous system various parts bioelectrical activity study is the cornerstone in neuro- and psychophysiological research of ionising radiation impact. Neurophysiological effects under radiation are of *phase* character. So the ionising radiation impact on peripheral nerve first induces spike potentials, transmission speed and irritability amplification. In further under continued exposure these effects are changed to the opposing ones with conductivity complete blockade that is mostly expressed in slow transmitting fibers compared to the quickly transmitting ones. Similarly the ionising radiation initially induce central nervous system agitation: electrographic activity evoked potentials arise thresholds decrease, thalamus and spinal reflexes involvement both with brain convulsive trim elevation. On the other hand exposure to high doses results in reflexes and central nervous system activity depression.

Phase nature of the central nervous system response on radiation impact corresponds the *three phases of organism reaction on increasing stimulus* where following phases are selected: 1st one — preventive inhibition; 2nd — stimulation and 3rd — over-limiting inhibition [Simonov P.F., 1962].

Irradiation with doses substantially less than 0.01 Gy can act as *central nervous system irritant* that was confirmed by brain bioelectrical activity alterations registration. Probably these reactions are resulted from neuronal or sensory structures direct irritation.

Alterations that occur in *afferent systems* under ionising radiation impact may occur within any serial stage of sensory information entry: in energy selective transformation and receptor input encoding, in this information

transmitting to the sensory systems and in analysis (decoding) of input on central nervous system various levels [Brickman R., 1962; Kimeldorf D., Hunt E., 1969; Carpenter D. et al., 1978].

According to A.V. Lebedinsky and Z.N. Nahilnitskaya (1960) opinions the *radiophosphene* (light sensations under ionising radiation impact) observation possibility is seems to be indisputable [Lipetz L.E., 1953, 1955]. Phenomenon characteristic for three-dimensional vision were observed under roentgen radiation application on both eyes retinas. Ionising radiation not refracts in eye and not produces eye substances fluorescence; light sensation is risen due to ionising radiation impact on light-sensitive elements of retina that in state of dark adaptation is sensitive to radiation within its whole extent up to edge periphery. According to the data by L.E. Lipetz (1955) one can suppose that phosphene rises under ionising radiation impact on eye as the result of visu purpure molecules irritation i.e. as the result of *photochemical reaction*. At the same time D. Kimeldorf and E. Hunt (1969) contest intentions to explain radiophosphene through retinal rhodopsin (visual purple) fading as that requires doses in million times more high than threshold effects required for irritation rise. Threshold value of roentgen radiation exposure dose for *radiophosphene* rise constitutes only about 0.5 mR under dose rate 1.6–8.7 $mR \cdot sec^{-1}$ according to R. Pape & J. Zakovsky (1954).

K.Motokawa et al. (1956, 1957) and J. Umetsu (1956) used the phosphene phenomenon rising during electric current run through the eye — *electrophosphene* as the test for roentgen radiation impact on human eye study. Japanese researchers demonstrated that exposure to the doses of 10–50 mR resulted in distinct elevation of electric current threshold value required for electrophosphene rise. Authors assumed that registered phenomenon is the result of roentgen rays impact on retina nervous elements.

V. Elenius & E. Sysimetsa (1957) observed electric phenomenon in retina under exposure to roentgen radiation in patients suffering elderly cataract and tuberculous iridocyclitis. According to the author's data the threshold dose for *electroretinogram reaction* rise in human under short-term exposition (flash) constitutes about 0.5 R that nearly in 1,000 times exceeds threshold value required for phosphene effect initiation. At that comparison of electroretinograms received after both roentgen and light stimulation occurred being practically identical.

With direct electrophysiological experiments they revealed that ionising radiation effect on retina evokes there slight *electric potentials* [Grigoryev U.G., 1963]. R.I.Pogosyan et al. (1961) demonstrated that retina biopotentials grow with their latent period decrease along with γ-irradiation intensity elevation. Threshold dose rate at that was 0.001 $R \cdot sec^{-1}$. Authors also noticed that adapted to darkness retina electric reaction on γ-rays from ^{60}Co had high similarity with electroretinogram.

D. Michel et al. (1980) received retinogram after roentgen radiation application on rat retina cell culture in dark adaptation conditions. *Electroretinogram after irradiation* with X-rays was identical to that after light application. Electroretinogram proportionality to logarithm of retina exposure dose value was demonstrated [Cited Grigoryev A.U., 1991].

B.N. Savchenko (1988) explained the *irritation* rise possibility *in retina* after ionising radiation direct impact on membranes with quasi-crystal structure where photoconductivity, hole-type conductivity electron migration is possible, besides that he referred to retina semi-conducting properties.

Retina functional properties alterations were observed under high exposure dose values. Ts.M. Avakyn (1958) marked distinct alterations in *electroretinogram* under frog isolated eye exposure to 10–60 R doses. Majority of works demonstrate that radiation injuries of visual tract and visual analyser cortical projections are possible under doses exceeding 400–500 R [Lebedinsky A.V., Nahilnitskaya Z.N., 1960; Kimeldorf D., Hunt E., 1969].

Mice express the highest sensitivity concerning *radiation cataract* genesis. According to K.W. Christenberry & I. Furth (1951) the lens turbidity can be observed in mice after roentgen irradiation with dose of only 16 - 32 R. At that threshold doses for cataract genesis in monkey (according to D.J. Kimeldorf (1962)) are substantially higher: 75 *rep* for quick neutrons, 500 *rep* for γ-quanta (^{60}Co) and 825 *rep* for thermal neutrons. At that neutrons in 0.5 Gy dose resulted in substantial number of lens turbidity cases that were expressed enough to obstruct the light go through and, obviously for visual perception. N. Fujii et al. (1986) noted the D-aspartic acid content elevation in lens that was followed with *lens pomutnenije* 1- 6 months after head exposure to 1.5 Gy. D-aspartat content is considered as the age*ing processes* indicator. Dose of 3 - 5 Gy is assumed as minimal *cataractogeneous dose* (for human) [Moscalev U.I., 1991]. At the same time the IAEA experts (1992) presented data concerning threshold dose for radiation cataract in human being only 0.5 Sv after single exposure.

Radiation pathology of *auditory organ* is described in cases of irradiation doses exceeding 400– 500 R (as a rule 1,000–6,000 R). At the same time the attempts of acoustic sensitivity radiogenic improvement were applied that resulted in somewhat positive results under 500 R doses of irradiation [Hendricks J., Smith J.C.]. But O. Novotny (1952) observed *cochlea microphone potential rise auditory threshold* elevation under doses over 1,000 R that reflected conductivity decrease in cochlea. M.Ya. Kozlov (1958) marked signs of *conductivity lost in cochlea* in guinea pigs under total irradiation doses exceeding 350 R. D. Kimeldorf and E. Hunt (1969) insisted on radiosensitivity recognition of receptive villiar cells of *auditory organ*.

Vestibular analyser function disorders after irradiation were observed in its peripheral and central parts. J. Ross, S. Leavitt, E. Holst, C. Clemente (1954) described the *nistagmus* rise in monkey after head exposure to 3,000 R. H.Quaster (1957) revealed several *labyrinth phenomenons* — rotation movements, orientation disorders under 7,500 R dose of ionising radiation impact on head in hamster. Z.A. Yanson (1957, 1958, 1961) demonstrated the sharp increase of *labyrinth reflex on extremities muscles* just after the total irradiation in rabbit with dose of 1,000 R. Tonic labyrinth reflexes alterations were confirmed in decerebrated animals too. Analysing these experiments results M.N. Livanov (1962) came to conclusion that after total radiation exposure in doses of 800–1,000 R the irritability

elevation with cortex, medullar and diencephalic centres irritation is observed. Afferentation coming in from periphery increase he presented as one of that phenomenon reasons.

Ionising radiation both in local and general application result in distinct alterations of *somatosensoric afferent system* functional state. N.A. Rokotova & I.M. Gorbunova (1957) conducted experiments that demonstrated the agitating effect of β-emitter ^{32}P on *skin and mucosal receptors*. Researchers observed the elevation of locomotive and secretory food conditioned reflexes after plane applicator containing ^{32}P impact on the skin with resulting dose of 2 R. Then some depression was observed with further reflexes normalisation. Directly after roentgen radiation local impact on rabbit footstep with dose of 500 R the periodical rise of *«spontaneous» electrical activity in skin nerves* was observed both with EEG reaction amplification on tactile irritation [Livanov M.N., Delitsyna N.S., 1956; Delitsyna N.S., 1969].

Ya.I. Geinisman & E.A. Zyrmunskaya (1952) conducted the experimental research for roentgen radiation with 4,500 R dose impact on *skin receptors* in frog. Authors demonstrated that in several minutes after the impact the skin nerve reactions in response on skin irritation are marked.

Pain reactions threshold elevation after irradiation was demonstrated in experiments. In guinea pigs this phenomenon was revealed also in total irradiation with dose of 10,000 R. Dose of 5,000 R induced no such phenomenon [Andrews H.L., 1957].

Indications concerning *interoceptive analyser* or *somatic-visceral afferent system* disorders under irradiation are present in literature. This system is imparted the decisive importance in the whole organism reaction on ionising radiation impact. Sharp alterations of interoceptive reflexes from vascular reflexogenic zones were revealed: from *sinocarotid zone* (I.A. Pejmer, 1952; A.S. Mozjuhin, 1953, 1954, 1956; R.M. Lubimova, 1955), *lymphatic nodes vessels and tissue* (U.M. Zaretskaya, 1956), *urinary bladder mechanoreceptors and intestinum chemoreceptors* (V.A. Chernichenko, 1955), *rectum* (N.S. Delitsyna, 1955; T.V. Popova, 1956), *gastrointestinal tract* (N.A. Lapshyn, 1955; T.V. Popova, 1956), *gastrointestinal tract baro- and thermal receptors* (T.K. Jarkjan, 1956), *bone marrow chemoreceptors* (I.A. Shevchenko, S.I. Erenburg, 1954). Interoceptive reflexes alterations most characteristic feature after irradiation is the phase pattern of their course [Lebedinsky A.V., Nahilnitskaya Z.N., 1960; Kimeldorf D., Hunt E., 1969].

Consequently wide enough amount of scientific works is present making of doubt statement of those radiation «invisibility» or «intactuality» contrary to the wide-spread opinion concerning ionising radiation detection possibility with sensory organs. *Visual and somatosensory* (including the *somatovisceral*) *afferent systems* are of the supreme radiosensitivity. These systems have also the leading informational importance [Shmidt R., 1984].

Kimeldorf D & Hunt E. (1969) noted that ionising radiation is the peculiar factor regarding nervous system organisation. Besides the ionising radiation impact on photochemical processes there are no any other data concerning adequate or even somewhat effective irritant for any receptive systems. Pathways of radiation stimulation remain nonrevealed. Hypotheses were pronounced about ionising radiation direct effect on energy-sensitive *synaptic processes* and about *radiation receptors existence* with pointing out to olfactory and taste ones, both with chemical sensitivity receptors in brain stem. *Photosensitive systems* participation possibility is considered in ionising radiation irritating effects realisation.

A.B. Tsipin (1955), A.B. Tsipin & U.G. Grigorjev (1960) formulated the statement that ionising radiation can lead to *irritability elevation of receptors themselves to adequate irritant*. As the result of such effect on receptors the adequate irritants that were of sub-threshold level before exposure can become the over-threshold ones and induce the analyser request reaction. Besides that the authors demonstrated that average time of nervous system reaction rise towards irradiation depending on radiation dose rate is described with typical for electric irritant curve by Gorveg—Vaice.

Within studies conducted in laboratory of M.N. Livanov the well-known *Law of Webber—Fechner*, describing sensation intensity dependence upon irritant power, was further developed regarding ionising radiation. Rabbits were exposed to the total γ-irradiation with dose rate 1.53 $Gy \cdot min^{-1}$. Continuous recording of brain bioelectrical activity was conducted within all the time. After the 7 minutes of radiation application the dose rate was elevated in one moment up to 4.59 $Gy \cdot min^{-1}$, i.e. for 3.06 $Gy \cdot min^{-1}$. Brain cortex biopotentials distinct alterations took place in animals at the moment of additional radiation exposure initiation [Grigorjev A.U., 1991].

