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CLINICAL, GENEALOGICAL AND PSYCHOGENIC FACTORS IN THE GENESIS OF RECURRENT DEPRESSION

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The survey covers the influence of inheritance endogenous mental disorders mechanisms, and the study of the genetics of depression. Significant risk factors for disease development are socio-economic and marital status (low social status correlates with an increase in mental pathology, particularly depression, and lack of family affects a person's adaptive resources, is also a risk factor in the formation of mental disorders). Numerous psychotraumatic factors are also extremely significant for the initiation of any depression. Prospective studies have also confirmed the significance of chronic psychiatric trauma as predictors of recurrent course of the disease. The authors have highlighted interpersonal relationship disorders preceding depression exacerbate the effects of childhood trauma, contributing to the development of recurrent depression. In the absence of chronic stress in adults, the effect of childhood mental trauma was not significant.

Key words: genesis of depression, heredity, social status, distress

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КЛІНІКО–ГЕНЕАЛОГІЧНІ ТА ПСИХОГЕННІ ЧИННИКИ У ГЕНЕЗІ РЕКУРЕНТНИХ ДЕПРЕСІЙ

У статті розглянуто вплив механізмів успадкування ендогенних психічних розладів та вивчення генетики депресії. Соціально-економічний статус та сімейний стан є суттєвими факторами ризику розвитку хвороби (низький соціальний статус корелює зі зростанням психічної патології, зокрема депресії, а відсутність сім'ї впливає на адаптивні ресурси людини, також є фактором ризику в формуванні психічних розладів). Численні психотравмируючи чинники також є надзвичайно значимими для ініціації будь–якої депресії. Проспективні дослідження також підтвердили значимість хронічних психічних травм у якості предикторів рекурентного перебігу захворювання. Автори показали, що розлади міжособистісних відносин, підсилюють ефект психічних травм, перенесених в дитинстві, сприяючи розвитку повторних депресій. При відсутності хронічного стресу у дорослих ефект дитячих психічних травм не був суттєвим.

Ключові слова: депресія, психогенні чинники, спадковість, соціальний статус, дистрес

The study is a fragment of the research project "Complex analysis of clinical–genealogical and pathopsychological features of patients with recurrent disorders", state registration No. 0120U100031.

The health and social status are the consequences for a wide range of clinical and social aspects and include a chronic course, relapses, reduced quality of life and degree of patient's adaptation, deterioration of professional and general functional capacity, accompanied by the job loss and social assistance, and family breakdown. Between 15 % and 30 % of depression' cases are characterized by a long and chronic course, with periods of relapse and remission [5, 6, 8].

The attention among scholars has long been focused on the mechanisms of inheritance of endogenous mental disorders, but the study of the genetics of depression has only recently started. In recent years, a number of new findings have been identified in the development of depressive disorders, and many patterns remain poorly defined, such as those concerning the mutual genetic and environmental factors influences [1, 9].

Depression breeds genetically, but there are many environmental and lifestyle factors that increase the risk of the disorder developing.

Significant risk factors for the disease development are socioeconomic and marital status (low social status correlates with increased mental pathology, particularly depression, and lack of family affects a person's adaptive resources are the risk factors in the formation of mental disorders). Numerous psychotraumatic factors are also extremely significant for any depression initiation. Prospective studies have also confirmed the significance of chronic psychological trauma as predictors of recurrent course of the disease. They demonstrated that impaired interpersonal relationships preceding major depression exacerbate the effects of childhood trauma, contributing to the development of recurrent depression. In the absence of chronic stress in adults, the effects of childhood mental trauma were not significant. Stress sensitization is the tendency to develop recurrent depression in response to psychotraumatic factors; it is considered specific to patients who have experienced childhood psychiatric trauma [5].

In recent years, there has been a fair amount of research into the genetic and environmental determinants of depressive disorders. The findings support the thesis that depression has a complex, multi-factorial nature.

Multiple genes may be involved in pathogenesis, affecting different neurobiological mechanisms that determine the predisposition to develop the disease. However, none of the possible candidate genes in repeated studies have shown a strong correlation to the depressive disorders formation and alone they contribute minimal to the overall etiological structure of mental disorders. The depressive phenotype is shaped by individual environmental factors and, in combination with genetic variability, leads to clinical heterogeneity [1, 6].

