Intelligence and Brain Damage in Children Acutely Irradiated in Utero As a Result of the Chernobyl Accident

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Abstract

The objective of the study was psychometric, neurophysiological and neuropsychiatric characterisation of acutely prenatally irradiated children. 100 randomly selected children who were in utero (born between April 26th, 1986 and February 26th, 1987) at the time of the Chernobyl accident and their mothers evacuated to Kiev as well as 100 classmates of the children were examined by the Wechsler Intelligence Scale for Children (WISC), electroencephalography (EEG) and clinical methods at the age of 10–12 years old. Foetal doses in the acutely exposed group were 11–92 mSv, in the comparison group — 0–3 mSv; foetal thyroid doses — 0.2–2 Gy and 0–0.04 Gy, respectively. The acutely exposed group showed a lower mean verbal IQ than in the comparison group (105.3±13.1 vs. 118.1±13; $p < .001$) and a lower mean full scale IQ (112.1±15.4 vs. 120.9±11.5; $p < .001$). In addition the followings were observed in the acutely exposed group; WISC performance/verbal discrepancies with verbal decrements; a higher frequency of low-voltage and epileptiformal EEG-patterns and left hemisphere lateralised dysfunction; an increase ($p < .001$) of δ- and β-power and a decrease ($p < .001$) of θ- and α-power; an increased frequency of paroxysmal and organic mental disorders, somatoform autonomic dysfunction, disorders of psychological development, and behavioural and emotional disorders. Cerebral dysfunction was etiologically heterogeneous. This study suggests that prenatal irradiation at a thyroid foetal dose range of 0.2–2 Gy and a foetal dose of 11–92 mSv can result in detectable brain damage.

Background

Considerable strides have been made in the recent past in the knowledge and understanding of the effects of ionising radiation on the developing brain. A dose of 10 mSv is postulated to cause a reduction in IQ (intellectual quotient) of 0.3 [*1*]. The developing human brain is substantially more susceptible to teratogenic insults than most other embryonic and foetal structures [*2*].

The brain develops in 4 overlapping stages. The main developmental event of the first stage (0–7 weeks after fertilisation) is the commencement of neuronal mitosis during which the brain produces two to three times the full adult complement of neurones [*3*]. Impaired cell division presumably gives rise to fewer neurones and may result in dysraphic abnormalities (at 3–4 weeks), cerebellar agenesis (at 4–10 weeks) and small head size (at 3–12 weeks) [*2*].

The second stage (8–15 weeks) is the first critical period of cerebrogenesis and corresponds to the most rapid proliferation of neuronal elements and substantial migration of neurones to the neocortex from their proliferative zones near the cerebral ventricles [*4–6*]. Disturbances in cell migration may result in ectopic grey matter and dysplasia [*2*]. Learning disorders and some form of mental retardation may arise from abnormal migration [*3*].

The third stage (16–25 weeks) is the second critical period of cerebrogenesis. This stage corresponds to the progress of neuronal differentiation and synaptogenesis, and the beginning of the formation of brain architecture [*2*]. The most striking neurobiological event at this stage is programmed cell death or apoptosis, when more than 50% of migrated neurones are eliminated prior to birth [*3*]. The recently proposed neurodevelopmental theory of the genesis of schizophrenia shows that the second trimester of pregnancy is critical, and disturbed neuronal apoptosis is considered as a key neurobiological abnormality leading to schizophrenia [*7*]. Programmed cell death, essential to the development of the normal brain and its adnexa, could be accelerated or otherwise altered by ionising radiation [*2*].

The fourth stage (26+ weeks) indicates cell differentiation, progressive growth of dendrites and axons, further formation of synapses and cerebral cytoarchitecture [*2,8*]. Synaptic development is also characterised by distinct waves of overproduction and elimination [*3*]. Possible damage of thalamocortical innervation (at 24–33 weeks) is indicated by abnormal cortical differentiation, and by involution of subpial granular layer (at 24–38 weeks) — so-called marginal heterotopias [*2*].

Over the years, the Atomic Bomb Causalty Commission (ABCC) and its successor, the Radiation Effects Research Foundation (RERF), have established several overlapping samples of individuals prenatally exposed to the atomic bombing of Hiroshima and Nagasaki. According to the DS86 system of dosimetry there are 1,544 clinical samples of prenatally exposed survivors from a sample of 1,599 (including 509 nonexposed persons) derived from the T65DR system of dosimetry. Severe mental retardation has been clinically diagnosed in 30 (5 in nonexposed) children [*2, 9*]. Analysis of the Koga intelligence test scores obtained in 1955 on the prenatally exposed survivors has revealed a progressive shift downwards in the distribution of these scores with increasing exposure. There is an apparent dose-related reduction in mean IQ for the groups irradiated in the periods 8–15 weeks and 16–25 weeks after fertilisation. This effect is still apparent when the seriously retarded persons are excluded from the analysed population [*10*].

Data on the incidence of severe mental retardation as well as variation in intelligence quotient (IQ) and school performance show significant effects on those survivors exposed 8–15 and 16–25 weeks after ovulation. Studies of seizures also exhibit a radiation effect in survivors exposed 8−15 weeks after ovulation. Magnetic resonance imaging of the brains of some mentally retarded survivors has revealed a large region of abnormally situated grey matter, suggesting an abnormality in neuronal migration. Radiation-related small head size is related to a generalised growth retardation [*11*]. A recent reanalysis of the dosimetry data indicated that the dose threshold for the development of mental retardation after intrauterine irradiation at gestation terms of 8–15 weeks is 0.06–0.31 Gy. At gestation term of 16–25 weeks, it is 0.28 Gy [*12*].

The question of the increased lifetime prevalence of schizophrenia in survivors prenatally exposed to atomic bomb radiation is still open to discussion [*13*]. Among 1,867 prenatally exposed individuals, 18 subjects (0.96%) had developed schizophrenia later in life. The prevalence was significantly higher in the people exposed in the second trimester of pregnancy than in those exposed in the third trimester. The closer they had been to the hypocentre, the higher was the prevalence. No statistically significant linear relationship was found [*14*].

Brain damage due to prenatal exposure was recognised by World Health Organisation (WHO) as a priority area in the assessment of the health consequences of the Chernobyl accident. Such acknowledgement led to the establishment of the WHO Pilot Project «Brain Damage in Utero» of the International Programme on the Health Effects of the Chernobyl Accident (IPHECA). Analysis of the results in three countries (Belarus, Russian and Ukraine) has shown the following:

a) incidence of mild mental retardation in prenatally irradiated children is higher when compared with the control group;

b) an upward trend was detected in cases of behavioural disorders and in changes in the emotional problems in children exposed *in utero*;

c) incidence of borderline nervous and psychological disorders in the parents of prenatally irradiated children is higher than that of controls.

On the basis of the investigations it was impossible to arrive at a final conclusion on the relationship between an increase in the number of mentally retarded children and exposure to ionising radiation due to the Chernobyl accident because of an absence of dosimetric support of the studies [*15–17*].

Recently some related studies have been published. Children irradiated *in utero*, living on the radioactively contaminated areas in Russian Federation (Tula Region, ^{137}Cs deposition density 185–555 kBq•m^{-2}) at the age of 1–7 years had the highest indices of mental morbidity and were more likely to display borderline intelligence and mental retardation. This morbidity was linked by the authors to radiation [*18*].

In Belarussian prenatally irradiated children, especially those exposed in 8–15 weeks, there were revealed more functional and organic disorders of central nervous system (CNS), borderline intelligence quotients (IQ) and abnormal EEG that were firstly linked to both radiation and psychosocial factors [*19*]. However, further these mental disorders among Belarussian children irradiated *in utero* were recognised as a result of sociodemographic and socio-cultural factors only [*20*]. Among these children there were revealed an increased prevalence of specific developmental speech-language and emotional disorders, as well as a lower mean full scale IQ and more cases of borderline IQ, which did not show the existence of a dose-effect relationships. No statistically significant distinctions in average IQ were found between the different subgroups of children in relation to the gestational age at the time of the Chernobyl accident. The authors attributed these disorders exclusively to unfavourable social-psychological and social-cultural factors [*21*]. At the same time, the same authors concerning the same children recently reported that average IQ for the subgroup of highly exposed children (thyroid doses more than 1 Gy) was lower in comparison with average IQ for the whole exposed group (85.7±6.4 vs 89.6±10.2 at the age of 6–7 years, P=.014; 89.1±7.1 vs 94.3±10.4 at age 10–12 years, P=.003) [*22*].

In contrast to the results of the WHO Pilot Project «Brain Damage in Utero» and another relevant studies, there are three recently published papers [*23–25*] where the authors concluded that 1) the mental and physical health of evacuee and non-evacuee children is similar and quite normal [*23*]; 2) the evacuee children (including irradiated *in utero*) were not different from their classmates based on data derived from objective and on the majority of the subjective measures used to assess attention, memory, intelligence and school performance [*25*]; 3) more evacuee mothers subjectively reported memory problems [*25*] and somatic symptoms [*23, 24*] in their children than classmates' mothers; 4) greater Chernobyl-focused anxiety is associated with slightly poorer performance on measures of attention [*25*]; 5) the most important risk factors were maternal somatization and Chernobyl-related stress [*24*]. However, as noted the authors, no dosimetric data were available, and there were no normative data in Ukraine for the measures used in the study [*24, 25*].

In the frame of the WHO Pilot Project «Brain Damage in Utero» we have previously revealed a significant increase of borderline and low range IQ, emotional and behavioural disorders, a decrease in high (IQ>110), as well as statistically significant higher prevalence of mental retardation (IQ<70) in Ukrainian prenatally irradiated children compared to the controls: 21 (3.9%) vs. 12 (1.6%) correspondingly (χ^2=6.27; df=1; P<.05) [*16, 26*]. Besides, we found that the thyroid-stimulating hormone (TSH) level grows with foetal thyroid dose increase with the 0.3 Sv threshold [*27*]. The radiation-induced malfunction of the thyroid-pituitary system was proposed as one important biological mechanism in the genesis of mental disorders in the prenatally irradiated children [*16, 26*]. It was hypothesised that the cerebral basis of mental disorders in the prenatally irradiated children is the malfunction of the left hemisphere limbic-reticular structures, particularly in those exposed at 16–25 weeks of gestation, which obviously reflects developmental abnormalities of brain structure and function as a result of interaction of prenatal and post-natal factors, including possible radiation effects on the developing brain. It was also proposed that the left hemisphere is more vulnerable to prenatal irradiation than the right [*28*].

Thus, in the majority of studies an increased prevalence of cognitive, emotional and behavioural impairments have been revealed in prenatally children exposed as a result of the Chernobyl accident. A point at issue remains the contribution of prenatal irradiation of a foetus and, especially, of the foetal thyroid gland to the genesis of brain damage in these children.

The objectives of the study was the psychometric, neurophysiological and neuropsychiatric (according to the International Classification of Disease, 10th Revision (ICD-10) criteria) characterisation of acutely prenatally irradiated children. This study involves acutely prenatally exposed children — born between April 26th, 1986 and February 26th 1987 from pregnant women at the time of the accident who had been evacuated from the 30-kilometer zone surrounding the Chernobyl NPP to Kiev — and their classmates. This sample seems to be optimal for examination of possible distinguished effects of exposure in different periods of cerebrogenesis.

