CLINICAL AND PSYCHOPHYSIOLOGICAL DATA OF THE CHERNOBYL PERSONNEL WORKING ON TRANSFORMATION OF THE OBJECT "SHELTER" INTO AN ECOLOGICALLY SAFE SYSTEM

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Abstract

Objective: The aim of this study is to assess possible changes in central nervous system, such as cognitive functions and brain bioelectric activity, after a period of work towards the conversion project of the "Shelter" into a safe and environmentally-safe system. This might lead to an improvement of clinical and psychophysiological criteria for professional selection and personnel admittance to work in particularly dangerous and harmful conditions amongst the presence of radiological and severe industrial risk factors.

Method: 196 males (age between 20-52 years old; M±SD: 35,9±8,2 years) were involved in this study and were being prospectively examined before, during and after the time of work at the "Shelter" object between 2004-2008. Based on the results of our psycho-neurological and neurophysiological investigations, an Excel database spreadsheets was created. This database contained 353 parameters for each of 196 examined individuals. Totally 69188 variables were analyzed.

Results: A prospective study showed that exposure to radiological (exposure in range 0 – 56.7 mSv, M±SD:19,9±13,0 mSv) and industrial risk factors may lead to the onset of a form of cognitive chronic fatigue syndrome characterized by dysfunction of cortical-limbic system, chiefly in the dominant (left) hemisphere with an important involvement of hippocampus. By the means of neurophysiological and neuropsychological assessments we could highlight early changes in brain likely caused by the presence of radiological and industrial risk factors occurring in conditions of high psycho-emotional tension at work. An effect of selection of "radiation resistant worker" was found. That is, individuals, who earlier were exposed to radiation without consequences for their health, were more resistant to further irradiation.

Conclusions: This work provides further evidence that implementing constant monitoring and rehabilitation are necessary measured for personnel employed within the "Shelter" project.

Key words: low doses, ionizing radiation, computer electroencephalography, cognitive functions, chronic fatigue syndrome, "Shelter" object

Declaration of interest: none

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Introduction

The Object "Shelter" (OS) of the Chernobyl Nuclear Power Plant (ChNPP) is unique in the world and its transformation into ecologically safe system is a unique problem whose solution requires the efforts of both Ukraine and the international community. At present, the main work of converting the Shelter into an environmentally safe system is implemented in the framework of the international project Implementation Plan (Shelter Implementation Plan, SIP). Medical and Dosimetric Means of the health personnel involved in these works, occupies a prominent place amongst the most urgent problems of modern clinical radiobiology, radiation hygiene and radiation protection (Bachner et al. 2006, Bebeshko et al. 2005, Bebeshko et al. 2007, Bebeshko et al. 2009, Bebeshko et al. 2010, National Report of Ukraine 2011). Mental health and physiological support work are key parts of the health maintenance on OS transformation into ecologically safe system (Bachner et al. 2006, Bebeshko et al. 2005, National Report of Ukraine 2011, Loganovsky et al. 2005, Loganovsky et al. 2009).

One of the unique features of working on OS is that the staff is required to perform tasks under conditions of high radionuclide ionizing radiation (IR) in areas destroyed by the 4th unit of ChNPP or close to it, that is, on radioactively contaminated territories. Whilst performing this type of work, there is a high risk of incorporating transuranic elements (plutonium- 238-

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241, americium -241) and strontium -90, cesium -137.

Debate on the radio-sensitivity of the central nervous system (CNS) is an ongoing matter. Recently, it has been collected a large amount of new neuro-radiobiological data on molecular mechanisms of radiation damage to the brain and new evidence of vulnerability of the brain to even low doses of IR emerged (Loganovsky 2009). CNS is radiosensitive, the degree of dysfunction has been proved by the electrophysiological, biochemical and behavioral parameters assessed (Gourmelon et al. 2009). Current views on the pathogenesis of radiation damage to the brain include dysfunction of neurogenesis in the hippocampus, changes in gene expression profiles, neuro-phlogistic reaction, neuro-signal alteration, apoptosis, neuronal death and injury as a result of secondary lesions (Lestaevel et al. 2008, Mancuso et al. 2008, Rola et al. 2008, Lowe et al. 2009, Rzeszowska-Wolny et al. 2009, Yang et al. 2010, Yang et al. 2011, Karlsson et al. 2012, Raber et al. 2011).