The clinical heterogeneity of depressive disorders is closely related to the genetic make-up that shapes the propensity to develop the disease and contributes to its manifestation under different environmental influences [2, 9].

The purpose of the study was to determine the influence of hereditary and psychogenic factors in the genesis of the recurrent depressive disorders.

Material and methods. The total of 154 persons were examined in common, while 108 patients among them had recurrent depression, (main group) and underwent stationary treatment in the Department of Borderline Psychiatry of SI "Institute of Neurology, Psychiatry and Narcology of the NAMS of Ukraine" (the diagnosis was made including criteria IDC-10, (F 3.0–F 33.2). 46 persons were representatives of the general population, without mental disorders and constituted the comparison group. There was also studied medicinal information on 394 patients' relatives and 314 persons' relatives that were included into the studied comparison group to investigate psychoneurological disorders and somatically developed diseases accumulation in families that are the basis in determination in the inclination to inherit this pathology.

To achieve the purpose and to implement the objectives of this study, we used the following methods: clinical, psychopathological, genealogical, psychodiagnostic evaluation and statistical methods of mathematical processing of the results.

The clinical–psychopathological method included analysis of complaints, medical history, life history, analysis of traumatic factors and assessment of the mental condition of patients. Genealogical research included the family tree method, taking into account the presence of mental disorders and concomitant somatic diseases of the proband's relatives. Each proband was informed on the purpose of the study and has given written informational consent to partcipate in the survey. According to the results of the study, a family tree was compiled for each proband. During the clinical and genealogical method, the family trees of each proband from I to IV degree of kinship and to a depth of three generation were studied [8].

While taking clinical-genealogical method there were studied each proband's tree from I to IV relative's level on the depth of three generation.

The sense of making clinical-genealogical research was in the following:

1) The collection of medicinal documentation with information on close relatives probands' health;

2) Making up the family tree of issued children;

3) Family tree analysis.

Psychodiagnostic evaluation included the scale of psychological stress (Lemyr–Tessier–Fillion (PSM–25). Scale is used for actual stress parameters and its phenomenological structure measurement. While processing scale data, the integral parameter of psychic tension is determined (NPS), that is evaluated by the following standards: (NPS more than 125 points – high level of stress, 124–100 points – average level of stress, less than 100 points – low level of stress [3].

The results of the study were mathematically processed in "Statistica" software for Windows. Their statistical significance was analyzed using the Student's t-test. Spearman's rank correlation coefficient was used to highlight the linear relationship between the values. Statistical significance was assessed at the level $\rho \leq 0.05$ (significance level not less than 95 %). Calculations of confidence interval were done by Wald's method in Agresti– Coull correction; calculations were done with online calculator. Particle comparison was performed using statistical criterion F. Statistical calculations and plotting were performed in Excel and Statistica 8.0. [1].

Results of the study and their discussion. According to our results, 74.07 % of the examined were women and 25.93% were men. The mean age of the main group was 46.79 years (52.25 years for women and 41.32 years for men). In the comparison group, the mean age was 43.2 years (46.8 years for women and 42.6 years for men).

Most of those surveyed in the main group had higher and specialized secondary education (47.22 % (51/108) and 33.33 % (36/108), respectively). The comparison group had higher and incomplete higher education (65.72 % (30/46) and 17.39 % (8/46), respectively.

By social status, the majority of those surveyed in the main group were unemployed (52.78 % (57/108)), while in the comparison group more were employed – 65.21 % (30/46). According to marital status, married persons prevailed in both groups (62.96 % (68/108) and 54.44 % (25/46) respectively), there were significantly fewer unmarried persons (14.81 % (16/108) and 19.56 % (9/46) respectively), p=0.05. Widows (widowers) in the main group were 11.11 % (12/108), divorced – 11.11 % (12/108), in the comparison group – 8.69 % (4/46) and 17.39 % (8/46) respectively.

