Neuropsychological state of the population living in the Aral Sea region (zone of ecological crisis)

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ABSTRACT

Background: The Aral Sea crisis has led to harmful effects on human habitat. In recent years, mild cognitive impairment is a growing problem.

Objectives: This article provides the results of studying the neuropsychological state of residents living in the crisis zone of the Aral Sea region in the case of Shalkar city. We have provided an assessment of the neuropsychological state of examined population and determined the leading pathology in this region.

Methods: The survey sample included 344 persons of reproductive age from 21 to 45 years. We have obtained results in biochemical studies, indicating perturbations of proteometabolism and lipid metabolism.

Results: A correlation analysis showed dependence between a decrease of albumin and high-density lipoproteins, an increase of low-density lipoproteins and parameters of cognitive function.

Conclusions: The research suggests a high prevalence of cerebrovascular pathology among the population, changes in cognitive function parameters, long-term and short-term memory problems and high levels of depression.

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Introduction

Aral Sea filling and partial drying affects the interests of all countries in Central Asia and is a matter of concern on the part of the world community. The pattern of filling and drying has been noted as an Aral Sea crisis and has led to significant economic damage and to harmful effects on human habitat [1–3]. Shalkar city of the Aktobe region (Population – 28,088 people) located in Western Kazakhstan, near the fresh lake Shalkar and far from Aral (approximately 100 km) is in the zone of ecological crisis due to drying. The Shalkar ambient air is polluted with salts of heavy metals (manganese, lead, cuprum, zinc, iron, silicon) that exceed the permissible level from 1.5 to 6 times [4]. In a control area – Atasu city, there is no excess of the above pollutants detected.

Chemical loading with salt and dust aerosols is one of the risk factors in the Aral Sea region. Long-term exposure to chemical xenobiotics causes a response from the body, where cognitive functions that reflect the state of the nervous system are of particular importance [2,3].

Recently, health status is a very relevant matter as an ecopathological problem, since there is an increased frequency and severity of diseases that are very difficult to explain without assessing environmental factors. Thus, there is an increasing number of central nervous system effects noted among the population in areas with anthropogenic load including: defective memory, low capacity to study, loop of verbal intelligence, delay in neuropsychic development (NPD), including development of motor and speech skills [5–7]. The search for a cause–effect relationship in the “environment and human health” system is important in evaluating the harmful effect of a chemical factor [8]. In recent years, much attention has been paid to the problem of mild cognitive impairment (MCI). This term corresponds to memory problems and to problems with other higher brain functions that are beyond the age norm, but do not cause social disadaptation [9].

In the International Classification of Diseases, 10th Edition (ICD-10), diagnostic criteria for MCI indicate

that MCI syndrome occupies an intermediate position between the changes in cognitive functions and dementia [2,3]. In 55–65% of cases, cognitive disorders are recorded in cerebrovascular diseases, in particular – discirculatory encephalopathy (DEP) that determines a disease progression [6,10,11]. Hypertensive disease, atherosclerosis affecting the main arteries of head and neck play a role in a cognitive disorder formation, based on the neurodegenerative changes in the brain tissue [7,12,13]. This circumstance necessitates the early diagnosis of MCI, allowing timely implementation of preventive measures aimed at preventing or slowing the social disadaptation. In this paper, we describe an assessment of the neuropsychological status of the population in the Aral Sea crisis zone in the case of Shalkar city.

Methods

Research design

Enrollment criteria

Three hundred and thirty-four people are without acute disorders of cerebral circulation, mental disorders, and severe physical illnesses. Persons from these groups have been living in their cities since they were born; they were not affected by harmful factors at the workplace and did not have a history of alcohol intake. The survey sample included persons of reproductive age from 21 to 45 years (Table 1).

Discontinuation criteria

Patients with acute disorders of cerebral circulation, craniocerebral injuries, and disabled people of group II, persons under 20 years old and over 46 years old, working in harmful working environment.