Chronic Fatigue Syndrome (CFS) is considered as a typical medical-biological effects of radiological disasters resulting by the concomitant influence of law and very law doses of IR and stress (Loganovsky 1998, Loganovsky 2000a, Loganovsky 2000b, Volovik et al. 2005). CFS may be caused by alteration of fundamental regulatory systems, such as, nervous, endocrine and immune systems (Hyde et al. 1992, Patarca-Montero et al. 2000, Prins et al. 2006, Light et al. 2010), and the cerebral dysfunction in CFS present with lateralization to fronto-temporal area of the dominant (left) hemisphere of the brain (Flor-Henry et al. 2010). Thus, CFS may be considered as a form of initial development of neurodegeneration, cognitive deficits and other neuropsychiatric disorders due to the influence of small doses of IP (Loganovsky 2000b, Volovik et al. 2005, Bazyka et al. 2009, Volovik et al. 2006, Volovik et al. 2005, Pall 2008).

The study of the brain information processing, using the most advanced technology analysis of bioelectric cerebral activity is a promising method for the assessment radio-cerebral effects and the developing of new ways for determining bio-indicators of exposure in humans. Quantitative electroencephalography (qEEG) with results chart data represent a relatively accessible, non-invasive method for screening and evaluating un-irradiated, irradiated and over-exposed people who happen to get in contact with the source IR and radiological emergency situations during their work (Loganovsky et al. 2008). Prospective Psychophysiological clinical observation, with assessments before, during and after the work on SO, of site personnel provided by personal dosimeters represents a unique opportunity to study the effect of low doses of IR on the human brain.

Methods

The study included 196 males, ranging from 20 to 52 years of age (M ± SD: 35,9 ± 8,2 years), who were prospectively surveyed between 2004-2008; the study involved persons who passed the preliminary medical tests and were eventually allowed to work at the Shelter (preliminary medical examinations were – a set of measures determined by medical expert to evaluate health and performance of staff prior to their involvement, as employees, to participate to the SIP for the Shelter). One hundred forty-three workers underwent special biophysical and medical monitoring, since they were found exceeding the limit value content of transuranic elements in daily fecal samples (239Pu content at levels exceeding 1.5 MBq in a sample of feces). All persons involved in the study were the final (output) control on completion of the works at the Shelter. Control test was to work on the OS.

Depending on different previous contacts with sources of IR, the subjects surveyed were divided into the following subgroups: subgroup A - participants of the accident (liquidators) at Chernobyl (n = 20); subgroup B – those who previously worked in the nuclear industry (n = 33); subgroup C – workers who previously not worked with the source IR (n = 143).

It was found that between 2004-2008 Shelter staff were exposed to external irradiation in the dose range of 0-54,3 mSv (M ± SD: 19,5 ± 12,8 mSv), internal irradiation in the dose range of 0-2,4 mSv (M ± SD : 0,4 ± 0,5 mSv) and total irradiation resulting as 0-56,7 mSv (M ± SD: 19,9 ± 13,0 mSv).

Clinical neurological and psychiatric examination were performed by the means of a routine scheme. The functional state of the brain was evaluated on the basis of qEEG topographic mapping results. The following neuropsychological and psychometric methods were used:

a) Rey Auditory Verbal Learning Test (RAVLT) to evaluate the nature and severity of memory dysfunction, learning capacities (immediate recall of 15 words, short-term memory) and a List A (15 words) 20-min delayed recall and recognition task (long term memory). The main is to learn 15 words (on 5 trials): there is a score for each call (corresponding to the total score for recalled words for each trial, a total 20-min delayed recall score and a total score for the words recognized) (Rosenberg et al. 1984);

b) General Health Questionnaire (GHQ-28), which assesses somatoform symptoms, anxiety and insomnia, social dysfunction and severe depression, was used to study psychopathology based on self-assessment (Goldberg 1981);

c) Zung Self-Rating Depression Scale (SDS) which determines the level of unmasked depression based on self-assessment (Thurber et al. 2002);

d) Brief Psychiatric Rating Scale (BPRS) for unified quantitative assessment of psychopathological symptoms (Overall et al. 1962).

Data analysis was performed using STATISTICA 7.0 software (StatSoft Inc.). Statistical processing included descriptive statistics, analysis of variance, Student's t-test, paired t-test, the chi-square test (criterion χ^2), Pearson's product-moment correlation, and regression analysis. The paired t-test was used to analyze data when a pair of measurements was obtained for each individual. The differences between groups were considered to be significant at alpha <0.05. If the expected frequencies of some of the cells of the 2x2 tables were too small (<5), the two-tailed Fisher's exact test was used instead of the chi-square test.

