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ORIGINAL PAPER

A comparison of adolescent- and adult-onset first-episode, non-affective psychosis: 2-year follow-up

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Abstract This study aimed to compare 2-year outcome among individuals with early-onset (EO; <18 years) versus adult-onset (AO) first-episode, non-affective psychosis. We compared clinical and treatment characteristics of 43 EO and 189 AO patients 2 years after their inclusion in a clinical epidemiologic population-based cohort study of first-episode psychosis. Outcome variables included symptom severity, remission status, drug abuse, treatment utilization, cognition and social functioning. At baseline, EO patients were more symptomatically compromised. However, these initial baseline differences were no longer significant at the 2-year follow-up. This study challenges the findings of a larger and older literature base consisting primarily of non-comparative studies concluding that teenage onset indicates a poor outcome. Our results indicate that adolescent-onset and adult-onset psychosis have similar prognostic trajectories, although both may predict a qualitatively different course from childhood-onset psychosis.

Keywords First-episode psychosis · Duration of untreated psychosis · Adolescence · Early-onset psychosis

Introduction

Early in brain development, synaptogenesis is followed by the elimination of weaker neural connections, a process often referred to as "synaptic pruning". In the sensory areas of the human brain, this process is generally completed by the age of 2 years, but in the prefrontal and association areas it reaches a critical level during adolescence. The onset of psychosis frequently occurs during this period, and it has been hypothesized that the process of

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synaptic pruning is a critical etiological factor influencing both the onset and the course of the illness [1]. Results from a recent study support previous findings of a generalized cognitive dysfunction in subjects with schizophrenia and other non-affective psychoses [2]. The developmental uniqueness of the teenage years renders the onset of psychosis during this period, here called early-onset (EO) psychosis, of particular interest, especially in comparison with AO cases. For this study, we have used the convention of defining EO psychosis as psychosis onset between the ages of 13 and 18 years [3].

A number of older studies have found that marked premorbid impairments are related to a more severe course and outcome in EO psychosis [4–9]. A more recent study demonstrates that EO psychosis patients show significant cognitive impairment [10]. However, three studies comparing EO with AO patients failed to demonstrate unambiguously a worse outcome for EO patients. The first investigation compared 19 EO and 19 AO patients and found more negative symptoms for the EO patients [11]. However, this study focused on children below the age of 15 years, not between 15 and 18 years of age; therefore, results may not represent a typical EO sample, but rather a mixture of very EO [3] and EO psychosis. The second was a file-audit study of 636 patients, of which 118 patients were younger than 18 years old [12]. No significant outcome differences were found between EO- and AO-onset psychosis. The third study compared adolescents (age: 15–19 years; $n = 69$) and adults (age: 26–50 years $n = 69$) presenting for treatment for the first time [11]. At 1-year follow-up, the two groups were similar clinically and functionally, but EO patients used more cannabis. At the 2-year follow-up, again few differences were found, although EO patients had experienced a greater number of relapses.

In summary, the course of EO psychosis clearly reflects deterioration. However, when this course is compared to a "control" group of AO psychosis, no greater downward trajectory of psychopathology has been consistently demonstrated.

The TIPS study (Early Treatment and Intervention of Psychosis; TIPS-I and TIPS-II) explores the clinical utility of an early detection and intervention program in reducing the duration of untreated psychosis (DUP) in a population-based catchment area [13]. As part of this study, baseline differences between EO and AO psychosis were investigated, with EO patients showing poorer premorbid functioning, more depressive symptoms and suicidality, and less cognitive impairment [14]. The current study aimed to investigate whether the previously demonstrated baseline differences between EO and AO patients with first-episode, non-affective psychosis remained significant at a 2-year follow-up.

