Schizophrenia in Palau

A Biocultural Analysis

by Roger J. Sullivan, John S. Allen, and Karen L. Nero

The Republic of Palau in the western Pacific has one of the highest rates of schizophrenia diagnoses in the world today. The expression of schizophrenia in Palau and greater Micronesia is also extraordinarily gendered, with rates of affliction approximately two times higher among males. This study uses contemporary clinical diagnostic and research tools to consider and reject the hypotheses that schizophrenia in Palau has a unique diagnostic profile, that it has a unique bio-behavioral expression, and that it is a consequence of "development" manifest in the introduction and use of psychoactive drugs. These results are used to critique an assumption that has emerged from previous cross-cultural research—that the expression of schizophrenia is necessarily more benign in "developing" settings—and to suggest that aspects of historical and contemporary social practices may contribute to a gender imbalance in the expression of symptoms of schizophrenia in this Pacific Island nation.

Schizophrenia is a debilitating mental illness with variable expression and uncertain etiology. If the causes underlying this illness are ever to be understood, its manifestations in diverse social, cultural, and ecological contexts will need to be examined in detail. Narrowly focused approaches to understanding the schizophrenic condition can provide valuable insights into particular aspects of the disease. However, to make sense of schizophrenia as a complex biocultural phenomenon, a synthetic perspective is required. Such a synthesis should incorporate not just bio-behavioral perspectives on schizophrenic illness but also analyses of social and cultural factors affecting the lives of people with schizophrenia in specific settings.

High hopes that the new era of human genomics research would uncover a gene or genes "for" schizophrenia have gone unfulfilled (Tsuang 1998; Brzustowicz et al. 2000). Instead, data emerging from the Human Genome Project and increasingly sophisticated gene-linkage studies indicate that genetic factors affecting schizophrenia are more complex than anticipated; a recent meta-analysis reported candidate "susceptibility genes" for schizophrenia on at least 10 and perhaps as many as 15 of 22 human autosomes (Lewis et al. 2003). This evidence of multilocus complexity in schizophrenia defies formulation of prescriptive relationships between genotypes and bio-behavioral phenotypes. Biological psychiatry has responded to this new reality with a conceptual tool, the "endophenotype," that models the relationship between an observable manifestation of the illness and its suspected but currently unidentified genetic basis (Gottesman and Gould 2003). Despite the failure to identify a specific genetic etiology, there is broad consensus in the biomedical sphere, based on decades of research, that the expression of schizophrenia requires a genetic predisposition (Gottesman and Shields 1972; Gottesman and Gould 2003). The expression of a genetic vulnerability to schizophrenia is also strongly influenced by epigenetic processes and environmental stressors; these three causal factors constitute current biomedical endophenotype models of schizophrenia (Gottesman and Gould 2003).

The difficulty in identifying "schizophrenia" at the level of the genotype or the bio-behavioral phenotype indicates that the "science" of schizophrenia is still at a descriptive stage. Much work remains to be done in terms of gathering basic data about different manifestations of the expression of illness in individuals, in societies, and globally. Nowhere is the paucity of basic data more evident than in detailed descriptions of the expression of schizophrenia within different geographical and cultural contexts. The literature describing the symptomatic expression of schizophrenia is heavily biased toward research conducted in clinical settings in Europe and the United States, and there is relatively little publication about research conducted in non-Western settings beyond the broad estimates of prevalence and incidence in epidemiological case-finding studies (Saha et al. 2005). With regard to the latter,

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meaningfully differentiating between studies conducted in societies transitioning between traditional and modern lifeways, societies that have completed the demographic transition, and urban industrialized societies remains both a challenge and an important objective for researchers.

A 1% average worldwide population prevalence of schizophrenic illness is routinely interpreted in the medical literature as implying a uniform distribution (Burns 2004). In this sense, the 1% figure is a myth that conceals considerable variability in actual prevalence between settings (Kleinman 1996; Murphy 1982; Sullivan and Allen 2004). The island nations of Micronesia are a good example, with point prevalence ranging from a low of approximately 0.4% in the Marshall Islands in eastern Micronesia to 1.7% in the western island nation of Palau—a *fourfold* difference within an average prevalence of 0.54% in Micronesia overall (Hezel and Wylie 1992). Recognizing this high variability in prevalence between populations is important because etiological models of schizophrenia depend on such data to validate or reject theoretical positions: genetic perspectives tend to emphasize uniformity in prevalence and symptomatic expression (Burns 2004), while contextual sociocultural perspectives tend to emphasize variability (Sass 1994). Determining whether such variability is more a function of biological, diagnostic, or contextual sociocultural factors is a critical issue.[1]

The World Health Organization (WHO) has sought to address the question of variable expression and outcome in schizophrenia with large-scale studies in multiple settings. The WHO and other studies have produced consistent findings that the expression of schizophrenia varies from setting to setting and that there is a trend toward reduced prevalence (Allen 1997*b*; Torrey 1987; Warner 1985) and more favorable outcome in "developing" versus "developed" settings (Leff et al.1992; Jablensky et al. 1992, 1994; Hopper and Wanderling 2000). However, there are significant problems with the WHO studies, including the sacrifice of detailed analysis in any one setting and the use of simplistic grouping categories and dichotomies such as "developed" versus "developing" and "urban" versus "rural." Hopper (2004, 76) has pointed out that developing settings in the most recent of the WHO follow-up studies are represented by research sited in a single country, "that great, teeming, post-colonial, sectarian-riven complicated place that is India." Clearly, the WHO research conclusion that outcome is more favorable in developing versus developed settings contributes little to explaining a fourfold variability of schizophrenia within "developing" Micronesia.

An alternative cross-cultural approach championed by H. B. M. Murphy is to compare high-incidence and low-incidence settings and analyze similarities at the extremes that might suggest contextual causes (Murphy 1982). These broadly comparative cross-cultural approaches have provided tantalizing clues rather than reliable facts about universal or particular aspects of the expression of schizophrenia. What is needed to move beyond the broad and shallow approach of the WHO-type studies is detailed research *within* settings, particularly those with extraordinary prevalence rates, for these may be more likely to provide "clues" about causal factors associated with schizophrenia in context. However, rather than emulate Murphy's explicit comparison of features of context X with those of context Y, we advocate thorough description of single cases using standardized data-gathering methods. Our method employs standardized clinical instruments to quantify symptomatic expression—what Jenkins and Barrett (2004, 3) describe as a "productive starting point for cross-cultural studies." The use of a standardized diagnostic methodology allows a "clinical definition of schizophrenia . . . operationalized in order to achieve agreement among researchers in diverse field sites that they are talking about more or less the same thing" (p. 4). We have chosen to use methods more commonly used by biomedical psychiatry because the data produced are comparable with a broad literature on the expression of schizophrenia in other settings (see also Browner et al. 1988). Using this approach, the standardized clinical data can be used with appropriate caution by any knowledgeable observer as a comparator with other such data from any setting in the literature.

Within-settings research requires recognition of the complexity of causal factors (the fact that the illness is affected by contextual cultural as well as biological variables), necessitating a *biocultural* approach to research design and practice (Allen 1990). Biological indicators are utilized in biocultural research to "assess the effects of constraining factors on health" and to "illustrate how people in different environments, cultural groups, and societies respond to illness and come to confront the constraints on their health and the quality of their lives" (Wiley 1992, 217). Conversely, biocultural research necessarily informs us about the expression of disease in a given cultural environment. A disease may be perceived as "genetic" or "infectious" (i.e., fundamentally the result of a biological process), but limiting inquiry to specific biological agents—however essential such knowledge may be for treatment or control—arbitrarily and artificially constrains the scope of investigation. Despite the potential benefits, integrative approaches are rare in psychiatric research and medical anthropology in general, with research tending to focus on either biological or cultural issues (Allen 1990; Browner at al. 1988). However, biocultural perspectives on mental health issues can be provided by anthropologists, as recent cross-cultural studies of attention-deficit hyperactivity disorder (Brewis, Schmidt, and Meyer 2001; Brewis and Schmidt 2003) and schizophrenia (Schmidt, Allen, and Attah Johnson 2000) have demonstrated.

Anthropologists have already made significant contribu-

1. The absence of incidence data for Micronesia limits comparisons with other data sets to the available prevalence data. Cross-cultural incidence data on schizophrenia are relatively rare (see Barbato 1998, 6–7; Kleinman 1988, 20–35), the notable exception being incidence studies carried out as part of the WHO Determinants of Outcome Study and Reduction and Assessment of Psychiatric Disability Study (Harrison et al. 2001; Sartorius et al. 1986).

tions to schizophrenia research in the form of detailed description in high-prevalence settings. For example, Scheper-Hughes's analysis of the effects of parenting style on the expression of schizophrenia in rural Ireland had an impact far beyond the boundaries of the discipline,[2] even though it now seems that the apparently high prevalence in 1970s Ireland was a statistical artifact (Scheper-Hughes 2001, 40). In contrast to Scheper-Hughes's findings for Ireland, the extraordinary prevalence of schizophrenia in Palau has been validated by several studies using different methodologies at different times. Hezel and Wylie (1992) used community-based case-finding methods to estimate a 1.7% point prevalence of chronic psychosis in the 1980s, and Myles-Worsely et al. (1999) used a combination of community-based and conventional epidemiological methods in their complete-ascertainment project in the 1990s to identify every individual with schizophrenia in the nation at that time. Myles-Worsley and colleagues (1999) calculated a 2% lifetime morbid risk for "strictly defined" schizophrenia among Palauans (i.e., the probability that an individual surviving the 15–54-years-of-age risk period will develop schizophrenia). Palau and Micronesia in general are also notable for profound variation in the expression of schizophrenia by gender. Hezel and Wylie (1992, 346) reported a Palauan prevalence of 2.2% for males and 1% for females within a 3.4:1 gender ratio in Micronesia overall. Myles-Worsley et al. (1999, 6) estimated a 2.8% lifetime morbid risk of strictly defined schizophrenia for Palauan males and 1.2% for females, a greater than 2:1 male-to-female risk ratio. Allen and Laycock (1997) note that while an excess of males with schizophrenia is typical in developing countries, the differences tend to decrease over time. Hezel and Wylie (1992, 348) contend that, when compared with the approximately 1:1 gender ratios reported in the WHO studies (Jablensky et al. 1992), a Micronesian gender imbalance in prevalence rates "represents a clear and unique difference from established patterns in the epidemiology of schizophrenia."

Recent research using genomewide linkage analyses in Palau and elsewhere in Micronesia have contributed to the complex emerging picture of the genetics of schizophrenia. A gene-linkage study carried out in the Micronesian nation of Kosrae identified potential susceptibility markers on eight chromosomes (Wijsman et al. 2003). Studies based on Palauan pedigrees have identified candidate loci on six chromosomes (2, 3, 5, 9, 13, and 17) (Camp et al. 2001; Coon et al. 1998; Devlin et al. 2002; Klei et al. 2005), leading Devlin and colleagues to suggest that "there are multiple genes conferring liability to schizophrenia even in the small population of Palau" (Devlin et al. 2002). One implication of this post-genomics uncertainty about the specific genetic etiology of schizophrenia is that the focus of research has shifted out of the genetics laboratory and back to "the field" in the sense of solving a myriad of lower-level etiological questions about the various domains of human functioning affected by the illness in context, from social problems to mood and perceptual and language difficulties.

From the perspective of biomedicine, contextual causes of variable expression in schizophrenia such as the possible effects of community/cultural attitudes toward mental illness (Leff et al. 1992; Kleinman 1996), membership in an "extended family," or drug abuse (Jablensky et al. 1992) are "soft" research questions that have received relatively little attention. In reality, accurate description of contextual causal factors is, literally at least, the hard problem because of the difficulties of demonstrating cause and effect with naturalistic methods in a field setting. We maintain, however, that explication of the contextual social, cultural, and ecological factors affecting the expression of schizophrenia can and should be pursued and that systematic research using contemporary methods, sensitively applied, will contribute significantly to a more holistic understanding of the causes of schizophrenia.