Subjects and Methods

Design and Sample

The design was a cross-sectional assessment of children who were *in utero* (born between April 26th, 1986 and February 26th, 1987) at the time of the Chernobyl accident (April 26th, 1986) and their mothers who have been evacuated to Kiev. This group was acutely prenatally exposed to both radiation and non-radiation factors at the time of explosion, being at the Chernobyl exclusion zone and evacuation route. Inhabitants of the town of Pripyat (n=49,360) and railway station Yanov (n=254) were evacuated on April 27th, 1986. Residents of the 10-kilometre zone surrounding of the Chernoby NPP (n≈10,000) were on May 2nd — 3rd, 1986. Since May 4th, 1986 stepwise evacuation of population of the 30-kilometer zone surrounding of the Chernobyl NPP was began. To the middle of August, 1986 there were evacuated 90,784 people from 81 settlements of Ukraine [*29*].

Obviously, these acutely prenatally exposed children-evacuees from Pripyat towards Kiev are the most adequate subcohort for comparison with the Japanese cohort prenatally exposed to the atomic bombs in Hiroshima and Nagasaki in view of 1) acute prenatal exposure, and 2) as much as possible urbanised sample.

The WHO Pilot Project «Brain Damage in Utero» International Advisory Board estimated the number of births to be identified in the interval between April 26th, 1986 and February 26th, 1987 in the Ukrainian radioactively contaminated areas (including the Chernobyl exclusion zone — 30-kilometer zone surrounding the Chernobyl NPP) as 1,400. However, when in 1993–1994 we could indeed identify 1,021 (73%) of these children, only 272 (27%) of them were evacuees from the Chernobyl exclusion zone. The reduced group of the identified prenatally irradiated children could be explained by both medical and spontaneous abortions (miscarriages) and migration. In the course of the WHO Pilot Project «Brain Damage in Utero» in Ukraine we have examined 544 (53%) prenatally irradiated children, only 115 (21%) of which were evacuees from the Chernobyl exclusion zone. The reduced number of the examined children irradiated *in utero* could be explained by: 1) migration and «dispersion» across Ukraine and other countries, 2) incorrect registration as prenatally irradiated children, 3) local organisational problems, and 4) refusals to be examined.

In 1997–1998, according to the database of the National Register of Ukraine, we identified the official cohort of prenatally irradiated children in Ukraine that consisted of 733 children, including 278 (38%) children born from mothers who had been evacuated from the Chernobyl exclusion zone in 1986. 145 (52%) of them live in Kiev, 133 (48%) — in 26 regions of Ukraine (3–10 children per region). Besides, we have identified additional 69 prenatally irradiated children-evacuees living in Kiev according to the data of the Specialised Clinical and Epidemiological Register (SCER) of the Research Centre for Radiation Medicine (RCRM) of Academy of Medical Sciences (AMS) of Ukraine. Thus, we have identified 347 prenatally irradiated children-evacuees including 214 (62%) living in Kiev. Among the latest there is the subcohort consisting of 182 (85%) children-evacuees from the town of Pripyat.

From the subcohort of 182 prenatally irradiated children-evacuees from the town of Pripyat living in Kiev we randomly selected 100 (55%) children for the study (acutely exposed group). The comparison group consisted of 100 gender- and age-matched children selected from the classrooms of the children of the acutely exposed group. Children of both groups were officially included to the SCER of the RCRM of AMS of Ukraine and were profoundly medically examined by general paediatrist, paediatrist-psychoneurologist, paediatrist-endocrinologist, paediatrist-Ear-Nose-Throat (ENT), paediatrist-ophtalmologist, paediatrist-cardiologist, paediatrist-haematologists, paediatrist-pulmonologists, paediatrist-gastroenterologists, paediatrist-surgeon, paediatrist-gynecologist (for girls), and genetics using general and biochemical blood tests, immunological tests, urine tests, coprogram, thyroid and visceral ultrasonography, electrocardiogram (ECG), electroencephalogram (EEG), rheoencephalogram (RhEG) as well as fibrogastoscopy, cardiac ultrasonography, and magnetoresonance imaging (MRI) for diagnostic reasons. These examinations have been carried out at the Children Department of the Out-Patients' Clinic of the Radiation Register of the RCRM of AMS of Ukraine.

It should be emphasised that neuropsychiatric assessments presented here are based on neurological and psychiatric examinations, psychometry of both children and their mothers, and conventional and computerised EEG, which have been carried out by us and associates at the Neurology Department of the RCRM of AMS of Ukraine. The assessments took place in 1997–1999 when the children were 10–12 years old.

Estimation of Prenatal Age at Exposure

The most important single factor in determining the nature of the insult to the developing brain from ionising radiation exposure is gestational age. There are possible errors in the estimation of prenatal age at exposure. Postovulatory age is usually estimated from the onset of the last menstrual period, and adjustment is then made for the differences between that date and the probable date of fertilisation (usually taken to be 2 weeks later). Women with irregular menstrual cycles or who miss a menstrual period could erroneously identify the onset of their last cycle [*2*].

In order to avoid the aforementioned uncertainties concerning the estimation of prenatal age at the time of the Chernobyl accident we used the adapted formulas offered for estimation of prenatal age at atomic bombing in Hiroshima and Nagasaki [*30*]:

$$\textit{Days of pregnancy } (Y) = 280 — (\textit{date of birth} — \textit{April } 26^{th}, 1986),$$

where the day of birth was obtained by interview with the mothers of the children and the mean duration of pregnancy is taken to be 280 days.

Gestational weeks after fertilisation at the time of the accident were calculated by the following equation:

$$\textit{Gestational weeks } (G) = (Y — 14 \textit{ days}) / 7 \textit{ days},$$

where G was taken to be zero if $G<0$.

Dosimetry

Individual reconstruction of foetal doses, foetal thyroid doses and foetal doses on the brain has been carried out in the Department of Dosimetry and Radiation Hygiene (Chief — Prof. I.A. Likhtariev) of the RCRM of AMS of Ukraine. It should be stressed that individual reconstruction has been carried out for all children of both the acutely exposed group and the comparison group because the residents in Kiev were also exposed to the Chernobyl accident fall-outs although significantly less than evacuees.

The main sources of irradiation of pregnant women were as follows: 1) external γ-irradiation of the whole body; 2) irradiation of thyroid by radioactive iodine isotopes; 3) internal irradiation by inhaled radionuclides; 4) internal irradiation by radioactively contaminated food. The dose depended on the settlement, the route of evacuation, and the places of intermediate and final evacuation. The estimation of individual doses was carried out by the methods of retrospective dosimetry that were elaborated on the base of measurements of the dynamic of exposure dose rate (EDR) at the settlements, analysis of 30,000 «route sheets» (information on clear address at the settlement, the date and the time of evacuation, the route of evacuation, the place of intermediate and final evacuation), direct measurements of radioactive iodine content in 10,000 evacuees, ^{137}Cs deposition density at the place of intermediate evacuation [*31, 32*].

Reconstruction of foetal doses was based on reconstruction of doses of pregnant women. For estimation of foetal dose due to external irradiation the screening properties of mother's body were taking into account, and for estimation of thyroid foetal dose — mother's thyroid dose. Shield factor of buildings in towns was taken to be 10, in rural settlements — 3. Behavioural factor (time fraction outside houses) for pregnant women was taken to be 0.4.

Summarised dose on the whole foetus was taken to be equal to the dose of pregnant woman. The tissue-equivalent human phantom was exposed to real Chernobyl fall-outs in order to calculate the dose on the foetal human brain. At the places of foetal organs in the phantom LiF detectors with sensitivity 0.01 mSv were disposed. The transfer coefficient from EDR to equivalent dose on the foetal brain ($K_{dbrain} = 0.57 \cdot 10^{-2}$ mSv per 1 mR) was obtained considering the screening effect of foetal head by mother's pelvic bones, which does not depend on the prenatal age [*32*]. Finally, the dose on the foetal brain was calculated as the summarised dose of mother's external irradiation multiplied by K_{dbrain}.

In the earliest period after the Chernobyl accident (April 26th — May, 1986) internal irradiation by radioactive iodine had the most impact on the absorbed dose forming in population. Radioiodine from pregnant woman transfers to foetus quite rapidly. The rate of transfer increases in hundreds times in proportion to the term of pregnancy. Foetal thyroid begins its functioning at about the 8–12 weeks when it absorbs 50–70% of the whole radioiodine transferred to foetus. The radioiodine transfer rate to foetal thyroid is maximal at about the 20–25 weeks [*33*]. Consequently, foetal thyroid doses were reconstructed since the 8th week after fertilisation.

Foetal thyroid doses were calculated on the base of direct measurements of radioiodine contents in mothers' thyroid, taking into account age and other correction factors; ratio of radioactive iodine isotopes release from the reactor, wind speed and direction. The mean standardised thyroid dose of the adult population of Pripyat was taken to be 0.605 Gy (standard error 7%). Protective effect of stable iodine was taken to be 0.75. At present there are no officially adapted model for calculation of foetal thyroid dose that can be by 1 to 10 times larger than mother's thyroid dose [*31, 32*]. Assuming that the coefficient of transplacentar transfer of iodine is 1 and iodine concentrations in maternal and foetal structures are equal, maternal and foetal thyroid doses were taken to be equal and not dependant on the prenatal age.

Intelligence assessment

The intellectual ability of children was assessed by the adapted and normalised version for the Ukrainian children of the WISC [*34*], which was carried out by Prof. Yu.Z. Gilbukh and colleagues from the Research Institute of Psychology of Academy of Pedagogic Sciences of Ukraine [*35*]. The child's performance was summarised in three composite scores, the verbal, performance and full scale IQs, which provide estimates of the individual's intellectual abilities.

Testing procedures were performed at standard conditions at the Neurology Department of the SCRM of AMS of Ukraine in a quite, adequately lit, well-ventilated room without an accompanying adult, seating and materials arrangement corresponded to recommendations by [*34, 35*] together with co-operative relationships between the child and the examiner. The entire test was administered in a single session.

Following subtests of the WISC were used: verbal scale — information, vocabulary, similarities, and digit span; performance scale — picture completion, block design, object assembly, and coding. We used eight subtests only of the WISC, as manuals permit it, to predict a possible fatigue of children due to following testing and examinations. The sum of subtest scaled scores on the affected scale was prorated to obtain the verbal and performance score that was used to derive the IQ score. To prorate the child's score on four verbal and four performance subtests we multiplied the sum of the four scaled scores by 1.25. The sums of verbal and performance subtest scaled scores were prorated separately and the resulting verbal and performance scores were summed to yield the full scale IQ score. Scaled score equivalents of raw scores, standardised to age, and IQ equivalents of sums of scaled scores for verbal, performance, and full scales were obtained from the norms and conversion tables for Ukrainian children [*35*].

Cerebral electrical activity assessment

Quantitative electroencephalography (QEEG) is a set of non-invasive tools that are capable of quantitatively assessing activity of the brain with sensitivity and temporal resolution superior to those of any other imaging methods. The EEG power spectrum is quite stable and characteristic for healthy human beings. At the same time many brain dysfunctions, including environmentally induced ones, can be distinguished by QEEG with specificity of about 95% and sensitivity of 60–95% [*36*]. The level of sensitivity and specificity of QEEG for brain injury (which is possible to expect in acutely prenatally irradiated children) meets the standards of sensitivity and specificity maintained for MRI, sonograms, blood analysis, and other common clinical diagnostic measures [*37*]. Thus, QEEG is one of the most adequate diagnostic technologies for assessment of radiation effects on the brain.

Neurophysiological investigations were carried out in the neurophysiological laboratory of the Department of Neurology, RCRM of AMS of Ukraine in the first half of the day during the passive awake state of a child. The children were nonmedicated for 3 and more days.

