Available online at www.sciencedirect.com

ScienceDirect

Comprehensive Psychiatry 55 (2014) 813–817

COMPREHENSIVE PSYCHIATRY

www.elsevier.com/locate/comppsych

Prognostic implications of paranoia and thought disorder in new onset psychosis

James Wilcox[a,*], David Briones[b], Syed Quadri[a], Ming Tsuang[c]

[a]University of Arizona, Tucson, AZ, USA
[b]Texas Tech University Health Sciences Center, El Paso, TX, USA
[c]University of California at San Diego, San Diego, CA, USA

Abstract

This study follows a group of 174 young people with new onset of schizotypal symptoms and examines factors which may lead to conversion to psychosis. These prodromal subjects were screened for symptoms and later given the Structured Clinical Interview of DSM-III-R at one year, two years and ten years post onset. We also included the Paranoia Scale of Fenigstein and Vanable and the Scale for Thought, Language and Communications of Andreasen in all interviews. Our analysis found that the addition of scales for paranoia and thought disorder enhanced prediction of conversion to psychosis and long term outcome. The early occurrence of ideas of reference and poverty of thought appear to be significant predictors of future deterioration even when considered among other high-risk variables.
Published by Elsevier Inc.

1. Introduction

The ability to predict the outcome of an illness has always been an important part of medical science. Similarly, many psychiatric syndromes have mild symptoms that appear prior the development of major illness. The use of prodromal terminology was introduced by Mayer-Gross in the early 20th century [1]. In recent years there has been increased interest in prognostic features of the schizophrenic prodroma [1–9]. The factors which predict conversion to psychosis are now the focus of considerable new research [2]. Several factors such as high genetic loading and substance abuse are known to be associated with poor outcome for many patients with prodromal symptoms [2–7]. Early onset of paranoia and thought disorder has also been noted as factors which may predict conversion into psychosis [8–10]. The use of psychiatric symptoms to examine the patient's progress has valuable clinical implications. With the development of prevention models in psychiatry, the ability to predict the course of an illness early on is gaining greater clinical importance [7–9,11]. The use of valid and reliable instruments to rate symptoms is, therefore, critical for proper longitudinal study of clinical syndromes over time. By using operational criteria in prospective work, the relative risk associated between early symptoms and later outcome can be assessed with a higher degree of precision.

Paranoid thinking has long been suspected to be a risk factor for the development of schizophrenia, yet it has not been well studied with operational criteria until recently [6,9,12,13]. Since unusual notions are found in normal populations and in a variety of syndromes [13–16], it is important to determine which cases are benign and which are more likely to deteriorate. It is, therefore, vital to ascertain which individuals with peculiar thinking are most at risk for decompensation. The Scale for Thought, Language and Communication (TLC) of Andreasen has been a very reliable standard for the evaluation of thought disorder for quite some time [17] and was chosen as one scale for examination of these problems. Fenigstein and Vanable have developed a scale for measuring paranoia that is both reliable and valid. This was used to examine paranoid thinking in detail [18]. By inclusion of these detailed scales, along with other measures, we hoped to determine the relative value of thought disorder and paranoia in the prediction of prognosis in early cases of prodromal illness.

This project was designed to examine the effect of early symptomatology on both conversion to psychosis and also

* Corresponding author at: Tucson VAMC, 3601 South 6th Avenue, Tucson, Arizona 85723, USA.
E-mail address: James.Wilcox2@VA.gov (J. Wilcox).

0010-440X/$ – see front matter. Published by Elsevier Inc.
http://dx.doi.org/10.1016/j.comppsych.2013.12.010

on long term prognosis. We wanted to assess the relative value of symptomatic and demographic variables at one year, two year and ten year intervals after the first onset of psychological impairment (Tables 1–6). We examined symptoms in subjects with the onset of new psychiatric symptoms (in the first 6 months) and followed up to see how these people progressed over the next ten years. Our efforts were concentrated on new cases of emotional illness regardless of their diagnosis. We thought that the addition of specific scales for thought disorder and paranoia would enhance prediction for conversion and later outcome.