The objectives of our research program in Palau are to identify a subset of these variable factors that may help explain the Palauan pattern of the illness. To do this, we employ several forms of biocultural and comparative analysis. First, we describe schizophrenia in Palau at the bio-behavioral level from two different perspectives: a quantitative survey of symptom expression and an assessment of an endophenotypic marker for schizophrenia, smooth-pursuit eye-tracking dysfunction. These two methods provide data with which to address basic questions about the generalizability of diagnostic practice in Palau, to test notions about the universality of the bio-behavioral expression of schizophrenia in Palau, and to comment on the likelihood that the expression of schizophrenia is relatively benign in "developing" settings, as suggested by the WHO cross-cultural findings on schizophrenia. Second, at the level of contextual behavioral response to illness, we analyze the use and abuse of psychoactive substances by people with schizophrenia in Palau. Previous researchers have suggested that the high prevalence of schizophrenia in Palau is an artifact of development manifested particularly in the arrival and widespread use of exotic drugs (Kauders, MacMurray, and Hammond 1982; Hammond, Kauders, and MacMurray 1983; Hezel and Wylie 1992). This hypothesis is widely accepted, permeating not only academic theory but also popular and medical opinion in Palau. We test it by analyzing the relationship between substance use and symptoms in a cohort of Palauans diagnosed with schizophrenia. Third, we articulate an interpretive perspective on the cultural and historical factors affecting the expression of schizophrenia in Palau. In this final analysis we describe and discuss unique cultural stressors that may contribute to gender differences

2. Other "classic" anthropological studies of major mental illness include Arthur Kleinman's (1982) research on the unique expression of depressive symptoms in Chinese culture, Sue Estroff's (1981) ethnography of "clients" in a day treatment setting, Alex Cohen's (2001) ethnography of mental illness among the homeless in Skid Row, Janis Hunter Jenkins's (1991) study of expressed emotion and schizophrenia in Mexican-American families, Nancy Waxler-Morrison's (1974) research on family dynamics and schizophrenia, and Jane Murphy's (1976) cross-cultural analysis of labeling theory and schizophrenia.

in schizophrenic morbidity in Palau and Micronesia. In the end, we reject the hypotheses that schizophrenia in Palau has a unique diagnostic profile, that it has a unique bio-behavioral expression, and that the high rate of the illness is a result of the introduction of drugs that accompanied "development" in Palau. Drawing on these findings, we argue that aspects of historical and contemporary Palauan social practices may affect the expression of schizophrenia and, in particular, link Palau's gender imbalance among people with schizophrenia to local practices more protective of young women than of young men.

The Setting and Methods

The Republic of Palau is the westernmost island group in Micronesia, comprising 340 islands with a total land area of 188 square miles (SAGRIC International 1996). From the latter part of the nineteenth century Palau was colonized consecutively by Spain, Germany, Japan, and finally the United States as part of the U.S. Trust Territory of the Pacific Islands (USTTPI). A Palauan constitutional government was established in 1981, but difficult negotiations continued on the terms of Palau's Compact of Free Association with the United States. Palau was the sole remaining trust territory from 1986 until it became a sovereign nation in free association with the United States in 1994. While it is still recognized as a developing country highly reliant upon U.S. transfers, as a middle-income nation it is not eligible for International Development Association funds (ADB 2005, 4). In 1999 the United Nations Development Programme reported that Palau had the Pacific's highest Human Development Index rating at 0.861 (UNDP 1999).

Estimates of the pre-European population size in Palau range from 20,000 to 50,000 (Gorenflo 1996, 46–47), declining to a low of 3,000 to 4,000 at the end of the nineteenth century (p. 75). From 1920 to 1990 the indigenous population recovered at a rate of 1.4% annually, despite the privations of World War II (p. 75). At the time of the 1995 census Palau had a population of 17,225 people, approximately 12,000 of whom were indigenous Palauans (Office of Planning and Statistics 2000). Over two-thirds of the population today live in or close to the main town of Koror.

Palauans have long recognized unusual behaviors, labeled *kebelung*, associated to some extent with certain families. Historically, such behavior was overlooked where possible or, if violent, contained by the family or village. Despite tolerance of many aspects of illness, long-term asocial behavior was stigmatized. Then, as now, Palauan herbal and other treatments were used by local healers to treat mental illness. The first USTTPI mental health service was established in Saipan only in 1969 with one psychiatrist later joined by a psychologist. Only minimal training programs and sporadic site visits were possible, leaving families and village communities to cope with the suffering of afflicted individuals. Only on Palau was a viable treatment program established, headed by a Palauan medical officer of chiefly status supported by a Palauan registered nurse, a high-ranking woman (Robillard 1987). A specialist in genealogies, the medical officer studied family histories in an effort to understand the increasing numbers of patients, and he and his staff focused on family and village interventions integrated with Western medical approaches. Their contemporary counterparts are trained health professionals conversant with Western biomedical approaches and grounded in traditional understandings of mental health.

The study data were collected during field trips to Palau in 1995 and 1998. Study participants were outpatients of the Behavioral Health Division, Belau National Hospital. Both analyses were cross-sectional and employed quantitative clinical assessments augmented and informed by close collaborative work with indigenous professionals and counterparts involved in key-informant and patient interviews. The principal study cohort (SYMPTOM cohort) was assessed in 1998 and consisted of 70 indigenous Palauans with a DSM-IV (APA 1994) diagnosis of chronic schizophrenia or schizoaffective disorder with mainly schizophrenic course.[3] The 1998 cohort was not a random sample but nonetheless constituted more than 50% of Palauans with "strictly defined" schizophrenia known to be on-island at that time. Illness-related characteristics of the principal study population are presented in table 1, and a breakdown of demographic data by gender is presented in table 2. The cohort included 49 men and 21 women, proportions that approximate the 2:1 overall sex ratio in Palau. The group was mature, with an average age of 39 years, and "chronic" in the sense that members had, on average, experienced the symptoms of schizophrenia for more than a decade. Most participants were receiving typical antipsychotic medications (haloperidol or fluphenazine). Other group characteristics will be discussed below.

Symptom Assessment

Schizophrenic symptomatology was assessed using the Positive and Negative Syndrome Scale (PANSS) (Kay and Sevy 1990; Kay, Opler, and Fiszbein 1992), and demographic data and self-reports of nonprescription substance use were recorded with a specially designed questionnaire. "Substance use" included consumption of the indigenous betel nut, cigarettes, alcohol, cannabis, and "ice" (methamphetamine). Self-reports of substance use were supplemented with reference to chart information on current medication and clinical histories of substance abuse.

The PANSS is a leading clinical and research assessment tool in biomedical psychiatry and has been used extensively in cross-cultural research on schizophrenia (Barrio et al. 2003; Haasen et al 2001). It is designed for use by lay researchers, but specialized training and experience are required. It is a

3. Of these, 21 had paranoid schizophrenia, 9 residual schizophrenia, 10 schizoaffective disorder, 20 undifferentiated schizophrenia, and 10 other schizophrenia (APA 1994).

Table 1. Clinical Data

	Palauan Sample ($N = 70$)	New York "Normative" Sample ($N = 240$)
	Mean (S.D.)	Mean (S.D.)
Age	39.2 (8.1)	33.1 (10.2)
Age at onset	22.5 (6.3)	
Age at first admission	22.8 (11.3)	
Number of admissions	5.1 (4.9)	
Duration of illness	16.7 (9.1)	10.7 (8.9)
PANSS positive symptom score	16.4 (6.5)	20[a]
PANSS negative symptom score	16.7 (7.3)	22[a]
PANSS general psychopathology	34.6 (9.1)	40[a]
PANSS depression cluster score	9.2 (3.6)	9–9.5[a]
Antipsychotic medication mg/day[b]	269.6 (244.5)	

[a] Transformed standardized *T* score: scale mean 50.0 (S.D. 10.0) (Kay, Opler, and Fiszbein 1992).
[b] Chlorpromazine equivalents.

novel methodology for anthropologists and was chosen after careful consideration of alternatives because of several methodological advantages. Previous research on the expression of schizophrenia in Palau has focused on the occurrence of symptom *types* in subject cohorts (Kauders, MacMurray, and Hammond 1982; Hammond, Kauders, and MacMurray 1983). The PANSS methodology is more nuanced in that it considers the *severity* of individual symptoms for each study participant. Quantified symptom severity then becomes a powerful dependent variable for statistical analysis in conjunction with independent research variables such as substance use. Because of the widespread use of the PANSS, the quantitative symptom ratings also provide benchmark data for comparison with symptom profiles of people with schizophrenia in other settings. The PANSS method entails a lengthy interview using open-ended questions to probe present-state symptoms associated with a diagnosis of schizophrenia. The interview is followed by quantitative rating of each interviewee in 30 symptom profiles grouped into three syndromes: "negative" symptoms, "positive" symptoms, and "general psychopathology." In broad terms, the negative syndrome refers to a cluster of symptoms associated with a diminution of emotional and sensory function, such as flattened emotional expression, the positive syndrome symptoms are those associated with an exaggeration of emotional and sensory function, such as auditory hallucinations, and the general-psychopathology syndrome refers to a broad category of important symptoms, such as anxiety, that fall outside the core symptomatic expression of schizophrenia (table 3).

The PANSS interview has considerable potential as a method for social scientists to generate detailed cross-cultural data on schizophrenia but suffers from the constraints of any cross-cultural methodology for the assessment of mental illness. Bridgman (1997, 103) has noted that "the diagnosis of schizophrenia in a person of one culture by a person of another is fraught with difficulties." Problems include confounding judgments about symptoms with cultural biases over the "meaning" of symptoms and miscommunication across language barriers. To minimize these biases, Palauan case workers were consulted on the range of PANSS items as they related to each participant with particular regard to delusional content, magical ideation, communication deficits, cognitive agility, and the interpretation of affect states. The PANSS Structured Clinical Interview (see Kay, Opler, and Fiszbein 1992) was translated into Palauan and then back-translated into English to provide a transcultural reference text for the rater and case workers. The Westernized "similarities" and "proverbs" items of the "abstract thinking" section of the PANSS were replaced with Palauan expressions and proverbs.

The test batteries were conducted in English with the assistance of the study participant's Palauan case worker, either a psychiatric nurse or a social worker. English is the language of instruction in Palauan schools, and all participants spoke English with varying degrees of fluency. The PANSS interviews ranged in length from approximately 40 minutes to 1.5 hours and allowed for discussion, often in Palauan, between case worker and participant as to the meaning of symptom-related questions in cultural context. Background information on the participant's social functioning was obtained from the participant's chart, case worker, and family (see Sullivan 2001 for further discussion).

The PANSS instrument was initially tested and validated using a "normative" sample of 240 medicated inpatients with

Table 2. Demographic Data by Gender

	Males ($N=49$)		Females ($N=21$)	
	Mean	S.D.	Mean	S.D.
Age	38.5	7	40.8	10.1
Number of children	0.5	1.1	2.3[a]	1.7
Years of education	10.4	3.2	10.8	2.6

[a] $p < 0.01$.

Table 3. Positive and Negative Syndrome Scale (PANSS)

Positive
P1. Delusions
P2. Conceptual disorganization
P3. Hallucinatory behaviour
P4. Excitement
P5. Grandiosity
P6. Suspiciousness/persecution
P7. Hostility
Negative
N1. Blunted affect
N2. Emotional withdrawal
N3. Poor rapport
N4. Passive/apathetic social withdrawal
N5. Difficulty in abstract thinking
N6. Lack of spontaneity and flow of conversation
N7. Stereotyped thinking
General Psychopathology
G1. Somatic concerns
G2. Anxiety
G3. Guilt feelings
G4. Tension
G5. Mannerism and posturing
G6. Depression
G7. Motor retardation
G8. Uncooperativeness
G9. Unusual thought content
G10. Disorientation
G11. Poor attention
G12. Lack of judgment and insight
G13. Disturbance of volition
G14. Poor impulse control
G15. Preoccupation
G16. Active social avoidance

schizophrenia recruited over a seven-year period in New York (Kay and Sevy 1990; Kay, Opler, and Fiszbein 1992; Lindenmayer, Bernstein-Hyman, and Grochowski 1994). The cohort included 179 males and 61 females (106 blacks, 60 whites, and 74 Hispanics) with an average age of 33.1 years (S.D. 10.2). The well-described symptomatic characteristics of the New York cohort were used as the principal comparative data in the analysis of Palauan symptomatology.

