MENTAL HEALTH AND NEUROPSYCHIATRIC AFTERMATH 35 YEARS AFTER THE CHERNOBYL CATASTROPHE: CURRENT STATE AND FUTURE PERSPECTIVES

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Abstract

Objective: The Chernobyl nuclear power plant (ChNPP) disaster that happened in Ukraine on the 26th of April 1986 still represents the most severe nuclear accident in human history. Its consequences, especially those involving mental health are increasingly emerging as long-term detrimental effects. Therefore, the aim of the present paper was to review the results of some of authors' studies and their personal reflections on this topic.

Method: The authors selected and commented on the findings mainly derived from their contributions on the prevalence of long-term psychopathological symptoms and neuropsychiatric disorders in different groups of exposed and non exposed individuals, including the workers at the NPP the so-called liquidators (CUWs), the most exposed group, evacuees and people living in more or less contaminated areas.

Results: The main findings derived from a series of studies carried out by the authors throughout the following decades after the disaster indicate the high prevalence of cerebrovascular diseases, organic mental and depressive disorders, cognitive impairment and even dementia that increase with the irradiation dose mainly amongst the liquidators. The organic disorders are probably related to a peculiar effect of radiation on left, dominant brain hemisphere. Interestingly, recent studies revealed abnormalities of the serotonin transporter and other genes disorders possibly at the basis of depression of exposed individuals.

Conclusions: The high prevalence of neuropsychiatric disorders amongst irradiated subjects following the ChNPP disaster highlights the impact of radiation exposure on the lifelong onset of neuropsychiatric disorders, for too long neglected by international agencies. Such findings require to be deepened in the future possibly within the frame of the so-called "ecological psychiatry".

Key words: nuclear accidents, chernobyl, ionizing radiation, liquidators, evacuees, central nervous system, cerebrovascular diseases, PTSD, depression, cognitive impairment, dementia, ecological psychiatry

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Introduction

Thirty five years ago, on the 26th April 1986 the n. 4 reactor explosion in the Chernobyl nuclear power plant (ChNPP), near the city of Pripyat in northern Ukraine (110 km from Kyiv, the capital) provoked the most sever NPP accident worldwide until now. According to the Nuclear and Radiological Event Scale (INES), the Chernobyl accident reached the 7th level, that is the highest, while triggering detrimental health and environmental effects requiring implementation of planned and extended countermeasures (Gresko, 2018). The impact of the Chernobyl catastrophe was 10 times higher than that following the Fukushima Daiichi nuclear disaster occurred on the 11th of March 2011 (ten years ago) (Shigemura et al., 2012, 2021).

For comparison, the worldwide annual exposure to natural radiation sources is expected to be in the range of 1–10 mSv. However, the average dose for Chernobyl workers (CUWs or "liquidators", 600,000 persons) was around 100 mSv (Gresko, 2017; National Research Center for Radiation Medicine, 2006), for evacuees (135,000 persons) 33 mSv, for strict control zone inhabitants (living in the territories with radioactivity deposition >555 kBq·m^{-2}) 50 mSv, for low exposed individuals (5,000,000 persons) 10–20 mSv (Gresko, 2017; National Research Center for Radiation Medicine, 2006).

With no doubt, different international agencies, with unfounded optimism tended to underestimate the

health consequences of the ChNPP catastrophe. Indeed, some international United Nations (UN)-associated organizations (International Atomic Energy Agency, IAEA, the World Health Organization WHO, and the UN scientific committee on the effects of atomic radiation, UNSCEAR) recognized that only 31 death cases could be directly related to the accident, 134 verified cases were suffering from acute radiation sickness (ARS, that is the acute illness deriving from irradiation of the total body in a short period of time), and around 6,000 cases from thyroid cancer mainly reported in children and adolescents exposed at the time of the accident. Their overall conclusions were that, although the ChNPP accident was a tragic event for its victims, there is no sufficient scientific evidence concerning other cancer and non-cancer effects, in spite of the evidence that several other people who dealt with the emergency lost their lives. Again, cataracts, leukemia, cardiovascular, including cerebrovascular and neurocognitive disorders were considered to be at the frame of radiation-associated effects in liquidators. Further, other several health problems noted in the victims/survivors were not attributed to radiation exposure, but to psychological consequences only. It is also noteworthy that the long-term effects in subjects exposed during childhood, who are at increased risk of radiation-induced negative effects, were totally neglected.

By contrast, ecologically oriented publications (Greenpeace-related) highlighted how a so-called "atomic lobby" had underestimated the environmental and health effects of the Chernobyl catastrophe (Bazyka et al., 2013; 2014; 2018b; Bolt et al., 2018).