Single general roentgen irradiation of rabbits with dose of 10 R induced the hip leg *flexor reflexes* time alterations [Kudritsky U.K., 1955; Fedorova I.V., 1958]. *Peripheral nerves* function and *segment reflexes* alterations were observed already under 1–10 mGy doses application. *Slow conducting fibers* radiosensitivity prevalence over the quick conducting ones was noticed. Afferent nerves and spinal cord tracts are considered as more radiosensitive than locomotive system elements. Radiogenic alterations on *receptors, neuromuscular contacts and spinal cord structure* levels were surveyed. Worth to mark that in the last cases both with peripheral nerves irradiation, the radiation effects were observed in most of studies under the very high radiation doses impact i.e. exceeding dozens and hundred of Grays [Livshits N.N., 1961; Livanov M.N., 1962; Kimeldorf D., Hunt E., 1969].

High radiosensitivity of *brain stem centres* was fixed. So the pituitary-intermediate zone exposure to roentgen radiation in human with dose of only 10 R induced the hand capillary permeability elevation and skin electroresistance phase alterations. Those reactions were explained through the *autonomous nervous system* high radiosensitivity to radiation [Pape R., Branter K., Jasky K., 1953; Hecht H., Neumayr A., Thurnher B., 1953].

A. Zuppinger (1953) underlined the *vegetative innervation* in reaction on irradiation, he noticed the effectiveness of preparations application suppressing *sympathetic and parasympathetic parts of autonomous nervous system* for suppression of organism general reaction on irradiation. Z.N. Nahilnitskaya (1957) observed the *postganglionic nervous fibers* functional state alterations after total exposure to 600 R dose.

A.V. Lebedinsky (1962) paid particular attention to the *autonomous nervous system* sensitivity to ionising radiation impact underlining *hypothalamus* disorders importance. He formulated hypothesis concerning the *sympathetic structures* extreme sensitivity to ionising radiation with synaptic membranes stable depolarisation rise and acetylcholinestherase system alteration.

G.Z. Abdullin (1962) reviewed the comparative radiosensitivity of brain different parts regarding their function alterations and concluded that *mesencephalic structures* functions are altered more rapidly and easily under ionising radiation impact. *Autonomous nervous system conditioned reflexes* were altered more sharply also under lower radiation doses compared to locomotive conditioned reflexes. Author marked the predominant injury of *brain subcortical-stem structures* (hypothalamus, medulla) functions by ionising radiation.

Hypothalamus irritability elevation through biopotentials frequency increase, polyrhythmia, acute waves and spike oscillations was revealed by N.P. Smirnova (1958, 1969) under cat total exposure to 50 R. Hypothalamus functional state alteration was of important role in *radiation vegetative-vascular dystonia* genesis as syndrome separated by the author.

T.A. Korolkova (1958) demonstrated that roentgen irradiation with doses of 5, 10, 25 and 50 R in single total exposure intensifies the *cortex irritation* processes. Stimulating effect of ionising radiation with 25 R dose was presented already in the day of exposure and with doses of 5 and 10 R — one day later. In study of human exposed to ionising radiation with dose values close enough to the maximally permissible ones the distinct alterations of conditioned reflexes were revealed that indicated mobility and equilibrium alterations of the main cortex processes [Livanov M.N., 1962].

Thus irradiation doses of 0.05, 1, 2, 5 and 10 R in single external irradiation are already enough to consider possible nervous system trace functional disorders registration. Presented values of irradiation doses cannot be surely enough considered as the threshold ones for nervous system various parts but there are all background points to state that the revealed disorders *in nervous system are initial ones* regarding to vascular and other alterations induced by ionising radiation impact. One cannot exclude that any impact of these radiation induce altering effect on biosubstrates that in its turn leads to opinion of threshold dose value absence within initial reactions on exposure. Thus one can conclude that even if the natural radiation background constantly makes damage to the separate elements of biosubstrate, the reparatory processes enable organism to overcome the effects. Pathology process genesis occurs only from the moment when injuring impact value starts to exceed reparation reparation capacities and threshold dependencies can be revealed here. At that the ionising radiation threshold sensitivity and injuring effects thresholds can divergence i.e. the *radiosensitivity and radioaffectability* concepts differentiation is required [Livanov M.N., 1962].

P.D. Horizontov (1964) wrote: *«...one not ought to confuse the radiosensitivity with radioaffectability concepts in radiobiology...»*. A.G. Sverdlov (1984) considered that combination of classical and newest research methods of just neurons and their ensembles is the background of success in the field of central nervous system radioresistance and radioaffectability studies. S.P. Yarmonenko is categorically against those concepts separation. At the same time according to opinion of A.U. Grigorjev (1991) the determined property of nervous system to response on ionising radiation impact with physiological reaction enables to approach differentially towards the ideas of radiosensitivity and radioaffectability where dose range differences can run up to size of 5–6 orders. At that the *individual* radiosensitivity and radioaffectability taking into account is required as both of them express dependence on organism initial functional state and its non-specific reactivity.

2.2.1.2. Brain Spontaneous and Evoked Bioelectric Activity

Summarising the results of more than ten-years-long research of ionising radiation impact on nervous system M.N. Livanov (1962) concluded that disorders in brain cortex under irradiation with substantial doses (500–1,000 R) are of *phase character*. Those disorders constitute cortex functional state initial elevation followed by deep and long-term depression. These shifts in brain cortex functional state are widely reflected in all viscera and tissues of exposed organism. Under doses impact of 1,000 R the *brain cortex and stem epileptic activity* was registered. Brain cortex functional state alterations dependence upon effects from periphery realised through *brain non-specific activating system* was demonstrated in experiments with single-sided disintegration of *mesencephalon reticular formation*. The *autonomous nervous system* and numerous *humoral mechanisms* are undoubtedly involved in process here. Ionising radiation impact is mainly focused on *neural processes weakening* with agitating weakness forming.

U.G. Grigorjev (1963) applied *EEG directly during the irradiation* as the central nervous system sensitivity indicator to ionising radiation, i.e. he registered brain early reactions on irradiation. This for the first time presented availability of threshold dose identification concerning nervous system functional sensitivity estimation under ionising radiation direct impact. Integral dose that resulted in brain biopotentials alterations with dose rate of 0.013 $R \cdot sec^{-1}$ constituted 0.05 R that was in 20–50 times less than doses resulting in stable disorders. U.G. Grigorjev (1963) concluded that biological effects of ionising radiation in its nature can be considered as non-threshold ones, but meaning its manifestation forms on the more high biological level where compensation and reparation phenomena are observed, those effects are modified into threshold response reactions. *Effect dependence on dose value* is best of all described with *S-type curve*.

Other authors described the EEG alterations only under the rather more high doses application. M. Betto (1970) considered that *minimal dose* resulting in EEG substantial alterations constitutes 4.5 Gy that is considerably less than that for morphological patterns — 7.6 Gy. High radiation doses induce EEG amplitude increase and waves

frequency decrease, and those alterations are considered being related mainly to the *synaptic irritability post-radiation elevation*. *Spikes, epileptiform discharges and EEG rhythms deceleration* were observed in monkey after exposure to 4,500–6,000 R. EEG oscillations *deceleration* combined with brain *serotonin* content decrease and *brain biopotentials depression* down to «bioelectrical silence» were revealed in rat after head irradiation with doses of 9,000–10,000 R [Andrews H.L. et al., 1953; Bailey O.T. et al., 1959; Ruebe W., 1959; Speck L.B., 1962; Nair V. et al., 1963; Sato M., 1978; Davidov B.I. et al., 1991].

Spike oscillations in hippocampus were observed without any clinical signs of radiation sickness or neurological damage under irradiation with doses of 200 and 400 R [Gangloff H., 1962; Haley T., 1962]. Besides that T. Haley (1962) marked that exposure to 400 R induced direct increase of *quick low-voltage* biopotential oscillations and EEG *slow* rhythmic quantity decrease. V.A. Hasabova (1969) revealed increase of expression and amplitude of *bioelectrical activity high frequency range* in locomotive, frontal, occipital, orbital and temporal cortex zones, thalamus, hippocampus and striopallidum nuclei just in first hours after exposure to 60, 100 and 400 R. At that early activation degree not depended on irradiation dose.

B.I. Davydov & I.B. Ushakov (1987) consider that *first phase — activation phase* — is hardly specific only for the radiation factor. U.G. Grigorjev (1982) qualified it as cortex electric activity temporary desynchronisation phenomenon arising following the irradiation source switching on («on—effect»). Irradiation termination also leads to desynchronisation («off—effect»). EEG desynchronisation followed by β-activity amplification as the result of up-going activating effect of reticular formation is considered the most universal reaction rising under various environmental factors impact. *Slowed* (θ- and δ-activity) and *irregular* waves both with periodical *paroxysmal waves and convulsive peak discharges* are characteristic for the *second phase* of bioelectrical activity alterations [Ross J.A.T. et al., 1954].

Studies of Georgian school of radioneurobiologists (K.Sh. Nadareishvili, O.S. Bakradze, 1968; O.S. Bakradze, 1971; K.Sh. Nadareishvili et al., 1972–1978) were concentrated on study of *brain various structures bioelectrical activity directly during irradiation*. Just after irradiation initiation (67–74 $mGy \cdot sec^{-1}$) bioelectrical activity alterations were observed in chiasm, tractus opticus, corpus geniculus lateralis, cortex primary and secondary visual zones, mesencephalon reticular formation, hypothalamus, hippocampus, motoric, somatic-sensory and limbic cortex. At the most extent the disorders were expressed in *bulbus olfactorius, hypothalamus and limbic system*. Rather contradictory results concerning interhemispheric asymmetry were received after *hemilateral irradiation*. Finally the authors came to conclusion that convulsions origin is related to ionising radiation direct impact on nervous cells, their ensembles and neuroglia-neuronal connections. The *evoked potentials* noticeble depression in reticular formation and tractus opticus was present under 90–100 Gy doses application. Further the evoked potentials restoration was observed excluding brain cortex where the respective normalisation was not observed. Authors concluded that the evoked potentials depression is the most early index of bioelectric activity alterations after exposure. Evoked potentials alterations both with convulsive activity were bilateral in experiments with rabbit brain hemilateral irradiation within dose range 80–120 Gy. N.R. Kiknadze (1975) and R.N. Kordzadze et al. (1983) noted the low-frequency rhythms marked alterations in irradiated cats during *the deep slow sleep* stage and less expressed — in *sleep paradox phase* when the high spike discharges were registered.

Thereby in spite of brain bioelectrical activity extremely high radiosensitivity, the enormous dispersion of radiation exposure dose values is marked concerning registration of EEG one or another alterations and EEG patterns interpretation ambiguity. That is why actuality of the *discussion concerning EEG adaptability as brain functional and organic alterations criterion* remains up to date.

Visual evoked potentials amplitude decrease in monkey cortex right visual zone was revealed 24–72 hours after roentgen irradiation with dose of 35 Gy [Caveness W.F., 1968]. T. Minamisawa et al. (1972, 1977) also observed v*isual evoked potentials* gradual reduction in rabbit under irradiation doses of 1–3 Gy once or 3–30 Gy fractionally. At the same time L.D. Diner (1971) observed conversely the positive phase increase of *evoked potentials from light and mechanical irritants* in mesencephalic reticular formation, cortex somatosensory zone and anterior hypothalamus after total roentgen irradiation in cat with dose rate of 1.5 $mGy \cdot sec^{-1}$. T.S. Kafarova (1973) demonstrated the evoked electrical activity of visual analyser structures depending on reticular formation functional state before and after the roentgen irradiation.

A.V. Mtskhvetadze (1972, 1984) demonstrated bioelectrical activity changes as the result of *ionising radiation direct impact* in studies of irritation transmission effect in *sympathetic vegetative ganglions* directly during irradiation. However V.U. Bolshakov and A.G. Sverdlov (1989) presented data about membranes structures high radioresistance providing nervous impulses transmission through the sympathetic ganglion. Authors assumed that possible alterations of synaptic mechanismes function under high radiation doses impact are not determinative in genesis of acute radiation sickness CNS-syndrome.

Evolving the nervous system high radiosensitivity concept S.I. Peimer, A.O. Dudkin and A.G. Sverdlov (1985) revealed *the ionising radiation in doses of 6–8 mGy direct activating impact on endogenous (pacemaker) mechanism of neural impulses generation*. Neural cells reaction character corresponded to that activation of hippocampus which is described in orientation behaviour. S.I. Peimer et al. (1988) marked that the described radiation reactions have characteristic signs of functional responses on irritants that enables their review from general physiological positions. At that authors considered that initially high-frequency neurones (over 4 Hz) and hypothetically containing high amounts of cAMP are more radioresistant.

