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DOCTORAL THESIS ABSTRACT

PSYCHOTRAUMATIC FACTORS IN PARANOID SCHIZOPHRENIA

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CONTENT

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GENERAL PART

INTRODUCTION

Schizophrenia is the most important neuropsychiatric disorder, with a severe clinical-evolutionary specificity and important psycho-social effects, becoming a priority in the field of psychiatry and public health. The study of schizophrenia and the complexity of the risk factors for onset and evolution keeps its level of interest high, any new results can contribute to elucidating the potential means of disease control. A correct interpretation of the psychological factors involved in the onset and evolution of the disease can lead to a better understanding of its mechanisms, as well as a closer perspective to the reality imposed by schizophrenia.

EPIDEMIOLOGY

The epidemiological studies have not been an easy approach in the case of schizophrenia, the obtained results varying widely due to non-unitary diagnostic criteria and the lack of specific indicators exclusively for the disease. In this specific context, we can mention a prevalence of about 5‰, and an incidence of 15.2/ 100,000 people, with a higher frequency of the disease in males, especially in the large urban areas and people with with low socio-economic status. Schizophrenia leads to significantly higher mortality rates, with values of the standard average rate between 1.5-3, especially in young people at the onset of the disease.

ETIOLOGY

The etiopathogenic mechanisms of the disease have not yet been fully elucidated, and the concerted action of the following categories of risk factors is discussed:

- biochemical: cerebral biochemical imbalances between the main neurotransmitters;
- genetics: some genes responsible for triggering the disease;
- biological: obstetric trauma, infections, malnutrition or diabetes in pregnant woman, high level of stress during pregnancy, smoking;
- behavioral: abuse or addiction to psychoactive substances;
- psychosocial: psychotrauma, hyperemotional climate, psychological and physical abuse, reduced social support, economic and financial difficulties.

MEDICAL SUBJECT MATTER OF SCHIZOPHRENIA

The disease has a long-term evolution with alternations between acute episodes and periods of remission, the clinical model based on evolutionary stages including the background represented by the neurodevelopmental abnormalities. According to this model, the advanced stages of the disease are dominated by symptoms with higher severity and intensity, progression to the advanced stages is characterized by a specific clinical picture, and the therapeutic intervention in the early stages is more effective.

THERAPY OF SCHIZOPHRENIA

The pharmacological treatment of schizophrenia is based on antipsychotic substances, their therapeutic effect being often supplemented with other psychotropic medications. The antipsychotic substances were classified chronologically and of the therapeutic effect into typical (first-generation, neuroleptic, classical) and atypical (second-generation, novel) antipsychotics. The non-pharmacological therapeutic methods include the full range of measures needed to supplement the effects of drug treatment and we refer here to a wide range of psychological interventions: psychosocial interventions, metacognitive therapies, peer support, psychoeducation, supportive psychotherapy, supportive counseling or family interventions.

PSYCHOTRAUMS AND SCHIZOPHRENIA

Starting from the diathesis-stress model, the role that stress and psychotraumatic events, especially those from childhood, have in schizophrenia was highlighted, both in terms of building a favorable environment for the onset of the disease and its evolution. The most important neurobiological effects of psychotraumas and stress are related to the hyperactivation of the pituitary-hypothalamic-cortico-adrenal axis, also confirmed by animal studies. The emotional disengagement during childhood has been associated with a high incidence of paranoid symptoms, ill-treatments are a marker of the unfavorable evolution of schizophrenia, and childhood psychotraumas have also led to impaired brain structure.

COGNITIVE DEFICIT IN SCHIZOPHRENIA

The deficit of the cognitive function is one of the most important features of schizophrenia, progressing with the evolution of the disease and being correlated with age at onset, being present in 61-78% of people with schizophrenia. Cognitive areas are affected such as: memory and learning functionality, global cognitive functioning, language, abstraction and executive functions, processing speed or attention. This dysfunction affects the ability to perform daily activities, the ability to solve social problems and has proven to be one of the marker elements of the possibility of social reintegration. One of the most important cognitive areas affected to a very high degree in schizophrenia is that of social cognition, this deficiency being in fact the cause of social functional disabilities specific to schizophrenia.

SCHIZOPHRENIA – SOCIO-ECONOMIC COSTS

The social and economic burden of schizophrenia is extremely important and is generated by disease-induced disabilities on the individual, disabilities which in turn are transposed to the family, community and society as a whole. The extremely high economic costs have as main cause the non-adherence to treatment, which leads to an increase in the number of recurrences that require repeated hospitalizations. The cognitive impairments and negative and affective symptoms are factors influencing the quality of life, functional recovery at a level as close as possible to the onset of the disease, being obtained through complex therapeutic programs that combine pharmacological and non-

pharmacological interventions and lead to limiting these negative effects. The difficulties created by the state of the disease are overlaid by the stigma and the whole range of its negative effects, at the individual level and by the family micro-group or even by the extended social group.

