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Perspectives in Early Intervention

What factors are related to delayed treatment in individuals at high risk for psychosis?

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Abstract

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Received 9 September 2009; accepted 6 February 2010 **Background:** Previous studies have shown that the individuals at high risk for psychosis suffer from depression, anxiety, and deficits in social functioning. The present report describes help-seeking behaviours, baseline psychopathology, and duration of attenuated psychotic symptoms (DUAPS) and their associations with other variables.

Methods: Using the Comprehensive Assessment of At-Risk Mental States (CAARMS), we conducted systematic evaluations of individuals at high risk for psychosis. Help-seeking behaviours, current Axis I diagnoses, DUAPS, and baseline psychopathology were investigated. Demographic and clinical characteristics of short and long DUAPS groups were compared.

Results: Thirty-eight subjects were recruited from nine centres.

Participants seldom sought psychiatric services at their first help-seeking contact, and the mean DUAPS was 22.00 ± 28.59 months. Most participants had current Axis I diagnoses, and depressive disorder NOS was the most common of these. Higher levels of depression, anxiety, obsessive-compulsive symptoms, and functional impairment were also identified. We found no significant differences between short and long DUAPS groups in baseline psychopathology. However, we observed significantly lesser distressing intensity of thought contents and significantly greater social impairment in the long-DUAPS group.

Conclusion: These findings suggest that high-risk subjects frequently received delayed treatment despite symptomatic distress and functional impairment. No direct evidence supporting the delayed effect of the DUAPS on baseline psychopathology was found.

Key words: duration of attenuated psychotic symptoms, high risk, prodrome, psychosis.

INTRODUCTION

With a peak onset in adolescents and young adults, schizophrenia represents the most severe of the mental disorders and often causes a high degree of disability. A study conducted by Üstün *et al.* study¹ on disability associated with physical and mental conditions reported that the general population ranked active psychosis as the third most disabling condition, next to quadriplegia and dementia. The Global Burden of Disease 2000² study reported that

23 182 deaths worldwide were related to schizophrenia, which was higher than the number related to unipolar depressive disorders (12 044) and schizophrenia accounted for 1.1% of the total disability-adjusted life years and 2.8% of the years lived with disability.³

Due to the devastating impact of this severe disease, major figures in psychiatry have been emphasizing the importance of the early identification of psychosis for many years. According to Kraepelin, 'It is of the greatest importance to diagnose cases of dementia praecox with certainty and at an early stage'.4 Sullivan noted, 'I feel certain that many incipient cases might be arrested before the efficient contact with reality is completely suspended, and a long stay in institutions made necessary'.⁵ Until recently, however, efforts towards the early detection of schizophrenia have been met with pessimism and neglect due to the non-specificity of prodromal symptoms and, possibly, the low priority assigned to schizophrenia in mental health policy. During the past 10 years, however, renewed interest in early intervention in psychotic disorders has emerged. Following the publication of several key papers⁶⁻⁸ in the Schizophrenia Bulletin, early intervention in psychotic disorders has generated significant interest and optimism in many countries, prompting policy-makers to give a high priority to this area. Close to 200 early intervention centres currently operate worldwide. In Korea, three centres provide special services to young people at high risk for psychosis: Seoul Youth Clinic at Seoul National University Hospital, Youth Clinic for You at Yonsei University Hospital, and the Early Assessment Clinic at Chonbuk National University Hospital.