In 2006, the UN Chernobyl forum identified the impact on mental health as a major problem following the ChNPP disaster, in particular, the increased prevalence of stress-related disorders, effects on developing brain, organic mental disorders and suicides, as well as cardiovascular and cerebrovascular disorders mainly in liquidators (Azizova et al., 2014; Bazyka et al., 2015; Bennett et al., 2006). Subsequently, the impact on mental health and neuropsychiatric consequences of the Chernobyl disaster was broadened and outlined as follows: 1) psychological and psychosomatic disorders; 2) long-term mental health disorders, including depression, post-traumatic stress disorders (PTSD), and alcohol abuse; 3) cerebrovascular and other organic disorders of the central nervous system (CNS), 4) cognitive disorders; 5) effects on the developing brain; 6) potential radiocerebral effects; 7) chronic fatigue syndrome; 8) suicide.

There are just a few well-designed systematic epidemiological studies of mental health following the Chernobyl catastrophe. However, interestingly, data are similar to those gathered after the A-bombing in Hiroshima and Nagasaki, (Japan, 1945) the Three Mile island crisis (USA, 1979), and the Daiichi accident (Loganovsky & Gresko, 2017; Loganovsky et al., 2018a; 2019a; 2020a; 2020b; 2020c; Shigemura et al., 2012, 2021; Terayama et al., 2021).

The aim of the present paper was to sum up the evidence of some studies carried out by our group showing "real data" on the prevalence and types of neuropsychiatric disorders in the long-term following Chernobyl disaster, together with personal authors' reflections.

Long-term effects on psychological wellbeing and mental health

The long-term impact on psychological wellbeing was and is one of the utmost medical and social consequences of the Chernobyl disaster. Immediately after this event, it was fueled by an excessive sense of health hazards from anticipated exposure, often caused by information from the local medical community and government officials. The CUWs, evacuees and people living in contaminated areas were and are still officially labeled as "survivors" or "victims of Chernobyl". Recognized as such, they received a right to receive financial, health, and educational compensation that, combined with ongoing monitoring by local and international organizations, had an iatrogenic effect on psychological wellbeing. Besides that, it should be mentioned that ionizing radiation is an invisible enemy that may induce long-term strong distress as the result of peculiarities of the perception of radiation and of the related traumatic experience (Marazziti et al., 2012; 2014). The latter affects the effectiveness of adaptation and constitutes a risk for emotional, behavioral and psychosomatic disorders (Loganovsky & Gresko, 2016; 2017). Retrospective-prospective data evaluation on the CUWs and evacuees from the Chernobyl exclusion zone showed that generally the premorbid personality of all subjects was characterized by high working capacity, discipline, perseverance, mood stability, optimism, energy, openness to new information, high motivation to achievements, propensity for empathy, altruism, and self-confidence (Loganovsky & Gresko, 2016; 2017). After the traumatic events some pathological personality changes were recorded, specifically, increased introversion and neuroticism, or exacerbation of personality traits, emotional reactivity, and pedantic, anxious, cyclothymic, excitable and dysthymic traits (Loganovsky & Gresko, 2016; 2017). Again, we detected high external reactivity, emotional instability, tendency to excessive vulnerability and sensitivity, inertia of mental processes, weakened self-control, tendency to panic reactions, lack of boundaries between fiction and reality, low tolerance to stress and feeling of helplessness and hopelessness (Loganovsky & Gresko, 2016; 2017). Some of these traits contributed to the inadequate, sometimes hypertrophic perception of the radiation threat that, in turn, was associated with some psychopathological symptoms typical of CUWs and evacuees from the Chernobyl exclusion zone. The most common of these symptoms are the following: low self-esteem, somatic uneasiness, social dysfunction, anxiety, sleep disturbances, low stress resistance and increased frequency of emotional and behavioral signs of distress. Significantly higher levels of psychological distress are observed amongst individuals affected by the two traumatic events (emergency work and evacuation) than in those suffering from one only (Gresko, 2017; 2018; Loganovsky & Gresko, 2017).

To sum up, available data indicate that the most vulnerable subjects to radiation exposure after the ChNPP disaster, that are liquidators, evacuees and people living in the contaminated areas, show significant long-term personality changes and psychopathological symptoms that are the cue of an underlying vulnerability towards the possible development of neuropsychiatric disorders.

The neuropsychiatric aftermath amongst Chernobyl liquidators (CUWs)

After analyzing the results of some of our recent retrospective-prospective studies on different exposed groups of subjects exploring neuropsychiatric effects, together with dosimetric monitoring of external

radiation doses, we present herein and comment on some of the ensuing data.