SPECIAL PART. OWN RESEARCH

HYPOTHESIS. OBJECTIVES. MATERIAL AND METHOD

By studying the possible correlations between the various categories of risk factors, among which the psychotraumatic ones occupy an extremely important position, the premises of a better and targeted approach are offered, in order to obtain positive long-term results, results that lead to a functional recovery of the individual affected by the disease based on an effective therapeutic management process.

The objectives of the study were the following:

1. Highlighting some psychological risk factors in the evolution of paranoid schizophrenia in a group of patients admitted to a psychiatric ward;
2. Specifying the clinical, cognitive, psychological and functional elements in the subjects from the study group;
3. Highlighting the presence of the psychotraumatic event with potential trigger for paranoid schizophrenia in the personal history of the subjects in the group;
4. Highlighting the role of the psychotraumatic event, of the psychological factors and of their possible correlations with the clinical elements in the paranoid schizophrenia.

A cross-sectional clinical study was performed on a group of 248 subjects diagnosed with paranoid schizophrenia according to ICD-10 criteria, hospitalized in the Psychiatry Clinic II of the Clinical Neuropsychiatric Hospital in Craiova, between January 1st, 2016 - December 31st, 2018.

From the medical documentation (observation sheets) and psychological evaluation at the level of the Clinic II Psychiatry - Clinical Hospital of Neuropsychiatry in Craiova were extracted clinical and socio-demographic data, and as clinical-psychological tools, there were used the scales *Mini Mintal State Examination (MMSE), Global Assessment of Functioning Scale (GAFS), Global Dementia Scale (GDS)*, *Koch's Baum Tree* Test and detecting the presence of psychotraumatic events in the personal history by calculating Wittgenstein's Index in the tree test.

The descriptive analysis of the tracked parameters and their graphical representation was performed in Microsoft Excel, with the help of the Functions-Statistical, Pivot Tables, Chart commands and the functions from the Data Analysis submenu, and commands from the XLSTAT module or the SPSS program were used for the data normality tests (*Shapiro-Wilks, Anderson-Darling*) and complex statistical tests (Z tests for proportions, *Chi square, Kruskal-Wallis, rho Spearman* correlation coefficient).

RESULTS

The distribution according to sex of the subjects from the study group N = 248, indicated a significantly higher frequency (62.90%) of women, the predominance of subjects aged 36-45 years (36.69%), followed by those in the age group 46-55 years (27.02%), and double frequency of the patients from urban areas (64.92%). Almost half of the research subjects (45.56%) are high school graduates, 55.24% are unmarried and 83.87% are beneficiaries of early retirement.

In the study group N = 248, approximately 90% of the subjects presented a duration of disease evolution of over 10 years (average duration of 20.89 $\pm$ 7.79 years), marked by numerous episodes of reexacerbation, 62.50% presenting over 5 hospitalizations. Drug treatment included atypical antipsychotics in all subjects of the group, associated in 95.56% of cases with other psychotropic substances (antidepressants, benzodiazepines, etc.).

The evaluation of functionality through GAFS scale indicated severe (64.11%) and moderate (16.13%) mental deficiencies, and the presence and severity degree of cognitive deficit, assessed longitudinally by MMSE scale, indicated a predominance of moderate and severe cognitive deficit (45.16 %). The scores of GDS scale indicated the presence of stages 1, 2, respectively 3 at 58.47%, characterized by moderate cognitive difficulties in the analysis and understanding of complex problems and an early stage of certain deficits specific to severe neurodegenerative disorders, and in 41.53% of patients, stages 4, 5 in which the cognitive decline is already moderate, characterized by difficulties in the more complex areas of daily life and the appearance of temporal-spatial disorientation.

We used the tree test in our research in order to objectify a psychological profile of the subjects from study group N = 248, the psychological diagnosis can be subsequently correlated with the clinical and socio-demographic data and, moreover, can lead to highlighting a characteristic psychological profile of people with vulnerability to the onset and development of schizophrenia. The existence of psychotraumas in the subjects' lives and the age at which they occurred can be detected by calculating Wittgenstein's index in the tree test, the psychotraumatic events can be considered by correlating with the psychiatric diagnosis and the subsequent evolution of the disease triggering and aggravating factors for the onset and severity of the disease. Wittgenstein's index was present in all subjects in the group, with an average value of 12.18 $\pm$ 2.87 years. We can thus consider that the presence of a psychotraumatic episode in the age range 9-15 years can be a real risk factor for the onset and development of paranoid schizophrenia, especially in the context of the existence of a premorbid personality with vulnerability to psychotic disorders.