Results

Subjects working for OS did not present significant changes in the frequency and no pathological pattern of the nervous system. However, we observed an increased frequency of mild cognitive disorder (F06.7), from 7 cases (3.6%) at the baseline to 22 (11.2 %) at the endpoint, that is, after their completion of their period of work on the site ($\chi2$ =8.4; p=0.004). We also found an increased frequency of abnormal qEEG (R 94.0). If work on OS was not allowed to any candidate with abnormal electroencephalogram at the initial assessment, after working at the site, 10 (5.1%) workers showed significant qEEG alteration (Fisher's exact test: $p < 0.001$) (**table 1**). Interestingly, neuro-psychiatric disorders occurred only in the C subgroup, that is, persons who had not previously been in contact with

Table 1. *Identified disorders in persons surveyed (n=196)*

Diagnosis	Before work on OS abs. (%)	χ2	p	After working on OS abs. (%)
Showed no illness	155 (79%)	8.64	<0.01	129 (65.8%)
Mild cognitive deficits (F06.7)	7 (3.6%)	8.38	<0.01	22 (11.2%)
Pathological EEG (R94.0)	0	--	<0.05	10 (5.1%)

IR sources.

The results of the analysis of neuropsychological assessment on verbal test Ray (RAVLT) traced the formation of a kind of cognitive deficits after work at OS (**figure 1**).

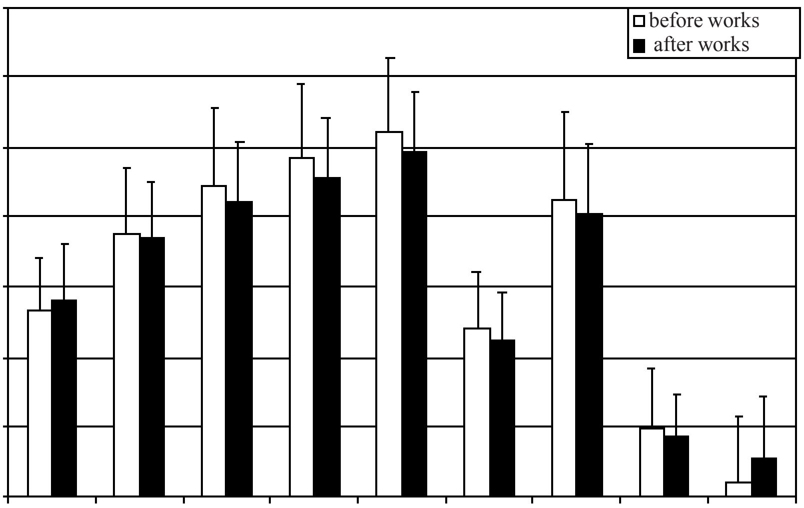


Figure 1. *Curve memorizes all examinees*

Although direct memory (the first presentation of words – A1) increased, other cognitive parameters deteriorated. We observed a statistically significant decrease in verbal learning (fifth presentation of words – A5). If prior to working at the site, the average memorized words were (M ± SD) 10,43 ± 2,09, after working at the Shelter the same variable was 9,86 ± 1,70 words (p <0,01). Particularly relevant seemed the deterioration of short-term verbal memory (word list reps A6) and the increased proactive interference effect of verbal information (number of repeated words list B); such as, the preservation of material degradation under the influence of information that has been previously memorized and which tend to interfere. In other words, after working at the Shelter people developed learning barriers caused by the exposure to information learned in the past. However, the effect of retroactive interference of verbal information (difference of repeated word lists A5 and A6 (A5-A6); i.e. the preservation of material degradation under the influence of learning or manipulation with further information, which might interfere, decreased.

Cognitive impairment was found mainly in subgroup C - employees who had not previously worked with IR sources. This may indicate that the subjects who had been exposed to IR, but remained healthy, may be more resistant to further exposure. These results can be explained by the selection effect of "radio-resistant employees".

The clinical (visual) assessment of EEG patterns showed a reduction of the frequency of an organized type of brain activity (the main component of which is organized by the α-activity) and several common types of disorganized EEG after working at the Shelter. Hyper-synchronous frequency and flat polymorphic EEG types reported at baseline did not change during EEG monitoring (**table 2**). Reduction in the organized type of EEG and increased frequency of disorganized EEG type after working at the Shelter were found in those workers who had been found exceeding the content limit value of transuranic elements. Alteration of brain activity was found amongst the OS staff, presenting with an excess of 239Pu at more than 1.5 MBq in a sample of feces. Moreover, EEG changes were identified amongst the subjects who had not previously worked in contact with IR sources.

