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Comparing schizophrenia symptoms in the Iban of Sarawak with other populations to elucidate clinical heterogeneity

Duncan McLean[1] **[Research Officer]**, **Robert Barrett**[2] **[Professor]**, **Peter Loa**[2,*] **[Researcher]**, **Rangaswamy Thara**[3] **[Director]**, **Sujit John**[3] **[Research Coordinator]**, **John McGrath**[1,4] **[Professor]**, **Jake Gratten**[1,4] **[Research Fellow]**, and **Bryan Mowry**[1,4] **[Professor]**

[1]Queensland Centre for Mental Health Research, The Park – Centre for Mental Health, Wacol, Queensland, 4076, Australia

[2]Department of Psychiatry, University of Adelaide, Royal Adelaide Hospital, North Terrace, Adelaide, South Australia, 5000, Australia

[3]Schizophrenia Research Foundation, R-7A North Main Road, AnnaNagar West (Extn.), Chennai 600 101, Tamil Nadu, India

[4]Queensland Brain Institute, Building # 79, Upland Road, University of Queensland, Brisbane, Queensland, 4072, Australia

Abstract

Introduction—The symptom profile of schizophrenia can vary between ethnic groups. We explored selected symptom variables previously reported to be characteristic of schizophrenia in the Iban of Sarawak in transethnic populations from Australia, India and Sarawak, Malaysia. We tested site differences to confirm previous research, and to explore implications of differences across populations for future investigations.

Methods—We recruited schizophrenia samples in Australia (n=609), India (n=310) and Sarawak (n=205) primarily for the purposes of genetic studies. We analyzed seven identified variables and their relationship to site using logistic regression, including: global delusions, bizarre delusions, thought broadcast/insertion/withdrawal delusions, global hallucinations, auditory hallucinations, disorganized behavior, and prodromal duration.

Results—We identified a distinct symptom profile in our Sarawak sample. Specifically, the Iban exhibit: low frequency of thought broadcast/insertion/withdrawal delusions, high frequency of auditory hallucinations and disorganized behavior, with a comparatively short prodrome when compared with Australian and Indian populations.

Discussion—Understanding between-site variation in symptom profile may complement future transethnic genetic studies, and provide important clues as to the nature of differing schizophrenia expression across ethnically distinct groups. A comprehensive approach to subtyping

Corresponding author: Bryan Mowry, Queensland Brain Institute, Building # 79, Upland Road, The University of Queensland, Brisbane, Queensland, 4072, Australia, Ph: +61 7 3346 6351, Fax: +61 7 3346 8836, b.mowry@uq.edu.au.
*Peter Loa is now a Medical Oncology Registrar, Canberra Hospital, Yamba Drive, Garran, Australian Capital Territory, 2605, Australia

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schizophrenia is warranted, utilizing comprehensively ascertained transethnic samples to inform both schizophrenia genetics and nosology.

Keywords

psychotic disorders; schizophrenia; culture; diagnosis; population characteristics

Introduction

In the past, the syndrome of schizophrenia has been treated as a single entity diagnosed according to reliable, internationally accepted criteria consisting of symptoms, disability, duration, illness course, and exclusion of allied disorders (APA, 1994; WHO, 1992). However, there is now clear evidence that schizophrenia shares a genetic predisposition with bipolar disorder (ISC, 2009; Lichtenstein *et al*., 2009), which challenges the dichotomous view of functional psychosis (Craddock, O'Donovan & Owen, 2009). There is currently little consensus on whether the latent structure of schizophrenia is best represented as a single (continuous) entity, with clinical variation represented as dimensions within a single class, or as two or more distinct, separate entities, with variation indicative of a number of distinct classes grouped under the label 'schizophrenia' (Fiedorowicz, Epping & Flaum, 2008; Kendler, Karkowski & Walsh, 1998; Linscott, Lenzenweger & van Os, 2009).