Materials and methods

Participants

Inclusion criteria were: living in the catchment area (Rogaland County) and recruited over two time periods (TIPS-1: 1997–2001 and TIPS-2: 2002–2004); age 15–65 years; meeting the *DSM-IV* [15] criteria for schizophrenia, schizophreniform disorder, schizoaffective disorder (core schizophrenia spectrum disorders) or brief psychotic episode, delusional disorder, affective psychosis with mood-incongruent delusions (affective psychosis MID), or psychotic disorder not otherwise specified; being actively psychotic, as measured by a Positive and Negative Syndrome Scale (PANSS) score [16] of four or more on at least one of the following PANSS items: P1 (delusions), P3 (hallucinations), P5 (grandiose thinking), P6 (suspiciousness) and G9 (unusual thought content); not previously receiving adequate treatment for psychosis (defined as antipsychotic medication of 3.5 haloperidol equivalents for 12 weeks or until remission of the psychotic symptoms); no neurological or endocrine disorders with relationship to the psychosis; no contraindications to antipsychotic medication; understands/speaks one of the Scandinavian languages; IQ over 70 (WAIS); willing and able to give informed consent. Age of onset was determined retrospectively at study entrance by patient report and additional information provided by relatives. To explore whether excluding patients with an IQ below 70 potentially introduced any selection bias, exclusion rates were compared based on this criterion. We found that 9% of the EO patients with an IQ below 70 were excluded, compared to 5% of the AO patients.

To summarize findings from the initial study, the two onset groups demonstrated the following demographics and clinical characteristics at baseline [14]: EO patients ($n = 43$) were younger and less educated than AO subjects ($n = 189$) according to definition of EO and AO patients. EO patients were more compromised than AO patients on childhood social and academic functioning, had a longer DUP, had more frequent outpatient visits, and displayed more suicidal behavior (plans and attempts). They were more depressed, but cognitively less impaired. Moreover, they had a higher mean GAFs score [15, 17] (Table 1).

A total of 189 patients participated at the 2-year follow-up, including 33 EO and 154 AO patients. No significant differences for age of psychosis onset, age at study inclusion, gender distribution, DUP, study site, drug abuse, suicidal behavior, or hospitalization existed between dropouts versus completers for either of the onset groups. Neither did we find significant differences between EO and AO dropouts for these variables.

Table 1 Clinical characteristics and demographics at baseline

	EO ($n = 43$)	AO ($n = 189$)	p value
Demographics			
Age at study entrance: mean (SD)/range	17.1 (2.3)/ 15.0–24.0	27.0 (8.6)/ 17.0–62.0	.00[c]
Age at psychosis onset: mean (SD)/range	15.6 (1.6)/ 9.5–17.9	26.4 (8.5)/ 18.0–62.0	.00[c]
Men (%)	22 (51)	119 (63)	.17[d]
Scandinavian origin	42 (98)	186 (98)	.51[e]
Mean (SD) length of education at study entrance, years	10.21 (1.05)	12.13 (2.27)	.00[c]
Clinical characteristics			
Diagnosis (%)			
Schizophrenia	7 (17)	58 (31)	.11[e]
Schizophreniform disorder	5 (12)	36 (19)	
Schizoaffective disorder	12 (28)	26 (14)	
Brief psychosis	5 (12)	15 (8)	
Delusional disorder	2 (5)	10 (5)	
Affective psychosis MID	6 (14)	29 (16)	
Organic psychosis	0	0	
Psychosis NOS	6 (14)	15 (8)	
Narrow schizophrenia spectrum diagnosis[a] (%)	24 (56)	121 (64)	.38[e]
Other psychoses[b]	19 (44)	68 (36)	
Drug abuse (%)	7 (17)	52 (28)	.13[d]
Alcohol abuse (%)	3 (7.1)	24 (13.0)	.29[d]
Suicidal behavior (plans or attempts) (%) lifetime	11 (26)	22 (12)	.02[d]
Treatment characteristics			
Included via detection team (%)	15 (34.9)	52 (27.5)	.30[d]
Outpatient at start of psychosis treatment (%)	15 (35)	30 (16)	.00[d]
Duration of untreated psychosis	77.12 (135.16)	33.20 (67.45)	.05[c]
Social/occupational functioning: seeing friends >2/month (%)	34 (73)	128 (83)	.18[d]
Having paid work (%)	16 (61)	85 (52)	.37[d]
Symptoms			
Mean (SD) PANSS pos comp	14.51 (3.65)	14.92 (4.24)	.56[c]
Mean (SD) PANSS neg comp	20.84 (9.54)	19.39 (7.67)	.29[c]
Mean (SD) PANSS cogn comp	5.35 (2.91)	6.79 (3.31)	.01[c]
Mean (SD) PANSS depr comp	12.72 (3.72)	11.13 (3.63)	.01[c]
Mean (SD) PANSS exc comp	8.70 (3.06)	8.69 (3.93)	.99[c]
GAF-symptoms	32.7 (6.1)	29. 7 (6.8)	.01[c]