Early intervention with high-risk (HR) subjects or those experiencing prodromal symptoms is a challenging area with many controversial issues, but it lies at the core of the early intervention movement and requires apostle-like devotion to implement. Development of semi-structured interview instruments, the Comprehensive Assessment of At-Risk Mental States (CAARMS)9 and the Structured Interview for Prodromal Symptoms,¹⁰ designed to evaluate HR individuals has catalyzed more systematic research in this domain. One of the pivotal studies demonstrated that more specific pharmacotherapy plus psychotherapy was more beneficial in terms of reducing the risk of early transition to psychosis in young people at ultra-high risk than needs-based intervention alone.¹¹ It should be noted, however, that cognitive therapy alone reduced the likelihood of progressing to psychosis during a 12-month period.¹² Several papers have been published on HR individuals in Korea; this literature has addressed neuropsychological abnormalities,¹³ 1-year follow-up,¹⁴ pre-attentive auditory processing,¹⁵ and social functioning deficits.¹⁶ In general, the major research focus with regard to HR individuals has involved identifying and exploring more reliable predictors of the conversion to psychosis, the rate at which HR individuals transit to psychosis over time, optimal treatment strategies, and so on. Surprisingly, however, research on the help-seeking behaviours and duration of untreated attenuated psychotic symptoms (DUAPS) at baseline and their impact on psychopathology are lacking. Thus, the aim of this study was to investigate the help-seeking behaviours, DUAPS, and baseline clinical characteristics in individuals at HR for psychosis.

METHOD

Subjects

The Korean Network of Early Psychosis, which includes 13 participating centres, was organized in 2004 for purposes of this study. Subjects were recruited from nine centres during 2005-2006. All participants were 18-35 years of age and had never experienced an episode of frank psychosis. Subjects at HR for psychosis were defined according to personal assessment and crisis evaluation criteria and diagnosed via a detailed clinical assessment using the Korean version of CAARMS which was developed through a standard procedure (translation, back-translation and rectification by comments from an original author, A. Yung). In summary, subjects met one or more of the following criteria: (i) the attenuated psychosis group, (ii) the brief limited intermittent psychosis (BLIP) group or (iii) the vulnerability group. Several training workshops were organized before the start of this study to enhance the interrater reliability amongst the centres. Exclusion criteria were: (i) history of previous psychotic disorder lasting longer than 1 week (treated or untreated), (ii) previous or current treatment with a neuroleptic for more than two consecutive weeks, (iii) presence of known organic brain disorder and (iv) learning disability as defined by ICD-10.17 The research protocol was approved by the institutional review board in each centre.

Measures

In addition to classifying HR individuals in terms of the subgroups defined by CAARMS, we also evaluated the frequency and intensity of three key symptoms: thought content, perceptual abnormalities, and disorganized speech. These were evaluated according to the following criteria: (i) frequency (≤ 1 time/week = 1, 2–5 times/week = 2, 6–9 times/week = 3 and ≥ 10 times/week = 4); and (ii) intensity of distress (0–10 on a visual analogue scale). Current Axis I diagnoses were determined, using DSM-IV criteria,¹⁸ via consensus reached in meetings with senior clinicians in which all clinical information was presented. Assessments of help-seeking behaviours were conducted for both HR subjects and their family members in terms of: (i) the presence of

active help-seeking behaviours (only self-initiated help-seeking actions were counted), (ii) the first person or resource contacted, (iii) whether this person or resource recommended seeing a psychiatrist and (iv) the total number of contacts to psychiatric services. DUAPS was defined as the time period from the onset of attenuated psychotic symptoms to the first visit to a psychiatric service, irrespective of medication prescribed. Great effort was made to identify the onset of attenuated psychotic symptoms, defined as the point when an individual suffered significant distressing symptoms for more than 1 month. In cases of inconsistent reports provided by the subject and family members, consensus was reached via discussion with the corresponding author (more weight was given to patient's report for subjective symptoms and family member's report for behavioural characteristics). In addition to basic demographic data, we also collected information on bullying experiences and stressful events related to the development of attenuated psychotic symptoms. Psychopathology was assessed with the Positive and Negative Syndrome Scale (PANSS),¹⁹ the Scale for the Assessment of Negative Symptoms (SANS),²⁰ the Clinical Global Impressions-Severity scale (CGI-S)²¹ and the Global Assessment of Functioning (GAF).²² We also used the Hamilton Rating Scale for Depression,²³ the Hamilton Rating Scale for Anxiety²³ and the Yale-Brown Obsessive-Compulsive Scale Symptom Checklist.24 Premorbid functioning was assessed with the Premorbid Adjustment Scale (PAS).²⁵ Based on a two-factor model of premorbid adjustment,²⁶ social withdrawal and peer relationship items were combined into the social factor, and school performance and adaptation to school were combined into the academic factor.

