UNIVERSITY OF SOUTHAMPTON

FACULTY OF MEDICINE, HEALTH AND BIOLOGICAL SCIENCES

School of Medicine

Development and Psychometric Properties of a Semi-structured Clinical Interview for Psychosis Sub-groups (SCIPS)

by

Yoshihiro Kinoshita

Thesis for the degree of Doctor of Philosophy

June 2009

UNIVERSITY OF SOUTHAMPTON
ABSTRACT
FACULTY OF MEDICINE, HEALTH AND BIOLOGICAL SCIENCES
SCHOOL OF MEDICINE
Doctor of Philosophy
DEVELOPMENT AND PSYCHOMETRIC PROPERTIES OF
A SEMI-STRUCTURED CLINICAL INTERVIEW FOR
PSYCHOSIS SUB-GROUPS (SCIPS)
By Yoshihiro Kinoshita

Background: Schizophrenia has long been considered to be remarkably heterogeneous, and there have been a number of attempts to identify sub-groups of this disorder which are more homogeneous. Nevertheless, most of these have not been used in either research or clinical practice to any great extent, because diagnoses by way of these strategies would be unstable over time and impractical. In such circumstances, the vulnerability-stress model has led to the development of a new concept of sub-grouping schizophrenia into 4 sub-types – drug related, traumatic, anxiety, and stress sensitivity. This conceptualisation is quite promising, not only because it may provide stable and practical diagnoses, but also because the terminology used therein is useful when it comes to destigmatising those who are currently diagnosed with schizophrenia.

Methodology: In order to adapt this concept for practical use, this project set out to develop a semi-structured interview for making diagnoses according to it. Thereafter, psychometric properties of the interview were examined. This assessment tool was then used to confirm the longitudinal stability of the diagnosis. In order to establish the construct validity of this classification system, it was examined if the anxiety and stress sensitivity sub-groups in this system were different in terms of their external validators. Three psychopathological variables – evaluative belief, fear of negative evaluation from others, and depression – were assessed in a cross-sectional study during this process of validation. Three other clinical variables – two for the duration of hospitalization and one for the risk of self harming – were also used in a retrospective cohort study for the evaluation of the predictive value of the differentiation.

Results and conclusion: Both the English and Japanese versions of the semi-structured clinical interview for psychosis sub-groups (SCIPS) were developed to sub-group patients into 4 categories, and their reliability and concurrent validity were established. The 6 month stability of SCIPS diagnoses of the drug related, anxiety and stress sensitivity sub-types was also indicated through a longitudinal study. A preliminary analysis provided little evidence of construct validity. The risk of self harming was, however, suggested as being associated with a distinction between the anxiety and stress sensitivity categories when the SCIPS was applied to a broader range of psychosis, including schizophrenia and schizoaffective disorder.

Table of Contents

List of Tables

List of Figures

List of Appendices

DECLARATION OF AUTHORSHIP

I, Yoshihiro Kinoshita, declare that the thesis entitled "Development and Psychometric Properties of a Semi-structured Clinical Interview for Psychosis Sub-groups (SCIPS)" and the work presented in the thesis are both my own, and have been generated by me as the result of my own original research. I confirm that:

- this work was done wholly or mainly while in candidature for a research degree at this University;

- where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated;

- where I have consulted the published work of others, this is always clearly attributed;

- where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work;

- I have acknowledged all main sources of help;

- where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself;

- none of this work has been published before submission.

Signed: ……………………………………………………………………….

Date:……………………………………………………………………….

Acknowledgements

List of commonly used abbreviations

ATPD	Acute and transient psychotic disorder
BDI or BDI-II	Beck depression inventory
BFNE	Brief fear of negative evaluation scale
BPD	Borderline personality disorder
CBT	Cognitive behavioural therapy
CGI	Clinical global impressions
CI	Confidence interval
DSM	Diagnostic and statistical manual for mental disorders
FNE	Fear of negative evaluation from others
GAF	Global assessment of functioning scale
ICD	International classification of diseases
IQR	Inter-quartile range
LSD	Lysergic acid diethylamide
n	Number of subjects
OR	Odds ratio
PANSS	Positive and negative syndrome scale
PAS	Pre-morbid adjustment scale
PDI or PDI-21	21item Peters delusions inventory
Pearson's r	Pearson product-moment correlation coefficient
%	Percent
RCT	Randomised controlled trial
RR	Relative risk
SD	Standard deviation
SE	Standard error
SCID	Structured clinical interview for the DSM
SCIPS	Semi-structured clinical interview for psychosis subgroups
Spearman's r	Spearman rank correlation coefficient
SRRSQ	Social readjustment rating scale and questionnaire
SUD	Substance use disorders
TCI	Temperament and character inventory

Chapter 1: Classification in Psychiatry

1.1   Historical background

From ancient times, people have long attempted to understand and classify mental illness adequately. Hippocrates, for instance, suggested that thoughts and feelings occur in the brain, while Plato believed that the soul struggles to find a balance between 2 conflicting impulses, one noble, the other driven by desire (Turner, 2007). By these attempts, a question of disease entities has both arisen and led to the development of a theory with which to form the basis of the main purposes of psychiatry: to identify natural disorders which are different to one another in principle, and to present the characteristic symptomatology, course, cause and physical findings thereof, in which there are no transitions (Jaspers, 1959).

Although the formulation of classifications of psychopathology according to this theory attracted a great deal of interest during the nineteenth century, the identification of mental disorders in that period was crude by current standards (Blashfield, 1984). Some of the categories seen in the records of nineteenth century asylums were highly idiosyncratic and lacked general validity. Moreover, their meanings did not seem to be mutually exclusive. Hurd addressed both the variation in terminologies between the different institutions and the importance of adopting a uniform system (Hurd, 1881). During the 1800s, the interest in psychiatric classifications, and the need for a more systematic approach, culminated with the work of German psychiatrist, Emil Kraepelin (1919). Kraepelin's organization of mental disorders was proposed in his text books, and became the foundation of modern psychiatric classification systems.

The Diagnostic and Statistical Manual of Mental Disorders (first edition-DSM-I) (American Psychiatric Association, 1952) was published by the American Psychiatric Association in 1952, with the aim of creating a classification which was a consensus of contemporary thinking. At about the same time, in 1951, the World Health Organization (WHO) proposed, for the first time, an international psychiatric classification scheme as part of the International Classification of Diseases (sixth edition-ICD-6) (World Health

Organization, 1948). Since that time, an international movement to develop a consensual classification system was accelerated. The result was the publication of the mental disorder section of the International Classification of Diseases (eighth edition-ICD-8) (World Health Organization, 1967), and the Diagnostic and Statistical Manual of Mental Disorders (second edition-DSM-II) (American Psychiatric Association, 1968). Although standardization was achieved with the earlier versions of the DSM and ICD, the reliability of clinical diagnoses was still poor. Accordingly, attempts were made to address this problem in the DSM-III (American Psychiatric Association, 1980) and the ICD-9 (World Health Organization, 1977). The former was then replaced by the DSM-III-R in 1987, and the most recent version, DSM-IV, was published in 1994. Similarly, the current version of the ICD is in its tenth edition (ICD-10) (World Health Organization, 1992). The next versions of both volumes (DSM-V and ICD-11) are now in the development stage, and are expected to be published in the near future. A release of a final, approved DSM-V is expected in May 2012, while the final ICD-11 is likely to be submitted to the World Health Assembly for approval by 2014.

1.2   The purpose of classification

As described above, classification has been a necessary and fundamental process in psychiatry. To understand why it is so important, it is helpful to consider the purposes behind a good classification scheme. The primary purpose of such a system is to provide nomenclature, which is essential for communication between those working in the field (Blashfield, 1984). A classification scheme can facilitate this by providing descriptive information about each entity included therein, and provides a basis upon which to make predictions. For instance, once a clinician is told that a patient's diagnosis is a major depressive disorder, this will help him or her to attempt to discover information about probable symptoms, the likely course of the condition and the treatment plan. In addition to this primary purpose, a classification system can also be useful for theory formulation. For example, Linnaeus's categorisation of living organisms in biology provided a firm foundation for Darwin's theory of biological evolution (Blashfield, 1984).

1.3 Limitations of classification in psychiatry

Although classification is thought to be an essential process in psychiatry, such systems are often criticised. There are 3 main complaints (Blashfield, 1984). Firstly, many of the schemes that have existed have been proved to have unacceptably low reliability values. This is something which should be taken seriously, because 'there is no guarantee that a reliable system is valid, but assuredly an unreliable system must be invalid' (Blashfield, 1984). Secondly, there are concerns about validity. As referred to above, a reliable classification scheme is not necessarily valid. In fact, there is little empirical support for the clinical validity of most major mental disorders, although the introduction of the current diagnostic systems, the DSM and the ICD, has led to improvements in the reliability of diagnoses (Kendell, 1989). In other words, a question of whether psychiatric disorders represent discrete entities, or are simply situated on a continuum, cannot be answered. Thirdly, classification systems in psychiatry are often criticised from the perspective of labelling theory. This proposes that labels may become self-fulfilling, and can have a major effect on the individuals being identified thereby. For instance, it is often the case that patients diagnosed with schizophrenia are stigmatised, with the disorder recently being renamed as 'disintegration syndrome' in Japan (Kingdon et al., 2007; Sato, 2006).

Accordingly, whenever a new classification system for psychiatric disorders or their sub-types is proposed, it should be designed to achieve acceptable levels of reliability and clinical validity. Moreover, it is essential that patients are comfortable with, and less stigmatised, by their diagnoses, or the sub-types thereof, in the scheme.

1.4 Procedure for validating a classification system

Six strategies for the evaluation of a syndrome's clinical validity were outlined by Kendell (1989) (Table 1). In this approach, disorders are firstly identified and described by cluster analysis or 'clinical intuition'. Next, the 'boundaries' between the syndromes or 'points of rarity' are identified using statistical forms of assessment, such as discriminant function and latent class analyses. The construct validity of the conditions is then established. To achieve this, many different predictions can be made, based upon the

theory or construct that is related to the conceptualisation of the disorders. In other words, follow-up studies can be conducted to prove a distinctive course or outcome, while a distinctive treatment response can be established by therapeutic trials. Distinctions in terms of aetiology (i.e., cause of the syndromes) and association with more fundamental abnormalities (e.g., histological, psychological, social, biochemical or molecular) is also important.

Table 1: Validators of clinical syndromes (Kendell, 1989).

1. Identification and description of the syndrome, either by 'clinical intuition' or by cluster analysis.

2. Demonstration of boundaries or 'points of rarity' between related syndromes by discriminant function analysis, latent class analysis, etc.

3. Follow-up studies establishing a distinctive course or outcome.

4. Therapeutic trials establishing a distinctive treatment response.

5. Family studies establishing that the syndrome 'breeds true'.

6. Association with some more fundamental abnormality, whether histological, psychological, biochemical or molecular.

In fact, it has been indicated that diagnostic categories should only be deemed valid when they are shown to be different in terms of several key variables, such as clinical descriptions, genetic factors and prognoses (Kendell & Jablensky, 2003; Robins & Guze, 1970). Possible diagnostic indicators were organised into 3 classes: antecedent (e.g., familial aggregation and pre-morbid personality), concurrent (e.g., psychological tests) and predictive validators (e.g., diagnostic stability and prognosis) (Kendler, 1980). In other words, a classification system can be validated and will be clinically relevant if the sub-types differ in the levels of the external validators, which are not included in the original diagnostic criteria. In addition, broad measures of clinical outcome can be introduced as such validators.

1.5   Summary

The history of classification in psychiatry can be traced back to, at least, the era of Hippocrates and Plato. Since the late nineteenth or early twentieth century, however, a

contemporary psychiatric classification system has been developed, to which Kraepelin made a significant contribution. Nowadays, 2 major schemes, the DSM and the ICD, are commonly employed for the categorisation of mental disorders. Although classification has been an essential and fundamental process in psychiatry, there have been many controversies relating to a number of both the previous and current systems, mainly because their levels of reliability and validity are unacceptable, and the labels employed tend to have self-fulfilling features which have a major effect on the individuals being identified thereby. In order to validate such a system, a procedure with 6 strategies was proposed, in which external validators can be employed to establish the construct validity of the classification.

Chapter 2: The Classification of Schizophrenia

2.1 Overview

Schizophrenia has a remarkably heterogeneous clinical presentation. In fact, there is general agreement that the patients who meet the criteria for the illness, according to the current versions of the DSM or ICD, are a very diverse group (Myin-Germeys, Delespaul, & van Os, 2005; van Os, 2009), which overlaps with bipolar disorder (Berrettini, 2000; Boks et al., 2007). Ever since the conceptualisation of schizophrenia by Kraepelin and Bleuler, it has been thought that there are sub-types thereof. Both the DSM-IV and ICD-10 provide the concepts behind and the diagnostic criteria for these sub-types, which are derived from the original schemes proposed by Kraepelin and Bleuler. Furthermore, other concepts for classification, such as positive vs. negative and familial vs. non-familial schizophrenia, have also been provided with the aim of achieving greater stability and validity.

2.2 Definition of psychosis and schizophrenia

In Kaplan and Sadock's Comprehensive Textbook of Psychiatry, psychosis is defined as 'a mental disorder in which the thoughts, affective response, ability to recognize reality, and ability to communicate and relate to others are sufficiently impaired to interfere grossly with the capacity to deal with reality; the classical characteristics of psychosis are impaired reality testing, hallucinations, delusions and illusions' (Sadock & Sadock, 2000a). Schizophrenia is described thus: 'Schizophrenia is the paradigmatic illness of psychiatry. It is a clinical syndrome of variable but profoundly disruptive psychopathology, which involves thought, perception, emotion, movement, and behaviour. The expression of these symptoms varies across patients and over time, but the cumulative effect of the illness is always severe and usually long lasting' (Sadock & Sadock, 2000b). In this thesis, I recognise that the conceptualisation of schizophrenia can be included in that of psychosis. In other words, the conceptualisation of the latter is broader and covers more than that of the former.

With regard to the diagnostic criteria for schizophrenia, those provided in the Diagnostic and Statistical Manual for Mental Disorders 4th edition (DSM-IV) (American Psychiatric Association, 2000) were used in this study.

2.3   The evolution of schizophrenia classification

Since Kraepelin (1919) first proposed the concept of dementia praecox, and, in his textbook (Bleuler, 1911), Bleuler broadened it, coining the term 'the schizophrenias' to refer to this conceptualisation, there have been a number of attempts to define the sub-groups of this illness by consensus classification. In this section, a perspective on the concepts of these sub-types will be described.

In his original thinking, dementia praecox, catatonia and dementia paranoides were proposed by Kraepelin as being 3 independent conditions (Kraepelin, 1919). In addition, he also listed 3 forms of dementia praecox: mild, severe and hebephrenia. Bleuler (1911), on the other hand, developed his conceptualisation of schizophrenia, including the dementia praecox, catatonia and dementia paranoides that were originally conceptualised by Kraepelin, by dividing the disorder into 4 sub-types: hebephrenic, catatonic, paranoid, and simple. This is the concept which was, essentially, adopted in the DSM-IV and the ICD-10 (see Table 2).

2.4   Classification systems in the DSM-IV and ICD-10

The schemes proposed by both the DSM and the ICD are widely used for classification purposes in schizophrenia research. The DSM-IV includes 4 main sub-types of the disorder: paranoid, disorganised, catatonic, and residual, as well as a further category, undifferentiated. Alternatively, the ICD-10 provides 5 main schizophrenia sub-groups: paranoid, hebephrenic, catatonic, residual and simple, as well as the additional categories of undifferentiated schizophrenia and post-schizophrenic depression. Table 2 presents the diagnostic criteria for these sub-types in the DSM-IV and the ICD-10.

Table 2: Diagnostic criteria for the sub-types of schizophrenia listed in the DSM-IV and the ICD-10 (American Psychiatric Association, 2000; World Health Organization, 1992).

DSM-IV

Paranoid Type

A type of schizophrenia in which the following criteria are met:

A. Preoccupation with one or more delusions or frequent auditory hallucinations.

B. None of the following is prominent: disorganised speech, disorganised or catatonic behaviour, or flat or inappropriate affect.

Disorganised Type

A type of schizophrenia in which the following criteria are met:

A. All of the following are prominent:

   (1) Disorganised speech

   (2) Disorganised behaviour

   (3) Flat or inappropriate affect

B. The criteria are not met for catatonic type.

Catatonic Type

A type of schizophrenia in which the clinical picture is dominated by at least two of the following:

(1) Motoric immobility as evidenced by catalepsy (including waxy flexibility) or stupor.

(2) Excessive motor activity (that is apparently purposeless and not influenced by external stimuli).

(3) Extreme negativism (an apparently motiveless resistance to all instructions or maintenance of a rigid posture against attempts to be moved) or mutism.

(4) Peculiarities of voluntary movement as evidenced by posturing (voluntary assumption of inappropriate or bizarre postures), stereotyped movements, prominent mannerisms, or prominent grimacing.

(5) Echolalia or echopraxia.

Table 2 continued.

Undifferentiated Type

A type of schizophrenia in which symptoms that meet Criterion A* are present, but the criteria are not met for the paranoid, disorganised, or catatonic type.

Residual Type

A type of schizophrenia in which the following criteria are met:

A. Absence of prominent delusions, hallucinations, disorganised speech, and grossly disorganised or catatonic behaviour.

B. There is continuing evidence of the disturbance, as indicated by the presence of negative symptoms or two or more symptoms listed in Criterion A for schizophrenia*, present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

*Criterion A for Schizophrenia

A. Characteristic symptoms: Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated):

(1) Delusions

(2) Hallucinations

(3) Disorganised speech (e.g., frequent derailment or incoherence)

(4) Grossly disorganised or catatonic behaviour

(5) Negative symptoms, i.e., affective flattening, alogia, or avolition

Note: Only one Criterion A symptom is required if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behaviour or thoughts, or two or more voices conversing with each other.