Brain electrical activity was recorded monopolarly using the International 10–20 System on 19 channels, referenced to linked ears on a brain potential analyser «Brain Surveyor», SAICO, Italy. EEG were registered at 1) passive awakeness, eyes closed — 1 min, 2) passive awakeness, eyes open — 30 s, 3) hyperventilation, eyes closed — 3 min, and 4) passive awakeness after hyperventilation, eyes closed — 1 min. Spectral analysis of brain electrical activity was conducted. Epochs of analysis consisted of 60 seconds, and analysed frequencies were in the 1–32 Hz range. Estimation and interpretation of conventional and QEEG activity were performed according to Zhirmunskaya's algorithm [*38*] together with paediatric EEG classic manuals [*39–41*].

Additional measurements

This paper focuses on intelligence and EEG assessment as well as clinical psychiatric and neurological diagnostic in the children. At the same time the children were also measured by a number of psychological tests, analysis of which we hope to present further. For this paper these measures were used for verification of clinical diagnosis.

Aiming to follow up the children who had been examined before, parents were asked to complete a Russian translation of the Rutter A (2) Behaviour Rating Scale which was used in the WHO Pilot Project «Brain Damage in Utero» in 1993–1994. Parental rating assesses problems associated with health, hyperactivity, and behavioural and emotional disorders [*42*]. Russian translation of Achenbach's Child Behaviour Checklist (CBCL), the questionnaires for the children and the parents, was also used [*43, 44*]. Moreover, the Children Questionnaire of Neurosis (CQN) by V.V. Sednev [*45*], validated and standardised for Ukrainian children, was applied for revealing of depression, asthenia, behavioural disorders, autonomic nervous system dysfunction, sleep disorders, anxiety, and sincerity.

Following the WHO Pilot Project «Brain Damage in Utero», mothers were also asked to complete the General Health Questionnaire (GHQ-28), reflecting the level of her mental adaptation, the level of anxiety and depression, and also social functions [*46, 47*]. The vocabulary subtest of the Wechsler Adult Intelligence Scales (WAIS) was used to estimate the verbal intelligence of the mother. Moreover, posttraumatic stress disorders (PTSD) in mothers were assessed by the Impact of Events Scale and Arousal Scale of PTSD [*48*], as well as mother's unmasking depression — by the Self-rating Depression Scale [*49*].

Finally, mothers were asked for demographic background, family history, educational level of the family, social and economical status as well as they completed a standardised questionnaire on radiation history. On the base of the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) Scale of Stress-Factors [*50*] we elaborated a standardised questionnaire on stress-factors related to the Chernobyl accident that reflects a severity of *real* stress events (but not affective symptoms or Chernobyl-focused anxiety) following the Chernobyl accident to the birth of the child. For instance, separation with the husband and family during evacuation; absence information about the husband, participating in emergency work at the Chernobyl NPP, and family; consumer problems at the places of evacuation; low level of medical care, etc.

Clinical Psychiatric and Neurological Assessment

The children of both the acutely prenatally exposed and the comparison groups were examined by standardised clinical psychiatric interview and standardised clinical neurological examination at the Department of Neurology, RCRM of AMS of Ukraine. The mental disorders and the diseases of the nervous system were assessed according to the diagnostic criteria of ICD-10 (Chapter V: Mental and Behavioural Disorders & Chapter VI: Diseases of the Nervous System). ICD-10 diagnostic was made on the base of clinical psychatric and neurological examinations, psychometry, conventional and QEEG, taking into account the results of the profound clinical, laboratory, and instrumental examination at the Children Department of the Out-Patients' Clinic of the Radiation Register of the RCRM of AMS of Ukraine, including MRI of the brain for diagnostic reasons.

Statistical Analysis

Statistical processing included descriptive statistics, *t* test, Chi-square tests, relative risk (RR) assessment, correlation and multiple regression analyses [*51*]. The paired *t* test was used to analyse data when a pair of measurements was obtained on each individual [*52*]. The Bonferroni correction was used when multiple statistical test were performed [*53*]. Statistical analysis was performed using STATISTICA 5.0 and MS EXCEL 97 software.

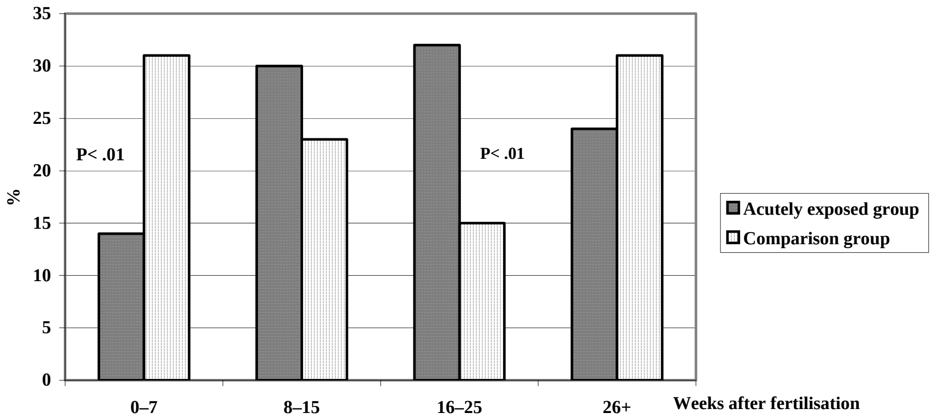


Figure 1. Distribution of children by prenatal age at the time of explosion (April 26th, 1986)

Results

Descriptive Characteristic

The age (M±SD) was 11.3±0.4 years for the children from the acutely exposed group and 11.48±0.82 for the classmates; 54% of the evacuee children and 56% of the comparison groups were male.

Distribution of children by prenatal age at the time of the Chernobyl accident is shown in Figure 1. In spite of a randomised procedure of the children selection, a significant reduction is found in the number of the children irradiated at 0–7 weeks after fertilisation in the acutely exposed group in comparison with the classmates (14% vs. 31%; χ^2=8.29; P<.01), which could be explained as the result of abortions and/or miscarriages among pregnant women-evacuees. However, it is difficult to explain why there is also a significant reduction of the number of the children from Kiev at 16–25 weeks after fertilisation in comparison with the acutely exposed group (32% vs. 15%; χ^2=8.04; P<.01).

Mean, standard deviation, and range of the individual foetal doses (summarised foetal dose of external irradiation, mSv; equivalent dose on the foetal brain, mSv; cumulated thyroid foetal dose (since the 8th weeks after fertilisation), Gy) for the two groups of children are presented in Table 1. It is clear that the children of the two groups correspond to the subgroups of the Japanese sample [*2*]: prenatally exposed survivors to atomic bomb radiation of the foetal dose category less than 0.01 Gy (n=1,201) — to the Ukrainian comparison group, and those of the dose category 0.01–0.09 Gy (n=322) — to the Ukrainian acutely exposed group.

Distribution of summarised foetal dose of external irradiation, equivalent dose on the foetal brain, mSv, and cumulated thyroid foetal dose (since the 8th weeks after fertilisation) among the children of the acutely

Table 1. Individual foetal doses.

Dose	Value	Acutely exposed group	*t*-test	P	Comparison group
Summarised foetal dose of external irradiation, mSv	M±SD Range	31.9±14.4 (10.74 – 92.52)	21.31	<.001	1.2±0.5 (0 – 2.67)
Equivalent dose on the foetal brain, mSv	M±SD Range	20.7±9.43 (6.98 – 60.12)	21.14	<.001	0.8±0.5 (0 – 2.52)
Cumulated thyroid foetal dose (since the 8th weeks after fertilisation), Gy	M±SD Range	0.66±0.32 (0.22 – 2.04)	17.52	<.001	0.04±0 (0.041)

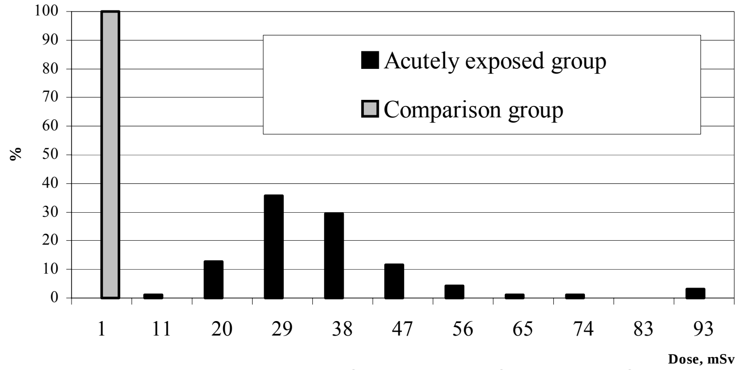


Figure 2. Distribution of summarised foetal dose of external irradiation

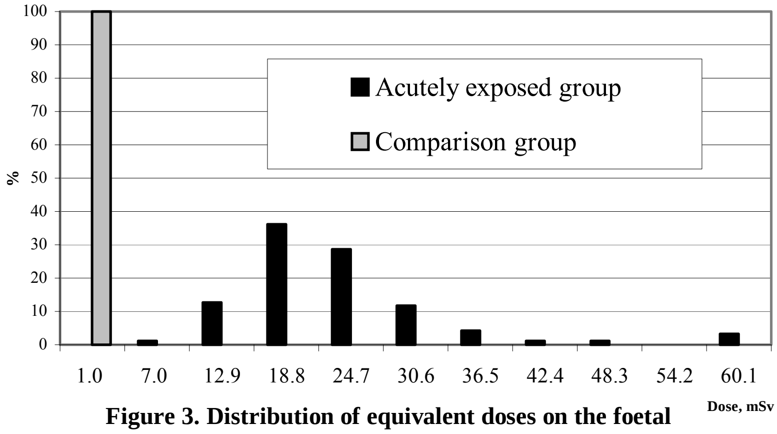


Figure 3. Distribution of equivalent doses on the foetal brain

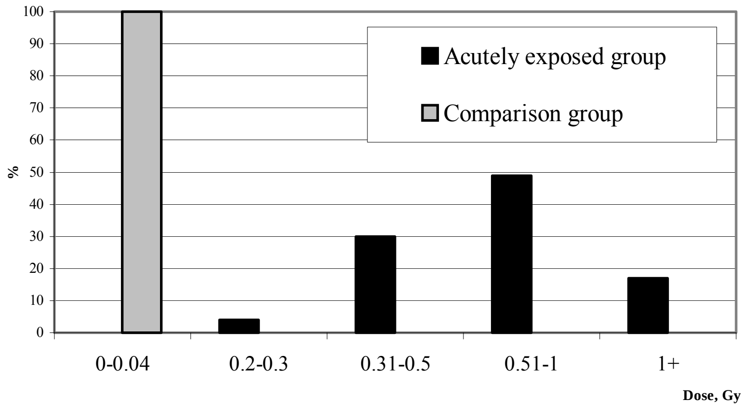


Figure 4. Distribution of foetal thyroid doses

exposed group are shown in Figures 2, 3 and 4, correspondingly. These foetal doses did not differ depending on the prenatal age at the time of the accident.

As seen in Figure 4, radiation exposure to foetal thyroid was quite significant: the permissible dose limit of 0.3 Gy on thyroid [*54*] was exceeded in 97% of the children of the acutely exposed group, moreover, the foetal thyroid of 17% of them was exposed to 1 Gy and more.