The results showed that CWs, who participated in the emergency works in 1986–1987 and were exposed to external radiation doses of 0.60–5900.00 mSv (M ± SD: 456.0 ± 760.0 mSv), were the group with the highest risk of neuropsychiatric disorders that exponentially increased with the radiation dose (≥ 50 mSv, $p < 0.001$). Cerebrovascular diseases, depression, organic mental disorders mild cognitive impairment and dementia to depend on radiation doses were the most common disorders amongst CWs >0.3 mSv.

The presence of specific brain alterations were revealed by using the non-invasive technology of cognitive auditory evoked potentials (event-related potentials, ERP, P300), as some radiation-associated changes at doses >50 mSv were identified, namely an increase of latency periods and decrease of amplitude of P300 component in Wernicke's area (Loganovsky & Kuts, 2018). (Damage to the Wernicke's area is known to impair perception and understanding of language/conversation, namely the comprehension of words, instructions, addressed speech that may lead to severe disability). Not surprisingly, verbal memory and learning of CWs were disturbed, and the IQ reduced due to verbal component. This last alteration can be also considered a neuropsychological marker of cognitive impairment in the CUWs, which reflects damage of the left (dominant) cerebral hemisphere (Loganovsky & Kuts, 2018). The EEG parameters in the left posterior temporal area (Wernicke's area) depended on the irradiation dose >0.25–0.3 mSv. The cerebral information processes were disrupted with lateralization to the Wernicke's area at doses >50 mSv. According to us, radiation-induced dysfunction of cortico-limbic system of the left dominant cerebral hemisphere with the specific involvement of hippocampus seems to be a key underpinning of the organic brain damage upon irradiation (Loganovsky et al., 2018a; 2020a).

Neuropsychiatric disorders amongst CUWs emerged quite early, about 3–5 years after the catastrophe, and only after 30 years these disorders become the same in the CUWs and unexposed control subjects. Several other neuropsychiatric disorders began to occur 7–10 years after the catastrophe amongst the CUWs who were also evacuated from the Chernobyl exclusion zone, rather than amongst those who were not evacuated. As already mentioned, this would indicate the negative impact of evacuation that would decrease the threshold towards the onset of neuropsychiatric disorders. During the first 15 post-accident years a dose-dependent effect on the onset of neuropsychiatric disorders was detected, namely at doses greater than 300 mSv they appeared almost immediately after the catastrophe, while at doses of 50–300 mSv they emerged after 2 years, and at doses less than 50 mSv after 10 years. Later on, this dependence disappeared (Loganovsky et al., 2018a; 2020a).

To summarize, the radiation risks for cerebrovascular diseases in CUWs, the most exposed group to CNPP radiation, were registered at radiation doses >0.15 Sv, and for mental disorders and also and mortality from stroke at doses >0.25 Sv. The CUWs (and also evacuees) showed a significantly elevated incidence of mental and behavioral disorders, vascular dementia, alcohol abuse, depression, and PTSD) that was even higher in those individuals facing the two events. Alcohol dependence and alcohol abuse syndrome were particularly increased amongst CUWs and probably developed as a consequence of the previous mental disorders, particularly of depression (Napryeyenko et al., 2019). The "post-radiation" PTSD deserves to be commented on, as it is characterized by the so-called "flashforward" phenomenon, i.e. predictive stress or anticipatory projection of fear and uncertainty to the future (i.e. "anticipatory stress") regarding cancer, congenital malformations in offspring, etc. Interestingly, the risk of stroke and atherosclerosis is increased in the CUW suffering from PTSD. It has been suggested that also chronic fatigue syndrome is a characteristic consequence of the impact of radiation in low doses and stress (Loganovsky et al., 2015; 2016; 2018b).

Depression was more common in the subjects with acute radiation sickness than in the CUWs ($p = 0.006$). A large international study exploring some possible pathophysiological mechanisms highlighted an important involvement of the serotonin transporter gene (SLC6A4). Its noteworthy that CUWs showed an increased number of *S/S SLC6A4* genotype carriers, as compared with a large group of Europeans with no mental disorders. Significant relationships were detected between depression and patient's age ($r = 0.503$; $p = 0.033$), time after accident ($r = 0.581$; $p = 0.011$), and radiation dose ($r = 0.515$; $p = 0.025$). Development of depression was also associated with a decrease of the highly functional *LA/LA* genotype (4.76% versus 31.25% in the absence of depressive symptoms) amongst subjects of 55 years of age and older (Abramenko et al., 2017).