A.O. Dudkin (1987) observed the spontaneous impulse activity frequency distinct alterations after roentgen irradiation with doses of 6–8 mGy of rat hippocampus section. Conclusion about *so low radiation doses direct effect on*

neurones was made because the replacement of standard incubation medium with calcium-free solution (in such conditions first of all the synaptic transmission is altered as the mediator release requires calcium entry in synapse) reaction on exposure dynamics was not different from that in standard conditions. At that the neurones reaction character corresponded the exact hippocampus activation type that is characteristic for orientation behaviour.

According to opinion of B.I. Davidov & I.B. Ushakov (1987) the held experiments results indicate that bioelectrical activity radiosensitivity is comparable with radiosensitivity of behaviour reactions on irradiation avoidance. B.I. Davidov & I.B. Ushakov (1987) noticed that *bioelectrical and neurochemical activity of hippocampus (paleocortex) — «the heart of limbic system»*, comparator, errors detector, action result acceptor, pragmatic indefinity detector etc. — is supplied now with still more importance in neurophysiological phenomenons explanation after irradiation.

V.B. Dutov, A.G. Sverdlov, A.A. Kuznetsov (1989) consider that experimental and theoretical basis is available that enables to review *the high power impulse ionising radiation under short exposition as physiological irritants, and explain the brain respective functional reactions on radiation as responses on such a irritating impact*. Authors exposed patients heads with impulse roentgen radiation. Tree impulses of 20 nsec duration constituted every whole exposition with dose rate of 1 Gy·sec^{-1} (for all the exposition). Dose rate produced by the single impulse constituted $1.7 \cdot 10^3$ Gy·sec^{-1} and the absorbed dose per 1 exposition — 0.1 mGy. Exposure was conducted in the single separate expositions regimen or with stimulation frequency 3, 10 and 20 Hz. Patients suffering schizophrenia with deficitive (apathetic–abulic) symptomatic and control group of healthy persons were examined. Both with EEG spectrum analysis the evoked potentials coherent accumulation was held.

Almost no any disorders in mental status were revealed either in EEG spectral analysis or evoked potentials results in healthy persons group. Author assumed that mentally healthy persons are enough resistant to low doses of high-power impulse roentgen radiation but not excluded individual peculiarities.

Emotional experience of patients suffering schizophrenia concerning their expression level and variability correlated rather exactly with psychics injury severity. Most frequently patients felt «sudden blow» or uncertain sensations «inside the head», sometimes — the reminiscences inflow or short-term actualisation of hallucination emotional experience directly at the moment of radiation impact. All the patients felt the anxious relief, some kind of peculiar «lightness in the body», cheerfulness, energies just after the seanse completion. EEG spectrum analysis demonstrated that desynchronisation reaction with 20–40 sec duration was risen directly at the time of exposure. Rhythmic stimulation led to the frequency-dependent effects in resonance spectrum part. Impulse roentgen radiation effect in sleep dynamics was characterised as mild irritant with some peculiarities: the impact was not realised in falling-asleep and slumber phases. Impulse roentgen radiation accelerated the sleep dynamics and redoubled it. Evoked potentials coherent computer accumulation (20 realisations) enabled to separate and describe the potentials polyphase oscillations under bipolar and unipolar registration channel. The most stable and meaningful negative component of evoked potentials had the peak latency 250–270 ms and in authors' opinion probably was the after-discharge analogue as was clearly connected to the dominating α-rhythm. V.B. Dutov, A.G. Sverdlov, A.A. Kuznetsov (1989) concluded that the held research results enable to consider being proven the impulse roentgen radiation stimulating impact presence with effect dependence upon dose rate.

These research works significance can hardly be overrated. In fact authors registered and described *the radiation brain evoked potentials*. Scientific boldness and creative newness of studies is obvious. Further application of methodological approaches presented above can enable to work out the principally new diagnostic methods and firs of all — for mental disorders, and widen substantially the opinions concerning ionising radiation impact on nervous system. Though for the one more time the thesis about neuropsychiatry ability to make substantial contribution in basic neurology and psychiatry progress is proved.

2.2.1.3. Behaviour and Neurological Reactions

Ionising radiation was demonstrated in series of experiments to be the reflex irritant making impact on animal *behaviour* under doses of 30–120 R [Garsia J. et al., 1955–1957; Garsia J., Kimeldorf D., 1957]. According to the opinion of B.I. Davidiv et al. (1989) *the changed biological motivations* are the «nucleus» of all the spectrum of *post-radiation behaviour disorders*.

C. Biagini & M. di Paola (1962), N.N. Livshits (1964) and some other authors again confirmed the concept about the elevated reaction on ionising radiation presence in subjects with *weak or unbalanced nervous system* or suffering *neurosis*.

S.P. Kernek & D.J. Kimeldorf (1975) demonstrated *behaviour and electrophysiological response* on ionising radiation impact in shrimps. The majority of intact shrimps escaped the further exposure through migration to the sheltered section of testing camera under roentgen irradiation with dose rate of 52 R·sec^{-1}. *Escape response* remained also after the «eye pedicels» and «antennas» extirpation. The significant escape activity was observed in case of body partial exposure that demonstrated the radiation-sensitive receptors existence in abdominal part. Electroretinogram induced by β- and roentgen sources was practically identical to that in visual light stimulation. Electrophysiological data indicated that eyes, antennules and probably chemoreceptors of abdominal segment serve the ways of ionising radiation detection.

K.T. Wheeler & K.A. Hardy (1985) observed the *retrograde amnesia* manifestations with effect threshold of 0.001 Gy. Other researchers observing no alterations of electroshock labyrinth transmission under doses exceeding 20 Gy supposed the memory function radioresistance [Kimeldorf D., Hunt E., 1969; Mu Z., Chen H., 1980]. N.G.

Darenskaya et al. (1994) revealed no ionising radiation significant effect in dose of 1 Gy on rat ability to fulfill the *memorised habit* and to *training* after irradiation.

I.O. Saneblidze et al. (1989) concluded that rat total exposure to 3.0–3.5 Gy induces *the conditioned-reflex memory* depression not involving reactions on the unconditioned irritant. At that the higher nervous function expressed deficiency was observed probably connected to the fear reaction sharp amplification.

Along with works demonstrating behaviour and psychophysiological reactions high radiosensitivity, the data are presented concerning *highly-motivated behaviour significant stability* under irradiation doses of 3.5–20 Gy and over despite initial radiation reaction symptoms rise both with several neurological symptoms [Davis R.T., 1965]. Some disorders of *training and memory* processes in monkey were registered under doses exceeding 4 Gy but the study results were controversial. Radiation effects of *attention* volume and general «psychological» or «living space» narrowing were described; general *locomotive activity* is depressed, *object-focused activity* and *«quick-wittedness»* are deteriorated with *locomotive co-ordination* alteration. At that according to G.W. Meier (1962) making difference is possible concerning behaviour disorders as the natural ageing result and ones resulting from *radiation-induced ageing*. They noted that *weakly motivated behaviour* is relatively easily altered by radiation whereas *the more strongly motivated one* is changes rather more slowly and under rather higher doses impact. «Dose—effect» dependence in relation to *«disability—incapacity»* is probably of complex nature and is full of contradictions according to numerous works [Brown W.L., Mc.Dowel A.A., 1962; Wickler J.E., Brown W.L., 1965; Kimeldorf D., Hunt E., 1969; Davidov B.I., Ushakov I.B., 1987; Davidov B.I. et al., 1991].

Vomiting is the most objective symptom of initial reaction on irradiation. Under total γ-irradiation in monkey vomiting was observed in doses 1.2–1.75 Gy. Radiation vomiting genesis explanations are based upon neurochemical hypotheses with data concerning endorphins content elevation, brain cholinergic and dopaminergic systems alterations. «Dose—effect» dependence with *vomiting* criterion under high and over-high doses is substantially complicated as then at doses of 20–30 Gy the «saturation» phenomenon of «vomiting dose—effect» is observed [Davidov B.I., Ushakov I.B., 1987].

M.O. Boyle (1976) reported about male rats *aggressiveness depression* after irradiation with dose of 0.96 Gy. B.I. Davidov & I.B. Ushakov (1987) noted *tranquilizing effect* of head irradiation in cat to 50 Gy dose that they connected to the γ-radiation direct impact on limbic system structures both with indirect depressive effect of other brain structures. K.Sh. Nadarejshvili et al. (1989) observed the *spontaneous aggressiveness* lost in rat after total roentgen irradiation with doses of 1.75–3.5 Gy explaining that with sharp alterations in serotonergic system.

Under massive irradiation doses (100–200 Gy) the trembling, convulsions, opisthotonus, ataxia, spreading out, astasia, extremities rigidity, dysmetria, balancing disorders, nystagmus, side position were observed. Radiocerebral patterns obvious similarity with *Parkinson's disease* was noticed. Data concerning post-radiation *Parkinson-type states* [Atadjanov M., 1982] and *lateral hypothalamus syndrome* are presented [Levitt D.R., Teitelbaum P., 1975]. G.A. Mickey & H. Teitelbaum (1978) observed the lateral hypothalamus injury effects — *lethargy, akinesia and various types motivated behaviour deterioration* in rat after exposure to electrons with 100 Gy dose.

Locomotive activity in rat decreased already after total irradiation with doses of 2 Gy [Szwaja S., 1978]. G.A. Mickey et al. (1983) under exposure dose of 15 Gy marked during first hours the *hyperactivity* phase analogous to activity after morphine injection in mice. Preliminary electroshock impact not induced the post-radiation hyperactivity. Authors concluded that hyperactivity was stipulated by *endorphins and enkephalins radiation release* that was confirmed by hyperactivation effect elimination with Naloxone and cross-adaptation with stress also releasing *endogenous opiates*.

Locomotive disorders are classifies as the central nervous system early functional disorders under ionising radiation high doses impact on organism. The γ-irradiation in absolutely lethal dose leads to alterations of behaviour reactions controlled by *brain dopaminergic structures*. Probably dopamine unbalance in striopallidum and nigrostriatum systems is the background for such disorders as that is observed in case of parkinsonism and hyperkinetic states [Mazuric V.K. et al. 1989].

B.M. Rabin et al. (1994) published the report concerning *behaviour reactions as the test—effects in radiation injury*. Irradiation with ^{56}Fe nuclei with 0.1 Gy dose decreases the taste disgust induced by 3 $mg \cdot kg^{-1}$ amphetamine intra-peritoneal injection that indicated the *dopaminergic system* integrity alteration. According to the authors opinion these data indicate the behaviour reactions alterations possibility during space flights.

R.B. Wallace et al. (1981) observed non-competitiveness of male rats in so-called *dominant situations* compared to the non-irradiated animals after roentgen irradiation with 2 Gy dose of hippocampal zone. At that granular cell content was for 70% decreased in hippocampus after exposure. But the exposed males dominated over the control group animals in *competition for females*. B.I. Davidov & I.B. Ushakov (1987) observed confidential shifts in *animal males sexual behaviour* only after head irradiation with 100 Gy dose. At the same time in the last research works [Miyachi Y., Yamada T., 1994] revealed that distinct *depression of sexual behavior* is observed in mice after total exposure to roentgen radiation with doses of 50—150 mGy. But higher doses (0.25–0.35 Gy) not induced such the effect. Head irradiation also induced such reactions confirming brain substantial role in this phenomenon realisation. Authors demonstrated that sexual behaviour depression was observed in stressed mice who lived in the long-term social isolation whereas such reactions were absent in the non-stressed animals. Japanese researchers underlined that in spite of that nervous system in adults is considered as the extremely resistant one, the presented results clearly demonstrate fact of *brain extremely high radiosensitivity regarding psychophysiological changes*.

2.2.2. Radiation-induced Neuromorphological and Neurochemical Disorders

Histochemical analysis results demonstrated the nucleoproteids isoelectric points shift to the acid side and afferent neurons and big hemispheres cortex neurones mitochondria and tigroid substance distinct damage under total irradiation with doses of 25–100 R. *Diencephalic zone* has the highest reactivity regarding the ionising radiation. Mammalian exposure to LD_{50}—LD_{75} stipulated immediate reactive alterations of nervous system *mitochondria* [Shabadash A.L., 1957, 1964]. Total single irradiation in dose of 50 R induced the following *morphological alterations*: cloudy swelling phenomenons in cortex cells, swelling combination with peripheral tigrolysis and cell vacuolisation in diencephalic, mesencephalic and medullar nuclei. Integral irradiation with 150 R dose led to the stable morphological alterations and with 250 Gy — to destructive ones that confirmed the biosubstrates ability to cumulate the ionising radiation relatively low doses effects [Alexandrovskaya M.M., 1957].