Among the acutely exposed group there were 5% disabled children and their disability was officially recognised to be caused by the consequences of the Chernobyl accident. Except one child with haemophilia, the four another children had neuromental disorders: moderate mental retardation (1), epilepsy (1), and encephalopathy (2). The child with haemophilia attended the school programme at home, and the child with moderate mental retardation was institutionalised into the special boarding school. Moreover, 7% of the

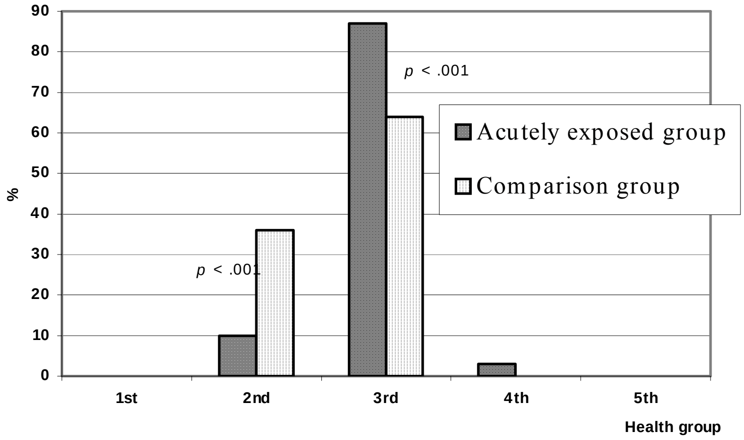


Figure 5. Distribution of children by the health groups

children-evacuee systematically missed school and attended the school programme at home due to different medical reasons except flu (epilepsy, paroxysmal states, behavioural problems, fatigue, headache, lack of concentration, exhaustion, etc). The other children attended public schools.

General health of children in the countries of the former U.S.S.R. is assessed according to the five «health groups»: the 1st health group includes absolutely healthy children; the 2nd — practically healthy children (no complaints, but there are some subclinical symptoms revealed by profound clinical, laboratory and instrumental examination only); the 3rd — children with chronic disease(s) in remission; the 4th — handicapped children with chronic disease(s) in exacerbation demanding active therapeutical intervention and/or institutialisation; the 5th — handicapped children with severe chronic disease(s) in decompensation stage demanding hospitalisation with absence of learning and self-service. As seen in Figure 5, among the children-evacuees there were significantly less practically healthy children (the 2nd health group) (10% vs. 36%; χ^2=19.09; P<.001) and significantly more children with chronic diseases in remission than in classmates (87% vs. 64%; χ^2=14.3; P<.001) (the 3rd health group). The 3rd health group in the both groups was predominantly comprised by chronic decompensated tonsillitis and adenoids of the 2nd–3rd severity degree; cardiomyopathy; chronic inflammatory diseases of stomach and intestine at the stage of exacerbation; diffusive thyroid hyperplasia of the 3rd degree, euthrosis (normal thyroid functions); moderate to severe disorders of refraction (hypermetropia, myopia, astigmatism). The conclusion about the health groups is given by the experts of the Children Department of the Out-Patient's Clinic of the Radiation Register of the RCRM of AMS of Ukraine. No single child from the both groups was recognised as absolutely healthy.

The acutely exposed children in comparison with the classmates had more often moderate complications of postnatal period, paroxysmal states, including epileptical, enuresis/encopresis at the age more than 4 years. The evacuated mothers had more often moderate abnormalities and toxicosis of pregnancy (63% vs. 32% correspondingly, χ^2=19.27; P<.001).

In the families of the acutely exposed children in comparison with the classmates living conditions were better; families with 2 and more children were more often; 85% of the fathers took part in the Chernobyl accident consequences clean up; 8% of the mothers were disabled and their disability was officially recognised to be caused by the consequences of the Chernobyl accident; the fathers took more alcoholic drinks and tobacco; less number of the parents graduated a university and more — had specialised secondary education.

According to our questionnaire on stress-factors related to the Chernobyl accident, a severity of *real* stress events was dramatically more pronounced in the mothers-evacuees than in the classmate's mothers: 14.9±6.1 vs. 3±5.3, t =10.56, P<.001. Although the mothers-Kyievers had not been apparently exposed to *real* Chernobyl-related stress-events (extreme situations) such as evacuation, family separation etc., in contrast to the mothers-evacuees, the mothers of the both groups have quite significant symptoms of Chernobyl-related PTSD, which were more pronounced in the mothers-evacuees. Mean score of the Impact of Events Scale and Arousal Scale of PTSD in the mothers-evacuees was 18.8±10.6 and the mothers-Kyievers — 14.8±9.9, t = 2.02, P<.05.

Mother's unmasking depression estimated by the Self-rating Depression Scale was higher in the mothers-evacuees than in the classmate's mothers: 56.3±10.4 vs. 42±12.5, t=5.22, P<.001.

The mothers-evacuees had also worse than the classmate's mothers mental adaptation and social functions as well as more symptoms of anxiety and depression estimated by the GHQ-28: 9.6±9.6 vs. 4.8±4.9, t=3.71, P<.001.

The verbal intelligence of the mother measured by the vocabulary subtest of the WAIS was lower in the mothers-evacuees than in the mothers-Kyievers: 43.2±10.9 vs. 52.4±8.4, t = –5.09, P<.001.

Intellectual ability of children

Distribution of verbal IQ, performance IQ and full scale IQ among the children of the both groups is presented in Table 2. Among the children of the acutely exposed group in comparison with the classmates there were significantly more children with an average verbal IQ of 91–110 (53% vs. 22%; χ^2=20.5; P<.001) as well as significantly less of children with an high-advanced verbal IQ of 121–> (9% vs. 45%; χ^2=32.88; P<.001) and an high-advanced full scale IQ of 121–> (27% vs. 55%; χ^2=16.21; P<.001).

Mean values of all verbal subtests and performance subtest — picture completion of the WISC were significantly lower in the acutely exposed children in comparison with the classmates (Table 3). Although the mean verbal IQ, performance IQ and full scale IQ in children of the both groups were in high range, the acutely exposed group had a significantly lower mean verbal IQ (105.3±13.1 vs. 118.1±13; t=–6.94; P<.001) and mean full scale IQ (112.1±15.4 vs. 120.9±11.5; t=–4.58; P<.001). The mean performance IQ, however, was not significantly different (117.3±18 vs. 119.2±10.2; t=–.92; P>.05).

In spite of a similar performance IQ in the both groups, significant WISC performance/verbal

Table 2. Distribution of verbal IQ, performance IQ and full scale IQ.

IQ range		Acutely exposed group	χ^2	P	Comparison group
Verbal IQ:	<70–80	3	3.05	>.05	0
	81–90	9	3.19	>.05	3
	91–110	53	20.50	<.001	22
	111–120	26	.04	>.05	30
	121–>	9	32.88	<.001	45
Performance IQ:	<70–80	3	3.05	>.05	0
	81–90	3	3.05	>.05	0
	91–110	20	.03	>.05	19
	111–120	27	.6	>.05	32
	121–>	47	.08	>.05	49
Full scale IQ:	<70–80	3	3.05	>.05	0
	81–90	3	3.05	>.05	0
	91–110	33	3.03	>.05	22
	111–120	34	2.97	>.05	23
	121–>	27	16.21	<.001	55

Table 3 WISC subtests, verbal IQ, performance IQ and full scale IQ.

Measure	Acutely exposed group (M±SD)	*t*-test	P	Comparison group (M±SD)
Verbal scale:				
Information	9.8±2.5	–4.53	<.001	11.4±2.5
Vocabulary	12.3±3.4	–6.84	<.001	15.4±3
Similarities	11,4±2.5	–4.89	<.001	13.2±2.7
Digit span	9.7±2.6	–3.6	<.001	11±2.5
Performance scale:				
Picture completion	14.8±3.4	–3.46	<.001	16.2±2.2
Block design	12.5±3.5	–1.61	>.05	13.2±2.6
Object assembly	10.9±3.3	–.72	>.05	11.2±2.5
Coding	11.7±3.2	2.55	<.05	10.6±2.9
Verbal IQ	105.3±13.1	–6.94	<.001	118.1±13
Performance IQ	117.3±18	–.92	>.05	119.2±10.2
Full scale IQ	112.1±15.4	–4.58	<.001	120.9±11.5

Note: Bonferroni corrected α-level of <.004 was used to assess statistical significance (.05 divided by 11 comparisons within measures of intelligence)

discrepancies ($IQ_{P–V}$ = performance IQ – verbal IQ) with verbal decrements were revealed in the acutely exposed group in comparison with the classmates: 12.1±13.8 (*paired t* = 8.7, P<.001) vs. 1.2±11.8 (*paired t* = 1, P>.05); *t*=6; P<.001.

WISC performance/verbal discrepancies take on clinical significance at the magnitude more than 25 points [55]. According to this criterion ($IQ_{P–V}$>25), among the acutely exposed group there were significantly more children with disharmoniously developed intelligence due to verbal decrements than in the comparison group (17% vs. 4%; χ^2= 8.99; P<.01), especially among those irradiated at 16–25 weeks after fertilisation. Among the children irradiated at 16–25 weeks after fertilisation (from acutely exposed group) there were 9 children with $IQ_{P–V}$>25 out of all 17 (more than $^1/_2$).

In Table 4 intellectual development of children of both groups corresponding to different periods of cerebrogenesis at exposure is presented. There is a tendency towards a deterioration of full scale IQ and verbal IQ, as well as an increasing of intellectual disharmony ($IQ_{P–V}$) in children of the acutely exposed group who were exposed at 16–25 weeks after fertilisation. Among those irradiated at 16–25 weeks, the full scale IQ and verbal IQ were the lowest in the acutely exposed.

There were 155 children (86 in the acutely exposed group and 69 in the classmates) who were at the 8th and more weeks after fertilisation at the time of the accident. For 154 (98%) of these children the foetal thyroid dose was reconstructured. IQs of the children in proportion to the foetal thyroid dose is presented in Table 5 and Figure 6. All classmates and 4 children from the acutely exposed group had the prenatal thyroid dose in the range of 0.04–0.3 Gy. It should be noted that the dose of 0.3 Gy on thyroid was the dose limit for the children at the time of the Chernobyl accident [54]. As it is shown in Table 5 and Figure 6, full scale IQ and, especially verbal IQ, were reduced in dependence to the foetal thyroid dose. Performance IQ was slightly reduced above the foetal thyroid dose of >1 Gy only.

According to the results of regression analysis, the children’s intelligence is etiologically heterogeneous (Table 6). Higher educational, intellectual, and economical levels of a family, as well as older parents at the time of childbirth (at the examined age ranges 18–35 years for the mothers and 19–42 — for the fathers) are the contributors towards a higher child intelligence. Higher doses of prenatal irradiation, especially foetal thyroid dose, more severe stressogenic events and additional mother’s hazards in the prenatal period, worse mother’s mental health, as well as childbirth problems are the contributors towards a lower child intelligence.

Foetal thyroid dose seems to be the main predictor of verbal intelligence deterioration (regression coefficient = –.34–(–.39); P<.001) nd WISC performance/verbal discrepancies with verbal decrements

Table 4. Intellectual development of children corresponding to different periods of cerebrogenesis at exposure.

