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A 45-year follow-up study of adolescent schizophrenia. Part II: Age of disease onset, type of onset of the disorder and presence of developmental burden in the context of disease course and long-term social functioning of patients

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Summary

Aim. Research on predictors of adolescent schizophrenia, especially that based on long-term follow-up studies, is rare in the literature. In our analysis, we examine the relationships of the age of disease onset, type of onset of the disorder and the presence of developmental burden with clinical and social indicators of the disease course.

Method. A total of 69 patients hospitalized at an average age of 16 years (time point 0) due to schizophrenia (retrospectively re-diagnosed according to ICD-10 criteria) and re-examined 5 years later (time point 1 – personal examination of 41 individuals) were re-evaluated for clinical and social parameters 45 years after initial hospitalization (time point 2 – personal examination of 21 individuals). Besides personal examination, other methods of data collection were also used, including hospital queries.

Results. The hidden type of onset of schizophrenia revealed numerous and various correlations with both the symptomatic picture and the clinical course of schizophrenia, and with distant social functioning of the subjects, translating into a classical Bleuler symptomatic picture, weaker response to treatment, and worse functioning in personal and professional life. The presence of significant separations in childhood proved to be a factor conducive to insight and less intense psychopathology in the distant course of schizophrenia. The family burden of schizophrenia correlated with the catatonic picture in the future and with more hospitalizations and earlier death.

Conclusions. The hidden type of onset of schizophrenia is the most important predictor of its later course.

Key words: schizophrenia, adolescence, prognosis

Introduction

Notes outlining the general theoretical context of the research project are included in the introduction to Part I of the cycle [1]. Part II of our follow-up study deals with the predictive value of the age of disease onset, type of onset of the disorder and some developmental burdens (organic, hereditary, separation trauma, and school difficulties). Both the age of onset and the type of onset (acute vs. hidden) are predictors that are often discussed in the literature; however, their position is somewhat different. The earlier age of disease onset has traditionally been associated with worse clinical and social prognosis [2, 3], with VEOS being given a distinguished position as the form with a particularly unfavourable prognosis [4, 5]. However, more recent research results often challenge the negative predictive value of earlier onset of schizophrenia [6], and even suggest that a younger age at disease onset may be associated with better prognosis [7], even when considering the VEOS subpopulation [8]. This situation reflects very well the heterogeneity of the phenomenon of schizophrenia.

On the contrary, the unfavourable prognostic value of the hidden onset of the disease is not generally questioned, and it even seems to be more important in the case of EOS and VEOS than in the case of schizophrenia with onset in adulthood [2, 4, 9]. The organic background of schizophrenia has remained a widely discussed topic for about 30 years, but the links between brain damage and the image of schizophrenia and its distant prognosis remain undefined. In attempts to define this predictor, recently, measurements of grey matter thickness in various cortex regions are often used; however, the follow-up periods considered in such studies are often very short [10].

Learning difficulties during adolescence are nowadays perceived as a developmental marker of schizophrenia [11] but there is no clear data on their prognostic value. Nowadays, analyses devoted to specific cognitive functions, such as perception, memory, attention, or executive functions are more frequent in the literature [12]. The predictive significance of hereditary genetic burden for the course of schizophrenia is questionable [13], also due to several methodological difficulties in its examination [14]. However, some studies have shown clinically and socially unfavourable correlations of this predictor [15, 16]. Traumatic experiences in the premorbid period as well as in earlier development were traditionally associated with the more severe onset of the disease, combined with the predominance of positive symptoms and better prognosis, i.e., features corresponding to type I schizophrenia according to Crow [17]. The etiopathological significance of such experiences is often emphasized in psychodynamic concepts [18] but the predictive role of episodes of early separation in relation to the course of the disease has not yet been empirically confirmed.

Material and method

The general methodology of the research project and the scenario of the study at individual points of the assessment are described in the chapter devoted to the methodology contained in Part I of our cycle [1]. Here, we will only point out that the starting group examined at time point 0 consisted of 69 people who were first hospitalized psychiatrically due to adolescent schizophrenia. Forty-one persons from this group were personally examined 5 years later (time point 1) and 21 persons another 40 years later (time point 2). In each of the time points, a similar examination pattern was attempted. In addition, lots of data were obtained through mailed questionnaires and analysis of medical records.