A.V. Lebedinsky & Z.N. Nahilnitskaya (1960) concluded that the dose of 50 R is to be considered as the «red line» for nervous system radiation damage genesis taking into account those disorders reversibility. Under irradiation with doses 50 R and over the phenomena of reflex irritation were observed on the disordered synaptic transmission, altered neurones trophic and intercentral relations background. Researchers reviewing the debatable question about *vascular disorders* role in brain tissue radiation reaction origin substantiated opinion concerning *nervous tissue radiation alterations initial character* and their certain independence from local circulation disorders.

Vascular factor in opinion of A.V. Lebedinsky & Z.N. Nahilnitsky (1960) has the pathogenic role in case of doses 300 R and over with its role elevation proportionally to the irradiation dose. At the same time authors not denied the vascular factor role for irradiation consequences in doses when they arise, especially concerning the disorders aggravation. At that some researchers pay particular attention to the vascular pathology role in nervous system radiation damage pathogenesis underlining vascular endothelium high radiosensitivity [Vorobjov E.I., Stepanov G.P., 1985; Moscalev U.I., Streltsov V.N., 1987; Torubarov F.S., 1991; Gutin P.H. et al., 1991 etc.].

B.I. Davidiv et al. (1987) observed the majority of alterations in *brain cortex* after dog irradiation with dose of 5 Gy. The highest polymorphism was surveyed in *sensomotoric cortex* where up to 24% of cells had reactive alterations and only 12% — the structural ones.

A.J. van der Kogel (1986, 1991) considers that there are two main ways of central nervous system radiation damage pathogenesis: one of them is characterised with *neuroglial cells progressing death* and another one — with *vascular alterations*. Irradiation with doses of 30–40 Gy induced the brain white substance necrosis and vascular alterations in thalamic zone. However in animals died after exposure to 20 Gy only the vascular disorders were revealed without white substance necrosis [Hopewell J.W., Wright E.A., 1970].

Death of oligodendrocytes both with *infarct and swelling* consequences are the white substance massive necrosis genesis explanation. Infarct and swelling underline the *vascular disorders* role in central nervous system remote radiation effects pathologic basis. *Demyelination and white substance necrosis* were observed only after iradiation with doses over 22.5 Gy and not earlier that 9 months after radiation impact. The most early and expressed alterations were revealed in blood vessels with intimate connection to astrocytes increase. Finally authors substantiated conception of *«vascular-neuroglial union in tissue damage»* under ionising radiation impact. The *limbic zone, corpus callosum and capsula interna* are most subject to the injury [Blakemore W.F., Palmer A.C., 1982; Calvo W. et al., 1988].

Blood-brain barrier damage under ionising radiation impact in rat with doses less than 20 Gy was not observed even 18 months after the exposure. However *the slowly progressing atrophy* genesis was noticed both in dog and human that was connected to oligodendroneuroglia chronic injury. *Blood-brain barrier* damage was observed after 20–60 Gy application on the brain. Authors concluded that after irradiation with doses exceeding 20 Gy the vascular injure rise is the trigging mechanism of further necrosis genesis [Remler M.P. et al., 1986; Fike J.R. et al., 1988; Asai A. et al., 1989; Bernstein M. et al., 1990].

Spinal cord damage after ionising radiation impact also was explained with vascular etiology of radiation necrosis. *Ataxia* was observed in some cases after exposure to 15, 20 and 30 Gy. Vascular alterations with fibrinoid necrosis and spinal arteries thrombosis were revealed in spinal cord. Spinal cord remote necrosis was studied after irradiation with doses of 29–54 Gy. Myelin, axons and neuroglia damage focuses were first signs of the necrosis [Innes J.R.M., Carsten A., 1961; Asscher A.W., Anson S.G., 1962].

P.A. Stewart et al (1995) after the single irradiation of spinal cord in rat with dose of 25 Gy observed the endothelium cells radiation damage, altering the *blood-spinal cord barrier* and leading to neurological deficiency. Authors concluded that endothelial cells radiation damage is of substantial role in spinal cord white substance necrosis pathogenesis.

Some researchers [Carsten A., Zeman W., 1966; Mastaglia F.L. et al., 1976] put in doubt the decisive role of vascular factor in brain white substance radiation necrosis genesis. Early alterations of myelin were observed after irradiation with doses of 5–10 Gy and they were basic for clinical *Lhermitte syndrome* forming. The named syndrome concerns the diffuse demyelination and is described as somnolence syndrome after brain irradiation.

A.L. Karpovsky (1985) selected the separate disease — *slowly progressing radiation sickness of the central nervous system*, its genesis he observed in experiment after single exposure to γ-radiation in doses of 1–6 Gy with dose rate 0.11 $Gy \cdot day^{-1}$ [Cited Moscalov U.I., 1991]. According to A.J. van der Kogel (1991) the so-called *central nervous system late delayed damage* can rise some time later (more than one year, as a rule) after relatively not high radiation doses

impact. After the early acute necrotic phase the chronic progressing damage can continue in genesis with three more or less independent mechanisms:

1. *Small necrotic focuses of white substance* with various degree of *mineralization.*

2. *Vascular reaction* presented with telangiectasis, capillary proliferation, vascular wall thinning, perivascular swelling, thrombosis, petechial hemorrhages, capillary and small venules dilatation. Complex *of vascular damage with endothelial and plain-muscular cells alterations* becomes of particular importance.

3. *Neuroglia atrophy* characterized with nervous tissue generalized atrophy probably induced by neuroglial cells exhaustion without distinct signs of vascular damage or tissue necrosis.

Neuroglia cells probably are the brain parenchyma main target of ionising radiation impact, as according to some authors they are more radiosensitive than neurons and their quantity is for one order higher than neurones [Van der Kogel A.J., 1986, 1991; Guskova A.K., Shakirova I.N., 1989].

Atrophic process rise possibility is marked after irradiation with relatively low doses and some time later. Progressing atrophy can be connected to the brain primary demyelination. *Lhermitte syndrome both with radiation myelopathy and leucoencephalopathy* are the clinical equivalents of those demyelination damages. *«Dose—effect»* dependence is described on the basis of linear-quadratic model with assumption of irradiation fractions with doses less than 2 Gy being *tolerant* for central nervous system. On the background of the traditional opinion of the nervous system *redioresistance*, the following tolerant dose values (integral) are adopted in the medical radiology field: 50 Gy on brain, 30 Gy on medulla, 30 - 35 Gy on spinal cord, 5 Gy on eye lens in case of daily exposure 5 times a week with dose not exceeding 2 Gy [Van der Kogel A.J., 1986, 1991; Fike J.R. et al., 1988; Asai A. et al., 1989].

Radiation damage of the central nervous system in space flights requires separate concern. J.W. Hopewell (1994) analysed brain damage possible acute and remote syndromes spectrum induced by ionising radiation and concluded that not all of them can be related to ionising radiation direct impact during space flight. Initial and gradual endothelial cells lost as the result of reproductive death can lead to capillary permeability elevation and swelling with further intracranial pressure increase. Author underlined that more low doses and probably very low doses can lead to *the central nervous system remote generalised atrophy* that can be extremely important for space flights.

Undoubtedly the vascular disorders inducing nervous system secondary damage are of significant importance in cerebral post-radiation pathology pathogenesis. Vascular endothelium high radiosensitivity is well-known [Vorobjov E.I., Stepanov G.P., 1985]. However from our opinion the role of hemodynamics disorders stipulated by initial radiation *alterations of vascular regulation centres* is to be taken into account concerning nervous system remote radiation damage genesis [Nadarejshvili K.Sh., 1966; Danijarov S.B., 1971; Bruner A., 1977; Mickey G.A., Teitelbaum H., 1978 etc.]. G.N.Krizanovsky (1980, 1987) first formulated definition of the so-called *nervous regulation diseases* for those pathology forms that are stipulated by the primary damage of not the target organ but its nervous regulation apparatus.

A.K. Guskova & I.N. Shakirova (1989) devote particular attention to the *immune disorders* role in radiation damage genesis [Chehonin V.P. et al., 1969 etc.] besides the described above alternative versions of nervous system radiation injury pathogenesis i.e. direct and indirect ones — through the vascular disorders. For the first time radiation injury *immune-pathologic conception* was presented by P. Lampert, M. Tom, M. Rider (1959) [Cited Guskova A.K., Shakirova I.N., 1989]. Authors proposed *the autoimmune theory* of radiation demyelination and necrosis genesis where the antigen substance was the *myelin shell* initial radiation damage product. K. Zulch (1969) considered that *vascular wall permeability alteration and blood-brain barrier destruction* are primarily phenomenon resulting in the high-molecular serum albumin penetrate white substance and coagulate there. This plasmatic transudate named *«amyloid»* and later — as *«paramiloid»* induces vascular destruction and myelin shell disintegration. Damaged myelin in its turn is the antigen inducing specific brain antibodies production that provoke myelin further destruction i.e. the *autoimmune disease* rise.

Summarising the research works results concerning autoimmune hypothesis of nervous system radiation damage genesis A.K. Guskova & I.N. Shakirova (1989) formulate three different pathogenesis versions:

- *olygodendromyelin complex* initial damage;
- *vascular wall and blood-brain barrier* initial damage;
- direct autoaggressive effect of autoantibodies on brain substance in *secondary damage focuses* directly not related to irradiated zone.

All these hypotheses are unified with the unanimity of all researchers concerning *myelin destruction* products are antigen substance stimulating autoimmune process genesis.

B.I. Davidov & I.B. Ushakov (1987), B.I. Davidov et al. (1991) considered the *brain hydration-electrolyte profile* and *blood-brain* permeability alterations (that are interconnected concepts) after irradiation as the important point in brain radiation damage genesis. Several works analysis results indicated that water, sodium and potassium content in neurocytes is subject to pronounced shifts in early terms starting with dose of 50 Gy where the big hemispheres hypo- and hyperhydration phases are marked both with neurocytes nuclei volume synchronous alterations. Registered disorders are first of all related to blood-brain barrier altered permeability. Significant amount of works is devoted to the *biomembranes ion permeability, ion balance and ion transport* alterations under irradiation but the presented results are rather contradictory. It makes possible to conclude that studies in this field require continuation with accent on complexity and multi-level approach to the radiobiological effects estimation [Patric. G., 1977; Sato C. et al., 1979; Vodolazskaya N.A. et al., 1989; Dvoretsky A.I. et al., 1990 etc.].

Alterations of *synaptoarchitectonics* are considered of important role in nervous system radiation damage. Synaptic damage under radiation exposure are revealed in central nervous system, neuro-muscular apparatus,

autonomous nervous system ganglions, spinal cord and hippocampus. F.E. D'Amelio et al. (1983) observed the *synaptic contour* length decrease in frontal cortex under total and local irradiation with 0.05 - 5 GY doses. In opinion of A.G.Sverdlov et al. (1986) the synaptic processes alteration threshold dose is 3.5 Gy.

A.V. Mtshvetadze (1972, 1984) on the example of autonomous nervous system demonstrated that ionising radiation induce alterations in *synapses* earlier than in nervous fibers and under lower doses. Nerves and ganglionic cells were found being substantially more radioresistant than integral effect of impulses transmission through the sympathetic nodule. According to the author's data the *acetylcholine receptors* one among firsts react on ionising radiation impact and ion permeability elevation in *subsynaptic membrane* is typical for their function. Ionising radiation direct effect on synapses was demonstrated (indirect and combined effects are not excluded) both with acetylcholine synthesis elevation and acetylcholinestherase activity increase in thalamus.

V.V. Antipov et al. (1987) revealed high reactivity ahead with interneuronal contacts plasticity in rats after head exposure to the doses of 2–100 Gy. In doses of 200–400 Gy the synaptic alterations moved to the first place and were of leading role in radiation sickness cerebral form genesis. Complete *asynapsy* was observed under exposure to the dose of 1,000 Gy and it could be according to the authors' opinion one of the leading causes of the death «under beam».

A.M. Kuzin (1986) substantiated *the structure-metabolic theory* in radiobiology concerning the radiation injuries genesis as chain-like cascade biochemical processes. The leading role in radiation pathology pathogenesis is rendered to the *free-radical processes and peroxidation* [Kuzin A.M., 1962, 1986; Shtreffer K., 1972; Kuzin A.V., Kopylov V.A., 1983; Yarmonenko S.P., 1988; Baraboj V.A. et al., 1991; Joseph J.A., 1992 etc.]. J.A.Joseph (1992) considers that joint mechanism of neurological damage under ionising radiation impact (just as in *ageing* process) is the membranes integrity free-radical damage through lipid peroxidation.