Analysis of an Endophenotype Marker for Schizophrenia

Genetic endophenotype markers are very useful for cross-cultural and within-cultural studies of psychiatric illness (Allen et al. 1990; Gottesman and Gould 2003). The eye movements we use when tracking a moving object across the visual field are known as smooth-pursuit eye movements; when smooth eye movements are replaced fully in or in part by short, jerky movements, the condition is called smooth-pursuit dysfunction (SPD). SPD is a robust endophenotype marker associated with schizophrenia. From 50 to 80% of patients diagnosed with schizophrenia and 40% of their first-degree relatives exhibit SPD; this is a finding confirmed in hundreds of studies from throughout the world (Levy et al. 1993; Calkins and Iacono 2000). The SPD marker is in effect culture-neutral in that it emerges from a very basic and fundamental aspect of human behavior (i.e., eye movements).

The 1995 cohort (MARKER cohort) was assessed for the prevalence of the SPD endophenotype marker. This group comprised 36 members of the Behavioral Health Division outpatient population: 26 men (average age 33.3 years; S.D. 6.3) and 10 women (average age 33.9 years; S.D. 5.9). The nonpsychiatric comparison group consisted of 26 individuals recruited from the Belau National Hospital staff: 15 men (average age 32.4 years; S.D. 9.1) and 11 women (average age 31.5 years; S.D. 9.6). Outpatient diagnoses were current at the time of testing and based on clinical records.

The methods used for the assessment of eye movements are discussed in detail by Allen (1997*a*; see also Allen and Johnson 1995). Although outpatient participants were receiving antipsychotic medications, numerous studies have shown that these drugs do not influence smooth-pursuit performance; in addition, there are no gender differences in pursuit performance (Levy et al. 1993). Eye movements were scored using the natural log of the signal-to-noise ratio (ln [s/n]) (Blackwood et al. 1991), a commonly used method for assessing eye-tracking performance globally (i.e., taking into account the entire tracking performance). A perfect tracking performance will have very little noise and will reflect the signal, which corresponds to the movement of the target. The perfect tracking score will be higher than the score derived from a tracking performance that is not so smooth and on target.

Results and Discussion

Clinical and Demographic Data on the SYMPTOM Cohort

The mean age of the study participants was consistent with that for a mature cohort with chronic schizophrenia (table 1). Age at onset and age at first admission were unremarkable. A later age of onset among females (mean 4.6 years) is also a characteristic of the illness in other settings. Most of the study participants were receiving typical dosages of antipsychotic medications. The level of employment was low (16.3% for males, 28.6 for females), as it tends to be among people with schizophrenia anywhere. Members of the cohort were well educated (mean 10.6 years) and very well traveled by any standards, with more than 50% (57% of males, 55% of females) having lived abroad for six months or more. Hammond, Kauders, and MacMurray (1983) found that a considerable number of Palauans diagnosed with schizophrenia had had their first break abroad and suggested that this might be related to a general pattern of increased mental illness among emigrant populations. While there may be stress as-

sociated with moving overseas, it should be pointed out that young adult Palauans frequently go overseas for work or education. For example, the 1990 census records 1,418 Palauans between the ages of 20 and 24 years (Levin, Gorenflo, and Hosie 1993), of whom 463 (33%) lived in Guam or the Commonwealth of the Northern Mariana Islands. The census did not include data from Hawaii, other parts of Micronesia, or the mainland United States, and therefore the 33% figure for Palauans in the vulnerable 20–24-year age-group residing overseas represents a minimum. Given this, the fact that a significant number of Palauans with schizophrenia had had their first break abroad is anticipated by the large proportion of young Palauans living abroad and is not necessarily an indication of the stress of emigration. Nevertheless, the degree to which migration is a schizophrenic stressor for young Palauans is an important research question that merits further study.

Quite different from the pattern in Western settings is the high proportion of Palauan study participants living with family (87%). This trend is less remarkable when compared with that for other developing countries: the WHO ten-country study results indicate that people with schizophrenia in developing settings are less likely to be living alone and more likely to be members of an extended family (Jablensky et al. 1992). However, the hypothesis that has emerged from the WHO studies that developing settings with "extensive kin-based stores of support" (Hopper 2004, 63) will be associated with a more benign expression of schizophrenia does not seem to be supported in the high-prevalence Palauan context.

Palauan women with schizophrenia are significantly more likely to be married and to have children than men: 48% (10) of the females in the Palauan cohort were "ever married" and only 10% (5) of the males. In contrast, the overall rate of "ever married" in the WHO ten-country study for people with schizophrenia was 60% of females and 30% of males (Jablensky et al. 1992, 22). Fertility rates in the SYMPTOM cohort were 2.3 (S.D. 1.7) and 0.5 (S.D. 1.1) offspring on average for women and men respectively. There can be little doubt, then, that people with schizophrenia have reduced fertility, but apparent fertility rates vary according to study, time, and place (Gottesman and Shields 1982; Larson and Nyman 1973; Nimgaonkar et al. 1997; but see Lane et al. 1995). In the 1990 census, Palauan women aged 30–34 years had an average of just over 2.0 children (or 2,044 children/1,000 women), and the total Palauan fertility rate was 2.8 (Levin, Gorenflo, and Hosie 1993). These figures indicate that Palauan women with schizophrenia were having the same number of children as other Palauan women. At the same time, the male fertility rate was well below the replacement level, and the marriage rate was extremely low. The low marriage rate could indicate that males with schizophrenia pay a very high social price for their illness such that it precludes marriage and reproduction.

Comparative Symptom Analyses

The PANSS positive and negative syndromes are the principal axes of symptom assessment, as they represent the least ambiguous or "signal" symptoms of schizophrenia, including Schneider's "first-rank" (positive) symptoms. Within a possible score range of 7 to 49, the mean cohort positive-scale PANSS score was 16.4 (S.D. 6.5) and the mean negative-scale score was 16.7 (S.D. 7.3) (table 1). In comparison, the standardized PANSS scores of the New York "normative" sample were 20 on the positive scale and 22 on the negative scale (Kay, Opler, and Fiszbein 1992, 14) (table 1). In terms of the interpretive clinical guidelines of Kay and colleagues (p. 12), the Palauan cohort positive-scale scores are in the "slightly below average" range and the negative-scale scores are "average." The Palauan cohort general-psychopathology-scale scores and depression-cluster scores are also clinically "average" (Kay, Opler, and Fiszbein 1992, 12) (table 1). These comparisons suggest that the Palauan cohort symptomatology is not extraordinary in terms of PANSS-score group means.

The cohort raw data were subjected to a factor analysis to extract principal components. The objective of this analysis was to determine whether the 30 Palauan-rated PANSS items would cluster on the predicted positive and negative axes and to describe the principal symptomatological dimensions of schizophrenia in the Palauan cohort. The results of the factor analysis are presented in table 4 and the factorial structure of the New York "normative" sample data in table 5 (Kay and Sevy 1990; Kay, Opler, and Fiszbein 1992).

An initial scree plot of eigenvalues suggested a four- or five-factor model for the Palauan cohort data. Following the methodological rationale of Lindenmayer, Bernstein, and Grochowski (1994) and von Knorring and Lindström (1995), the data were analyzed using orthogonal rotation of a five-factor model accounting for 55.5% of the total variance (table 4). The two largest factors explained 34.7% of the total variance and were made up of items associated with negative symptoms (factor 1) and positive symptoms (factor 2); these factors may be interpreted as representing the negative and positive syndromes of schizophrenia. Factor 3 ("excited") included items associated with excitement and poor impulse control. Factor 4 ("depressive") was composed mainly of items associated with mood but also included a loading of the positive-symptom item "hallucinatory behavior." The fifth factor ("others") grouped the remaining items. Factors 1–3 had high internal consistency: "negative" $\alpha = 0.86$, "positive" $\alpha = 0.84$, "excited" $\alpha = 0.71$, "depressive" $\alpha = 0.56$, "others" $\alpha = 0.53$.

In comparison, the New York "normative" data are composed of seven orthogonal factors accounting for 64.7% of the total variance (table 5). In their initial analysis of these data, Kay and Sevy (1990) retained the first four factors with eigenvalues > 2 and labeled them "negative," "positive," "excited," and "depressive." The remaining three factors were disregarded as error variance. Kay and Sevy's four-factor py-

Table 4. Factor Loadings of PANSS Items, Palau Sample

	Equamax Rotated Component Loadings				
Component/Symptoms	1	2	3	4	5
Negative					
N6. Lack of spontaneity	.83	–	–	–	–
N3. Poor rapport	.76	–	.30	–	–
N1. Blunted affect	.75	–	–	.23	–
N2. Emotional withdrawal	.73	–	–	.33	–
G7. Motor retardation	.69	–	–	–	–
N4. Passive social withdrawal	.66	–	–	.38	–
G16. Active social avoidance	.53	–	.38	.44	.28
G13. Disturbance of volition	.30	–	–	–	–
Positive					
G9. Unusual thought content	–	.80	–	.32	–
P1. Delusions	–	.77	–	.28	–
P2. Conceptual disorganization	–	.69	–	–	–
P5. Grandiosity	–	.65	.27	–	–
N7. Stereotyped thinking	–	.64	–	–	–
G12. Lack of judgment and insight	.21	.58	.24	–	–
G15. Preoccupation	.41	.52	–	.23	–
P6. Suspiciousness/persecution	–	.50	.36	.40	–
N5. Difficulty in abstract thinking	.36	.47	–	–	–
G1. Somatic concerns	.22	.39	–	.25	–
G10. Disorientation	.25	.28	–	–	–
Excited					
G14. Poor impulse control	–	–	.82	–	–
P7. Hostility	–	–	.78	–	–
G8. Uncooperativeness	.29	–	.64	–	–
P4. Excitement	–	.26	.51	–	.35
G11. Poor attention	–	.21	.46	–	–
Depressive					
G6. Depression	.38	–	–	.68	–
G3. Guilt feelings	–	–	–	.67	–
G2. Anxiety	–	–	.32	.58	–
P3. Hallucinatory behaviour	–	.30	–	.53	–
Others					
G4. Tension	.35	–	–	–	.68
G5. Mannerism and posturing	–	.28	–	–	.59
Eigenvalue	6.43	3.97	2.61	2.16	1.48
Variance	21.45	13.25	8.71	7.20	4.20

Note: Loadings < .20 are not shown.

ramidal model of schizophrenia described the predicted division of negative and positive symptoms "alongside more unspecific factors, which would give the individual mark to specific patient samples and also reflect the extensiveness of pathology" (Lindenmayer, Bernstein, and Grochowski 1994, 632).

Our Palauan cohort results were sufficiently similar to the New York model that we have used the same descriptive labels for the rotated scale factors. The Palauan factorial structure is more variable than the normative sample data in that less of the total variance is included in the five-factor model but is similar in explaining most of the variance (50.6%) within the first four factors with eigenvalues > 2. The first four factors describing the two cohorts are very similar, but the leftover items in factor 5 are different. A notable difference in the Palauan data is the loading onto different factors of items associated with cognitive functioning such as "abstract thinking" and "conceptual disorganization," items that loaded onto factor 5 in the normative sample data. This result suggests that our evaluations of the study participants' cognitive performance were flawed and that further Palauan-led research design is required on this axis of assessment.

The factorial structure of the Palauan cohort data describes a unique expression of schizophrenia emerging around the core positive and negative symptom syndromes predicted by Kay and Sevy's (1990) model. The principal four-factor structure of the Palauan PANSS data is remarkably similar to the structure of the normative New York sample despite the temporal, geographical, and cultural differences between the cohorts. Overall, the results of the factor analysis reinforce the group-mean findings in suggesting that the symptomatic expression of schizophrenia in Palau is broadly comparable to its expression in other settings.

