Preventive Intervention for Early Psychosis in Adolescents - The Palau Youth At Risk Project

Hilda Ngiralmau*
Francisca Blailes*
Marina Myles-Worsley**
Lisa M. Ord**

**Ministry of Health, Republic of Palau, Koror, Palau 96940, **Dept. of Psychiatry, University of Utah School of Medicine, Salt Lake City UT 84132*

Abstract:
We have studied a total of 393 adolescents 14 to 19 years from Palau, where the lifetime morbid risk for broadly defined schizophrenia is 2.67% and cases cluster in large extended families. These Palauan adolescents included 52 offspring of a schizophrenic parent designated as "Genetically Highest Risk" or GHR+ and 61 nieces/nephews of affected sib-pairs/trios, designated "Genetically High Risk" or GHR. The remaining 280 subjects were recruited based on the results of a survey of Palauan high school students that was designed to screen for clinically HR and normal control adolescents with no close affected relatives. Among the selected high school students were 60 adolescents with one affected second or third degree relative who were designated as "Genetically Moderate Risk" (GMR). The remaining 220 subjects with no close affected relatives were designated as "Genetically Low Risk" (GLR). Based on a comprehensive clinical assessment using the K-SADS, we identified a total of 230 Palauan adolescents with early psychosis, 48 or 21% of whom had already transitioned to a DSM-IV psychotic disorder, predominantly schizophrenia. Together, the two highest genetic risk groups contributed 35% of the adolescent-onset DSM-IV psychosis cases and 26% of the prodromals. More than half of the early psychosis cases (55%) had no close affected relatives, indicating that genetic liability provides only a partial explanation of elevated risk. Our results support the value of screening for early psychosis in the high schools, conducting a full-scale clinical assessment to identify adolescents with early "prodromal" symptoms, and initiating a family-based intervention program designed to delay or even prevent the onset of florid psychosis. This intervention program comprises regular symptom reassessments so that referrals for treatment can be made as needed plus family psycho-education designed to engage the family in a program of care and support for the early psychosis patient (PHD, 2005 Vol 12 No 1 Pages 43 - 46)

Introduction

Schizophrenia is a complex neuropsychiatric disorder that typically appears during late adolescence or early adulthood. A number of prospective studies of high risk (HR) subjects are being conducted in an effort to identify the risk factors that predict future onset of schizophrenia. Prospective studies can identify HR subjects either genetically, through family history (e.g., the New York High Risk Project, Erlenmeyer-Kimling et al 1997), or clinically, through referrals of young people with pre-psychotic or prodromal symptomatology (e.g., The Early Psychosis Prevention and Intervention Center in Melbourne Australia, McGorry et al., 1996). The prodromal phase is defined as that period preceding the onset of the first florid psychotic episode when there is increasing symptomatic presentation and functional deterioration.

We have been conducting a prospective study of HR adolescents in the Republic of Palau, an isolated island nation in Micronesia where the prevalence of schizophrenia is significantly elevated and cases cluster in large, multigenerational families (Myles-Worsley et al., 1999). The Palau Youth At Risk Study combines the genetic HR and clinical HR strategies by studying both the genetically HR adolescent offspring in multiply affected families and also clinically HR adolescents with prominent symptomatology but no close relatives with a psychotic illness. These HR adolescents are being compared to normal control adolescents in the same 14 to 19 year age range with respect to clinical, psychosocial, and neurocognitive functioning.

The isolated population of Palau, with only 20,000 people, represents a unique resource for studies of early psychosis because extended high-density pedigrees with 4 to 25 cases of schizophrenia have already been ascertained and large families are the norm in Palau, even for schizophrenia patients Furthermore, we were able to conduct a government-sponsored survey of high school students to screen for "potentially prodromal" adolescents (Ord et al., 2004). Consequently we were able to study a community-based sample prior to any referral or psychiatric treatment.

Methods

Subjects.