The 7th Framework Program of the European Union "Nuclear Fission and Radiation Protection" has implemented a joint European project CEREBRAD ("Cognitive and Cerebrovascular Effects Induced by Low Dose Ionizing Radiation"), in which the National Research Centre for Radiation Medicine, National Academy of Medical Sciences of Ukraine (NRCRM) was participating. Clinical and new molecular-biological features of cognitive and cerebrovascular effects of irradiation in low doses were established there (Bazyka et al., 2013; 2014; 2015; Marazziti et al., 2016). As far as possible neurobiological mechanisms of cerebral radiosensitivity and pathogenesis of radio-cerebral effects, data are accumulating featuring the inhibition of neurogenesis, mainly in hippocampus, changes in telomere and gene expression, apoptosis, neuroinflammation, autoimmune processes, "glio-vascular complex", multiorgan dysfunctions, and others. Recently, we studied the *TERF1*, *TERF2* and *TERT (GE)* gene expression by means of RT-PCR and relative telomere length (RTL) assessment in CUWs (n = 258, 22–2800 mSv radiation dose range) and in a control group of patients with vascular cognitive deficits (n = 78). A significant shortening of telomeres in the CUWs upon irradiation at 100–500 mSv doses was detected. The decreasing of RTL correlated with radiation dose increase and overexpression of negative telomere length regulators. The results of the study indicate the parallel changes in decrease of cognitive functions and telomere length, as well as features in the *TERF2*, *TERT* and *TERF1* gene regulation in the late period upon irradiation at doses above 500 mSv (Bazyka et al., 2013; 2014; 2015).

More recently, cellular, molecular, genetic, and noninvasive (including neurophysiological) functional occupational biomarkers were studied in workers exposed to a combination of external gamma radiation and transuranic elements (alpha emitters). The study was conducted in personnel (n = 688) working on the project of "Shelter" unit transformation into an environmentally safe system. The average external radiation dose was 26.06 mSv (0.1-113.35 mSv range) at the background risk of internal exposure to transuranic

elements (plutonium and americium). Parallel changes were observed in the decrease of cerebral electrical activity, telomere length, and difference in *CCND1, CDKN1A, CDKN2A, VEGFA, TP53*, and *DDB2* gene expression. Increase in the number of such chromosome aberrations as dicentric and paired fragments both with TCR-variant lymphocytes at doses exceeding the established occupational limits indicate the mandatory requirement of biological dosimetry. These findings confirmed the presence of radiation-induced changes in the regulation of cell proliferation genes, telomere function, and apoptosis in nuclear workers (Bazyka et al., 2018a).

Ionizing radiation and the visual organ

Recently, there has been a growing research interest in the effects of ionizing radiation on brain and visual organ, given the evidence that the eye structures are easily accessible, and retina, that is part of the brain, may represent a useful and indicator of the actual conditions of the CNS. The eye lens is one of the most radiosensitive human tissues, and retina is at risk for suffering from severe consequences induced by ionizing radiation such as angiopathy and angiosclerosis (Ciarmatori et al., 2016). Therefore, it has been proposed that targeting the eye might useful to design early detection strategies and prevention of radiotoxicity not only at its level, but also in the brain, on the basis of what we called "eye-brain axis", as supported by evidence that the eye, specifically the retina, is just a brain expansion (Loganovsky et al., 2020b; 2020c).

One of our studies revealed a significant increase of retinal angiopathy and angiosclerosis in a cohort of CUWs of the CNPP accident (314.8±14.5 per 1000 people in 1993 and 911.9±19.7 per 1000 people in 2004). In comparison with a control group, the relative risk of angiopathy was 2.6 for a dose up to 0.05 Gy, 2.75 for doses ranging from 0.05 to 0.099 Gy, 2.86 for doses between 0.1 and 0.249 Gy, and 2.93 for dose of 0.25 Gy or higher. In several CWs who were initially diagnosed with angiopathy and followed up, a transformation of angiopathy into angiosclerosis was noted: walls of arteries became thicker, the lumen of vessels decreased and the caliber became uneven. That is why, prevalence of the retina angiosclerosis increased considerably by time, mainly in relatively young age groups (Loganovsky et al., 2020b; 2020c).