Smooth-Pursuit Eye-Tracking Dysfunction

In this study, we addressed the issue of whether people diagnosed with schizophrenia in Palau demonstrate poorer smooth-pursuit performance compared with Palauan control subjects. In addition, we looked within the schizophrenia subject group to see if there were differences in SPD frequency associated with substance abuse status. Our results showed that smooth-pursuit performance was worse in the patient group relative to the comparison group (table 6). The outpatients with schizophrenia had an average eye-tracking performance score (ln(s/n)) of 4.69 (s.d. = 1.07), while the Palauan comparison subjects had an average score of 5.36 (s.d. = 0.64); this difference was significant ($t = 2.85$, d.f. = 60, $p < 0.01$). There were no significant differences between male and female patients with schizophrenia and male and female controls. Eye-tracking performance was not significantly correlated with age. Sixteen members of the patient group, all males, had a clinical history of substance abuse. They had an average ln(s/n) score of 4.79 (s.d. = 1.08), which is not significantly different from that of the non-substance-abusing patients: ln(s/n) = 4.79 (s.d. = 1.01). Among the schizophrenia patients, 10 of 36 subjects (27.8%) had ln(s/n) scores at least two standard deviations below the control mean (4.08), compared with only one of the 26 comparison subjects (4%). The two-standard-deviation threshold is a very conservative way of estimating the percentage of patients with SPD. A less conservative estimate can be derived by looking at the percentile distributions of scores in each group (the percentile equivalents) and finding the score at which the two groups are most divergent. In this case, the most differentiating score is 4.83: 4 of 26 controls (15.4%) scored below this compared with 20 of 36 patients (55.6%).

Table 5. Factor Loadings of PANSS Items, New York Sample

	Equamax Rotated Component Loadings						
Component/Symptoms	1	2	3	4	5	6	7
Negative							
N2. Emotional withdrawal	.80	–	–	–	–	–	–
N4. Passive social withdrawal	.79	–	–	–	–	–	–
N6. Lack of spontaneity	.76	–	–	–	–	–	–
N1. Blunted affect	.71	–	–	–	–	–	–
N3. Poor rapport	.71	–	.22	–	–	–	–
G11. Poor attention	.68	–	.24	–	.22	–	–
G16. Active social avoidance	.56	–	–	–	–	.45	–
G7. Motor retardation	.55	–	–	–	–	–	–
G13. Disturbance of volition	.51	–	.24	.31	–	–	–
G5. Mannerism and posturing	.38	–	–	–	.26	–	–
Positive							
G9. Unusual thought content	–	.84	–	–	–	–	–
P1. Delusions	–	.84	–	.26	–	–	–
P5. Grandiosity	–	.76	–	–	–	–	–
G12. Lack of judgment and insight	.32	.52	–	–	.36	–	–
P3. Hallucinatory behaviour	–	.43	–	.39	.25	–	–
Excited							
P4. Excitement	–	–	.83	–	–	–	–
G14. Poor impulse control	–	–	.71	–	–	–	–
G4. Tension	.22	–	.66	.39	–	–	–
P7. Hostility	–	–	.61	–	–	–	–
G8. Uncooperativeness	.48	–	.49	–	–	.38	–
Depressive							
G2. Anxiety	–	–	.28	.71	–	–	–
G3. Guilt feelings	–	–	–	.66	–	.28	–
G6. Depression	–	–	–	.64	–	.31	–
G1. Somatic concern/delusions	–	.21	–	.60	–	–	–
G15. Preoccupation	.30	.32	–	.53	–	–	.49
Cognitive and Others							
N5. Difficulty in abstract thinking	.52	–	–	–	.57	–	–
G10. Disorientation	.51	–	–	–	.56	–	–
P2. Conceptual disorganization	.39	.48	–	–	.52	–	–
P6. Suspiciousness/persecution	–	.47	–	.23	–	.61	–
N7. Stereotyped thinking	.30	.41	.27	.31	–	–	.45
Eigenvalue	5.68	3.54	2.94	2.92	1.58	1.53	1.25

Note: Loadings < .20 are not shown.
[a] After Kay and Sevy (1990).

These results are comparable, although with some differences, with those from studies conducted elsewhere using similar methods. They indicate that SPD is common among Palauans with schizophrenia. The percentage of study participants scoring two standard deviations below the comparison mean is quite high relative to comparable studies in New Zealand (Allen 1997*a*) and Scotland (Blackwood et al. 1991), and the percentile-equivalent threshold indicates that over half of the patients have SPD. The percentile-equivalent threshold is somewhat lower in the Palauan sample than in the New Zealand sample, suggesting that smooth-pursuit performance is somewhat worse in nonpsychiatric Palauan subjects than in nonpsychiatric New Zealand subjects. This result could indicate that the genetic factors underlying the SPD endophenotype marker are more broadly distributed in the Palauan population, which may be associated with the higher prevalence of schizophrenia in Palau than in other Micronesian populations. However, given the small sample size, this conclusion should be taken as preliminary.

Overall, with approximately 55% of the schizophrenia patients exhibiting SPD, a genetic endophenotye marker for schizophrenia, it is reasonable to conclude that schizophrenia in Palau has a similar biophysiological basis to schizophrenia in other populations. The results reported here are in agreement with those found in Palau for other endophenotype markers, such as antisaccadic eye-movement performance (Allen et al. 1996; McDowell et al. 1999) and P50 gating deficits (Myles-Worsley 2002). The results of these studies, which are very consistent with results obtained in carefully diagnosed research populations in other countries, indicate

Table 6. Smooth-Pursuit Eye-Tracking Dysfunction (1995 Palau MARKER Cohort)

			Age		Smooth-Pursuit Eye-Tracking Performance	
Subject Group	Males	Females	Mean	S.D.	ln(s/n) Score[a]	S.D.
Palau ($N = 62$)						
Schizophrenia group	26	10	33.5	6.2	4.69[b]	1.07
Nonpsychiatric comparison group	15	11	32.0	9.3	5.36	0.64
Schizophrenia group, substance abusers	16	0	35.9	6.2	4.79	1.08
Schizophrenia group, non-substance abusers	8	10	32.4	5.6	4.79	1.01
New Zealand ($N = 60$)[c]						
Schizophrenia group	19	7	36.4	10.2	4.99[b]	0.84
Nonpsychiatric comparison group	17	17	33.3	9.3	5.60	0.86

[a] Natural log (signal/noise ratio).
[b] $p < 0.01$.
[c] Data from Allen (1997*a*).

that the diagnosis of schizophrenia in Palau not only reflects a common symptomatic profile based on overt behavior but also is consistent with the hypothesis of a genetic susceptibility for the condition.

Although the numbers are small, the fact that substance abusers scored no differently from the others does not support the idea of substance abuse as a general explanation for the relative "excess" of schizophrenia in Palau. If substance abuse were a schizophrenogenic stressor independent of underlying genetic susceptibility (revealed by SPD), then the substance-abuse patients would be expected to have better smooth-pursuit performance than the other patients. Substance abuse could, of course, still be a schizophrenogenic stressor at the individual level; however, these results fail to provide evidence in support of the hypothesis that substance abuse alone can explain the distribution of schizophrenia in Palau at the population level.

Substance Use

The use of street drugs was associated with a less-favorable outcome in schizophrenia in the WHO ten-country study (Jablensky et al. 1992, 79). Both Hammond, Kauders, and MacMurray (1983) and Hezel and Wylie (1992) have emphasized the role of substance abuse as a potential environmental causative factor in schizophrenia in Palau. Hammond, Kanders, and MacMurray (1983) noted in particular the association between substance use and violence, and Hezel and Wylie (1992, 349) interpreted the "strong differentiation along sex lines with respect to drug use" as a potential cause for the relatively higher rates of male mental illness.

Given the importance attributed to substance use as a factor affecting the expression of schizophrenia in the WHO studies and the direct causal association with the high prevalence of schizophrenia in Palau reported by previous researchers, we analyzed the relationship between substance use and symptomatology in some detail. A self-report survey of substance use by the 1998 SYMPTOM cohort and retrospective analyses of patient case histories were conducted. The nonprescription psychoactive substances most favored by people with schizophrenia in Palau were betel nut (*Areca catechu*), tobacco (chewed or smoked), cannabis, and alcohol (table 7). Methamphetamine use was negligible and is not shown.

Betel nut was used by 74% of the cohort (52 individuals), a similar rate to that for the general population (Ysaol, Chilton, and Callaghan 1996). When the symptoms of the 40 "chewers" in the cohort were compared with those of the 30 non- or "casual" chewers (≤ 2 quids/day), the chewers had significantly lower negative and positive symptoms as measured by the PANSS scale (see Sullivan et al. 2000 for analysis and discussion) (table 8).

The tobacco-use patterns were complex. Whereas only 37 participants (53%) were cigarette smokers, 64 participants (91.4%) either smoked cigarettes, broke up cigarettes and included the tobacco as a chewed ingredient of the betel quid, or both chewed and smoked cigarettes. Betel nut and cigarette chewing were negatively correlated with cigarette smoking; participants tended to be either exclusively chewers or smokers ($r = -0.43$, $p < 0.01$). This trend was particularly evident

Table 7. Self-Reported Substance Use ($N = 70$)

Substance	Mean	S.D.	*N*	%
Betel nut (whole nuts/day)	8.4	6.4	52	74.3
Alcohol (servings/week)[a]	8.5	6.7	18	26.1
Cannabis ("joints"/week)	10.9	21.2	22	31.4
Cigarettes (smoked/day)	26.1	16.2	37	53.0
Cigarettes (chewed with betel nut/day)	8.9	6.5	46	66.0
Cigarettes (chewed + smoked/day)	21.0	15.1	64	91.4

[a] U.S. standard servings of beer, wine, and spirits.

Table 8. Substance Use and PANSS-rated Symptoms (N = 70)

Substance and Type of Symptom	Users Mean (S.D.)	Nonusers Mean (S.D.)	t	p
Betel (N = 40/30)				
Positive	14.3 (5.7)	19.2 (6.6)	−3.3	0.001
Negative	14.4 (6.7)	19.7 (7.1)	−3.2	0.002
Cigarettes (N = 37/33)				
Positive	18.2 (6.8)	14.3 (5.5)	2.6	0.01
Negative	18.3 (6.5)	14.9 (7.9)	1.9	0.055
Cannabis (N = 20/29)[a]				
Positive	17.4 (7.1)	18.1 (6.0)	−0.3	n.s.
Negative	15.7 (4.5)	19.8 (7.9)	−2.3	0.03
Alcohol (N = 17/31)[a]				
Positive	18.2 (6.7)	17.9 (6.2)	0.1	n.s.
Negative	16.3 (5.5)	19.1 (7.6)	−1.3	n.s.

[a] Males only.

among the female group, of whom 17 (81%) were cigarette chewers and 4 (19%) were smokers. Overall the quantity of tobacco chewed in the betel quid was considerably less than that consumed by smoking. Although the majority of both men and women used tobacco, women consumed half as much as men (t = 4.4, p = 0.000). The prevalence of smoking in the study group (53%) was also much higher than in the general Palauan population (18.1%) (Futterman and Lyman 1998, 17). Finally, the relationship between cigarette smoking and schizophrenic symptoms was a reversal of the betel-nut data, with smokers on average having significantly worse positive symptoms than nonsmokers (table 8). This result is consistent with those of a number of studies describing a relationship between cigarette smoking and more severe positive symptoms (see Chong and Choo 1996).

The self-reported rates of substance use were distinctly gendered. Betel nut and tobacco was used widely by both male and female participants, but use of alcohol and cannabis was limited mainly to a subgroup of males. Twenty-four males (49%) reported using either alcohol or cannabis. The use of alcohol and cannabis among females was negligible, with only one reporting the use of alcohol and two reporting the use of cannabis.

Males who used alcohol or cannabis were not significantly different from male nonusers in terms of demographic or preassessment clinical variables. Contrary to the anticipated adverse effects of cannabis on the symptoms of schizophrenia, male cannabis users had significantly lower negative symptoms (table 7) and depression-cluster scores (t = −2.4, p = .02) than nonusers as measured by the PANSS. Similarly, there were no significant differences in PANSS-rated symptoms between male drinkers and nondrinkers, with the exception of a significantly lower depression-cluster score (t = −2.2, p = .04) among the drinking group.