EO early onset psychosis, *AO* adult-onset psychosis

[a] Narrow schizophrenia spectrum diagnosis: schizophrenia, schizophreniform disorder, or schizoaffective disorder; [b] other psychoses: brief psychosis, delusional disorder, affective psychosis MID, psychosis NOS

[c] t test; [d] Pearson Chi-square; [e] Fisher exact test

Instruments and procedure

Symptom levels were measured with the PANSS. The duration of untreated psychosis (DUP) was defined as the time from onset of psychosis until the start of adequate treatment [18]. The 30 PANSS items were grouped into the following five factors: positive, negative, cognitive, depressive, and excitement [19]. Misuse of alcohol and other substances was measured by the Drake Clinician Rating Scale [20]. Social functioning was measured by the Strauss Carpenter Level of Functioning Scale [21].

After referral to the TIPS early detection team, cases identified with potential psychosis were invited to undergo a more comprehensive psychosis screening involving the PANSS. Individuals with a score >3 on one or more of the PANSS subscale items designated above were then referred for a longer interview using the Structured Clinical Interview for DSM-IV (SCID) [22]. Diagnoses were set based on data from SCID and available patient registry data. Any individuals diagnosed with a non-affective psychosis were subsequently included in the study. The treatment system was based on a single catchment area and was publicly

funded. Within this catchment area, treatment of first-episode patients was designated as the responsibility of the specialized psychiatric treatment system, with rapid transfer of identified cases from the primary care to the speciality services. The treatment program adopted a standard treatment algorithm with a combination of antipsychotic medication (low dose, mostly second-generation antipsychotic medication), individual psychosocial treatment, and psychoeducational multi-family groups.

At follow-up, remission was defined as "a period of at least one week without positive psychotic symptoms corresponding to a PANSS score of 3 or below on positive subscale items 1,3,5 or 6 or on general subscale 9". Relapse was defined as "PANSS item scores 4 or more on one of the above items, over a period of at least seven days".

Assessment raters

The assessment team for the two study inclusion periods was the same except for one new psychologist in TIPS-II. The team consisted of clinically experienced and trained research personnel which performed all evaluations [23]. The raters were trained for reliability in the use of the study instruments. Reliability tests were blind and based on randomly drawn study participants (for details, see previous publications [23, 24].

Consent

The project has been approved by the Regional Committee for Medical Research Ethics Health Region West (015.03) and the Regional Committee for Medical Research Ethics Health Region II (#S-95189). Written informed consent was obtained from all study participants. For patients younger than 18 years of age, informed consent was also provided by their parents or legal guardians.

Statistical analyses

Statistical analyses were performed using SPSS 15.0 (SPSS Inc. Chicago, Illinois). Continuous data were represented as means with standard deviations (SD) and analyzed using Student's t tests. Categorical variables were analyzed using Chi-square (χ^2) or Fisher's exact test. All tests were two tailed with a level of significance of $p < 0.05$.

Results

Although no significant differences in diagnostic distribution were found either at baseline or at the 2-year follow-up, the onset groups were more similar diagnostically at 2 years compared to baseline. Specifically, the proportion of schizoaffective patients in the EO subsample at baseline was twice the proportion of AO schizoaffective patients. At the 2-year follow-up, however, the percent of EO schizoaffective patients had decreased, such that a greater percentage of EO patients now received a diagnosis of schizophrenia. As shown in Table 2, no significant group differences existed at the 2-year follow-up for symptoms (including suicidal thoughts), remission status, substance abuse, numbers of patients on antipsychotic medication, type of antipsychotic medication, participation in psychotherapy, or hospitalization. A greater number of EO subjects and their families had participated in the psychoeducational multi-family groups. Additionally, no differences existed at the 2-year follow-up for the number of friends as measured by the Strauss–Carpenter indices or employment held during the previous year (Table 2).

Discussion

At a 2-year follow-up, no significant differences were found between the EO and AO groups on the five PANSS components. Except for multi-family group therapy, we found no differences in treatment utilization, and no differences existed for suicidal behavior, substance abuse, or functional outcomes. At baseline, in contrast, the EO patients were clearly more compromised both premorbidly and morbidly than AO patients. Moreover, the EO patients had a longer DUP, and had higher levels of depression and suicidal behavior. At 2 years, however, the differences between the two groups were no longer apparent and fewer EO subjects had been continuously psychotic. Since EO and AO patients are in different stages of life (EO: mean age = 17 years and AO: mean age = 27), obviously their social and occupational aspects of life will have different features. For example, since more older subjects will have entered regular occupational activities before psychosis onset, we expected a higher degree of AO patients having returned to paid work at follow-up. However, this expectation was not confirmed.