Age in weeks after fertilisation	Acutely exposed group	*t*-test	P	Comparison group
Total				
Subjects	100			100
Full IQ (M±SD)	112.3±15.4	–4.58	<.001	120.9±11.5
Verbal IQ (M±SD)	105.3±13.1	–6.94	<.001	118.1±13
Preformance IQ (M±SD)	117.3±18	–.92	>.05	119.2±10.2
Intellectual disharmony IQ_{P-V} (M±SD)	12.1±13.8	6	<.001	1.2±11.8
paired t	*8.7*			*1*
P	<.001			>.05
0–7				
Subjects	14			31
Full IQ (M±SD)	110±14.7	–2.73	<.01	122.2±11.9
Verbal IQ (M±SD)	103.9±15.3	–3.26	<.01	119.4±13.5
Preformance IQ (M±SD)	115±14.6	–1.47	>.05	121.4±10.7
Intellectual disharmony IQ_{P-V} (M±SD)	11.1±12.8	2.28	<.05	2±11.4
paired t	*3.3*			*1*
P	<.001			>.05
8–15				
Subjects	30			26
Full IQ (M±SD)	113.1±10.9	–1.37	>.05	117.6±12.5
Verbal IQ (M±SD)	106.3±10.5	–2.59	<.01	114.9±13
Preformance IQ (M±SD)	117.9±12	.74	>.05	115.6±10.5
Intellectual disharmony IQ_{P-V} (M±SD)	11.6±10.9	3.29	<.001	.8±12.5
paired t	*5.8*			*.3*
P	<.001			>.05
16–25				
Subjects	32			15
Full IQ (M±SD)	109.2±20	–2.28	<.05	120.5±13.5
Verbal IQ (M±SD)	102.7±15.5	–2.88	<.01	117.1±16.2
Preformance IQ (M±SD)	114.7±23.3	–.75	>.05	118.3±9.7
Intellectual disharmony IQ_{P-V} (M±SD)	12±14	2.62	<.01	1.3±12.6
paired t	*4.8*			*.4*
P	<.001			>.05
26–term				
Subjects	24			31
Full IQ (M±SD)	116±13.1	–2.01	>.05	122.3±9.1
Verbal IQ (M±SD)	108.3±11.2	–3.78	<.001	119.6±10.7
Preformance IQ (M±SD)	121.4±18	.3	>.05	120.2±9.4
Intellectual disharmony IQ_{P-V} (M±SD)	13.1±17.6	3	<.01	.6±11.8
paired t	*3.7*			*.3*
P	<.001			>.05

Table 5 Full scale IQ, Verbal IQ and Performance IQ at prenatal exposure to different thyroid dose.

Thyroid doetal dose, Gy	Full scale IQ, M±SD	Verbal scale IQ, M±SD	Performance scale IQ, M±SD
0.04–0.3 (n=76)	119.6±10.8	116.6±12.3	118.0±9.5
0.31–0.6 (n=31)	113.3±15.2	106.9±12.1	118.0±17.9
0.61–1.0 (n=33)	113.2±14.9	105.5±12.7	119.3±19.2
1.0+ (n=14)	108.4±18.9	102.3±15.2	112.9±20.7

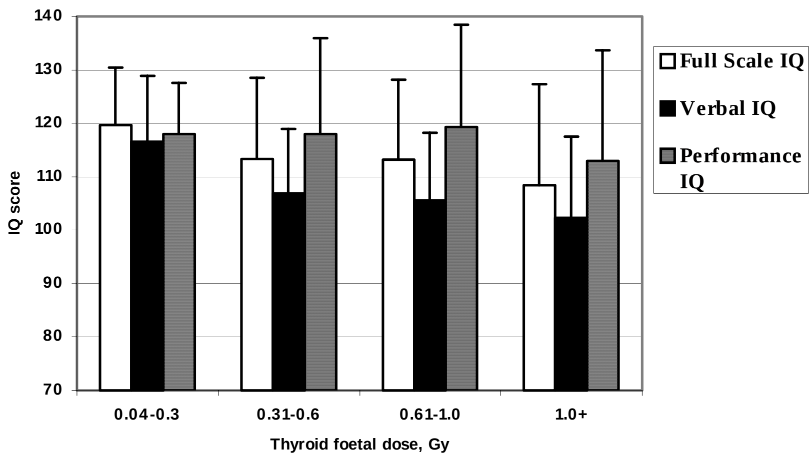


Figure 6. Children intelligence in proportion to the thyroid foetal dose

Table 6 Regression analysis of the predictors of the children's intellectual development.

Predictor	Regression coefficient	$F_{(df1, df2)}$	P
Information subtest of WISC			
Mother's intelligence (vocabulary subtest of WAIS)	.21	$9.2002_{(1,198)}$	.003
Father's age	.20	$8.1679_{(1, 198)}$	.005
Father's educational level	.18	$6.6469_{(1, 198)}$	.01
Mother's age	.18	$6.3917_{(1, 198)}$	.01
Mother's educational level	.14	$4.0504_{(1, 198)}$	.04
Vocabulary subtest of WISC			
Thyroid foetal dose	–.39	$25.7159_{(1,152)}$	.000001
Mother's intelligence (vocabulary subtest of WAIS)	.36	$28.9968_{(1,198)}$	.000000
Foetal dose	–.29	$18.3566_{(1, 198)}$	.00003
Dose on the foetal brain	–.29	$17.6903_{(1, 198)}$	.00004
Stress-events after the accident during pregnancy	–.15	$4.6808_{(1, 198)}$	.03
Similarities subtest of WISC			
Thyroid foetal dose	–.24	$8.4675_{(1,152)}$	.004
Mother's intelligence (vocabulary subtest of WAIS)	.22	$9.7155_{(1,198)}$	.002
Dose on the foetal brain	–.21	$9.0083_{(1, 198)}$	.003
Foetal dose	–.20	$8.5392_{(1, 198)}$	.004
Stress-events after the accident during pregnancy	–.16	$5.1838_{(1, 198)}$	.02
Economic level of family	.16	$5.0957_{(1, 198)}$	.02
Mother's GHQ-28	–.15	$4.6937_{(1, 198)}$	.03
Digit Span subtest of WISC			
Thyroid foetal dose	–.26	$10.5202_{(1,152)}$	.001
Mother's intelligence (vocabulary subtest of WAIS)	.24	$11.8890_{(1,198)}$	.0007
Dose on the foetal brain	–.24	$11.5737_{(1, 198)}$	.0008
Foetal dose	–.23	$11.0999_{(1, 198)}$	.001
Mother's additional hazards during pregnancy	–.15	$4.8516_{(1, 198)}$	.03
Mother's Self-rating Depression Scale (Zung)	–.15	$4.3983_{(1, 198)}$	.04
Father's educational level	.14	$4.2379_{(1, 198)}$	.04
Verbal IQ			
Thyroid foetal dose	–.34	$18.7662_{(1,152)}$	.00003
Mother's intelligence (vocabulary subtest of WAIS)	.33	$24.6009_{(1,198)}$	.000002
Dose on the foetal brain	–.28	$17.2540_{(1, 198)}$	.00005
Foetal dose	–.28	$17.1946_{(1, 198)}$	.00005
Father's educational level	.16	$4.8868_{(1, 198)}$	.03
Economic level of family	.15	$4.5543_{(1, 198)}$	.03
Stress-events after the accident during pregnancy	–.14	$3.9069_{(1, 198)}$	.049
Mother's educational level	.14	$3.9227_{(1, 198)}$	.049

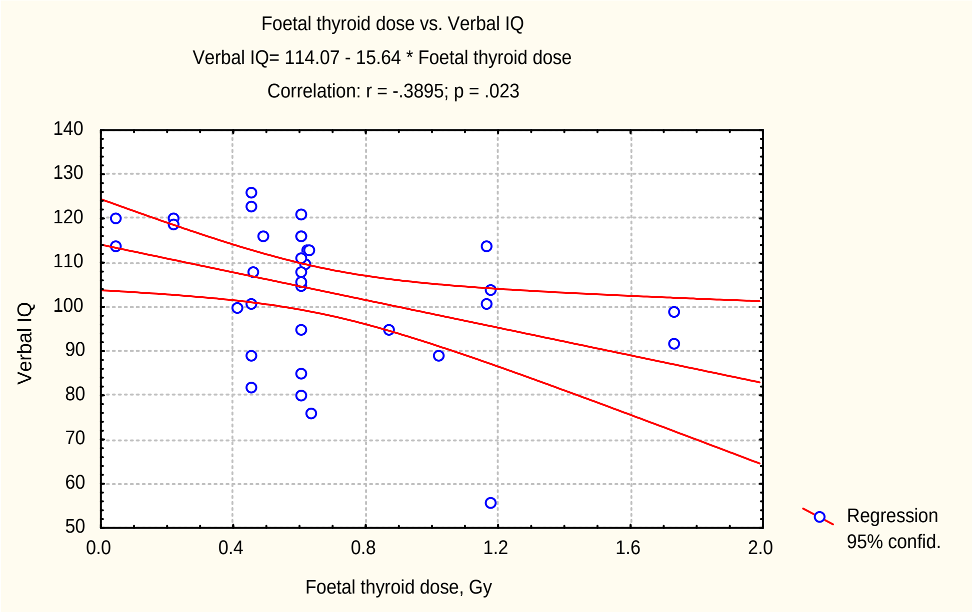
(Table 6 continued)

Predictor	Regression coefficient	$F_{(df1, df2)}$	P
Picture completion subtest of WISC			
Economic level of family	.26	$14.2983_{(1, 198)}$	.0002
Mother's intelligence (vocabulary subtest of WAIS)	.22	$10.0078_{(1,198)}$	.002
Dose on the foetal brain	–.19	$7.1427_{(1, 198)}$	.008
Foetal dose	–.18	$6.4733_{(1, 198)}$	.01
Father's age	.17	$6.2598_{(1, 198)}$	.01
Father's educational level	.16	$5.0650_{(1, 198)}$	.02
Mother's GHQ-28	–.16	$5.1748_{(1, 198)}$	.02
Mother's educational level	.15	$4.7358_{(1, 198)}$	.03
Childbirth abnormalities	–.15	$4.3178_{(1, 198)}$	.04
Block design subtest of WISC			
Mother's educational level	.18	$6.9333_{(1, 198)}$	.009
Economic level of family	.17	$6.0673_{(1, 198)}$	.01
Mother's PTSD	–.14	$4.1347_{(1,198)}$	.04
Object assembly subtest of WISC			
Father's educational level	.18	$6.5096_{(1, 198)}$	.01
Economic level of family	.17	$6.1768_{(1, 198)}$	.01
Mother's intelligence (vocabulary subtest of WAIS)	.14	$4.0587_{(1,198)}$	.04
Coding subtest of WISC			
Economic level of family	.28	$17.1997_{(1, 198)}$	.00005
Father's educational level	.16	$5.3818_{(1, 198)}$	.02
Mother's GHQ-28	–.14	$4.0682_{(1, 198)}$	.04
Performance IQ			
Economic level of family	.32	$22.9500_{(1, 198)}$	.000003
Mother's intelligence (vocabulary subtest of WAIS)	.23	$10.6177_{(1,198)}$	.001
Father's educational level	.21	$8.7027_{(1, 198)}$	.004
Mother's educational level	.17	$5.8003_{(1, 198)}$	.02
Disharmony of intellectual development $IQ_{P–V}$			
Thyroid foetal dose	.31	$15.8215_{(1,152)}$	.0001
Foetal dose	.23	$11.5167_{(1, 198)}$	.0008
Dose on the foetal brain	.22	$10.5278_{(1, 198)}$	.001
Economic level of family	.19	$7.1229_{(1, 198)}$	.008
Mother's Self-rating Depression Scale (Zung)	.16	$4.9322_{(1, 198)}$	.03
Full scale IQ			
Mother's intelligence (vocabulary subtest of WAIS)	.32	$22.3837_{(1,198)}$	.000004
Economic level of family	.26	$14.4738_{(1, 198)}$	.0002
Dose on the foetal brain	–.20	$8.0329_{(1, 198)}$	.005
Thyroid foetal dose	–.20	$5.8691_{(1,152)}$	.02
Father's educational level	.20	$7.9749_{(1, 198)}$	.005
Foetal dose	–.19	$7.5897_{(1, 198)}$	.006
Mother's educational level	.15	$4.6695_{(1, 198)}$	.03
Verbal IQ *(children exposed at 16–25 weeks after fertilisation, n=47)*			
Thyroid foetal dose	-.39	$5.7221_{(1,45)}$	.022
Mother's intelligence (vocabulary subtest of WAIS)	.42	$5.8961_{(1,45)}$	.022
Vocabulary sutest of WISC *(children exposed at 16–25 weeks after fertilisation, n=47)*			
Thyroid foetal dose	-.51	$11.0984_{(1,45)}$	.002
Mother's intelligence (vocabulary subtest of WAIS)	.42	$6.0628_{(1,45)}$	.02

(regression coefficient = .31; P<.001) (Table 6), especially among the children irradiated at 16–25 weeks after fertilisation (Figure 7).