ICD-10

Paranoid schizophrenia

A. The general criteria for schizophrenia must be met.

B. Delusions or hallucinations must be prominent (such as delusions of persecution, reference, exalted birth, special mission, bodily change, or jealousy; threatening or commanding voices, hallucinations of smell or taste. sexual or other bodily sensations).

Table 2 continued.

C. Flattening or incongruity of affect, catatonic symptoms, or incoherent speech must not dominate the clinical picture, although they may be present to a mild degree.

Hebephrenic schizophrenia

A. The general criteria for schizophrenia must be met.

B. Either of the following must be present:

(1) Definite and sustained flattening or shallowness of affect;

(2) Definite and sustained incongruity or inappropriateness of affect.

C. Either of the following must be present:

(1) Behaviour that is aimless and disjointed rather than goal directed;

(2) Definite thought disorder, manifesting as speech that is disjointed, rambling, or incoherent.

D. Hallucinations or delusions must not dominate the clinical picture, although they may be present to a mild degree.

Catatonic schizophrenia

A. The general criteria for schizophrenia must eventually be met, although this may not be possible initially if the patient is uncommunicative.

B. For a period of at least 2 weeks one or more of the following catatonic behaviours must be prominent:

(1) Stupor (marked decrease in reactivity to the environment and reduction of spontaneous movements and activity) or mutism;

(2) Excitement (apparently purposeless motor activity, not influenced by external stimuli);

(3) Posturing (voluntary assumption and maintenance of inappropriate or bizarre postures);

(4) Negativism (an apparently motiveless resistance to all instructions or attempts to be moved, or movement in the opposite direction);

(5) Rigidity (maintenance of a rigid posture against efforts to be moved);

(6) Waxy flexibility (maintenance of limbs and body in externally imposed positions);

(7) Command automatism (automatic compliance with instructions).

Table 2 continued.

Undifferentiated schizophrenia

A. The general criteria for schizophrenia must be met.

B. Either of the following must apply:

　(1) Insufficient symptoms to meet the criteria for any of the following: paranoid schizophrenia, hebephrenic schizophrenia, catatonic schizophrenia, post-schizophrenic depression, or residual schizophrenia.

　(2) So many symptoms that the criteria for more than one of the sub-types listed in (1) above are met.

Post-schizophrenic depression

A. The general criteria for schizophrenia (F20.0-F20.3) must have been met within the past 12 months, but are not met at the present time.

B. One of the conditions in criterion G1 (2) a, b, c, or d* for F20.0-F20.3 must still be present.

C. The depressive symptoms must be sufficiently prolonged, severe, and extensive to meet criteria for at least a mild depressive episode.

Residual schizophrenia

A. The general criteria for schizophrenia must have been met at some time in the past, but are not met at the present time.

B. At least four of the following 'negative' symptoms have been present throughout the previous 12 months:

　(1) psychomotor slowing or underactivity;

　(2) definite blunting of affect;

　(3) passivity and lack of initiative;

　(4) poverty of either the quantity or the content of speech;

　(5) poor non-verbal communication by facial expression, eye contact, voice modulation, or posture;

　(6) poor social performance or self-care.

Simple schizophrenia

A. There is slow but progressive development, over a period of at least 1 year, of all three of the following:

Table 2 continued.

(1) a significant and consistent change in the overall quality of some aspects of personal behaviour, manifest as loss of drive and interests, aimlessness, idleness, a self-absorbed attitude, and social withdrawal;

(2) gradual appearance and deepening of 'negative' symptoms such as marked apathy, paucity of speech, under-activity, blunting of affect, passivity and lack of initiative, and poor non-verbal communication (by facial expression, eye contact, voice modulation, and posture);

(3) marked decline in social, scholastic, or occupational performance.

B. At no time are there any of the symptoms referred to in criterion G1 for paranoid schizophrenia, hebephrenic schizophrenia, catatonic schizophrenia, and undifferentiated schizophrenia, nor are there hallucinations or well formed delusions of any kind, i.e., the individual must never have met the criteria for any other type of schizophrenia or for any other psychotic disorder.

C. There is no evidence of dementia or any other organic mental disorder listed in F00-F09.

* Criterion G1 for F20.0-F20.3

G1. Either at least one of the syndromes, symptoms, and signs listed under (1) below, or at least two of the symptoms and signs listed under (2) should be present for most of the time during an episode of psychotic illness lasting for at least 1 month (or at some time during most of the days).

(1) At least one of the following must be present:

(a) thought echo, thought insertion or withdrawal, or thought broadcasting;

(b) delusions of control, influence, or passivity, clearly referred to body or limb movements or specific thoughts, actions, or sensations; delusional perception;

(c) hallucinatory voices giving a running commentary on the patient's behaviour, or discussing the patient among themselves, or other types of hallucinatory voices coming from some part of the body.

Table 2 continued.

(d) persistent delusions of other kinds that are culturally inappropriate and completely impossible (e.g., being able to control the weather, or being in communication with aliens from another world).

(2) or at least two of the following;

(a) persistent hallucinations in any modality, when occurring every day for at least 1 month, when accompanied by delusions (which may be fleeting or half-formed) without clear affective content, or when accompanied by persistent over-valued ideas;

(b) neologisms, breaks, or interpolations in the train of thought, resulting in incoherence or irrelevant speech;

(c) catatonic behaviour, such as excitement, posturing or waxy flexibility, negativism, mutism, and stupor;

(d) 'negative' symptoms, such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses (it must be clear that these are not due to depression or to neuroleptic medication).

2.5   Other proposed classification systems

Although the diagnostic criteria for sub-types of schizophrenia are provided in both the DSM-IV and the ICD-10, there has been some criticism that these diagnoses are not stable over time (Kendler, Gruenberg, & Tsuang, 1985), and that their validity is not sufficiently high (Goldberg & Weinberger, 1995). Accordingly, other concepts for classification have been provided, so as to achieve greater stability and validity. Two main schemas, and some less significant others, have been adopted to provide such conceptualisation (Goldberg & Weinberger, 1995).

2.5.1   Positive vs. negative schizophrenia

Based upon the symptoms of schizophrenia, it was proposed that the illness could be divided into 2 main categories where there are positive and negative symptoms, and a remaining sub-type of 'mixed schizophrenia' for the patients who do not meet the aforementioned criteria, or meet the criteria for both (Andreasen & Olsen, 1982). In this concept, discrimination between positive and negative schizophrenia is based upon whether the symptoms of the disorder are predominantly positive (or florid), or predominantly negative (or deficit) (Table 3). Furthermore, an additional proposal was presented in which positive symptoms could be further divided into 2 classes, one of which is related to disorganised symptoms, while the other is associated with reality distortion, such as delusions and hallucinations (Liddle & Barnes, 1990). Alternatively, the concept of the deficit sub-type, developed by Carpenter and others, is almost the same as that behind negative schizophrenia, as proposed by Andreasen and her colleagues (Kirkpatrick et al., 1989). In this context, the deficit sub-type of schizophrenia is defined in terms of prominent, primary negative symptoms which endure for a long period of time (Kirkpatrick et al., 2001) (Table 4).

Table 3: Diagnostic criteria for positive and negative schizophrenia (Andreasen & Olsen, 1982).

Positive schizophrenia

1. At least one of the following is a prominent part of the illness.
    a. Severe hallucinations that dominate the clinical picture (auditory, haptic, or olfactory)(The judgement of severity should be based on various factors such as persistence, frequency, and effect on lifestyle.)
    b. Severe delusions (may be persecutory, jealous, somatic, religious, grandiose, or fantastic)(The judgement of frequency should be made as described for severity.)
    c. Marked positive formal thought disorder (manifested by marked incoherence, derailment, tangentiality, or illogicality)
    d. Repeated instances of bizarre or disorganised behaviour.
2. None of the following is present to a marked degree.
    a. Alogia
    b. Affective flattening
    c. Avolition-apathy
    d. Anhedonia-asociality
    e. Attentional impairment

Negative schizophrenia

1. At least two of the following are present to a marked degree.
    a. Alogia (e.g., marked poverty of speech, poverty of content of speech)
    b. Affective flattening
    c. Anhedonia-associality (e.g., inability to experience pleasure or to feel intimacy, few social contacts)
    d. Avolition-apathy (e.g., anergia, impersistence at work or school)
    e. Attentional impairment
2. None of the following dominates the clinical picture or is present to a marked degree.
    a. Hallucinations
    b. Delusions
    c. Positive formal thought disorder

Table 3 continued.

   d.   Bizarre behaviour

Mixed schizophrenia

This category includes those patients that do not meet criteria for either positive or negative schizophrenia, or meet criteria for both.

Table 4: Diagnostic criteria for deficit schizophrenia (Kirkpatrick et al., 2001).

1. At least 2 of the following 6 features must be present and of clinically significant severity:

    Restricted affect

    Diminished emotional range

    Poverty of speech

    Curbing of interests

    Diminished sense of purpose

    Diminished social drive

2. Two or more of these features must have been present for the preceding 12 months, and always have been present during periods of clinical stability (including chronic psychotic states). These symptoms may or may not be detectable during transient episodes of acute psychotic disorganisation or decompensation.

3. Two or more of these enduring features are also idiopathic, i.e., not secondary to factors other than the disease process. Such factors include:

    Anxiety

    Drug effect

    Suspiciousness

    Formal thought disorder

    Hallucinations or delusions

    Mental retardation

    Depression

4. The patient meets DSM criteria for schizophrenia.

2.5.2 Familial vs. non-familial schizophrenia

Based upon the concept of heredity schizophrenia, there have been some attempts to classify the illness into familial and non-familial sub-types (Roy & Crowe, 1994). The former is defined by a family history of psychotic disorders, while 'sporadic schizophrenia' is defined by the absence of such a history (John et al., 2007).

2.5.3 Other classification schemes

In terms of neurophysiology and neuroanatomy, it was recognized that there is a group of schizophrenia patients who demonstrate either prefrontal cortical hypofunction (Weinberger & Berman, 1996) or small ventricular size (Crow, 1985). In addition, other researchers have attempted to identify specific groups by using other approaches (John et al., 2007; Magri et al., 2007). Indeed, John and his colleagues sub-group patients with schizophrenia according to neurometric analyses of quantitative electroenchephalography (John, Prichep, & Easton, 1994). On the other hand, Magri et al attempted to demonstrate the association between mitochondria DNA haplotypes and the onset of the disorder (Magri et al., 2007).

2.6 Summary

Schizophrenia has a remarkably heterogeneous clinical presentation. Indeed, since Kraepelin (1919) first proposed the concept of dementia praecox, and Bleuler (1911) extended it, coining the term schizophrenia when referring to this conceptualisation in his book , there have been several attempts to define categories of the illness by consensus classification. Both the DSM-IV and the ICD-10 provide the conceptualisation and diagnostic criteria for schizophrenia sub-types, which are derived from the original schemes proposed by Kraepelin and Bleuler. In addition, concepts for classification, such as positive vs. negative and familial vs. non-familial schizophrenia, have also been utilized to achieve greater stability and validity.

Chapter 3: Arguments on the Classification of Schizophrenia

3.1   Overview

As with classification systems in general, a number of difficulties in relation to the sub-types of schizophrenia have been proposed. In fact, although quite a few concepts have been used to identify sub-groups of the illness, these categories have not been utilised in research or clinical practice to any great extent, mainly because these concepts for classification have not been properly validated. Accordingly, in this chapter, the validity of the current schemes for the categorisation of schizophrenia is discussed. The focus is on 2 of the major components thereof, namely the stability and prognostic value of classification, since their establishment is an essential process for confirming the value of such systems in research and clinical practice.

3.2   Controversies about the DSM and ICD schemes for the classification of schizophrenia

Two key problems, namely the instability of diagnoses and a lack of prognostic quality, are proposed as reducing the worth of these 2 major classification systems. Indeed, one study revealed that diagnoses obtained through these strategies were unstable over time and impractical (Kendler, Gruenberg, & Tsuang, 1985). In that research, the long term stability of the sub-types of schizophrenia, as defined by 4 diagnostic systems (DSM-III, Research Diagnostic Criteria, ICD-9, and the criteria proposed by Tsuang and Winokur), were examined, with the consequence being that their constancy was not satisfactorily established. For example, the corrected kappa values of all of the sub-groups diagnosed with the DSM-III and the ICD-9 were 0.19 (Standard error (SE) = 0.08) and 0.45 (SE = 0.16) respectively. These results indicate that the diagnoses would not be useful for research or clinical practice purposes, because it is necessary to reconsider them over time as a consequence of changes that occur. The limited stability of the sub-types was also indicated in other work conducted by Deister and Marneros (1993). This study examined the long-term stability of the sub-groups of patients diagnosed with schizophrenia (n = 100) according to the DSM-III-R and the ICD-10. As summarized in Table 5, a category change was found in many cases, and particularly in some of the

specific sub-types (DSM-III-R: disorganized and catatonic; ICD-10: hebephrenic, catatonic and residual). In fact, no instances of a stable course were discovered at all, with the kappa values for the concordance of the sub-types between the first and second episodes, using the DSM-III-R and ICD-10 schemes, being 0.24 and 0.30 respectively.

Table 5: Summary of the long-term stability of the sub-types as shown in Deister's paper (n = 100) (Deister & Marneros, 1993).

Initial sub-type	Patients with stable course
DSM-III-R	
Paranoid type (n = 31)	14 (45.2%)
Disorganised type (n = 7)	0 (0.0%)
Catatonic type (n = 6)	0 (0.0%)
Undifferentiated type (n = 33)	3 (9.1%)
Residual type (n = 23)	4 (17.4%)
ICD-10	
Paranoid (n = 48)	18 (37.5%)
Hebephrenic (n = 7)	0 (0.0%)
Catatonic (n = 6)	0 (0.0%)
Undifferentiated (n = 28)	7 (25.0%)
Residual (n = 11)	0 (0.0%)

In terms of the predictive value of the classification systems, 2 key studies have been conducted to demonstrate that these sub-types are predictors of important patient outcomes, such as prognoses and response to medication. Firstly, Kendler and his colleagues examined the short (2.5 years) and long term (24 years) outcomes in terms of social and clinical factors (i.e., residential, occupational and psychiatric status) (Kendler, Gruenberg, & Tsuang, 1984). However, no statistically significant differences were found in the short term outcomes of the sub-types diagnosed with the DSM-III or ICD-9. In terms of the long term outlook, although differences were revealed between the paranoid and the non-paranoid sub-groups (see Table 6), there was no distinction between the hebephrenic and undifferentiated categories.

Although differences which implicate the predictive quality of the paranoid sub-type of schizophrenia were found, this study has 2 critical problems in terms of its design and the procedure used for statistical analysis. Firstly, all of the diagnoses were made by

retrospectively reviewing the index admission charts of the patients from the IOWA 500 study, which had been conducted for other purposes. Indeed, the diagnoses of the sub-types may well be biased by the information which was recorded in the charts, which gave each patient's outcome. Secondly, type I errors, or false positives, caused by multiple comparisons, were not considered when the statistical analyses were carried out. This means that differences might be found where, in truth, there are none.

Table 6: Summary of the differences in long-term outcome shown in Kendler's paper (Kendler, Gruenberg, & Tsuang, 1984).

Diagnostic system	Comparison P v H			Comparison P v U		
	R	O	P	R	O	P
DSM-III		X			X	X
ICD-9	X	X	X	N/A	N/A	N/A

P: Paranoid sub-type; H: Hebephrenic sub-type; U: Undifferentiated sub-type.
R: Residential outcome; O: Occupational outcome; P: Psychiatric outcome.
Comparisons which showed significant differences (p < 0.05) were indicated with an 'X'.
N/A: Undifferentiated sub-type is not provided in the ICD-9.
There was no difference between the hebephrenic and undifferentiated sub-types.

Another study which examined the difference in outcomes between sub-groups, and used a procedure which was similar to that applied in the earlier piece of work, was conducted by Kendler and his colleagues (1994). In this research, outcomes were assessed from clinical (e.g., chronicity and hospitalization) and functional (e.g., occupation and social interaction) perspectives. It was reported that paranoid schizophrenia had a substantially better outcome than the other categories of the disorder. However, as in the case of the previous work, this study was not prospective, and did not involve an independent assessment of diagnosis and outcome. In addition, the number of patients with the catatonic sub-type was limited, with only 4 individuals diagnosed as having this category of the illness by both the DSM-III and the ICD-9. Accordingly, it was difficult to reach a conclusion where this form of the illness was compared to the others.

On top of these 2 main studies, Fenton and McGlashan also conducted research which aimed to establish the longitudinal stability and prognostic value of a similar classification system (Fenton & McGlashan, 1991a). In this study, neither the DSM nor

the ICD schemes were used for the classification. Instead, diagnostic criteria based on items from Tsuang-Winokur's work and the DSM-III were developed and used. The issue examined was the differences in short and long-term outcomes between the sub-types, with regard to clinical course (e.g., chronicity and hospitalization) and social functioning (e.g., occupation and social interaction). As in Kendler's study (Kendler, Gruenberg, & Tsuang, 1984), no statistically significant distinction was found in short-term outcome between the sub-types. So far as the long-term outlook was concerned, differences were revealed in the paranoid, hebephrenic, and undifferentiated categories (Table 7). However, this study's design is also retrospective. Moreover, the stability of the sub-types was unsatisfactory. Indeed, on the basis of the diagnostic criteria used therein, only 66% of all patients remained in the same sub-group over the 2 time points of the assessment (kappa coefficient = 0.44).

Table 7: Summary of the differences in long-term outcome shown in Fenton's paper (Fenton & McGlashan, 1991a).

	Significant Post Hoc Differences at P < 0.05
Hospital time since discharge	P > H, U > H
Frequency of social contact	P > H, U > H
Time symptomatic since discharge	P > H, U > H
Sum global outcome since discharge	P > H, U > H
Clinical global outcome, No. (%) fair, good, recovered	P > H, U > H
Current living situation, No. (%) sheltered or with family of origin	P > H, U > H

P: Paranoid sub-type; H: Hebephrenic sub-type; U: Undifferentiated sub-type.