These findings are intriguing and challenge the notion that EO cases have poorer outcome. In the model of psychosis as a product of developmentally aberrant synaptic pruning, the normal transition from late childhood to early adulthood involves reductions (pruning) of cortical–cortical connections. Psychosis ensues when the reduction exceeds a normal level, generating positive and negative symptoms of psychosis. EO of psychosis in adolescence can arise from two possible mechanisms. First, synaptic connectivity in childhood may already be reduced due to genetics or other factors, such as perinatal trauma. In these cases, normal adolescent pruning reduces connectivity below the psychotic threshold before leveling off. Alternatively, normal levels of synaptic connectivity from

Table 2 Demographics and clinical characteristics including symptoms at 2-year follow-up

	EO ($n = 33$)	AO ($n = 154$)	p value
Clinical characteristics[a]			
Diagnosis (%)			
Schizophrenia	12 (39)	70 (45)	.58[d]
Schizophreniform disorder	1 (3)	7 (4)	
Schizoaffective disorder	6 (19)	30 (19)	
Brief psychosis	1 (3)	9 (6)	
Delusional disorder	0 (0)	7 (5)	
Affective psychosis MID	8 (26)	24 (16)	
Organic psychosis	0 (0)	1 (1)	
Psychosis NOS	3 (10)	6 (4)	
Narrow schizophrenia spectrum diagnosis	22 (61)	107 (72)	.84[d]
Other psychoses	11 (39)	47 (28)	
Drug abuse (%)	4 (11)	29 (18)	.27[d]
Alcohol abuse (%)	2 (6)	18 (11)	.28[d]
Suicidal behavior (plans or attempts) (%) during follow-up period	16 (57)	68 (47)	.42[e]
Remission status[a]			
Continuously psychotic (%)	4 (13)	39 (25)	.10[d]
Social/occupational functioning[a]			
Seeing friends ≥2/month (%)	26 (69)	109 (81)	.18[e]
Having paid work (%)	9 (36)	65 (41)	.61[e]
Living alone (%)	33 (89)	120 (70)	.02[e]
Mean (SD) length of education at study entrance, years	11.28 (1.20)	12.32 (2.63)	.00[f]
Symptoms			
Mean (SD) PANSS pos comp	8.84 (4.97)	9.36 (4.97)	.24[f]
Mean (SD) PANSS neg comp	13.78 (5.66)	15.91 (6.78)	.10[f]
Mean (SD) PANSS cogn comp	4.26 (2.22)	4.29 (2.06)	.97[f]
Mean (SD) PANSS depr comp	9.03 (4.28)	8.18 (3.03)	.48[f]
Mean (SD) PANSS exc comp	6.20 (2.37)	6.53 (2.72)	.33[f]
Mean (SD) GAF-symptoms	54.91 (18.00)	51.27 (17.15)	.28[f]
Treatment[a]			
Mean no. of weeks of antipsychotic medication (SD)	67.28 (38.17)	74.19 (34.37)	.28[e]
No. of subjects not on medication at follow-up (%)	12 (32)	48 (29)	.70[d]
Use of first-generation antipsychotics[b] at follow-up (%)	9 (24)	35 (21)	.67[e]
Use of second-generation antipsychotics[c] at follow-up (%)	16 (43)	81 (49)	.59
Mean no. of weeks of psychotherapy (SD)	89.44 (25.75)	82.13 (29.65)	.71[e]
Participated in multifamily group therapy (%)	24 (77.4)	71 (46.1)	.00[e]
Mean number of hospital admissions during follow-up (SD)	2.00 (1.70)	2.18 (1.8)	.59[f]
Mean duration (no. of weeks) of all admissions (SD)	28.10 (33.84)	26.23 (28.52)	.72[f]

EO early-onset psychosis, *AO* adult-onset psychosis

[a] Percentages of non-missing data on this variable

[b] First-generation antipsychotics: perphanizine, zuclopenthixol, haloperidol, chlorpromazine, chlorprothixene, levomepromazine, pimozide

[c] Second-generation antipsychotics: olanzapine, risperidone, sertindole

[d] Fisher's exact test; [e] Pearson Chi-square; [f] t test

childhood are carried into adolescence, but pruning is abnormally aggressive and reduces connectivity below the psychotic level before leveling off. In the first instance, the onset is slow and insidious with high levels of negative symptoms, while in the second, the onset is rapid and acute with a high level of positive symptoms.

