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Implications Of Ionizing Radiation Exposure to Patients' Mental Health During Diagnosis and Treatment: A Systematic Review

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Abstract

Both humans and animals may experience fear and stressful conditions as a result of radiation exposure's psychological and cognitive impacts. There is evidence connecting radiation exposure to neuro-inflammation, apoptosis, and the death of neural stem cells in addition to cognitive decline. The goal of this systematic review is to provide a thorough assessment of the body of research on the psychological and cognitive effects of ionizing radiation exposure during diagnosis and patient treatment. Ionizing radiation can affect people's mental and cognitive health. It can come from a variety of sources, including medical operations, nuclear accidents, and space exploration. To improve our knowledge of these consequences, this review aims to analyze the evidence that is currently available. An exhaustive exploration of various electronic databases, such as PubMed, Research Gate, Google Scholar, Academia, and Web of Science, was carried out to find pertinent research articles published in peer-reviewed publications. Studies that looked at the psychological and cognitive effects of ionizing radiation exposure were included in the study. The results were synthesized qualitatively and presented. 53 studies out of the 1000 that were found during the original search satisfied the inclusion criteria. Radiation occurrences, occupational exposure, medical imaging, and treatments were among the several sources of ionizing radiation exposure included in the examined research. Research has indicated that individuals receiving radiation therapy and diagnostic radiological procedures may encounter immediate psychological side effects, which could have an impact on mental health. The symptoms of these psychological reactions can include discomfort, nausea, exhaustion, difficulty sleeping, and shortness of breath. This research documented a variety of psychological and cognitive outcomes, such as low self-esteem, anxiety, depression, post-traumatic stress disorder (PTSD), cognitive deterioration, and dread. In situations including both acute and prolonged exposure, these effects were noted. Notably, those who were subjected to higher ionizing radiation doses for example, those who survived nuclear accidents showed signs of more severe and persistent cognitive and psychological deficits. The analysis has brought attention to the wide range of impacts that ionizing radiation can have on the mind and body. This variance can be explained by variables including individual susceptibility variations and exposure parameters like dose, duration, and frequency. Furthermore, the results emphasize that ionizing radiation can cause a variety of psychological reactions, ranging from short-term stress reactions to long-term mental health issues even at 0.0Gy. The consequences on cognition likewise show a wide range, with memory, attention, and executive function impairments among them.

Keywords: ionizing radiation; psychological effects; cognitive effects; systematic review; radiation exposure; mental health; cognitive function; radiation-induced psychopathology

1.Introduction

Radiation surrounds every living thing on our planet. On hot days, the sun radiates, and our homes' radiators radiate as well. Radiation exposure occurs to passengers each time they board an aircraft. These identical passengers are exposed to another little dosage of cosmic radiation from the atmosphere when the plane ascends in altitude. Along with the surrounding ground, the stone that we use to construct our homes and buildings also contains natural radiation. In addition, there is radiation from medical devices like CT scans and X-rays, as well as radionuclides such as potassium, which can be present in some fruits and vegetables. The entire amount of potassium that we consume contains some radioactive potassium, and the radiation from these forms of potassium makes up some of the fundamental radiation kinds that we are continuously exposed to [55] . Radiation exposure is a necessary part of human life. Regardless of the effect, it has always existed. The question is, are we more vulnerable to anything that the reactor might release? Almost always, the risk is exceedingly minimal, regardless of how much it is increased. Paul Slovic divides risk perception into two categories: unknown risk and fear of danger. At its highest point, "dread risk" is characterized by feelings of helplessness, terror, catastrophic potential, deadly outcomes, and an unfair distribution of risks and rewards. Nuclear power and weapons get the highest scores among the attributes that comprise this component. When it comes to risks that are deemed to be novel, unobservable, and have a delayed manifestation of harm, they are classified as "unknown risks." [55].

The word is mostly employed psychologically to explain the public's emotional responses to situations with which one should rationally interact, as nearly every radiation-related story makes "conscientious" and "unprofessional" citizens feel afraid and rejected [31]. The dread that comes with being exposed to radiation can have considerably more negative effects than the radiation's real damaging effects. The mass media has shaped public perception over the last 70 years regarding the lethal consequences of radiation. For this reason, the majority of people fear radiation, and the very concept of radiation evokes negative emotions and associations. Since people have been hearing and absorbing the fact that radiation is lethal for such a long time, these terms have come to define and comprehend radiation exposure. Only when exposed to extremely high radiation levels can radiation result in death. Since natural radiation is all around us and will always exist, there is always a theoretical or epidemiological risk associated with it [42, 43]. It also serves as a natural lower bound for radiation protection in terms of dose and risk reduction due to its inevitable exposure to natural radiation. It is not justified to lower the contribution of radiation exposure below natural limitations [55]. To preserve function at all ages, cognitive function must be maintained. Cognitive skills are predictive of children's academic success, adults' professional success, and older individuals' ability to maintain their independence and general well-being. Cognitive functioning can be maintained by elements including physical exercise, education, career position, and mentally challenging activities.

Ionizing radiation exposure can have a profound effect on one's mental state. Radiation accidents can result in widespread and protracted psychological symptoms, such as PTSD, anxiety, and depression. The public's fear and rejection of radiation can be linked to false beliefs and information spread by the media. Although we cannot completely escape being exposed to radiation in our daily lives—both natural and man-made—it is crucial to comprehend the possible long-term effects of low radiation dosages. Myths and visuals about the effects of radiation exposure frequently feed people's worries. Furthermore, radiation exposure has been connected to neurodegenerative consequences and could be involved in the etiology of mental illnesses.

All things considered, the mental effects of ionizing radiation exposure ought to be taken into account in addition to the physical health. To successfully handle the fallout from radiation disasters, the psychological effects of ionizing radiation exposure should be taken into account in addition to the effects on physical health. Examining the effects of ionizing radiation on mental health was the goal of this review.

2.0 Material and Method

Using the PubMed, Research Gate, Google Scholar, Academia, and Web of Science Articles databases, a literature search was done to address the possibility that radiation exposure, even at 0.0 Gy above background dose, can have psychological effects that could ultimately lead to cognitive damage. Radiation anxiety, psychological stress from radiation, cognitive functioning and radiation, cognitive impairment and radiation, neuroinflammation and radiation, and psychological stress and cognitive functioning were among the search phrases that were covered. English-language peer-reviewed articles were the only ones selected. The data extracted and tabulated involved title, objective, result and conclusion of the research.