Brain electrical activity of children

The children of the acutely exposed group had significantly less age normal patterns of brain electrical activity in comparison with the classmates (16% vs. 54%, $\chi^2 = 31.74$, $p < .001$) (Table 7). There were four



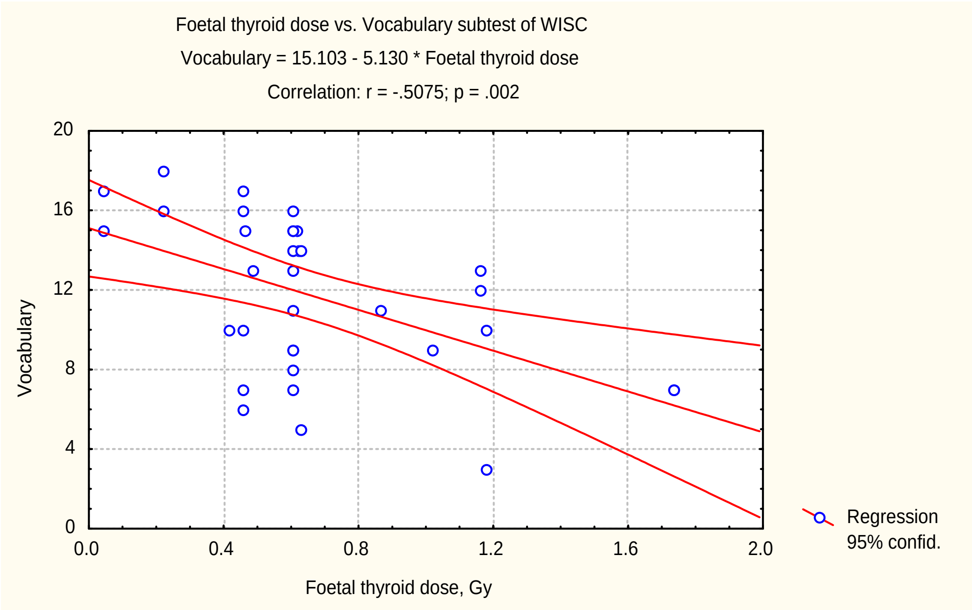


Figure 7. Relationships between Verbal IQ and Vocabulary subtest of WISC vs foetal thyroid dose, in children of the both groups (n=47) exposed at 16–25 weeks after fertilization.

abnormal EEG-patterns in the prenatally irradiated children as follows:

(1) *Low-voltage EEG* (20–25 μV) with excess of slow (δ) and fast (β) activity together with depression of α- and θ-activity with paroxysmal activity shifted to the left fronto-temporal region was one of the most distinguished conventional EEG-pattern in the children of the acutely exposed group (31% vs. 8%, χ^2=16.85, P<.001).

(2) *Disorganised slow EEG-pattern* with δ-activity domination characterised by disorganised activity of moderate (40–55 μV) or high (70–80 μV) amplitude with a mainly δ-range slow activity domination and non-regular α-activity where hyperventilation led to bilateral paroxysmal activity discharges, as well as 3) *disorganised EEG-pattern with paroxysmal activity*, similar in general to the one described above, but characterised by generalised paroxysmal discharges and bursts of acute, θ- and δ-waves of high amplitude where the hyperventilation led to the bilateral paroxysmal activity increase, were found equally in the both groups.

(4) *Epileptiformal EEG* with «spike» or «polyspike—wave» complexes in the fronto-temporal region,

Table 7 Conventional EEG-patterns.

EEG-pattern	Acutely exposed group	χ^2	P	Comparison group
Age norm	**16**	**31.74**	**<.001**	**54**
Organised	0	4.08	<.05	4
Disorganised with predominance of α-activity	10	5.36	<.05	22
Hypersynchronous	6	17.15	<.001	28
Abnormal	**84**	**31.74**	**<.001**	**46**
Low-voltage	31	16.85	<.001	8
Disorganised slow	16	.16	>.05	14
Disorganised with paroxysmal activity	20	.27	>.05	23
Epileptiformal	17	15.63	<.001	1
Interhemispheric asymmetry	**73**	**24.8**	**<.001**	**38**
Left hemisphere lateralised dysfunction	37	15.36	<.001	13
Right hemisphere lateralised dysfunction	15	.87	>.05	20
Cross-hemispherical dysfunction	21	11.32	>.001	5

mainly of the left hemisphere, and bilateral paroxysmal activity in the form of δ-waves of very high amplitude (higher than 100 μV) was another of the most distinguished conventional EEG-pattern among the children of the acutely exposed group (17% vs. 1%, χ^2=15.63, P<.001).

Interhemispheric asymmetry of the EEG was revealed significantly more often in the acutely exposed children compared with the classmates (73% vs. 38%, χ^2=24.8, P<.001) according to an asymmetry index >5%. An increase of the abnormal or/and a decrease of the normal EEG-signs in one hemisphere in comparison with another were the criteria adopted for the lateralised dysfunction detection (Table 7). Three types of interhemispheric asymmetry were found in the children of the both groups. A *left hemisphere lateralised dysfunction* was characterised by slow and/or epileptiformal activity in the fronto-temporal region together with α-activity depression in the left hemisphere. The left-hemispherical type of EEG-laterality was found more often among the acutely exposed children in comparison with the classmates (37% vs. 13%, χ^2=15.36, P<.001). A *right hemisphere lateralised dysfunction* characterised by abnormal activity in the right fronto-temporal region did not differentiate the acutely exposed children from the classmates (15% vs. 20%, χ^2=0.87, P>.05). We described a so-called cross-hemispherical dysfunction, which consisted of abnormal activity simultaneously in the fronto-temporal region of one hemisphere and in the parieto-temporal region of another hemisphere. This was found in 21% of the children from the acutely exposed group and 5% of the children from the comparison group (χ^2=11.32, P<.001).

According to the spectral EEG-analysis, a significant difference was found between the acutely exposed and the comparison groups (Table 8). The acutely prenatally irradiated children were dramatically distinguished from the classmates by an increase (P<.001) of δ- and β-power and a decrease (P<.001) of θ- and α-power. However, the pattern of summarised EEG spectral power in the children of the both groups exposed at 0–7 and 26+ weeks after fertilisation was statistically equal (except more δ-power among those acutely exposed at 26+ weeks). The children prenatally acutely exposed at 16–25 weeks of gestation had the most distinguished pattern of summarised EEG spectral power (increased δ- and β- and decreased θ- and α-power), as well as those exposed at 8–15 weeks (increased δ- and decreased θ-power) in comparison with the classmates.

Obviously, children's pattern of cerebral electrical activity is, like intelligence, etiologically heterogeneous. On the basis of correlation and regression analyses we found that the children's EEG-pattern was associated with age, current neuropsychiatric disorder, perinatal pathology, mother's mental health, as well as exposure to the disaster — both to stress and radiation. Foetal dose was the predictor for an increase

Table 8 EEG spectral analysis.

Age in weeks after fertilsation	Acutely exposed group	*t*	*p*	Comparison group
Summarised δ (1–4 Hz)-power (%)				
All	**47.65±12.54**	**8.65**	**<.001**	**33.59±10.34**
0–7	44.99±10.71	3.2	=.001	33.36±12.51
8–15	48.53±15.03	4.25	<.001	32.98±12.34
16–25	49.81±13.10	5.46	<.001	34.05±8.17
26–term	45.05±8.41	4.01	<.001	33.99±10.12
Summarised θ (4–7) –power (%)				
All	**15.96±5.61**	**–8.9**	**<.001**	**23.32±6.07**
0–7	16.75±6.08	–3.05	<.01	23.12±7.27
8–15	17.76±7.04	–4.99	<.001	26.35±5.84
16–25	14.01±4.05	–8.47	<.001	23±3.79
26–term	15.89±4.68	–3.12	<.01	21.09±6.42
Summarised α (7–12) –power (%)				
All	**26.62±10.24**	**–5.5**	**<.001**	**33.50±7.17**
0–7	29.79±12.77	–1.07	>.05	33.7±8.28
8–15	24.55±7.88	–3.12	<.01	30.93±7.39
16–25	25.25±11.63	–3.36	<.001	33.74±6.95
26–term	29.31±8.37	–2.55	<.01	35.42±7.85
Summarised β (12–32) –power (%)				
All	**16.49±6.42**	**4.28**	**<.001**	**13.33±3.63**
0–7	15.86±7.13	1	>.05	13.94±2.75
8–15	14.97±7.72	1.48	>.05	12.75±2.59
16–25	17.76±5.8	3.7	<.001	13.2±3.1
26–term	17.09±7.06	2.27	<.01	13.92±4.63

Note: Bonferroni corrected α-level of <.001 was used to assess statistical significance.

of summarised δ-power (regression coefficient =.46; P<.001) and β- power (regression coefficient =.22; P=.002), and for a decrease of θ- power (regression coefficient =–.48; P<.001) and α-power (regression coefficient =–.35; P<.001) (Table 9). This dose-effect relationship was the most pronounced in the children exposed at 8–25 weeks, especially at 16–25 weeks after fertilisation. Thyroid foetal dose was also the predictor for an increase of summarised δ-power (regression coefficient =.49; P<.001) and for a decrease of θ- power (regression coefficient =–.5; P<.001) and α-power (regression coefficient =–.32; P<.001). This dose-effect relationship was the most pronounced in the children exposed at 16–25 weeks after fertilisation (Figure 8).

The correlations between intelligence and spectral power of EEG were revealed as follows. Full scale IQ deterioration was associated with an increase of δ-power (r=.25–.35; P<.001), especially at the left frontal region (r=.31–.35; P<.001), a decrease of α-power (r=.27–.36; P<.001), especially at the left parieto-occipital region (r=.33–.36; P<.001), as well as a lateralisation of β-power to the left fronto-temporal region (r =.2; P=.02).