Conditions and methods for recording outcomes

Diseases of the nervous system were diagnosed based on a neurological examination (examination of cranial nerves, motor, sensorium, reflex, cerebellar spheres and coordination, finding meningeal symptoms, determination of cortical functions) [14]. Diagnosis included the complaints of the patient, medical case history and function tests data. Transcranial dopplerography of the cerebral vessels was performed by the Sonomed-300 (SPECTROMED, Russia).

Neuropsychiatric testing included: short-term memory for numbers (STMN), short-term memory for words

(STMW), long-term memory for numbers (LTMN), long-term memory for words (LTMW) [15]; attentional capacity (AC) [16,17]; degree of depression (DD) [18].

The assessment “memory for numbers” makes it possible to evaluate the ability to directly memorize. The subjects were asked to listen to 10 two-digit numbers within 30 s. After that, the subjects should have recorded the memorized numbers on the form for 1 min. In evaluating their performance, we took in to account the total number of numbers that the subjects have remembered.

In assessing “memory for words,” subjects were offered to listen to 10 words within 30 s. The words were one- and two-syllable and not connected with each other by logical meaning, as it could facilitate memorization. After that, the subjects should have recorded the memorized words on the form for 1 min. In evaluating their performance, we took in to account the total number of words that the subjects have remembered. Memory was assessed according to the four-point system: 8 numbers out of 10 – indicator is regarded as excellent, 6–7 numbers – as well, 4–5 numbers – as good, and less than 4 numbers out of 10 – as bad.

Biochemical studies of blood plasma parameters were carried out with an automatic biochemical analyzer Humastar-80 (Wiesbaden, Germany) and a semiautomatic analyzer SturDast MC-15 (Diagnostic Systems International, Germany). They have included: alanine transaminase level (ALT level), aspartate transaminase level (AST level), total amylase and total protein levels, levels of glucose, gamma-glutamyltransferase (GGT), creatinine, urea, alkaline phosphatase (ALP), cholesterol, triglycerides, uric acid (UA). Protein (albumin, alpha, beta 1, beta 2, and gamma) and cholesterol (high-density lipoproteins – HDL, low-density lipoproteins – LDL, intermediate-density lipoproteins – IDL) fractions were determined with an automatic analyzer Hydrasis 2 SCAN (Sebia, France).

Statistical analysis

Data analysis was carried out with a Statistica 10 software package (StatSoft, USA). Processing operations have included the calculation of arithmetic mean values (M), standard errors of arithmetic mean (m), confidence intervals (CI), and standard deviation for variables with normal distributions. The latter was verified by the Shapiro–Wilk test and by the Kolmogorov–Smirnov test. Differences between the groups with normal distribution

Table 1. Description of experimental groups.

No.	Survey sample	Residence	Clinical description
1	108	Shalkar	DEP – cognitive impairment with a long-term memory problem related to words and numbers, a decrease of attentional capacity in connecting with depressive disorders
2	106	Shalkar	In the group of healthy subjects, there were no clinical manifestations of DEP
3	130	Atasu	In the group of healthy subjects, there were no clinical manifestations of DEP

Note: In Atasu, the expected number of patients with encephalopathy was not recorded. There were found only five patients with DEP; the group was not formed.

were found by means of parametric statistical methods and Student's *T*-test for two unrelated groups. Linear dependence was determined by means of the Pearson correlation coefficient for indicators with normal distribution [19–22].

Results

Neurologic state analysis of examined Shalkar residents has revealed that nervous system impairment comes with asthenic-neurotic, vegetative-vascular syndromes and psycho-emotional, cognitive disorders (based on complaints and examination). Thus, patients with DEP were complaining about permanent headaches (77%), non-systemic vertigo (53%), buzzing and head noises (41%), and bad memory for current events (78%) and for distant events (91%). At the time of examination, all subjects with DEP had cerebral symptoms (headache, non-systemic vertigo, various motor, and sensory disorders). Ultrasound scan of brachiocephalic arteries in DEP has revealed signs of non-stenosing cerebral atherosclerosis (CA) with flat homogeneous atherosclerotic plaques in examined groups. Thus, there were 78% of cases recorded in the first group, 56% – in the second group, 23% – in the third group. Ultrasound scan has revealed signs of stenosing atherosclerosis of vessels of the brain and neck: 51% in the first group, 16% in the second group, and 11% in the third group.