The *radiation stress* conception is worth separate consideration [Baraboj V.A. et al., 1991]. H.Selye (1936, 1947) considered the pituitary-adrenal system activation (with corticotropin secretion elevation, adrenal glands cortex hypertrophy and corticosteroids hypersecretion), thymus-lymphatic system involution, gastric ulcers and hemorrhage rise (*Selye triad*) as the typical for human and animal organism stress-reaction. Stress concept is considered as *«general non-specific neurohumoral reaction rising in organism under conditions threatening with homeostasis alteration»* [Goncharenko E.N., Kudryashov U.B., 1985]. Lipids peroxidation activation is considered as the stress-reaction link. Specification of Selye theory led to sympathetic-adrenomedullar and at less extent — choline-, histamine- and serotonergic systems activation phenomenon inclusion to the stress mechanisms.

The stress-reaction includes three stages.

1. *Anxiety* stage — reserves mobilisation and general resistance short-term decrease.
2. *Elevated stability* stage — homeostatic regulation systems activation.
3. *Exhaustion* stage — resistance decrease.

Under the continuing impact of extreme factor the last terminal stage can be completed with the lethal exit [Horizontov P.D., 1976; Meyerson F.Z. 1981].

According to the up-to-date views the two types of stress-reactions are singled out.

1. *Somatic (biological) stress* — response on direct impact of irritant including the ionising radiation.
2. Chronic and acute *psycho-emotional stress* — stress-reaction without direct contact to the stressor due to the so-called distant reception [Meyerson F.Z., 1981].

The afferent branches of reaction both in somatic and psycho-emotional stress are different, whereas *the central* (hypothalamus, reticular formation) and *efferent* (hypothalamic-sympathetic-adrenomedullar and hypothalamic-pituitary-corticoadrenal systems) branches are similar or analogous. V.A. Baraboj et al (1991) underline that radiation injury both with any other stress type besides the general regularities is different with specific peculiarities too. Stochastic genetic disorders and cells reproductive death are considered related to them. Authors demonstrated the *lipids peroxidation* role in stress mechanism. *Lipid peroxidation* is considered as the initial mediator branch of the stress. Non-specific stressoric form of cell death under exposure can be defined as interphasal one that is not related to the cell genetic mechanism and mitosis damage and mainly stipulated by membrane processes.

The study of *neurochemical processes* risen in nervous system after irradiation is of particular importance in radiocerebral effects mechanisms understanding. L.C. Cherkasova (1964) demonstrated that radiation dose of 40 Gy is the threshold for damage effect induction on *biochemical processes in the central nervous system.* After such dose application author observed the pronounced disorders of protein and carbohydrate-energetic metabolism in central nervous system and other tissues. Deoxyribonucleoprotein metabolism disorders were marked. Author considers that these disorders are the enough background for explanation of the central nervous system alterations under ionising radiation low doses impact.

P.F. Minajev (1962) considered *brain proteins* are radiosensitive whereas A.D. Reva (1974) regarded that *protein* metabolism and related to it *nuclein* one as the main task of radiation biochemistry. *Nucleic acid biosynthesis* radiosensitivuty is well-known. Stimulating effect of irradiation with doses of 0.2 – 1 Gy on brain DNAse and RNAse is determined [Petrusenko G.P., 1982].

N.P. Taranova (1975) revealed sharp inhibition of *gangliosides, cerebrosides, phospholipides and cholesterol synthesis.* Author supposed that the nervous tissue redioresistance is determined (realised) through its ability for gangliosides synthesis enzyme systems quick repair that maintain the neuron membranes required polarisation level and its capacity for phospholipids (antioxidants) and cholesterol qualitative and quantitative constant content preservation. Lipids metabolism and biosynthesis alteration under irradiation was also demonstrated in study of E. Pavlukova & A. Sedlakova (1988).

A.S. Sobolev (1987) analysed the post-radiation disorders of *cyclic nucleotides* cell system. He considered the *cAMP* and *cGMP* system post-radiation dysfunction is stipulated first of all by *adenylate cyclase, guanilate cyclase and phosphodiesterase* activity alterations. Cyclic nucleotides biological and clinical role is that through their system the specific extracellular primary messenger (neurohormone, neurotransmitter) passes commands to the intracellular enzymes. Neuron integrates effects of numerous inhibiting and stimulating chemical messengers just through the cyclic nucleotides system [Fedorov N.A., 1979]. Synaptic transmission alterations mechanisms in brain tissue under encephalopathy of various origin are connected to the cyclic nucleotides concentration disorders. Ca^{2+} — metabolism enzyme systems high radiosensitivity was marked, at that the phosphorylation impact on transport Ca^{2+} — dependent system of synaptosome membranes is changed under irradiation [Davidov B.I., Ushakov I.B., 1987; Davidov B.I. et al., 1991].

N.V. Gamezo et al. (1984) and U.B. Belkin (1984) observed the initial elevation of *cAMP* concentration taking turns with the phase changes in hypothalamus, brain hemispheres and cerebellum after irradiation with doses of 0.2–0.5 Gy. Minimal values of *adenylate cyclase* activity were registered in early terms after irradiation mainly in central nervous system and adrenals.

At present the main concept describing radiation-stipulated disorders of the central nervous system is the so-called *radiation polyneuromediator effect* i.e. *neuromediators* and *neuromodulators* concentration alterations — dopamine, acetylcholine, histamine, serotonin, bradikinine, *neuropeptids,* prostaglandins etc. [Mickley G.A., Teitelbaum H., 1978; Skopec F., 1981; Mickey G.A. et al., 1983; Davidov B.I., Ushakov I.B., 1987; Pastorova B., Arendarcik J., 1989; Davidiv B.I. et al., 1991; Gromov L.A. 1991 etc]. So for example A.V. Lebedinsky & Z.N. Nahilnitskaya (1960) concluded that *phenomenon of parasympathetic innervation* irritation *with cholinergic mediation alteration* dominates under radiation exposure and radiation Parkinson-type pathology is interpreted as *dopamine, acetylcholine and serotonine* unbalance [Atadjanov M., 1982].

Literature data concerning *cholinergic* mediator systems disorders after irradiation are contradictory: data are presented about their both high radiosensitivity and radioresistance under extremely high doses. No complete clearness is present in the field of radiation effects among *monoaminergic* mediator systems including norepinephrine, According to the data of K. Shtreffer (1972) the catecholamines content elevation in mesencephalon was noted whereas respective levels in blood, brain stem and hypothalamus were decreased in monkey after irradiation to the 6–8 Gy. E.Pavusecu et al. (1973) observed the norepinephrine content elevation in brain under 4 Gy dose impact. The early *post-radiation activity* of *dopaminergic systems* was demonstrated in cycle of works by V.I. Legeza et al. (1979, 1982, 1986). *Dopaminic hypothesis* — main neurotransmitter hypothesis of schizophrenia — postulates that dopaminergic systems hyperactivity takes place in *schizophrenia* [Kaplan G.I., Sadok B.J., 1994]. Dopamine content decrease in striapallidum system is considered pathognomonic for Parkinson's disease [Gromov L.A., 1992].

The concept of brain structures mediator processes dyscoordination in low doses impact is substantiated in several studies with those structures key role in hypothalamic functions regulation. *Serotoninergic mechanisms* involving hypothalamus-pituitary-adrenal cortex system and glucocorticod-dependent oxidation-reduction processes into the reaction on irradiation are identified. The 6 months after combined impact of external irradiation with 0.5 Gy and intraperitoneal injection of ^{131}I (6.5 $mCi \cdot kg^{-1}$) in rat with relative thyroid function insufficiency the decrease of the depression processes indices in cortex perietal zone, medium-basal hypothalamus, lateral vestibular nuclei, locus coeruleus and stitch nuclei was noted. These disorders occurred on the background of tricarboxylic acids cycle dehydrogenases activity decrease in brain mitochondria and adrenal cortex glucocorticoid function relative insufficiency [Tajtz M.U. et al., 1988; Gurin V.N. et al., 1989; Dudina T.V. et al., 1989]. According to the modern opinion the mood disorders connection to the heterogeneous alterations in biogenic amines regulation is remarkable [Kaplan G.I., Sadoc B.J., 1994].

Post-radiation disorders links to serum *histamine* content elevation were fixed. Histamine content elevation is considered possible after irradiation in epiphysis, cortex and subcortex structures, especially in hypothalamus where histaminergic neurons are present. Hemodynamics and behaviour effects of radiation exposure are considered connected to the histamine system [Mickey G.A., 1981]. Histamine effect importance was demonstrated towards peripheral vessels, in disseminated intravascular coagulation syndrome genesis both with blood-brain barrier permeability alterations [Doyle T.F., Strike T.A., 1977; Alter W.A. et al., 1983; Cockerham L.G. et al., 1986; Davidiv B.I., Ushakov I.B., 1987].

Prostaglandins (neuromodulators) group E content elevation was revealed in hypothalamus, hypophysis and adrenals after rats exposure to 0.5 Gy that was explained by the hypothalamic-pituitary system activation [Cherkasova L.S., Mitykova T.A., 1984]. According to B.I. Davidov and I.B. Ushakov (1987) both with several other experts the prostaglandins brain tissue content alterations after irradiation are undoubtedly the complex phenomenon.

G.A. Mickey et al. (1983) demonstrated *the endogenous opiates hypersecretion* role in behaviour reactions post-radiation disorders. Authors exposed to 25 Gy of radiation the mice tolerant to morhine. Behaviour reactions alterations in animals tolerant to morphine were rather less expressed than in non-tollerant ones. Besides that the pharmacological blockade of opiate receptors with antagonist *naloxone* just after irradiation with doses of 10–15 Gy prevented radiogenic stereotype locomotive hyperactivity similar to the hyperactivity induced by morphine. C.C. Teskey & M. Kavaliers (1984) demonstrated the *«radiation analgesia»* possibility with opiate receptors involvement. Dose—dependent elevation of the pain threshold was registered in mice in early terms after irradiation with doses of 2.5–15 Gy. Naloxone injection prior to radiation exposure blocked the radiation effect. L.A. Gromov (1992) presented data concerning β-endorphins serum content substantial decrease in patients suffering *affective psychoses* in

depressive phase. At the same time in *schizophrenia* the average value of β-endorphins serum content is higher than in norm an that is why the naloxone application was recommended in patients suffering *schizophrenia* — being used 0.4 mg i.v. it resulted in positive therapeutic effect.

K.S. Rayevsky & V.L. Georgijev (1986) mark that *gamma-aminobutyric acid* (GABA) is the depressive action mediator providing irritation/depression balance in brain. That stipulates GABA role in radiation effects. Besides that the GABA deficiency in corpus striatum, globus pallidum and substantia nigra under Parkinson's disease is well-known. They suppose that GABA activity decrease can be basic for dopaminergic neurons hyperactivity and also be of certain role in schizophrenia [Kaplan G.I., Sedok B.J., 1994]. Some researchers received data concerning GABA content elevation in brain after exposure to doses of 1–6 Gy [Stansky Z., 1966; Savitsky I.V. et al., 1982; Snisar I.A., 1984]. A.S. El-Kashef (1980) observed glutaminic acid, asparaginic acid and GABA content elevation after irradiation with doses of 1 Gy. Dose of 6 Gy application resulted in opposite effects. GABA content elevation occurred along with electrocardiogram depression signs rise and correlated with disorders of the central nervous system reactions on light irritants. A.T. Piculev et al. (1976) demonstrated the GABA-system high radiosensitivity. Glutamate decarboxylase activity depression was marked after irradiation with dose of 0.4 Gy. Adrenergic system role was fixed in radiation effect modification towards GABA metabolism in central nervous system. Reasons of unequal post-radiation shifts in brain GABA metabolism are to me considered as GABA-system interaction disorders with pituitary-adrenal, cholinergic and other neuromediator systems [Davidov B.I., Ushakov I.B., 1987].

So the presented above literature data indicate on the one hand the *polyneurotransmitter radiation effect* presence where the pathognomonic alterations hardly can be identified at present, and on the other hand — the known neural and mental diseases neurochemical similarity is obvious with central nervous system post-radiation disorders. The last point is the biological precondition for hypothesis of several neural and mental diseases genesis elevated risk after irradiation.

New approaches in radiation injuries pathogenesis study — *informational* ones — are worth to mark. U.V. Markov (1989) formulated the hypothesis concerning leading role of *information transmission electric path alteration* in the basis of disorders occurring in organism as the result of radiation impact. From this hypothesis positions author considers that pathogenetic therapy of radiation injuries is not to be the pharmacological but physical one — through electromagnetic and other field application.