While the field has been mindful of within-group heterogeneity of schizophrenia, the between-group, transethnic differences in the phenotypes have received less scrutiny. Examination of transethnic schizophrenia samples provides an opportunity to elucidate differences in schizophrenia expression, which are important to a comprehensive understanding of this disorder (Kleinman, 1988).

Previous anthropological (Barrett, 2004) and psychiatric (Barrett *et al*., 2005) research on the Iban of Sarawak has proposed the following symptoms as characteristic of schizophrenia in that population: low rates of bizarre delusions, specifically thought broadcast, insertion and withdrawal delusions; and high rates of auditory hallucinations, disorganized behavior, restlessness and insomnia. Additionally, a comparatively short prodrome has been consistently noted in case review, particularly in comparison with other studied populations.

The Genetics Research group at the Queensland Centre for Mental Health Research (QCMHR) and our collaborators recruited three cohorts of individuals with psychosis for genetic analyses: European Australians (n=821); Tamil Brahmin and proximal caste groups from Tamil Nadu, India (n=520); and the Iban of Sarawak, Malaysia (n=298). In this paper, we examined nine variables previously associated with schizophrenia in the Iban, and compared the frequencies of these variables in the Iban sample with our Australian and Indian cohorts.

Our available Iban sample is an extension of the sample described in a previous publication (Barrett *et al*., 2005). Their sample included individuals with schizophrenia identified through an initial medical records screen (n=275). We recontacted and comprehensively assessed 122 of these individuals plus an additional 23 individuals who were primarily new cases diagnosed after the initial screen. Thus we increased both sample size (of included

individuals with schizophrenia) and quality of clinical information available. We aimed to confirm the previous research proposing these characteristic symptoms, and explore the implications of differences across populations.

We hypothesized that (a) hallucinations (specifically auditory), disorganized behavior, sleep disturbance, and psychomotor changes would occur more frequently in the Iban than in samples derived from Australian or Indian populations; (b) bizarre delusions (specifically broadcast, insertion and withdrawal delusions) would occur less frequently in the Iban than in Australia or India; and (c) the prodrome would be shorter in the Iban than in Australia or India.

Methods

Sample details

Sample recruitment across sites and clinical ascertainment are detailed elsewhere (see McLean *et al*., 2012). Briefly, recruitment at each site involved: Australia – sibling pairs and unrelated individuals were recruited as part of a major US/Australian collaboration (Molecular Genetics of Schizophrenia [MGS] Consortium) from multiple sources, including local treatment facilities, physician referrals, community organizations, supported accommodation facilities and advertisements; India – sibling pairs, trios and unrelated individuals were identified and invited to participate through The Schizophrenia Research Foundation India (SCARF); and Sarawak – Iban individuals were identified through Malaysian census data, an initial medical records assessment was undertaken, then a subset of individuals and families were contacted for in-depth follow-up. We included all individuals with a Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) (APA, 1994) diagnosis of schizophrenia or schizoaffective disorder who met the (self-reported) ethnicity inclusion criterion. Ethnicity was subsequently confirmed through genetic analysis (Australia: Shi et al., 2009; India and Sarawak: manuscripts in preparation). Exclusion criteria for individuals were: (i) inability to give informed consent; (ii) psychosis assessed as secondary to substance use or a neurological disorder; and (iii) severe intellectual disability. Informed consent was obtained across all sites, and local Institutional Ethics Committee approval was obtained for each study. This research conforms to the provisions of the Declaration of Helsinki (as revised in Edinburgh 2000).

Clinical ascertainment

Clinical ascertainment included five elements.

- **i.** Trained clinicians used the semi-structured Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger *et al*., 1994) to obtain DSM-IV relevant diagnostic information.
- **ii.** A family informant, when possible, or the proband was interviewed about the family psychiatric history using the Family Interview for Genetic Studies (FIGS) (Gershon *et al*., 1988; Maxwell, 1992). The cultural equivalence of the DIGS and FIGS was extensively addressed by the chief investigators at the three sites, and

each instrument was translated into Iban (Sarawak) and Tamil (India) with appropriate back-translation procedures.

iii. All available medical records were retrieved for each participant and *assessed* by trained clinicians.

iv. A trained clinician prepared a case summary based on all available information, which facilitated diagnostic review.

v. DIGS interview, case summary, available medical records, and FIGS reports formed the basis for diagnostic review. Diagnoses were assigned using the Best Estimate Final Diagnosis (BEFD) procedure (Leckman *et al*., 1982), with two experienced psychiatrists independently reviewing all available information then conferring to assign a consensus diagnosis. Approximately half the Sarawak sample had diagnoses formulated by one experienced psychiatrist, with a BEFD generated in a random subset (20 cases).