Memory disorders in patients with DEP from group 1 and from group 2 were qualitatively different in nature. In studying cognitive function, we have recorded significant problems with STMN in the first and the second groups in comparison with the control group (Table 3). A similar trend was recorded in relation to STMW in the main group in comparison with the control group (Atasu city).

Indicators of LTMN in the compared groups had almost identical values. In the learning test for patients with DEP, there were recorded defections of long-term memory for words in comparison with the control group.

In analyzing the degree of depression (DD), we have found that it was increased by 59% in the main group in comparison with the control group. Attentional capacity was reliably reduced to 20% in groups 1 and 2 in comparison with the control group (Table 2).

Degree of depression is higher in the main group than in the control group (by 59%) and is higher than in the second group (by 38%). The fact of increasing depression rates is also indicated by the following – 58% of the patients from the first group were in a “highly depressive state.” At the same time, the percentage of “highly depressive” people was 26% in the second group and 23% in the control group. On the contrary, there were almost no people with such an indicator as “no depression” in the first (main) group – only 5%. This is significantly less than in the second group (comparison) and the third group (control), in which the indicator “no depression” was observed in 25% and in 28% of people, respectively (Table 3).

Metabolic profiles of the main group have showed a slight, but definite increase in total protein and glucose levels, as well as a decrease in the level of urea and uric acid in comparison with the comparison and control groups (Table 4). In the second group, there is an increase in glucose level and a decrease in urea level in comparison with the control group. Changed biochemical indicators point to adaptive possibilities, which, apparently, are related to metabolic changes in the state of systems and organs, since cells of various tissues and organs are subject to chemical factors. There are no significant changes recorded on the part of other indicators (ATT, ALT, GGT, TG, and ALP).

In terms of protein fractions, the analysis has showed a significant decrease in albumin and γ -globulin levels and excess of β_1 -globulins (Table 5). Decrease in albumin level points to an endotoxiosis. This protein is responsible for the transport of various metabolites and xenobiotics [23,24]. The data also point to damage of antioxidant defense systems, because albumin makes a significant contribution to antioxidative activity due to (normal) free thiol group [25]. It is known that patients with acute exposure to psychotropic drugs have a decreased albumin level. In addition, there was recorded a decrease in the level of thiols. This affects the quantitative content of albumin in blood serum of patients with mental disorders [25]. Thus, the average albumin level is within the lower limit of normal in the main group, namely – it is reduced only by 4% in comparison with the control group, while the number of people having a decrease in this index was 65%. In the control group, only 10% of the subjects have a decrease in albumin level. The comparison group occupies an intermediate position – 57%. The amount of albumin in blood likely determines the performance of its functions and some authors suggest that a decrease in the albumin level can lead to different psycho-emotional states [25,26]. At the same time,

Table 2. Indicators of cognitive function in the population living in Shalkar or Atasu city.

Indicators	Group 1	Group 2	Group 3
	M $\pm$ SEM (CI) N = 108	M $\pm$ SEM (CI) N = 106	M $\pm$ SEM (CI) N = 130
STMN	0.389 $\pm$ 0.02* (0.35–0.42)	0.40 $\pm$ 0.01 (0.37–0.43)	0.45 $\pm$ 0.01 (0.42–0.48)
STMW	0.45 $\pm$ 0.01* (0.42–0.47)	0.43 $\pm$ 0.02 (0.39–0.46)	0.53 $\pm$ 0.01 (0.50–0.55)
LTMN	0.30 $\pm$ 0.01 (0.27–0.33)	0.30 $\pm$ 0.01 (0.27–0.32)	0.34 $\pm$ 0.01 (0.31–0.37)
LTMW	0.34 $\pm$ 0.01* (0.32–0.37)	0.37 $\pm$ 0.01 (0.34–0.40)	0.44 $\pm$ 0.01 (0.41–0.46)
AC	19.47 $\pm$ 0.63* (18.21–20.73)	20.50 $\pm$ 0.57 (19.35–21.64)	22.67 $\pm$ 0.42 (21.83–23.51)
DD	16.48 $\pm$ 0.83* (14.84–18.12)	11.94 $\pm$ 0.95 (10.04–13.84)	10.36 $\pm$ 0.74 (8.89–11.83)

*significant differences with respect to benchmarks, $p < 0.05$

Table 3. Prevalence of depression in compared groups (% M $\pm$ SEM, CI).