2.3. Chronic Irradiation Effects

M.N. Livanov (1962) considered the methodological approaches advances reduce adopted minimal threshold dose values. L.I. Kotlyarevsky (1958, 1959) revealed the conditioned reflexes alterations in dog and rat in series of irradiation seances with doses of 0.05 R after integral dose reaching 3 R. In other words even the so low doses effect can *cumulate*. Effect of ionising radiation low doses comes out being more expressed in case of numerous exposure episodes even through the long time intervals. Three-time irradiation of dog with 10 R in 5 days interval induced the conditioned-reflex activity distinct alterations that normalised only 4 months after the exposure [Yaroslavtseva O.P., 1958].

In more prolonged impact of ionising radiation with doses of 3–15 R (2–3 days interval or daily) the higher nervous function disorders were observed through irritation and depression processes slackening both with cortex working capacity decrease after the short-term cortex irritability rise following integral dose attainment of 130–190 R [Malukova I.V., 1958; Mejzerov E.S., 1958; Yarullin H.H., 1958]. E.N.Klimova (1960) marked the similar alterations in conditioned-reflex activity in dog after 0.02 and 1 $\mu Ci \cdot kg^{-1}$ ^{90}Sr daily consumption with food. V.M. Zakharov (1961) observed transient disorders of higher nervous activity in rat under 0.04–0.4 $\mu Ci \cdot kg^{-1}$ of radioactive sodium injection.

Repeating irradiation (5, 10, 25 and 50 R) applied with one-week interval induced less expressed effects than previous ones. At the same time *effects* cumulating was observed through the brain cortex depression rise after 3 - 4 exposures to radiation: irritability, reactivity, biopotentials lability and amplitude decrease. Cortex state with dose value elevation became more and more unstable: its activity increase periods were changing into depression and more further more rarely stimulation risen with *depression* occurring more and more often [Korolkova T.A., 1958].

U.K. Kudritsky (1955) and I.V. Fedorova (1958) studied the chronic irradiation in low doses impact on *spinal unconditioned reflexes*. Single total roentgen irradiation with 10 R dose resulted in noticeable lability of back extremities flexor reflexes latent periods. In case of rabbit daily exposure to 0.1 R and 0.05 R during 14 days (integral dose 1.5 R or 0.7 R) the reflexes irritability depression occurred. Unconditioned reflexes alterations increased after 32 seances of irradiation (integral dose 3.2 R or 1.6 R).

M.N. Livanov (1962) concluded that the unconditioned-reflex activity can also cumulate under several even very slight impacts of ionising radiation. At that he marked that not only the physiological experiments but morphological data too indicate *the nervous system sensitivity to small doses of ionising radiation*.

U.M. Olenov (1950) after the new-born mice brain exposure to 40, 80 and 120 R doses revealed big hemispheres cortex neural cells disintegration and significant alterations rise in epindymal layer of lateral ventriculums anterior horn. As marked earlier A.L. Shabadash (1957, 1964) observed the nucleoproteids isoelectric points shift to the acid side both with afferent neurons and big hemispheres cortex cells mitochondria and tigroid

substance distinct damage after total irradiation with 25–100 R doses. *Diencephalic* zone was the most radiosensitive there. M.M. Alexandrovskaya (1957) observed *reversible morphological alterations* as cortex cells cloudy swelling, swelling combination with peripheral tigrolysis and cells vacuolisation of mesencephalic, diencephalic nuclei after total single irradiation with dose of 50 R. Already *stable morphological alterations* arose in remote period after thrice-repeated irradiation (integral dose 150 R with weekly intervals) and fivefold repeated exposure resulted in alterations of destructive nature that also confirms the ability of biosubstrates for relatively low radiation doses impact cumulating. At that M.M. Alexandrovskaya (1957) demonstrated that morphological vascular disorders in brain cortex after single total irradiation with dose of 50 R were slight and could not stipulate observed alterations in nervous cells. Thereby the nervous tissue radiation damage was *initial* one in such dose values

Thereby presented data indicate that repeated irradiation results in gradual amplification – cumulating of nervous system disorders. At the same time every separate repeated irradiation results in more slight and less prolonged effect on nervous centres state compared to initial one. Some authors interpret the last facts as *adaptation* to irradiation. But according to opinion of M.N. Livanov that is related not to the adaptation but to the gradual decrease of central nervous system response, that is the consequence of nervous tissue radiation damage cumulating.

M.N. Livanov (1962) underlined that the more high doses from 25 R and over are required for morphological alterations rise — initially reversable and further stable, compared to that required for the functional disorders genesis registered with physiological methods. Author considered that nervous system sensitivity thresholds divergence with damage thresholds is possible. That is why in reality the nervous system radiosensitivity can be even more high than that is indicated by stable functional and morphological alterations available for observation. *Electrophysiological studies* are considered the most suitable ones for those most slight shifts registration.

A.B. Tsipin & U.G. Grirorjev (1960) demonstrated that ratio between dose rate value and exposure time required for brain cortex electrophysiological alterations rise corresponds with square *Gorveg—Vaise hyperbola* characteristic for electric current impact on excitable tissue.

Significant difference in *individual radiosensitivity* presence is demonstrated. Radiosensitivity and radioinjurability are not in constant ratio between each other: animal persons with nervous system low radiosensitivity have lower injurability and vice-versa — animals higher radiosensitivity thresholds die substantially more easily [Livanov M.N., 1962].

Works of numerous researchers are devoted to the *hypothalamus* role in radiation disease pathogenesis [Nemenov M.I., 1950; Alexandrovskaya M.M., 1957; Gvozdikova Z.M., 1959; Lebedinsky A.V., Nahilnitskaya Z.N., 1960; Yanson Z.A., 1961; Smirnova N.P., 1969 etc.]. Hypothalamic regio is one of the most radiosensitive structures in the central nervous system. According to data of U.A. Holodov (1955, 1982) the hypothalamus is capable for light rays and electromagnetic fields perception. It is not possible to exclude that *diencephalon* and hypothalamic region in particular are to considerable extent able to ionising radiation direst reception. *Autonomous nervous system dystonia* under radiation impact corresponds to the hypothalamus functional state disorders: its initial excitability elevation, further lability decrease and phase reactions onset. Radiation modifies intensity and quality of hypothalamic region effects on other parts of central nervous system.

Alterations in brain cortex under ionising radiation impact can be considered as the brain stem *reticular formation* state shifts results due to afferent impulsation and hormonal impact. *Brain functional state* alterations are determined being of phase pattern under radiation impact: first the short-term activation is registered followed by its deep depression [Livanov M.N., 1962].

U.G. Grigorjev et al. (1988) following the advice of A.I. Burnazyan, academicians A.V. Lebedinsky and V.V. Parin conducted the so-called «Chronic experiment» — complex clinical-physiological survey of 246 dogs exposed daily to γ-irradiation for several years with various dose rate. Authors concluded that year integral doses of 0.21 Gy and 0.62 Gy not altered animals general state and resulted in no disorders of haemopoietic and reproductive systems. Exposure to integral doses of 1.2 Gy per year resulted in reversible disorders of the named systems without pronounced alterations in animals general state.

Higher nervous function state was estimated in dogs exposed for 3 years to dose rates 3.4 $mGy \cdot day^{-1}$. Integral year dose constituted 1.25 Gy. Delays in stabilisation of unconsolidated chain locomotive conditioned reflexes, high amount of wrong reactions and conditioned reactions latent period confidential lengthening were marked after integral dose of 0.1 Gy accumulation per one month. However the conditioned reflexes reached the control level and remained so for the following year of exposure after the 4 - 8 month of radiation impact with integral doses of 0.4–0.8 Gy accumulation. Authors observed the conditioned reflexes improvement after 2 Gy dose accumulation, in their opinion — due to the compensatory processes mobilisation. Orientation-search reaction weakening also was marked that they related to the reticular formation radiation activating impact on brain cortex. Locomotive reactions latent periods increase remained for 3 years of exposure that indicated the reflex chains lability and conductivity decrease. Received results reflected the agitation process strength and mobility decrease, depression process inertness rise and these processes co-ordination alteration in chain locomotive reflex after 3-year chronic irradiation.

According to U.G. Grigirjev et al. (1988) the *vestibular analyser* excitability under chronic irradiation in dog not modified for 36 months. Chronic radiation exposure with integral doses of 0.63, 1.86 and 3.75 Gy also not altered the response *vestibulo-somatic reactions*. Thrice-repeated for each year acute irradiation in combination with chronic one was followed with analyser excitability and reactivity undulating modification. At that the maximum disorders were observed in 18–24 months of combined exposure. No confidential alterations were registered 3–5 months after the irradiation.

Organism compensatory capacities significant decrease was marked up to the 6th year of irradiation. That manifested through the *hypothalamus-hypophysis-adrenal* system sclerotic and necrotic degenerative alterations rise and functional capacity decrease. Hypofunctional shifts and exhaustion were observed in thyroid gland and gonads. Physical working capacity decreased for long time period after irradiation termination. Besides that *the remote consequences specific* for radiation impact forming was observed after 3–6 year-long chronic irradiation. *Spermatogenesis and reproductive function* disorders in dogs remained pronounced. Some animals have got *tumours*. *Life duration* shortened. *Proliferation processes* activation in some organs and systems is untypical for age-related disorders. *The initially multiple tumours* rise was the characteristic feature of tumor genesis in exposed animals.

S the result of conducted studies U.G. Grigorjev et al. (1988) substantiated the radiation impact permissible dose values for cosmonauts in long-term space flights: 3.25–4.15 Sv for 2-year and 4.5–5.6 Sv for 3-year flights. At that no any undesirable early radiation symptoms decreasing the crew working capacity are to be observed but only the slight transient concentration deviations of peripheral blood granulocytes and lymphocytes within physiological norm.

Permissible radiation doses for spacemen adopted in the former USSR and being currently in force in Russia are shown in Table 2.1.

Table 2.1

NORMALISED PARAMETERS VALUES FOR SPACE FLIGHTS OF VARIOUS DURATION

Flight duration *T*, months	**Normalised parameter**	
	Radiation risk normed value, 10^{-4}	Maximum permissible equal dose, Sv
1	0.6	0.105
3	1.8	0.215
6	3.6	0.37
12	7.2	0.665
18	10.8	0.935
24	14.4	1.1185
30	18	1.405
36	21.5	1.625

The maximum permissible equal dose for all the professional activity period for cosmonaut i.e all term in cosmonaut team involvement is not to exceed 4 Sv [Gusev N.G. et al., 1990].

Worth to note that permissible doses high values not respond to the possible remote consequences. So N.A. Meshkov et al. (1993) demonstrated in experiments on monkey exposed to ionising radiation during space flight that *stable organic alteration rise in various cerebral structures* is one of the most serious consequences of low and medium radiation doses impact.

Data of biochemical, morphological and physiological studies in dogs within «Chronic experiment» indicate that enough profound alterations gradually accumulate in several systems, especially in the non-renewing or slowly regenerating tissues (first of all — *nervous* one) under the long-term radiation exposure with high dose values (integrally 1.5–2.25 Sv). That indicates the one or another form of *chronic radiation sickness* (CRS) rise. In such cases the hypofunctional and morphological alterations take place in highest nervous regulatory centres and endocrine system. According to U.G. Grigorjev et al. (1988) that leads to the various diseases rise probability elevation including the malignancies and dogs life duration substantial decrease in doses exceeding 3.6–3.8 Sv.

P. Mele et al. (1988) exposed rats to the thrice-time γ-irradiation in 43 days interval with doses of 0.5, 1.5 and 4.5 Gy. Integral dose constituted 6.5 Gy. Authors concluded that *radiogenic disorders of training* depended upon irradiation dose value, were reversible and non-cumulating, and also depended on refresh regimen.

Sympathetic-adrenal system state under chronic and fractionated irradiation was studied by A.B. Uteshev and G.M. Musagalijeva (1989). Authors examined the epinephrine, norepinephrine, dopamine and DOPA concentrations in rat brain, kidneys, liver, thymus, heart and adrenals under exposure to 0.05 Gy two times a week. Integral dose of chronic irradiation 10 - 12 months after constituted 4 Gy. *Epinephrine* content significant increase in brain, kidneys and liver was marked with *norepinephrine* content decrease in thymus and liver under chronic irradiation. Fractionated irradiation led to the more substantial alterations in catecholamines content.

Experimental research results by V.N. Gurin et al. (1989) indicated that mediator processes alterations are observed in brain structures responsible for hypothalamic functions regulation are observed in remote terms after ionising radiation impact in low doses. Those disorders occurred against the backgroung of tricarboxylic acids cycle dehydrogenases activity decrease in *brain neurones mitochondria* and other biochemical shifts.