Inter-rater reliability was assessed within the Australian/US sample (Shi *et al*., 2009; Suarez *et al*., 2006); within the Indian sample (Thara *et al*., 2009); within the Sarawak sample; between the Australian and Indian samples (disagreement in one of 20 cases; κ=0.886); and between the Australian and Sarawak samples (disagreement in one of 20 cases; κ=0.828). One psychiatrist (BM) was a Principal Investigator on all studies, and has reviewed all included cases.

Data analysis

We analyzed nine clinical variables identified in previous research: (i) lifetime delusions; (ii) bizarre delusions; (iii) delusions of thought broadcast, insertion or withdrawal; (iv) lifetime hallucinations; (v) auditory hallucinations; (vi) lifetime disorganized or catatonic motor behavior; (vii) sleep disturbance; (viii) psychomotor changes; and (ix) length of prodromal period. We also included the following potentially confounding variables: (x) sex; (xi) age; and (xii) presence of lifetime major depressive episodes.

Prodromal duration was obtained from all available information (DIGS interview, case summary, medical records, FIGS reports), and was assessed as the period between when social and/or occupational decline was first observed and when definite psychotic symptoms were first recorded. It was coded as dichotomous: rapid=onset within 4 weeks; gradual=onset longer than 4 weeks. Two outcome variables (sleep disturbance and psychomotor changes) were dropped from the model due to a lack of equivalence across sites.

Sources of data were audited (both electronic and hard copy), and all potential cases were identified for whom comprehensive diagnostic information was available. Data were extracted from diagnostic interview databases, where possible, then responses were checked, corrected, and missing values retrieved from all available sources, including a detailed review of all narrative summaries.

Due to the potential confounding effect of including both related and unrelated individuals in our sample, we selected a conservative model. Individuals within families may be more

similar with regard to demographic and symptom characteristics than unrelated individuals owing to shared socioeconomic and environmental circumstances. Given that between-site similarities and differences across these variables were a focus of this study, and the degree of inter-relatedness differed across sites, we included only unrelated individuals, with a single individual randomly selected from each of the 1124 families across the three sites.

Outcome variables were then assessed individually by logistic regression, fitting site, presence of lifetime depressive episode(s), age, and sex as explanatory variables, plus all second level effects (e.g. site-by-sex) for these variables. We performed model simplification based on AIC, with the least significant effect being removed from the model at each iteration, until all remaining effects were significant. The minimal adequate model is presented for each outcome variable. Statistical analyses used Proc Logistic in SAS software, version 9.3 for Windows (SAS Institute Inc.). We used Bonferroni correction to account for multiple testing.

The present study was drawn from 1831 individuals from Australia (*n*=821), India (*n*=524) and Sarawak (*n*=486). We excluded 192 individuals because their DSM-IV diagnosis was a psychotic disorder other than schizophrenia or schizoaffective disorder (Australia, *n*=0; India, *n*=4; Sarawak, *n*=188). Of the resulting 1639 individuals we then excluded all individuals with missing data for any of the eleven variables (seven outcome, four explanatory) of interest (Australia, *n*=136; India, *n*=24; Sarawak, *n*=62), leaving 1417 individuals from 1124 independent families. One individual from each family was randomly selected to constitute the final sample of 1124 individuals (Australia, *n*=609; India, *n*=310; Sarawak, *n*=205). DIGS and FIGS data were available for over 90% of participants in Australia and India, and approximately 50% of participants in Sarawak. Case summaries were available for over 90% of participants in Australia and Sarawak, and for over 75% of participants in India. Best-estimate final diagnoses were available for all participants across the three sites (except as previously noted).