The following variables are of primary importance for part II of the cycle: "age of onset", "accuracy of the date of onset", "family burden", "organic burden", "EEG pathology", "significant separation", and "school problems". "Age of onset" means the age of the patient at the beginning of the disease. Clinical descriptions from the years 1968–1972 turned out to be precise enough to relate this variable to the beginning of the disease, not to the beginning of treatment or even to admission to hospital. The "accuracy of the date of onset" indicates how accurate the age of disease onset can be determined. This allows to assess, at least to some extent, how acute and rapid the onset of the disease was. A five-point order scale is used, where the level of accuracy "up to one week" (i.e., with an acute onset) has been set at the bottom of the scale and the level of accuracy "less than one year" (thus, with a hidden onset) at the top of the scale. "Family burden" means the burden of the occurrence of schizophrenia in the family. This scale is quantitative, and the number of points awarded depends on the number of close family members of the examined person treated in hospital for schizophrenic psychosis. In the case of the patient's parents and siblings, 10 points were added per person, and in the case of the parents' siblings and grandparents of the examined person, it was 5 points per person. "Organic burden" means the presence of brain diseases, pathology of pregnancy or childbirth that may affect brain development, somatic diseases that may have similar effects or skull injuries in the patient's history. The occurrence of each of these cases added 5 points on the organic burden scale.

The remaining explanatory variables ("EEG pathology", "significant separation", "school problems") were dichotomized, with the following values at the top of the scales, respectively: the occurrence of pathology in EEG recording, the presence of longer periods of separation of the child from their closest persons during the childhood of the examined person, and the occurrence of significant difficulties at school during the premorbid period, both intellectual and emotional. EEG was performed during the first hospitalization. It was abandoned in cases of previously initiated intensive biological treatment potentially distorting the record. Results corresponding to the borderline of the norm were classified as normal. Periods of separation from the closest relatives (parents or other primary caregivers) that were taken into account

could be related to such circumstances as, for example: stays in orphanages, stays in other care institutions, repeated or prolonged hospitalizations, or stays with relatives. These periods had to last at least several months in total, taking into account the age of the child at the time of separation (shorter periods were considered more important for younger children, compared to older youth). Apparent signs of the child's suffering and stress accompanying the separation were not considered essential.

The psychopathology of schizophrenia recorded at individual time points of the study was divided into the following categories: "autism", "apathy and abulia", "symptoms of splitting", "formal thought disorders", "catatonia symptoms", "hebephrenic symptoms", "delusions", and "hallucinations". The severity of each symptom was assessed by personal examination using a four-point order scale. The sum of the whole schizophrenic psychopathology ("sum of schizophrenia symptoms") was also calculated by adding together the intensity of all eight groups of symptoms. Cognitive deficits were assessed using the same four-point scale. "Cognitive deficits" here mean the impairment of cognitive functions such as thinking and memory, understood as secondary to the development of the schizophrenic process. In the evaluation of this variable at time point 2, attempts have been made to take into account the impact of possible other somatic and, in particular, neurological conditions on the cognitive functions of the subjects, while retaining the possibility of waiving the evaluation in doubtful cases. The "number of hospitalizations" and the total number of days spent in hospital ("days in hospital in total") were assessed on quantitative scales, taking into account only in-patient hospitalizations in general psychiatric wards. The other order variables included were classified on a three-point ("regression"), five-point ("relational abilities", "education", "professional life") or six-point ("insight", "clinical improvement") scale – in the case of which the following values were set at the top of the scales: deep regression, ability to establish mature bonds, higher education, very good professional life, full insight, and full remission, respectively. The scale system was taken from the TSAF and FAF forms constructed in Turku (see Part I of our cycle), and adapted by our predecessors examining the patients at time point 0, in order to maintain methodological continuity of the study.

"Regression" was understood as a return to previous developmental patterns of mental functioning, particularly in the area of defence mechanisms and relations with the object, entailing loss and helplessness. "Insight" was understood as the awareness of mental illness. The following variables were dichotomized: "psychotherapy during follow-up", "marriage", "death before time point 2", "death before the age of 50" in the case of which the following values were set at the top of the scales: psychotherapy between time points 0 and 1, getting married, death before time point 2, and death before the age of 50. The GAF (Global Assessment of Functioning) is a hundred-point order scale combining the assessment of the intensity of psychopathology and the level of social functioning. The conditions of this study were considered to allow for an

assessment with an accuracy corresponding to the five-point range. The "number of children" was regarded as a quantitative variable. It is worth noting that most of the parameters relating to the premorbid period and time points 0 and 1 were evaluated at these two time points, in direct contact with patients and their parents. The only exceptions were: "age of onset", "number of hospitalizations", "total days at hospital" and "GAF", which were assessed retrospectively on the basis of clinical descriptions prepared by the first researchers and data obtained in hospital queries.