When studying the factors of psychic traumatization, in the genesis of depressive disorders, it was found that 52.78 % (57/108) of examined patients associated the development of a primary depressive episode directly to the influence of psychogenic factors. With the course of the disease, the number of those who cited psychic traumatization factors as provoking factors for the current episode was 42.59 % (46/108) of those surveyed. However, it should be noted that the majority of those in this group were over 50 years of age (88.89 % (96/108)) and had between 3 and 5 depressive episodes in their medical history (78.70 % (85/108)). Some differences were also observed in the very structure of psychiatric trauma factors at the onset compared to the current episode.

In the structure of psychiatric traumatization factors identified in the examined patients during the primary episode, social-psychological factors prevailed – 31.58% (34/108). So, such factors as "uncertainty about the future" (fear of worsening socio-economic situation in the future/changes in living conditions in general, media information). Socio-economic factor was – 24.07% (26/108) (in particular, worsening/dissatisfaction with the material and domestic situation, deterioration/loss of social status) factors (p=0.05). At the same time, in the current episode the number of people who mentioned social-psychological factors as a cause of the disease increased, and was 59.25 % (64/108) of cases. At the same time, the components of this group of psychogenic factors changed somewhat and included both "insecurity about the future" and the experience of loneliness, in particular due to the loss of a loved one or separation from loved ones (8.33 % (9/108)). Health-related factors, mostly self-reported (13.89 % (15/108) of the cases), also accounted for a significant proportion. In the comparison group, there was also a preponderance of social-psychological – 2.41 % (35/108) and family/personal relationship factors of psychological trauma – 21.29 % (23/108).

One of the purposes of the study was to investigate, in patients with recurrent depressive disorder and individuals in the general population (without mental disorders), the degree of heritable burdening with depression, alcohol dependence, auto-aggression, somatic pathology (cardiovascular (CVD), cerebral (CNS), endocrine, gastrointestinal (GI), respiratory and oncological).

To accomplish the task, clinical and genealogical study was performed, during which medical information was collected and processed for 394 relatives, 195 of whom were maternal relatives, 185 were paternal relatives, and in 14 cases were siblings. As a comparative analysis, information on 314 relatives of persons in the comparison group was processed, of whom 167 were maternal relatives, 136 were paternal relatives, and in 11 cases were siblings.

The familial accumulation of psychiatric and somatic disorders in the families of patients in the main group was investigated by comparing the percentages of pathology in the family tree of the patients and in the family tree of the comparison group. All members of the family trees and separately male and female relatives were included in the comparison.

The family trees of the probands were analyzed for the presence of relatives with mental disorders and somatic diseases. Percentages of relatives of probands–patients in the main group with different types of disorders compared with the corresponding percentages of probands in the comparison group.

The results are presented in table 1.

There was a statistically significant predominance of persons with mental disorders among the relatives of patients in the main group compared to those in the comparison group. The percentage of individuals under psychiatric observation (18 %, CI: 14.5–22.1) was 15 times higher than in the comparison group (p=0.0001), those with depression (33 %, CI: 28.5–37.8) was 7.3 times higher (p=0.0001), suicides (7.9 %, CI: 5.6–11.0) was 4.2 times higher (p=0.05), and alcohol dependence (25.6 %, CI: 21.6–30.2) was 1.8 times higher (p=0.0001).

Genealogical analysis showed a significant family accumulation of mental disorders in the family trees of patients with recurrent depression, evidence of a genetic component in the occurrence of this disease's clinical forms. The severity of recurrent depression manifestations in patients (main group) in general is not determined by the percentage of relatives with mental disorders, but the tendency to increase

the severity of recurrent depression with increasing number of suicides in the family tree was revealed. On the other hand, the opposite result was observed with somatic diseases. The percentage of relatives with coronary heart disease (CHD), hypertension (HT), diseases of the CVD, CNS, and GI, as well as cancer and allergic diseases was higher in the family trees of the comparison group (p=0.05) than among relatives of patients.