The hospital records of each participant were retrospectively analyzed for a clinical history of "substance abuse" (mainly alcohol and cannabis abuse) and associated problems, particularly violent behavior and incarceration. The proportion of participants with a clinical history of "substance abuse," excluding smoking and betel chewing, was 67% (N = 47), four females (19%) and 43 males (88%). A clinical history of substance abuse, particularly heavy drinking, was associated with clinically recorded violence and incarceration. All 20 male participants with a history of violence also had a history of substance abuse—an association that was statistically significant (x^2 = 4.7, p = 0.3). Eighteen of the 19 male participants who had spent time in jail were also substance abusers. In contrast, only one of the female participants had a history of violent behavior, which was unrelated to any history of substance abuse, and none of the female participants had been jailed.

In summary, the hypothesis that substance abuse might explain the extraordinary prevalence of schizophrenia in Palau is not well supported by the data presented here. The rates of substance use in the study group, though extreme in comparison with nonclinical populations, are not unique (Lohr and Flynn 1992). In contrast to the clinical assumption that substance use will worsen symptoms of schizophrenia, substance use in this chronic cohort was not related to increased severity of symptoms (with the exception of cigarette smoking). On the contrary, the use of betel nut, cannabis, and alcohol was related to milder aspects of symptomatology. Substance-use patterns among the mentally ill are quite distinct from those among nonclinical populations and reflect attempts by afflicted individuals to respond to and cope with the experience of illness. Our results suggest that Palauans with mental illness are exploiting the contextual ecology, in the form of indigenous and exotic substances, in order to "adapt" to aspects of their experience of illness. In biomedicine, nonmedication substance use by mentally ill persons is called "self-medication." The finding that several of the substances were associated with decreased symptom severity is predicted by the self-medication hypothesis: that people with schizophrenia seek out substances that ameliorate their suffering, either by relieving emotional suffering (the psychodynamic perspective [see Khantzian 1997]) or by modulating neurotransmitter imbalances (Schneier and Siris 1987). However, it is important to remember that this is an adult population in a chronic stage of the illness. This cross-sectional "snapshot" does not advance our understanding of the interaction between drug use and symptoms during the initial onset and acute phases of the illness. The prevalence of violent events and incarceration among male Palauan substance abusers is also not unique, and studies in Finland and Denmark have reported similar findings (Räsänen et al. 1998; Soyka 2000). The institutional histories of violence and incarceration in the Palauan cohort indicate that drug use is associated with social problems and pathology not detected with a cross-sectional study. A longitudinal study is currently under way in Palau to test whether these initial findings remain consistent over time.

Sociocultural and Historical Factors Affecting the Expression of Schizophrenia

The comparative analyses of symptom expression, the SPD endophenotype marker, and the effects of substance use in two cohorts of Palauans with schizophrenia have not identified any manifestations of the illness that reflect or explain the high prevalence of schizophrenia in Palau. These assessments have used standardized methods designed to quantify presumptively universal manifestations of schizophrenic expression. The absence of a unique bio-behavioral expression of the illness in the study population suggests that contextual processes external to the study cohorts should be considered in the search for insight into the unusual rate of mental illness in Palau.

Kauders, MacMurray, and Hammond (1982) postulated that recent external influences have destabilized "traditional" gender roles and contributed to a differential risk of schizophrenic morbidity of Palauan men and women. They especially emphasized the increasing anomie of Palauan males in the rapidly changing and modernizing social environment of the 1960s and 1970s. In contrast, they claimed, the female role was less affected by these changes and, if anything, the trend toward nuclearized roles had emphasized the "female's mothering role, and increased her long-standing importance as a central cultural figure." Micronesianist researchers have cautioned that Western models positing social and mental pathology as a consequence of colonization and development cannot be directly transferred to Micronesian contexts (Hezel 1987; Marshall 1979; Nero 1990; Nero, Brel Murray, and Burton 2000; Rubinstein 1992). Hezel and Wylie (1992) and Marshall (1996) have argued that sex differences in traditional social stressors may have preceded the era of modernization. Acknowledging the earlier observations by Gladwin and Sarason (1953) and Lessa (1951), Hezel and Wylie contend that after World War II "the social pressures on men were greater and the supports fewer" (1992, 349). In age-ranked Micronesian societies young people, and particularly young males, are "especially vulnerable" (Hezel 1987, 286). In Truk (Chuuk), Hezel describes young males as experiencing

> repeated dislocation in contrast with women, who enjoy greater stability in their lives, even if at the price of far more restriction as to occupation, dress and other features of life. The male customarily left his house at puberty in compliance with incest taboos against sleeping in the same house with his sisters. He often had no residence throughout his adolescence, and at marriage he usually moved to his wife's lineage estate to work for her family, even while retaining obligations to his own lineage. The Trukese male, then, seems to have always been in a somewhat more precarious position than the female, especially during his younger years.

The traditional virilocal Palauan residence pattern differs from the matrilocal Chuukese pattern (a Palauan wife usually moved to her husband's father's house), but many of the male-specific stressors described by Hezel also occur in the Palauan context. In the past "young men were eased out of their families due to strong brother-sister avoidance mores" and would spend most of their time with age-mates at village club houses (Nero 1990, 71). Today, young men tend to move among residences and brother-sister relationships are still marked by some distance and respect (Smith 1983, 76). Nero notes that a young Palauan man is not considered a mature adult "until he demonstrates his stability and establishes his home, career, and family—now perhaps in his thirties. Such processes require active clan support, although a high paying job can allow increased independence" (1990, 75). Because of increased urbanization, today's residence patterns are increasingly neolocal, compounding the financial pressures on new couples.

A major source of stress for young Palauans is the requirement to observe and fulfill customary obligations. Traditional patterns of reciprocal exchange continue in Palau today, although transformed by imported goods and currencies (Nero, Brel Murray, and Burton 2000; Smith 1983). The roles and expectations with regard to customary obligations are different for young men than for young women. A young Palauan man's identity, potential wealth, and social standing are not just dependent on his ability to earn money in the wage economy but linked to his sister's support and efficiency within the traditional reciprocal exchange system; she mediates major types of exchanges on his behalf, including collections made to finance the construction of his house and payments to his wife's family on the occasion of his marriage, the birth of a child, and divorce (Nero 1990; Smith 1983). Traditionally, a sister earned money to fulfill this responsibility through services to her husband's family.

Whereas women bring money into the Palauan clan lineage ("savers"), men are a cause of expenditure ("spenders" [Smith 1983, 141]). This responsibility may burden a Palauan woman with stressful obligations, but it also places her securely within a cultural tradition and underpins her identity and social standing as foundational within the clan lineage. Young Palauan women have a secure position within the household and lineage whether or not they have a wage job, and they are drawn into the family in times of trouble.

To some extent a young Palauan man has no meaningful identity until he earns an income, marries, has children, and engages in the matrix of social relationships and economic and political exchanges channeled through the brother-sister dyad and their respective spouses. In terms of social roles and responsibilities, those of young men are "floating" in comparison with the more prescribed roles of young women in Palauan society. This vulnerable phase in the lives of young Palauan men overlaps with the prodromal period and age of onset of males diagnosed with schizophrenia in Palau (table 1). Whereas an estranged or mentally ill daughter will be drawn back into the family and protected, particularly if she has become pregnant, a wayward son is likely to receive less direct support from his family and clan; he may find food

and shelter among his relatives, but his residence is more provisional. A similar pattern of relative familial support for males and females has been identified elsewhere in Micronesia. According to Lowe (1999), young Chuukese females receive significantly more social support classified as "instrumental" from both their mothers and fathers and significantly more "expressive" and "global" support from their mothers than males (Lowe 1999, 296–98). At the same time, young males receive significantly more instrumental and global support from same-sex extended parents than females (pp. 296–98; see also Lowe 2002).

Smith has noted that "all relationships . . . *must be validated by fulfilling the behavioral obligations* inherent in the status of 'blood kin"' (1983, 51, emphasis added). The differences in customary roles of young men and women in Palauan society and the relative degrees and types of support provided by family and lineage suggest that young men and women with schizophrenia are differently able to meet these behavioral obligations. A young Palauan woman with schizophrenia can maintain a relatively secure customary role identity: living at home, she may participate in domestic chores, gardening for the family and exchanges, and child care and may even bear children. She is also more likely to receive support and protection from her family and clan group and to be married before the average age of schizophrenic onset (table 1). In contrast, the problems faced by a young Palauan man with schizophrenia are compounding: he has few "traditional" roles that he can adopt (with the exception of fisherman) and is unlikely to find the employment in the wage economy necessary to fulfill his customary obligations. Consequently, as an undesirable marriage partner, he cannot participate in and benefit from the flow of wealth from customary exchanges that is available to married men. As the costs of customary obligations have become inflated by the wage economy and store-purchased goods, the pressures faced by young men with schizophrenia are likely to have increased accordingly.

Cultural performance is exacerbated by the social impairment associated with schizophrenia in any context and perhaps more so in Micronesia. Marshall (1996, 253) has noted that "cultural competence" is especially valued in the "group-centered" and "other-directed" Micronesian cultural context:

> Personal competence . . . is contingent upon a continually demonstrated ability to respond to others, to be a mature adult, and not to be governed by one's emotions or personal whims. To be incompetent is to be crazy and beyond reach of the social universe that provides order and guides behavioral conformity . . . necessary for successful life in these small face-to-face communities.

According to Marshall, it is *only* mentally impaired people who are recognized as truly "disabled" in Micronesian societies because even people with major physical impairment or disease can still participate in the social realm. Sullivan and Allen (1999) have stressed that social deficits are a fundamental defining and experiential characteristic of schizophrenia and that these deficits are maximized in face-to-face situations. Allen (1997*b*) has argued that societal expectations are more pervasive and therefore more schizophrenogenic in small-scale societies than they are in the relative anonymity of urban settings. The premium placed on "cultural competence" in Micronesian society may represent a unique burden for individuals suffering from schizophrenia there, relative to other cultural settings in which personhood is not so closely associated with cultural/social performance.

Summary and Conclusions

We have carried out analyses on several levels to build a synthetic biocultural picture of the expression of schizophrenia in Palau. The two bio-behavioral methodologies—assessment of symptom expression and evaluation of an endophenotypic marker—are particularly important because they produce independent descriptive data about the expression of schizophrenia. These independed methods and data sets have provided converging evidence that the bio-behavioral expression of schizophrenia in Palau is not particular to this setting but reflects patterns of illness observed elsewhere and that the diagnosis of schizophrenia has not been in any way looser or more inclusive in Palau than elsewhere. In comparisons between the Palauan and "normative" New York cohorts, uncorrelated clusterings of PANSS items associated with the negative and positive syndromes of schizophrenia emerged alongside of more particular manifestations of the expression of the illness in each setting. In terms of endophenotypic factors, smooth-pursuit eye-tracking dysfunction was relatively common in Palauans with schizophrenia, indicating a biophysiological etiology shared with carefully diagnosed cohorts from other populations.

Our intention has not been to present a case that schizophrenia has a homogeneous cross-cultural expression emerging from a universal genetic etiology, and we do not subscribe to such a view. These analyses have identified unique aspects of the expression of schizophrenia in Palau, but more striking to us are the similarities that emerge when comparing the Palauan data with research findings in other settings, particularly the differentiation of symptomatic expression in the predicted positive/negative syndrome axes in widely divergent contexts. Emphasizing similarities in the expression of mental illness is a point of contention in cross-cultural research on schizophrenia. For example, Kleinman (1988, 1996) and Sass (2004) have criticized a bias in biomedicine toward seeking cross-cultural similarities and universals in mental disorders while deemphasizing cultural particularities because of perceived biologically determinist assumptions about the "cause and structure" of mental disease. Yet Kleinman (1988, 44), for one, also acknowledges that there are "significant uniformities" in the cross-cultural expression of schizophrenia and other mental disorders and has expressed frustration at the lack of progress in exploring factors underlying salient

features of the cross-cultural expression of mental illness such as the more favorable prognosis of individuals in "developing" settings. It is the symptomatic detail within this uniformity of expression in schizophrenia that is one of the areas we have chosen to research. To do so does not trivialize perspectives critical of such research or deny the importance of describing and analyzing the most variable aspects of mental illness (for example, see the discussion of "brief reactive psychosis" in Kleinman 1988, 36).