	Group 1	Group 2	Group 3
Indicator	(N = 108)	(N = 106)	(N = 129)
High rate of depression	57.84 $\pm$ 4.89 (56.91–58.77)	26.41 $\pm$ 4.28 (17.85–34.97)	23.25 $\pm$ 3.72 (15.82–30.69)
Average rate of depression	28.43 $\pm$ 4.46 (27.57–29.29)	38.67 $\pm$ 4.73 (29.22–48.14)	35.65 $\pm$ 4.21 (27.22–44.09)
Low rate of depression	7.84 $\pm$ 2.66 (7.33–8.36)	9.43 $\pm$ 2.83 (3.75–15.11)	12.40 $\pm$ 2.90 (6.59–18.20)
No depression	5.88 $\pm$ 2.33 (5.43–6.35)	25.47 $\pm$ 4.23 (17.01–33.93)	28.68 $\pm$ 3.98 (20.71–36.64)

Table 4. Biochemical indicators in examined subjects (comparison and control groups).

		Group 1	Group 2	Group 3
Indicator	Reference value	M $\pm$ SEM (CI)	M $\pm$ SEM (CI)	M $\pm$ SEM (CI)
Total protein level	65–85 g/L	70.27 $\pm$ 0.46 (69.35–71.18)	68.29 $\pm$ 0.45 (67.39–69.18)	68.96 $\pm$ 0.40 (68.17–69.76)
Glucose level	4.2–6.1 mkmol/L	5.30 $\pm$ 0.18* (4.94–5.66)	5.61 $\pm$ 0.14* (5.33–5.90)	4.86 $\pm$ 0.07 (4.71–5.01)
Urea level	1.7–8.3 mkmol/L	6.14 $\pm$ 0.15* (5.83–6.45)	6.15 $\pm$ 0.47 (5.21–7.10)	6.57 $\pm$ 0.14 (6.28–6.85)
ALP up to 117 ea/L		78.54 $\pm$ 4.59 (69.44–87.65)	78.47 $\pm$ 3.81 (70.91–86.04)	80.03 $\pm$ 5.39 (69.36–90.71)
Cholesterol level	5.17 mkmol/L	4.64 $\pm$ 0.08 (4.46–4.81)	4.67 $\pm$ 0.09 (4.47–4.86)	4.63 $\pm$ 0.07 (4.49–4.78)
UA level	142–416 mkmol/L	237.68 $\pm$ 7.54* (222.73–252.63)	232.38 $\pm$ 7.23 (218.04–246.73)	275.9 $\pm$ 4.09 (267.84–284.04)

*significant differences with respect to benchmarks, $p < 0.05$

Table 5. Indicators of protein fractions in examined subjects (comparison and control groups).

		Group 1	Group 2	Group 3
Indicator	Reference value	M $\pm$ SEM (CI)	M $\pm$ SEM (CI)	M $\pm$ SEM (CI)
Albumins	60.3–72.8%	60.38 $\pm$ 0.59* (59.21–61.55)	62.15 $\pm$ 0.29 (61.58–62.73)	63.09 $\pm$ 0.29 (62.51–63.67)
α_1 -globulins	1.0–2.6%	2.21 $\pm$ 0.05 (2.12–2.31)	2.11 $\pm$ 0.05 (2.01–2.20)	2.29 $\pm$ 0.08 (2.13–2.46)
α_2 -globulins	7.2–11.8%	8.91 $\pm$ 0.17 (8.55–9.26)	8.63 $\pm$ 0.18 (8.26–9.00)	9.06 $\pm$ 0.09 (8.88–9.25)
β_1 -globulins	5.6–9.1%	7.60 $\pm$ 0.14* (7.31–7.89)	7.40 $\pm$ 0.16* (7.08–7.73)	7.03 $\pm$ 0.09 (6.85–7.22)
β_2 -globulins	2.2–5.7%	3.11 $\pm$ 0.17 (2.76–3.45)	2.99 $\pm$ 0.13 (2.73–3.25)	2.98 $\pm$ 0.06 (2.85–3.12)
γ -globulins	6.2–15.4%	14.65 $\pm$ 0.36* (13.93–15.37)	15.53 $\pm$ 0.35 (14.84–16.22)	15.59 $\pm$ 0.22 (15.15–16.03)