A total of 393 Palauan adolescents 14 to 19 years of age participated in the study. Table 1 presents

sample sizes by level of genetic risk and gender. We assessed 52 offspring of a parent with a psychotic illness, predominantly schizophrenia, designated as "Genetically Highest Risk" or GHR+, and 61 offspring of an unaffected parent with two or more affected siblings, designated "Genetically High Risk" or GHR. The remaining 280 adolescent subjects were identified by surveying high school students in all four Palauan high schools as described in Ord et al., 2004. Briefly, we developed a self-report questionnaire, the Y-PARQ (Youth Psychosis At Risk Questionnaire) based on the Comprehensive Assessment of at Risk Mental States (CAARMS, McGorry et al., 1996) which presents 92 questions covering positive, affective, and negative symptoms. The total number of endorsements on the 24 most discriminating positive symptom items was used as a positive symptom score. We identified "potentially prodromal" and "probably normal" adolescents by identifying students in the upper and lower tails of the distribution of positive symptom scores. For all participating subjects, family trees for the mother and father were constructed in order to identify any affected relatives. We found 60 adolescents with a second or third degree relative with a psychotic disorder, and these subjects were designated "genetically moderate risk" or GMR. The remaining 220 subjects with no first, second or third degree relatives with a psychotic disorder were designated as "Genetically Low Risk" or GLR. Among these 220 GLR subjects, 126 adolescents were diagnosed with early psychosis and 94 adolescents were identified as normal. All adolescents were assessed prior to any psychiatric treatment.

Clinical Assessment and Diagnosis.

The clinical assessment instrument was a modified Kiddie-SADS-PL (Schedule of Affective Disorders and Schizophrenia, Kaufman et al, 1997). Modifications were made to incorporate prodromal and early psychotic symptomatology as evaluated by the CAARMS and to reflect cultural norms in Palau. One experienced Palauan clinician, Francisca Blailes, BSN, conducted all adolescent interviews. In addition, the interviewer used the first two pages of the CBCL (Child Behavior Checklist) Youth Self Report to inquire about psychosocial functioning.

All interview data were reviewed by the diagnostic panel together with informant report data in order to reach a Best Estimate diagnosis using DSM-IV criteria. The diagnostic panel was blind to the subject's risk category and all non-diagnostic data (e.g., neurocognitive functioning). Each diagnostician made best-estimate diagnoses using DSM-IV criteria for a psychotic disorder and the PACE criteria (Phillips et al., 2000) for the prodrome.

Results

Table 2 presents the distribution of early psychosis cases by level of genetic risk. We identified a total of 230 Palauan adolescents with early psychosis, 48 or 21% of whom had already transitioned to a DSM-IV psychotic disorder, predominantly schizophrenia. Together, the two highest risk groups, the GHR+ and GHR adolescents, contributed 35% of the adolescent-onset DSM-IV psychosis cases and 26% of the prodromals. However, more than half of the early psychosis cases (55%) had no first, second or third degree relatives affected with a psychotic disorder.

Table 1. Sample sizes by level of genetic risk and gender

	Total	Female	Male	% Male
GHR+: Genetically highest risk (1st deg relative)	52	28	24	46.2
GHR: Genetic high risk (≥2 2nd deg relatives)	61	31	30	49.2
High School Survey:				
GMR: Genetically moderate risk	60	37	23	38.3
Low genetic risk & early psychosis	126	70	56	44.4
Low genetic risk & normal	94	50	44	46.8
Total sample	**393**	**216**	**177**	**45.0**

Table 2. Distribution of early psychosis cases by level of genetic risk

	Psychosis		Prodromal		Total Early Psychosis	
	No.	%	No.	%	No.	%
Highest: GHR+	9	18.7	21	11.5	30	13.0
High: GHR	8	16.7	26	14.3	34	14.8
Moderate: GMR	10	20.8	30	16.5	40	17.4
Low	21	43.8	105	57.7	126	54.8
Total cases	48	100.0	182	100.0	230	100.0

Table 3 shows that the affection rates in the GHR+ and GHR adolescents were equivalently high. Almost 60% of these adolescents were diagnosed with early psychosis, including 15% who had already transitioned to a DSM-IV psychotic disorder prior to the clinical assessment.

