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Screening for schizophrenia in initial prodromal phase: Detecting the sub-threshold psychosis

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ABSTRACT

Objectives: The aim of the study is to screen and evaluate the efficacy of the screening tools in detecting subjects with sub-threshold psychosis among asymptomatic individuals at genetic risk, as compared with persons in the general public.
Methods: This was a two-stage study of the relatives of patients with schizophrenia and general individuals. Subjects were screened with a Screening Questionnaire (SQ) and General Health Questionnaires (GHQ-12) in the initial stage. Those who screened positive were reassessed using the Comprehensive Assessment of At-Risk Mental State (CAARMS) in the second stage.
Results: A total of 190 (29%) subjects initially screened positive from a sample of 660 individuals. The proportion of persons in the general public (63%) who progressed to the second stage was significantly higher than at-risk relatives (37.4%) ($X^2 = 17.028$, $df = 1$, $p < 0.001$). After final assessment, about 4% of the sample was positive; subjects at sub-threshold UHR (ultra-high risk) was higher (69%) than subjects at UHR (31%). Detection rate was higher when both GHQ and SQ (26.4%) measures were positive in the initial screening. In both categories of sub-threshold psychosis, the percentage of subjects at genetic risk was higher (62%), and the proportion steadily increased as the psychosis progressed.
Conclusion: The prevalence of sub-threshold psychosis was higher in subjects at genetic risk. Clinical assessment following a self-report questionnaire should be mandatory as the rate of false positive results is high. The SQ has poor validation indexes, which is partly contributed to low detection rate and the GHQ is not suitable for screening early psychosis.

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1. Introduction

It is believed that individuals who will develop schizophrenia go through a variety of abnormal subjective experiences that progressively develop during pre-puberty and puberty. Genetic high-risk studies have indicated that subtle deficits can be identified long before psychosis emerges and these deficits can serve as predictors for later development of schizophrenia. Ideally, the prevention should be conducted during these years to detect the disease before symptoms are evident and progress to psychosis. The participants in most of the studies were help-seeking adolescents who were already affected by psychotic-like symptom. Such people cannot be targeted with primary prevention because it is highly probable that an actual disease process has already begun (Cornblatt et al., 2002). The intervention should be aimed at high risk individuals showing minimal but detectable signs of possible incipient mental disorder, and who do not meet the current diagnostic criteria.

There are a number of variables that confer some indication of vulnerability to schizophrenia. Screening instruments have been developed that incorporates vulnerable factors. However, there is no single instrument capable of detecting individuals in the prodromal phase with satisfying degrees of sensitivity and specificity (Kline et al., 2012). Basic Symptoms (BSs) which is presumably characterise the early prodromal phase, are closely linked to hypothetical core vulnerability of schizophrenia. These disturbances are presumed to be the phenotype of underlying neurophysiological deficits. The BSs are experiential, not behavioural in kind and only recognisable by the self-report of the patients. BSs are subjectively experienced disturbances of perception, cognition, language, motor function, will, initiative, level of energy and stress tolerance (Gross, 1997), operationalized by the

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Bonn Scale for Assessment of Basic Symptoms (BSABS, Gross et al., 1987), or the shorter version, Schizophrenia Prediction Instrument-Adult Version (SPI-A, Schultze-Lutter et al., 2004). The BSABS operationalization of prodromal symptoms performed well in the early detection of schizophrenia (Klosterkotter et al., 2001).

The ability to identify asymptomatic individuals at high risk for psychosis through low cost screening is greatly beneficial. The screening instrument is used in the first phase of a two-stage study, which is followed by assessment either with the Comprehensive Assessment of At-Risk Mental State (CAARMS, Yung et al., 2002) or the Structured Interview for Prodromal Symptoms (SIPS, McGlashen et al., 2003) in the second stage. The CAARMS and SIPS as well as the other commonly used screening instruments such as Prodromal Screening (PROD-Screen, Heinima et al., 2003), Prodromal Questionnaires (PQ, Loewy et al., 2005) and SIPS Screen (Miller et al., 2004) are based on the attenuated positive syndrome (APS) approach, which is aimed to detect the late prodromal phase, but less useful for detecting early psychosis (Olsen and Rosenbaum, 2006). While the BSABS (Gross et al., 1987) is more sensitive in detecting early prodromal phase.