Verbal IQ deterioration was associated with an increase of δ-power (r=.25–.41; P<.001), mainly in the left hemisphere, especially at the left frontal region (r=.38–.41; P<.001), a decrease of α-power (r=.22–.38; P<.001), also mainly in the left hemisphere, especially at the left frontal region (r=.34–.38; P<.001), as well as an increase of β-power (r=.27; P<.001). Performance IQ deterioration was associated with an increase of δ-power (r=.15–.28; P<.001), mainly in the right hemisphere, especially at the right parietal region (r=.21–.28; P<.001), a decrease of α-power (r=.17–.26; P<.001), also especially at the right parietal region (r=.23–.26; P<.001), as well as an increase of β-power (r=.21–27; P<.001) at the right temporal region. WISC performance/verbal discrepancies with verbal decrements were associated with lateralisation of δ-power towards the left parietal region (r=.24; P=.04), a decrease of θ-power in the left fronto-temporal region

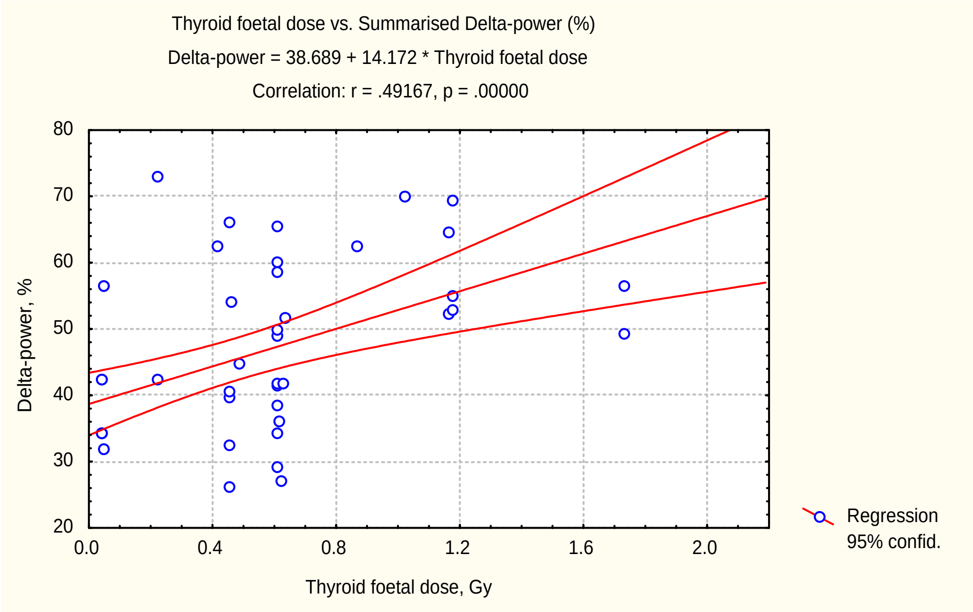
Table 9 Relationships between EEG and doses of prenatal irradiation.

Age in weeks after fertilsation	Dose	Regression coefficient	$F_{(df1,\ df2)}$	*p*
		Summarised δ (1–4 Hz)-power (%)		
All	**Thyroid foetal**	**.49**	**61.2214$_{(1,152)}$**	**.000000**
	Foetal	**.46**	**54.5663$_{(1,198)}$**	**.000000**
0–7	Foetal	.45	12.7301$_{(1,\ 43)}$	.0008
8–15	Thyroid foetal	.43	11.3462$_{(1,54)}$	.001
	Foetal	.42	10.7512$_{(1,54)}$	.002
16–25	Thyroid foetal	.49	15.6218$_{(1,45)}$	.0002
	Foetal	.46	13.3483$_{(1,45)}$	.0006
26–term	Thyroid foetal	.54	18.6339$_{(1,53)}$	.00009
	Foetal dose	.49	13.91842$_{(1,53)}$	.0005
		Summarised θ (4–7) –power (%)		
All	**Thyroid foetal**	**–.5**	**64.3190$_{(1,152)}$**	**.000000**
	Foetal	**–.48**	**60.3387$_{(1,198)}$**	**.000000**
0–7	Foetal	–.34	6.9570$_{(1,\ 43)}$	.01
8–15	Thyroid foetal	–.51	17.2614$_{(1,54)}$	.0001
	Foetal	–.53	19.1616$_{(1,54)}$	.00006
16–25	Thyroid foetal	–.63	32.0500 $_{(1,45)}$	.000001
	Foetal	–.59	26.8140$_{(1,45)}$	.000004
26–term	Thyroid foetal	–.43	10.2321$_{(1,53)}$	.002
	Foetal dose	–.44	11.0047$_{(1,53)}$	.002
		Summarised α (7–12) –power (%)		
All	**Thyroid foetal**	**–.32**	**22.9415$_{(1,152)}$**	**.000003**
	Foetal	**–.35**	**27.0970$_{(1,198)}$**	**.000000**
0–7	Foetal	–.26	3.6292$_{(1,\ 43)}$	.06
8–15	Thyroid foetal	–.26	3.5650$_{(1,54)}$	.06
	Foetal	–.31	5.3726$_{(1,54)}$	.02
16–25	Thyroid foetal	–.35	6.7276$_{(1,45)}$	.01
	Foetal	–.39	8.6232$_{(1,45)}$	.005
26–term	Thyroid foetal	–.39	8.2347$_{(1,53)}$	.006
	Foetal dose	–.3	4.4584$_{(1,53)}$	.04
		Summarised β (12–32) –power (%)		
All	**Thyroid foetal**	**.14**	**3.7750$_{(1,152)}$**	**.05**
	Foetal	**.22**	**9.9334$_{(1,198)}$**	**.002**
0–7	Foetal	.09	0.4783$_{(1,\ 43)}$	.5
8–15	Thyroid foetal	.11	0.6035$_{(1,54)}$	.4
	Foetal	.23	2.8587$_{(1,54)}$	.1
16–25	Thyroid foetal	.14	0.944$_{(1,45)}$	.3
	Foetal	.44	6.6197$_{(1,45)}$	.01
26–term	Thyroid foetal	.17	1.3397$_{(1,53)}$	.2
	Foetal dose	.11	0.5989$_{(1,53)}$	.4

(r=.27–31; P<.001), as well as an increase of β-power (r=.2–.27; P<.001).

Although intelligence is an integrative function of the human brain, full scale IQ and, especially, verbal IQ are closer associated with the left hemisphere functions, whereas performance IQ — with the right hemisphere ones. According to the data obtained a possible cerebral basis of full scale IQ and verbal IQ deterioration as well as WISC performance/verbal discrepancies with verbal decrements in the prenatally irradiated children is dysfunction of the left frontal, temporal and parietal lobes. This dysfunction apparently involves the cortico-limbic system, prefrontal cortex (frontal associative area), the secondary cortical receptor fields (temporal associative area), and the tertiary parietal associative area at the left, dominating, hemisphere [*56, 57*].

It seems to be possible to attribute this central nervous system dysfunction to prenatal exposure to ionising radiation, especially at the second critical period of cerebrogenesis (16–25 weeks after fertilisation)



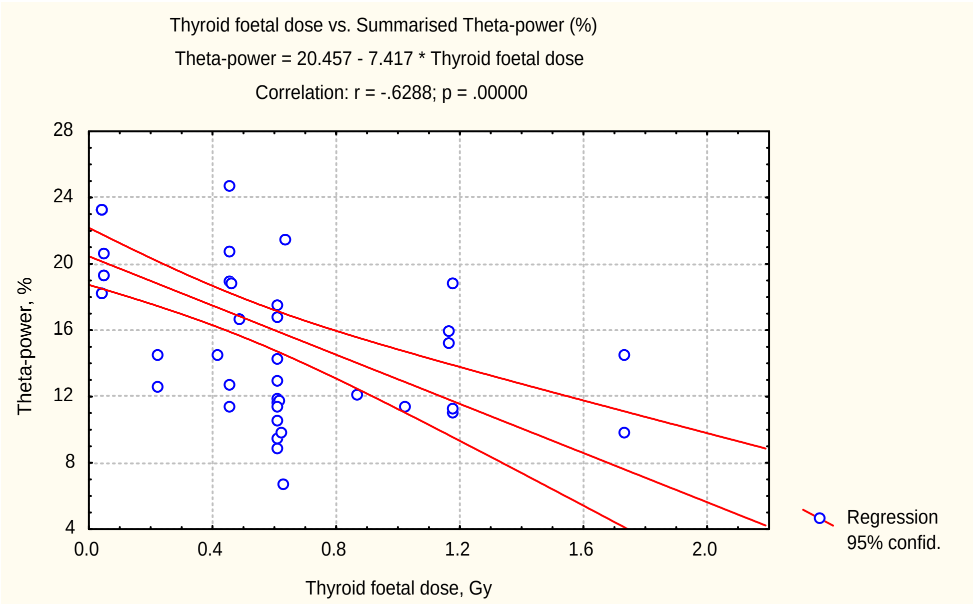


Figure 8. Relationships between summarised δ (1–4 Hz)-power (%) and summarised θ (4–7) – power (%) vs. foetal thyroid dose, in children of the both groups (n=47) exposed at 16–25 weeks after fertilization.

— the time of the most sophisticated events of brain creation, as well as limbic system, brain asymmetry and hemisphere dominating forming [*58–60*]. Moreover, radiation-induced malfunction of the foetal thyroid-pituitary system cannot be excluded.

ICD-10 diagnosis

According to the ICD-10 clinical descriptions and diagnostic guidelines, neurological disorders were revealed in 65 of the children of the acutely exposed group and in 25 of the classmates (χ^2=27.85; P<.001) (Table 10). The overwhelming majority of this pathology were episodic and paroxysmal disorders, which were revealed significantly more often in the acutely exposed group than in the comparison group (61% vs. 29%; χ^2=20.69; P<.001). The children-evacuee had significantly more epilepsy (G40) and migraine (G43) than the classmates. Epilepsy and other paroxysmal disorders were verified by clinical EEG, when clinical pattern of episodic or paroxysmal disorder corresponded to paroxysmal brain electrical activity (spikes, spike-waves, acute and slow waves of high amplitude >100 mkV).

Mental and behavioural disorders according to the ICD-10 criteria were revealed in 90 of the children of the acutely exposed group and in 52 of the classmates (χ^2=35.97; P<.001) (Table 10). Organic, including symptomatic, mental disorders (F06, F07), somatoform autonomic dysfunction (F45.3), disorders of psychological development (F80–F89), and behavioural and emotional disorders with onset usually occurring in childhood and adolescence (F90–F98) were diagnosed significantly more often in the acutely exposed group than in the comparison group. Mental comorbidity was 24% in the acutely exposed group and 7% in the comparison group (χ^2=11.03; P<.001).

Organic mental disorders were verified by Brain Mapping of QEEG and Visual Evoked Potentials (VEP) and in a number of cases by MRI and CT. Two cases of F07 (Personality and behavioural disorders due to brain disease, damage and dysfunction) and 6 cases of F06 (Other mental disorders due to brain damage and dysfunction and to physical disease) from the acutely exposed group were due to epilepsy (G40), while 1 of F06 from the comparison group was due to epilepsy. Two cases of F07 from the acutely exposed group were linked to mental retardation (F70 and F71). One case of F07 and 14 cases of F06 from the acutely exposed group, as well as 5 cases of F06 from the comparison group were attributed to the evidences of perinatal, predominantly pre- and intrenatal, pathology, i.e. pathology during *in utero* period and delivery, such as moderate to severe toxicosis of pregnancy, uterine haemorrhage during pregnancy, risk of miscarriage, waterless period during delivery, too short- or too long-time period of delivery, hypoxia of foetus and asphyxia of newborn.

The more severe neuropsychiatric disorders — mental retardation, epilepsy, and organic mental

Table 10 Diseases of the nervous system, mental and behavioural disorders according to the ICD-10 criteria.