3.0 Results and Discussion

Individuals may experience psychological impacts from radiation exposure. Irrational worry and anxiety resulting from the public's fear and rejection of radiation can have more detrimental effects than the real physical harm caused by radiation [31]. Mental health effects such as depression, anxiety, and post-traumatic stress disorder are highly represented in populations affected by radiation disasters (Snežana and Milan 2020). The atomic bombings of Hiroshima and Nagasaki and the Chernobyl nuclear accident have shown long-term effects on the psychological and social processes of victims and their families [9]. Vulnerable populations such as children, women, clean-up workers, and migrants are particularly at risk for mental health issues in radiation-affected areas [25]. Additionally, radiation exposure can have an impact on cognitive processes and psychological functions, potentially contributing to the pathophysiology of psychiatric disorders [36]. Radiation exposure has multiple effects on the brain, behavior, and cognitive functions. It has been reported that high-dose (>20 Gy) radiation-induced behavior and cognitive aberration are partly associated with severe tissue destruction. Low-dose (<3 Gy) exposure can occur in radiological disasters and cerebral endovascular treatment. However, only a few reports analyzed behavior and cognitive functions after low-dose irradiation.

3.1 Radiation Exposure Anxiety and Depression

Radiation anxiety is defined as the negative cognition regarding the potential adverse health effects following radiation exposure [26]. It is also associated with problems such as perceived stigma and discrimination. Most non-single-item measures of radiation anxiety are based on Slovic’s model of risk perception [49], which posits two psychological dimensions: dread risk and unknown risk. Radiation anxiety is a common issue among head and neck cancer patients undergoing radiation therapy. The use of thermoplastic masks for immobilization during treatment can cause significant anxiety [7]. Patients have reported various triggers of anxiety, such as claustrophobia and fear of the mask [12]. Healthcare providers need to address mask anxiety and provide support to patients. Strategies that may help reduce mask anxiety include increased communication, delivery of visual information, exposure to the mask before treatment, and increased control of music/soundtrack selection [27]. Additionally, radiation therapy can lead to acute psychological side effects, including anxiety, depression, fear, and low self-esteem. Therefore, support and care for the psychological well-being of radiation therapy patients are crucial (**Forbes *et al.*, 2022).** Non-pharmacological interventions, such as biofeedback and breathing techniques, are being explored to reduce procedural anxiety during radiation therapy. Radiation emergencies can have significant psychological consequences, including depression, anxiety, and post-traumatic stress disorder [31]. Depression is a long-term effect of atomic bombings, nuclear testing, and radiation emergencies, with increased prevalence observed in individuals exposed to radiation. Infrared radiation has been shown to have antidepressant and anxiolytic effects in animal models [50]. Some patients undergoing radiation therapy for cancer may experience depression, with cognitive rand endogenous symptoms being helpful in distinguishing those with depressive symptoms [23]. Depression is not inevitable with cancer, and a personal or family history of treated depression is associated with an increased risk of depressive symptoms in radiation oncology patients [20].

Loganovsky and Vasilenko (2013) Investigated the genesis of depressive disorders caused by ionizing radiation and found that Depression is one of the most significant and long-term effects of atomic bombings, nuclear testing, and radiation emergencies. The participants in the accident at the Chornobyl nuclear power plant increased prevalence of depression (18.0% and 13.1% in controls) and suicide rates. Depression is mainly observed in the structure of an organic mental disorder against cerebrovascular disease. The clinical pattern is dominated by asthenoadynamic and asthenoapathetic depression. Depressive disorders in radiation emergencies are multifactorial, that is the result of exposure to complex psychogenic and radiological accident factors, the impact of traditional risk factors, somatic and neurological diseases, genetic predisposition, predisposition, etc. At the same time, exposure to ionizing radiation is a factor in the genesis of depression. This impact can be direct (to the Central Nervous System), and indirectly through the somatic and neurological abnormalities (multiorgan dysfunction) as well as by a variety of pathogenic mechanisms of ionizing radiation on the brain that have been discovered recently. It is strongly necessary for analytical clinical and epidemiological studies with verification of depression and evidence-based establishment of the role of radiation and non-radiation risk factors. In another investigation, it was documented the trajectory of situational anxiety during HNC treatment delivery and explored radiation therapists' (RTs') ability to identify it. Participants with Head and Neck Cancer commencing radiation therapy completed the state-trait anxiety inventory at their mask-making session, and once each week immediately before and after their radiation treatment. Treating RTs independently rated their perception of participant's anxiety at the same time points. Participant- and RT-rated anxiety scores were calculated at each time point together with the proportion of participants reporting clinically significant anxiety (state-trait anxiety inventory $\geq$ 40). Intraclass correlations were calculated to assess concordance between participant- and RT-ratings. Sixty-five participants and 16 RTs took part in the study. Participants were classified into 1 of 5 trajectory groups: stable high (16%), increasing (19%), decreasing (27%), fluctuating (19%), and no anxiety (19%). Nearly half (43%) of participants reported clinically significant anxiety before their mask-making session, and between 30% and 43% across trajectories reported significant anxiety immediately before treatments. Intraclass correlation values indicated poor agreement between participant- and RT-ratings. Situational anxiety is prevalent in people receiving HNC radiation therapy with mask immobilization. RTs did not reliably capture patients' situational anxiety. There is no single best time point to provide intervention, suggesting people should be screened for anxiety regularly throughout their treatment. Resources and education should also be available to improve RT's skills in providing psychosocial support.