Conclusions

Current planning of the nuclear disaster response in European countries is largely technical in nature, with less attention paid to social, psychological and ethical issues. The SHAMISEN consortium (Nuclear Emergency Situations - Improvement of Medical And Health Surveillance) with participation of 50 experts from 10 countries has critically reviewed the current recommendations and experience on dose assessment and reconstruction, evacuation decisions, long-term health surveillance programs and epidemiological research. The case studies and lessons learned from the living conditions and health of population affected by the Chernobyl and Fukushima accidents were assessed using an integrated approach to the health and well-being. A set of comprehensive recommendations have been developed to improve the preparedness, response, long-term observation and living conditions of populations that were affected by the past radiation accidents or may be harmed by such accidents in future with the purpose to meet their needs while minimizing an unnecessary anxiety (Ohba et al., 2021).

The WHO believes that the experience of Chernobyl and Fukushima accidents clearly demonstrates that nuclear emergencies can lead to subsequent low and very low levels of radiation exposure, in which the psychological and social effects in the affected population will dominate over the actual biological effects of ionizing radiation itself. According to the international protection standards and guidelines, it is required that both radiological and non-radiological health effects should be considered in the readiness and response to the real emergencies. There is an urgent need to expand the philosophy of radiological protection system beyond the metrics of radioactivity and radiation dose. Over the last decade, a number of multidisciplinary projects have been set up to assess the management options according to the social, economic and ethical criteria, in addition to the technical capacity of achieving this goal. The WHO and partners from the intergovernmental standing committee on mental health and psychosocial support in emergency settings have developed a comprehensive framework and guidelines that can be applied to any type of emergency or catastrophe, regardless of its origin. There is a need to include available scientific expertise and technical, managerial, and personal resources what will be considered in a similar “decision-making structure” to be applied to the radiation emergencies. The radiological protection (Marazziti et al., 2015), medical support (especially primary care and emergency care, mental health support), social sciences (anthropology, psychology, ethics) and communication issues are the key areas of knowledge required to develop such a system. The implementation of such a multidisciplinary concept in operational terms requires the personnel extra education and training, which significantly exceeds current level of knowledge and experience (Carr et al., 2018).

At the same time, there is a wide discussion and debate on mental health. Impact on mental health is the most important consequence of the accident for public health in the three most radiologically contaminated countries, i.e. Ukraine, Republic of Belarus and the Russian Federation (Zablotska, 2016). Some incidence excess of mental disorders, cerebrovascular disease including mortality from the latter with certain radiation risks, as well as eye problems, was revealed especially amongst CUWs, but also evacuees and people living in irradiated areas some decades after the disasters (Bazyka et al., 2018b). It is interesting to mention that CUWs were selected on the basis of their good physical and mental health. Unfortunately, after the CnNPP catastrophe, some of them showed pathological change of personality and psychopathological symptoms impairing their social and familial adjustment. Others were suffering from cerebro-vascular, organic mental and psychiatric disorders (depression alcohol abuse, PTSD), cognitive impairment, dementia and eye angiopathy that disrupted their lives in an irreversible way. Some of our findings would indicate that the radiation-induced dysfunction of the cortico-limbic system in the left dominant hemisphere of the brain, especially of the hippocampus might be the basis of post-radiation organic brain damage leading to both neurological and psychiatric disorders. The association of genotypes by 5_HTTLPR and rs25531 polymorphisms of the SLC6A4gene with affective and cognitive disorders supports the link between ionizing radiation and certain gene polymorphisms. Last, but not least, we cannot exempt ourselves from mentioning that

such findings highlight the biological risk of irradiated-in utero subjects and children who have the most radio-sensitive brain.

Although the ChNPP disaster occurred 35 years ago (and Fukushima 10 years ago), their health and particularly mental health consequences continue and probably will continue to be documented for a long time. Therefore, it is fundamental that not only the memories of the disaster are maintained, but also the awareness that their consequences are not finished, so that that long clinical and epidemiological psychiatric studies in all categories of the Chernobyl disaster survivors with reliable dosimetric support should be constantly implemented.

A lesson derived from Chernobyl was the need of a branch of psychiatry devoted to ecology and ecological disasters that led to the establishing of a separate section of World Psychiatric Association (WPA) called "Ecology, psychiatry, mental health" where Ukraine is engaged, and one of the authors (K. Loganovsky) is its representative (Loganovsky et al., 2019b). We are of the opinion that this is just the beginning of the story. Indeed, the past nuclear disasters of Chernobyl and Fukushima and their apparently never-ending aftermath, together with the current COVID-19 pandemic and its psychological and neuropsychiatric consequences (Marazziti et al., 2021), require the emergence of a brand new and real ecological awareness that should lead to a total (re)shapening of policy and human way of living, if it is true that every catastrophe has its own origin" (Neyrat, 2008).

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