Table 3. Affection rates in GHR+ and GHR adolescents

	GHR+: Highest		GHR: High		Total	
	No.	%	No.	%	No.	%
Psychosis	9	17.3	8	13.1	17	15.0
Prodromal	21	40.4	26	42.6	47	41.6
Normal	22	42.3	27	44.3	49	43.4
Total	52	100.0	61	100.0	113	100.0

Discussion

The results indicate that the adolescent population in Palau has significantly higher rates of early psychosis than have been found in other countries. Over half of the 230 cases of early psychosis were found among Genetically Low Risk adolescents with no close affected relatives, who were identified as "potentially prodromal" via a high school survey.

Not all prodromal adolescents will transition to frank psychosis. Yung et al. (2003) recently reported that the 40% transition rate found in the first wave of subjects referred to the PACE Clinic in Melbourne Australia for an "At Risk Mental State" has dropped to 20-25%, possibly because referrals are now encompassing a broader range of symptomatology.

The 230 cases of early psychosis identified in Palau represent a relatively unprecedented community-based sample that was not help-seeking. These young subjects can contribute valuable information about transition rates from prodromal to frank psychosis. Follow-up reassessments are in progress. Our long-term goal is to accelerate progress toward preventive intervention strategies for young people at risk for a psychotic disorder like schizophrenia.

References

1) Erlenmeyer-Kimling L, Adamo U, Rock D et al. (1997): The New York High Risk Project: prevalence and comorbidity of axis I disorders in the offspring of schizophrenic parents at 25-year followup. *Arch Gen Psychiatry* 54:1096-1102.

2) McGorry PD, Edwards J, Mihalopoulos C et al. (1996) EPPIC: an evolving system of early detection and optimal management. *Schiz Bull* 22:305-326.

3) McGorry PD, Phillips LJ, Yung AR, Francey S, Velakoulis D, Brewer W et al (1999): The identification of predictors of psychosis in a high risk group. *Schizophrenia Research* 36:49.

4) McGorry PD et al. (2000). The Comprehensive Assessment of At Risk Mental States (CAARMS). University of Melbourne, Melbourne Australia.

5) Myles-Worsley M, Coon H, Tiobech J, Collier J, Dale P, Wender P, Reimherr F, Polloi A, Byerley W. A genetic epidemiological study of schizophrenia in Palau, Micronesia: Prevalence and familiality. *Am J Med Genet: Neuropsychiatr Genet* 1999;88:4-10.

6) Ord LM, Myles-Worsley, Blailes F, Ngiralmau H. Screening for prodromal adolescents in an isolated high risk population. *Schizophr Research* 2004;71:507-508.

7) Phillips, L., Yung, A.R., McGorry, P.D., 2000. Identification of young people at risk of psychosis: validation of Personal Assessment and Crisis Evaluation Clinic intake criteria. Aust. *N. Z. J. Psychiatry* 34:164-169.

8) Yung A, McGorry P, McFarlane C, Patton GC (1995): The PACE Clinic: development of a clinical service for young people at high risk of psychosis. *Aust Psychiatry* 3:345-349.

9) Yung A, McGorry P (1996): The initial prodrome in psychosis: descriptive and qualitative aspects. *Aust N Z J Psychiatry* 30:587-599.

10) Yung A, McGorry P (1996): The prodromal phase of first-episode psychosis: past and current conceptualizations. *Schizophrenia Bulletin* 22:353-370.

11) Yung A, Phillips L, Yuen HP, Francey SM, McFarlane C, Hallgren M, McGorry P (2003): Psychosis prediction: 12-month follow up of a high-risk ("prodromal") group. *Schizophrenia Research* 60:21-

Hard work never killed a men. Men die of boredom, psychological conflict and disease. In deed the harder your people work, the happier and healthier they will be.
(David Ogilvy - 1911)