3.3   Controversies about other proposed classification systems

As described in Chapter 2 ("The Classification of Schizophrenia"), 2 other classification systems, positive vs. negative and familial vs. non-familial schizophrenia, have been proposed, and attempts have been made to validate them. The value of these schemes is discussed below.

3.3.1   Positive vs. negative schizophrenia

As in the case of the DSM and ICD systems, the instability of diagnoses is the major problem. Deister and Marneros (1993) evaluated the long-term stability of the sub-types

(positive, negative, and mixed schizophrenia) therein, and revealed that an initial allocated category frequently changed over time (see Table 8). Indeed, in their study of positive/negative schizophrenia, the kappa value for the concordance of the sub-types between the first and second episodes was 0.21. Kay and Singh (1989) also examined the stability of positive and negative syndromes by assessing the correlation between drug-free baseline and post-neuroleptic treatment for both positive and negative symptoms. The correlation coefficients for these symptoms (Pearson product-moment correlation coefficient (Pearson's r) = 0.37 and 0.43, respectively) did not seem to be large enough to establish the stability thereof, although the correlations themselves were statistically significant.

Table 8: Long-term stability of positive/negative schizophrenia shown in Deister's study (Deister & Marneros, 1993).

Initial sub-type	Patients with stable course
Positive schizophrenia (n = 50)	18 (36.0%)
Mixed schizophrenia (n = 20)	2 (10.0%)
Negative schizophrenia (n = 30)	6 (20.0%)

3.3.2 Familial vs. non-familial schizophrenia

In order to provide theoretical and empirical support for the validity of this classification system, a review was completed in which 69 articles comparing familial and sporadic schizophrenic patients were analysed (Roy & Crowe, 1994). Despite a substantial number of comparisons between groups of patients with these forms of the disorder, very few differences were found in terms of clinical symptomatology, age of onset, pre-morbid functioning, outcome, and treatment response.

With regard to the prognostic value of this distinction, 2 studies among the 69 articles reviewed examined long-term outcomes. One of these (Alda et al., 1991) compared clinical variables (i.e., illness course, residual symptoms and number and duration of hospitalizations) between the 2 sub-types, while the other (Kendler & Tsuang, 1988) examined social factors (i.e., marital, residential and occupational status). However, neither study revealed any differences between the 2 sub-groups. In addition, other

research evaluated the response to neuroleptics, which was assessed by symptom severity before and after 6 weeks of treatment with no less than 600mg/day of chlorpromazine equivalents. No differences were found in the improvement of symptoms between the 2 groups.

3.4   Summary

Concepts relating to sub-types of schizophrenia are proposed in the DSM-IV and ICD-10, which are, in turn, derived from the conceptualisation by Kraepelin. Nevertheless, there is little empirical support for the predictive value of these systems. Moreover, diagnoses made with these schemes demonstrate little longitudinal stability. Likewise, the clinical validity of 2 other classification systems, positive vs. negative and familial vs. non-familial schizophrenia, has not yet been established. It is, therefore, questionable whether these approaches are useful, either clinically, or for research purposes.

Chapter 4: Psychosocial Factors and Psychosis

4.1 Overview

As described in Chapter 1 "Classification in Psychiatry", the first step in the development or validation of a new classification system is to identify and describe syndromes (or sub-types) by 'clinical intuition' or cluster analysis. This process should commence with the selection of potential variables that can be used to describe the conditions (Kendell, 1989). In this chapter, the psychosocial and clinical factors which have been proved to be associated with psychosis are explained, and a new conceptualisation for the classification of this disorder, in which these same elements are employed, is described.

4.2 Vulnerability-stress model

In the vulnerability-stress hypothesis of schizophrenia (Nuechterlein et al., 1994; Nuechterlein & Dawson, 1984; Zubin & Spring, 1977), vulnerabilities and stresses are thought to combine to produce the characteristics of the disorder. The precise symptoms (e.g., voices or delusions) and combinations thereof (e.g., any of the clinical sub-groups described later) which occur are determined by the nature of the vulnerabilities and stresses experienced. People who are susceptible due to genetic weighting, poor obstetric care, and negative schemas may become psychotic through the occurrence of environmental stressors such as drug use, trauma, or the accumulation of social problems. These negative schemas, the lack of support, the use of hallucinogens, and a generally impoverished social environment in which there is victimization, will then act to maintain psychotic symptoms.

4.3 Psychosocial factors associated with psychosis

With regard to the vulnerability-stress model, some specific psychosocial factors have been demonstrated to be associated with psychosis or schizophrenia (Cantor-Graae, 2007). These include ethnic minority or migration (Boydell et al., 2001; Cantor-Graae & Pedersen, 2007), childhood trauma (Janssen et al., 2004), borderline personality (Miller et al., 1993), drug misuse (Talamo et al., 2006), stressful life events (Cullberg, 2003), and stress sensitivity (Myin-Germeys et al., 2001; Myin-Germeys & van Os, 2007). For

instance, in terms of the relationship between migration and schizophrenia, immigration has been shown to be linked to the development of the illness. Indeed, in one meta-analysis (Cantor-Graae & Selten, 2005), it was found that the overall relative risk of developing schizophrenia in first and second-generation immigrants in Europe and Australia was 2.9 (95% confidence interval (CI) = 2.5-3.4). The association between other psychosocial factors and schizophrenia and psychosis will be discussed below.

4.3.1 Trauma and psychosis

It has been suggested that trauma is linked to psychosis (Morrison, Read, & Turkington, 2005). Indeed, various studies have demonstrated that there is a high incidence of trauma in the histories of individuals with this condition (Bebbington et al., 2004; Mueser et al., 1998; Read et al., 2005). It has also been shown that early childhood trauma increases the risk for positive psychotic symptoms (Janssen et al., 2004). In that research, data was derived from a general population sample of 4,045 subjects, aged 18-64 years, and the baseline reported childhood abuse was predictive of the development of positive psychotic symptoms associated with the need for care (Odds ratio (OR) = 7.3, 95% CI = 1.1-49.0). Indeed, several lines of evidence suggest that there is an association between trauma and psychosis.

Nevertheless, others have suggested that the evidence that childhood trauma causes psychosis is controversial and contestable (Morgan & Fisher, 2007). These researchers insisted that the findings from studies which demonstrated a relationship between early trauma and psychosis were not totally consistent, and had a number of methodological limitations. For instance, in many of the population-based studies which aimed to demonstrate the relationship between childhood trauma and psychotic symptoms, sexual abuse was assessed with a single question, and no account was taken of timing, duration, or the severity of the abuse, and no distinction was made between childhood and adult exposure thereto.

The evidence is even more controversial when it comes to which type of trauma is the most powerful predictor of later psychiatric symptoms. Childhood trauma is generally classified into 4 categories: sexual, physical, and emotional abuse and neglect (Morgan & Fisher, 2007). Read and Argyle reported a high incidence of physical and sexual abuse in particular, in patients with psychosis (Read & Argyle, 1999). It has also been noted that physical abuse is associated with positive psychotic symptoms, while sexual abuse is specifically related to hallucinations (Kilcommons & Morrison, 2005). In another study, in which data from a general population sample of over 8,000 individuals in the US was analysed, physical abuse was shown to predict psychosis, while sexual abuse or neglect was not (Shevlin, Dorahy, & Adamson, 2007). Although very few articles can be found which have explored a link between childhood emotional abuse and psychosis, there is one which suggested that physical neglect and emotional abuse demonstrate a significant correlation with dissociative symptoms in patients with schizophrenia spectrum disorders (Schafer et al., 2006).

In conclusion, there is an increasing amount of evidence which suggests that there is an association between childhood trauma and psychosis, although it should be interpreted cautiously. Further research is, therefore, clearly needed into which type of trauma best predicts the development of psychotic symptoms.

4.3.2 Borderline personality and psychosis

Although the evidence of an association between borderline personality and psychotic symptoms is not strong, some studies and case reports (Suzuki et al., 1998) have suggested that psychosis can be related to this personality disorder. Dowson and his colleagues demonstrated that the DSM-III diagnosis of borderline personality disorder (BPD) predicts the past experience of psychotic phenomena, 2 of which are "smelling things that other people couldn't" and "thoughts were taken out of your head" (Dowson et al., 2000). Furthermore, it was revealed that 27% of patients with BPD (n = 92) had had psychotic episodes, typically lasting many weeks (Miller et al., 1993).

Nevertheless, in clinical practice, patients with a diagnosis of schizophrenia can demonstrate characteristics of borderline personality, even before their first psychotic episodes. Moreover, the co-morbidity of BPD with schizophrenia or other psychotic disorders should be taken into consideration. This is particularly the case when cognitive behavioural therapy (CBT) is conducted with patients with schizophrenia, since co-morbid BPD could have a major impact on the treatment plan. There is one study which examined the impact of co-morbid BPD on patients with schizophrenia (Kingdon et al. in submission). In it, the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 1997) was administered to people with schizophrenia who did, or did not, have co-morbid BPD. It was demonstrated that sexual and emotional abuse is more associated with individuals who have this co-morbidity than those who do not. On the other hand, it was also found that the difference between these patient groups was less, although still, significant, with regard to childhood physical abuse.

In conclusion, it has been suggested in some studies that BPD predicts the development of psychotic symptoms. Accordingly, the existence of co-morbid BPD with schizophrenia should be considered when CBT is conducted with schizophrenic patients. It also seems to be important to provide a definition of a sub-group of psychosis, or schizophrenia, with co-morbid BPD. Moreover, co-morbid BPD with schizophrenia is predictive of the existence of childhood sexual or emotional abuse.

4.3.3 Drug misuse and psychosis

Co-morbid substance misuse is common among patients with schizophrenia, both in the UK and elsewhere (Talamo et al., 2006). Although it should be taken into account that different types of substances have been included in studies (e.g., cannabis, stimulants), the prevalence of substance use disorders (SUD) in patients with schizophrenia has been estimated to be around 33%, and even as high as 60% (Fowler et al., 1998). This latter percentage is almost five times as great as drug abuse rates in the general population (Regier et al., 1990; Talamo et al., 2006). In fact, it has been suggested that schizophrenia patients 'self-medicate' after the onset of the illness to relieve negative symptoms,

depression, and the adverse effects of their medication (Addington & Duchak, 1997; Dixon et al., 1991; Fowler et al., 1998). In other words, substances are used by patients to relieve boredom, facilitate social interactions, or for novelty purposes (Talamo et al., 2006), although some data has disproved this theory (D'Souza et al., 2005; Salyers & Mueser, 2001; Sevy et al., 1990). Alternatively, SUD (especially cannabis abuse) may either precede, and even precipitate, psychosis (Hambrecht & Hafner, 1996; Zammit et al., 2002), or the neuropathophysiology of psychosis may increase vulnerability to SUD (Abi-Dargham, 2004; Chambers, Krystal, & Self, 2001; Green et al., 1999; Lieberman, Kane, & Alvir, 1987). Indeed, it has been suggested that psychosis could be induced by cannabis (Fergusson, Horwood, & Ridder, 2005), amphetamine (Angrist et al., 1974; Angrist & Gershon, 1970), including its synthetic derivatives N-Methyl-3,4-methylenedioxyamphetamine (Ecstasy) (Landabaso et al., 2002; Morgan, 2000; van Kampen & Katz, 2001), and cocaine (Brady et al., 1991; Shaner et al., 1998; Sherer et al., 1988). Moreover, it has also been proposed that lysergic acid diethylamide (LSD) induces psychosis (Vardy & Kay, 1983), although the number of studies which have examined the causal relationship between use of the substance and the onset of this condition is limited. Illicit drug use has also been revealed to be one of the key factors identified by patients as leading to the onset of their psychosis (Dudley et al., 2009).

Alternatively, in terms of the influence of substance misuse on patients with psychotic disorders, poor long-term clinical outcomes have been shown to be related to the co-morbid use of drugs (Dixon, 1999; Green, 2005; Mueser et al., 1990). Indeed, with regard to the association between cannabis use and the clinical outcomes of individuals with psychosis, a systematic review (Zammit et al., 2008) was conducted to examine whether cannabis affects the outcome of psychotic disorders. In this study, cannabis use was, fairly consistently, demonstrated to be linked to an increased rate of relapse or rehospitalization and reduced treatment adherence.

It has also been suggested that co-morbid substance use is associated with more prominent positive psychotic symptoms (D'Souza et al., 2005; Green et al., 1999; Lieberman, Kane, & Alvir, 1987; Lysaker et al., 1994; Negrete et al., 1986; Rosenthal,

Hellerstein, & Miner, 1994), impulsive or aggressive behaviours (Green, 2005; Walsh, Buchanan, & Fahy, 2002), and the risk of suicide (Hawton et al., 2005). At the same time, it is also significantly associated with the young and the male gender (DeQuardo, Carpenter, & Tandon, 1994; Mueser et al., 1990; Zammit et al., 2002).

With regard to the link between co-morbid substance use and pre-morbid adjustment in patients with schizophrenia, Arndt and his colleagues (1992) found that the former was related to better pre-morbid adjustment. In that study, a cohort of 131 schizophrenic patients was divided into 2 groups by their co-morbid substance misuse, and the pre-morbid adjustment level was compared between them. As a result, the pathological users (n = 64) experienced better pre-morbid adjustment than the non-users (n = 67), although both groups were similar in terms of current symptomatology and clinical history. The same study also revealed that only alcohol and, to some extent, cannabis use contributed to this effect, while stimulants or hallucinogens did not.

Alternatively, from the perspective of the treatment of patients with co-morbid schizophrenia and substance abuse, approaches which are specific to such a condition have been developed and seem to be effective (Barrowclough et al., 2001; Haddock et al., 2003). Indeed, motivational interviewing, combined with individual CBT and family or caregiver intervention, was shown to be beneficial for such people. This randomised controlled trial (RCT) (Haddock et al., 2003) compared the effects of motivational intervention combined with individual CBT and routine care, and routine care alone, on patients with co-morbid schizophrenia and substance use. It was revealed that the newly developed treatment not only resulted in significant improvements in patient functioning (assessed with the Global Assessment of Functioning Scale: GAF) when compared to the routine treatment, but that these benefits lasted for up to 18-months. These findings were supported by another RCT (James et al., 2004), which highlighted that an approach specifically targeting substance misuse in people with psychosis could be employed in a group-based intervention, and would be beneficial in reducing substance misuse.

In terms of a diagnosis of drug induced psychosis and schizophrenia, the diagnostic criteria for the latter in the DSM-IV excludes patients with psychotic symptoms that are, apparently, due to the direct physiological effects of a substance (American Psychiatric Association, 2000). Nevertheless, a number of patients with psychotic symptoms and co-morbid substance use could, and should, be diagnosed as suffering from schizophrenia, even using the DSM-IV criteria, because they either start to use the substance after the onset of their psychosis, or continue to have these symptoms long after they have stopped using it. In such a situation, it might be useful to conceptualise a sub-type of patients with schizophrenia, whose substance misuse precedes the onset of psychotic symptoms. Indeed, by defining this sub-group, it would become possible to compare clinically important characteristics, such as long-term clinical outcome and response to a pharmacological or psychological treatment, between this sub-group and others. In addition, intensive treatment for drug misuse might be more effective for patients with this sub-type.

In conclusion, co-morbid substance use has been associated with psychotic symptoms and an unfavourable clinical outcome in schizophrenia. Moreover, specific approaches, developed to target substance misuse in people with psychosis, have been shown to be effective. It, therefore, seems to be useful to conceptualise a sub-group of patients with the illness, whose substance misuse precedes the onset of their psychotic symptoms.

4.3.4 Pre-morbid adjustment and psychosis

It has been suggested that pre-morbid adjustment would be a useful way of identifying sub-types within the heterogeneous syndrome of schizophrenia. It was demonstrated by Strauss and Carpenter (1974) that past employment function and social relationships were the best predictors of respective outcome functions in patients with the disease. Indeed, it was empirically demonstrated that a deterioration in pre-morbid functioning is associated with the development of negative symptoms in schizophrenia (Kelley et al., 1992). In another study, conducted by Gupta et al. (1995), it was found that poor pre-morbid adjustment was significantly associated with the prominence of negative symptoms, an

early age of onset, educational problems, chronicity, and neurological soft signs. The link between pre-morbid social impairment and early age of onset was also demonstrated in a study by Hollis (2003). In addition, Larsen and his colleagues used the pre-morbid adjustment scale (PAS) (Cannon-Spoor, Potkin, & Wyatt, 1982) to examine 335 patients experiencing their first episode of non-affective psychosis, and revealed that those with a stable social course, compared to those with a deteriorating one, had a shorter duration of untreated psychosis, were older, had more friends, and had fewer negative symptoms. Furthermore, patients with a stable academic course were older at admission (Larsen et al., 2004). On the other hand, schizophrenic patients with good pre-morbid functioning are more likely to commit suicide (Pompili et al., 2007).

In terms of the association between pre-morbid function and treatment response in the first episode of schizophrenia, it was proposed that good pre-morbid adjustment is linked to a better response to pharmacological treatment and fewer extrapyramidal symptoms (Rabinowitz et al., 2006). In that study, 530 patients with schizophrenia who were treated with risperidone or haloperidol were assessed by the PAS and categorized into 3 groups, 'stable good' (n = 251), 'stable poor' (n = 198), and 'declining' (n = 81). Response to pharmacological treatment, which was evaluated by the Positive and Negative Syndrome Scale (PANSS) (Kay & Singh, 1989) and the Clinical Global Impressions (CGI) scale (NIMH, 1985), was then compared between them. Consequently, a significantly greater improvement was demonstrated in the 'stable-good' group than the 'stable-poor' one. This difference was found on the mean change in the PANSS total, the positive, negative and general psychopathology scales, and in CGI severity and improvement. On the other hand, patients in the 'declining' group improved the least among these 3 categories.

In conclusion, it may be useful to propose a sub-type of schizophrenia with poor pre-morbid adjustment, early age of onset, and prominent negative symptoms. It might also be helpful to define a further sub-group with good pre-morbid adjustment, late age of onset, and fewer negative symptoms.

