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## Examining the continuum of psychosis: Frequency and characteristics of psychotic-like symptoms in relatives and non-relatives of patients with schizophrenia

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### ABSTRACT

**Background:** A key finding underlying the continuum of psychosis concept is the presence of psychotic-like experiences (PLEs) in healthy subjects. However, it remains uncertain to what extent these experiences are related to the genetic risk for schizophrenia and how far they actually resemble attenuated forms of psychotic symptoms. **Methods:** Forty-nine adults with no history of mental illness in first-degree relatives and 59 siblings of patients with schizophrenia were rated on the psychosis section of the Computerized Diagnostic Interview Schedule IV (C DIS-IV) and the Rust Inventory of Schizotypal Cognitions (RISC). Those who rated positive on the C DIS-IV were re-interviewed using the lifetime version of the Present State Examination 9th edition (PSE-9) and the Structured interview for Schizotypy (SIS).

**Results:** Seventeen (34.69%) of the non-relatives and 22 (37.29%) of the relatives responded positively to one or more of the psychosis questions on the DIS. This difference was not significant. RISC scores were also similar between the groups. At follow-up interview with the PSE-9, 13/40 PLEs (32.50%) in the non-relatives were classified as possible or probable psychotic symptoms compared to 11/46 (23.91%) in the relatives. Using liberal symptom thresholds, 5 of those who attended the follow-up interview (2 non-relatives and 3 relatives) met SIS criteria for schizotypal personality disorder.

**Conclusions:** Rates of PLEs, however considered, do not differ substantially between relatives and non-relatives of patients with schizophrenia. Only a minority of PLEs picked up by screening interviews resemble attenuated forms of psychotic symptoms.

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Following pioneering studies by Verdoux et al. (1998) and van Os et al. (2000), it is now accepted that a proportion of the healthy adult population – 5–6% according to current estimates (van Os et al., 2009; McGrath et al., 2015) – report unusual beliefs and experiences that seem to represent attenuated forms of schizophrenic symptoms (psychotic-like experiences or PLEs). Occurrence of PLEs has been found to be associated with demographic factors such as male sex, urbanicity, lower educational level, being a migrant and belonging to an ethnic minority, which are also risk factors for schizophrenia (van Os et al., 2000;

van Os et al., 2009). Experience of PLEs in childhood has also been found to increase the risk of development of psychosis in adult life (Poulton et al., 2000; Welham et al., 2009). Taken together, these findings have led to the influential continuum of psychosis concept, that schizophrenia is an arbitrarily defined severe and/or distressing end of what in reality is a spectrum of psychotic symptoms in the population.

Nevertheless, there are unanswered questions about PLEs. One of these is how far they are a manifestation of the genetic predisposition to schizophrenia. Some evidence on this point comes from the literature on schizotypy, the concept of which was originally based on the observation that relatives of schizophrenic patients often show features reminiscent of the disorder (Kendler, 1985; Spitzer et al., 1979). Pooling data from 8 studies, Tarbox and Pogue-Geile (2011) found evidence for significantly higher rates of social-interpersonal schizotypal symptoms (excessive social anxiety, lack of close friends, constricted affect

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and suspiciousness) and disorganized schizotypal symptoms (odd speech and behaviour) in the first-degree relatives of schizophrenic patients compared to healthy controls and to relatives of patients with affective disorder. However, contrary to expectations, cognitive-perceptual symptoms (ideas of reference, magical thinking, and unusual perceptual experiences) showed only a small increase among relatives compared to both the control groups.

One study has also examined the frequency of PLEs in relatives of patients with schizophrenia directly. [Johnstone et al. \(2000\)](#) obtained detailed information on adolescents and young adults who had at least two first- or second-degree relatives with schizophrenia and a matched group of individuals with no known family history of the disorder. Over three years of follow-up, 37/152 high risk subjects reported one or more partially or fully rated psychotic symptoms on the Present State Examination 9th Edition (PSE-9) ([Wing et al., 1974](#)), compared to 4/36 individuals without familial risk. Although the rate was substantially higher in the relatives, the difference did not reach significance ( $p = 0.11$ ).

Another issue concerning PLEs is the degree to which they are actually understandable as attenuated forms of delusions and hallucinations as seen in psychosis. Thus, in the study of [Verdoux et al. \(1998\)](#) presence of PLEs was based on responses to self-report questionnaires, which are known to face problems about whether the respondent has adequately understood the questions, or whether the questions themselves are misleading ([David, 2010](#)). [van Os et al. \(2000\)](#) addressed this problem by using information from the psychosis section of the Composite International Diagnostic Interview (CIDI) ([WHO, 1990](#)), a structured psychiatric interview designed to be administered by trained non-clinicians. Positive responses to psychosis items were probed and characterized as 'true psychiatric symptom', or as 'present, but not clinically relevant (not bothered by it and not seeking help for it)', 'result of ingestion of drugs', 'result of somatic disease', or 'not really a symptom because there appears to be some explanation for it'. Among 4165 adults with no psychiatric diagnosis they found a rate of 10.4% for any psychotic symptom; this was made up of rates of 6.8% for true + not clinically relevant delusions and 3.7% for true + not clinically relevant hallucinations, plus much lower rates for symptoms due to drug use or physical disease and those which had a plausible explanation.