Data concerning the *mitochondrial genome* as the possible target for radiation is considered interesting. The mitochondria genome structure alterations role is demonstrated at present in genesis of several neurological diseases classified as *mitochondrial cytopathology*. There is the formulated idea that mitochondrial DNA state is the direct index

of both impact degree and remote consequences prognosis because of its high radiosensitivity due to respective reparation system complete absence [Beregovskaya N.N., Savich A.V., 1989; Beregovskaya N.N. et al., 1994].

The Ukraine-Italian Symposium *«Fundamental Aspects of Radiation Medicine and Radiobiology»* took place in Kiev 23–24 September, 1992. Scientific Report *«Ionising Radiation Impact on Human and Monkey Brain Functional State»* by A.I. Nyagu, A.G. Noschenko, G.D. Kuznetsova, N.L. Fedorova and K.N. Loganovsky was presented there. Unfortunately, the Symposium proceedings were not wide enough presented that is why we consider rational to summarise the main content of this work. Comparison of ionising radiation impact on brain functional state in clinic and experiment was the study aim. Clinical part (concerning the Chernobyl NPP accident consequences cleaning up participants including those — acute radiation sickness survivors) will be presented further here in details. Experimental part for ionising radiation impact study *on monkey central nervous system functional state* (operational activity, brain electric activity, lipids metabolism state) was conducted by research team from Moscow: N.L. Fedorova (Scientific-Research Cebter for Space Objects Radiation Security of Russian Federation Ministry of Public Health), G.D. Kuznetsova, P.B. Kazakova, A. Podolets (Institute for Higher Nervous Function and Neurophysiology of Russian Academy of Sciences) and N.B. Holodova (Moscow Scientific-Research Institute for Diagnostics and Surgery of Russian Federation Ministry of Public Health).

Study was held among 8 Macaque Rhesus monkey with body weight 4–5 kg, age 5–6 years. Monkeys were first exposed to radiation with doses 1.5 Gy and than (few months later) repeatedly to 0.75+0.75 Gy. Close and remote consequences of radiation impact were studied concerning *operational activity*. *Brain electric activity mapping* and brain lipid metabolism state study by means of *single-photon emission computer tomography* were conducted in four animals in remote terms after irradiation (1.5–2 years later). Besides that control experiments with the last two methods application were held among intact monkeys. Morphological study of the exposed animals brain was conducted at the end of the work.

Instrumental conditional reflexes with food support were worked out in all animals before the irradiation. Number of correct reactions towards positive and negative irritant both with reactions latent period and intersignal reactions number were indices of operational activity completion quality. This methodology is the monkey operational activity model and is applied for monkey working capacity estimation under extreme conditions.

All the monkeys managed perfectly with the settled task before the irradiation. *Operational activity* was stable. Mild signs of the acute radiation sickness rise were revealed after first exposure seance (1.5 Gy dose) in monkeys: arterial pressure decrease, apathy, locomotive activity lowering. Single episode of vomiting was registered in one animal 2.5 hour after irradiation. Animal state normalised one day after the first exposure. Blood analysis revealed alterations characteristic for this form of radiation sickness.

Number of correct reactions decrease towards positive irritant within range 30–65% and differentiation unbreaking was observed in all involved animals after single irradiation with dose of 1.5 Gy. The most expressed alterations were observed in first 1–3 hours after irradiation during initial radiation reaction presentation. Maximal disorders of reactions on positive signal were observed 3 hour after the exposure. Almost complete restoration of reactions on positive irritant occurred to the 3rd–4th day. One monkey demonstrated the secondary decrease of correct responses number 10–12 days later. In further terms the operating activity reached the normal values. More expressed disorders of operating activity were observed in reactions study towards differentiating signal especially in early terms after irradiation. Number of correct responses on differentiating irritant 1–3 hour after the irradiation not exceeded 35–50% with 80–90% in norm before exposure. Received data indicate that for monkey the irradiation dose value of 1.5 Gy is about the minimal-limit level capable to induce the detectable alterations in complex purposeful behaviour reactions modeling the operating activity.

Four monkeys were repeatedly exposed to the γ-irradiation (twice exposure to 0.75+0.75 Gy with 6 hours interval) on the background of main physiological functions and operating activity complete restoration 10 months after the initial seance. This radiation application both as the first one resulted in the mild form of acute radiation sickness with respective peculiar symptomatic. More pronounced alteration of operating activity compared to the first episode was observed in all the animals. Operating activity was almost altered 3 hours after the secondary radiation impact (0.75+0.75 Gy) and the restoration took place only the next day (1 animal) or lasted for several days with one case of incomplete recovery within one month. If the initial radiation exposure (0.75 Gy) induced relatively mild decrease of operating activity quality, the secondary impact of the same power (0.75 Gy) was followed by collapsible and prolonged enough deterioration of operating activity.

Face muscles convulsive twitching and anterior extremity convulsive movements were noted in two monkeys on the *immobilisation stress* background. In one animal under sharp change of surrounding environment the obsessive penduliform trunk movements appeared. The first and second phenomenon were signs of *brain pathology*.

Monkey brain electric activity study was conducted 1.5 years after the initial radiation exposure on the background of operating activity complete restoration. EEG pathological alterations were revealed in exposed monkeys. Mainly the pathology was presented with various epileptiform discharges that were of definite individual peculiarities in every animal. Both single and rhythmic epileptiform discharges were registered. Epileptiform activity focuses localizsation was unstable changing within one experiment and from one test to another one.

Activity pathological forms were amplified in response to the applied functional tests: hypnoidisation, more strict fixation of the animal in primatological chair («immobilisation stress»), difficult breathing (by accident occurred uncomfortable pose of the animal). Prolonged convulsive attack with high-voltage discharges occurred twice. Discharges generalisation without noticeable convulsions was marked many times. Hypnosis and immobilisation

stress elevated the electrical activity pathological forms probability up to 50% and over, at that the big hemispheres cortex electric activity pathological forms substantial generalisation was registered.

Spectral power of EEG main rhythms in right and left hemispheres was unequal in monkeys within remote terms after irradiation. Asymmetry was revealed both in EEG mapping and spectrum power analysis. Power spectrums with β-range activity substantial domination in right hemisphere were characteristic ones. EEG high asymmetry was noted in α- and β-ranges and to the less extent — in the more low frequencies. Generalised hypersynchronous discharges were surveyed involving left hemisphere major part.

Metabolism mapping with *single-photon computer emission tomography* method was conducted in remote terms after irradiation in four exposed and one intact animal. On the contrary to the normal animal (control) monkeys exposed integrally to the 3 Gy dose the lipid activity distribution in brain was irregular with lipid activity decrease zones registration. Computer analysis enabled to reveal in two monkeys the interhemisphere asymmetry of lipid activity distribution that coincided with interhemisphere data asymmetry received in those animals with EEG.

Monkey brain morphological study was conducted 1.5 years after the irradiation. Hemodynamics disorders through the pronounced perivascular swelling of intermediate and small vessels down to capillary was the dominant disorders presented in all studied cortex zones with prevalence in precentral, postcentral, temporal cortex and hippocampus. To the less extent alterations were present in parietal-occipital zone, cerebellum and brain stem some parts (mainly in the ponts Warolii). Pia mater both with lateral ventricules subepindymal zone loosening and swelling were revealed. In some places the vascular hyalinosis of subarachnoidal and subepindymal zones was present.

Pronounced body swelling of neurones was noted with substantial tigrolysis and diffuse karyocytolysis. The named alterations were most of all expressed in neurones of layer III. Significant alterations were surveyed in cerebellum Purkinje's cells presented through bodies swelling, tigrolysis and lysis in some of them. Neuroglia nuclei proliferation was marked especially in white substance along the nervous fibers direction.

The work demonstrated that *brain hidden pathology* signs are revealed by means of additional study methods (EEG, single-photon emission tomography) in animals in remote period after irradiation on background of satisfactory clinical-physiological state and normal operating activity. Revealed lipid metabolism disorders can be reason of neurones and neuroglia cells membrane alterations that in its turn can be reflected in brain paroxysmal electric activity forming. Regional blood circulation disorders are of important role in brain functions pathological changes. Data received with single-photon emission tomography indicate such monkey brain alteration presence in remote terms after irradiation. That was confirmed by the monkey brain morphological study results. Significant perivascular swelling of intermediate and small vessels, capillary was registered both with expressed hypoxic alterations in neurones that enables to characterise the observed histological pattern as the *dyscirculatory-hypoxic syndrome* of moderate degree.

Though monkey exposure to γ-irradiation with 1.5 Gy dose led to the symptoms complex rise of acute radiation sickness of mild degree and induced operating activity temporary disorders with restoration for one month period. But in remote terms after repeated irradiation (0.75 Gy+0.75 Gy, 3 Gy integrally) the *stable organic alterations* were revealed in brain structures.

Monkey brain organic damage signs revealed in experiment corresponded to the clinical-neurophysiological pattern of the ChNPP accident consequences cleaning up participants who were engaged in works in estrangement zone since 1986–1987 for 3–5 and more years both with persons — acute radiation sickness survivors. That enables us to conclude that the brain organic damage rise is possible after chronic radiation exposure and in acute radiation sickness in remote period.

Metabolism, regional circulation and brain electrogenesis mapping in four monkeys 2 years after the irradiation with 0.7 Gy dose also revealed *brain organic damage* signs [Zubovsky G.A. et al., 1991; Meshkov N.A. et al., 1993].

Complex experimental study results among four monkeys exposed to 1.5 Gy of γ-radiation are presented in the further work of N.B. Holodova et al (1996). Authors revealed brain cortex electrogenesis distinct pathological alterations, regional circulation and lipid metabolism disorders 1.5–2 years after the irradiation.

Results by N.B.Holodova et al. (1996) of the *irradiated monkey brain histological studies* confirming brain organic damage presence occurred being principally important for clinical field. Vessels of all degree including capillary walls permeability pronounced alterations were revealed in *brain tissue* — perivascular swelling with surrounding zones loosening, subepindymal swelling, single small hemorrhages mainly in cortex and subepindymal zone.

Neurones were characterised with dystrophy-destructive alterations. Almost complete tigroid disappearance, in substantial cells part among the cortex was observed both with nuclei contours unclearness, spread karyocytolysis of various degree up to the cells complete disintegration that led to the cortex remarkable diffuse and focal loosening especially of its upper layers II and III (in more profound cortex layers i.e. V and VI such alterations were presented to the less extent). Besides that the groups of wrinkled, hyperchromic or pale elongated cells were revealed in all cortex layers. Described alterations were distinctly registered in all cortex zones with leading *frontal, parietal and temporal zones damage.*

Pyramid cells in *hippocampus* were in karyocytolysis various stages down to the complete death. Other cells of this layer were swelled with disseminated tigroid. Small and especially big cells death was distinctly registered in *nucleus caudatus and nucleus lentiformis*. *Thalamus* cells occurred being less altered. Their bodies moderate swelling, tigroid dissemination and some cells karyocytolysis were noted. *Brain stem* neurons, especially of cranium-brain nerves nuclei were relatively safe with partial hyperchromatosis and wrinkling. Purkinje's cells of *cerebellum* were noticeably altered where the cells focal death with cell layer empty spots forming was observed. The remained cells partial atrophy and lysis were marked. Numerous cells in cerebellum nucleus dentatum were atrophic or in the stage of karyocytolysis.

Pathology of *neuroglia* constituted in astracytes moderate proliferation with their bodies and outgrowth coarsening, especially that of vascular stalks. Dystrophy signs were revealed in *microglia* — bodies and outgrowth coarsening, secondary branching lost, bodies and outgrowth swelling and fragmentation.

Authors concluded that brain structural alterations in animals corresponded the *chronic progressing dyscirculatory-hypoxic syndrome* with expressed vascular walls permeability pronounced alterations, nervous cells wide-spread dystrophy-destructive disorders of unreversible type with neuroglia proliferation-dystrophic reaction in remote period after exposure to 1.5 Gy dose. These experimental data completely corresponded to the clinical pattern in 60 studied persons — ChNPP accident consequences clean-up participants that enabled authors to recognise the radiation factor leading role in brain pathology genesis in remote terms after irradiation. On the basis of own experimental studies N.B. Holodova et al. (1996) state that stress amplifies the existing pathology manifestations but separately itself is not able to be all the pathologic changes symptoms complex reason in remote terms after irradiation.