Table 1

Frequency of relatives with mental and somatic disorders

Disorder	Comparison group, n=314			Main group, n=394			p
	N	%	DI	N	%	DI	
Observation at the psychiatrist	8	2.5	1.2–5.0	71	18.0	14.5–22.1	0.0001
Depression	14	4.5	2.6–7.4	130	33.0	28.5–37.8	0.0001
Suicidal behavior	6	1.9	0.8–4.2	31	7.9	5.6–11.0	0.05
Alcohol addiction	45	14.3	10.9–18.7	101	25.6	21.6–30.2	0.0001
Drug addiction	3	1.0	0.2–2.9	6	1.5	0.6–3.4	0.5090
Mental retardation	17	5.4	3.4–8.6	16	4.1	2.5–6.5	0.3974
CHD	104	33.1	28.1–38.5	68	17.3	13.8–21.3	0.0001
HD	93	29.6	24.8–34.9	76	19.3	15.7–23.5	0.0001
CS	56	17.8	14.0–22.5	48	12.2	9.3–15.8	0.0001
CNS	57	18.2	14.3–22.8	56	14.2	11.1–18.0	0.0001
Bronchial asthma	20	6.4	4.1–9.7	21	5.3	3.5–8.1	0.5563
Pulmonary system diseas	5	1.6	0.6–3.8	9	2.3	1.1–4.4	0.5122
Allergies	41	13.1	9.8–17.3	15	3.8	2.3–6.2	0.0001
Oncological pathology	55	17.5	13.7–22.1	35	8.9	6.4–12.1	0.0001
Diabetes	21	6.7	4.4–10.1	26	6.6	4.5–9.5	0.9619
Thyroid gland disease	25	8.0	5.4–11.5	40	10.2	7.5–13.6	0.3164
GI tract	65	20.7	16.6–25.5	50	12.7	9.7–16.4	0.0001
Gynecological pathology	37	22.2	8.6–15.9	27	13.8	4.7–9.8	0.3975

Note: n – number of people in the group, N – number of people with the study, p–significance level, CI – 95 % confidence interval. The difference between the percentages in the control group and the patient group was assessed using F criterion. The difference is statistically significant, p=0.05.

Due to the data of Lemyr–Tessier–Fillion Scale of psychological stress (PSM–25), there were shown such level of neuro-psychic tension parameters of patients suffered from recurrent depression, that were 137.15±11.26 points, which indicated a high level of psychological stress. While in the comparison group, the level of neuropsychological tension was significantly lower and was 82.74±10.12 points (p=0.001), which corresponded to a low stress level with normal gradations and indicated their adaptability to daily stress.

Manifestations of stress in patients with recurrent depression (main group) included changes in all levels of mental functioning: emotional, cognitive, motivational, behavioral and somatic, and in their totality defined the presence of mental discomfort and state of maladjustment. The most prominent manifestations of stress in patients with recurrent depression were: disturbances in the emotional sphere in the form of low mood and irritability; in the motivational and behavioral sphere in the form of lethargy, apathy, increased fatigue, feeling of loss of control, disorganization and reduced capacity for work; disturbances of somatic state and physiological functions: sleep disorders, appetite, disorders of sexual function, pain symptoms – that formed the clinical picture of a depressive disorder.

The distribution of the examined patients according to the level of psychological distress according to normative gradations are presented in fig. 1.

As we can see from the following figure, there was no great difference on the psychological stress level among the comparison group. But for the patients suffering from the recurrent depression their stronger indicators of medium and high level prevailed. Patients were mostly defined with medium (54.63±3.44 %) and high levels of psychological stress (43.52±3.06 %). Amount of persons with low stress levels among depressed patients were 1.85±0.17 %. While those in the comparison group also determined as having predominantly moderate (50±8.86 %) and low (45.65±4.48 %) levels of psychological distress, and high levels were recorded in only 4.35±0.94 %.