The analysis of topographic charting spectral power and dominant frequency of brain activity after working at the Shelter showed the following changes: 1) increase in relative and absolute spectral power δ-activity, mainly in the anterior brain (frontal-temporal area) (**figure 2**), 2) reduction of relative θ-power in the right temporal area with increasing absolute θ-power

Table 2. *Changes in the types of electrical activity of the brain after working on OS*

Type of EEG	Before work on OS (n=196)	χ^2	p	After working on OS (n=196)
Organization EEG	38 (19%)	9.33	<0.01	17 (9%)
Gipersynchronic EEG	63 (32%)	0.43	>0.05	57 (29%)
Disorganized EEG	25 (13%)	5.20	<0.05	42 (21%)
Flat polymorphic EEG	70 (36%)	0.06	>0.05	80 (41%)

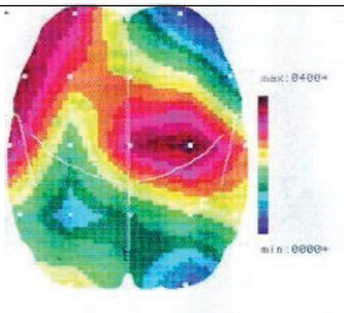
Table 3. *Characteristics of the relative power of informative indicators kEEG Shelter staff have surveyed (n = 196)*

Setting and retracting	Before work on OS M±SD	*paired t*-test	p	After working on OS M±SD
δ-power, % F7	20.78±4.65	-2.49	<0.05	21.81±5.46
T3	19.64±4.59	-2.02	<0.05	20.38±4.82
T5	18.54±4.35	-2.83	<0.01	19.47±4.97
θ- power, % T4	26.11±3.63	2.67	<0.01	25.37±3.56
α- power,% T4	33.07±6.43	-3.59	<0.001	34.60±7.30
T5	36.92±8.43	2.23	<0.05	35.83±7.84
β- power,% C4	19.64±4.63	2.96	<0.01	18.82±4.35
T6	19.08±4.34	2.42	<0.05	18.42±4.43

Table 4. *Characteristics of the absolute power of informative indicators kEEG Shelter staff have surveyed (n = 196)*

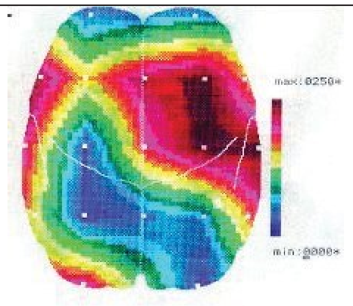
Setting and retracting	Before work on OS M±SD	*paired t*-test	p	After working on OS M±SD
δ- power, mkV^2·Hz$^-$	10.58±3.66	–3.54	<0.05	11.79±4.27
F3	8.01±2.75	–2.79	<0.05	8.69±3.10
F4	8.13±2.88	–2.21	<0.05	8.69±3.05
F7	8.08±2.64	–4.67	<0.05	9.23±3.44
T3	6.26±1.75	–3.56	<0.05	6.92±2.48
T4	6.95±2.25	–2.59	<0.05	7.43±2.45
C4	5.70±1.99	–4.39	<0.05	6.49±2.27
T6	9.11±4.08	–2.37	<0.05	10.02±4.21
P4	7.13±2.61	–1.98	<0.05	7.60±3.03
O1	10.11±4.01	–2.49	<0.05	10.84±4.57
θ- power, mkV^2·Hz$^-$	11.14±3.42	–3.15	<0.05	11.98±3.96
F4	9.54±3.18	–3.16	<0.05	10.37±3.71
F7	9.43±3.17	–2.88	<0.05	10.15±3.36
T3	7.79±2.45	–2.00	<0.05	8.20±2.89
T4	8.30±2.69	–3.29	<0.05	9.03±3.08
C4	7.20±2.54	–3.57	<0.05	7.98±3.11
T6	11.46±5.08	–2.01	<0.05	12.35±5.59
O1	12.85±5.57	–2.08	<0.05	13.56±6.11
α- power, mkV^2·Hz$^-$	18.37±9.60	–2.05	<0.05	19.81±10.59
F4	15.61±8.19	–2.29	<0.05	16.87±8.67
T4	11.80±5.46	–5.26	<0.05	14.02±7.39
C4	11.80±6.12	–3.53	<0.05	13.40±7.54
T6	21.03±12.94	–2.02	<0.05	23.08±13.68
β- power, mkV^2·Hz$^-$	7.82±2.67	–2.28	<0.05	8.25±2.70
T4	7.04±2.85	–2.65	<0.05	7.56±2.71
C4	6.05±2.67	–2.19	<0.05	6.43±2.65
Dominant frequency, Hz	8.35±0.54	3.24	<0.05	8.22±0.55