Statistical methods

Due to the multitude of dependent variables and potential predictors that we decided to take into account, we stopped the analyses at the level of bilateral correlations without moving to the level of regression analysis, which would have required a significant pre-selection of data. We considered non-parametric tests (Spearman's coefficient) to be more adequate than parametric tests because of the lack of clarity about the normal distribution of the examined traits, a large amount of data outliers from the average, and also because of the large amount of dichotomous and sequential data, not typically quantitative. The statistical significance level was assumed to be $p < 0.05$; however, due to interesting trends emerging from the analyses at a weaker significance level (< 0.1) we decided to also present them, bearing in mind the weak statistical basis of such conclusions. For analyses, we made use of statistical software IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp., Released 2012.

Limitations of the work

We recognize very serious methodological limitations of our work. Fifty years have passed since the period when the first data were collected. During this time, the entire psychiatry has changed significantly, including the understanding of schizophrenia. The decisions of the first researchers concerning the diagnosis of the patients, the division of the symptoms of schizophrenia into categories, how to account for family burdens, organic or significant separations during childhood (to remain with selected examples only) were certainly anchored in the (not only psychiatric) culture and knowledge of those times. The mere re-diagnosis of psychopathological syndromes according to ICD-10 criteria (although, thanks to the reliability and inquisitiveness of the first researchers' descriptions, it seems relatively reliable) certainly does not eliminate these differences entirely. The construction of the scales, which have been preserved for methodological continuity, is not devoid of a certain arbitrariness. The perception of "school problems" as having both intellectual and emotional aspects is certainly too broad and fuzzy. Also, the category of relevant separations is constructed at an unsatisfactory level of accuracy. Undoubtedly, the weakness of the work is the fact that, except in particularly doubtful cases, the results of the examination of individual

persons were not discussed, and the researchers individually and independently made decisions about scores in particular categories.

The work is also limited by the fact that the number of people surveyed personally is clearly decreasing over time: at time point 0 there were 69 people, at time point 1 – 41, and at time point 2 only 21. It should be noted that only 12 people (9 women and 3 men) were examined personally at each of the points of the study. The fact that a lot of data (concerning the course of treatment, education, work, personal life, survival) could be obtained from other sources can only be a partial compensation, burdened by its own limitations.

From the statistical point of view, the work stops at a rather superficial level of analysis, which has already been discussed and justified in the previous subsection. When discussing the limitations of the work, it is worth noting that the analyzed material was developed by researchers to whom psychodynamic theories of schizophrenia etiopathogenesis are particularly close. From our point of view, the psychodynamic paradigm is a very useful model in which – without any claim to superficial and often false integration – psychoanalytical, neurobiological, and medical perspectives can meet [19, 20].

Results

The first area of analysis encompassed correlations between the main explanatory variables and the image of the disease recorded both during the first hospitalization and 5 years and 45 years later. This is illustrated by Tables 1-3.

Table 1. **Age of onset, type of onset of the disorder, and presence of developmental burden and clinical picture of the disease at time point 0**

	Age of onset	Accuracy of the date of onset	Family burden	Organic burden	EEG pathology	Significant separation	School problems
Autism 0	-0.20	0.17	-0.10	-0.13	-0.26	-0.17	-0.02
Apathy, abulia 0	-0.02	0.30*	-0.14	-0.04	0.20	-0.13	0.01
Symptoms of splitting 0	0.00	0.21+	0.16	-0.04	-0.05	0.10	0.17
Formal thought disorders 0	0.08	-0.31*	0.09	-0.16	0.37*	0.05	-0.31*
Catatonia symptoms 0	-0.16	-0.35***	-0.10	0.05	0.12	-0.11	-0.09
Hebephrenic symptoms 0	-0.03	-0.12	-0.07	-0.13	0.09	0.16	-0.17
Delusions 0	0.13	-0.07	0.28*	0.03	-0.34*	-0.01	0.10

table continued on the next page

Hallucinations 0	0.06	-0.07	0.23+	0.00	-0.01	0.12	-0.12
Sum of schizophrenia symptoms 0	0.05	-0.21+	0.15	-0.17	0.02	-0.03	-0.21