Collett *et al.* (2020) addressed the question that perceived radiation exposure - even where the actual absorbed dose is 0.0 Gy above the background dose - can result in psychological stress, which could in turn lead to cognitive dysfunction. Overall, the evidence shows that prenatal exposure to low and moderate doses was detrimental to brain development and subsequent cognitive functioning, however, the evidence for adolescent and adult low- and moderate-dose exposure remains uncertain. The persistent psychological stress following accidental exposure to low doses in adulthood may pose a greater threat to cognitive functioning. Indeed, the psychological implications for instructed cohorts (e.g., astronauts and radiotherapy patients) are less clear and warrant further investigation. Nonetheless, the psychosocial consequences of low- and moderate-dose exposure must be carefully considered when evaluating radiation effects on cognitive functioning, and to avoid unnecessary harm when planning public health response strategies. **Yuya *et al*. (2020)** noted that One of the biggest public health impacts of the Fukushima Daiichi Nuclear Power Station accident is psychosocial. Anxiety about radiation is still present, and radiation risk perception, particularly about genetic effects, is known to affect mental health. However, the roles of other risk factors such as health anxiety and mindfulness remain to be proved. Here, we examined how radiation risk perception (genetic effects) mediates health anxiety and psychological distress, and how mindfulness influences those variables. Seven years after the accident, a self-reported online survey with 832 participants was commissioned, 416 each from Fukushima and Tokyo, and the relationship between those variables using Structural Equation Modelling. Health anxiety had a much stronger influence on psychological distress than radiation risk perception. Mindfulness was significantly correlated with both health anxiety and psychological distress, but not with radiation risk perception. The total effects on psychological distress were -0.38 for mindfulness and +0.38 for health anxiety. These results suggest the potential application of mindfulness-based interventions to alleviate health anxiety and psychological distress rather than therapy focused on radiation anxiety. The results underline the effectiveness of community support efforts in Fukushima and highlight the importance of enhancing mindfulness during the chronic phase following a disaster. **Van Beek *et al.*, (2020)** identified sociodemographic and clinical factors, health-related quality of life (HRQOL), and head and neck cancer (HNC) symptoms associated with the course of symptoms of anxiety and depression from pretreatment to 24-month follow-up among HNC patients after (chemo) radiation. Patients (n = 345) completed questionnaires on anxiety and depression (HADS), HRQOL, and symptoms (EORTC QLQ-C30/QLQ-H&N35) before treatment, and 6-weeks,3-,6-12-,18-, and 24-months after treatment. Mixed model analyses were used to investigate the course of anxiety and depression from pretreatment to 24 months with factors assessed at baseline, and the course of anxiety and depression from 6- to 24 months, about factors assessed at 6 months. Increased risk for anxiety (HADS-anxiety > 7) was 28.7% among patients before treatment, which declined to 10.0% at 24-months. Increased risk for depression (HADS-depression > 7) was 15.1% before treatment, 18.2% at 3 months, 7.2% at 12 months, and 16.0% at 24 months. Factors assessed at baseline that were significantly associated with the course of anxiety were age, pain, problems with social contact, and feeling ill, whereas chemotherapy, worse emotional functioning, speech problems, and weight loss were significantly associated with the course of depression. Regarding factors assessed at 6 months, chemotherapy, worse cognitive and social functioning, insomnia, swallowing problems, and trouble with social eating were associated with the course of anxiety. Nausea/vomiting, dyspnea, coughing, and feeling ill were associated with the course of depression (p-values Discussion Factors associated with a worse course of anxiety and depression are younger age, treatment with chemotherapy, worse HRQOL, and higher symptom burden.

Khurshid *et al.* (2023) investigated the prevalence of anxiety and depression in cancer patients undergoing radiation therapy and identified the factors associated with the multidimensional model, including sociodemographic, clinical, function well-being, and symptom variables. Methodology: The research was conducted at the Shifa International Hospital Ltd. In Islamabad's radiation oncology clinic from February 2022 to May 2022. Assessments of side effects and the intensity of typical symptoms experienced by cancer patients receiving radiation therapy have been carried out using the MD Anderson Symptom Inventory (MDASI) questionnaire. Version 20.0 of the Statistical Package for the Social Sciences (SPSS) has been used to analyze the data. They were described using categorical statistics using frequency and percentage. Results: The majority of participants were women. During the treatment, patients experienced various psychological reactions, such as nausea, Pain, anxiety, depression, fear, fatigue, disturbed sleep, and shortness of breath. Many patients also reported feeling sad, losing enjoyment of life, and having disturbed relationships with people around them. However, the psychological state of patients improved at the end and after the Intervention. Conclusion: Acute psychological side effects appeared in several patients receiving radiation therapy, such as anxiety, depression, fear, and low self-esteem. Hence, we concluded it has a high incidence. So, radiation therapy patients should receive support and care for their psychological well-being.

Fukasawa *et al.* (2017) assessed the associations among radiation exposure or psychological exposure to the Fukushima nuclear power plant accident (i.e., fear/anxiety immediately after the accident), current radiation anxiety, and psychological distress among non-evacuee community residents in Fukushima five years after the Great East Japan Earthquake, which occurred in March 2011. A questionnaire survey was administered to a random sample of non-evacuee community residents from 49 municipalities of Fukushima prefecture from February to April 2016, and data from 1684 respondents (34.4%) were analyzed. Environmental radiation levels at the time of the accident were ascertained from survey meter data, while environmental radiation levels at the time of the survey were ascertained from monitoring post data. In the questionnaire, immediate fear/anxiety after the accident, current radiation anxiety, and psychological distress were measured using a single-item question, a 7-item scale, and K6, respectively. Multilevel linear or logistic regression models were applied to analyze the determinants of radiation anxiety and psychological distress. The findings showed that environmental radiation levels at the time of the survey were more strongly associated with radiation anxiety than radiation levels immediately after the accident. Disaster-related experiences, such as direct damage, disaster-related family stress, fear/anxiety after the accident, and demographic characteristics (e.g., younger age, being married, low socioeconomic status) were significantly associated with radiation anxiety. Environmental radiation levels at the time of the accident or survey were not significantly associated with psychological distress. Radiation anxiety largely mediated the association between fear/anxiety after the accident and psychological distress. In addition to environmental radiation levels, respondents' radiation anxiety was affected by multiple factors, such as disaster-related experiences and demographic characteristics. Radiation levels were not associated with psychological distress in non-evacuee community residents. Rather, fear/anxiety after the nuclear power plant accident may be a determinant of psychological distress, mediated by radiation anxiety