A second point of contention is the use of "objective" diagnostic techniques to quantify or categorize manifestations of behavioral disorders. In calling for a "culturally sensitive" use of diagnostic techniques, Fabrega (1996, 12) warns that "the discourse and language of scientific objectivism [can] handle persons as mechanical objects and eschew or disregard the view that persons are socially, culturally, and morally situated." Fabrega's concerns should be heeded while at the same time remembering that no methodological approach can necessarily claim to be intrinsically "culturally sensitive," as is demonstrated by recent reflexive *mea culpas* by anthropologists who have employed more subjective, person-centered approaches to research in the field of mental illness (Estroff 2004; Scheper-Hughes 2001). In short, anthropological research should be able to include objective perspectives about salient or universalistic features of mental illness while maintaining a cultural sensitivity in the design and execution of research. Some will disagree with this assessment, but we believe that the data we have presented here are a good example of the use of contemporary definitions of schizophrenia to allow a discussion "more or less about the same thing" when comparing research findings from different settings (Jenkins and Barrett 2004, 4); we consider these data to be a starting point for discussion, critique, and formulation of new hypotheses about the expression of schizophrenia in Palau and elsewhere.

However, the bio-behavioral data from the SYMPTOM and MARKER cohorts have not provided insight into the extraordinary prevalence of schizophrenia in Palau, and we have turned to aspects of Palauan culture and history in an attempt to understand and analyze the causes of mental illness in this context. The SYMPTOM cohort demographic data describe profound gender differences in the consequences of mental illness, with marriage and fertility rates markedly lower among men. In contrast to previous researchers, who have argued that "modernization" and anomie are the root causes of the differential risk of schizophrenic morbidity for Palauan men (e.g., Kauders, MacMurray, and Hammond 1982), we have suggested that aspects of Palauan social practices that are supportive of young women and uniquely stressful for young men are historical and predate the colonial era. Having made this case, our intention has not been to claim that schizophrenia in Palau is "caused" by the differential treatment of young Palauan men and women. Instead, it has been to engage with the manifold factors that could potentially affect the expression of schizophrenia in this setting and to suggest a relevant dimension of the contextual social and cultural dynamics affecting young Palauans that is amenable to further investigation. Further collaborative quantitative and qualitative person-centered studies are being designed as we attempt to understand the complex interplays between genetic, epigenetic, and environmental factors affecting the symptomatic expression of schizophrenia. Our arguments are currently being tested in a longitudinal study carried out in conjunction with Palauan mental health professionals that explores the relationships between the severity and course of illness in Palauans with schizophrenia and their social functioning, degree of participation in customary obligations, "traditional" role identities as perceived by others, and the degrees and types of support that they receive from their families and kin groups.

The key finding from 40 years of cross-cultural studies by the WHO and others that prevalence rates and outcome tend to be more favorable in "developing" settings is not well supported in the Palauan context. Hopper (2004) has pointed out that the WHO categorizations are simplistic and based on broad generalizations from a few settings, particularly the Indian subcontinent. To the extent that Palau can be considered a "developing" country (the label would have applied throughout the formative years and much of the lives of many of the study participants), we see little evidence of a relatively benign expression of schizophrenia. Drawing on the data presented here, we have argued that the high rates of schizophrenia are not an artifact of diagnostic practice and that the symptomatic expression in Palau is similar in pattern and severity to that in other settings. Although not an incidence study that can provide causal data about the course of illness, the 1998 SYMPTOM cohort is a mature population that represents a large proportion of living Palauans with psychotic mental illness at the time of research. The average age (39.2 years; S.D. 8.1) and mean duration of illness (16.7 years; S.D. 9.1) in this cohort are not consistent with an assumption that course or outcome is in any way more favorable in the Palauan setting than it is in others, "developed" or otherwise.

Several researchers have invoked "development" as a the principal causal factor for schizophrenia in Palau (Kauders, MacMurray, and Hammond 1982; Hammond, Kauders, and MacMurray 1983). "Development" is a complex concept to operationalize, and this makes it difficult to test or falsify this widely held perspective. However, as a recent exotic import, substance use is a reasonably concrete proxy identified by several researchers as an "effect of development" in Palau that we have analyzed in some detail. Our findings that use of the exotic agents alcohol and cannabis was not negatively associated with symptoms and that use of the indigenous betel nut was associated with milder symptoms undermine the simplistic notion that presumptively harmful correlates of "development" are necessarily schizophrenogenic. Further detailed research on correlates of development within settings is required to move beyond the current dependence on this problematic concept toward a more sophisticated understand-

ing of factors affecting the expression of schizophrenia in particular cultural contexts.

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Comments

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Sullivan, Allen, and Nero seek to explain the high point prevalence for schizophrenia in Palau and account for the male-female ratio of 2:1. They interviewed 70 Palauans with schizophrenia using Kay, Opler, and Fiszbein's (1992) Positive and Negative Syndrome Scale and performed factor analysis on 30 variables to extract principal components which were similar to those found by Kay in his New York study of 240 cases. From this they inferred that "the symptomatic expression of schizophrenia in Palau is broadly comparable to its expression in other settings," leading them to "reject the hypothesis that schizophrenia in Palau has a unique diagnostic profile."

Readers cannot be sure, however, that it is reasonable to conduct factor analysis of the principal-components type on these data, for the authors provide no indication of whether variables are normally distributed or relationships between variables are linear—they do not share with us their appraisal of factorability of the matrix. A clear factor structure emerged from this analysis, but even so the number of cases is well below the minimum of about 150 cases required for such an analysis (Tabachnick and Fidell 2007, 613), even the most generous authorities advising a minimum of 100 cases (Kline 1994, 73).

Beyond this, it is likely that if one asks questions pertaining to 30 items of people with schizophrenia in New York and then repeats these questions to people in Palau with the same diagnosis one will record fairly similar answers. Given that the PANSS is based on the construct of negative and positive symptoms, it is not surprising that "negative" and "positive" emerge as two principal factors. The PANSS measures what it sets out to measure—it has construct validity—and keeps on doing this whether in New York or Palau—it is reliable. To infer from this finding, based on the use of a tightly focused instrument, that the "bio-behavioral" expression of schizophrenia is broadly comparable between Palau and other settings involves an overabundance of interpretation.

How do Sullivan et al. arrive at the conclusion of broad comparability? First, they elide difference. The greater variability of the Palauan factorial structure is mentioned in the results not the conclusions, the different factorial configuration of conceptual disorganization is apologized for, and one factor is dropped from the discussion. Second, they widen the claims of their two-site comparison. New York becomes "other settings," and its cohort becomes a "'normative' sample." We find here a tendency to render the West the normative frame of reference for the rest of the world, as if it were the "white man's burden" to serve as a sort of psychometric benchmark for all the "new-caught sullen peoples" of the earth (Kipling 1940, 323).

With respect to the study of smooth-pursuit (eye-movement) dysfunction (SPD), I have similar qualms about extrapolating from the finding that 20 of 36 cases showed SPD to the conclusion that "schizophrenia in Palau has a similar biophysiological basis to schizophrenia in other populations."

Sullivan and colleagues recognize the tension between the impulse to render schizophrenia globally universal and the impulse to render it locally distinctive but succumb to both. They universalize the biological ("bio-behavioral") to talk of the "presumptively universal manifestations of schizophrenic expression," at the same time particularizing the cultural ("behavioral response", "contextual processes"). Theirs is an equation wherein biological is to invariant is to universal is to comparable is to same as cultural is to variable is to local is to unique is to different. This formula prestructures their explanatory framework, because in trying to account for difference (in prevalence, gender ratio) one would hardly invoke sameness (biological); one would invoke difference (cultural). Their answers are contained in cells A and B of my table 1. A broader approach might also contemplate the possibility of explanations that lie in the C and D cells, by which I mean cultural universals and biological variations. This would encourage consideration of the role of, say, that universal cultural commodity, stigma, perhaps quite intense in this tiny island population, or the contribution made by the distinctive

Table 1. Explanatory Frameworks

	Sameness	Difference
Cultural	C	B
Biological	A	D

genetic profile of this isolated population in seeking to account for the findings.

With rare conditions like schizophrenia, variations in the number of incident cases usually make little contribution to prevalence. Forces that keep people ill account for the steady accumulation of cases that results in high prevalence. It is these forces—probably cultural entwined in close embrace with biological, with universal and particular crosscutting both—that Sullivan et al. have a mandate to invoke to explain the unique prevalence and gender ratio of schizophrenia in Palau. We anticipate that their forthcoming study will address these issues.

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Why do some groups suffer more from the phenomenon we call schizophrenia?

Using preexisting prevalence data, Sullivan and colleagues present the "extraordinary prevalence" of schizophrenia amongst Palauan men, 2.2% versus 1% for women (Hezel and Wylie 1992). They interview 50% (70) of the island's patients, who have an average age of 39.2 and a mean duration of illness of 16.7 years. The latter is said to imply a tendency towards chronicity. Given this increased rate of chronic schizophrenia in a developing setting, they ask "whether such variability is more a function of biological, diagnostic, or contextual sociocultural factors."

For the biological aspect they perform a nested case-control study, comparing 36 patients with 25 controls, recording the presence of smooth-pursuit eye-tracking dysfunction (SPD). They find SPD more common in the nonpsychiatric population than expected, suggesting a possible genetic propensity to SPD and by association schizophrenia. This interesting result is not mentioned in the conclusions. Fifty-five percent their schizophrenic sample have SPD, significantly more than the controls, which leads to the conclusion that the illness has a similar biophysiological basis as in other populations. It must be emphasized for nonpsychiatrist readers that schizophrenia is diagnosed phenomenologically. There are no predictive biological markers. Associations with SPD or other endophenotypes in any population remain debatable and are not necessarily specific to schizophrenia. This is the only part of the paper that mentions a control group.

To ensure diagnostic precision, Sullivan et al. interview their sample with a well-known symptom inventory. As they state, this allows researchers to ensure that they are talking about "more or less the same thing" when they use the term schizophrenia.

Lastly, they address several sociocultural factors.

Drug use is measured. Current cannabis use (for some reason conflated in men with alcohol) is 49% men, 9.5% women. Past history of drug use is 88% men, 19% women. However, despite the disparity they conclude that the data do not support drugs' being responsible for the increased prevalence. Those admitting to using drugs do report fewer symptoms, but in this the difference between a cause of an illness and an aggravator/reliever of its symptoms is not distinguished. More broadly, the inability to distinguish cause from effect is, of course, a function of the use of prevalence rather than incidence data.

The effect of migration, another well-known risk factor (Cantor-Graae and Selton 2005), is touched on but cannot be addressed with this data set. It is said to be of minimal importance because "many Palauans go overseas"—at least 33% in the 20–24-year age-group. However, 50% of the patients had been migrants, and a "significant" proportion had had their first break abroad. Sullivan et al. accept that the issue warrants further study.

Finally, they elegantly describe the social and family structures and practices that lead to women's being protected from isolation and looked after when ill while men can be isolated in both cases. Hence a powerful rhetorical point is made about a possible factor in the aetiology of the extraordinary rates amongst men and their chronic course.

The paper's stated aim is to perform a biocultural analysis to help determine why the prevalence of schizophrenia varies in Palau. It gives an in-depth description of the position of men and of women and how the former may act as a risk factor. By couching this in the language of anthropological enquiry, it does capture a sense of how it might be to face the challenges of a Palauan man. An important link to the disconnected phenomenology of schizophrenia forms a seductive hermeneutic that transcends the simple correlations in psychiatric epidemiology of risk factor with disease. This is possibly a good thing (Harland, Morgan, and Hutchinson 2004). But this controversial sleight-of-hand is not made explicit, so it is hard to know if it is intentional and if the well-known pitfalls have been considered. At times Sullivan et al. appear to be talking in the language and method of risk factors and causality and at others in terms of meaningful understanding.