mainly in the anterior brain (**figure 3**), 3) an increase in absolute and relative α-power, especially in the temporal areas of the redistribution of α-activity to the front of the brain (**figure 3**), 4) reduction of the relative β- power in the right temporal area with an absolute increase β-power in the anterior brain, and 5) reduction of the dominant frequency in the left temporal area (**figure 4**). In general, changes in brain activity after



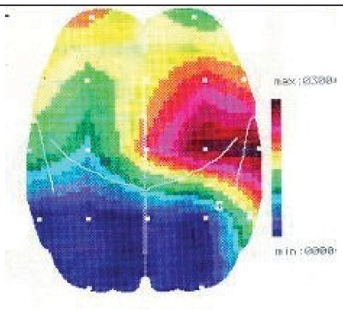
F1: 0354 Fz: 0250 C3: 0164 T5: 0191
T6: 0237 F2: 0000 F4: 0220 Cz: 0350
P3: 0105 O1: 0249 F7: 0466 F8: 0066
C4: 0438 Pz: 0150 O2: 0047 F3: 0279
T3: 0355 T4: 0259 P4: 0198

Figure 2. *t-test increase in δ-absolute power in all the examined*



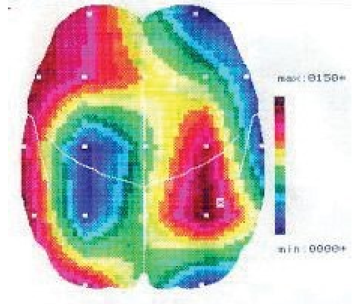
F1: 0035 Fz: 0225 C3: 0028 T5: 0168
T6: 0200 F2: 0051 F4: 0316 Cz: 0190
P3: 0019 O1: 0208 F7: 0288 F8: 0131
C4: 0357 Pz: 0045 O2: 0020 F3: 0155
T3: 0200 T4: 0329 P4: 0070

Figure 3. *t-test increase in θ -absolute power in all the examined*



F1: 0205 Fz: 0180 C3: 0087 T5: 0000
T6: 0202 F2: 0127 F4: 0228 Cz: 0220
P3: 0000 O1: 0005 F7: 0183 F8: 0188
C4: 0352 Pz: 0005 O2: 0000 F3: 0135
T3: 0141 T4: 0525 P4: 0011

Figure 4. *t-test increase in α -absolute power in all the examined*



F1: 0129 Fz: 0095 C3: 0003 T5: 0324
T6: 0067 F2: 0000 F4: 0070 Cz: 0065
P3: 0006 O1: 0129 F7: 0155 F8: 0000
C4: 0135 Pz: 0085 O2: 0003 F3: 0119
T3: 0133 T4: 0000 P4: 0180

Figure 5. *t-test decrease in the dominant frequency in all the examined*

working at the Shelter can be interpreted as a damage of the cortico-limbic system with a key involvement of the hippocampus (**table 3**, **4**).

In Shelter workers who were found as exceeding the limit content value of transuranic elements (239Pu content of 1.5 MBq in a sample of feces) the most significant changes in qEEG parameters were found; specifically: 1) an increase in the relative and absolute δ-capacity in the anterior brain, 2) an increase in the absolute θ-power, 3) redistribution of α- power to the front of the brain, and 4) reduction of the dominant frequency in the left frontal- temporal area. Moreover, in accordance with the above, amongst those OS workers who were found as not exceeding the limit content value of transuranic elements (239Pu content of 1.5 MBq in a sample of feces) such qEEG alterations were absent.

Risk factors potentially affecting neurophysiological functioning were also evaluated, such as, slowed down brain activity (increased δ-and θ-power, reduced α-power) dependent on alcohol, smoking and time spent at the Shelter. However, the detected increase in θ-power brain activity resulted dependent on radiation dose.

Cognitive impairment and changes in qEEG parameters were found mainly in the subgroup C – employees who not previously worked with the source IR. However, amongst the subgroup A of OS workers – cleaning workers of Chernobyl and those who had worked in the nuclear industry -subgroup B, qEEG changes observed were minor. This would support the impression regarding possible effect of selection "radio-resistant workers", i.e. that subjects who had been exposed to IR, but remained healthy, may be more resistant to further exposure.