3.2 Brain Neurochemistry and Behavioural Disruption

Brain neurochemistry and behavioral disruption can occur due to ionizing radiation exposure. Studies have shown that radiation-induced impairments in behaviors and cognition are associated with molecular mechanisms that lead to damage in neuronal cells, disrupting normal communication between cells in the neural network. Cognitive impairment, such as memory deficits and attention performance deficits, is a significant risk for patients undergoing conventional radiotherapy for brain tumors. Radiation exposure can cause damage to various cell populations in the brain, including neural stem cells, mature neural cells, and glial cells, leading to lasting repercussions on neurocognitive functions. The combination of ionizing radiation and hypo gravity can also affect the central nervous system, leading to changes in behaviors and metabolism of monoamines in the brain. An overview of the result was tabulated in **Table 1**. The study undertaken by [5] assessed the relationship between brain neurochemistry and behavioral disruption in irradiated mice. The irradiated mice (0.5 Gy, 1 Gy, and 3 Gy) were tested for alteration in their normal behavior over 10 days. Serotonin (5-HT), Dopamine, gamma-aminobutyric acid (GABA), and cortisol analysis was carried out in blood, hippocampus, amygdala, and whole brain tissue. There was a significant decline in the exploratory activity of mice exposed to 3 Gy and 1 Gy radiation in an open-field test. We observed a significant short-term memory loss in 3 Gy and 1 Gy irradiated mice in Y-Maze. Mice exposed to 1 Gy and 3 Gy radiation exhibited increased anxiety in an elevated plus maze (EPM). The increased anxiety and memory loss patterns were also seen in 0.5 Gy irradiated mice, but the results were not statistically significant. In this study, we observed that neurotransmitters are significantly altered after irradiation, but the neuronal cells in the hippocampus were not significantly affected. This study suggests that the low-dose radiation-induced cognitive impairment may be associated with the neurochemical in low-dose irradiation and unlike the high-dose scenario might not be directly related to the morphological changes in the brain.

A similar study conducted by **Guo *et al.* (2023)** assessed relationships between the perception of radiation risks and psychological distress among evacuees from the Fukushima nuclear power plant disaster. Psychological distress was classified as present or absent based on the K6 scale. Respondents recorded their views about the health risks of exposure to ionizing radiation, including immediate, delayed, and genetic (inherited) health effects, on a four-point Likert scale. The associations between psychological distress and risk perception were examined using logistic regression models. Age, gender, educational attainment, history of mental illness, and the consequences of the disaster for employment and living conditions were potential confounders. Findings Out of the 180 604 people who received the questionnaire, we included 59 807 responses in our sample. 8717 respondents were reporting psychological distress. Respondents who believed that radiation exposure was very likely to cause health effects were significantly more likely to be psychologically distressed than other respondents: odds ratio (OR) 1.64 (99.9% confidence interval, CI: 1.42-1.89) for immediate effects; OR: 1.48 (99.9% CI: 1.32-1.67) for delayed effects and OR: 2.17 (99.9% CI: 1.94-2.42) for genetic (inherited) effects. Similar results were obtained after controlling for individual characteristics and disaster-related stressors. Conclusion Among evacuees of the Fukushima nuclear disaster, concern about radiation risks was associated with psychological distress.

S/N	Type of Research	Objective	Result	Conclusions	References
1	Radiation damage to neuronal cells: Simulating the energy deposition and water radiolysis in a small neural network.	To investigate the early biological damage caused by ionizing radiation in a neural network, suggesting that radiation-induced oxidative damage may disrupt normal communication between neurons	The results indicate that the neuron morphology is an important factor determining the accumulation of microscopic radiation dose and water radiolysis products in neurons, and the estimation of the radiolytic yields in neuronal cells suggests that the observed enhancement in the levels of reactive oxygen species may potentially lead to oxidative damage to neuronal components disrupting the normal communication between cells of the neural network.	Neuron morphology affects radiation damage and water radiolysis. Reactive oxygen species may cause oxidative damage.	(Belov *et al.*, 2016)
2	Radiation-induced cognitive impairments	To discuss the cognitive impairments caused by ionizing radiation and the challenges in delivering targeted radiation to the brain	To avoid hippocampus impairment in cranial irradiating, allowing for the same dose sent to the remainder of the brain, poses severe challenges given the central position and unique anatomic shape of the hippocampus	Radiation-induced cognitive impairments pose significant risks for patients undergoing conventional radiotherapy. - Modern intensity-modulated radiotherapy methods can help minimize hippocampus impairment.	(Refahi *et al.*, 2018)
3	Neurocognitive decline following radiotherapy: Mechanisms and therapeutic implications	To review the current knowledge about radiation-induced damage in stem cells of the brain and its potential treatment interventions to prevent and mitigate radiation-related cognitive decline	Ionizing radiation exposure can lead to neurocognitive decline, affecting neurogenesis, neural differentiation, and apoptotic cell death, resulting in lasting disruptions in brain neurochemistry and behavior.	Cranial radiation therapy is associated with long-term neurocognitive decline. Radiation-induced damage affects stem cells and neural cells.	(Pazzaglia *et al.*, 2020)
4	Evoked bioelectrical brain activity following exposure to ionizing radiation.	To investigate the potential neurocognitive deficits and behavioral changes that can occur due to ionizing radiation exposure.	An overview of modern physiological evidence is provided to support the hypothesis on cortical limbic system dysfunction due to the hippocampal neurogenesis impairment as a basis of the brain interhemispheric asymmetry and neurocognitive deficit after radiation exposure.	Cortico limbic system dysfunction due to hippocampal neurogenesis impairment was observed with Potential risks to CNS during space travel	(Loganovsky and Kuts, 2017)
5	An investigation of the single and combined effects of hypogravity and ionizing radiation on brain monoamine metabolism and rats' behavior	To investigate single and combined effects of hypogravity and ionizing radiation on brain monoamine metabolism and rats' behavior	The study found that ionizing radiation had a slight effect on behavior and monoamine metabolism in the brain, but when combined with hypogravity, it reduced the negative effects of hypogravity on locomotor activity and memory.	A combination of hypogravity and ionizing radiation affects behavior and monoamine metabolism.	(Kokhan *et al.*, 2019)