In the former voice they say that the data suggest that other confounding factors are less probable. These include well-established risk factors established by meta-analysis such as migration, cannabis (Henquet et al. 2005), and urbanization (van Os 2004). But when choosing a cross-sectional design (a nonrandom snapshot of patients) it is bold in epidemiological terms to do more than comment on associations. They say towards the end, "Our intention has not been to claim that schizophrenia in Palau is 'caused' by differential treatment of young Palauan men." But at other times they do suggest more: "The hypothesis that substance abuse might explain the extraordinary prevalence of schizophrenia in Palau is not well supported by the data."

This research presents anthropological data that would enrich mainstream psychiatric research. It furthers understanding of the predicament of the Palauan man. But in converting

this material into an objective local risk factor related to disease prevalence it is important to be clear about epistemology and to follow its constraints. Given the assumption of a discrete entity called schizophrenia, a further study (case-control or cohort) could help separate cause from aggravator and clarify the issue of reverse causality and confounders.

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Palau, an island group with a small population of some 20,000 (one-third of them Asian laborers) and an unusually high rate of schizophrenia, has gained recognition in some circles as an unparalleled laboratory for the study of mental illness. When Palau was "discovered" by researchers in the early 1980s (Kauders, MacMurray, and Hammond 1982; Hammond, Kauders, and MacMurray 1983), their explorations into the etiology of the disease were stimulated by an unusually large gender imbalance in a disease that was not commonly regarded as sex-linked. Hammond et al. (1983) recorded a 4:1 ratio of male to female prevalence in Palau, an imbalance that was confirmed by later studies, although modified to about 2:1, as the authors of this article point out. These initial studies, as well as our study a decade later (Hezel and Wylie 1992), suggested various explanations for the skewed prevalence rates by gender.

This present article offers strong evidence that one of these hypotheses, the contribution of drug use (largely alcohol, cannabis, and cocaine or heroin) to the early onset and more severe course of male patients should be discounted. For this we who were mapping various paths of possible future research can be grateful. Another hypothesis, however, was that female schizophrenics may present more attenuated symptoms than male patients, allowing the latter to be more easily identified than females. The authors might have provided similar guidance regarding the plausibility of this avenue of research if they had broken down their Palau data on the Positive and Negative Syndrome Scale (PANSS) by gender. In doing so, they might have helped us understand whether the severity of schizophrenia, or at least its mode of expression, differs markedly between Palauan males and females, thus allowing female schizophrenics to go undetected. The other possible explanation suggested by early researchers was that the cultural environment, which presumably had an effect on the onset and severity of the disease, was more benign for women than for men. This, of course, is the avenue of exploration endorsed by the authors in this article.

During the 1990s, however, exploration of the cultural environment for clues on the skewed gender rates of schizophrenia in Palau was put on hold. Because the scientific community was entranced by the possibilities of gene mapping laid out in the Human Genome Project, a whole new thrust was introduced into schizophrenia research in Palau. Gender disparity was disregarded for the time as researchers used the extensive genealogical data there to plot genetic pathways or else joined their colleagues throughout the world in the race to identify the schizophrenia-carrying gene (Myles-Worsley et al. 1999). As Sullivan and colleagues indicate, however, the genetic factors affecting schizophrenia are proving to be far more complex than anticipated; the simple links once hoped for are proving to be a chimera.

The merit of this article is that it redirects us toward what I regard as the key issue in the Palau data: the extraordinarily high rate of male schizophrenia relative to the female rate. While the article is by no means dismissive of the obvious genetic components of schizophrenia, its focus on the unique cultural context in Palau is a summons to take seriously once again environmental factors that seem to have long been sidelined, if not ignored, in general schizophrenia studies. Perhaps the neglect of environmental factors in recent years is a reaction to the studies of an earlier period, now largely discredited, that sought to explain schizophrenia exclusively in terms of these factors. Sullivan et al. mention Scheper-Hughes's (2001) study of schizophrenia in rural Ireland, originally published in 1979, but the pedigree goes back to Gregory Bateson (1956), R. D. Laing (1965), and Thomas Szasz (1970). With such extremes behind us, we should now be in a position to assess in a clear-headed fashion what those old studies of the concordance rates in monozygotic twins (e.g., Gottesman and Shields 1972) have long indicated to us—namely, that while genetic factors are extremely important in determining the etiology of schizophrenia, they must be complemented by studies of the particular cultural environment.

All of this suggests that Palau, small and isolated as it is, could serve as a useful laboratory not so much for plotting the genetic pathways of schizophrenia as for revealing the social and environmental factors affecting the disease. The article underscores the urgency of leaving the clinical lab for the field, a summons that many of us who have been struggling to explain not just high prevalence rates in Palau but an extraordinarily high male-female differential must strongly applaud. The challenge today, of course, is to find the tools to identify and assess the impact of these environmental factors on the course and severity of schizophrenia.

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This paper makes a valuable contribution to the schizophrenia literature by taking an anthropological approach to the role of sociocultural context in the epidemiology of schizophrenia in a developing country. Sullivan and colleagues conclude that their results support a symptom profile in Palau that is basically similar to that found in schizophrenia patients from developed countries. However, they have based their conclu-

sions on a sample of 70 chronic schizophrenia outpatients who regularly receive neuroleptic medication, a sample that is not necessarily representative of Palauan individuals with schizophrenia.

Our genetic epidemiological study (Myles-Worsley et al. 1999) identified a total of 160 Palauan individuals with strictly defined schizophrenia. Many of these individuals either were medication-naïve or had been treated with neuroleptics for a limited period, discontinued medication when their symptoms resolved, and then resumed relatively normal lives. If the PANSS and substance-use assessments of the Sullivan et al. study had included a broader cross-section of Palauans with schizophrenia, including those whose symptoms had remitted after a shorter period of neuroleptic treatment and those who had remained unmedicated throughout their lives, the symptom assessment data might have revealed a different and relatively "benign" version of the illness compared with schizophrenia in developed countries.

In-depth studies of Palau's unmedicated schizophrenia patients, which are now under way, can help to clarify how neuroleptic treatment influences the expression and developmental course of illness. One of these is the Palau Early Psychosis Study (Myles-Worsley et al. 2006*a*), conducted with a community-based, non-help-seeking sample of Palauan adolescents with varying levels of genetic risk. This study identified 62 adolescents (40 females and 22 males, close to a 2:1 female-to-male ratio) with a DSM-IV psychotic disorder, predominantly schizophrenia. To date, only three male cases have received treatment with antipsychotic medication. The remaining adolescent-onset cases have declined to be referred for treatment, stating that they prefer to manage their symptoms without medication. These young Palauans want to avoid the stigma of being one of the "Behavioral Health patients," (the Sullivan et al. sample), many of whom exhibit clearly visible signs of long-term treatment with high doses of the conventional neuroleptics available in Palau. In this close-knit, family-based Pacific Island community, psychotic symptoms may be better tolerated, less distressing, and consequently less likely to lead to a referral for treatment than in the large urban settings of developed countries. Because Palauan males have higher rates of problems that precipitate referral for treatment, such as drug abuse, violence, and criminal behavior, we hypothesize that more young females than males with schizophrenia will remain unmedicated. If this hypothesis is confirmed and untreated relatives are found to be disproportionately female, the gender imbalance we previously reported may even out.

One important distinction between schizophrenia in developing countries like Palau and schizophrenia in developed countries is the role of treatment in defining cases. In most developed countries, "first-episode" schizophrenia is typically defined in terms of first admission for antipsychotic medication, implying that the diagnostic threshold for schizophrenia is reached only when medication is prescribed. Sullivan and colleagues acknowledge this issue by stating that "the literature describing the symptomatic expression of schizophrenia is heavily biased toward research conducted in clinical settings in Europe and the United States." Yet the studies reported in this paper fail to reach beyond the clinical setting in Palau to the rich data that can be provided by the large proportion of Palauans with schizophrenia who choose to manage their illness without medication.

Is the expression of schizophrenia different or more benign in developing countries compared with developed nations? This question will remain unanswered until we conduct systematic studies of people who meet DSM-IV criteria for schizophrenia but are never medicated.

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Sullivan, Allen, and Nero's interesting article refutes the expectation of a straightforward association or unmediated correlation of schizophrenia with modernity—the idea, which they attribute to the WHO, that "the experience of schizophrenia is *necessarily* more benign in 'developing' settings" (emphasis added). Upon reflection, one realizes that the simplistic idea of such a "necessary" connection was never very plausible. To believe in such a correlation, one would have to think that sociocultural factors were virtually the *only* factors affecting differential prevalence and illness outcomes. For this to be so, genetic factors (among others) would have to be irrelevant—either causally inefficacious or of uniform prevalence and penetrance across all sociocultural settings; neither view is consistent with the available data. Sullivan et al. mention the high prevalence of schizophrenia in Palau, the high male-female gender ratio (over 2:1) in Micronesia, and the fourfold variation in schizophrenia prevalence across cultures as apparently similar as different islands in "developing" Micronesia. All of these provide empirical evidence against the simplistic hypothesis.

Sullivan et al.'s way of presenting the epidemiological data they report could, however, obscure the fact that these data (and, even more, their interpretation of them) actually support a *refined* version of the modernity/schizophrenia hypothesis already suggested by the WHO studies. This is the notion that, *in interaction with such factors as genetic predisposition* (perhaps more prevalent in Micronesia, is as suggested by Sullivan et al.'s eye-movement data), key psychosocial or psychocultural factors associated with modernity though not unique to it may play a significant contributory role in the development or prolongation of schizophrenic symptoms. The findings showing gender imbalance in expression of schizophrenia (Hezel and Wylie 1992; Myles-Worsley et al. 1999) could even be viewed as offering a kind of replication, *within* Palau society, of the WHO cross-cultural findings. To see how this could be so, it is sufficient to rec-

ognize that these studies can themselves be viewed as cross-cultural in nature, with the differing "cultures" at issue being the sociocultural "micro-climates" of male versus female life in Palau.

Drawing on their results and review, Sullivan et al. suggest that "aspects of historical and contemporary social practices may contribute to a gender imbalance in the expression of symptoms of schizophrenia in [Palau]." The aspects that particularly affect Palau males (according to their hypotheses) are precisely those typically associated with modernity: absence of readily available and "secure customary role identity" and the requirement of independent action to demonstrate "personal competence" and even "personhood" and establish a "meaningful identity" and respected place in society. All this implies greater risk of isolation, dislocation, role insecurity, and anomie—the latter being Durkheim's characterization of the detachment from guiding frameworks and identities typical of modern societies. Some of these features are implicit in *traditional* male roles in Palau (might we say that Palau males have always been more "modern"?), but, as Sullivan et al. suggest (citing Kauders, MacMurray, and Hammond 1982; Hezel and Wylie 1992; Nero 1990), they are likely to have been exacerbated by modernization and globalization.

Modernity is a multifaceted phenomenon; its key features can be conceived in various ways. I myself have speculated on the possible role of exaggerated disengagement, individualism, and self-consciousness (Sass 1994, 1997) and of disembedding from traditional "commonsense" frameworks (2004), arguing that such features could be conducive to (and interact with) the "hyperreflexivity" (1992) and alienation from "common sense" (Blankenburg 2001) central to schizophrenia. Sullivan et al.'s description of Palau suggests that such modernity-related factors (and others that one may postulate) are likely to play a more prominent role for Palau males, especially under conditions of modernization.

Another issue concerns Sullivan et al.'s use of the PANSS and associated claims concerning the universality of clinical symptomatology. They are more struck by similarities than by differences in the expression of schizophrenia in Palau and other settings. It seems obvious that mental disorders have both universal and culturally specific aspects; different perspectives and methodologies will bring out one or the other aspect.

One must be grateful for the careful attempt that Sullivan et al. have made to apply uniform criteria across diverse cultural contexts and to look beyond diagnosis toward a richer psychopathological profile. It is certainly of interest that, on PANSS measures, Palau schizophrenia is "broadly comparable" to what is found in other settings including New York City. It is suggestive, however, that key PANSS scores (positive and negative symptoms, general psychopathology) are somewhat lower among schizophrenia patients in Palau (albeit not statistically significant, I assume—though this is not reported).