DISCUTIONS. STATISTICAL CORRELATIONS.

Taking into account the distribution of subjects according to sex (62.90% women), it was possible to find an inverse report compared to epidemiological studies worldwide and European that indicated an almost double frequency of this pathology in males, associating higher levels of symptom severity. The distribution of subjects according to age and duration of long evolution are similar to the

data from other epidemiological studies. The level of education is directly correlated with that of social dysfunction and with the onset of the disease, its precocity influencing the intellectual performance and the socio-economic status of people with schizophrenia. The socio-economic functioning capacities are drastically reduced, the disabilities produced representing elements that lead to dependence on social and financial assistance services for 96.37% of patients included in the research, results similar to those presented by previous international studies, similar to the inability to to create and maintain social relationships.

The duration of the disease with a large number of hospitalizations are similar to the models presented in the specialized literature, and psychopharmacological associations have highlighted the low level of therapeutic responsiveness. The level of mental deficiency did not highlight significant differences (p ANOVA = 0.712; p> 0.05) between the distributions of the subjects according to the three categories of global dysfunction, thus emphasizing the heterogeneous nature of the disease according to the particular profile of each patient.

Longitudinal follow-up during the period of assessment of the cognitive status of subjects revealed a relatively linear evolution at the end of the treatment periods, which indicated the inefficiency of the drug therapy in this field, results confirmed by other research. The analysis of mean frequencies of MMSE scores indicated an uneven distribution of the level of cognitive deficit (p ANOVA = 0.949, p> 0.05), similar to the mean frequencies recorded on GDS scale (p Student = 0.0669; p> 0.05).

It was possible to demonstrate the existence of a significant correlation (p Chi square = 0.029; p <0.05) between the level of global functionality of the subjects in the study group and their moderate to severe cognitive difficulties, the direct influence of cognitive decline on the evolution from socio-functional perspective of subjects being also underlined by the statistically significant high correlation ($p = 3.396E^{-51}$; p <0.001) between the scores of GAF scale and those of MMSE. The results obtained by the statistical analysis of our study group thus underline the importance that the cognitive deficit has on the quality of the evolution of schizophrenia and the level of functionality.

The cognitive deficit was also significantly correlated with the distribution according to the age groups of the subjects in the study group N = 248 (p = 0.002; p <0.01; $p = 4.808E^{-06}$; p <0.001), thus being able to claim that there is a direct dependence between advancing age and the decline of cognition in the conditions of long-term paranoid schizophrenia, as well as between the level of functionality and residence in the urban environment (p = 0.049; p <0.05). The long-term evolution of the disease was significantly associated between the duration of evolution and GDS scores (p = 0.019; p <0.05), GAFS (p = 0.018; p <0.05), and highly significant for MMSE scores (p = 0.0002; p <0.01), similar situation also in the correlation between the level of cognitive deficit expressed by MMSE scores and the number of hospitalizations (p = 0.030; p <0.05).

The results obtained by applying the tree test, used in this research to highlight the psychological profile of the subjects and, in particular, to identify the presence of a psychotraumatic event with impact on the individual's further development and age at which it occurred, were analyzed

compared to clinical data. The accentuated mental deficiency was significantly associated with the attachment to tradition, steadiness, conformity (49.19%), respectively minor intelligences (50.81%) (p Chi Square = 0.028, p <0.05); impulsivity, impressionability, exuberance, non-conformism, agitation, immediate will or inconstancy, irresponsibility, confusion, present in 64.11% of subjects - p Chi Square = 0.016 (p <0.05); insecurity, shyness, adaptation difficulties, aggression, nonconformism, refusal to submit to effort present in 64.52% of patients - p Chi Square = 0.034 (p <0.05). Cognitive dysfunction was significantly correlated with difficulties in adapting to the environment, existential fear, reserve, shyness, present in 49.60% of subjects, respectively uncontrolled exuberance, fanaticism, hyper-self-assessment and the need to compensate for some internal gaps encountered in 50.40% of the patients included in research (p <0.05).

The exposure to psychotrauma around the age of 12 years (12.18 $\pm$ 2.87 years) is a risk factor for paranoid schizophrenia with cognitive deficiencies and long-term adverse evolution, significantly associated with the current socio-professional status of the subjects (p ANOVA = 0.015; p <0.05) and with a large number of hospitalizations (p ANOVA = 0.000; p <0.01).