Data analyses

Descriptive statistics and frequencies were calculated for demographic variables, and scale scores were calculated for psychopathology variables. One-way repeated-measures analyses of variance (ANOVA) were used for the subscale scores of the PAS to verify change over time. To investigate the delayed effects of DUAPS, we divided subjects into long-(\geq 1 year) and short- (<1 year) DUAPS groups. When comparing the two groups, we used *t*-tests and chi-square tests or Fisher's exact test for quantitative and categorical variables, respectively. All analyses were performed using SPSS for Windows (version 14.0, SPSS Inc., Chicago, IL, USA). The *alpha*-level for testing the significance of effects was P = 0.05.

RESULTS

Demographic characteristics and help – seeking behaviours

A total of 38 subjects from nine centres were included in this study. The demographic characteristics of the subjects are presented in Table 1. Of particular importance is the substantially higher proportion of men, the prevalence of histories of bullying, and the long DUAPS. Most subjects met criteria for membership in the attenuated psychosis group (n = 35, 92.1%); of these, 34 were subthreshold in terms of intensity, and one was subthreshold in terms of frequency. One subject met criteria for the past BLIP group and two met criteria for both the subthreshold intensity subtype of the attenuated psychosis group and the vulnerability group. A greater proportion of family members who served as the first contacts for both HR individuals and their relatives reported undertaking active helpseeking behaviours (Table 2). A modest portion of HR subjects and family members contacted psychiatrists initially. The key resources recommending psychiatric consultation to HR subjects and relatives were family members and patients themselves, respectively. The total number of contacts to psychiatric services were rather minimal, 2.0 ± 0.77 and 1.7 ± 0.59 for HR subjects and family members, respectively (Table 2).

Baseline clinical characteristics

Current Axis I diagnoses were given to 29 (76.3%) subjects; depressive disorder NOS and major

TABLE 1. Demographics of high risk subjects (n = 38)

	N (%)			
Sex	Male	31 (81.6)		
	Female	7 (18.4)		
Mean age (SD), year	24.24 (6.43)		
Stressful event	22 (57.9)		
Bullying	12 (31.6)		
DUAPS, months	Mean \pm SD	22.00 ± 28.59		
	Median	10.5		
	Minimal/maximal	0.07/120		
Familial history of	Psychosis	2 (5.3)		
psychiatry	Depression	2 (5.3)		
	OCD	2 (5.3)		
	Alcohol abuse	1 (2.6)		
	Mental retardation	1 (2.6)		
	Total	8 (21.1)		

DUAPS, duration of attenuated psychotic symptoms; OCD, obsessive compulsive disorder.

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	High risk subjects No (%)	Family No. (%)
Active help-seeking behaviour	19 (50)	18 (81.8)
First person most frequently contacted	Family (42.1)	Other family member (44.4)
Number of person contacted psychiatrist first	5 (26.3)	6 (33.3)
Types and number of person recommended to	Family 19 (50)	Self-seeking 8 (36.3)
see psychiatrist	Self-seeking 5 (13.2)	Other family member 6 (27.3)
	Military doctor 6 (15.8)	General practitioner 4 (18.2)
	General practitioner 5 (13.2)	Others 4 (18.2)
	Others 3 (7.8)	
Total number of contact to psychiatric service†	2.0 ± 0.77	1.7 ± 0.59

†Include the contact of psychiatrist.