2. Methods

This was a prospective follow-up of patients with the new onset of psychiatric symptoms. These subjects were collected from mental health clinics and hospitals in Western Texas. Appropriate permission was obtained from the proper ethics and institutional review board before the study and all subjects gave informed consent to be interviewed. Subjects were at least 18 years old at the time of enrollment and were primarily English speaking. Each subject was screened to assess the presence of prodromal symptoms (these were essentially new onset of schizotypal symptoms of 6 months duration or less) by the author, JW. We did initial recruitment from the years 1997–2003. Patients were subsequently followed at intervals of one, two and ten years. We screened 200 original subjects. Our recruitment was successful and 87% of potential subjects agreed to participate. Each person provided demographic information about their family history, education, drug use and age of onset of psychiatric symptoms. Each subject was also interviewed using the Paranoia Scale (PS) [18], Scale for the Assessment of Thought, Language and Communication (TLC) [17], the Brief Psychiatric Rating Scale (BPRS) [19] and the SCID [20].

The administration of the TLC was done in the manner of Andreasen [17]. This required a 45 minute interview conducted in a standardized nonclinical format. The subject was allowed to talk about themselves for about 15 minutes. The topics were neutral and discussion of symptoms was avoided. Ratings were done by taking notes and then transferred to score sheets immediately afterward. The interviewer was kept blinded to the diagnosis of the subject.

The Paranoia Scale used in this study was designed to detect symptoms in nonclinical populations and was, therefore, appropriate to capture subtle changes of the prodromal phase. Using this method of recruitment, we were able to enroll 174 subjects in the study. Follow up interviews using the PS, TLC, SCID and BPRS were conducted one, two and ten years after the initial assessment. All assessments were done by investigators JW and SQ. Kappa scores for reliability between the two raters were found to be high (.89). The mean age of subjects was 21 years with a range of 18–26 years. Eighty nine of the subjects were male. All subjects were in good physical health.

Table 1
Demographic and symptomatic variables associated with conversion to psychosis at 1st year of follow up.

By correlation coefficient post multivariate analysis, not significant = NS

Variable	r	Significance
Level of education	.09	p > .05 NS
Affective symptoms	.04	p > .05 NS
Positive family history	.32	p < .05
Unusual thoughts	.65	p < .001
Paranoia	.77	p < .001
Substance abuse	.19	p < .05
Gender	.08	p > .05 NS
Age onset	.09	p > .05 NS
Hallucinations	.18	p < .05
Poverty of thought	.79	p < .001

Table 2
Correlation of BPRS scores to original index factors in converters at 1 year.

Variable	r	Significance
Positive family history	.17	p < .05
Unusual thoughts	.61	p < .001
Paranoia	.62	p < .001
Substance abuse	.18	p < .05
Poverty of thought	.70	p < .001

3. Statistical analysis

Analysis of findings used Chi square test where appropriate. Student's t test was used as appropriate. Pearson correlations were run to examine random correlations of possible interactions. Multiple regression analysis was performed to evaluate variation in effect of demographics, BPRS, and TLC and PS scores at one year, two years and ten years, as a method of assessing effects upon symptom variation over time. SCID findings at these intervals were assessed for diagnosis separately as qualitative data using appropriate logistic analysis. A separate analysis was performed to evaluate the impact of demographic information, the initial TLC and PS scores on later diagnoses as indicated by SCID exams at follow up. Statistical tests were conducted 2 tailed, using an alpha value of .05, unless otherwise noted. Multivariate analysis

Table 3
Overall regression analysis of significant predictive factors for conversion at 1 year.

Variable	F value	Significance
Substance abuse	3.84	p < .05
Positive family history	3.90	p < .05
Poverty of thought	7.77	p < .001
Paranoia	7.50	p < .001

Table 4
Demographic and symptomatic variables associated with conversion to psychosis at 2nd year of follow up.