4.3.5   Stressful life events and psychosis

An interaction between events which occur in an individual's life and the onset or relapse of their illness has been observed in many psychiatric disorders, including schizophrenia (Kingdon & Turkington, 1994). Falloon commented that 'the impact of life stress on the course of schizophrenia has been observed frequently. In 1913 Emil Kraepelin remarked that remissions were often terminated by changes in the patient's environment' (Falloon, 1984).

So far as empirical support for the link between stressful life events and psychosis is concerned, it was suggested in one study that very recent life events trigger onset (Brown & Birley, 1968). Furthermore, in other explorative work conducted by Cullberg (2003), it was found that significant releasing factors could be observed in the majority of cases of first episode psychosis patients. Indeed, this research proposed that a stressful life event would be regarded as a more or less important boosting factor for psychosis, although it may not be considered to be the 'cause'.

Van Os et al. (1994) also demonstrated the influence of life events on the subsequent course of psychosis. In this prospective study, the existence of stressful life events in the 3 months before onset was suggested to be associated with milder symptom severity and less time spent in hospital. This research also demonstrated that the presence of the life events were linked to less need of anti-psychotic maintenance medication over the follow-up period and more time in complete remission in patients with schizophrenia. However, there may be two major limitations in this study, namely recall bias relating to patients' report about the existence of stressful life events, and difficulty in the demonstration of the causal relationship between such events and the clinical features in psychosis or schizophrenia.

For such a situation, the category of acute and transient psychotic disorder (ATPD) was created by the WHO (F23 of ICD-10), with it being proposed that the diagnosis thereof is associated with a negative life event preceding the first episode, good social adaptation,

reduced psychological impairment, and fine global function (Marneros et al., 2003). This description suggests that a negative event, which precedes initial psychotic symptoms, may predict a favourable prognosis in patients with schizophrenia or psychosis.

In conclusion, the existence of a significant life event which precedes the first episode might predict a favourable prognosis, although it is difficult to demonstrate a causal relationship between such an event and the development of psychotic symptoms.

4.3.6 Significance of specific psychosocial factors that have been revealed in studies of acute and transient psychotic disorder (ATPD)

The new category of ATPD was introduced by the WHO (F23 of ICD-10) (World Health Organization, 1992). There is one prospective longitudinal case control study thereof, which revealed the differences and similarities between ATPD and schizophrenia (Marneros et al., 2003). In this research, inpatients with the former were compared to matched controls with 'positive' schizophrenia and with mentally healthy controls. It was suggested that individuals with ATPD and schizophrenia were similar (but different to the healthy control) in terms of the prevalence of coming from a 'broken home' and a family history of mental disorders, while ATPD patients had better pre-morbid social adjustment than those with schizophrenia. Moreover, those with ATPD more frequently displayed rapidly changing symptoms in the index episode and had experienced a negative life event preceding it. Comparisons between patients with ATPD and its related disorders, as well as those with schizophrenia, were made in other studies which identified more acute onset, less non-schizoid pre-morbid personality, and greater precipitating stress as the features of the former disorder (McCabe, 1975; Stephens, Shaffer, & Carpenter, Jr., 1982).

Nevertheless, the facts that diagnoses of ATPD are not stable, and that a considerable proportion of these patients go on to develop schizophrenia over the course of the illness, does make the situation more complicated in terms of the relationship between the 2 conditions (Jorgensen, 1985; Jorgensen et al., 1997). In this kind of situation, Suda and

her colleagues (2005) demonstrated that the lack of an acute upsurge in insomnia in an early phase of the episode, and poor pre-morbid heterosexual relationships, predict the later development of schizophrenia in patients who are currently diagnosed with ATPD.

If all these data on ATPD and schizophrenia are taken into consideration, it seems possible to propose a sub-group of schizophrenia or psychosis which is characterized by acute onset, good pre-morbid social function, and heterosexual relationships. The existence of stressful life events in the period leading up to an acute upsurge of insomnia, which precedes the first episode, might also be included in the diagnostic criteria for this sub-type.

4.3.7 Stress sensitivity and psychosis

Sensitivity to stress has been recognized as a component of schizophrenia ever since the term was first proposed by Bleuler (1911). In other words, it has long been considered to be an area of vulnerability that is associated with the onset and relapse of schizophrenia and other psychotic disorders (Myin-Germeys et al., 2001). Two types of study have now cast light on this area of evaluating the 'daily hassles' of life (Norman & Malla, 1991) and recording unsettling experiences (Myin-Germeys et al., 2001). In fact, Malla and his colleagues (1990) suggested that comparatively minor daily stressors can have a significant effect on patients with schizophrenia. On the other hand, Myin-Germeys and others (2001) investigated the emotional reactivity of patients with psychosis to daily life stress as a vulnerability marker for psychotic illness. They demonstrated that individuals with psychosis had a more intense emotional reaction to subjective appraisals of stress in daily life than the control subjects. Stress sensitivity, including social anxiety, was also shown to be one of the key factors which people believed led to the onset of their psychotic symptoms (Dudley et al., 2009).

In conclusion, stress sensitivity is considered to be a component of vulnerability which is related to the onset and relapse of schizophrenia and other psychotic disorders.

4.4   Age and mode of onset as important clinical factors in schizophrenia

Along with the psychosocial elements which were described above, two clinical factors relating to onset of schizophrenia, namely age and mode thereof, have also been proved to be associated with clinical features of the illness (Dernovsek & Tavcar, 1999; Harrison et al., 1996). Indeed, early age at onset was suggested to be associated with chronic course of the disorder (Krausz & Muller-Thomsen, 1993), frequent rehospitalizations (Eaton et al., 1992), less favourable prognosis (Hafner & Nowotny, 1995), and poorer response to treatment (Meltzer et al., 1997). On the other hand, with regard to the mode of onset, an insidious onset was demonstrated to predict a longer duration of first or subsequent episodes (Wiersma et al., 1998). Association between the insidious onset and more negative symptoms was also suggested in patients with schizophrenia (Fenton & McGlashan, 1991b; Larsen et al., 1996). Moreover, both the age (Gupta et al., 1995) and mode (Bailer, Brauer, & Rey, 1996; Larsen et al., 1996) of onset was indicated to be linked to pre-morbid functioning . In fact, good pre-morbid functioning was proved to be associated with both the lateness and acuteness of the onset.

Therefore, as discussed above (see section 4.3.4, "Pre-morbid adjustment and psychosis"), it may be useful to propose two sub-types of schizophrenia; one is with poor pre-morbid adjustment, early age of onset, and prominent negative symptoms, while the other is with good pre-morbid adjustment, late age of onset, and fewer negative symptoms. Furthermore, it might be reasonable to use the mode of onset as an additional factor for distinction between these two sub-groups. That is to say, an insidious onset may also be included in the definition of the former sub-type, while an acute onset may become an element in the conceptualisation of the latter.

4.5   Significant psychosocial factors from patients' perspectives

Some of the psychosocial factors described above have also been revealed to be important from the perspective of those with psychosis. Indeed, Dudley and his colleagues (2009) investigated the factors that patients believed led to the onset of their symptoms. In this study with 21 patients with psychosis, 4 main factors were identified as being perceived causal factors for the onset of the condition: the drug related explanation

(e.g., use of illegal drugs), the adult trauma explanation (e.g., sexual assault and physical violence as an adult), the personal sensitivity explanation (e.g., social anxiety and an inability to deal with problems), and the developmental vulnerability explanation (e.g., abusive experiences in childhood [but not sexual abuse]). In other words, people with psychosis believe that the psychosocial factors referred to did cause the onset of their symptoms. The findings suggest that these kinds of explanations could be comfortably accepted by the patients and, importantly, may be less stigmatising.

4.6   A concept of clinical sub-groups integrating psychosocial factors

Due to both the lack of practically useful concepts of sub-types of schizophrenia which have been previously established, and the significance of the psychosocial and psychopathological factors mentioned in previous sections, it is worth integrating these elements into a concept of the sub-types of the illness. In fact, the conceptualisation of 4 sub-groups of schizophrenia – drug related, traumatic, anxiety, and stress sensitivity - was established on the basis of the model produced by Kingdon and Turkington (2005).

This classification scheme for individuals with schizophrenia employed a multi-dimensional approach. Most of the previous attempts to sub-group the disorder have been dependent upon only one aspect of this psychiatric phenomenon, such as its symptoms, cognitive deficit, or neurological anatomical issues. Nevertheless, the criteria proposed are based equally on age and mode of onset, pre-morbid adjustment, and aetiology, such as drug-misuse and traumatic experience. Theoretically, these factors never change after the onset of schizophrenia, and may contribute to the stability of the classification. This approach may, therefore, lead to a holistic and more precise understanding of those with this specific mental disorder.

4.7   Summary

The vulnerability-stress model is deemed useful for understanding the association between psychosocial factors and psychosis or schizophrenia. Some specific psychosocial factors, such as trauma and stress sensitivity, have been shown to be related to psychosis. In such a situation, a new classification system, in which these psychosocial factors were

integrated, was put forward. This employs these elements to identify and describe each of the 4 sub-types proposed.

Chapter 5: Description of the Four Sub-groups of Schizophrenia

5.1   Overview

As described in the previous chapter, the conceptualisation of the 4 sub-groups of schizophrenia, which arose from clinical observations in the development and use of cognitive behavioural therapy, was developed by integrating psychosocial factors into the classification scheme (Kingdon & Turkington, 2005). In this chapter, a description of each of the 4 sub-groups - drug related, traumatic, anxiety, and stress sensitivity - is presented.

5.2   Description of the four sub-groups of schizophrenia

Drug Related Sub-group:

The core characteristic of this sub-group is that the individual will have used at least 1 of the hallucinogens/stimulants listed below in the 2 weeks before the onset of the first psychotic episode.

List of hallucinogens/stimulants

Amphetamine, cocaine, LSD, ecstasy, cannabis, and others[1]

Age of onset will usually be in their teens or 20s, and mode of onset is either acute or insidious. With regard to lifetime patterns of social interaction, individuals with this sub-type will tend to be relatively sociable (Arndt et al., 1992), having many friends at school and possibly a number of partners or wives/husbands. Moreover, the symptom patterns will tend to be diverse, with negative ones being less prominent (D'Souza et al., 2005; Green et al., 1999; Lieberman, Kane, & Alvir, 1987; Lysaker et al., 1994; Negrete et al., 1986; Rosenthal, Hellerstein, & Miner, 1994).

---

[1] Any other types of drugs which are known to cause psychotic symptoms (e.g., diethylpropion) can be included.

The conceptualisation of this sub-type is supported by the suggested differences between patients with and without co-morbid substance misuse that are discussed in Chapter 4 (see section 4.3.3, "Drug misuse and psychosis").

Traumatic Sub-group:
The core characteristic of this sub-group is that the person meets the criteria for co-morbid borderline personality disorder, and has also experienced childhood sexual or emotional abuse.

Additionally, the age of onset will usually be in the patients' teens or 20s, and the mode of onset[2] is either acute or insidious. In terms of lifetime patterns of social interaction, individuals with this sub-type will tend to have chaotic relationships with others (e.g., severe conflicts with their families, and unstable sexual relationships with many boy/girlfriends). With regard to symptom patterns, abusive hallucinations (auditory or visual) may well occur in those in this sub-group.

The conceptualisation of this sub-type is supported by research findings wherein childhood trauma is linked to psychosis (Morrison, Read, & Turkington, 2005). Moreover, as described in Chapter 4 (see section 4.3.2, "Borderline personality and psychosis"), in patients with schizophrenia, sexual and emotional abuse is more associated with the individuals who have co-morbid BPD than with those who do not (Kingdon et al. in submission).

Anxiety Sub-group:
The core characteristic of this sub-group is that the individual has had good peer relationships in early adolescence, and will have generally developed close relationships with a partner or spouse. Age of onset will usually be in the patients' 30s or older, and the

---

[2] Mode of onset is defined as the period between the first reported symptom or noticeable behavioural change and the patient's subjective peak of this first episode. The subjective peak means the point at which distress at the psychotic symptoms is at its height. 'Acute' onset means that the period is less than 1 months whereas 'insidious' onset means that it is as long as, or longer, than 1 months.

mode of onset is likely to be acute. In terms of the lifetime pattern of social interaction, those in this sub-group are relatively sociable, having had both many friends at school, and partners or wives/husbands, before onset. In many cases, individuals will have experienced stressful life events immediately preceding the psychotic symptoms (generally considered to be within 3 months of onset). So far as symptom patterns are concerned, delusions (especially those that are systematized or well organized) are prominent. In addition, hallucinations (auditory, visual, or with other modals) occur, but are less to the fore, as are negative symptoms.

This sub-type was established in order to classify the patients with schizophrenia who had experienced the psychosocial factors associated with a good clinical outcome which are described in Chapter 4 (see sections 4.3, "Psychosocial factors associated with psychosis" and 4.4, "Age and mode of onset as important clinical factors in schizophrenia").

The conceptualisation of this category overlaps, to some extent, with Kraepelin's description of paranoia (Kraepelin, 1919). However, patients with hallucinations, or other symptoms which are characteristic of those suffering from schizophrenia, including confusion of speech and stereotyping, are excluded from the concept behind paranoia. We, therefore, proposed the concept of anxiety psychosis which can be applied to individuals with schizophrenia.

Stress Sensitivity Sub-group:
The core characteristic of this sub-group is that the individual is more stress sensitive[3] and less sociable. Age of onset is usually in the patients' teens or early 20s, and the mode of onset is likely to be insidious. In terms of lifetime patterns of social interaction, those with this sub-type are less sociable, having few friends, (even in childhood), and do not have partners or wives/husbands. With regard to symptom patterns, negative symptoms are prominent, even in the first episode, whereas a range of positive symptoms occur as well.

---

[3] 'Stress sensitive' means that emotional reactivity is high to daily life stress, or 'daily hassles' (Myin-Germeys et al., 2001; Myin-Germeys & van Os, 2007)

This sub-type was established to classify patients with schizophrenia who had experienced the psychosocial factors associated with a poor clinical outcome which are described in Chapter 4 (see sections 4.3, "Psychosocial factors associated with psychosis" and 4.4, "Age and mode of onset as important clinical factors in schizophrenia").

Although the conceptualisation of schizophrenia in the DSM-IV is based upon that of dementia praecox proposed by Kraepelin (1919), the former is broader than the latter, and the patients diagnosed with schizophrenia by the DSM-IV have a more heterogeneous clinical presentation than those with dementia praecox. As mentioned in Chapter 2 ("The Classification of Schizophrenia"), this is mainly due to Bleuler's expansion of the concept. Nevertheless, the discrepancy of the conceptualisations of dementia praecox and schizophrenia in the DSM-IV cannot be fully explained by this historical process in the development of the initial concept of schizophrenia. For instance, Schneider (1959) emphasised that the categorisation of schizophrenia should be based upon the nature of symptoms, rather than their content, and it initially seemed that the definition could be made tighter by doing so. However, the first-rank symptoms proposed by Schneider have proved to be less specific than was initially hoped. For example, they have been demonstrated as occurring in association with trauma (Ross & Joshi, 1992), as well as in those whose first psychotic experience was due to the effects of stimulant and hallucinogenic drugs. The inclusion of the second group became increasingly important from the 1960s onwards, and led to a substantial increase in the numbers of those who could be included within the diagnostic category (Kingdon et al., 2008a; Kingdon et al., 2008b) It might, therefore, be useful to define one sub-group of schizophrenia which corresponds to the original conceptualisation of dementia praecox. Accordingly, the concept behind the stress sensitivity sub-type better reflects that of dementia praecox than it does that of schizophrenia in the DSM-IV or the ICD-10.

5.3   Differentiation between the anxiety and stress sensitivity sub-types

As described in the previous chapter, late and acute onset, good pre-morbid social function and heterosexual relationships, the existence of stressful life events, and an acute

upsurge in insomnia preceding the onset or recurrence of the first episode of schizophrenia have been found to be associated with good outcomes in patients with that illness. Moreover, some of these factors have been revealed to be related to each other in such individuals. These characteristics are employed for differentiating between the anxiety and the stress sensitivity sub-types. In other words, the diagnostic criteria for the anxiety category were designed to include late and acute onset, good pre-morbid function, including good sociability in early or late adolescence and an experience of heterosexual relationships, and the existence of stressful life events which are followed by an acute upsurge in insomnia and the first psychotic episode. On the other hand, the diagnostic criteria for the stress sensitivity sub-type consist of early and insidious onset, poor pre-morbid function, including poor sociability since early adolescence and a lack of pre-morbid heterosexual relationships, and an absence of stressful life events preceding the onset of the first episode (Appendix A).

Chapter 6: Stigmatisation of Patients with Diagnoses of Schizophrenia

6.1   Background

The term schizophrenia has consistently proved difficult to use with many patients, who reject it either on the basis of the associations that it now has with aggressive behaviour and a deteriorating symptom course, or because they do not consider themselves to be ill (British Psychological Society, 2000). It is, therefore, clear that a diagnosis of schizophrenia is associated with a great degree of stigma (Angermeyer & Matschinger, 2003). This makes it difficult for patients with this condition to accept their diagnoses. What is even worse is when patients deny the need for treatment because of its association with this unacceptable diagnosis. Indeed, it is suggested that insight into the need for treatment is at least as important as insight into the fact that an individual has an illness (Rathod et al., 2005). In any case, it is a common experience for psychiatrists to either disagree with a patient about the diagnosis, or negotiate an acceptable alternative term, which is imprecise but less stigmatising. Developing terms which might be acceptable and meaningful to both psychiatrists and patients would, therefore, be a step forward in communication and therapy.

6.2   Impact of this concept of sub-grouping schizophrenia on research and in clinical practice

The concept of sub-grouping schizophrenia based upon the vulnerability-stress model could be valuable for both research and in clinical practice. Firstly, this scheme could establish a basis for the further study of the characteristics of each sub-type. In other words, although additional investigations are required, this classification system may lead to more precise prognoses and more appropriate therapeutic interventions. Secondly, a set of terms which may be acceptable, and less stigmatising, as an alternative to that of schizophrenia could be provided. Indeed, by accurately defining and introducing these terms for the sub-groups, it may become possible for both psychiatrists and patients to discuss this disorder more openly and constructively (Kingdon et al., 2007).