Screening instrument with good validation indexes should be able to assess correctly asymptomatic individuals at risk (Corcoran et al., 2005). The objective of the study is to detect subjects at sub-threshold psychosis among the relatives of patients with schizophrenia and people of the general public; and evaluate the efficacy of the screening tools. There is a growing consensus in the field that UHR and BSs approach are complementary, providing criteria to detect different prodromal stages (Phillips et al., 2005). In contrast, this study is exploring the utility of a single screening instrument in detecting subjects at the earlier (sub-threshold UHR) and late prodromal stage (UHR). We would use a previous local screening questionnaire (Razali et al., 2011), which is design mainly to cover APS psychopathology, and the General Health Questionnaires (GHQ-12) in the initial stage. We hope to evaluate the sensitivity of APS psychopathology and usefulness of GHQ-12 in screening early psychosis.

2. Methods

2.1. Subjects

The selected subjects were divided equally into two groups, which were chosen through convenience sampling. The first and second degree relatives of patients with schizophrenia (DSM-IV-TR, American Psychiatric Association, 2000) between 12 and 30 years formed the first group; while the second group consisted of individuals from the general population within the same age group. The relatives of patients was selected for the study when they visited psychiatric ward during visiting hours or when they accompanied psychiatric patients to the psychiatric clinic of Hospital USM. Other members of the family were then contacted through telephone to arrange for an interview at home with the assistance of the Community Mental Health Team (CMHT) if they agreed for the study. Members of the general public were chosen from among the patients' neighbours, house-wives, hospital visitors, pedestrians, civil servants, hospital administrative staff, schools and college students. The Ethical Committee (Human), Universiti Sains Malaysia (USM) reviewed the research protocol and then approved the study.

2.1.1. Exclusion criteria

Subjects in both groups were excluded if they:

(i) declined to sign informed consent, or
(ii) had past history of psychotic illness or being treated with neuroleptics, or
(iii) had co-morbid substance abuse, mental retardation or organic mental disorders

Individuals from the general population were excluded if they:

(i) had history of major psychotic illness among the first and/or second degree relatives.

2.2. Assessment

2.2.1. Initial screening

Research assistance (RA) started the preliminary (first stage) screening using a validated Malay version of Screening Questionnaire (SQ) (Table 1) and the General Health Questionnaires (GHQ-12). The SQ is a 10-item question mainly covering APS psychopathology, which was modified from the SIPS (McGlashen et al., 2003). The cut-off scores of the SQ and GHQ-12 was 2 and 3 respectively (Razali et al., 2011).

2.2.2. Second stage screening

The research psychiatrists conducted the second stage assessment using the Comprehensive Assessment of At-Risk Mental State (CAARMS) and two other research tools, as summarized in the flow chart (Fig. 1). If positive findings were detected from CAARMS, they were further explored to assess the severity, frequency and duration of the symptoms. The Global Assessment of Function (GAF) scale (DSM-IV-TR, American Psychiatric Association, 2000) was then used to evaluate the current level of function. The presence of schizotypal personality disorder (PD) in second degree relatives and general individuals when their GAF scores dropped more than 30% from premorbid level was assessed with The Structured Clinical Interview for DSM-IV (SCID, American Psychiatric Association, 1994).

The positive subjects were classified according to two main categories: UHR (early prodromal stage) and sub-threshold UHR (late prodromal stage)

(i) The UHR category is further divided to two sub-groups (Yung et al., 2004a):
  (a) Brief limited intermittent psychotic symptoms (BLIPS) or attenuated psychotic symptoms (APS).
  (b) Vulnerable group (VG): The primary degree relatives and other subjects with schizotypal PD who sustained at least 30% drop in GAF score from premorbid level for a month.
(ii) A sub-threshold UHR category consists of sub-threshold APS (STAPS) and sub-threshold BLIPS (STBLIPS) in which the positive symptom (severity scale score) is less severe or the

Table 1
The Screening Questionnaires (SQ).

No.	Psychphatology assessed
1	Perceptual disturbances (auditory)
2	Suspiciousness/Persecutory idea
3	Perceptual disturbances (visual)
4	Unusual thought content
5	Impaired ability to initiate social contact
6	Delusional ideas
7	Delusion of being controlled/thought interference
8	Clairvoyance/Sixth sense
9	Conceptual disorganisation
10	Distorted body experiences/impaired bodily sensation

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