Spearman's correlation coefficient
+ = $p < 0.1$
*= $p < 0.05$
***= $p < 0.005$

A later age of onset increases the likelihood of the decompensation being productive rather than autistic, but these relationships are weak. Much more important than age is the onset of the disorder. The hidden onset of the disorder quite clearly correlates with a higher intensity of apathy and abulia symptoms and (to a lesser extent) autistic and splitting symptoms, as well as with a lower probability of formal thought disorders and catatonic symptoms (in this case the correlation is particularly strong). This kind of onset of schizophrenia results in the first decompensation of a rather scarce type. The existence of family burden of schizophrenia translates into a rather rich, delusional-hallucinatory picture of the first decompensation. In cases where EEG pathology was diagnosed, delusions were less frequent, while formal thought disorders were more frequent.

Negative correlations of premorbid school problems with the severity of formal thought disorders and with the total severity of schizophrenia symptoms at time point 0 resemble the data obtained for the blurred type of the onset of the disorder. It can be assumed that these two subpopulations overlap to a significant extent. On the other hand, correlations of the organic burden and significant separation in childhood with the initial psychopathology proved to be vague and uncharacteristic.

Table 2. **Age of onset, type of onset of the disorder, and presence of developmental burden and clinical picture of the disease at time point 1**

	Age of onset	Accuracy of the date of onset	Family burden	Organic burden	EEG pathology	Significant separation	School problems
Autism 1	-0.08	0.35*	-0.20	-0.10	0.49*	-0.12	-0.01
Apathy, abulia 1	-0.13	0.17	-0.19	-0.10	0.56*	-0.06	-0.02
Symptoms of splitting 1	-0.03	0.29+	-0.14	-0.12	0.03	-0.04	-0.18
Formal thought disorders 1	-0.11	0.17	-0.28+	-0.20	0.03	-0.07	-0.20
Catatonia symptoms 1	0.21	0.17	0.29+	0.24	0.46*	-0.07	0.09
Hebephrenic symptoms 1	-0.13	0.22	-0.07	-0.10	-	0.41**	-0.16

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Delusions 1	-0.10	0.08	-0.22	0.12	0.14	0.04	-0.20
Hallucinations 1	0.01	-0.18	-0.16	-0.10	0.24	-0.12	-0.17
Sum of schizophrenia symptoms 1	-0.09	0.30+	-0.22	-0.09	0.42+	-0.03	-0.13

Spearman's correlation coefficient
+ = $p < 0.1$
* = $p < 0.05$
**= $p < 0.01$

The hidden onset of the disorder at time point 1 translates into a rather autistic-splitting image; however, at this stage, the schizophrenia is already much richer symptomatically. In people with a family history of schizophrenia, the intensity of symptoms is weaker, except for catatonic symptomatology. Patients in whom at time point 0 a significant pathology in EEG was diagnosed revealed a significantly higher intensity of autistic, apathy-abulia, and catatonic symptoms at time point 1. It is also the strongest predictor of the rich overall manifestation at time point 1. Significant separation in childhood correlates with the very significant and very selective severity of hebephrenic symptoms at time point 1. The organic burden begins to show some preference for catatonic expression after 5 years of illness. Patients with premorbid school problems at time point 1 are characterized by a rather certain silencing of the dynamics of the disease.

Table 3. **Age of onset, type of onset of the disorder, and presence of developmental burden and clinical picture of the disease at time point 2**

	Age of onset	Accuracy of the date of onset	Family burden	Organic burden	EEG pathology	Significant separation	School problems
Autism 2	-0.11	0.45*	0.27	0.20	0.00	-0.37+	-0.11
Apathy, abulia 2	-0.09	0.27	0.29	0.08	0.00	-0.23	-0.19
Symptoms of splitting 2	-0.05	0.53*	0.20	0.05	-0.07	-0.38+	-0.21
Formal thought disorders 2	-0.15	0.63***	0.21	-0.05	-0.30	-0.39+	-0.14
Catatonia symptoms 2	0.15	0.27	0.51*	-0.17	0.32	-0.18	-0.30
Hebephrenic symptoms 2	-0.06	0.69***	0.18	0.07	-0.22	-0.37+	0.00
Delusions 2	0.05	0.06	0.19	0.12	-0.41	-0.16	0.11

table continued on the next page

Hallucinations 2	0.32	0.16	-0.12	0.19	-	-0.07	0.17
Sum of schizophrenia symptoms 2	-0.01	0.51*	0.36	0.10	0.07	-0.40+	-0.17