6	Fetal Programming of Brain and Behavior through Ionizing Radiation	To perform fetal Programming of the Brain through ionization	Early gestational exposures to ionizing radiation cause damage to multiple organs and molecular processes while Late gestational changes and behavioural phenotypes are varied and not always investigated	The peer-reviewed support for the fetal programming of neural-genetic activity and behavior in multiple neural regions was provided such as the prefrontal cortex, the cerebral cortex, the hippocampus, the cerebellum, and the hypothalamic-pituitary-adrenal axis.	(Lalonde *et al.*, 2023)
7	Pathological changes in the central nervous system following exposure to ionizing radiation.	Exposure to ionizing radiation can lead to changes in brain neurochemistry and behavior, including cognitive impairment.	Radiation-induced injury can alter neuronal, glial cell population, and brain vasculature. - Hippocampal avoidance prevents radiation-induced cognitive impairment	Pathological changes in the central nervous system were observed	(Bálentová and Adamkov, 2020)
8	Effects of ionizing radiation on the mammalian brain	To examine the effects of ionizing radiation on the mammalian brain	Ionizing radiation can cause damage to the brain, leading to cognitive impairment and disruption of neurochemistry and behavior	Ionizing radiation causes damage to the mammalian brain. - Strategies for prevention and treatment are being developed.	(Hladik and Tapio, 2016)
9	Neurophysiological and Behavioural Dysfunctions After Electromagnetic Field Exposure: A Dose-Response Relationship	To discuss the effects of electromagnetic fields (EMF) on neurophysiological and behavioral dysfunctions	Neurophysiological and behavioral dysfunctions were affected by EMF exposure.	The effects of RF-EMF are cumulative and dose-dependent.	(Sharma *et al.*, 2017)
10	Dose-dependent long-term effects of a single radiation event on behavior and glial cells	The study investigates the long-term effects of low-dose ionizing radiation on the brain, behavior, and its potential association with neurodegenerative diseases	The findings demonstrate long-term and late-onset effects on the brain and behavior after a single radiation event in adulthood and indicated heightened immune activity after high-dose irradiation while conversely, low dose induced more neuroprotective features.	Long-term effects of low-dose radiation on behavior studied. There is a Possible association between neurodegenerative diseases and single radiation dose	(Ung *et al.*, 2021)
11	Fractionated low-dose radiation induces long-lasting inflammatory responses in the hippocampal stem cell niche.	To investigate whether Fractionated low-dose radiation induces long-lasting inflammatory responses in the hippocampal stem cell niche	Low doses of radiation induce long-lasting inflammatory responses. Glial cell activation and transient neuroinflammation occurred	Fractionated low-dose radiation-induced long-lasting inflammatory responses. However, limiting radiation dose to the hippocampus is important for preserving neurocognitive functions.	(Schmal *et al.*, 2021)
12	Effects of low dose ionizing radiation on the brain- a functional, cellular, and molecular perspective	To study, the effects of low-dose ionizing radiation on the brain- a functional, cellular, and molecular perspective	The findings indicated that Low dose ionizing radiation can cause neurological effects and disrupt brain neurochemistry and behavior.	Low-dose radiation can have neurological effects. However, a re-evaluation of low-dose radiation usage is required.	(Narasimhamurthy *et al.*, 2022)
13	Detrimental impacts of mixed-ion radiation on nervous system function	To investigate the detrimental impacts of mixed-ion radiation on nervous system function	The results show that mixed-ion GCR irradiation alters hippocampal neurotransmission and network activity. Finally, Perturbed learning, memory, and anxiety behavior were observed.	The detrimental impacts of mixed-ion radiation on nervous system function were observed	(Klein *et al.*, 2021)

14	Ionizing radiation: brain effects and related neuropsychiatric manifestations.	To discuss the effects of ionizing radiation on brain neurochemistry and the potential for behavioral disruption.	Findings indicated that the brain effects of ionizing radiation (IR) are diverse. Finally, brain abnormalities occurred following medical radiation.	Brain effects of ionizing radiation vary depending on dose and severity.	Marazziti *et al.* (2012)
15	The geomorphological correlation of radiation dose rate	To examine the neuro morphological correlation of radiation dose rate	The study found that low-dose ionizing radiation exposure led to changes in brain neuron function and structure, potentially causing central nervous system disorders.	Ionizing radiation does not cause significant organic changes in brain neurons. However, increasing radiation exposure leads to an increase in dysfunctional and altered neurons, potentially resulting in CNS disorders.	(Ushakov *et al.*, 2019)

Exposure to ionizing radiation during diagnosis and treatment can have implications for patients' mental health. Studies have shown that patients undergoing radiation therapy and Diagnostic radiological procedures may experience acute psychological side effects such as anxiety, depression, fear, and low self-esteem. These psychological reactions can manifest as symptoms including nausea, pain, fatigue, disturbed sleep, and shortness of breath. However, it has been observed that the psychological state of patients tends to improve at the end and after the intervention [56]. Radiation therapy patients need to receive support and care for their psychological well-being. Additionally, the effects of ionizing radiation on the human body can vary depending on the exposure time and absorbed dose, leading to different symptoms and prognosis for the patient. Efforts to minimize radiation risk and protect patients' mental health are crucial in the field of radiation protection[8, 37]

3.3 Radiation Risk Perceptions on Mental Health

Perceived radiation exposure is often described in the context of excessive psychological stress. The impact on mental health is argued to be the largest public health consequence following the Chornobyl disaster, with reports of increased levels of anxiety and depression irrespective of the dose received [10]. The following terms were used to describe the psychological effects of radiation exposure. Radiophobia has been used to denote the fear of radiation exposure following Chernobyl. Phobias are an excessive or unreasonable persistent fear regarding an object or situation. However, in the absence of dosimetry, it is difficult to assess whether or not an individual’s fear of radiation is unreasonable or excessive. Following the Fukushima disaster, where the psycho-societal impact was also reported to be significant [26] despite no deaths being directly caused by acute radiation exposure [48], a new term was introduced *Radiation-anxiety.* In the context of radiation exposure, dread risk typically refers to the negative health effects on the individual and future generations. Unknown risk refers to the possibility that the true health consequences of exposure are not understood.

Fukasawa *et al.* (2020) explored the effects of prolonged radiation risk perceptions on mental health after the Fukushima nuclear power plant accident occurred in 2011. The longitudinal associations of radiation risk perceptions were investigated five years after the accident with psychological distress and posttraumatic stress symptoms two years later among non-evacuee community residents of Fukushima prefecture. A two-wave questionnaire survey was administered to 4,900 randomly sampled residents in 49 municipalities of Fukushima prefecture excluding the evacuation area designated by the Japanese government. Radiation risk perceptions were assessed with a seven-item scale. Psychological distress and posttraumatic stress symptoms were measured by the K6 and the six-item abbreviated version of the Posttraumatic Stress Disorder Checklist-Specific version, respectively. The associations of radiation risk perceptions in the first survey conducted in 2016 were investigated with psychological distress and posttraumatic stress symptoms in the follow-up survey conducted in 2017-18, controlling for the baseline level of distress or symptoms using multivariate logistic regression analyses. Valid responses were obtained from 1,148 residents (23.4%). Higher risk perceptions of radiation exposure in the first survey predicted later posttraumatic stress symptoms but not psychological distress after controlling for baseline symptoms or distress. High-risk perceptions of radiation exposure after nuclear power plant accidents can lead to posttraumatic stress symptoms.