ICD-10 code	Acutely exposed group	χ^2	P	Comparison group
Diseases of the nervous system (G00—G99)				
Without neuropathology	38	27.85	<.001	75
Episodic and paroxysmal disorders (G40—G47):	61	20.69	<.001	29
G40 Epilepsy	8	5.7	<.05	1
G43 Migraine	8	8.33	<.05	0
G44 Other headache syndromes	36	3.43	>.05	24
G47 Sleep disorders	9	2.06	>.05	4
G90.8 Other disorders of autonomic nervous system	5	5.13	<.05	0
Mental and behavioural disorders (F00—F99)				
Without psychopathology	10	35.07	<.001	48
Organic, including symptomatic, mental disorders (F00–F09):	25	13.78	<.001	6
F06 Other mental disorders due to brain damage and dysfunction and to physical disease	20	8.66	<.01	6
F07 Personality and behavioural disorders due to brain disease, damage and dysfunction	5	5.13	<.05	0
F12 Mental and behavioural disorders due to use of cannabinoids	1	1.01	>.05	0
Neurotic, stress-related and somatoform disorders (F40–F48):	36	0.56	>.05	31
F45.3 Somatoform autonomic dysfunction	23	10.04	<.01	7
F48.0 Neurasthenia	13	4.01	<.05	24
F51 Nonorganic sleep disorders	6	2.08	>.05	2
Mental retardation (F70—F79):	2	2.02	>.05	0
F70 Mild mental retardation	1	1.01	>.05	0
F71 Moderate mental retardation	1	1.01	>.05	0
Disorders of psychological development (F80–F89)	12	12.77	<.001	0
Behavioural and emotional disorders with onset usually occurring in childhood and adolescence (F90–F98)	33	4.34	<.05	20
Mental comorbidity	24	11.03	<.001	7

disorders — were diagnosed in 25 acutely exposed children and in 6 classmates (χ^2=13.78; P<.001). The majority (16) of the acutely exposed children with these disorders (including 2 cases of mental retardation) were irradiated at 8–15 and 16–25 weeks after fertilisation. Thyroid foetal dose of these children with severe neuropsychiatric disorders was significantly higher than in other children of the acutely exposed group (.78±.31 vs. .59±.28, t = 2.79, P<.01).

It is clear that the children's neuromental disorders are etiologically heterogeneous. Higher economical level of a family, better somatic health of a child, better mental health of parents are the contributors towards a better children's neuromental health. Higher doses of prenatal irradiation, especially foetal thyroid dose, more severe stress events, and additional mother's hazards in the prenatal period, worse mother's mental health, as well as problems of the perinatal period are the contributors towards children's neurological and mental health deterioration.

Discussion and Conclusions

The UNSCEAR Report-2000, Annex J: Exposure and Effects of the Chernobyl Accident [*61*] touched the problem of the psychological development of the children who were exposed to radiation from the Chernobyl accident *in utero* basing on one publication only [*21*] where cognitive, emotional and behavioural disorders in prenatally irradiated children were attributed exclusively to unfavourable social-psychological and social-cultural factors.

The WHO Pilot Project «Brain Damage in Utero» International Advisory Board assumes that prenatal exposure to the Chernobyl disaster can give rise to a dysfunctional child, either because of organic damage to the developing brain or because of the disturbed psychosocial milieu. Indeed, intelligence peculiarities, neurophysiological abnormalities, and neuromental health deterioration in the children acutely prenatally exposed to both radiation and stress are etiologically multifactorial. Although the children were affected by multiple exposure including prenatal stress and current social, economical and medical problems in their families, the «dose—effects» relationships concerning both intelligence and EEG-parameters, which are the most marked at the critical periods of cerebrogenesis, testify to significant contribution of prenatal irradiation into the brain damage.

This study confirms and develops the results of the WHO Pilot Project «Brain Damage in Utero» [*15, 17*] and relevant studies [*18–22*] concerning mental health and intelligence deterioration in children exposed *in utero* as a result of the Chernobyl disaster. Unlike to the study [*21*] where the authors did not find evidences of the contribution of prenatal irradiation on the children's intelligence deterioration, we have done it. The differences between the results of the study [*21*] and ours we can explain by the followings: 1) different sample: we examined acutely exposed in 1986 children, but they — those resettled in 5–7 years after the disaster, and 2) different measures: they analysed full scale IQ only, but we — verbal IQ (including subtests), performance IQ (including subtests), WISC performance/verbal discrepancies, and full scale IQ. Exactly deterioration of verbal IQ and WISC performance/verbal discrepancies with verbal decrements, were in proportion to the foetal thyroid dose.

Our data do not confirm the results of the studies [*23–25*] concerning similarity and normality of mental and physical health, intelligence similarity of acutely prenatally exposed children in the Chernobyl exclusion zone evacuated to Kiev and children-classmates living in Kiev, as well as that the most important risk factors were maternal somatization and Chernobyl-related stress. A possible explanation of the differences between the results of the studies [*23–25*] and ours study seems to be as follows: 1) Restricted neuropsychological battery for children's intelligence assessment allowed them [*25*] to measure spatial intelligence only, which indeed looks likely to be intact; 2) An absence of clinical neuropsychiatric examination by ICD-10 or DSM-IV criteria and screening-like physical examination in the works [*23, 24*] resulted their conclusion concerning evacuee children's mental and physical welfare to be the point at issue. 3) Inadequate using of gestation months for analysis, but not periods of cerebrogenesis (0–7, 8–15, 16–25, and 26+ weeks after fertilisation), and possible uncertainties in the gestation term estimation did not enable in the studies [*23–25*] to estimate the most important factor in determining the nature of the insult to the developing brain from ionising radiation [*2*] — exposure in critical and «non-critical» periods of prenatal development. 4) An absence of dosimetric data for both children-evacuee and non-evacuee did not enable them [*23–25*] to study a possible dose-effect relationship and to estimate the contribution of ionising radiation towards intelligence and psychological development of the children. However, the most important reason of the differences between their and our studies seems to be the different paradigms of the researches: psychosocial model of the studies [*23–25*], and neuropsychiatric or neurobilogical — in us.

It should be noted limitations and uncertainties of this study. First of all, there is a problem of representativeness of the sample: a possible bias towards «improving selection» where some disabled children due to neuropsychiatric problems could be dropped out from the study, or «deteriorating selection» when for instance prodigy infants attending special advanced schools were also out of the sample. Ideally, all parentally exposed children, or at least all those who had been evacuated from the Chermobyl exclusion zone, should be involved in the study. However, our sample — evacuee in Kiev and non-evacuee classmates living in Kiev — looks quite good from the point of view of similarity about informational and urban saturation environment, providing as much as possible in Ukraine. It should be also stressed that the uncertainties of individual doses estimation are due to an absence at present of generally accepted methodology concerning model of foetal dose assessment. Probably, like in Japan, there will be further new dosimetric systems and reassessment of psychometrical, neurophysiological and other data.

As it was mentioned above, our sample corresponds to subgroups of the Japanese sample [*2*]: prenatally exposed survivors to atomic bomb radiation of the foetal dose category less than 0.01 Gy (n=1,201) — to the Ukrainian comparison group, and those of the dose category 0.01–0.09 Gy (n=322) — to the Ukrainian acutely exposed group. However, there is an extremely important radiological difference between the Japanese and Ukrainian samples — prenatal exposure to radioactive isotopes of iodine. The prenatally exposed to atomic bomb radiation had not been irradiated by radioiodine, but the prenatally exposed children as a result of the Chernobyl disaster received quite significant foetal thyroid doses. This fact makes difficult to extrapolate all data (risks, thresholds of the effects, etc.) from the Japanese sample on the Chernobyl one. It seems that the acutely prenatally exposed children at the Chernoby exclusion zone is a unique sample that should be used for reassessment of risks of prenatal irradiation at radiation accidents on nuclear reactors.

The results of this study agree with the Japanese studies concerning 1) dose related full scale IQ reduction [*10*], 2) an increase of paroxysmal disorders [*62*], 3) critical periods of cerebrogenesis — 8–15 and, especially, 16–25 weeks after fertilisation [*2*]. The highest vulnerability of the brain under exposure at 16–25, but not 8–15 weeks after fertilisation as in the Japanese sample, we can explain by 1) maximal radioiodine transfer rate in foetal thyroid at about 20–25 weeks [*33*], 2) more «delicate» examination of intelligence disturbances that corresponds exactly to the events of the brain creation at 16–25 weeks after fertilisation (neuronal differentiation, limbic system and brain asymmetry forming, apoptosis beginning etc. [*58–60*]). An absence of dramatic increase of mental retardation, especially its severe form, as well as microcephalia obviously can be explained by significantly lower foetal doses of irradiation than that in the atomic bomb survivors.

Following recommendations of Shull & Otake [*63*] concerning future studies of the prenatally exposed survivors and the WHO Pilot Project «Brain Damage in Utero» International Advisory Board for the second phase of the project, we used QEEG and WISC. This resulted in interesting findings of verbal IQ reduction and WISC performance/verbal discrepancies with verbal decrements, which were in proportion to the foetal thyroid dose, especially among those children exposed at 16–25 weeks after fertilisation. Previously we reported [*16, 26, 27*] about TSH level grows with foetal thyroid dose increase with a 0.3 Sv threshold. Probably, these children had been affected by intrauterine hypothyroidism that resulted in intelligence disturbances during their life. Obviously, an international psychoendocrine study should be organised for exploration of functions of the pituitary-thyroid system as a possible biological basis of mental health problem in children irradiated in utero as a result of the Chernobyl disaster.

The prenatally acutely exposed children have quite distinguished pattern of summarised EEG spectral power (increased δ- and β- and decreased θ- and α-power), in comparison with both the classmates and literature normative data [*41, 55*]. Foetal dose and thyroid foetal dose were the predictors of this QEEG-pattern, especially among the children irradiated at 16–25 weeks after fertilisation.

Neurophysiological abnormalities together with intelligence disturbances, both dose-related, especially at 16–25 weeks after fertilisation, as well as a «concentration» of the most severe neuropsychiatric disorders among the children exposed at the critical periods of cerebrogenesis, can testify to the developing brain abnormalities due to multiple factors including the effects of prenatal irradiation.

Verbal IQ deterioration together with lateralisation of abnormal electrical activity to the left hemisphere supports our previous report about the predominance of the left hemisphere dysfunction in prenatally irradiated children [*28*]. Association of verbal IQ and left hemisphere is well-known [*64*], and full scale IQ is closer related to the left than to the right hemisphere [*56*]. It seems that the left hemisphere is more vulnerable to exogenous impacts including ionising radiation than the right hemisphere, probably due to dominating of the left brain and, consequently, its more functional activity.

A possible cerebral basis of intelligence disturbances in prenatally irradiated children is dysfunction of the left frontal, temporal and parietal lobes, involving the cortico-limbic system, prefrontal cortex, temporal associative area, and the tertiary parietal associative area at the left dominating hemisphere [*56, 57*]. However, the predominance of the left hemisphere dysfunction is leading towards higher risk of schizophrenia spectrum disorders in prenatally irradiated children, which is why the long-term follow up study of this cohort is of great importance for clinical medicine and neuroscience.

Thus, the neuromental health of the acutely prenatally irradiated children at the Chernobyl exclusion zone is deteriorated in comparison with the non-evacuee classmates living in Kiev due to more frequent occurrences of episodic and paroxysmal disorders, organic, including symptomatic, mental disorders, somatoform autonomic dysfunction, disorders of psychological development, and behavioural and emotional disorders with onset usually occurring in childhood and adolescence. Obviously, their neuromental health disorders are etiologically heterogeneous including psycho-social and economic factors, medical problems in their families. The effect of real stress events (but not only their perception) during pregnancy together with prenatal irradiation cannot be excluded.

Intelligence of the acutely prenatally irradiated children is deteriorated due to reduction of full scale and verbal IQ, as well as WISC performance/verbal discrepancies with verbal decrements. Although the children's intelligence is multifactorial, the contribution of prenatal irradiation was revealed.

Characteristic neurophysiological changes of the acutely prenatally irradiated children are also etiologically heterogeneous, but the dose-effect relationship, especially at critical periods of cerebrogenesis, testifies the impact of prenatal irradiation.

This study suggests that prenatal exposure to ionising radiation at thyroid foetal dose 0.2–2 Gy and foetal dose 11–92 mSv can result in detectable brain damage.

The data obtained reflect great importance, interdisciplinarity, and complexity of such problem as brain damage *in utero* following radioecological disaster and a necessity to integrate international efforts to its solving.

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