Indeed, a study conducted by Kingdon et al. (2008b) suggested that patients with a diagnosis of schizophrenia, as well as their carers and mental health staff, considered that the current terminology was impairing communication and increasing stigmatisation, and that alternatives needed to be sought. In that research, patients with schizophrenia (n = 27) were shown 5 cards which described the 4 sub-groups and schizophrenia, as well as a sixth which simply stated 'none of these'. Participants were then asked to consider which description best matched their experiences, with particular reference to how their problems had begun. It was demonstrated that patients were more positive about the terms used for the 4 sub-groups than the word, schizophrenia. Furthermore, the 4 terms which were put forward as defining the 4 sub-groups of the disorder, according to the concepts of Professors Kingdon and Turkington, were also shown to reduce the negative attitudes of medical students to it (Kingdon et al., 2008a). In that particular study, attitudes to schizophrenia in a sample of medical students (n = 241) were compared to their attitudes to the proposed groups and to the alternative terminology (Kingdon et al., 2008a).

Although the concept of sub-grouping may well be useful, the sub-types still require validation. Indeed, the validity of this classification scheme should be established with the procedures proposed by Kendell (1989), as described in Chapter 1 (see section 1.4, "Procedure for validating a classification system"). Nevertheless, the validity of the categories cannot be established unless the diagnosis thereof is reliable. Therefore, it is also important to improve the reliability of the diagnosis. A semi-structured interview, as discussed in the next chapter (Chapter 7, "Semi-structured Interview for Sub-grouping Schizophrenia"), can be considered to be a promising tool for improving the reliability of collected data.

Chapter 7: Semi-structured Interview for Sub-grouping Schizophrenia

Even though the concept for categorizing the disorder has been established, it may still be difficult to sub-group patients according thereto. The conceptualisation is not useful on its own, and requires a number of devices which may facilitate its practical use. The semi-structured interview is a promising tool, and would be valuable both when it comes to applying the concept in research or clinical use, and improving the reliability of a diagnosis (Richardson SA, Dohrenwend BS, & Klein D, 1965; Tsuang, Woolson, & Simpson, 1980). A semi-structured interview contains questions which are posed by an interviewer, and explains how to assess a respondent's answers thereto. Such devices could minimise discrepancies in the assessments made by different interviewers, and assist them in reproducing the same judgements when they have to undertake the questioning twice.

Tsuang defines a structured (standardized) interview as follows: 'Standard questions are asked in a predetermined order, and the set of available responses is often fixed' (Tsuang, Woolson, & Simpson, 1980). Structured interviews can be further divided into 2 categories, 'scheduled' and 'non-scheduled' (Richardson SA, Dohrenwend BS, & Klein D, 1965). Tsuang's definition would correspond to a scheduled standardized interview, whereas a semi-structured one is equivalent to a non-scheduled standardized interview, which indicates the specific information to be obtained, but allows for flexibility in the form and sequence of the questions (Helzer, 1983). These instruments may improve the validity and reliability of the relevant clinical information obtained during the assessment process (Calinoiu & McClellan, 2004).

Therefore, in the study herein, a semi-structured clinical interview for psychosis sub-groups (SCIPS) was developed to facilitate research into both the concept of schizophrenia sub-groups and the clinical application thereof, and to achieve an acceptable degree of reliability for such classifications.

Chapter 8: Potential External Validators of the Sub-types in the Current Study

8.1   Overview

As described in Chapter 1 (see section 1.4, "Procedure for validating a classification system"), specific external validators are needed to assess the construct validity of the sub-types in the present study (see Table 1). Nevertheless, such validators are still to be identified. Indeed, specific variables which are not included in the original diagnostic criteria, and differ between the sub-types, should be identified and then utilised for the validation of these categories. Three variables, namely evaluative beliefs, fear of negative evaluations from others, and depression were identified as possible validators.

8.2   Criteria for the identification of the candidates to be validators

The criteria, which consist of 4 items, were used to identify candidates to be the validators examined in the present study (Table 9).

Table 9: The criteria for the identification of candidates for the validators.

1. A variable which is not included in the SCIPS.
2. A variable which is expected to differ among the sub-types.
3. A variable which is suggested as being associated with the intensity of psychotic symptoms (e.g., delusions and hallucinations).
4. A variable which is indicated as being a target for cognitive behavioural therapy (CBT).

As described briefly in Chapter 1 (see section 1.4, "Procedure for validating a classification system"), if a classification system is valid and clinically relevant, then the sub-types of schizophrenia should differ in some specific variable that is relevant in research or clinical practice, and is not included in the original diagnostic criteria. Thus, items 1) and 2) should be included therein. In addition, item 3) was included in the criteria because variables which are related to the intensity of psychotic symptoms would influence clinical outcome and response to treatment. On the other hand, item 4) was

included because the concept behind the sub-groups was originally developed to be applied to CBT for the sub-types, and validators which indicate the difference in responses to this form of treatment would be clinically relevant and useful.

Three variables, which were: evaluative beliefs, the fear of negative evaluations from others, and depression, were confirmed as fulfilling the criteria described above.

Temperament, pre-morbid or co-morbid schizotypal or schizoid personality disorder, and neurobiological variables including results of neuroimaging testing were also considered to be the candidates. However, these variables were not assessed in the present study, mainly because a large amount of time would be required to implement these types of evaluation for each participant. Furthermore, the diagnostic criteria for schizotypal or schizoid personality disorder and the stress sensitivity sub-type do overlap to some extent (i.e., both criteria include poor social relationships as an item). This was also the reason why these sorts of personality disorders were not used as the external evaluators in this thesis.

8.3 Evaluative beliefs

Evaluative, or schematic, beliefs can be defined as the way in which people make judgements or evaluate themselves and other people (Fowler et al., 2006). These beliefs are considered to be a central process in mediating an individual's adaptation to the social world, and form a part of a basic human response to social stresses and threats (Gilbert, 1992). Indeed, moment-to-moment evaluations of the self and others are suggested as being associated with current external events, current mood and cognitive state, and memory processes in the form of schema which synthesise past reactions (Beck, 1976; Gilbert, 1992; Teasdale & Barnard, 1993). In other words, these evaluative beliefs might be a key component of stress sensitivity, as described in Chapter 4 (see section 4.3.7, "Stress sensitivity and psychosis"), and the levels of these beliefs may be higher in patients with the stress sensitivity sub-type.

The evaluative beliefs can be assessed with a high construct validity by using the Brief Core Schema Scale (see Appendix D) (Fowler et al., 2006). Negative evaluative beliefs about the self were shown to be associated with persecutory delusions, even after the confounding effects of depression and low self-esteem were controlled (Smith et al., 2006). Moreover, evaluative beliefs are a main target of CBT in a wide range of mental illnesses, including schizophrenia and other psychotic disorders (Wright et al., 2008).

Evaluative beliefs have been implicated to be associated with stress sensitivity and thus, in hypothesis, useful to differentiate between the anxiety and stress sensitivity sub-types. Social stress is thought to be one of the key elements of stress. For example, Myin Germeys (2001) described that social stress can be divided into 4 components, namely, 1. Event related, 2. Acivity related, 3. Thought related and 4. Social element. Therefore, a stress sensitive person would be more likely to have social anxiety. For example, according to Rusch's study (2009), social anxiety predicted lower self-esteem in patients with mental illness. At the same time, according to Fowler's work (2006), negative evaluative beliefs about self are significantly associated with self-esteem. Accordingly, negative evaluative beliefs about self may be higher in patients with stress sensitivity sub-type than in those with anxiety sub-type.

8.4 Fear of negative evaluation from others (FNE)

The fear of negative evaluation from others can be defined as apprehension about receiving negative appraisal from other people (Watson & Friend, 1969). FNE has been considered to be a crucial cognition in social anxiety disorder (Collins et al., 2005; Endler et al., 1991; Schlenker & Leary, 1982; Winton, Clark, & Edelmann, 1995), and might also be involved in the development and maintenance of symptoms other than social anxiety (Kingsep, Nathan, & Castle, 2003; O'Connor et al., 2002; Swoboda et al., 2003). In other words, this cognition might be an important element in stress sensitivity, as described in Chapter 4 (see section 4.3.7, "Stress sensitivity and psychosis"), and the levels of these beliefs may be higher in patients in the stress sensitivity sub-group.

In terms of the relationship between high FNE and subclinical paranoid ideations, it has been demonstrated that the former is one of the best predictors of the latter in a non-clinical population (Martin & Penn, 2001). In this study of a student group (N = 193) (Martin & Penn, 2001), greater paranoid ideation, measured by the Paranoia Scale (Fenigstein & Vanable, 1992), was associated with a higher score in the BFNE (Pearson's $r = 0.39$, p < 0.01). Nevertheless, the direct relationship between high FNE and psychotic symptoms in patients with schizophrenia and other psychotic disorders is still to be demonstrated.

The FNE can be assessed by using the Brief Fear of Negative Evaluation Scale (see Appendix E) which has high reliability and validity (Rodebaugh et al., 2004). The FNE might also be a significant target for CBT for those suffering from schizophrenia (Kingsep, Nathan, & Castle, 2003). This study suggests that when group CBT for social anxiety is conducted with these patients, the improvement of positive symptoms in those with this illness is associated with a reduction in FNE.

FNE has been implicated to be associated with stress sensitivity and thus, in hypothesis, useful to differentiate between the anxiety and stress sensitivity sub-types. As discussed above, a stress sensitive person would be more likely to have social anxiety. On the other hand, FNE is considered to be a crucial cognition in social anxiety disorder (Collins 2005). Therefore, extent of FNE may be higher in patients with stress sensitivity sub-type than in those with anxiety sub-type.

8.5   Depression

A body of evidence from epidemiological, questionnaire, experimental, and treatment studies support the notion that low mood can contribute to the development of psychotic symptoms (Drake et al., 2004; Freeman & Garety, 2003; Hafner et al., 2005; Iqbal et al., 2000; Krabbendam et al., 2005; Smith et al., 2006). In addition, it has been suggested that the enduring effect of psychotherapy, which enables clients to effectively manage their sensitivity to stress, may contribute to a reduction in depressive symptoms (Hawley et al., 2007; Zuroff & Blatt, 2006). It is, thus, implied that the level of depression is greater in

patients with the stress sensitivity sub-type of schizophrenia. At the same time, depression is also a significant target for CBT, even when it is associated with schizophrenia or other psychotic disorders (Iqbal et al., 2000; Wright et al., 2008). The Beck Depression Inventory-II (BDI-II) (see Appendix F) (Beck, Steer, & Brown, 1996) was used for the assessment of this condition in the present study.

Depression may be useful to differentiate between the anxiety and stress sensitivity sub-types. On the basis of its definition, individuals with higher stress sensitivity would show higher emotional reactivity to daily life stress, or 'daily hassles' (Myin-Germeys et al., 2001). This means that a stress sensitive person would more likely to become depressive due to daily life stress. Therefore, level of depression may be higher in patients with stress sensitivity sub-type than in those with anxiety sub-type.

8.6   Summary

Criteria were developed and used for the identification of candidates for external validators. Three variables: evaluative beliefs, fear of negative evaluations from others, and depression were identified as possibilities which would both fulfil the criteria, and could be used to establish the construct validity of the sub-types of schizophrenia.

Chapter 9: Summary of Chapters 1 to 8 Providing the Background to This Thesis

As described in the previous chapters, schizophrenia has long been considered to be remarkably heterogeneous, and there have been a number of attempts to identify sub-groups of this disorder which are more homogeneous. Nevertheless, most of these have not been used in either research or clinical practice to any great extent, because diagnoses by way of these strategies would be unstable over time and impractical.

In such circumstances, the vulnerability-stress model has led to the development of a new concept of sub-grouping schizophrenia into 4 sub-types – drug related, traumatic, anxiety, and stress sensitivity. This conceptualisation is quite promising, not only because it may provide stable and practical diagnoses, but also because the terminology used therein is useful when it comes to destigmatising those who are currently diagnosed with schizophrenia.

In order to adapt this concept for practical use, this project set out to prepare a semi-structured interview for making diagnoses according to it and examine its reliability and validity. This assessment tool could then facilitate the evaluation of the validity of this classification system. In other words, the sub-types in this system may be demonstrated as being different in terms of their external validators. Three psychopathological variables – evaluative belief, FNE, and depression – could be assessed during this process of validation. Moreover, longitudinal stability and a distinctive course or outcome or treatment response can be established for the sub-types determined with the interview.

Chapter 10: Method

10.1 Justification for the present study

As discussed above, the classification of schizophrenia continues to be problematic. The illness has a remarkably heterogeneous clinical presentation, and although a number of classification schemes for sub-types thereof have been developed, they lack the empirical support required for clinical validity and utility. In these circumstances, and based upon the vulnerability-stress model (Kingdon et al., 2008a; Kingdon et al., 2008b), the concept of 4 sub-groups of schizophrenia - drug related, traumatic, anxiety, and stress sensitivity- was established. This system employs a multi-dimensional approach. In other words, the criteria proposed are based equally on age and mode of onset, pre-morbid adjustment, and aetiology, such as drug-misuse and traumatic experiences. Theoretically, these factors never change after the onset of psychosis, and may contribute to the stability of the classification. At the same time, significant prognostic value is also anticipated, because the factors used for classification purposes have been shown to predict clinical outcome, as discussed in Chapter 4 ("Psychosocial Factors and Psychosis").

The primary aim of this thesis was to develop a semi-structured interview to aid the diagnosis of schizophrenia according to the classification system described in Chapter 5 ("Description of the Four Sub-groups of Schizophrenia"). The factors to be included were decided following a careful review of the potential variables discussed in Chapter 4 ("Psychosocial Factors and Psychosis"). A semi-structured clinical interview for psychosis sub-groups (SCIPS) was then developed by integrating these elements. Thereafter, inter-rater reliability and concurrent validity of this assessment tool were evaluated, and longitudinal stability of the classification over a 6 month period was also examined. In addition, a preliminary assessment of construct validity of the distinction between the anxiety and stress sensitivity sub-types was conducted through the exploration of their potential differences. These 2 particular sub-groups were chosen for this purpose because there may be an overlap in the concepts behind them, and differentiating between them, thus, seemed to be especially important. Accordingly, and as discussed in Chapter 8 ("Potential External Validators of the Sub-types in the Current

Study"), external evaluators, which had been hypothesised to differentiate between these 2 specific sub-types, were chosen to be utilised herein. These validators, namely negative and positive evaluative beliefs, fear of negative evaluation from others (FNE), and depression were carefully chosen, again as described in Chapter 8. During this process, 2 cross-sectional studies were also conducted to highlight the clinical significance of the FNE. Moreover, the prognostic quality of the distinction was extensively analysed by comparing clinical outcomes between these 2 sub-types.

10.2   Study design
The main body of this research employed a systematic cross-sectional design, which was based on the collection of data from a consecutive sample of patients who were recruited from outpatient clinics and psychiatric hospitals. Three cross-sectional studies (with patients suffering from schizophrenia in the UK and Japan, and the non-clinical population in Japan) were conducted for the purpose of this thesis. To establish the longitudinal stability of the classification, a prospective follow-up piece of work was also carried out. In addition, a retrospective cohort study, evaluating the association between the sub-types and clinical outcome, was conducted. For this latter research, a detailed retrospective audit of the participants' case notes was performed to collect data about clinical outcomes. In addition, the SCIPS was used to determine the patients' sub-types.

10.3   Objectives of the study
1. The following aims were identified for the cross-sectional study in the UK and in Japan:

1.1 The primary aims were to:

1.1.1 Establish the inter-rater reliability and concurrent validity of the English and Japanese versions of the SCIPS. That is to say, the null hypotheses examined were:

1)   There is no statistically significant concurrence in the SCIPS diagnoses between two independent raters (for the inter-rater reliability).

2)   There is no statistically significant concurrence between the SCIPS diagnosis and sub-groups determined with the highest achievable validity (for the concurrent validity).

1.1.2 Confirm the sensitivity and specificity of the SCIPS diagnosis for each of the 4 sub-types in the UK and in Japan.

1.2 The secondary aims were to:

1.2.1   Determine if the anxiety and stress sensitivity sub-types differed in their psychopathological characteristics (i.e., evaluative beliefs and fear of negative evaluation from others in the UK and evaluative beliefs, fear of negative evaluation from others and depression in Japan).

1.2.2   Examine if the sub-types determined with the SCIPS were not related to those determined with the DSM-IV;

1.2.3   Determine if the FNE was associated with the severity of delusional ideations, in order to confirm the clinical significance of FNE as a potential external validator of the classification scheme implicated in the cross-sectional study with the non-clinical population in Japan.

2. The aim of the longitudinal study with patients suffering from schizophrenia in Japan was to establish if the sub-types determined with the SCIPS were stable over a 6 month period. That is to say, the null hypothesis examined was that there is no statistically significant concurrence between the two SCIPS diagnoses for each patient determined on 2 different days with an interval of at least 6 months.

3. The following aims were identified for the retrospective cohort study in Japan:

3.1 The primary aim was to establish whether the anxiety and stress sensitivity sub-types differed in relation to the total duration of patient hospitalization during the period of 3 years after the date of the first admission and the length of the first hospitalization. That is to say, the null hypothesis examined was that there is no statistically significant difference in these 2 variables between the 2 sub-types.

69

3.2 The secondary aim was to determine if the anxiety and stress sensitivity sub-types differed with regard to the risk of patients self harming.

4. The aim of the cross-sectional study with the non-clinical population in Japan was to determine if the FNE was associated with delusional thinking; the purpose being to find supporting evidence of the clinical significance of FNE as a potential external validator of the classification scheme. That is to say, the null hypothesis examined was that there is no statistically significant association between the FNE and delusional thinking in the sample.

The cross-sectional studies, which aimed to establish an association between the FNE and delusional thinking in both the non-clinical population (objective 5, described above) and patients with schizophrenia (objective 2.2.3, described above) in Japan, were independent of the other research, which was attempting to directly develop and assess the psychometric properties of the SCIPS. For the purpose of clarity, the method used in these 2 studies are not described in detail in this chapter, instead being included in Chapter 12 ("Relationship between the Fear of Negative Evaluation from Others and Delusions").