Results

A summary of symptom variable frequencies by site, including all outcome and explanatory variables, is provided in table 1.

A summary of the logistic regression performed is provided in table 2, with associated odds ratios and 95% confidence intervals provided in table 3.

Each of the seven outcome variables had significant site effects, while all outcome variables except global delusions and disorganized behavior had significant age effects. Both lifetime hallucinations and length of prodrome had significant sex effects, whereas only lifetime delusions had a significant depressive episode(s) effect.

Multiple testing correction

The site effect for six of the seven outcome variables remained significant using a Bonferroni corrected p-value=0.0007, with only the disorganized behavior effect (p=0.041) failing to reach this threshold. Age remained significant for bizarre delusions, with younger

individuals having greater odds of reporting bizarre delusions. No other effects remained significant for any of the outcome variables.

Discussion

Consistent with previous reports (Barrett, 2004; Barrett *et al*., 2005), we found that individuals with schizophrenia from the Iban sample differed on key symptom variables. In addition, we identified a range of differences for these variables between the Iban, Australia and India.

Delusions

While the proportion of individuals reporting bizarre delusions and delusions of thought broadcast, insertion and withdrawal was lowest in the Iban, it is noteworthy that the frequencies in India were also low in contrast to Australia, and that India and Sarawak were similar in their reported frequencies of broadcast/insertion/withdrawal delusions (India 14.2%; Sarawak 10.7%). The difficulty of assessing bizarreness of beliefs is widely recognized (Kendler et al., 1983), particularly across cultures (APA, 1994). Moreover, the greater frequency of Schneiderian first-rank symptoms reported in Western populations has been attributed to bizarre experiences in Western cultures being considered normative in non-Western cultures (Barrett, 2004). However, several alternative explanations for these cross-cultural differences have also been proposed (for a summary see Barrett, 2004).

Younger individuals had significantly greater odds of experiencing lifetime bizarre delusions, after correction for multiple testing. This somewhat counter-intuitive result may reflect recall bias, with an under-reporting of bizarre delusions in older individuals, since age has been associated with decreased occurrence of delusions and hallucinations (Schultz *et al*., 1997).

Hallucinations

Auditory hallucinations were, as expected, reported most frequently in the Iban, although rates of both lifetime hallucinations and auditory hallucinations did not differ between Sarawak (lifetime 94.6%; auditory 93.7%) and Australia (lifetime 92.9%; auditory 90.5%), with Indian rates (lifetime 81.6%; auditory 78.7%) significantly lower. A ‘striking resemblance’ in the appearance of auditory hallucinations, between Australian and Iban samples with schizophrenia, has been noted (Barrett, 2004). This finding offers an interesting contrast to our delusion finding, in that any explanation relying on Western/non-Western cultural norms explaining site differences is not sufficient to explain the significant difference in rates of auditory hallucinations between the non-Western cultures of India and Sarawak.

Disorganized behavior

The frequency of disorganized behavior was marginally higher in the Iban (86.3%) than in Australia (76.2%) or India (78.7%), although this site difference was non-significant after correction for multiple testing.

Onset type

The clear site difference regarding greater frequency of rapid onset in Sarawak (43.9%) in contrast to Australia (17.9%) and India (22.6%) is of particular interest. A later age of onset (~6 years) finding in the Iban compared with Australia and India has been previously reported (McLean et al., 2012), yet the greater proportion of Iban individuals with rapid onset type is equally stark. Because the majority of Iban live with close family contact, and there is a societal propensity to seek early medical treatment (Barrett *et al*., 2005), early changes in behavior would likely be readily noted; thus, a longer reported prodrome may be expected, with social/occupational decline prior to psychosis onset identified more readily than in other populations. Clearly, the data do not support this. Alternatively, help-seeking behavior may prompt earlier diagnosis, truncating the period regarded as prodromal, with definite psychosis detected earlier in the Iban, in contrast to other populations, where later detection may 'artificially' lengthen the period regarded as prodromal. Cultural considerations may also be fundamental to the identified site difference: e.g. the Iban may be more tolerant of aberrant behavior than other societies, and may not rate atypical behavior as 'prodromal' until immediately prior to recognition of definite psychosis.