By correlation coefficient post multivariate analysis, not significant = NS		
Variable	r	Significance
Level of education	.09	p > .05 NS
Affective symptoms	.04	p > .05 NS
Positive family history	.22	p < .05
Unusual thoughts	.62	p < .001
Paranoia	.79	p < .001
Substance abuse	.17	p < .05
Gender	.08	p > .05 NS
Age onset	.09	p > .05 NS
Hallucinations	.19	p < .05
Poverty of thought	.80	p < .001

was performed to examine possible redundancies [21]. All analyses were done using the SPSS program (SPSS, Chicago, IL) [25].

4. Results

Of the 174 subjects enrolled, 144 (83%) completed at least one year of follow up. We subsequently re-interviewed 134 (77%) at two years and 122 (70%) at ten year follow up. Post hoc analysis demonstrated that patients lost at the 1st, 2nd and 3rd follow up did not significantly differ from original enrollees in race, ethnicity, family history, education or initial PS, TLC, SCID or BPRS ratings. More males than females were lost to follow up (difference of 5%, 8% and 12% between genders for each wave of contact, respectively). The prognostic variables associated with conversion to psychosis by simple correlation were subjected to multivariate analysis to remove redundancies among related measures. Several variables survived multivariate analysis to indicate significant risk for conversion. We found that conversion to psychosis in the first year was highly related to genetic risk for schizophrenia (chi Square = 9.68, $p < .001$), unusual thought content (chi square = 5.3, $p < .01$), paranoia (chi square = 6.3, $p < .01$) and substance abuse (chi square 4.9, $p < .01$). Those who converted to psychosis tended to develop either schizophrenia (75%) or schizoaffective disorder (25%) according to our SCID findings by the end of year two. Paranoia Scale items changed little in follow up visits for most patients, with 78% maintaining mild to moderate degrees of paranoid thinking in years one, two and ten. Only 7% were found to develop sophisticated paranoid delusions at follow up in any of the three waves of interviews. Ideas of reference continued to be a major feature in most of the cases that converted, accounting for nearly all of the 78% noted above. Multivariate analysis of all endorsed items on the combined rating scales found that ideas of reference had significant non-redundant predictive value for conversion to psychosis within two years ($p < .001$). Educational level, age of onset and handedness were not found to have predictive value in our population. Almost all conversions had taken place by the second year of follow up for our study subjects. We found little progression towards new levels of psychosis between the second and third waves of evaluations. See tables for data on years one and two. No tables were made for year ten because 92% of conversions had occurred by year two and the conversions during the period between years two and ten were negligible.

Table 5
Correlation of BPRS scores to original index factors in converters at 2 years.

Variable	r	Significance
Positive family history	.20	p < .05
Unusual thoughts	.68	p < .001
Paranoia	.70	p < .001
Substance abuse	.18	p < .05
Poverty of thought	.73	p < .001

Table 6
Overall regression analysis of significant predictive factors for conversion at 2 years.

Variable	F value	Significance
Substance abuse	3.45	p < .05
Positive family history	3.29	p < .05
Poverty of thought	7.34	p < .001
Paranoia	7.30	p < .001

5. Discussion

Our findings suggest that early paranoia and poverty of thought were highly predictive of conversion to psychosis in a sample of young adults. While the various scales used in this study all contain information about unusual thoughts, the analysis controlled for redundancies and found that persistent ideas of reference were among the most important predictive variables for conversion to psychosis, if the subject also had poverty of thought. This suggests that such ideation is important in the development of psychotic thinking and decompensation. The literature agrees that most conversions to psychosis occur in the first two to five years of illness [7–16,22–27]. As in previous studies we found high rates of conversion at the one year point (34%) with much lower rates at later contacts, 8.5% at two years and 1.5% at the ten year point. This is consistent with other studies [5,23–26,28]. This work suggests that the rate of conversion is highest in the first 2 years of the onset of symptoms and then rapidly tapers off [5,23–28]. The present study presents information on new measures at one, two and ten years post onset, therefore, producing a unique set of data. The use of highly specific operational criteria allowed for substantial predictive validity in our model. The prediction of conversion is now enhanced by the knowledge that paranoia and poverty of thought carry great prognostic