CONCLUSIONS

1. In study group N = 248 subjects with the diagnosis of paranoid schizophrenia according to ICD-10 criteria, hospitalized in Clinic II Psychiatry of the Clinical Neuropsychiatric Hospital in Craiova, between January 1st, 2016 - December 31st, 2018, the distribution by sex was predominantly in the favor of women (62.90% vs. 37.10%), aged between 36-45 years (36.69%), 46-55 years (27.02%), respectively 26-35 years (22.18%), 64.92% of subjects from the environment urban, with average educational level (45.56%), professional (19.35%) or secondary (17.34%), not involved in family or couple relationships, without involvement in couple relationships (66.13%) or in socio-professional activities (95.97%).

2. The duration of the disease was 10-19 years (44.35%), 20-29 years (41.94%), and over 30 years (9.68%) (average duration 20.89$\pm$7.79 years), with the time of onset at a young age and multiple episodes that determined repeated hospitalizations (over 5 hospitalizations - 62.50%, 4 hospitalizations - 14.92%; 3 hospitalizations - 11.69%), indicator of an unfavorable evolution with incomplete therapeutic response.

3. The pharmacological treatment was performed in the entire study group with antipsychotic substances in combination with other psychotropic substances (mood stabilizers, antidepressants, benzodiazepines) (95.56%).

4. The level of social adaptation was one specific to the accentuated deficiency (64.11%), severe (19.76%), respectively medium (16.13%), without being registered a statistically significant difference of distribution at the level of the study group significant (p ANOVA> 0.05).

5. The cognitive deficit in the patients of the study group was mostly severe (MMSE scores 0-23) (47.18%), respectively medium and severe (MMSE scores 20-23 (32.26%) with a relatively linear evolution during the evaluation period and presenting an uneven distribution (p ANOVA> 0.05).

6. The level of functional and cognitive impairment (GDS scores) fell into the category of moderate cognitive difficulties in the analysis and understanding of complex problems and an early stage of deficits specific to the severe neurodegenerative disorders (58.47%), respectively difficulties in more complex areas of daily life and temporo-spatial disorientation (41.53%), without a statistically significant frequency distribution (p Student> 0.05).

7. The cognitive deficit leads in patients with paranoid schizophrenia to disabilities of adaptation and social functioning ($p < 0.05$; $p < 0.001$), being influenced by the age of people affected by the disease ($p < 0.01$), the long duration of its evolution ($p < 0.01$) , large number of episodes ($p < 0.05$), uncontrolled exuberance, fanaticism, hyper-self-assessment and the need to compensate for some internal gaps ($p < 0.05$).

8. The diagnosis of paranoid schizophrenia leads to significant global functioning disabilities associated with the urban environment of residence ($p < 0.05$), the long duration of the disease ($p < 0.05$) and the following psychological elements: solid foundations, attachment to tradition, steadiness, conformism, respectively minor intelligences ($p < 0.05$); impulsivity, impressionability, exuberance, non-conformism, agitation, immediate will or inconstancy, irresponsibility, confusion ($p < 0.05$); insecurity, shyness, difficulties in adapting, aggression, nonconformism, refusal to submit to effort ($p < 0.05$).

9. Criticality, bizarreness character and good observation capacity, adaptability and need for social contact, susceptibility, depression, introversion tendencies and phantasmagorias were statistically significantly associated ($p < 0.05$) with the impairment of functional and cognitive abilities (GDS), similar to discipline, self-control, selflessness and shyness ($p < 0.05$).

10. The presence of the first psychotraumatic event during life, expressed by calculating Wittgenstein's index in the tree test (Koch) was identified in all subjects in the group at an average age of 12.18 ± 2.87 years, the age range 9-15 years being a risk factor for the onset and development of paranoid schizophrenia and the prolonged duration of adverse disease progression.

11. The presence of the psychotraumatic episode with the potential to trigger paranoid schizophrenia at the average age of 12.18 ± 2.87 years is statistically significantly correlated with the low socioeconomic status of people with this diagnosis ($p < 0.05$) and the large number of disease episodes that led to readmissions ($p < 0.01$).

12. The results of this research are confirmed in similar data presented by previous studies, but at the same time draw attention to the importance of identifying the presence of psychotraumatic events in the personal history of individuals with paranoid schizophrenia and when psychotrauma occurred to better monitor the disease progression and of achieving a complex therapeutic approach, which should include psychological interventions in order to ameliorate the effects of these events. Thus, the current therapeutic objectives can be achieved through the multidisciplinary approach, psychiatrist - clinical psychologist, which are not limited to the remission of psychotic symptoms, but also to the psycho-social recovery of people with this diagnosis.