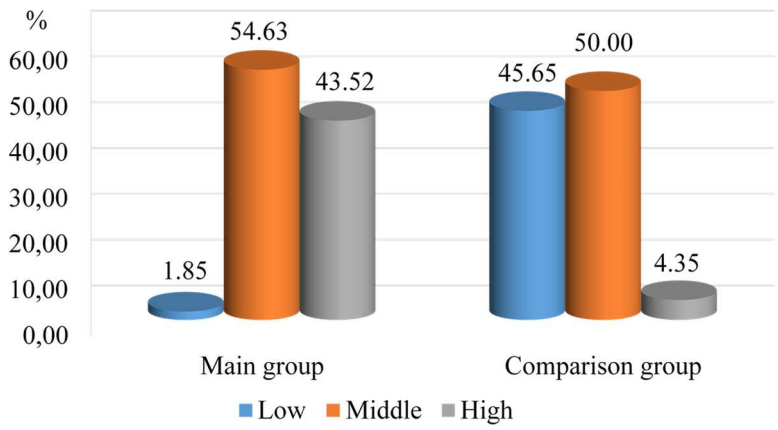

Fig. 1. Distribution of the examined persons according to the level of psychological stress (according to the Lemyr–Tessier–Fillion psychological stress scale (PSM – 25)) * – significant differences between comparison groups

The prevalence of high levels of psychological distress among depressed individuals was statistically confirmed at the p=0.0001 level, DC=–11.42, MI=1.36. Whereas the comparison group was significantly dominated by those with low levels of psychological distress, p=0.0001, DC=11.82, MI=2.40. The high level of psychological distress in patients with recurrent depression determined the presence of emotional, somatic, behavioral and cognitive equivalents of psychological distress, which correlated with the manifestations of depressive symptoms, and reflected general maladaptation, emotional and behavioral conformity to the depressive type. The results obtained suggest that neuropsychological instability parameters may serve as prognostic markers of depression, in particular, a high level of NPS is an informative marker of the presence, and a low level – of the absence of a depressive disorder.

To define diagnostic value and informativeness of the allocated signs and possibility of their use as markers of depressive disorders, the procedure of the sequential statistical analysis by A. Wald in updating by E.V. Gubler has been applied. Diagnostic coefficients (DC) and normativity measures (MI) for the selected features were calculated according to the results of frequency analysis.

The obtained results are given in table 2, where only statistically significant attributes are available, whose frequencies of representation in the groups of examinees differed significantly (p=0.05).

□□bl□2

Hereditable, socio-demographical and socio-psychological recurrent depressive disorders' markers

Parameter	Main group	Comparison group	p	DC	MI
Genetic factors:					
Proband's relative's observation at the psychiatrist	18	2.5	0.0001	–5.78	1.40
Depression	33.0	4.5	0.0001	–8.69	1.24
Suicidal behavior	7.9	1.9	0.0004	–6.15	0.18
Alcohol addiction	25.6	14.3	0.0002	–2.53	0.14
CHD	17.3	33.1	0.0000	2.83	0.22
HD	19.3	29.6	0.001	1.86	0.10
CS	12.2	17.8	0.03	1.66	0.05
CNS	14.2	18.2	0.01	1.06	0.02
Allergic disease	3.8	13.1	0.001	5.35	0.25
Oncological pathology	8.9	17.5	0.0006	2.95	0.13
GI tract	12.7	20.7	0.004	2.13	0.09
Sociodemographic factors					
high/incomplete higher education	53.7	82.61	0.0005	1.87	0.27
Secondary/special secondary education	46.29	16.89	0.0003	–4.25	0.61
Sociopsychological factors (stress load)					
Psychotraumas of sociopsychological nature	50.00	36.96	0.047	–1.31	0.09
High level of psychological distress (NPS)	43.52	4.35	0.0001	–11.42	1.36
Low level of psychological distress (NPS)	1.85	45.65	0.0001	11.82	2.40
High level of stress	30.56	15.22	0.02	–3.03	0.23

The marker diagnostic features of recurrent depressive disorders were hereditary associations with psychopathology, in particular "seeing a psychiatrist in the proband's family" (DC=–5.78, MI=1.40), depression (DC=–8.69, MI=1.24), suicidal ideation (DC=–6.15, MI=0.18), and alcohol dependence (DC=–2.53, MI=0.18). Suicidal behavior (DC=–6.15, MI=0.18) and alcohol dependence (DC=–2.53, MI=0.14); thyroid pathology (DC=–2.32, MI=1.01) and diabetes (DC=–5.1, MI=0.92) low education level (in particular having a secondary or secondary special education (DC=–4.25, MI=0.61)) high level of psychological distress (DC=–11.42, MI=1.36), high level of stressful events during the last year (DC=–3.03, MI=0.23).