significance. While this may have previously existed in clinical opinion, the validity of the notion has been improved by the use of operational criteria and reliable instruments. Multivariate analysis found that both ideas of reference and negative thought disorder strongly predicted conversion to psychosis at two years post onset. Analysis of data suggests that unusual thinking can be divided into two very significant, independent subtypes, paranoid thinking and poverty of thought content.

Prediction algorithms which incorporate paranoia and poverty of thought along with genetic risk, may have greater prognostic value than assessment of general symptoms alone. Negative thought disorder has been associated with poor prognosis in previous studies [10,26]. Our previous work has found that poverty of thought content predicts conversion to psychosis in high risk individuals [9]. The most sensitive indicator of conversion, among the paranoid items in our study, appeared to be ideas of reference. This has been noted in the past, but seldom examined with operational criteria [1,6,13]. Within our sample this seemed to take the form of persistent belief that one was the topic of unkind attention, malicious gossip or persistent comments (in 81% of cases). This description would generally translate into a clinical picture of a socially isolated, emotionally guarded and suspicious individual.

The authors acknowledge potential problems in this or any long term prospective study. Our study population was relatively small. A larger group may have provided for analysis of a larger, more diverse set of variables [29], but this was not the goal of the study. The high follow-up rates and high rates of inter-rater reliability were good for the integrity of the study and strengthened our findings. We looked at young people that were seeking treatment or psychiatric evaluation. This group may not fully generalize to other young people with early symptoms of mental illness. The family data we collected were amenable to the family history method of comparison. More detailed family information and follow up would have allowed the more precise family study method.

We found that the inclusion of the scales for paranoia and thought disorder allowed us to detect various elements of unusual thinking with a high degree of sensitivity. If these scales had not been used, gross description by nonoperational means would have limited the accuracy of symptom detection. The prediction of psychotic deterioration among subjects with high genetic loading is enhanced by a history of substance abuse, negative thought disorder and ideas of reference. Previous studies that lacked these operational scales were unable to capture data on quality of thought content [26–28]. Based on our findings, poverty of thought and paranoia are highly predictive of conversion to psychosis in populations with positive genetic loading for schizophrenia. We encourage ongoing research on prodromal phenomena and assessment of symptoms which may predict conversion to psychosis. Further work including the family study method and genetic risk assessment on subjects who had been tested with operational criteria would improve our understanding of the interaction of heredity and symptoms.