10.4   Settings

Given that the SCIPS aimed to identify sub-groups of patients with schizophrenia seen in clinical settings, it was decided that the study in the UK would be conducted at an adult community mental health service. Accordingly, people with schizophrenia were recruited at the psychiatric outpatient clinics and psychiatric hospitals that were part of the Hampshire NHS Trust. In Japan, it was decided that the research would be conducted in psychiatric hospitals with both outpatient clinics and psychiatric beds. Community mental health teams are not as developed in Japan as in the UK, and the former country's psychiatric hospitals function more like community mental health out-patient clinics.

10.5   Participant eligibility criteria

Patients were recruited for the study if they:

- Were aged 18-65 in the UK and 21-65 in Japan
- Had schizophrenia and other psychotic disorders (i.e., schizoaffective disorder, schizophreniform disorder and delusional disorder) diagnosed according to the DSM-IV

NB.

1. It was originally intended that patients aged between 18 and 65 would also be recruited in Japan. However, the eligibility criteria were changed on the basis of advice from the ethics committee of the Graduate School of Medicine at Nagoya City University.

2. Because the main purpose of this thesis was to evaluate the psychometric properties of the SCIPS for patients with schizophrenia, most of the analyses were conducted by excluding those with a diagnosis of schizoaffective disorder, schizophreniform disorder and delusional disorder, unless otherwise stated.

Patients were not recruited for the study if:

- They expressed a wish not to participate and/or were unable to give informed consent
- There was evidence of an organic central nervous system disorder
- They had mental retardation (with a documented IQ of less than 70, or a history of special needs education)
- They had severe psychotic symptoms which made it difficult for them to complete the questionnaire

NB.

Patients were not excluded from the study even if there was co-morbid substance misuse.

10.6   Sample size

The issue of sample size was considered in detail prior to the commencement of data collection, and the relevant calculations are described in each chapter containing the results of each investigation. In outline, it was planned that at least 40 patients would be recruited for a preliminary small-scale investigation in the UK. Of these 40 participants, the SCIPS interview was conducted twice with at least 20 of them to examine inter-rater reliability. At the same time, sub-groups were determined with the highest achievable validity (as described below) for a minimum of 20 patients, in order to assess the concurrent validity of the SCIPS diagnosis (using the English version of the test). The results of this preliminary study in the UK were then taken into consideration, with the decision being made that at least 100 participants would be required for the research in Japan. Data from at least 30 of this sample of 100 was used to evaluate the inter-rater reliability of the SCIPS diagnosis (using the Japanese version thereof). In order to assess the concurrent validity of the SCIPS diagnosis (with the Japanese version of the interview), sub-groups were determined with the highest achievable validity (as described below) for the greatest possible number of the patients recruited in Japan.

10.7   Determination of the sub-groups with the highest achievable validity

In order to evaluate the concurrent validity, specificity and sensitivity of the SCIPS diagnosis, sub-groups with the highest achievable validity were determined for the participants and then compared with the SCIPS outcomes. In the UK study, DK, who was one of those who had originally conceptualised the 4 sub-types and was blind to the SCIPS diagnosis, collected appropriate information by reading case notes and then classified the patients. DK also interviewed the participants if there was not enough information in their notes and it was possible to see the individuals concerned. Such data included age and mode of onset, symptom profiles, experience of substance misuse, childhood trauma, co-morbid borderline personality disorder, pre-morbid adjustment, and significant life events. For classification purposes in the study in Japan, a rater who was blind to the SCIPS diagnoses gathered the necessary data by reading case notes,

interviewing the patients' psychiatrists and having several discussions with DK, who was also blind to the SCIPS outcomes.

10.8   Measures

Along with the sub-types which were obtained by using the SCIPS, the following critical measures were also identified: socio-demographic characteristics; severity of delusional ideations, (which is one of the most important psychotic symptoms); the psychological characteristics which are potential external validators of the SCIPS diagnoses; and mood. Broad measures of clinical outcome were also identified.

The most appropriate measure of each variable was identified by the following procedure: a literature search was conducted using the Medline and Psycinfo databases. The key words used included 'measurement', 'assessment' and relevant variable descriptors, such as schizophrenia, evaluative beliefs and fear of negative evaluation. Significant papers relating to classification and the use of cognitive behavioural therapy (CBT) for schizophrenia were also reviewed, and renowned researchers in these fields were contacted for their input and advice about measurement selection. Potential measures for each variable were then systematically reviewed and examined according to the following criteria: psychometric quality, prior use within the schizophrenia field, relevance of sub-scales, language, length, and whether the measure was assumed to have sufficient utility within a research setting (see Appendix B for a sample of a systematic review record).

Following this procedure, the following scales were selected for use in this study:

10.8.1 Socio-demographic information

Socio-demographic information relating to age, gender, marital status, ethnicity and educational history was gathered in interviews with the participants.

10.8.2 Age at the time of the first psychotic episode and the number of years since then

Data about patient age at the time of the first psychotic episode was mainly obtained from case notes. If there was not enough information in the notes, a psychiatrist, social worker, or nurse who was responsible for the patient was consulted. A researcher who was blind to the participants' sub-types was the individual responsible for reviewing the case notes and extracting the relevant data.

The number of years since the age at onset of the first psychotic episode was calculated by subtracting the age at the time of this event from a patient's current age.

10.8.3 Severity of delusional ideations

The 21item Peters Delusions' Inventory (PDI-21) (see Appendix C) (Peters et al., 2004): This questionnaire was designed to measure the unusual subjective beliefs and experiences which relate to the dimension of delusional ideation in the general population (Peters et al., 2004; Peters, Joseph, & Garety, 1999). Indeed, it has been shown that the Japanese version of the PDI could assess delusional experiences in the general population with significant validity and reliability (Yamasaki et al., 2004).

The 21original questions are derived from items used in the Present State Examination to assess delusional symptoms (Wing, Cooper, & Sartorius, 1974), and each of them is comprised of 3 sub-scales (distress, pre-occupation and conviction) which are, in turn, answered on a 5-point scale (1-5). A 'Yes' answer to each item is followed by an assessment of these 3 sub-scales, while a 'No' answer automatically leads to a zero (0) score for each of them. The PDI-21 score is obtained by assigning 1 to each 'Yes' answer and 0 to each 'No' answer, and distinguishes psychotic patients from healthy subjects (Verdoux & van Os, 2002). The score correlates well with the Brief Psychiatric Rating Scale (BPRS) (Verdoux & van Os, 2002) and the Positive and Negative Syndrome Scale (PANSS) (Yamasaki et al., 2004) in patients with a confirmed diagnosis of schizophrenia, but who are stable clinically (Khazaal et al., 2006; van Os et al., 1999). The PDI-21 can, thus, be considered to be one of the 'best-available' tools with which to assess the

presence of delusions in both patients with schizophrenia, as well as in a normal population.

10.8.4 Candidate external validators

10.8.4.1 The Brief Core Schema Scale (BCSS) (see Appendix D) (Fowler et al., 2006):

The BCSS contains 24 items concerning beliefs about the self and others that are answered on a 5-point scale (0-4). Four scores are obtained which represent beliefs about the negative-self (NS: 6 items), negative-others (NO: 6 items), positive-self (PS: 6 items), and positive-others (PO: 6 items) (Fowler et al., 2006). The content of the negative-self component, as globally negative self-descriptors of personality, is derived from the self-devaluative words used by Teasdale and Dent (1987) and, subsequently, by Teasdale and Cox (2001). The 4 scores assessed in this scale are compared in this study. The BCSS was originally developed to evaluate the core schema of patients with schizophrenia or psychosis. It has been translated into Japanese, and both the English and Japanese versions thereof demonstrate strong evidence of construct and criterion validity (Fowler et al., 2006; Yamauchi, Sudo, & Tanno, 2009). The BCSS was chosen for a number of reasons: it is a brief, well validated questionnaire that measures evaluative beliefs; it has originally been developed for use within the field of psychosis; and its Japanese version exists.

10.8.4.2 Brief Fear of Negative Evaluation Scale (BFNE) (see Appendix E) (Rodebaugh et al., 2004):

The BFNE is a self-reporting questionnaire which assesses the degree to which people worry about how they are perceived and evaluated by others. It is a shortened version of the original 28 item, Fear of Negative Evaluation scale (FNE), and contains 12 items which are answered on a 5-point scale (0 = not at all characteristic of me, 4 = extremely characteristic of me) (Watson & Friend, 1969). The FNE score is provided by the sum of the scores of the 12 items, and there is strong evidence of its construct and criterion

validity (Leary, 1983; Rodebaugh et al., 2004). This scale was also used for patients with schizophrenia in research which demonstrated the effectiveness of CBT in managing the social anxiety of those diagnosed as suffering from this mental disorder (Kingsep, Nathan, & Castle, 2003). The BFNE was translated into Japanese, and a back translation thereof was carried out to achieve maximum reliability and validity (Ishikawa, Sasaki, & Fukui, 1992). The BFNE was selected for a number of reasons: it is a brief, well validated questionnaire that measures fear of negative evaluation from others; its Japanese version exists; and it has previously been used within the field of psychosis.

10.8.4.3 Mood

Beck Depression Inventory (BDI-II) (see Appendix F) (Beck, Steer, & Brown, 1996): The BDI-II is a self-reporting 21 item, 4-point scale (0-3) for the assessment of depression (Beck, Steer, & Brown, 1996), wherein mood is analysed over the fortnight prior to taking the test. It has also been used for patients with schizophrenia (Rector, Seeman, & Segal, 2003; Smith et al., 2006). Internal consistency, reliability, criterion validity and factor validity of the Japanese version of the BDI-II have also been established (Kojima et al., 2002). This measure was selected because it is a brief, well validated measure of depression widely used in psychological research.

10.8.5 DSM sub-types

DSM sub-types were determined according to the DSM-IV diagnostic criteria by a rater who conducted the first assessment of each participant. The Structured Clinical Interview for the DSM-IV Axis I Disorders (SCID-I) (First & Gibbon, 2004) was used for this purpose. If this was difficult to do with only the information obtained directly from the patient, a psychiatrist, social worker, or nurse who was responsible for this individual was consulted to ensure that enough information was collected to be able to make a diagnosis.

10.8.6 Clinical outcome

Data about the past hospitalization of the members of the sample was mainly obtained from their case notes, but to improve the quality of the information collected in this way,

comparisons were made between what was learnt from these notes and what was discovered from the patients. In this process, the participants were asked about their history of hospitalizations, including the names of all of the relevant establishments, and the frequency of their stays. If there was a discrepancy between the data in the case notes and what the patients said, a psychiatrist, social worker, or nurse who was responsible for the individual concerned was consulted. Data was excluded if it was difficult to judge whether it was correct, even after consultation with professionals. A researcher who was blind to patient sub-types was responsible for reviewing the case notes, extracting the data and determining if it should be omitted, in the circumstances described above.

10.8.6.1   Two variables for the comparison related to hospitalization

Variable 1: Total time [the number of days] spent in hospital in the 3 year period after the date of first admission:

This variable is thought to be one of the most important components of clinical outcome, and is determined for each patient by calculating the total duration of all hospitalizations in a 3 year period after the date of his/her first admission. Data was excluded if the development of psychotic episodes was obviously not the cause of the hospital stay (e.g., treatment of physical illness and training in blood sugar control).

Variable 2: Duration [the number of days] of the first hospitalization:

This variable is also a good indicator of short-term clinical outcome. The data was collected from the case notes as described above. As in the case of variable 1, information was excluded if the development of psychotic episodes was obviously not the cause of the hospital admission.

In terms of the time unit of the variables 1 and 2, the number of days was counted for each of them.

10.8.6.2   History of self harming

Data about self harming was obtained from patients' case notes, and collated using the Structured Clinical Interview for the DSM-IV Axis II Disorders (SCID-II, section for

borderline personality disorder, item 97) (First & Gibbon, 2004). In order to confirm whether they had actually hurt themselves at least once after the onset of their first episode of schizophrenia, participants were asked 2 additional questions - (1. "Did you really hurt yourself or did you just threaten to do so?" and 2. "Did you hurt yourself after the onset of your psychotic symptoms?"). To improve the quality of the data, comparisons were made between the information in the case notes and that obtained in the SCID interviews. If there was a discrepancy, a psychiatrist, social worker, or nurse who was responsible for the patient was consulted. A researcher who was blind to the patients' sub-types was responsible for reviewing the case notes and extracting the data. In terms of the history of self harming, those who had actually hurt themselves at least once after the onset of their first episode of schizophrenia were rated as positive, while those who only did so beforehand, or did not actually harm themselves at all, were rated as negative.

10.9   Procedure

Figures 1 and 2 set out the outlines of the studies conducted in the UK and Japan, respectively.

Figure 1: Outline of the study in the UK.

Participants with schizophrenia for the 1st assessment (n = 42)

1. To assess concurrent validity of the SCIPS (n = 21) (Chapter 13).

2. To calculate sensitivity and specificity of the SCIPS diagnosis (n = 21) (Chapter 13).

3. To establish construct validity of the classification; assessment with BCSS and BFNE (n = 42) (Chapter 15).

At least 2 weeks after the 1st assessment

For the 2nd SCIPS interview (n = 20)

To assess inter-rater reliability of the SCIPS (Chapter 13).

Figure 2: Outline of the study in Japan.

Participants with schizophrenia for the 1st assessment (n = 117)

1. To examine if delusional ideation is associated with FNE (Chapter 12).

2. To assess concurrent validity of the SCIPS (Chapter 13).

3. To calculate sensitivity and specificity of the SCIPS diagnosis (Chapter 13).

4. To establish construct validity of the classification; assessment with BCSS, BFNE and BDI (Chapter 16).

5. To examine predictive value of the classification (about hospitalization and history of self-harming) (Chapter 17).

At least 2 weeks after the 1st assessment

For the 2nd SCIPS interview (n = 35)

To assess inter-rater reliability of the SCIPS (Chapter 13).

At least 6 months after the 1st assessment

For the follow-up SCIPS interview (n = 43)

To assess longitudinal stability of the subtypes (Chapter 14).

10.9.1 Recruitment of participants in the UK

Seven consultants, who usually saw their patients at 3 different psychiatric outpatient clinics (Cannon House, Bay Tree House, and College Keep in Southampton) and at 3 psychiatric hospitals (Royal South Hants Hospital in Southampton, Melbury Lodge in Winchester, and Ravenswood House in Fareham), were asked to nominate individuals with schizophrenia and other psychotic disorders (i.e., schizoaffective disorder, schizophreniform disorder, and delusional disorder) who might be suitable for the project. The patients were first asked by their consultants whether they would be willing to participate in the study, and, if they agreed, they were then contacted by one of the researchers. Information sheets (Appendix G) were given to all potential participants at that time. They were also provided with an overview of the assessment process, and were told about the study, its objectives and what their participation would involve. At this time, potential subjects were also given the opportunity to ask questions, and were reassured that a decision to not take part would not affect their access to services or treatment. Those who wished to be involved were asked to complete questions 1 -5 of the consent form (see Appendix H). At that time, patients were also reminded that the audio taping of part of the interview was related to quality control, and they could refuse to co-operate with this element and still take part in the study.

During this recruitment period (October 2007-August 2008), 51 patients were selected and referred to take part in the project by their consultants, and were then formally invited to participate. Of these, 45 agreed and 6 declined. Clinically experienced and trained research personnel confirmed the subjects' diagnoses using the SCID (sections for psychotic disorders and borderline personality disorder) (First & Gibbon, 2004). Forty-two of the patients were diagnosed with schizophrenia, and 3 with schizoaffective disorder, delusional disorder and bipolar disorder. Of the sample of 42, 33 were male (78.6%) and 9 were female (21.4%). They ranged in age from 18 to 64, with the mean being 42.1 (Standard deviation (SD) = 12.3, median = 42.0). The median for the number of years the patients had spent in formal education was 11.0 (Inter-quartile range (IQR) = 10.0-13.0). Twenty-five of the participants were single (59.5%), 8 were married or living with a partner (19.0%), and 9 were divorced/separated (21.4%). In terms of ethnic

breakdown, 39 patients (92.9%) were white British, 1 (2.4%) was African and 2 (4.7%) were Asian. Thirty-five (83.3%) were outpatients and 7 were inpatients (16.7%). Table 10 sets out this demographic data.

YK conducted the first interviews for 39 of the 42 participants, and DU questioned the other 3.

10.9.2 Assessment of the inter-rater and test-retest reliability of a diagnosis with the English version of the SCIPS

In order to assess inter-rater reliability, the SCIPS interview was carried out twice for each participant by 2 independent raters who were blind to each other's diagnoses. The results were then compared. YK, KK, SS and DU, who are clinically experienced and trained research personnel, conducted these interviews. A patient's first and second interviews were carried out on 2 different days, with an interval of at least 2 weeks between them, in order to assess test-retest reliability, as well as inter-rater reliability. Of the 42 individuals who were diagnosed with schizophrenia, 41 completed the first SCIPS interview. Of the 41, 36 were asked to take the second interview, and 30 of these agreed to make appointments for this purpose. Five were not asked because they lived some distance away from Southampton. Of the 30 who made appointments, 20 attended and completed the second interview. Of these 20 participants, 16 (80.0%) were male and 4 (20.0%) female. Their mean age was 41.7 years (SD = 11.2, median = 41.0), and 10 were single (50.0%), 4 were married or living with a partner (20.0%), and 6 were divorced/separated (30.0%). In terms of ethnic breakdown, 19 (95.0%) were white British and 1 (5.0%) was African. All of the participants were outpatients, and 2 (10.0%) met the criteria for borderline personality disorder (Table 10).

YK carried out the second interviews with 3 of the 20 participants, and SS and KK did so for 6 and 11 of them, respectively.