Brain morphological and biochemical alterations after rat internal irradiation in low doses were estimated in experimental works of staff team under leadership of academician A.P. Romodanov (1993). The ^{137}Cs with 620 Bq·day^{-1} activity and ^{85}Sr with 1,200 Bq·day^{-1} activity were applied, their administration with food resulted in doses accumulation up to 0.03–0.1 Gy for 1–3 months. O.A. Mirgorodsky et al. (1993) revealed the ^{137}Cs activity growth in brain for 25% during 3-month administration compared to that in one month term. Authors received data concerning 0.2–0.5% of total nuclide amount accumulation in brain tissue compared to that in whole animal bode. Accumulation of ^{85}Sr in brain was low that authors explain through ^{85}Sr short half-life period ($T_{1/2}$=64.8 days). Resarchers concluded the *brain ability to absorb the radionuclides* and ^{137}Cs in particular. A.T. Nosov et al. (1993) studied the brain morphological alterations applying electron microscopy in 30 mature female mice under ^{137}Cs and ^{85}Sr chronic intake for three months with integral doses 0.03–0.1 Gy. Authors revealed brain cortex neurones and neurones synaptic apparatus destructive-dystrophic disorders on the intracerebral microcirculation progressing alteration. At the same time neurones energy-producing and protein-producing functions remained safe. Microcirculation disorders were revealed in form of microvessels progressing dilatation, capillary stasis, vascular wall integrity alteration with further thrombosis and perivascular swelling phenomenon both with brain tissue perivascular and intracerebral focuses of softening rise.

At the same time A.K. Guskova et al. (1996) put under doubt the neurones primarily damage possibility under chronic irradiation with doses of 0.03–0.1 Gy. They apply to the brain morphological alterations study results among dead persons with exposure doses of up to 17 Gy total irradiation and 30–40 Gy local radiation impact on brain where according to the authors no any confirmation was found concerning neurons damage. A.K. Guskova and I.N. Shakirova (1989) present the following values of threshold doses for nervous system radiation morphological damage: 10–50 Gy for local exposure and 2–4 Gy for general irradiation.

Though the nervous system interaction with ionising radiation problem continues remaining debatable often with considerations polarity even regarding the experimental results having adequate dosimetry support. Thesis of *nervous system tolerance* towards ionising radiation injuring impact is vindicated in the majority of today works.

2.4. Conclusion

The completion of experimental radioneurobiological research results review we as clinicians faced as the complex enough task. Both with experimental works technical specificity, the surprising results contradictoriness and radiocerebral effects interpretation polarity occur the major problems here. Undoubtedly that indicates the radioneurobiology dynamic progress and its leading position among natural sciences. Undoubtedly also is the radiation neuropsychiatric pathology diagnostics, management and prophylactic impossibility without knowledge about its pathogenesis.

From our experience just the clinicians face actual need in radioneurobiological knowledge. First of all exactly to them the present review is addressed aiming the excessive considerations categoricity avoidance in the field of ionising radiation role in etiology and pathogenesis of some nervous and mental diseases.

Table 2.2 shows *ionising radiation neuropsychiatric effects dose thresholds* presented by various authors.

Table 2.2

NEUROPSYCHIATRIC EFFECTS THRESHOLDS FROM EXPERIMENTAL DATA

Effect	Threshold	Information source
Radiophosphene	0.5 mR (1.6–8.7 mR·sec^{-1})	Pape R., Zakovsky J., 1954
Electric potentials rise *in retina*	1 mR·sec^{-1}	Pogosyan R.I. et al., 1961
Stimulating effect on the CNS with *evoked potentials* generation under impulse roentgen irradiation	0.1 mGy (single impulse dose rate $1.7 \cdot 10^3$ Gy·sec^{-1})	Dutov V.B. et al., 1989
Memory disorders	1 mGy 3–3.5 Gy 20 Gy	Wheeler K.T., Hardy K.A., 1985 Sanablidze I.O. et al., 1989 Kimeldorf D., Hunt A., 1969 Mu Z., Chen H., 1980

Peripheral nerves and *segmental reflexes* functions alteration	1–10 mGy	Livshits N.N., 1961 Kimeldorf D., Hunt A., 1969
Direct activating impact on *endogenous* (pacemaker) *mechanism of nerve impulse generation*	6–8 mGy	Peimer S.I. et al., 1985 Dudkin A.O., 1987
Electric current threshold value elevation for *phosphene* rise	10–50 mR	Motokawa K. Et al., 1956, 1957
EEG alteration	50 mR (13 mR·sec^{-1}) 4.5 Gy	Grigorjev U.G., 1963 Betetto M., 1970
Nervous system functional state alterations	0.05–10 R (single dose)	Livanov M.N., 1962
Electroretinogram rection	0.5 R 10–60 R	Elenius V., Sysimetsa, 1957 Avakyan Ts.M., 1958
Skin and mucosa *receptors* irritation	2 R	Rokotova N.A., Gorbunova I.M., 1957
Nervous tissue *morphological* alterations	0.03–0.1 Gy 25 R 25–100 R 50 R 50–250 R 0.7 Gy 1.5 Gy 2 – 4 Gy 3 Gy 5 Gy 10–50 Gy 30–40 Gy	Romodanov A.P. et al., 1993 Livanov M.N., 1962 Shabadash A.L., 1957, 1964 Lebedinsky A.V., Nahilnitskaya Z.N., 1960 Alexandrovskaya M.M., 1957 Zubovsky G.A. et al., 1991; Meshkov N.A. et al., 1993 Holodova N.B. et al., 1996 Guskova A.K., Shakirova I.N., 1989 Fedorova N.L. et al., 1992 Davydov B.I. et al., 1987 Guskova A.K., Shakirova I.N., 1989 Van der Kogel A.J., 1986, 1991
Cortex agitation	5–50 R	Korolkova T.A., 1958
Synaptoarchitectonics alterations	0.05–5 Gy 3.5 Gy	D'Amelio F.E. et al., 1983 Sverdlov A.G. et al., 1986
Sexual behaviour depression	50–150 mGy 2 Gy 100 Gy	Miyachi Y., Yamada T., 1994 Wallace R.B. et al., 1981 Davydov B.I., Ushakov I.B., 1987
Flexing reflexes alteration	10 R	Kudritsky U.K., 1955; Fedorova I.V., 1958
Autonomous nervous system reactions	10 R	Pape R. Et al., 1953; Hecht H. Et al., 1953
Cataract mice monkey human	 16–32 R 75–825 rep 0.5 Sv (single dose) 3–5 Gy	 Christenberry K., Furth I., 1951 Kimeldorf D.J., 1962 IAEA, 1992 Moskalev U.I., 1991
CNS *biochemical* alterations	0.2–0.5 Gy 0.2–1 Gy 40 R 0.5 Gy	Gamezo N.V., et al., 1984; Yelkin U.B., 1984 Petrusenko G.P., 1982 Cherkasova L.S., 1964 Taitz M.U. et al., 1988
Behaviour reactions	30–120 R 1.5 Gy 3.5–20 Gy	Garsia J. Et al., 1955 – 1957 Fedorova N.L. et al., 1992 Davis R.T., 1965
Hypothalamus irritability elevation. *Radiation autonomous nervous system dystonia* rise	50 R	Smirnova N.P., 1958, 1969
Rapid activity elevation in EEG	60–400 R 400 R	Hasabova V.A., 1969 Haley T., 1962
Aggression depression	0.96 Gy 1.75–3.5 Gy 50 Gy	O'Boyle M., 1976 Nadarejshvili K.Sh. et al., 1989 Davydov B.I., Ushakov I.B., 1987
Slowly progressing *CNS radiation sickness*	1–6 Gy	Karpovsky A.L., 1985; Moscalev U.I., 1991

Vomiting	1.2–1.75 Gy	Davydov B.I., Ushakov I.B., 1987
Chronic radiation sickness	1.5–2.25 Sv	Grigorjev U.G. et al., 1988
Visual evoked potentials reduction	1–3 Gy (single dose) or 3–30 Gy in fractions	Minamisawa T. Et al., 1972, 1977
Locomotive activity lowering	2 Gy	Szwaja S., 1978
«Radiation analgesia» with opiate receptors concern	2.5–15 Gy	Teskey C.C., Kavaliers M., 1984
Spike discharges in *hippocampus*	200–400 R	Gangloff H., 1962; Haley T., 1962
Cerebral vessels morphological damage	300 R 20 Gy	Lebedinsky A.V., Nahilnitskaya Z.N., 1960 Hopewell J.W., Wright E.A., 1970
Cochlear conductivity lost	350 R	Kozlov M.Ya. 1958
Visual tracts and visual analyser cortical projections	400–500 R	Lebedinsky A.V., Nahilnitskaya Z.N., 1960 Kimeldorf D., Hunt A., 1969
Hearing organ damage	400–500 R	Kimeldorf D., Hunt A., 1969
«Spontaneous» *electrical activity* rise in skin nerves and *EEG reaction amplification* on tactile stimulus	500 R	Livanov M.N., Delitsyna N.S., 1956; Delitsyna N.S., 1969;
Brain cortex disorders *phase pattern*	500–1,000 R	Livanov M.N., 1962
Demyelination, Lhermitte syndrome forming	5–10 Gy	Carsten A., Zeman W., 1966; Mastaglia F.L. et al., 1976
Epileptic activity in brain stem	1,000 R	Livanov M.N., 1962
Cochlea microphone potential rise *auditory threshold* elevation	1,000 R	Novotny O., 1952
Labyrinth reflex elevation	1,000 R	Yanson Z.A., 1957, 1958, 1961
Spinal cord damage	15–30 Gy	Asscher A.W., Anson S.G., 1962
Blood-brain barrier injury	20 Gy	Remler M.P. et al., 1986
Blood-myelitic barrier injury	25 Gy	Stewart P.A. et al., 1995
Nystagmus in monkey	3,000 R	Ross J. et al., 1954
Epiactivity in EEG	45–60 Gy	Davydov B.I. et al., 1991
Brain hydration-electrolyte profile alterations	50 Gy	Davydov B.I., Ushakov I.B., 1987
Labyrinth damage in hamster	7,500 R	Quastler H., 1957
Evoked potentials alterations, bilateral *convulsive trim*	80–120 Gy	Nadarejshvili K.Sh. et al., 1972 – 1978
EEG rhythms slowdown, brain *«bioelectrical silence»*	90–100 Gy	Davydov B.I., Ushakov I.B., 1987
Evoked potentials depression in reticular formation and tractus opticus	90–100 Gy	Nadarejshvili K.Sh. et al., 1972 – 1978
Lateral hypothalamus damage syndrome	100 Gy	Levit D., Teitelbaum P., 1975
Postradiation *Parkinson's disease – like states*	100–200 Gy	Atadjanov M., 1982

Summarising the presented above we consider available to state *the main mechanisms of ionising radiation impact on nervous system:*

1. *Direct* impact including the reflected or *afferent* one.
2. *Indirect*, realised through
   - polyneuromediator,
   - dysmetabolic,
   - dyscirculatory and
   - autoimmune processes.

We consider the further research perspective can be related to the two principal directions: *neuro- and psychophysiology* and also to the *neurochemistry*. In any case not diminishing the importance of morphological and other research methods for radiocerebral effects study, we still consider the *physiological and chemical fields* are linked to the progress in understanding of biological processes taking place in nervous system under irradiation. Effective remedies for brain radiation damage prophylactics and management will be also worked out on that background. The *neuro-* and *psychophysiological fields* worth especial attention. Spontaneous and evoked brain bioelectrical activity registration exclusive importance under radiation exposure is out of doubt. Computer technologies progress enabled to widen the diagnostic and research capabilities of EEG and evoked potentials methods. Actually the radiation evoked brain potentials were received. However, rather much more is to be done here than is already completed.

However the *non-invasive registration of brain electrical activity* has principal limitation: the electric conductivity irregularities and first of all — that of cranium bones disables precise mathematical processing of signals aiming cerebral activity pattern completion similar to the density distribution images in roentgen tomography or MRI-

introscopy. That is why the spontaneous and evoked *brain magnetic activity* studies without EEG disadvantages can present the extremely interesting data concerning brain functional state both directly during irradiation and in remote period of radiation damages. This method advantages (self-descriptiveness, non-invasiveness and contact-free nature) within studies in human are obvious [Okada Y.C. et al., 1982; Hari R. et al., 1983; Weinberg H. et al., 1983; Fiumara R. et al., 1985; Vvedensky V.L., Ojogyn V.I., 1986; Hari R., Kaukoranta K., 1987].

In conclusion we one more time underline the radioneurobiology role in natural sciences as the radioneurobiology always is followed by the fundamental neurosciences progress.