However, even this strategy may not be sufficient to exclude false positive responses. [Kendler et al. \(1996\)](#) re-interviewed 446 community-dwelling individuals who screened positive on CIDI psychosis items. They found that a substantial number of the responses that had been rated as 'possible, at least a suspicion of psychosis' or 'probable or definite' were not in fact psychotic symptoms; examples included culturally sanctioned beliefs such as in witchcraft, isolated ideas of reference, or seeing a ghost or a recently deceased relative. They noted that CIDI items assessing common persecutory themes and thought transfer-like experiences performed particularly poorly, being frequently misunderstood by the respondents and misinterpreted by the interviewers. Similarly, [Ochoa et al. \(2008\)](#) examined the CIDI responses of 44 individuals who responded positively to one or more psychosis questions but were not found to have a diagnosis of non-affective psychosis based on re-interview with the Structured Clinical Interview for DSM IV (SCID) ([First et al., 2002](#)). None of the responses concerning perceptual experiences were considered to represent true hallucinations, consisting mostly of hearing or seeing a family member in the days after he or she died, hypnagogic/hypnopompic hallucinations or hearing a voice when there were actually people around. Answers to questions concerning mind control, being affected by strange forces, plots to harm the person, etc. were also mostly found not to reflect genuine psychotic symptoms.

In the present study we aimed to examine the occurrence of PLEs in samples of individuals with and without a family history of schizophrenia. We also tried to establish the 'authenticity' of the phenomena by re-interviewing individuals who reported them using a detailed structured psychiatric interview. The relationship of PLEs to presence of schizotypy was examined at both stages of the study.

## 1. Method

### 1.1. Subjects

The sample consisted of 108 healthy adults, 49 with no history of major mental illness in first-degree relatives and 59 who were the siblings of patients with schizophrenia. The non-relatives were recruited via poster and web-based advertisement in the hospital and local community, plus word-of-mouth requests from staff in the research unit. They were excluded if they reported having a first-degree relative with an established diagnosis of major mental illness, or who had symptoms suggestive of this, such as having spent time in a mental hospital or being on psychotropic drug treatment. The relatives all had a sibling who met DSM-IV criteria for schizophrenia, based on review of case-notes by two members of the research team (PJM and SS).

Subjects were excluded if: (i) they were younger than 18 or older than 65 years; (ii) they had a personal history of major mental illness (schizophrenia, bipolar disorder, major depression, confirmed by a computerized diagnostic interview – see below) or treatment with psychotropic medication; (iii) they had a history of brain trauma or neurological disease; (iv) they had shown alcohol/substance abuse within 12 months prior to participation; and (v) there was evidence of learning disability.

The two samples were recruited so as to be similar in age and sex. IQ was estimated using the Word Accentuation Test (Test de Acentuación de Palabras (TAP) ([Del Ser et al., 1997](#); [Gomar et al., 2011](#)), which is conceptually similar to the UK National Adult Reading Test (NART) ([Nelson and Willison, 1991](#)) and the US Wide Range of Achievement Test ([Jastak and Wilkinson, 1984](#)). Socio-economic status (SES) was measured using the Hollingshead-Redlich index of social position ([Hollingshead and Redlich, 2007](#)). The groups were not prospectively matched for this variable, as it seemed possible that being at familial risk for schizophrenia might itself impact on social and occupational functioning, similar to schizophrenia itself (e.g. [Goldberg and Morrison, 1963](#)).

All participants gave written informed consent and the study was approved by the hospital research ethics committee. All procedures were carried out according to the Declaration of Helsinki.

### 1.2. Procedure

#### 1.2.1. Screening for PLEs

Participants underwent assessment using the Computerized Diagnostic Interview Schedule IV (C DIS-IV) ([Robins et al., 2000](#)), a structured psychiatric interview similar in scope to the CIDI, administered by a psychologist (2) or a psychiatrist (1) who were trained in its use. The psychosis section of this interview contains 22 items, 17 for delusion-like and 5 for hallucination-like experience (see [Table 1](#)). Responses are explored and then rated as 'absent', 'plausible' (i.e. do not represent a psychiatric symptom because they have a real basis) or implausible (i.e. represent a psychiatric symptom); in some cases whether the symptom has occurred in relation only to alcohol or drug use is also noted.

The subjects were also rated on a measure of schizotypy, the Rust Inventory of Schizotypal Cognitions (RISC) ([Rust, 1989](#)). This contains 26 statements to which the participant is asked to respond, with a 4-point forced choice response set (strongly agree, agree, disagree, strongly disagree).

#### 1.2.2. Further exploration of reported PLEs

Participants who endorsed any of the C DIS-IV psychosis section questions, irrespective of whether they were rated as plausible, implausible drug-related, etc., were invited for a follow-up interview. In this, their experiences were explored in depth using relevant questions from the lifetime version of the Present State Examination 9th edition (PSE-9) ([McGuffin et al., 1986](#); [Wing et al., 1974](#)). This establishes the presence or absence of a wide range of psychotic symptoms according

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