Spearman's correlation coefficient
+ = p < 0.1
*= p < 0.05
***= p < 0.005

At time point 2, the age of onset remains an insignificant predictor. The later age of disease onset correlates with a rather lower intensity of many symptoms, but one important exception are catatonic symptoms, especially hallucinations ($p < 0.16$). The hidden type of onset confirms its significant predictive value. Individuals with this type of onset have significantly more symptoms when entering seniority, which is particularly evident in the area of hebephrenia, formal thought disorders, splitting symptoms, and autism. The familial burden of schizophrenia, while it also correlates with the overall symptomatology at time point 2, turns out to be a much less important predictive factor against this background. It points out, however, that in the timeline, there is another clear strengthening of the positive relationship between the family burden of schizophrenia and the intensity of catatonic symptoms. After years, the developmental organic burden and school problems appear to be factors without significant influence on the dynamics of the psychopathology. The effects of early EEG pathology also tend to disperse over time. The presence of significant separations in childhood correlates negatively with any kind of late psychopathology. This applies in the least to strictly productive symptoms. This predictor is by far the strongest of all and translates into lower overall severity of symptoms.

Table 4 describes the relationship between the examined explanatory variables and the treatment effects achieved during the first hospitalization.

Table 4. **Age of onset, type of onset of the disorder, and presence of developmental burden and effects of treatment at time point 0**

	Age of onset	Accuracy of the date of onset	Family burden	Organic burden	EEG pathology	Significant separation	School problems
Clinical improvement 0	0.00	-0.33***	0.05	0.22+	-0.12	-0.04	0.15
Insight 0	0.11	-0.20	0.04	-0.15	-0.02	0.00	-0.10
Relational abilities 0	-0.04	-0.16	0.04	-0.01	-0.13	-0.03	0.03

Spearman's correlation coefficient
+ = p < 0.01
***= p < 0.005

As can be seen, the only really important predictor is the type of disease onset. The hidden type of onset of schizophrenia clearly translates into a weaker clinical improvement at the end of the first stay in hospital.

Tables 5 and 6 show correlations of the analyzed predictors with selected indicators of the later course of the disease and its treatment at time points 1 and 2.

Table 5. **Age of onset, type of onset of the disorder, and presence of developmental burden and certain indicators of the later course of the disease and its treatment at time point 1**

	Age of onset	Accuracy of the date of onset	Family burden	Organic burden	EEG pathology	Significant separation	School problems
Cognitive deficits 1	-0.38*	0.28+	0.14	-0.10	0.24	0.05	-0.09
Number of hospitalizations 1	0.10	-0.03	0.03	0.10	-0.02	0.14	0.00
Days in hospital in total 1	0.10	0.01	-0.06	0.00	-0.06	0.05	-0.03
Regression 1	-0.07	0.33*	-0.11	0.05	0.53*	-0.03	-0.07
Insight 1	0.03	-0.31*	-0.01	-0.12	-0.44+	0.28+	0.04
Clinical improvement 1	0.09	-0.23	0.19	0.03	-0.52*	0.14	0.07
Relational abilities 1	-0.01	-0.20	0.39*	0.01	-0.15	0.13	-0.03
Psychotherapy in follow-up 1	0.07	-0.06	-0.34*	-0.32*	-0.20	0.13	-0.24
GAF 1	-0.06	-0.28+	0.00	0.00	-0.26	0.08	0.16

Spearman's correlation coefficient

+= $p < 0.1$

*= $p < 0.05$

A later age of onset correlates with significantly fewer cognitive deficits at time point 1. The hidden onset of the disorder clearly casts a shadow at time point 1 already. These people are at this time point in a deeper regression, have worse disease insight, more cognitive deficits, and are already quite distinctly different from other subjects in terms of general psychosocial functioning (GAF 1). Contrary to this, the level of family and organic burden at time point 1 does not reveal any correlation with GAF 1. The only outstanding correlation of those two parameters is a significantly negative correlation with the using of psychotherapy in the follow-up period. The existence of EEG pathology at time point 0 means a significant burden especially in the areas of regression, clinical change, and insight at time point 1. This result is consistent with that which has previously emerged from the analysis of the psychopathological picture at time point 1. Patients with significant separations during their development have

better insight into their disease at time point 1, and those with school problems during development use psychotherapy less frequently in the follow-up period.