We hypothesized a synergistic role of duration of working at the Shelter and the total radiation dose to determine changes in the frequency pattern of cerebral bioelectrical activity. The qEEG dominant frequency decreases was proportional to the duration of woring at the Shelter and IR dose, especially in the central area of the right C4 ($r = -0,19$; $p < 0,05$) and left temporal area T5 ($r = -0,18$; $p < 0, 05$).

The dominant frequency amongst the subjects also increased proportionately with age.

Amongst the OS workers who had previously taken part as liquidators to deal with consequences of the 1986 Chernobyl nuclear disaster (subgroup A), it was found decreased δ- and θ- EEG power and dominant frequency, and α- power increase, mainly in the fronto- parietal areas, in proportion to the radiation dose. Duration of working at OS in this group may have caused to slow the cerebral bioelectrical activity. In Shelter staff who had previously worked in nuclear power plants (subgroup B), it was observed a slow qEEG pattern depending on the radiation dose and time works for OS.

Analysis of correlation between performance assessment, using questionnaires, diagnostic psychological tests and qEEG parameters on the sample, reported the following: the smaller was the dominant frequency of bioelectrical cerebral activity, the greater was the rate of the total score BPRS (in lead F4 $r = -0,18$; $p < 0.05$); the larger was the figure A5 in the study of verbal learning, the lower was the value of δ-power (in lead T5 $r = -0,20$; $p < 0,05$); moreover, the larger was the value of α-power, the better were cognitive performance functions. These parameters provided a likely but still weak correlation power.

In the subgroup A, with increasing β-power there was an increase in the performance of RAVLT A5 test (in lead T3 $r = -0,66$; $p < 0,05$) and in the subgroup B (in designated F3 $r = -0,55$; $p < 0,05$), an increase in qEEG dominant frequency (in lead T5 $r = -0,59$; $p < 0,05$) accompanied by the reduction of BPRS scores. The subgroup showing an increase of the spectral power in all qEEG ranges, accompanied by a decline in A4 and A5 test RAVLT, and an increase in β-power (in lead F8 $r = -0,47$; $p < 0,05$), correlated with a decrease in the overall BPRS rate. In the workers it was noted an increase in spectral power, which may be a key indicators of qEEG bands that correlated with the reduction of verbal learning RAVLT; increase in dominant qEEG frequency (at leads F3, O1) was accompanied by a decrease of BPRS scores, while an increase in δ- power (in leads T3, F3, O1) associated with the increase in BPRS scores.

Discussion

Our work is intending to highlight the demand existing for evidence-based data to further expand clinical expertise in this field and to stress the importance of ad hoc neurophysiological and neuropsychological research to optimize health monitoring of subject candidates for working and the staff already working at OS. We also want to bring the scientific community attention to the importance of developing and implementing a system of psycho-physical health monitoring aimed at prevention of severe neuropsychiatric diseases during work at the Shelter, in particular when considering the severely dangerous and hazardous conditions of being exposed to IR and other common industrial risk factors. It was observed that the influence of risk factors for mental health amongst OS staff minor, which may be explained by the high quality selection of healthy personnel to work on the site.

However, several neuropsychiatric alteration, such as, changes in cognitive function and brain activity in some employees were dependent on radiation risk factors linked with working at OS, which in turn would suggest a possible role of low doses of IR and the likely neurotoxicity of transuranic elements.

Our observations indicate that people who had been previously exposed to IR, but were allowed to work at OS, remained healthy after initial radiation exposure and tended to be more stable to further irradiation. This may indicate a selection effect suggesting that there might be a sort of “radio-resistant employee “.

Our data confirmed the hypothesis on radiation-induced reduction of neurogenesis in the hippocampus as a possible mechanism of cognitive deficits and the involvement of cortical- limbic changes in the dominant hemisphere of the brain after exposure to low doses of IR. In particular, it is worth pointing out the alteration of verbal parameters that are a function of the dominant hemisphere, as well as memory and θ-range electrical activity of the brain in which the hippocampus is implicated.

Overall, neuropsychiatric, cognitive and neurophysiological brain pattern changes after working at the Shelter can be interpreted as a cognitive type of chronic fatigue syndrome due to the influence of dangerous and hazardous working conditions on this site, including the effects of low and very low doses of IR and possible neurotoxicity of transuranic elements.

These results indicate that personnel working at converting the Shelter into an environmentally safe system requires constant medical monitoring and rehabilitation.

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