3.4 Cognitive Impairment and Ionizing Radiation

Cognitive functioning refers to mental abilities such as learning, reasoning, problem-solving, decision-making, and attention [11]. The maintenance of cognitive function is crucial to maintain function at all ages. Cognitive abilities have been identified as predictors of school performance in children, work performance in adults, and maintaining independent living and positive well-being in older adults. Factors such as physical activity, education, occupational status, and cognitively stimulating activity can help preserve cognitive functioning. Ionizing radiation (IR) may cause cognitive defects via two broad mechanisms, stemming from perceived and actual exposure (fig 1). First concerning actual exposure effects observed at high doses (>1.0 Gy) and potentially moderate (0.1–1.0 Gy) and low doses (<0.1 Gy), and second concerning psychological effects following perceived exposure at any dose level (0.0 Gy). Both actual IR effects and psychological effects on cognitive function share common mediators such as vascular inflammation, neuroinflammation, and decreased neurogenesis. The mediators of cognitive defects specific to psychological stress include elevated cortisol and health-risk behaviors as shown in the figure. These stress-specific mediators may further exacerbate any possible cognitive defects caused by actual IR exposure. **Collett *et al.* (2020)** identified radiotherapy and diagnostics, occupational roles, space travel, Chernobyl and Fukushima nuclear accidents as possible risk factors for cognitive dysfunction. The deleterious effects of high doses (1.0 Gy) on cognitive functioning are fairly well understood, while the consequences of low (0.1 Gy) and moderate doses (0.1–1.0 Gy) have been receiving more research interest over the past decade.

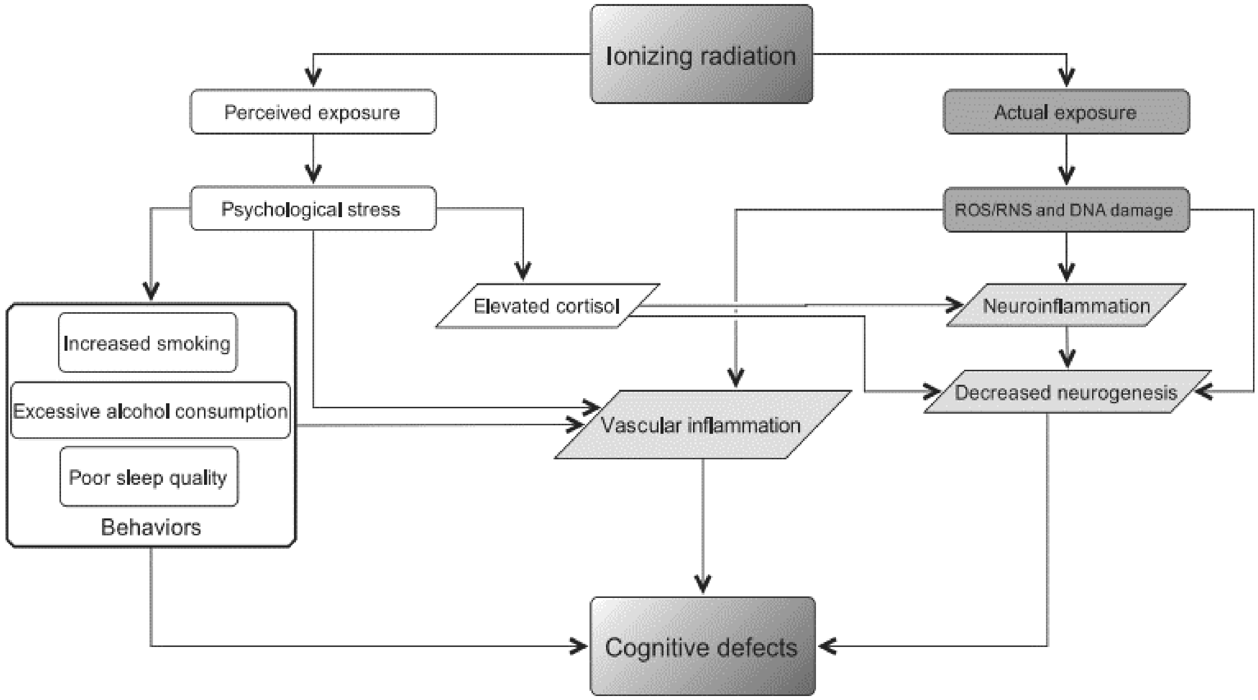

Figure 1: Cognitive effect caused by IR [9]

Studies have shown that accidental radiation exposure can result in cognitive impairments such as mild cognitive impairment, insomnia disorder, and difficulty remembering current events (AlJasem *et al.*, 2023). Additionally, radiation therapy for head and neck tumors can also cause cognitive impairments, with hippocampal dysfunction playing a key role [33]. Repeated low-dose radiation exposure over time can lead to reduced neuronal proliferation, altered neurogenesis, and neuroinflammation, which can contribute to various neurological complications, including cognitive impairment [54]. Furthermore, microwave radiation at 2.45 GHz has been found to have effects on cognitive dysfunction induced by vascular dementia, with chronic exposure leading to recovery of learning-memory performance and hippocampal cell loss. These findings highlight the importance of further research in understanding the risks and mechanisms of radiation-induced cognitive impairment.