TABLE 3. Current Axis I diagnoses in high risk subjects

DSM-IV diagnoses	Number	Percent
Depressive disorder NOS	7	18.4
Major depressive disorder	4	10.5
Adjustment disorder	3	7.9
Anxiety disorder NOS	3	7.9
Dysthymia	3	7.9
Social phobia	2	5.3
OCD	3	7.9
PTSD	1	2.6
Dual diagnosis		
OCD and Dysthymia	1	2.6
Depressive disorder NOS & Social phobia	1	2.6
Major depressive disorder & Alcohol abuse	1	2.6
Total	29	76.3

OCD, obsessive compulsive disorder; PTSD, post-traumatic stress disorder.

depressive disorder were the most common of these conditions (Table 3). The results of the baseline psychopathology assessment indicated that subjects suffered from substantial numbers of positive and negative symptoms, depression, anxiety, and significant functional impairment (Table 4). The most prevalent obsessivecompulsive symptoms were aggressive (95.8%), contamination (62.5%) and sexual obsessions (37.5%) and checking (79.2%), cleaning (54.2%) and repeating compulsions (54.2%). The analysis of the PAS showed a significant deterioration over time in all social, academic and socio-sexual areas (Table 5).

Comparison of demographic and clinical characteristics of short and long DUAPS groups

We found no significant differences between groups in terms of demographic characteristics and scores on the psychopathology scales (data not shown). TABLE 4. Psychopathological rating scale scores of high risk subjects

Measure	Mean \pm SD
PANSS	
Total	69.34 ± 12.19
Positive	14.74 ± 3.08
Negative	16.74 ± 4.27
General	37.87 ± 7.41
SANS	
Total	33.53 ± 12.03
Affective flattening fflattening	10.03 ± 5.42
Alogia	4.37 ± 2.69
Avolition/Apathy	5.63 ± 2.24
Anhedonia/Asociality	10.24 ± 3.69
Attention	3.26 ± 1.73
HAM-D	18.24 ± 5.78
HAM-A	20.68 ± 8.17
CGI-S	4.11 ± 0.86
GAF	46.74 ± 8.81
Subscales of CAARMS	
Thought content	
Frequency	2.37 ± 0.54
Distressing intensity	6.92 ± 1.73
Perceptual abnormalities	
Frequency	1.59 ± 1.15
Distressing intensity	4.21 ± 2.56
Disorganized speech	
Frequency	1.46 ± 0.78
Distressing intensity	2.92 ± 2.29

CAARMS, comprehensive assessment of at risk mental states; CGI-S, clinical global impression-severity; GAF, global assessment of functioning; HAM-A, hamilton rating scale for anxiety; HAM-D, hamilton rating scale for depression; PANSS, positive and negative syndrome scale; SANS, scale for the assessment of negative symptoms.

The intensity of the content of distressing thoughts was significantly lower in the long-DUAPS group (P = 0.01) (Table 6). Total scores on the PAS, scores for negative childhood and adolescent social experiences, and total social scores were significantly higher in the long-DUAPS group (Table 7).

Delayed treatment in high risk subjects

TABLE 5. Premorbid Adjustment Scale in high risk subjects†

Adjustment domain	Childhood (n = 38)	Early adolescence (n = 38)	Late adolescence (n = 38)	Adulthood (n = 36)	Р
Social	2.84 ± 3.00	3.39 ± 2.88	4.61 ± 2.97†	5.92 ± 2.59†‡	0.000
Academic	4.61 ± 2.03	4.97 ± 2.37	5.95 ± 2.16†‡		0.000
Socio-sexual		1.71 ± 1.54	$2.45\pm1.80\ddagger$	3.22 ± 1.46 ‡§	0.000

 \pm Statistically significant differences from the Childhood group (P < 0.05). Data are given as mean \pm SD. \pm Statistically significant differences from the Early adolescence group (P < 0.05).

Statistically significant differences from the Late adolescence group (P < 0.05).