During adolescence, both of these processes level off and symptom severity plateaus. In AO psychosis, the same pruning process occurs, reducing connectivity to psychotic threshold and also leveling off, but it does so later than adolescent cases. This may explain our finding that at baseline, the EO cases were symptomatically more compromised than the AO cases. Nevertheless, the pruning process continues until synaptic density plateaus. Each mode of onset involves a comparable loss of connectivity, but the EO cases are affected earlier than AO cases. Eventually, however, both EO and AO groups will reach the same level of reduced connectivity, albeit at different

time points. This can be observed in our sample, as the EO cases were significantly more compromised than AO cases at the initial evaluation (baseline), but differences attenuated over time and both onset groups demonstrated equivalent levels of severity and impairment at follow-up.

The limitations of the present study deserve acknowledgment. Despite similar treatment protocols, the administration of treatment may have differed between groups. Another shortcoming of the study regards the lack of a specific measure of cognition. Cognitive functioning was only measured by the PANSS, which is a notably poor measure of cognitive functioning [24]. Further, our study excluded patients with an IQ below 70. Given that low IQ is associated with a more severe prognosis in EO psychosis [25, 26]), a selection bias may have occurred, such that we selected a subset of EO patients with a better prognosis than the average EO patient. However, our data showed that 9% of the EO patients were excluded based on this criterion, compared to 5% of the AO patients. Owing to the relatively few patients and relatively small difference between EO and AO, we feel that any potential bias cannot severely threaten the validity of our results. In contrast to the study by Pencer et al. [27], we did not exclude AO subjects with the lowest age of psychosis onset. Therefore, it is possible the two groups might not be optimally delineated. However, since our aim was to evaluate the 2-year outcome of baseline differences between EO and AO patients, we chose to use the same definitions of EO and AE at both time points to ensure continuity in the research design [14]. Lastly, a 2-year follow-up period is a relatively short duration of time. Owing to the attenuation of group differences already observable during the 2-year time frame, however, it seems unlikely that a longer follow-up period would have provided additional or contradictory evidence to our findings. Results showing a similar long-term (i.e., 2 years) outcome strongly suggest that an adolescent onset of psychosis is an earlier manifestation of the same neurobiological processes as observed in adult-onset cases. Until recently, the literature suggested that adolescent-onset cases were different somehow, more severe and malignant, yet none of these studies actually compared adolescent versus adult-onset cases at follow-up. Our study replicates findings by Pencer et al. [27] and questions the prevailing assumption that earlier-onset cases of psychosis are more severe.

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References

1. McGlashan TH, Hoffman RE (2000) Schizophrenia as a disorder of developmentally reduced synaptic connectivity. Arch Gen Psychiatry 57(7):637–648
2. Tuulio-Henriksson A, Perala J, Saarni SI, Isometsa E, Koskinen S, Lonnqvist J, Suvisaari J (2011) Cognitive functioning in severe psychiatric disorders: a general population study. Eur Arch Psychiatry Clin Neurosci 261(6):447–456
3. Werry JS, McClellan JM (2001) Practice parameter for the assessment and treatment of children and adolescents with schizophrenia. J Am Acad Child Adolesc Psychiatry 40(7 suppl): 4S–23S
4. Bender L (1973) The life course of children with schizophrenia. Am J Psychiatry 130(7):783–786
5. Werry JS, McClellan JM (1992) Predicting outcome in child and adolescent (early onset) schizophrenia and bipolar disorder. J Am Acad Child Adolesc Psychiatry 31(1):147–150
6. Asarnow JR, Tompson MC, Goldstein MJ (1994) Childhood-onset schizophrenia: a followup study. Schizophr Bull 20(4):599–617
7. Hafner H, Nowotny B (1995) Epidemiology of early-onset schizophrenia. Eur Arch Psychiatry Clin Neurosci 245(2):80–92
8. Lay B, Blanz B, Hartmann M, Schmidt MH (2000) The psychosocial outcome of adolescent-onset schizophrenia: a 12-year followup. Schizophr Bull 26(4):801–816
9. Hollis C (2003) Developmental precursors of child- and adolescent-onset schizophrenia and affective psychoses: diagnostic specificity and continuity with symptom dimensions. Br J Psychiatry 182:37–44
10. Zabala A, Rapado M, Arango C, Robles O, de la Serna E, Gonzalez C, Rodriguez-Sanchez JM, Andres P, Mayoral M, Bombin I (2010) Neuropsychological functioning in early-onset first-episode psychosis: comparison of diagnostic subgroups. Eur Arch Psychiatry Clin Neurosci 260(3):225–233
11. Yang PC, Liu CY, Chiang SQ, Chen JY, Lin TS (1995) Comparison of adult manifestations of schizophrenia with onset before and after 15 years of age. Acta Psychiatr Scand 91(3):209–212
12. Schimmelmann BG, Conus P, Cotton S, McGorry PD, Lambert M (2007) Pre-treatment, baseline, and outcome differences between early-onset and adult-onset psychosis in an epidemiological cohort of 636 first-episode patients. Schizoph Res 95:1–8
13. Melle I, Larsen TK, Haahr U, Friis S, Johannessen JO, Opjordsmoen S, Simonsen E, Rund BR, Vaglum P, McGlashan T (2004) Reducing the duration of untreated first-episode psychosis: effects on clinical presentation. Arch Gen Psychiatry 61(2):143–150
14. Joa I, Johannessen JO, Langeveld J, Friis S, Melle I, Opjordsmoen S, Simonsen E, Vaglum P, McGlashan T, Larsen TK (2009) Baseline profiles of adolescent vs. adult-onset first-