Cultural considerations

Categorization of research participants by ethnicity and/or culture is problematic and highly contested (Egede, 2006; Ma *et al*., 2007). The fact that our cohorts are both ethnically homogeneous and geographically constrained enables assessment of cultural confounders because these two factors represent the best available proxy for culture (Azuonye, 1994). Our sample is large for a transethnic comparative schizophrenia study (n=1124), individuals were assessed using the same battery of instruments, and individuals were diagnosed using the best-estimate final diagnosis method, which offers consistently high diagnostic reliability and stability (Beckmann, Franzek & Stober, 1996; Calkins *et al*., 2007), and is the benchmark method available with current methods of classifying schizophrenia (McLean *et al*., 2012). We assessed ethnicity by self-report, which is considered the research 'gold standard' in transcultural research (Ma *et al*., 2007). Furthermore, we ascertained birthplace for individuals' parents and grandparents, confirmed ethnic homogeneity genetically, and interviewed individuals in their home countries using local interviewers. These measures avoid many confounding factors frequently experienced in cross-cultural research, which can limit generalizability of findings (McKenzie & Crowcroft, 1996a, 1996b).

Methodological limitations

First, a lack of measurement equivalence was unavoidable. The samples were collected for specific genetic studies, thus there were differences in selection methods of included individuals. Both the Indian and Sarawak samples were chosen from ethnically homogeneous populations, whereas the Australian sample was not specifically recruited as such (although we did focus on Caucasian ethnicity). Furthermore, the Australian and Indian cohorts included sib-pairs as well as unrelated individuals recruited opportunistically, while only the Sarawak sample can be considered relatively epidemiologically sound (Barrett *et al*., 2005). As previously noted, we negated any effect of familial relatedness in our model by randomly selecting one individual per family for analyses. The different recruitment

methods also resulted in DIGS and FIGS data being unavailable for approximately half the Sarawak sample (see McLean *et al*., 2012).

Second, caution must always be exercised when using diagnostic instruments across cultures, since converting thoughts, feelings, and concepts such as bizarreness across languages can be difficult (Barrett, 2004). Consequently, we addressed cultural equivalence extensively in the preliminary planning for the studies (for a cultural equivalence framework see Herdman, Fox-Rushby & Badia, 1998). We also employed state-of-the-art methods, translating and back-translating the DIGS, and using local interviewers who interviewed in the native language across the three sites, and recorded responses in Iban (Sarawak) and English (India and Australia). The reliability of the instrument (inter-rater reliability within and across the samples) was also tested across sites, although diagnostic inter-rater reliability was not assessed between India and Sarawak.

Third, the generalizability of our findings is limited, particularly given that both the Iban in Malaysia and the Tamil Brahmin and other geographically proximal castes in India are homogeneous groups within diverse societies. Furthermore, we did not specifically collect socioeconomic data across our samples, which further limits the generalizability of any findings attributed to ethnicity/culture, as socioeconomic position has been proposed as a stronger determinant of health outcomes than ethnicity (Egede, 2006).

Fourth, utilizing a sample of individuals meeting the DSM-IV criteria for either schizophrenia or schizoaffective disorder to study the nature of psychosis and/or schizophrenia itself may be problematic, in that we are not able to make comparisons with other DSM-IV diagnoses such as bipolar disorder, which would give a ‘broader perspective’. Furthermore, restricting the sample to those meeting DSM-IV schizophrenia criteria excludes cases with psychosis demonstrating the most clinical variation; these may be important to cultural understanding of psychosis (Kleinman, 1988).