TABLE 6. Comparison of subscale scores of the CAARMS between the short DUAPS (<12 months) and long DUAPS (\geq 12 months) groups

Subscales of CAARMS	<12 mon	<12 months (<i>n</i> = 19) Mean ± SD		\geq 12 months (<i>n</i> = 19) Mean ± SD	
	Mea				
Thought content					
Frequency	2.32	± 0.48	2.42	± 0.61	0.556
Distressing intensity	7.63	± 1.16	6.21	± 1.93	0.010
Perceptual abnormalities					
Frequency	1.27	± 0.88	1.93	± 1.33	0.123
Distressing intensity	4.47	± 2.83	3.92	± 2.29	0.585
Disorganized speech					
Frequency	1.83	± 0.98	1.14	± 0.38	0.154
Distressing intensity	3.83	\pm 2.71	2.14	± 1.68	0.196

CAARMS, comprehensive assessment of at risk mental states; DUAPS, duration of attenuated psychotic symptoms.

PAS		<12 months (<i>n</i> = 19)		≥12 months (<i>n</i> = 19)		P value
		Mear	$n \pm SD$	ſ	$Vlean \pm SD$	
Childhood	Social	1.74	± 2.35	3.95	± 3.22	0.021
	Academic	4.05	± 2.07	5.16	± 1.89	0.094
Early adolescence	Social	2.11	± 2.08	4.68	± 3.04	0.004
	Academic	4.32	± 2.38	5.63	± 2.22	0.086
	Socio-sexual	1.26	± 1.24	2.16	± 1.71	0.074
Late adolescence	Social	2.95	± 2.32	6.26	± 2.64	0.000
	Academic	5.37	± 1.95	6.53	± 2.25	0.098
	Socio-sexual	2.05	± 1.51	2.84	± 2.01	0.179
Adulthood	Social	5.53	± 2.44	6.35	± 2.76 (<i>n</i> = 17)	0.346
	Socio-sexual	3.42	± 1.30	3.00	± 1.62 (<i>n</i> = 17)	0.394
Total social		12.32	± 7.06	20.58	± 7.21	0.001
Total academic		13.74	± 5.27	17.32	± 5.71	0.052
Total socio-sexual		6.74	± 3.49	7.68	± 3.73	0.424
Total		22.79	\pm 7.48	28.00	± 11.92	0.115

TABLE 7. Comparison of Premorbid Adjustment Scale between the short DUAPS (<12 months) and long DUAPS (\geq 12 months) groups

PAS, premorbid adjustment scale.

DISCUSSION

Thirty-eight HR subjects from nine centres participated in the study over the course of

2 years. We investigated baseline demographic and clinical characteristics, help-seeking behaviours, and DUAPS and their associations with other variables.

Experiences with bullying were reported by 31.6% of the HR subjects. Associations between bullying and psychotic-like experiences or psychotic symptoms have been reported consistently.²⁷⁻³⁰ More specifically, Schreier et al.,²⁹ reported that these associations were stronger (odds ratios up to 4.60) when victimization was chronic or severe. Psychological studies of the consequences of being bullied have focused primarily on affective disorders or on psychological constructs such as self-esteem or aspects of personality.³¹⁻³³ Given that experiences with being bullied can lead to feelings of isolation, social withdrawal, and anhedonia, which constitute part of the constellation of negative symptoms, the role of being bullied as a possible predictor of transition to psychosis in HR subjects should be further investigated.

Active help-seeking behaviours were reported by half of the HR subjects, but only about 20-30% of subjects and their families initially contacted a psychiatrist. Although no previous data on the help-seeking behaviours of HR subjects have been reported, passive and reluctant attitudes towards getting help from mental health services are consistent with the attitudes exhibited by those experiencing their first episode of psychosis.³⁴⁻³⁶ Family was the most frequently cited first resource contacted by both subjects and family members and played a significant role in recommending psychiatric consultations. These results are strikingly different from those indicating that general practitioners or family physicians played important roles in first episodes of psychosis.^{36,37}