Table 6. **Age of onset, type of onset of the disorder, and presence of developmental burden and certain indicators of the later course of the disease and its treatment at time point 2**

	Age of onset	Accuracy of the date of onset	Family burden	Organic burden	EEG pathology	Significant separation	School problems
Cognitive deficits 2	-0.15	0.54*	0.32	0.08	-0.08	-0.47*	-0.18
Number of hospitalizations 2	-0.10	-0.06	0.28*	0.10	-0.08	-0.12	-0.07
Days in hospital in total 2	-0.12	0.08	0.19	0.04	-0.13	-0.14	-0.10
Regression 2	-0.13	0.48*	0.29	0.18	-0.17	-0.34	-0.04
Insight 2	0.16	-0.55**	-0.39+	0.01	0.08	0.38+	0.16
Relational abilities 2	0.26	-0.45*	-0.29	-0.35	0.16	0.34	-0.05

Spearman's correlation coefficient

+= $p < 0.1$

*= $p < 0.05$

**= $p < 0.01$

The significance of late onset of the disease seems to be mildly protective; however, correlations of this parameter do not reach statistical significance at any point. Similarly, correlations of organic burden, EEG pathology and school problems turn out to be of little importance after the years. Again, the type of disease onset proves to be the most significant predictor. A hidden onset means above all much weaker insight into the disease at time point 2 but also more cognitive deficits, deeper regression, and weaker relational abilities. The effects of the family burden follow basically the same direction but are much weaker. There is a significant difference in the number of hospitalizations and (to a lesser extent) days spent in hospital. In this respect, the family burden of schizophrenia turns out to be an important predictor of the total number of hospitalizations during the 45-year course of a patient's disease. It is the only significant predictor in this matter among all that have been analyzed in this article. The presence of significant separations in childhood is a protective factor with directions of correlations close to that of the age of disease onset but these correlations are much stronger. This is particularly true for the negative correlation with the development of late cognitive deficits but there is also a clear negative correlation with the level of regression and a positive relationship with the quality of insight and relational abilities.

Table 7 illustrates the relationships between the analyzed independent variables and some indicators of later social functioning.

Table 7. **Age of onset, type of onset of the disorder, and presence of developmental burden and certain indicators of later social and psychosocial functioning**

	Age of onset	Accuracy of the date of onset	Family burden	Organic burden	EEG pathology	Significant separation	School problems
GAF 2	0.26	-0.55***	-0.27	-0.13	-0.02	0.26	-0.03
Education 2	0.49***	0.10	-0.10	-0.10	-0.12	0.00	0.03
Professional life 2	0.18	-0.47***	0.18	-0.04	-0.04	-0.03	-0.01
Marriage 2	0.16	-0.32**	0.17	0.01	-0.11	-0.10	-0.03
Number of children 2	0.17	-0.34*	0.31*	0.11	0.08	-0.01	-0.12
Death before time point 2	0.10	0.16	0.25*	0.19	-0.10	0.03	0.01
Death before age of 50	0.06	0.22+	0.11	0.15	-0.01	-0.10	-0.11

Spearman's correlation coefficient

+= $p < 0.1$

*= $p < 0.05$

**= $p < 0.01$

***= $p < 0.005$

Pathologies in the picture of EEG, the presence of organic burden and the presence of school problems are distantly insignificant. The later age of onset and the presence of significant separations in childhood correlate similarly positively with general psychosocial functioning but as for other parameters, the impact of the age of onset is clearly more significant and the impact of significant separation experiences is virtually insignificant. The significance of the later age of onset can be seen primarily in the highly positive correlation with the final level of education; other parameters benefit at a considerably lower extent. The type of disease onset, also in the area of social adaptation, proves to be by far the most important predictor. A hidden onset translates with great force into worse general psychosocial functioning, as well as worse professional and family functioning (less chance of getting married and a lower number of children). People with this type of onset died more often before the age of 50. The impact of family burden is much weaker but also more varied. Although the general psychosocial functioning of such people is worse, positive correlations are observed in the areas concerning professional and personal life. The statistically significantly higher number of children is particularly noticeable. It is also seen that

people with a family burden of schizophrenia lived shorter, although those were not necessarily very early deaths.