Moreover, there is growing evidence that exposure of the adult brain to moderate doses may be detrimental to cognitive functioning. Following the Chernobyl nuclear accident, researchers observed poorer cognitive functioning in clean-up workers, as compared to foresters and agricultural workers over 4 years, with each group receiving mean doses of 0.63, 0.13, and 0.09 Gy, respectively. Furthermore, in a cohort working on the Chernobyl 'Shelter Object' project (0–0.0567 Sv total dose from external and internal sources), an increase in verbal memory deficits was observed compared to before the project (Loganovsky and Vasilenko, 2013). Other studies observed no significant difference in verbal memory between clean-up workers exposed to greater than 0.5 Sv and clean-up workers exposed to less than 0.02 Sv but observed reduced brief global cognitive scores in the former group. The recent NASA twins study observed reductions in cognitive efficiency persisting for up to 6 months post-flight in the flight subject (physical dosimeter = 0.07618 Gy, effective dose = 0.146 Sv) compared to the ground subject (Garrett-Bakelman *et al.*, 2019) and there is emerging evidence from animal studies that support this. Prenatal exposure in rodents is primarily characterized by gross morphological defects of the brain, more subtle hippocampal anomalies, and cognitive defects in later life. Behaviors associated with psychological stress such as cigarette smoking, excessive alcohol, consumption and decreased sleep quality may also impact cognitive functioning**.** Psychological distress was observed to be a risk factor for smoking initiation amongst Fukushima evacuation area residents (Nakano *et al.*, 2018), while research elsewhere observed no association in exposed residents near the Semipalatinsk nuclear test site, despite an increase in anxiety and somatic distress (Semenova *et al.*, 2019)**.** The totality of any direct and psychological stress effects of low/moderate-dose IR exposure on cognitive functioning has implications for policy and public health. The psychological stress associated with nuclear accidents may be further exacerbated through stigma discrimination and social change associated with displacement. Therefore, effort is required at the community level to ameliorate these psychosocial consequences and prevent further psychological stress.

Litvinchuk *et al.* (2022) evaluated cognitive impairments in persons affected by accidental radiation exposure. The study involved residents of the settlements located in the Techa River basin that are included in the database «Man» of the URCRM. The main group «case» consisted of 38 people with the dose to soft tissues ≥0.07 Gy. 38 people with a dose of soft tissues not exceeding the background level were selected using the matched pair case-control method («control»). The following methods were used: clinical method, method of evaluation of cognitive evoked potentials, clinical and psychological method, and statistical methods. In the group «case» the number of examined people with mild cognitive impairment (F06.7) increased. There are statistically significantly more people with cognitive impairments (p=0.039; OR=2.9; 95% CI: 1.2-7.5), insomnia disorder (p=0.022; OR=2.6; 95% CI: 1.04-6.6), complaints of difficulty remembering current events (p=0.034; OR=2.8; 95% CI: 1.1-7.5). In this group, statistically significant differences between the groups in terms of individual values of P300 latency (p=0.009) are observed. The number of people with P300 latency increased by ≥3 Σ is also statistically significantly higher (p=0.025; OR=6.4; 95% CI: 1.3-31.7) in this group. In the group «case»: cognitive impairments are more pronounced. It is manifested in the increase in the number of examined people with organic cognitive impairment, cognitive decline, complaints of deterioration of cognitive functions, and prolongation of P300 latency. **Refahi *et al.* (2018) indicated that** Ionizing radiation is a non-surgical treatment of brain tumors and metastases. Preclinical studies have shown main insights into the harmful effects of radiation on the nervous system in vivo and in vitro. Cognitive impairment such as progressive memory, executive and attention performance deficits indicate a significant risk for patients experiencing conventional radiotherapy. Changes in hippocampus-dependent cognition often state radiation-induced cognitive destruction. Radiation-induced brain injury can impair neuronal, glial, and vascular parts of the brain and may cause molecular, cellular, and functional alterations. To avoid hippocampus impairment in cranial irradiating, allowing for the same dose sending to the remainder of the brain, poses severe challenges given the central position and unique anatomic shape of the hippocampus. Recently, previous studies showed the ability of modern intensity-modulated radiotherapy methods, like LINAC-based intensity-modulated radiotherapy and helical tomotherapy, to permit the delivery of extremely conformal dose distribution**s.**

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4.0 Reduction to radiation-induced psychological and cognitive effects

Radiation-induced cognitive impairment is a significant concern for brain cancer survivors and individuals exposed to radiation. Several studies have explored strategies to mitigate the risk of cognitive dysfunction. One approach involves targeting Toll-like receptor 9 (TLR9) and mitochondrial reactive oxygen species (mtROS) to prevent endothelial damage and dysfunction. Another potential mitigating agent is EUK-207, a catalytic ROS scavenger that has shown promise in mitigating radiation-induced cognitive injury. Additionally, hippocampal sparing intensity modulated proton therapy (HS-IMPT) has been investigated as a means to reduce neurocognitive impairment. By sparing the hippocampus from high radiation doses, the risk of cognitive impairment can be significantly reduced without compromising tumor control. Modern intensity-modulated radiotherapy methods, such as LINAC-based intensity-modulated radiotherapy and helical tomotherapy, have also been shown to allow for the delivery of conformal dose distributions, potentially minimizing hippocampus impairment (Gram *et al.*, 2023; Lindsey *et al.*, 2022). Here are some findings for the reduction of ionizing radiation's impact on mental health

Gram *et al.* (2023) irradiated Mice at a dose of 15 Gy and showed cognitive impairments in the water maze probe trial. EUK-207 mitigated these impairments while not affecting the cognitive performance of sham-irradiated mice in the water maze probe trial. Thus, EUK-207 has attractive properties and should be considered an ideal candidate to mitigate radiation-induced cognitive injury. Gram *et al.* (2023) investigated the predicted risk of neurocognitive impairment of craniospinal irradiation (CSI) and the deliverability and effects of hippocampal sparing. The risk estimates were derived from published NTCP models. Specifically, research leveraged the estimated benefit of reduced neurocognitive impairment with the risk of reduced tumor control. For the dose planning study, a total of 504 hippocampal sparing intensity modulated proton therapy (HS-IMPT) plans were generated for 24 pediatric patients who had previously received CSI. Plans were evaluated for target coverage and homogeneity index to target volumes, the maximum, and the mean dose to OARs. Paired t-tests were used to compare hippocampal mean doses and normal tissue complication probability estimates. The median mean dose to the hippocampus could be reduced from 31.3 GyRBE to 7.3 GyRBE ($p < .001$), though 20% of these plans were not considered clinically acceptable as they failed one or more acceptance criteria. Reducing the median mean hippocampus dose to 10.6 GyRBE was possible with all plans considered clinically acceptable treatment plans. By sparing the hippocampus to the lowest dose level, the risk estimation of neurocognitive impairment could be reduced from 89.6%, 62.1%, and 51.1% to 41.0% ($p < .001$), 20.1% ($p < .001$) and 29.9% ($p < .001$) for task efficiency, organization, and memory, respectively. Estimated tumor control probability was not adversely affected by HS-IMPT, ranging from 78.5 to 80.5% for all plans. The estimates of potential clinical benefit in terms of neurocognitive impairment were presented and demonstrate the possibility of considerably reducing neurocognitive adverse effects, minimally compromising target coverage locally using HS-IMPT.