Our finding that depressive disorder NOS was the most common diagnosis in HR subjects slightly differs from previous results indicating that major depressive disorder,³⁸ cannabis dependence³⁹ or dysthymia40 were most common. Amongst the subdomains of the SANS, affective flattening and anhedonia/asociality were more prominent than were other subdomains in the HR subjects. In addition, our study sample was found to have moderate depression and anxiety, and severe impairment of functioning, and comorbid obsessive-compulsive symptoms were very common. PAS results showing a deteriorating course over time are fairly consistent with those reported by Miller et al. study.⁴¹ Social deterioration, in particular, was more pronounced than were the other components, with marked declines in this domain starting in late adolescence. Taken together, these data can be construed as suggesting that careful assessment of attenuated psychotic symptoms is warranted when young people gradually withdraw socially and complain of depressive and obsessive-compulsive symptoms.

DUAPS varied widely amongst subjects, ranging from 0.07 to 120 months, with a median of 10.5 months and a mean of 22 months. Only a few studies have investigated the time between symptom onset and first contact with psychiatric services; these reported durations of 344 ± 490 days $(11.5\pm16.3\text{ months})^{11}$ and 565 \pm 816 days (18.8 \pm 27.2 months).⁴² Such lengthy DUAPS, like long duration of untreated psychosis, constitute a serious problem in that these may prolong the period of distress and lead to greater deteriorations in social functioning, more severe symptoms, and a greater chance of transitioning to psychosis. Given that family was a major focus of the help-seeking behaviours of HR subjects, public education and awareness campaigns should be at the forefront of strategies to reduce DUAPS. The development of a more acceptable alternative name to 'prodrome' is essential to the success of public campaigns. Although such terms as 'at-risk mental state', 'ultrahigh-risk', 'clinical high risk' or 'hypopsychosis' may be less stigmatizing, they remain negative and possibly indicative of danger. We recently conducted a nation-wide survey to 508 psychiatrists in Korea in which we described a case of the attenuated psychosis group and asked them to choose the best name for the case amongst high-risk state, crisis state, thought-perception sensitive state, at-risk mental state, hypopsychosis, prodrome and borderline state. The answers, in order of frequency, were: thought-perception sensitive state (43.4%), prodrome (19.4%), hypopsychosis (13.7%), borderline state (6.7%), at-risk mental state (5.9%), high-risk state (5.7%) and crisis state (5.4%) (unpublished data). Based on this finding, the authors proposed Thought-Perception Sensitivity State and Thought-Perception Sensitivity Disorder as alternative names for prodrome and schizophrenia, respectively.⁴³

We divided subjects into short- and long-DUAPS groups to examine the effect of delayed treatment. Contrary to our hypothesis that delayed treatment would lead to more severe psychopathology, no significant difference between the groups was found on the PANSS, SANS, HAM-D, HAM-A, CGI and GAF. Instead, we found that the long-DUAPS group reported less distressing intensity of thought contents and more impaired social functioning during childhood and adolescence. The former finding might be understood in the context that mild levels of distress could lead to less active help-seeking behaviours. The latter finding might be understood in the context that further deteriorations in social functioning or modest complaints of symptoms would not be noticeable to family members when social functioning has been low since childhood. Alternatively, poor social functioning might be the consequence of long DUAPS. Although direct evidence supporting the possibly toxic effect of long DUAPS was not found, this is the first examination of the association between DUAPS and psychopathology. The effect of DUAPS on the cognitive functioning or brain morphology of HR subjects might serve as interesting and important topics for in future investigations.

This study is limited in that its cross-sectional design and small sample size might undermine its ability to detect the effect of DUAPS on psychopathology. In addition, specifying the time at which attenuated psychotic symptoms first emerged would have been much easier had we employed a standardized instrument for establishing onset time. In spite of these caveats, this study demonstrated that young people at high risk for psychosis seldom sought help from psychiatric services despite substantial depression, anxiety and functional impairment; we also found that the DUAPS of this population was quite long.

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