*significant differences with respect to benchmarks, $p < 0.05$

long-term chronic exposure to chemical factors, as well as changing biochemical parameters, reflects the changing process of protein-synthesizing function of the liver due to microsomal oxidation. In evaluating the cognitive impairment dependence on the metabolic profile, we report a potential correlation between the STMW and the level of albumins by conducting related calculations. Pearson correlation coefficient was $r = 0.3$, $p < 0.05$. We have made a prognostic model based on the revealed correlation relationship to find the dependence of STMW on albumin level in blood $Y(\text{STMW}) = -0.26 + 0.01 \cdot x$; regression coefficient is $R = 0.33$, $p < 0.01$.

Comparative analysis of cholesterol level among the study groups has showed no statistically significant changes. In analyzing fractional distribution of lipoproteins, we have recorded a decrease in HDL in the main group – by 19% in comparison with the control group (Table 6). Although the average level of HDL was within the lower limit of normal in the first group, 65% of the subjects had low rates. In the control group, a decrease in HDL was recorded only in 24% of subjects; in the second group a decrease was observed in 36% of subjects. We have recorded a significant decrease in IDL compared with the comparison and control groups. The level of LDL has increased in the first group in comparison with the second – by 23%, and by 36% in comparison with the third group. In the first group, β_1 -globulin level is exceeded by 8% in comparison with the control group.

We have found a direct correlation between the STMW and the level of high-density lipoproteins; the correlation coefficients were $r = 0.4$ $p < 0.05$. We have made a prognostic model based on the revealed correlation relationship to find the dependence of STMW on the level of HDL $Y(\text{KPS}) = 0.23 + 0.01 \cdot x$; regression coefficient is $R = 0.45$, $p < 0.01$. This supports that a qualitative composition in lipid metabolism is significant in terms of short-term memory.

We also note a relationship between the DD and the low-density lipoproteins. The correlation coefficients is $r = 0.36$, $p < 0.05$. We have made a prognostic model based on the revealed correlation relationship $Y(\text{UD}) = 2.42 + 0.24 \cdot x$; regression coefficient is $R = 0.37$, $p < 0.01$.

Discussion

Cognitive disorders (CD) and metabolic changes are one of the most characteristic clinical implications of DEP. In a number of cases, cognitive disorders were the first signs in the clinical picture of a disease and were the main reason for visiting a physician. At the same time, CD in our patients has always been combined with other neurological symptoms typical for cerebral vascular insufficiency [40–44]. Chemical stress in the Shalkar city is one of the environmental risk factors in found cognitive impairments. We have found a close relationship, based on correlation dependence, between the levels of LDL and albumin and the cognitive impairments as a degree of depression severity.

We have recorded disorders of attention and motor learning, and problems with short-term memory for words and numbers (STMW/STMN) in the most of our patients. These disorders were based on metabolic and neurodynamic disorders and on inadequate regulation of cognitive activity, which may reflect brain dysfunction according to the concept of cognitive activity dynamic organization [5].

This type of cognitive and metabolic disorders is the most typical for cerebral vascular insufficiency. It is assumed that neurodynamic cognitive disorders in

Table 6. Indicators of lipid metabolism in examined groups.