Finally, because the samples were collected for specific genetic studies, there are limitations to the assumptions and generalizations we can make regarding difficult-to-quantify culturally-sensitive concepts such as length of prodrome, notwithstanding our extensive cross-cultural equivalence work and use of carefully ascertained ethnicity as our distinguishing factor between sites. In order to validate and interpret our finding of significantly shorter prodrome in Sarawak, further qualitative in-depth interviews specifically addressing cultural interpretations of illness progression and associated concepts across sites should be undertaken. This follow-up research, while worthwhile, was beyond the scope of this study.

Conclusions

We have observed significant differences in the frequency of symptoms of schizophrenia across three ethnically different populations. A comprehensive search for clinical subtypes using ethnically distinct populations is warranted, as this may contribute to our understanding of between-group clinical variation, which may not only benefit future genetic studies, but also inform the ongoing nosological debate regarding schizophrenia.

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Table 1

Demographic and symptom characteristics of affected individuals by site †

Variable	Australia	India	Sarawak	Total
N	609 (54.2%)	310 (27.6%)	205 (18.2%)	1124 (100%)
Demographic variables				
Age, Mean ± SD	38.95 ± 11.55	36.57 ± 11.37	47.19 ± 14.67	39.80 ± 12.66
Sex				
Female	173 (28.4%)	128 (41.3%)	85 (41.5%)	386 (34.3%)
Male	436 (71.6%)	182 (58.7%)	120 (58.5%)	738 (65.7%)
Symptom variables				
Diagnosis				
Schizoaffective, depressed	22 (3.6%)	1 (0.3%)	30 (14.6%)	53 (4.7%)
Schizoaffective, bipolar	26 (4.3%)	0 (0%)	16 (7.8%)	42 (3.7%)
Schizophrenia	561 (92.1%)	309 (99.7%)	159 (77.6%)	1029 (91.6%)
Onset type				
Rapid (4 weeks or less)	109 (17.9%)	70 (22.6%)	90 (43.9%)	269 (23.9%)
Gradual (longer than 4 weeks)	500 (82.1%)	240 (77.4%)	115 (56.1%)	855 (76.1%)
Presence of any delusions (lifetime)	599 (98.3%)	283 (91.3%)	164 (80.0%)	1046 (93.1%)
Presence of bizarre delusions (lifetime)	410 (67.3%)	113 (36.5%)	40 (19.5%)	563 (50.1%)
Presence of thought broadcast/insertion/withdrawal delusions (lifetime)	322 (52.9%)	44 (14.2%)	22 (10.7%)	388 (34.5%)
Presence of any hallucinations (lifetime)	566 (92.9%)	253 (81.6%)	194 (94.6%)	1013 (90.1%)
Presence of auditory hallucinations (lifetime)	551 (90.5%)	244 (78.7%)	192 (93.7%)	987 (87.8%)
Presence of disorganized behavior (lifetime)	464 (76.2%)	244 (78.7%)	177 (86.3%)	885 (78.7%)
Presence of major depressive episode(s) (lifetime)	261 (42.9%)	9 (2.9%)	44 (21.5%)	314 (27.9%)

† One affected family member randomly generated from each family included in the sample.

Table 2

Logistic regression showing predictors of the presence of identified characteristic Iban symptoms †

Outcome Variable	Explanatory Variables ‡	DF	Wald X^2	P-value §
Global Delusions				
	Intercept	**1**	**19.85**	**<0.0001*** **
	Site	**2**	**23.78**	**<0.0001*** **
	Age	1	0.84	0.36
	Major depressive episodes	1	7.59	0.006**
	Age by Site	2	4.62	0.10
Bizarre Delusions				
	Intercept	1	7.77	0.005**
	Site	**2**	**38.67**	**<0.0001*** **
	Age	**1**	**16.56**	**<0.0001*** **
	Sex	1	3.56	0.06
	Age by Site	2	9.63	0.008**
	Sex by Site	2	5.17	0.08
Broadcast/Insertion/Withdrawal Delusions				
	Intercept	**1**	**19.09**	**<0.0001*** **
	Site	**2**	**65.97**	**<0.0001*** **
	Age	1	10.57	0.001**
	Major depressive episodes	1	2.57	0.11
	Age by Site	2	6.38	0.041*
Global Hallucinations				
	Intercept	**1**	**51.18**	**<0.0001*** **
	Site	**2**	**24. 24**	**<0.0001*** **
	Age	1	4.82	0.028*
	Sex	1	5.68	0.017*
	Major depressive episodes	1	0.96	0.33
	Sex by Major depressive episodes	1	4.31	0.038*
Auditory Hallucinations				
	Intercept	**1**	**90.76**	**<0.0001*** **
	Site	**2**	**65.40**	**<0.0001*** **
	Age	1	4.89	0.027*
	Sex	1	0.16	0.69
	Sex by Site	2	9.39	0.009**