10.9.3 Assessment of the concurrent validity of a diagnosis with the English version of the SCIPS

In order to evaluate the concurrent validity of a SCIPS diagnosis, the sub-types determined with the initial interviews were compared to those with the highest achievable validity. Among the 41participants, who completed the first SCIPS interview, the first 21 individuals recruited from Cannon House, Bay Tree House, College Keep and the Royal South Hants Hospital were sub-grouped with the highest achievable validity as described above. Of these 21 participants, 17 (81.0%) were male and 4 (19.0%) female. The mean age was 37.1 (SD = 11.4, median = 38.0), 14 were single (66.7%), 5 were married or living with a partner (23.8%) and 2 were divorced/separated (9.5%). In terms of ethnic breakdown, 20 (95.2%) were white British and 1 (4.8%) was African. Nineteen were outpatients (90.5%), 2 inpatients (9.5%), and 2 (9.5%) met the criteria for borderline personality disorder (Table 10).

Table 10: Participant demographics (Study in the UK).

	Participants for 1st interview (n = 42)	Participants for 2nd interview (n = 20)	Participants sub-grouped with the highest achievable validity (n = 21)
Mean age (SD)	42.1 (12.3)	41.7 (11.2)	37.1 (11.4)
Median age (IQR)	42.0 (33.0-51.0)	41.0 (33.0-50.8)	38.0 (28.0-46.0)
Median years in education (IQR)	11.0 (10.0-13.0)	11.0 (10.0-13.0)	11.0 (10.0-13.0)
Male, No. (%)	33 (78.6)	16 (80.0)	17 (81.0)
Outpatients, No. (%)	35 (83.3)	20 (100.0)	19 (90.5)
Mean years after the age of onset (SD)	16.1 (8.3)	15.1 (9.8)	11.6 (6.7)
Median years after the age of onset (IQR)	15.0 (9.0-22.0)	14.0 (9.0-17.0)	12.0 (5.5-16.5)
The SCIPS interview completed, No. (%)	41 (97.6)	20 (100.0)	21 (100.0)

10.9.4 Recruitment of participants in Japan

Participants were recruited from 3 psychiatric hospitals (Kusunoki Mental Hospital, Yagoto Hospital, and Minamichita Hospital) in Aichi, Japan, all of which have psychiatric beds, day care units and outpatient clinics. All of the psychiatrists working in these hospitals were asked to nominate patients with schizophrenia and other psychotic disorders (i.e., schizoaffective disorder, schizophreniform disorder, and delusional disorder) who might be suitable for the project. During the recruitment period (September 2008-October 2008) 129 patients were put forward by their consultants. Information sheets were given to all potential participants when they were first approached by the researcher, and they were also given an overview of the assessment process at that time. Patients were told about the study, its objectives and what their participation would involve. They were also given the opportunity to ask questions, and were reassured that a decision to not take part would not affect their access to services or treatment. Those who did wish to become involved were asked to complete questions 1-4 of the consent form (these were Japanese translations of the questions contained in Appendix H). They were then formally invited to take part in the research, with 121 agreeing to do so and 8 declining. Clinically experienced and trained research personnel confirmed the subjects' diagnoses using the Structured Clinical Interview for the DSM-IV. Sub-types of schizophrenia were also determined for each participant according to the DSM-IV. Of the sample of 121 patients, 117 had schizophrenia and 4 were diagnosed with schizoaffective disorder. Of this 117, 76 were male (65.0%) and 41 were female (35.0%). Their ages ranged from 21 to 65, with the mean age being 44.5 (SD = 12.3, median = 43.0). The median for the number of years spent in education was 12.0 (IQR = 9.0-12.0); 86 participants were single (73.5%), 8 were married or living with a partner (6.8%) and 13 were divorced/separated (11.1%). Information about their marital status was unclear for 6 individuals (5.1%), because they withdrew from the study at the start of their interviews. All of the participants were of Japanese origin, and 94 (80.3%) were outpatients and 23 were inpatients (19.7%) (Table 11).

YK carried out the first interviews with 60 of the 117 participants and KK did so with the remaining 57.

10.9.5 Assessment of the inter-rater and test-retest reliability of a diagnosis with the Japanese version of the SCIPS

As in the study in the UK, and in order to assess inter-rater and test-retest reliability, the SCIPS interviews were conducted twice for each patient by 2 independent raters, YK and KK, who were blind to each other's diagnoses. These first and second interviews were held on 2 different days with an interval of at least 2 weeks between them. The interviewers spent 6 days (2 for each of the 3 hospitals) recruiting patients for the second interviews. Of the sample of 117, 46 individuals (all of whom were either hospitalized, had appointments at outpatient clinics, or attended the day care units on these 6 days) were asked if they would be interviewed again and 35 agreed to do so. Of these 35 participants, 18 (51.4%) were male and 17 (48.6%) female. Their mean age was 46.8 years (SD = 10.7, median = 44.0), and 26 were single (74.3%), 4 were married or living with a partner (11.4%) and 5 were divorced/separated (14.3%). All of the subjects were of Japanese origin, and 31 of them (88.6%) were outpatients and 4 were inpatients (11.4%) (Table 11).

YK carried out the interviews with 17 of the 35 patients who had agreed to be questioned again, and KK did so with the remaining 18.

10.9.6 Assessment of the concurrent validity of a diagnosis with the Japanese version of the SCIPS

In order to evaluate the concurrent validity of a SCIPS diagnosis, the sub-types which were determined with the first interviews were compared to those with the highest achievable validity. A determination of the sub-groups with this highest achievable validity (as described above) was attempted for all of the participants who completed the first SCIPS questionnaire (n = 107). Of the 107 individuals in this sample, 88 patients (82.2%) could be sub-grouped with the highest achievable validity, while not enough information was available, and sub-types could, therefore, not be determined, for 19 participants (17.8%).

10.9.7 Evaluation of the longitudinal stability of the SCIPS diagnosis in Japan

In order to establish if the sub-types determined with the SCIPS were stable over time, participants were recruited from day care units in the 3 hospitals in Japan. The researchers worked over 4 days (31st March-3rd April, 2009, 2 days in 1 hospital and 1 day in each of the other 2), at least 6 months after the first interviews, to recruit subjects for follow-up questioning. A notice which sought such participation, and set out the likely dates, was displayed in advance (1 or 2 weeks before the dates of the interviews) at each of the day care units. All of the patients who had taken part in the initial interviews, and then went on to declare an intention to participate further in the assessment process, were interviewed again using the SCIPS. A total of 44 individuals declared an intention to be, and were, questioned again. Of these 44, according to the DSM-IV, 43 of them had schizophrenia and 1 had schizoaffective disorder. Of the 43 schizophrenics, 27 (62.8%) were male and 16 (37.2%) female. The mean age was 42.3 years (SD = 10.0, median = 42.0) (Table 11); 31 were single (72.1%), 5 were married or living with a partner (11.6%) and 7 were divorced/separated (16.3%). All of the participants were of Japanese origin.

YK did the follow-up interviews with 18 of the 43 in this sample, while KK did the remaining 25.

Table 11: Participant demographics (Study in Japan).

	Participants for 1st interview (n = 117)	Participants for 2nd interview (n = 35)	Participants in 6 month follow-up interview (n = 43)
Mean age (SD)	44.5 (12.3)	46.8 (10.7)	42.3 (10.0)
Median age (IQR)	43.0 (35.0-55.0)	44.0 (39.0-58.0)	42.0 (37.0-51.0)
Median years in education (IQR)	12.0 (9.0-12.0)	12.0 (9.0-12.0)	12.0 (9.0-12.0)
Male, No. (%)	76 (65.0)	18 (51.4)	27 (62.8)
Outpatients, No. (%)	94 (80.3)	31 (88.6)	43 (100.0)
Mean years after the age of onset (SD)	18.9 (12.0)	20.5 (11.6)	16.7 (10.3)
Median years after the age of onset (IQR)	18.0 (10.0-29.0)	19.0 (10.0-29.0)	17.0 (8.0-25.0)
The SCIPS interview completed, No. (%)	107 (91.5)	35 (100.0)	43 (100.0)

10.9.8 Data collection and the assessment process

After giving their consent, participants were provided with the additional research questionnaires (BCSS, BFNE and PDI-21 in the UK study, and BCSS, BFNE, PDI-21 and BDI-II in the Japanese study) to complete and were interviewed using the SCIPS. The whole process took about an hour per respondent. In the current study, the patients were instructed to assess the BFNE and PDI-21 over the past month, because in our previous use of these scales, we noticed that the BFNE and the PDI-21 scores of patients with schizophrenia sometimes changed within a few months or a year, apparently in conjunction with the changes in their symptomatology, whereas no instruction was given to the students with regard to the period which the assessment of these scales covered. Thus, it should be noted that the scores of BFNE and PDI-21 cannot be compared directly between the student sample and the patient sample, because the instruction for the patients about how to complete these scales was different to that for the students in terms of the time period which they covered. The SCIPS interview element of the process was repeated for some of the patients who had completed the first assessment (20 in the UK and 35 in Japan). To assess the inter-rater and test-retest reliability thereof, these 2 interviews were conducted by 2 independent raters on 2 different days, with an interval of at least 2 weeks between them. The SCIPS interview part of the process was then repeated for some of those who had completed the first assessment in Japan, in order to assess the longitudinal stability of the classifications (n = 43). This interview was carried out at least 6 months after the date of the first assessment, and took about 10 minutes per participant. Confidentiality was guaranteed in terms of the answers given, and written informed consent was obtained from each subject. The sections for psychotic disorders in the SCID-I and for borderline personality disorder in the SCID-II were applied to all of the participants in order to confirm the diagnoses.

Clinical outcome data relating to hospitalization and a history of self harming was collected using the procedure described above (see section 10.8.6, "Clinical outcome").

10.10 Ethics approval

The Isle of Wight, Portsmouth & South East Hampshire Research Ethics' Committee (REC) approved the protocol for the study in the UK. The ethics committee of the Graduate School of Medicine at Nagoya City University, in turn, approved the protocol for the research in Japan. Participants were enrolled in the study only where consent was unambiguously given. The identification of respondents, as a result of any kind of analysis, was not possible because of the use of codes. All of the information has been, and will be, kept strictly confidential.

10.11 Pilot work and quality control

The draft questionnaires, information sheets and consent forms were all checked by a member of the general public to ensure that all of the items in the measures, as well as the content of the forms, were understandable to a lay audience. All of the researchers who collected the data were clinicians who are experienced in the clinical practice of psychiatry, and the use of both the DSM-IV diagnostic criteria and the SCID-I and -II. Prior to the start of data collection, these researchers were trained in how to administer the interviews and questionnaires by the principal investigator. Throughout the period of data collection, the researchers held regular meetings and frequently discussed any relevant issues (once a week, on average). The aim of these sessions was to clarify rating queries and maintain standards.

10.12 Statistical methods

Data were analysed using the Statistical Package for the Social Sciences, version 15 (SPSS Inc, 2006), and Stata, version 8 (StataCorp, 2005). Primary analyses were conducted for the participants who had a diagnosis of schizophrenia, because the primary objectives of this thesis were to both test the psychometric properties of the SCIPS, as well as assess the validity of the classification scheme when applied to patients with this psychiatric disorder.

In Chapter 12 ("Relationship between the Fear of Negative Evaluation from Others and Delusions"):

1. In order to determine if the FNE was associated with delusional thinking, Pearson product-moment correlation coefficients (Pearson's *r*) were calculated to evaluate the association between the PDI, BFNE, and BDI-II scores. Linear regression analyses were conducted to assess if the BFNE scores continued to be associated with the PDI scores once the confounding effects of depression were controlled. Spearman rank correlation coefficients (Spearman's *r*) were also calculated to examine the relationship, in scores, between the BFNE and the 6 factors of the PDI-21(Preti, Sardu, & Piga, 2007).

In Chapter 13 ("Psychometric Evaluation of the English and Japanese Versions of the SCIPS"):

2. Kappa coefficients were calculated with regard to the assessment of the inter-rater reliability and concurrent validity of the SCIPS.
3. The sensitivity and specificity of the SCIPS diagnoses were calculated by preparing 2x2 tables for each of the 4 sub-types.

In Chapter 14 ("Six Month Stability of the SCIPS Diagnosis: A Longitudinal Study in Japan"):

4. Kappa coefficients were calculated to examine the longitudinal stability of the sub-types which were determined with the SCIPS.

In Chapter 15 ("Construct Validity of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types: A Preliminary Study in the UK") and Chapter 16 ("Construct Validity of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types: A Study with a Larger Sample in Japan"):

5. The Mann-Whitney U Test was employed to determine if the anxiety and stress sensitivity sub-types differed in their psychopathological characteristics (i.e., evaluative beliefs, fear of negative evaluation from others, and depression). This non-

parametric test was chosen for this purpose because all of the variables analysed were not normally distributed.

6.   The Chi-square test or the Fisher's exact test was conducted to assess if the sub-types determined with the SCIPS were related to those determined with the DSM-IV.

In Chapter 17 ("Predictive Value of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types"):

7.   The Mann-Whitney U Test was employed to examine if the anxiety and stress sensitivity sub-types differed in their clinical outcome (total time spent in hospital over a period of 3 years after the date of first admission [variable 1] and the length of the first hospitalization [variable 2]). This non-parametric test was chosen for this purpose because all of the variables analysed were not normally distributed.

8.   The Chi-square test was conducted, and relative risk (RR) was calculated, to examine if the anxiety and stress sensitivity sub-types differed in terms of the risk of self-harm.

10.13   Data management

All data was entered into a database using Microsoft Office Excel 2003, and was double entered to check for systematic errors. The error rates for all of the questionnaires were acceptable at 0.1%.

10.14   Missing values

Upon completion, questionnaires were examined for missing data and, where possible, participants were asked to answer any questions they had missed. All of the missing data was excluded from the statistical analyses.

Chapter 11: Development of the English and Japanese Versions of the SCIPS

11.1   Overview

As discussed in Chapters 4 ("Psychosocial Factors and Psychosis") and 5 ("Description of the 4 Sub-groups of Schizophrenia"), the vulnerability-stress model led to the development of the new concept of sub-grouping schizophrenia into 4 sub-types: drug related, traumatic, anxiety and stress sensitivity (Kingdon & Turkington, 2005). In order to adapt this for practical use, a semi-structured interview for the purpose of making diagnoses was developed. This interview is known as a Semi-structured Clinical Interview for Psychosis Sub-groups (SCIPS), and an original English version thereof was translated into Japanese to be used with natives of that country. In this chapter, the characteristics of the SCIPS are discussed, as is its development, structure, and mode of operation.

11.2   Development of a semi-structured clinical interview for psychosis sub-groups (SCIPS)

The SCIPS was initially developed, and the first draft version thereof was then prepared. Four psychiatrists, who had extensive clinical experience with the diagnosis and treatment of schizophrenia, were asked to review the existing version of this assessment tool and final refinements thereto were made on the basis of the recommendations made. As a result of this process, the second version of the SCIPS, to be used for research purposes (Appendix A), was established with high face validity.

11.3   Preparation of the Japanese version of the SCIPS

The Japanese version of the SCIPS was prepared by translating the English document into Japanese. YK, one of the founders of the SCIPS, did this first, and then, MI, who had no knowledge of this English version, back translated the Japanese document into English. Next, DK, the other originator of the SCIPS, examined the differences between the original English version and the back translation. If he concluded that there were significant differences in some places between these 2 versions, DK told YK which

sentence in the Japanese document should be modified and back translated again. This process was repeated until there were no critical differences between the original version and the back translation. Thereafter, four psychiatrists who had extensive clinical experience of the diagnosis and treatment of schizophrenia, and could understand Japanese, were asked to review this Japanese version, and confirmed that high face validity was sustained, even after translation.

11.4 Terminology used in the SCIPS

11.4.1 Limitation on the use of the word 'psychosis' in the thesis

The SCIPS was developed on the basis of the assumption that it would be extensively applied to patients with psychotic disorders other than schizophrenia. In addition, the interview attempts to reduce the stigma associated with the word 'schizophrenia' by using the term 'psychosis' to apply to individuals with the illness. Thus, the word 'psychosis' is used in this tool instead of the phrase 'sub-type of schizophrenia'. However, as described in Chapter 2 ("The Classification of Schizophrenia"), the conceptualisation of psychosis is broader than that of schizophrenia. This means that the use of the word 'psychosis' might be ambiguous when it is applied to a sub-type of schizophrenia, at least from a scientific perspective. Moreover, and as explained in Chapter 10 ("Method"), the key objectives of this thesis were to test the psychometric properties of the SCIPS, and assess the validity of the classification scheme when applied to patients with a diagnosis of schizophrenia. Therefore, the utilisation of the word 'psychosis' was deliberately limited in this study, and the terms 'sub-type' or 'sub-group' were used instead.

11.4.2 Definition of late and early age at onset

The term 'late age at onset of schizophrenia' has been used inconsistently (Luoma et al., 2008). For instance, the international consensus (Howard et al., 2000) recommends that the term 'late onset schizophrenia' is used in cases where 'the onset occurs between age 40 and 60'. Alternatively, age at onset between 20 and 29 years were defined as young-onset by Schulz et al. (2000).

In such circumstances, a study (Schurhoff et al., 2004) carried out an admixture analysis to demonstrate that an age at onset is a marker identifying schizophrenia sub-types. In the study, it was proved that the observed distribution of the age at onset was a mixture of two separate Gaussian distributions, with a cut-off point of 28 years for the two sub-types.

Accordingly, in the SCIPS (item 1-1), a cut-off point of 30 years is used for the differentiation between the early and late age onset. Figure 3 presents the distribution of age of onset in the present study (in the UK and Japanese samples).

Figure 3: Distribution of age of onset in the present study.