episode psychosis in an early detection program. Acta Psychiatr Scand 119(6):494–500
15. American Psychiatric Assosiation (2005) Diagnostic and statistical manual of mental disorders, 4th edn. American Psychiatric Assosiation, Washington, DC
16. Kay SR, Fiszbein A, Opler LA (1987) The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull 13(2):261–276
17. Pedersen G, Hagtvet K, Karterud S (2007) Generalizability studies of the Global Assessment of Functioning-split version. Compr Psychiatry 48(1):88–94
18. Larsen TK, McGlashan TH, Moe LC (1996) First-episode schizophrenia: I. Early course parameters. Schizophr Bull 22(2):241–256
19. Bentsen H, Munkvold OG, Notland TH, Boye B, Bjørge H, Lersbryggen AB, Oskarsson KH, Berg-Larsen R, Malt UF (1996) Inter-rater reliability of the positive and negative syndrome scale. Int J Methods Psychiatr Res 6:226–235
20. Drake RE, Osher FC, Noordsy DL, Hurlbut SC, Teague GB, Beaudett MS (1990) Diagnosis of alcohol use disorders in schizophrenia. Schizophr Bull 16(1):57–67
21. Strauss J, Carpenter WJ (1972) The prediction of outcome in schizophrenia: I. The characteristics of outcome. Arch Gen Psychiatry 27:739–746
22. Spitzer RL, Williams JB, Gibbon M, First MB (1992) The structured clinical interview for DSM-III-R (SCID). I: History, rationale, and description. Arch Gen Psychiatry 49(8):624–629
23. Friis S, Larsen TK, Melle I, Opjordsmoen S, Johannessen JO, Haahr U, Simonsen E, Rund BR, Vaglum P, McGlashan T (2003) Methodological pitfalls in early detection studies—the NAPE Lecture 2002. Nordic Association for Psychiatric Epidemiology. Acta Psychiatr Scand 107(1):3–9
24. Joa I, Johannessen JO, Auestad B, Friis S, McGlashan T, Melle I, Opjordsmoen S, Simonsen E, Vaglum P, Larsen TK (2008) The key to reducing duration of untreated first psychosis: information campaigns. Schizophr Bull 34(3):466–472
25. Gunnell D, Harrison G, Rasmussen F, Fouskakis D, Tynelius P (2002) Associations between premorbid intellectual performance, early-life exposures and early-onset schizophrenia. Cohort study. Br J Psychiatry 181:298–305
26. Zammit S, Allebeck P, David AS, Dalman C, Hemmingsson T, Lundberg I, Lewis G (2004) A longitudinal study of premorbid IQ Score and risk of developing schizophrenia, bipolar disorder, severe depression, and other nonaffective psychoses. Arch Gen Psychiatry 61(4):354–360
27. Pencer A, Addington J, Addington D (2005) Outcome of a first episode of psychosis in adolescence: a 2-year followup. Psychiatry Res 133(1):35–43