Anti-risk markers for the formation of depression were defined as: being burdened with somatic pathology (specifically, allergic diseases (DC=5.35, MI=0.25), CHD (DC=2.83, MI=0.22), cancer pathology (DC=2.95, MI=0.13), GB (DC=1.86, MI=0.10), GI (DC=2.13, MI=0.09) and CNS (DC=1.06, MI=0.02)) tertiary or incomplete higher education (DC=3.71, MI=0.19) adaptability to daily normal activities (DC=11.82, MI=2.40).

Thus, the results of a comprehensive analysis using clinical and genealogical, sociodemographic, and social psychological methods confirm the multifactorial genesis of depressive disorders as in different recent studies [6, 9]. Our results sequenced with [6, 8], which perform data on possible influence of hereditary, social, environmental factors and pathopsychological individual's peculiarities. Thus, a substantial family accumulation of psychiatric disorders in the family trees of patients with recurrent depression: the percentage of those under observation by a psychiatrist, those with depression, suicides, and alcohol dependence is evidence of an important genetic component in the occurrence of clinical forms [2, 4]. As a sociodemographic factor, low educational attainment was diagnostically significant in the genesis of depression. Also, the data obtained on the greater number of unemployed among patients with depressive disorder and the identified socio-psychological factors, high levels of psychological stress and high levels of stressful events, may indicate social maladjustment of this category of persons, which is consistent with scientific sources [2, 7].

Conclusion

This clinical-genealogical research has given an opportunity to determine that the accumulation of psychic disorders in patients' with recurrent depression family tree indicates the important role of inherit and family factors in clinical forms of this disorder combining with social and environmental factors (social and demographic factors, factors of psychic trauma) and socio-psychological factors (peculiarities in perception of important life events that is a high level of psychological distress).

References

1. Vodopyanova NYe. Psikhodiagnostika stressa: SPb: Piter. 2009:117 [in Russian]

2. Lapach SN, Chubenko AV, Babich PN. Statisticheskiye metody v mediko–biologicheskikh issledovaniyakh s ispolzovaniyem Excel. Kiev: "Morion".2000; 320 s. [in Russian]

3. Maruta NO, Fedchenko VYu, Linska KI. Genetichni peredumovy depresyvnykh rozladiv. Ukrayinskiy visnyk psikhonevrolohiyi. 2017; 25(3):43–39 [in Ukrainian]

4. Tetushkin YeYA. Geneticheskaya genealogiya: istoriya i metodologiya. Genetika.2011; 47(5):596–581[in Russian]

5. Ferrari AJ, Somerville AJ, Baxter AJ. Global variation in the prevalence and incidence of major depressive disorder: A systematic review of the epidemiological literature. Psychological Medicine. 2013; 43(3): 481–471. Doi: 10.1017/S0033291712001511

6. Kendler KS, Aggen SH, Neale MC. Evidence for multiple genetic factors underlying DSM –IV criteria for major depression. JAMA Psychiatry. 2013; 70(6):607–599. Doi:10.1001 /jamapsychiatry.2013.751

7. Mullins N, Power RA, Fisher HL. Polygenic interactions with environmental adversity in the aetiologic of major depressive disorder. Psychological Medicine. 2016;46(4):770–759. Doi: 10.1017/S0033291715002172

8. Müller B, Wilcke A, Boulesteix AL. Improved prediction of complex diseases by common genetic markers: state of the art and further perspectives. Human Genetics. 2016; 135(3):272–259. Doi: 10.1007/s00439-016-1636-

9. Sharma S, Powers A, Bradley B. Gene × environment determinants of stress-and anxiety-related disorders. Annual Review of Psychology. 2016; 67: 239–261. Doi: 10.1146/annurev-psych-122414-033408.

10. Villanueva R. Neurobiology of Major Depressive Disorder. Neural Plast. 2013. Doi: 10.1155/2013/873278

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