More important is the fact that PANSS scores (Kay, Opler, and Fiszbein 1992) describe signs and symptoms in extremely general terms. For example, in PANSS "delusions" is a single item. Two patients who receive the highest "delusions" score may differ dramatically, since either "highly systematized" or "very numerous" delusions can justify a 7-point rating. No attention is paid to whether the delusions would qualify as "bizarre." The "conceptual disorganization" item ignores differences between types of formal thought disorder that have been shown to characterize schizophrenic versus manic versus schizo-affective patients (Holzman, Shenton, and Solovay (1986). It is possible that a more fine-grained assessment of symptoms would show interesting differences between schizophrenia in Palau and schizophrenia elsewhere. It is clear, in any case, that (as Sullivan et al. acknowledge but perhaps insufficiently emphasize) it would be imprudent to conclude from their PANSS findings that there is an absolute uniformity of symptomatic expression between Palau and New York.

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The criticisms made by Sullivan, Allen, and Nero of the well-established tendency to address complex problems with gross quantitative methods and simplistic dichotomies are very welcome, particularly because they come from researchers who prove to have a sound knowledge of the methodologies that they question, using them in their favour in a masterful way. Indeed, the variability in the prevalence of schizophrenia in different regions and even within the same location calls into question the appropriateness of explanations founded on a genetic or bio-behavioural determinism and large-scale studies based on necessarily far too general sociological criteria. I share their criticisms of the pseudo-scientific argument that a gene (which is always on the verge of being discovered) can explain complex phenomena such as schizophrenia, criminality, or patriotism. I also agree with the questions that they raise about the World Health Organization's cross-cultural findings based on a duality such as developed-versus-developing-settings, which provides few answers other than the tautological conclusion that everything is better in a "developed" world. Similar studies on the distribution of other medical or socioeconomic phenomena are so frequent in the WHO and similar organizations, often financed with large costs, that it would be worth questioning the purpose of those initiatives. As a social anthropologist, I am equally in agreement with the need for monographic studies that represent a "productive starting point for cross-cultural studies" as well as placing much more emphasis on a qualitative and detailed analysis of particular social and cultural contexts. However, I believe that the article generates some ambiguity. Indeed, when the reader is expecting detailed criticism of bio-deterministic approaches and sterile quantitativism, the authors seem to pull back, particularly when they claim that "an-

thropological research should be able to include objective perspectives about salient or universalistic features of mental illness while maintaining a cultural sensitivity in the design and execution of research. Some will disagree with this assessment, but we believe that the data we have presented here are a good example of the use of contemporary definitions of schizophrenia to allow a discussion 'more or less about the same thing' when comparing research findings from different settings." This precision considerably reduces the scope that the article initially appears to promise. Granted that if one truly wants understanding of the sociocultural context, the aim cannot be an "object" like schizophrenia, whose "objective" reality has been established, as the authors themselves recognize, with studies based almost exclusively on cases under European or North American clinical conditions. For truly cross-cultural work, the first "productive starting point" would be to question the reality of a phenomenon as complex as schizophrenia in populations that may have quite original ways of conceiving the scope of the pathology and how to treat it. However, in a brief appendix titled "Sociocultural and Historical Factors" Sullivan et al. describe what could be the historical, social, and cultural cases of the gender bias in the schizophrenia found in Palau on the basis of a series of assumptions—traditional versus modern—as simplistic as the ones they question. If the stress suffered by men from "traditional" societies due to modernization encouraged the appearance of schizophrenia, the characteristics that it presents in Palau should be common to a large section of humanity. The risk involved in not being sufficiently radical is falling into the same errors we intend to combat. Although it is true that the authors postpone an in-depth sociocultural study to the near future, the preview presented here does not promise results on a par with the criticisms that this article makes of other methodologies. The main problem is conceiving the historical and sociocultural factors as positive facts within the framework of a functional system which, with epithets such as patterns of postmarital residence, reciprocal interchange, and parental obligations, reminds us of the anthropology of times past.

Reply

Schizophrenia and AIDS have commonalities that might suggest that they are equally interesting as research topics for anthropologists: they have comparable scale in terms of global burden of illness, and both have complex social, cultural, and biological causes. However, a search of AnthroSource for scholarly articles published in the past decade using the title keyword "schizophrenia" yields a single hit (excluding book reviews and news items): Anne Lovell's (1997) account of schizophrenia and homelessness. In contrast, a search using the title keyword "AIDS" yields 20 articles for the same period, with the most recent in 2006. Hezel notes that environmentally deterministic models of schizophrenia, including those of anthropologists such as Gregory Bateson and other social scientists such as Frieda Fromm-Reichman and Thomas Scheff, have been very influential in the discipline. The recent relative silence on schizophrenia in anthropology may reflect a rejection of or unwillingness to engage with the ascendant biological etiological models. And yet the major biomedical perspectives have never been biologically deterministic—the watershed 1967 international conference on schizophrenia at Dorado Beach, Puerto Rico, championed the diathesis-stressor model (Gottesman 1991), and senior authors of the WHO multicountry studies in the 1960s and 1970s formally concluded that "culture" was a causal factor in schizophrenia and appealed for research to address putative hypotheses (Jablensky et al. 1992, 1994) such as that "traditional" or "developing" societies may have "greater tolerance and acceptance of symptomatic patients" (Leff et al. 1992, 142). The challenge of addressing these objective research questions has not been taken up by anthropologists—the majority of writing on mental illness by anthropologists in the past two decades has been focused on criticism of biomedicine, criticism of reductive objective methods and theory, and assertion of subjective person-centered approaches to cross-cultural research on mental illness.

This sentiment is captured in the commentary by Surrallés, who applauds our criticism of biological deterministic approaches but questions whether an objective assessment of schizophrenia is possible and concludes that attempting to reduce complex phenomena to operationalized research variables "reminds us of the anthropology of times past." This tone of disapproval is also captured in Barrett's appeal to Kipling's "white man's burden" and colonized "new-caught sullen peoples." Without restating our arguments about universalistic perspectives of mental illness or the value of objective research, we suggest that the a priori expectation that correct anthropological perspectives should be particular and subjective emerges from a history of resistance to universalistic aspects of mental illness among anthropologists. This opposition may have been legitimate some years ago, when the genetic underpinnings of schizophrenia were more contentious, but is less so now with the broad acceptance of a heritable basis to schizophrenia. We argue that anthropology can benefit tremendously by complementing the undoubtedly useful critiques of biomedicine with cautious use of the data and methods that biomedicine provides.

Barrett makes several specific comments about sample size and statistical method. While it is undoubtedly correct that an $N > 150$ is desirable in factor analyses, ideal sample sizes are frequently unmet, particularly in psychiatric research, where there are many obstacles to finding willing participants in the settings of Western research hospitals, let alone in "the field," as Barrett must be aware from his own remarkable research among the Iban ($N = 50$ [Barrett 2004]). There are several guidelines about sample sizes for factor analyses in the

literature. We applied that of Mertler and Vannatta (2005, 258) that "components with four or more loadings above 0.6 in absolute value are reliable, regardless of sample size."

We disagree with Barrett's claim that, "given that the PANSS is based on the construct of negative and positive symptoms, it is not surprising that 'negative' and 'positive' emerge as two principal factors." We expect that components emerging from a data set will correspond with the factorial structure of an instrument only if the data—the study participants' responses—are in accord with the factorial structure of the instrument. If the symptomatology of the Palauan sample were not characterized by negative and positive symptom syndromes, then the results of the factor analysis would be other than those presented.

The use of "normative" is criticized by Barrett as invoking a colonial paternalism toward the research participants, but the term was enclosed in quotation marks in the text to both draw attention to and avoid a lengthy discussion about the original rationale for its use by the designers of the PANSS instrument.

Harland is critical of the interpretation that drug abuse might be less of a risk factor in chronic schizophrenia than has been claimed and feels that we should have been more supportive of risk factors that he claims are "well-established" elsewhere: migration, cannabis, and urbanization. These factors are associations that remain contested as causal variables in schizophrenia (e.g., Schiffman et al. 2005 on cannabis), and this reinforces our belief that detailed analyses within settings are preferable to an averaging of data between settings (i.e., in this case, invoking meta-analyses of studies from different settings).

Myles-Worsley suggests that our sampling, based on BHD out-patients, may have missed a "relatively 'benign' version" of the illness in afflicted but unmedicated individuals in the broader community. This assumption is not necessarily warranted. Our sample included 16 unmedicated individuals (11 men and 5 women); the BHD has an excellent program that maintains contact with diagnosed individuals in the community who are not medicated, and this allowed inclusion in the study of other than walk-in medicated patients. Study participation was voluntary (if paid), a process that tends to select less-afflicted individuals. Individuals suffering acute symptoms were excluded from the study. Finally, the overall dosages of antipsychotic medication in the sample were quite low (table 1). Nonetheless, Myles-Worsley's comments about the importance of studying individuals who remain untreated are well-taken, and goals for future research include longitudinal study of the life course of illness in individuals with mental illness.

Second, Myles-Worsley's description of a possibly more benign expression of schizophrenia in Palau is at least somewhat contradicted by findings from her own research. The Myles-Worsley et al. (1999) study confirmed the high rates and gender bias reported in the earlier Hezel and Wylie study (1992) and was based explicitly on cases identified with "strictly defined" schizophrenia, that is, individuals with unambiguous symptoms indicating an active episode of schizophrenia. Nor are the results of Myles-Worsley and colleagues' most recent research on early-onset psychosis in Palauan adolescents particularly optimistic. Their Palau Early Psychosis Study reports a total of 221 adolescents with "early psychosis" identified from a "non-help-seeking sample" of 404 adolescents (14–19 years) stratified by "level of genetic risk" (Myles-Worsley et al. 2006*a*). Given that the adult Palauan population already carries a very high 2.7% lifetime morbid risk of psychotic illness assessed in the late 1990s (Myles-Worsley et al. 1999), this figure represents an additional burden of mental illness emerging in a younger cohort. Myles-Worsley and colleagues also observed that the Palauan expression of adolescent illness is comparatively negative in that "even [genetically low-risk] adolescents with no close affected relatives have elevated rates of early psychosis" (2006*a*) and that "risks to 1st- and 2nd-degree offspring were approximately double the rates found in the smaller Western European families" [of a large data set of Western European families] (2006*b*).

Sass provides a thoughtful evaluation of notions of modernity and mental illness. We acknowledge his excellent point that particular aspects of male gender roles in Palau are also "typically associated with modernity" elsewhere. However, our argument is that the relationships between such factors and mental illness should be systematically assessed and tested, rather than assuming that "modernization" per se is schizophrenogenic, particularly when imposed on a "traditional" set of sociocultural values and practices.

Sass queries the validity of drawing conclusions from a single PANSS item, in this case the "depression" item. We should clarify that the discussions about reduced symptoms of depression in relation to male alcohol and cannabis use are based on ratings of the PANSS "depression *cluster*," including the items "depression," "anxiety," "guilt feelings," and "somatic concerns."

As noted by Hezel, the burden of evidence for a heritable component in schizophrenia allows us to move on from the etiological squabbles of the past—the hard positions about the primary cause of schizophrenia—and to redirect our energies toward identifying the nongenetic factors that affect the expression of the illness in people and how that expression varies in different ecological, social, economic, and cultural contexts. There are questions about major mental illness, in addition to criticism of biomedical epistemology and method, that anthropologists are uniquely qualified to address: In non-Western societies undergoing economic and demographic transitions, is there "greater tolerance and acceptance of symptomatic patients" (Leff et al. 1992)? Do "extensive kin-based stores of support" (Hopper 2004) affect the onset and course of mental illness? Are societal and economic changes associated with these transitions causal in mental illness? These and related questions should be systematically studied and tested rather than becoming de facto truisms about the cross-cultural expression of mental illness. Not only might

these basic research questions increase our understanding of schizophrenia in identifying and delineating the multiple causal pathways affecting biocultural illness processes, they may also provide insights into more general issues of pathology, health, and the human condition.

—Roger J. Sullivan, John S. Allen, and Karen L. Nero

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