Outcome Variable	Explanatory Variables ‡	DF	Wald X^2	P-value §
Disorganized Behavior				
	Intercept	**1**	**60.33**	**<0.0001*** **
	Site	2	6.38	0.041*
	Age	1	3.10	0.08
	Major depressive episodes	1	3.46	0.06
Rapid Onset Type				
	Intercept	1	2.52	0.11
	Site	**2**	**43.03**	**<0.0001*** **
	Age	1	10.56	0.001**
	Sex	1	6.90	0.009**
	Major depressive episodes	1	1.42	0.23
	Age by Site	2	5.18	0.08
	Sex by Site	2	5.96	0.05
	Age by Sex	1	8.06	0.005**
	Sex by Major depressive episodes	1	2.81	0.09

* p<0.05

** p<0.01

*** p<0.001

† Iteration with best AIC (model fit) that passes overdispersion test shown for each outcome variable

‡ Odds ratios and 95% confidence intervals for relevant effect combinations presented as Table 3

§ Effects surpassing Bonferroni correction shown in bold

Table 3

Odds ratios and 95% confidence intervals for all variable combinations presented in Table 2

Outcome Variable	Explanatory Variable Combinations	Estimate (95% CI)
Global Delusions		
	Site (Australia vs. India) at mean age	5.06 (1.94 − 13.18)
	Site (Australia vs. Sarawak) at mean age	15.57 (6.17 − 39.32)
	Site (India vs. Sarawak) at mean age	3.08 (1.71 − 5.57)
	Age in Australia	0.21 (0.04 − 1.05)
	Age in India	0.22 (0.09 − 0.52)
	Age in Sarawak	0.70 (0.33 − 1.49)
	No major depressive episodes vs. one or more ma jor depressive episodes	0.26 (0.10 − 0.68)
Bizarre Delusions		
	Site (Australia vs. India) at mean age, males	3.64 (2.40 − 5.54)
	Site (Australia vs. Sarawak) at mean age, males	11.91 (6.32 − 22.43)
	Site (India vs. Sarawak) at mean age, males	3.27 (1.64 − 6.51)
	Site (Australia vs. India) at mean age, females	4.40 (2.53 − 7.65)
	Site (Australia vs. Sarawak) at mean age, females	4.61 (2.31 − 9.18)
	Site (India vs. Sarawak) at mean age, females	1.05 (0.50 − 2.18)
	Age in Australia	0.73 (0.50 − 1.07)
	Age in India	0.49 (0.28 − 0.88)
	Age in Sarawak	0.17 (0.07 − 0.39)
	Sex (Male vs. Female) in Australia	1.15 (0.76 − 1.74)
	Sex (Male vs. Female) in India	1.39 (0.81 − 2.38)
	Sex (Male vs. Female) in Sarawak	0.44 (0.19 − 1.03)
Broadcast/Insertion/Withdrawal Delusions		
	Site (Australia vs. India) at mean age	6.29 (4.08 − 9.70)
	Site (Australia vs. Sarawak) at mean age	9.15 (5.09 − 16.44)
	Site (India vs. Sarawak) at mean age	1.45 (0.74 − 2.85)
	Age in Australia	0.65 (0.46 − 0.93)
	Age in India	0.79 (0.37 − 1.71)
	Age in Sarawak	0.15 (0.05 − 0.47)
	No major depressive episodes vs. one or more ma jor depressive episodes	0.76 (0.54 − 1.06)
Global Hallucinations		
	Site (Australia vs. India)	3.58 (2.00 − 6.39)
	Site (Australia vs. Sarawak)	0.73 (0.32 − 1.66)
	Site (India vs. Sarawak)	0.20 (0.09 − 0.47)
	Age	0.58 (0.35 − 0.94)
	Sex (Male vs. Female), no major depressive episodes	0.46 (0.25 − 0.87)
	Sex (Male vs. Female), one or more major depressive episodes	1.68 (0.59 − 4.74)
	Depressive episodes (none vs. one or more), males	0.66 (0.29 − 1.52)