References

[1] Bleuler E. Dementia Praecox of the Group of Schizophrenias. New York: NY International Universities Press; 1911.
[2] McGorry P, Yung A, Phillips L. The “close-in” of ultra high-risk model: a safe and effective strategy for research and clinical intervention in prepsychotic mental disorder. Schizophr Bull 1996;22(2):771-90.
[3] Yung A, McGorry P. The prodromal phase of first-episode psychosis: past and current conceptualizations. Schizophr Bull 1996;22(2):353-70.
[4] Cannon T. Clinical and genetic high-risk strategies in understanding vulnerability to psychosis. Schizophr Res 2005;79(1):35-44.
[5] Cannon T, Cadenhead K, Cornblatt B, Woods S, Addington J, Walker E, et al. Prediction of psychosis in youth at high clinical risk. Arch Clin Psychiatry 2008;65(1):28-35.
[6] Kraepelin E. Clinical Psychiatry: A textbook for students and physicians. 7th ed. New York: Macmillan; 1915.
[7] Ruhrman S, Schultze-Lutter F, Saloakngas R, Heinman M, Linszen D, Dingemans P, et al. Prediction of psychosis in adolescents and young adults at high risk: results from the prospective European prediction of psychosis study. Arch Clin Psychiatry 2010;67(3):241-51.
[8] Cannon T, Cornblatt B, McGorry P. The empirical status of the ultra high-risk (prodromal) research paradigm. Schizophr Bull 2007;33(3):661-4.
[9] Skalli L, Nicole L. Specialized first-episode psychosis services: a systematic review of the literature. Encéphale 2011;37(Suppl 1):S66-76.
[10] Wilcox J, Winokur G, Tsuang M. Predictive value of thought disorder in new-onset Psychosis. Compr Psychiatry 2012;53(6):674-8.
[11] Lenciu M, Romosan F, Bredicean C, Romosan R. First episode psychosis and treatment delay – causes and consequences. Psychiatr Danub 2010;22(4):540-3.
[12] Jaspers K. Allgemeine psychopathologie. Berlin: Springer; 1913.
[13] Cameron N. The development of paranoic thinking. Psychol Rev 1943;50:219-33.
[14] Freeman D, Philippa G, Bebbington P, Smith B, Rollison R, Fowler D, et al. Psychological investigation of the structure of paranoia in a non-clinical population. Br J Psychiatry 2005;186:427-35.
[15] Spitznagel M, Suhr J. Neuropsychological impairment associated with symptoms of schizotypy: role of depressive and paranoid symptoms. J Nerv Ment Dis 2004;192(5):382-4.
[16] Fernyhough C, Jones S, Whittle C, Waterhouse J, Bentall R. Theory of mind, schizotypy, and persecutory ideation in young adults. Cogn Neuropsychiatr 2008;13(3):233-49.
[17] Andreasen N. The Scale for the Assessment of Thought, Language and Communication (TLC). Iowa City: the University of Iowa; 1978.
[18] Fenigstein A, Vanable P. Paranoia and self-consciousness. J Pers Soc Psychol 1992;62:129-38.
[19] Overall J, Gormann D. The Brief Psychiatric Rating Scale. Psychol Rep 1962;10(2):799-812.
[20] Spitzer R, William J, Gibbon M, First M. Structured Clinical Interview of DSM-III-R. Washington D.C.: American Psychiatric Press, Inc.; 1990.
[21] Abraham B, Ledolter J. Statistical methods for forecasting. New York: Wiley & Sons; 2004.
[22] Leversque R. SPSS programming and data management: a guide of SPSS and SAS for users. 4th ed. Chicago: SPSS Inc.; 2007.
[23] Cornblatt B, Lencz T, Smith C, Correll C, Auther A, Nakayama E. The schizophrenia prodrome revisited: a Neurodevelopmental perspective. Schizophr Bull 2003;29(4):633-51.
[24] Cannon T, Van Erp T, Bearden C, Loewy R, Thompson P, Toga A, et al. Early and late Neurodevelopmental influences in the prodrome

to schizophrenia: contributions of genes, environment and their interactions. Schizophr Bull 2003;29(4):653-69.

[25] Owens D, Miller P, Lawrie S, Johnstone E. Pathogenesis of schizophrenia: a psychopathological perspective. Br J Psychiatry 2005;185: 386-93.

[26] Yung A, Stanford C, Cosgrave E, Killackey E, Phillips L, Nelson B, et al. Testing the ultra high (prodromal) criteria for the prediction of psychosis in a clinical research sample of young people. Schizophr Res 2006;84(1):57-66.

[27] Opjordsmoen S, Retterstol N. Dimensions of delusional experience and their value as predictors of long term outcome. Psychopathology 2007;40(5):278-81.

[28] Helgason L. Twenty year's follow-up of first psychiatric presentation for schizophrenia: What could have been prevented? Acta Psychiatr Scand 1990;81:231-5.

[29] Biau D, Kerneis S, Porcher R. Statistics in Brief: The Importance of Sample Size in the Planning and Interpretation of Medical Research. Clin Orthop Relat Res 2008;466:2282-8.