Discussion

Concerning the importance of the age of onset and type of onset of the disease, it can be stated that the results of our analyses confirm the data from the literature described in the introduction of this paper. The later age of disease onset appears to be only a mildly beneficial prognostic factor. It promises a smaller number of cognitive deficits 5 years after the first hospitalization and the only significant distant correlation is with the level of education of the subjects. This should be considered as rather obvious. It can be assumed that a more mature, better formed ego turns out to be more resistant to a disease we know to threaten the psychological integrity of the individual. In comparison with this, the correlations of the hidden onset are, however, much more significant. In particular, it means more splitting and autistic symptoms, and with time also hebephrenic symptoms and symptoms of formal thought disorders. In the case of respondents with this type of onset of the disorder, there is a perspective of increasing intensity of symptoms at subsequent time points. In the course of such an onset of schizophrenia, worse improvement during the first hospitalization, more cognitive deficits, deeper regression, weaker insight, and weaker relational abilities can be expected clinically. From the social point of view, such patients scored much lower on the GAF scale, functioned worse professionally, coped less well in personal life and died more often before the age of 50. It can be argued that a hidden onset increases the probability of the development of a Bleuler-type disease, i.e., one in which the symptoms called by Bleuler the basic symptoms (*Grundsymptome*) will play an important role: autism, affective disorders, disorders of associative processes, and splitting-based (*Spaltung*) ambivalence. This form of schizophrenia, having such a processional core, would be associated with poorer prognosis.

In the broad field of schizophrenia recognized according to ICD-10 criteria (based, after all, largely on the Schneider approach), it would obviously be only a part of the cases, one of many possible etiopathogenic pathways. In our study, the organic burden and school difficulties during development only announce less frequent use of psychotherapeutic treatment during the first 5 years after the first hospitalization. Perhaps they translate into a lower level of reflexivity, which is, after all, a feature that clearly facilitates the use of the psychotherapeutic relationship.

Quite interesting but difficult to interpret are correlations of pathologies in the EEG. They correlate in a contrasting way with initial disorders of content (negatively) and the form of thinking (positively), and 5 years later, they show generally more vivid symptomatology of schizophrenia, especially in terms of autistic-apathic-abulic, and catatonic symptoms. These effects dissipate in the long term. Apparently, the vividness

of mental transformation, which is undeniable in the early stages of schizophrenia, also has its neuroelectric representation.

In our analyses, distant correlations of the family burden of schizophrenia turned out interesting. Such study participants more often had catatonic symptoms, which easily refers to a common view of the importance of biological and genetic components in the etiology of catatonia. They were also more frequently hospitalized and died slightly earlier, although this does not seem to be caused by a more severe course of the disease. It is possible that these relationships (as well as the higher number of children in this group of patients) can be explained by the identification of the patients with their schizophrenic relatives, especially their parents.

In our study, the presence of significant separations during development correlated positively with the severity of hebephrenic symptoms 5 years after the first hospitalization and with lower intensity of each type of psychopathology but especially with classical Bleuler symptoms at time point 2. In both time points of the follow-up, this parameter translated into a fuller insight, and at time point 2 also into fewer cognitive deficits. Therefore, those correlations can be said to have a protective effect concerning clinical aspects, and the strength of these correlations even seems to increase slightly with time. Perhaps, in specific contrast to the schizophrenia discussed earlier, with its hidden onset, we are dealing with a form having a more psychogenic character, which would constitute another possible etiopathological path within the extremely capacious circle of schizophrenia understood according to ICD-10 categories. The positive correlation with the severity of hebephrenic symptoms at time point 1 is very interesting because phenomenologically, these symptoms are often confused with dissociative symptoms, which in turn are a typical clinical consequence of mental trauma.

Conclusions

1. The most important predictive factor in both the clinical and social area was the blurred type of EOS onset.
2. Later age of onset and the presence of significant separations during development are likely to be predictors of mild protective significance, where the role of separation seems to be more important, especially clinically.
3. Significant correlations between the organic burden during the premorbid period and the subsequent course of schizophrenia have not been revealed.
4. The family burden of schizophrenia correlates with the presence of catatonic symptoms in the later course of the disease, with a higher frequency of hospitalization, and with slightly earlier death.

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