S/N	Types of research	Objective	Results	Conclusions	References
1	Innovative leakage stabilization system for mitigation of ionizing radiation-induced effects	Focuses on the development of a novel radiation leakage stabilization circuit using ionizing radiation sensors	The proposed LSC reduces VTC shift by 98.5% for up to 1 Mrad radiation exposure. Sensor's sensitivity: 0-10 krad: 20 mV/krad, 10-100 krad: 3.9 mV/krad, 100 krad-1 Mrad: 0.6 V/krad.	The proposed LSC reduces radiation-induced effects significantly. The capacitive radiation sensor used in LSC is reliable.	(Anjankar and Dhavse, 2023)
2	Selective Inhibition of Microglia-Mediated Neuroinflammation Mitigates Radiation-Induced Cognitive Impairment	To discuss the use of MW-151, a selective inhibitor of proinflammatory microglial cytokine production, as a potential mitigation strategy for radiation-induced cognitive impairment.	Neuroinflammation mediated by activated microglial cytokines contributes to radiation-induced cognitive impairment. - Selective inhibition of microglia can mitigate neuroinflammation.	Neuroinflammation mediated by activated microglial cytokines contributes to radiation-induced cognitive impairment. - Selective inhibition of microglia can mitigate this impairment.	(Jenrow *et al.*, 2013)
3	Radiation Sensor Design for Mitigation of Total Ionizing Dose Effects	To design a radiation sensor to minimize radiation effects on CMOS ICs.	Design of radiation sensor for minimizing radiation effects - The sensitivity of the sensor for 0-1 Mrad is 0.5 mV/krad	- Novel radiation sensor designed to minimize radiation effects - Sensor sensitivity for 0-1 Mrad is 0.5 mV/krad	(Anjankar and Dhavse, 2022)
4	Use of rice bran oil distillate extract for prevention and mitigation of the effects of radiation	The provided paper does not mention anything about the mitigation of radiation-induced psychological and cognitive effects. The paper focuses on the radioprotective and antioxidant properties of a local-rich fraction of rice bran oil distillate extract.	- Rice bran oil distillate extract is radioprotective. - Rice bran oil distillate extract protects against oxidative damage.	- Rice bran oil distillate extract is radioprotective. - It can protect against oxidative damage.	Compadre *et al.* (2021)
5	Mitigation of Radiation Effects in SRAM-Based FPGAs for Space Applications	The provided paper does not discuss mitigation techniques for radiation-induced psychological and cognitive effects. The paper focuses on mitigation techniques for radiation effects in SRAM-based FPGAs for space applications.	- Comprehensive survey of literature on radiation effects mitigation - Tutorial for space engineers and decision-makers	- SRAM-based FPGAs require mitigation techniques for radiation effects. - Design guidelines for mitigation techniques are provided.	(Siegle *et al.*, 2015)
6	Molecular Pathways: Radiation-Induced Cognitive Impairment	The paper discusses the use of neuronal stem cells and clinically prescribed drugs, such as PPAR and RAS blockers, to prevent radiation-induced neuroinflammation and cognitive impairment. These interventions show promise in improving the quality of life of brain tumor patients who receive radiotherapy.	- Late radiation effects cause progressive cognitive impairment. - Preclinical studies suggest stem cell therapies can prevent cognitive impairment.	- Late radiation effects cause progressive cognitive impairment. - Stem cell therapies may prevent radiation-induced cognitive impairment.	Greene-Schloesser *et al.* (2013)

7	Reliability analysis of radiation-induced fault mitigation strategies in field programmable gate arrays	The provided paper does not discuss mitigation strategies for radiation-induced psychological and cognitive effects. The paper focuses on the engineering design and analysis of a radiation-tolerant computer system for use in space flight applications.	Design and analysis of a radiation tolerant computer system - Reliability analysis of radiation effects mitigation strategy	The inclusion of spare circuitry increases system reliability. - Migrating single points of failure to an older technology node improves reliability.	(Hogan, 2014)

Table 2: Some findings on mitigating the impact of ionizing radiation

Conclusion

In conclusion, the systematic review of the psychological and cognitive effects of ionizing radiation exposure underscores the critical importance of understanding the multifaceted impact of such exposure on human well-being. The body of research analyzed in this review provides valuable insights into the intricate interplay between radiation exposure and the human psyche. The review has highlighted the substantial variability in the psychological and cognitive effects of ionizing radiation. This variation can be attributed to factors such as the dose, duration, and frequency of exposure, as well as individual differences in susceptibility. Additionally, the findings emphasize that ionizing radiation can induce a range of psychological responses, from acute stress reactions to long-term psychiatric disorders. The cognitive effects also exhibit a diverse spectrum, including impairments in memory, attention, and executive functions. Furthermore, it is evident from this study that the psychological and cognitive effects of ionizing radiation are not limited to the individual alone. The impact extends to families, communities, and societies as a whole. This emphasizes the necessity of adopting a holistic approach to address the psychosocial consequences of radiation exposure. Several studies have explored strategies to mitigate the risk of cognitive dysfunction as indicated in this review. The review also underscores the need for continued research in this field, particularly in the assessment of long-term and low-dose radiation exposure. Understanding the delayed effects and cumulative impact of radiation on psychological and cognitive well-being remains an important avenue for future investigation. In practical terms, the findings call for the development of comprehensive support systems and interventions for individuals exposed to ionizing radiation. Such initiatives should encompass not only the physical health but also the psychological and cognitive well-being of those affected. Moreover, raising awareness about the potential psychosocial consequences of radiation exposure is vital in promoting resilience and mitigating the stigmatization often associated with such exposure. Finally, this systematic review illuminates the intricate relationship between ionizing radiation exposure and its psychological and cognitive effects. It highlights the importance of recognizing and addressing these psychosocial consequences, not only to support affected individuals but also to foster a deeper understanding of the broader implications for society as a whole. As our understanding of this field continues to evolve, so too must our efforts to ameliorate the psychological and cognitive burdens borne by those exposed to ionizing radiation.

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