Indicator	Reference value	Group 1	Group 2	Group 3
		M ± SEM (CI)	M ± SEM (CI)	M ± SEM (CI)
Cholesterol level	5.17 mkmol/L	4.64 ± 0.08 (4.46–4.81)	4.67 ± 0.09 (4.47–4.86)	4.63 ± 0.07 (4.49–4.78)
HDL	38.6–69.4%	39.81 ± 1.31* (37.19–42.42)	43.49 ± 1.38 (40.75–46.25)	48.91 ± 1.04 (46.84–50.97)
IDL	4.4–23.1%	7.68 ± 0.43* (6.83–8.54)	13.47 ± 1.08 (11.33–15.62)	12.25 ± 0.37 (11.50–12.99)
LDL	22.3–53.3%	53.05 ± 1.29* (50.48–55.62)	43.15 ± 1.33 (40.51–45.79)	39.01 ± 1.18 (36.67–41.35)

*significant differences with respect to benchmarks, $p < 0.05$

*significant differences relative to the comparison group, $p < 0.05$

DEP are based on functional dissociation of brain and subcortical structures due to diffuse changes in the white matter of brain [45–47].

These changes are likely occurring due to chronic cerebral ischemia in hypertension and arteriosclerosis of small vessels. Besides the aforementioned cognitive disorders in patients with CD syndrome in DEP, there were signs of amnesic disorders: impaired concentration and problems with long-term memory for words. Similar memory problems are inherent in organic hippocampal lesions [5].

We have found definite signs of cerebral vascular insufficiency in all patients with DEP during clinic-based studies. At the same time, we have noted a slightly greater severity of cerebral vascular disease. Cognitive and metabolic disorders were recorded in the “comparison” group under mild cerebral vascular disease and less pronounced neurological symptoms.

Dyscirculatory encephalopathy was accompanied by cognitive impairment, problems with long-term memory for words and numbers, decreased attentional capacity with predominant depressive disorders [12,48,49].

Hyperlipoproteinemia is accompanied by an increase in LDL [27]. The results indicate a perturbation of lipid metabolism in the main group with DEP. The observed redistribution is an unfavorable process. It indicates a higher atherogenic index and a higher probability of excess cholesterol deposition in the intima. Chemical stress leads to lipolysis – fatty acids and glycerin enter the liver, where triacylglycerols are resynthesized and lipoproteins are rich in these compounds, in particular – low-density lipoproteins (LDL) are synthesized [28].

The current literature has shown that cognitive dysfunction is the main sign of DEP. Clinical features of DEP can be explained by the fact that the most cases of DEP, unlike acute cerebral circulatory disorders, are related not to extracranial arteria pathology and its main intracranial branches, but to small cerebral arteria involvement (cerebral microangiopathy) [29–32]. The signs of this process are the following: slow mental activity, detraction, decline of speech activity, violation of planning, memory impairment. Progression of

neuropsychological disorders in DEP leads to vascular dementia [32,33]. Higher level of low-density lipoproteins in blood can lead to impaired blood flow and to damaged vascular wall cells [34].

According to our developed model, we can assume that an increase in LDL in blood indicates a statistically significant probability of higher depression rates. Thus, we can assume that an increase in LDL in blood can lead to undesirable consequences in blood supply to the brain, which in turn can result in changing cognitive function, namely – higher depression rates. There are a number of studies showing the relationship between the degree of depression and various biochemical indicators, including indicators of lipid metabolism [35–39].

Conclusion

Changed metabolic profile, in particular – increase in LDL and decrease in the albumin level in blood, is of great importance in pathogenesis of cognitive disorders that can lead to cerebrovascular diseases, in particular – discirculatory encephalopathy. An increase in LDL in blood can lead to undesirable consequences in blood supply to the brain, which in turn can result in changing cognitive function, namely – higher depression rates. According to correlation analysis, changed spectrum of protein and cholesterol fractions is one of factors determining the state of cognitive function, in particular – degree of depression and memory. Cognitive disorder as a neurological symptom in dyscirculatory encephalopathy increases the risk of a neurodegenerative process in brain, which signs are: problems with long-term memory for numbers and words and decreased attentional capacity under less pronounced neurological symptoms. The current study supports the conclusion that at least in part some of these physiological relationships are potentially heightened in populations living in areas with significant ecological disturbances.

Disclosure statement

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