Outcome Variable	Explanatory Variable Combinations	Estimate (95% CI)
	Depressive episodes (none vs. one or more), females	2.39 (0.89 − 6.40)
Auditory Hallucinations		
	Site (Australia vs. India), males	3.73 (2.61 − 5.34)
	Site (Australia vs. Sarawak), males	0.58 (0.31 − 1.10)
	Site (India vs. Sarawak), males	0.16 (0.08 − 0.30)
	Site (Australia vs. India), females	1.47 (0.86 − 2.50)
	Site (Australia vs. Sarawak), females	0.62 (0.30 − 1.30)
	Site (India vs. Sarawak), females	0.43 (0.20 −0.90)
	Age	0.72 (0.54 − 0.96)
	Sex (Male vs. Female) in Australia	1.12 (0.72 − 1.76)
	Sex (Male vs. Female) in India	0.44 (0.28 − 0.70)
	Sex (Male vs. Female) in Sarawak	1.19 (0.50 − 2.83)
Disorganized Behavior		
	Site (Australia vs. India)	0.96 (0.67 − 1.38)
	Site (Australia vs. Sarawak)	0.57 (0.36 − 0.89)
	Site (India vs. Sarawak)	0.59 (0.36 − 0.97)
	Age	1.31 (0.97 − 1.76)
	Depressive episodes (none vs. one or more)	1.38 (0.98 − 1.94)
Rapid Onset Type		
	Site (Australia vs. India) at mean age, males	0.80 (0.50 − 1.29)
	Site (Australia vs. Sarawak) at mean age, males	0.20 (0.13 − 0.32)
	Site (India vs. Sarawak) at mean age, males	0.25 (0.15 − 0.43)
	Site (Australia vs. India) at mean age, females	0.34 (0.17 − 0.68)
	Site (Australia vs. Sarawak) at mean age, females	0.23 (0.12 − 0.43)
	Site (India vs. Sarawak) at mean age, females	0.66 (0.35 − 1.23)
	Age, males in Australia	0.66 (0.42 − 1.05)
	Age, males in India	0.88 (0.46 − 1.67)
	Age, males in Sarawak	0.36 (0.19 − 0.66)
	Age, females in Australia	1.62 (0.88 − 2.99)
	Age, females in India	2.15 (1.14 − 4.07)
	Age, females in Sarawak	0.87 (0.43 − 1.73)
	Sex (Male vs. Female) at mean age, no major depressive episodes in Australia	1.59 (0.83 − 3.04)
	Sex (Male vs. Female) at mean age, no major depressive episodes in India	0.68 (0.39 − 1.17)
	Sex (Male vs. Female) at mean age, no major depressive episodes in Sarawak	1.76 (0.95 − 3.25)
	Sex (Male vs. Female) at mean age, one or more ma jor depressive episodes in Australia	0.84 (0.48 − 1.47)
	Sex (Male vs. Female) at mean age, one or more ma jor depressive episodes in India	0. 36 (0.15 − 0.88)
	Sex (Male vs. Female) at mean age, one or more ma jor depressive episodes in Sarawak	0.93 (0.42 − 2.07)
	Depressive episodes (none vs. one or more), males	0.77 (0.50 − 1.18)
	Depressive episodes (none vs. one or more), females	0.41 (0.22 − 0.75)