The UK sample
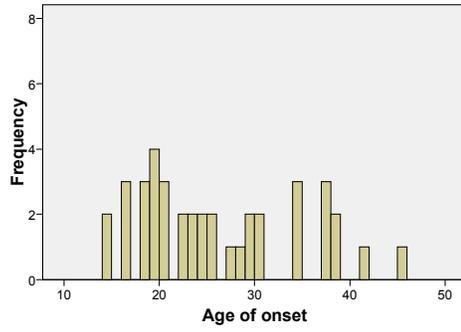
Japanese sample
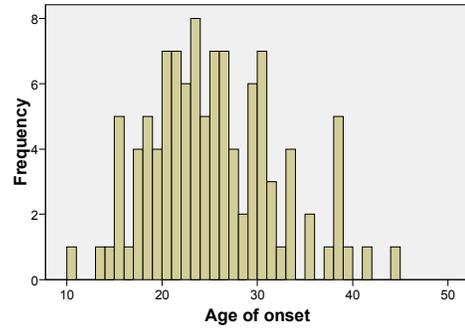
11.4.3 Definition of acute and insidious onset

In a number of studies for which mode of onset was assessed (Harrison et al., 1996; Morgan et al., 2006; Singh et al., 2000), distinction of the acute and insidious onset was made with a cut-off point of 1 month. The same cut-off point (= 1 month) was also used for the differentiation between the acute and insidious onset in the SCIPS (item 1-2).

In the UK sample for the present study, the numbers of patients with acute onset and insidious onset were 11 (26.2%) and 26 (61.9%) respectively. 5 (11.9%) could not give enough information about their mode of onset. Of the 11 whose onset was acute, 4 were with drug related sub-type and 6 were with anxiety category. The sub-type could not be determined for one of the participants because he could not give enough information about the timing of his use of stimulants/ hallucinogens. Of the 26 whose onset was insidious, 9 were with drug related sub-type, 2 were with traumatic category, 3 were with anxiety sub-group, and 12 were with stress sensitivity sub-type. On the other hand, in the Japanese sample, the numbers of patients with acute onset and insidious onset were 31 (29.0%) and 75 (70.1%) respectively. 1 (0.9%) could not give enough information about his mode of onset. Of the 31 whose onset was acute, 1 were with drug related sub-type, 14 were with anxiety category, and 16 were with stress sensitivity sub-group. Of the 75 whose onset was insidious, 4 were with drug related sub-type, 1 were with traumatic category, 12 were with anxiety sub-group, and 58 were with stress sensitivity sub-type.

11.5   Structure of the current version of the SCIPS

The second English and the first Japanese versions of the SCIPS have a common structure and include the same items. The second version (Appendix A) is comprised of 3 sections: the SCIPS interview, a rating sheet, and the diagnostic criteria for the sub-groups, and 3 appendices. The interview includes items with which to obtain relevant information for the sub-grouping of patients, and has 3 sub-sections: 1. onset of psychosis; 2. social functioning; and 3. factors related to psychosis. Each section contains questions to be put to the respondents and instructions about how to rate each item. The rating of these items is recorded on the rating sheet, and enables each patient to be sub-typed by using the diagnostic criteria. Appendix 1 of the SCIPS is the Social

Readjustment Rating Scale and Questionnaire (SRRSQ) (Holmes & Rahe, 1967). This can be used as a list of the major life events with which to rate items 1-3: triggers of the first psychotic episode. Appendix 2 is the Diagnostic Criteria for Borderline Personality Disorder in DSM-IV, and can be used to make a diagnosis of that condition. Appendix 3 is the Diagnostic Guidelines for Psychosis Sub-types. This guideline is a comprehensive overview of the concept of the sub-types of schizophrenia which are utilised in the instrument. The characteristics of each are described therein to enable clinicians and researchers to understand the general idea behind the SCIPS and its conceptualisation.

11.6   Items and questions in the interview section of the SCIPS

The first section of the SCIPS interview concerns the onset of psychosis, and begins by listing the psychotic symptoms which have been experienced by a respondent. Item 1-1 is used to determine age of onset by asking how old a patient was when he/she first experienced psychosis. Item 1-2 aims to identify the mode of onset, with respondents being asked about when they first noticed that something was wrong in the lead up to the first episode of the illness. Mode of onset is also determined by asking the interviewee about how much time passed between when he/she first noticed that something was wrong and the subjective peak of this first episode. The term, subjective peak, means the point at which the respondent's subjective distress about his/her psychotic symptoms is at its height. The precise definition of mode of onset has been described in a previous study (Morgan et al., 2006), and was referenced in order to develop this item herein. Mode of onset of less than 1 month is rated as acute, while that equal to or more than 1 month is rated as insidious.

Item 1-3 aims to identify stressful life events which could lead to psychotic symptoms. This is especially important when seeking to differentiate between the anxiety and stress sensitivity sub-types of schizophrenia. Whether a life event is major or not is determined according to the SRRSQ (Holmes & Rahe, 1967), and on the basis thereof, events with a score of at least 40 are considered to be significant. Furthermore, whether a major life event has led to the development of psychotic symptoms and is, thus, considered to be

stressful, is estimated by identifying whether what happened changed a respondent's sleeping patterns.

The second section of the SCIPS interview concerns social functioning, and was developed mainly by referencing the Pre-morbid Adjustment Scale (PAS) (Cannon-Spoor, Potkin, & Wyatt, 1982). Item 2-1 aims to identify pre-morbid changes in work or school performance. The pre-morbid period is defined as being up to 2 years before the onset of the first episode. Changes which started within 6 months of this time are rated as acute, while those which began more than 6 months before onset are rated as gradual.

Items 2-2 and 2-3 concern pre-morbid social relationships, and are particularly important for the diagnosis of the stress sensitivity sub-type. Item 2-2 aims to assess relationships since early adolescence, while item 2-3 evaluates marital and/or sexual relationships.

The third section of the SCIPS interview concerns factors related to psychosis. Item 3-1 is used to identify the use of illicit drugs, and the type thereof, if applicable. Both the current and the previous Drug Use Scale (DUS) (Drake et al., 1990) were referenced to develop this item. The misuse of drugs just before the onset of a first episode (within 2 weeks) is rated as positive for this item, whereas other time-scales (after or well before onset) is rated as negative.

Item 3-2 relates to early traumatic experiences. As mentioned before, in one study which compared the characteristics of patients with both schizophrenia and borderline personality disorder to those with schizophrenia only (Kingdon et al. in submission), it was found that emotional and sexual abuse in childhood were more associated with the dual diagnosis of the former condition. The difference between these patient groups was less marked, although still significant, when it came to childhood physical abuse. Accordingly, the existence of early emotional and sexual abuse is dealt with in this item, with the Childhood Trauma Questionnaire (CTQ) (Bernstein et al., 1997) being referenced in the preparation thereof.

Individuals who have disclosed their childhood trauma should be carefully supported and followed up. Thus, item 3-2 also provides two questions to take action to this issue; one is for clarifying if they have already discussed their childhood trauma with their care managers, psychiatrists or therapists, and the other is for asking them if information about the trauma could be passed onto their care managers, psychiatrists or therapists when necessary.

11.7   Rating sheet for the SCIPS

The rating sheet is designed to both record the data collected with the SCIPS interview and facilitate the diagnosis of the sub-groups. The ratings for most of the items are dichotomized, and recorded by simply circling one of a number of pre-determined options on the sheet. With particular regard to the ratings for the items involved in the differentiation between the anxiety and stress sensitivity sub-types (items 1-1, 1-2, 1-3, 2-2 and 2-3), the rating '1' applies to a diagnosis of anxiety, while the rating '0' relates to stress sensitivity. Two specific numbers: (A) number of items which are rated as '1' and (B) those which are rated as '0', are used to differentiate between these 2 sub-groups. Item 2-1 is not included for the reasons described in Chapter 13 (see section 13.5.1, "Omission of item 2-1 from the SCIPS"). A table for these 2 numbers is prepared on this sheet, and they are counted and recorded therein.

11.8   Basic concept of the diagnostic criteria for the SCIPS sub-groups

The diagnostic criteria for the SCIPS sub-groups are in 2 parts, one for making a diagnosis that a patient belongs to the drug related and traumatic categories, and the other to enable a differentiation between the anxiety and stress sensitivity forms of the disease. For a diagnosis of the former 2 sub-types, the ratings for items 3-1 and 3-2, respectively, are used. In the SCIPS interview, the ratings for the items in sections 1 and 2 (Items 1-1, 1-2, 1-3, 2-2 and 2-3) help to differentiate between the anxiety and stress sensitivity sub-types.

In the drug related/traumatic part of the criteria, if the rating for item 3-1 "precipitating use of hallucinogens" is 1 'Yes', the patient is put into the former sub-group. If the

ratings for both items 3-2 "traumatic experience" and 3-3 "borderline personality disorder" are 1 'Yes', the patient is put into the traumatic category. On the other hand, if the ratings for either of these 2 items are 'No', the patient is not assigned to this latter sub-group. The rating of 0 'not discussed' is treated as missing for item 3-2. The criteria do allow for the co-existence of the drug related and traumatic categories, whereas the anxiety and stress sensitivity classifications should not exist with any other sub-types. A hierarchical approach is used in this system, meaning that a diagnosis that a patient belongs to the drug related and/or traumatic sub-groups precedes consideration of their status in the anxiety and stress sensitivity forms of the illness. In other words, these latter criteria are only applied to the patients who have been excluded from the drug related and traumatic categories.

In the latter part of the criteria, which are set out in the table entitled "Scores for differentiation between the anxiety and the stress sensitivity sub-groups" on the rating sheet, (A) number of items which are rated as '1' and (B) items which are rated as '0', are considered for the purpose of differentiation between these 2 sub-types. A patient is assigned to the former sub-group if (A) (number of items which are rated as '1') is equal to or more than the pre-determined cut-off point. Alternatively, the patient is assigned to the latter sub-group if (B) (number of items which are rated '0') is equal to or more than the cut-off point which is pre-determined for this parameter. The diagnostic criteria for both of these categories are designed so that these 2 sub-types cannot coexist. To ensure that this is, indeed, the case, the cut-off point for (B) was determined by the following formula:

[Cut-off point for (B)] = [Total number of items involved in the diagnostic process] – [Cut-off point for (A)] + 1

In this formula, the total number of items involved in the diagnostic process is 5.

The ways in which the cut-off points set out in the final version of the SCIPS were determined are discussed in Chapter 13 (see section 13.5.2, "The best diagnostic criteria

for making a distinction between the anxiety and stress sensitivity sub-groups (English version)").

11.9   Conclusion

The English version of the SCIPS was developed to enable the sub-grouping of patients with schizophrenia into 4 sub-types, namely, drug related, traumatic, anxiety and stress sensitivity. Thereafter, a Japanese version of the test was prepared by translating the English document. The 2 versions share a common structure and include the same items. The SCIPS is made up of 3 sections: the SCIPS interview, a rating sheet, and the diagnostic criteria for the sub-groups, and 3 appendices. The information obtained by using the SCIPS interview is recorded on the rating sheet, and the diagnostic criteria are designed to produce an accurate diagnosis of which category a patient belongs to by using the ratings recorded on the rating sheet.

Chapter 12: Relationship between the Fear of Negative Evaluation from Others and Delusions

12.1 Overview

As described in Chapter 8 ("Potential External Validators of the Sub-types in the Current Study"), the fear of negative evaluation from others (FNE) is one of the most promising ways of establishing the construct validity of the stress sensitivity sub-type of schizophrenia, especially in terms of how it is differentiated from the anxiety sub-type. Indeed, the FNE is expected to differentiate between these 2 categories of the illness, and is not included in the diagnostic criteria of the SCIPS. In addition, clinical significance is implied by one study which has revealed that FNE is one of the best predictors of paranoid ideation in a non-clinical population (Martin & Penn, 2001). Nevertheless, such evidence is not in itself robust enough to prove the psychopathological significance of this association in patients with schizophrenia, since the sample used was non-clinical, and other confounding factors for the association (e.g., depression) were not considered. Accordingly, the link between the levels of FNE and delusional ideation was examined in both the non-clinical and clinical samples, and depression was acknowledged as the confounding factor in the analyses which followed. The results of the study are discussed in this chapter.

12.2 Aims of this study

The aims of this study are to examine the hypotheses described below:

1. Delusional ideation is directly associated with FNE in the normal population.
2. Delusional ideation is directly associated with FNE in patients with schizophrenia.
3. FNE continues to be independently associated with delusional ideation in the normal population once the confounding effect of depression is controlled, whilst there would be associations between low mood and the severity of delusional ideation.
4. FNE continues to be independently associated with delusional ideation in patients with schizophrenia once the confounding effect of depression is controlled, whilst there would be associations between low mood and the severity of delusional ideation.

12.3 Procedure

Participant recruitment

Student sample:

282 undergraduate students, who were studying pharmaceutical science at Nihon Pharmaceutical University, were asked, and agreed, to anonymously complete our questionnaires, which included demographic questions about age and sex, the PDI-21, the BFNE and the BDI-II. The participants were initially approached by a teacher when they were attending lectures. Of the 282 individuals, 140 were male (49.6%) and 142 female (50.4%). Their age ranged from 18 to 40 years, with the mean age being 21.0 years (SD = 3.5) and the median age 21.0 (IQR = 19.0-22.0). All of the subjects were of Japanese origin, and were selected because it was assumed that such a group would be healthy.

Patient sample:

The same patient sample, which had been recruited for the assessment of the inter-rater reliability and concurrent validity of the SCIPS, was employed for this study (see Figure 2). The descriptive data and the procedure for the recruitment of the sample are described in Chapter 10 (see section 10.9, "Procedure" and Table 11).

12.4 Measures

The participants were informed that the questionnaire was not an examination; that there were no right or wrong answers; that they did not have to take part in it if they did not want to; and that they could withdraw from the study at any time. Confidentiality was guaranteed in terms of the answers given to the questionnaire. Each participant subsequently received a booklet containing the following questionnaires, which he/she was asked to complete:

The Brief Fear of Negative Evaluation Scale (BFNE) (Collins et al., 2005)

The 21-item Peters et al. Delusions Inventory (PDI-21) (Peters et al., 2004)

The Beck Depression Inventory II (BDI-II) (Beck, Steer, & Brown, 1996)

Details of the scales have been provided in Chapter 10 (see section 10.8, "Measures").

12.5   Sample size

To be able to produce a statistically significant correlation coefficient of at least 0.3 with a two-sided test at the 5% level and with a power of 80% would require a minimum sample of 85 individuals. To allow for missing data, we aimed to recruit 100 individuals to each of our student-volunteer and patient groups. All sample sizes were calculated using the nQuery advisor 7.0.

12.6   Statistical analysis

All of the data was analysed using Microsoft Office Excel and the statistical package, SPSS for Windows (version 15). Pearson product-moment correlation coefficients were calculated to evaluate the association between the PDI, BFNE, and BDI-II scores. Linear regression analyses were carried out to assess if the BFNE score continued to be associated with the PDI scores once the confounding effects of depression were controlled. Spearman rank correlation coefficients were calculated in order to examine the relationship in scores between the BFNE and the 6 factors of the PDI-21(Preti, Sardu, & Piga, 2007).

12.7   Results

12.7.1 The mean scores of all of the scales assessed in this study

Table 12 presents the mean scores of the PDI-21, BFNE, and BDI-II questionnaires in the student and patient samples.

Table 12: Mean scores for all of the scales assessed in this study.

	Student sample (n = 282)	Patient sample (n = 117)
PDI-21 score	6.43 (SD = 4.29, n = 228)	5.44 (SD = 4.95, n = 106)
BFNE total score	23.93 (SD = 10.59, n = 241)	17.55 (SD = 10.14, n = 107)
BDI-II total score	14.34 (SD = 9.72, n = 235)	14.03 (SD = 10.07, n = 105)

12.7.2 The relationship between depression, fear of negative evaluation and delusional ideation

In the student sample, the BDI-II (Pearson's r = 0.46, p < 0.001) and the BFNE (Pearson's r = 0.37, p < 0.001) results were related to the PDI-21 score, and these

relationships were statistically significant. The BDI-II and the BFNE were also associated with each other (Pearson's $r = 0.49$, p < 0.001) (Table 13). Moreover, in the patient sample, the BDI-II (Pearson's $r = 0.44$, p < 0.001) and the BFNE (Pearson's $r = 0.33$, p = 0.002) results were related to the PDI-21 score. An association was also found between the BDI-II and the BFNE outcomes (Pearson's $r = 0.36$, p < 0.001) (Table 14).

Table 13: Pearson's bivariate correlation (two-tailed probabilities) between delusional ideations, depression and fear of negative evaluation from others in the student sample.

	BDI-II	BFNE
PDI-21 score	0.46 (95%CI = 0.35-0.55, n = 228)	0.37 (95%CI = 0.25-0.48, n = 223)
BDI-II		0.49 (95%CI = 0.39-0.59, n = 220)

Table 14: Pearson's bivariate correlation (two-tailed probabilities) between delusional ideations, depression and fear of negative evaluation from others in the patient sample.

	BDI-II	BFNE
PDI-21 score	0.44 (95%CI = 0.28-0.59, n = 105)	0.33 (95%CI = 0.14-0.49, n = 106)
BDI-II		0.36 (95%CI = 0.18-0.52, n = 105)

12.7.3 Linear regression analyses to control the confounding effects of depression

Linear regression analyses were used to evaluate a model in both the student and patient samples. In this model, the BFNE and BDI-II scores were entered as independent variables, and the dependent variable was the PDI-21 score. The adjusted R squared (R^2) for these models in the student and patient samples were 0.24 and 0.21, respectively. In the student sample, the un-standardized regression coefficient for the BFNE was 0.08 (95%CI = 0.03-0.14, p = 0.002), while that for the BDI was 0.16 (95%CI = 0.10-0.22, p < 0.001) (Table 15). In the patient sample, the un-standardized regression coefficients for the BFNE and the BDI were 0.09 (95%CI = 0.001-0.18, p = 0.048) and 0.19 (95%CI = 0.09-0.28, p < 0.001) respectively (Table 16).

Table 15: Linear regression for the PDI-21 score in the student sample: with the BFNE and BDI-II scores as independent variables (n = 213).

Independent variable	Un-standardized Coefficients	t value	p value	95% CI
BFNE	0.08	3.07	0.002	0.03-0.14
BDI-II	0.16	5.12	< 0.001	0.10-0.22

Table 16: Linear regression for the PDI-21 score in the patient sample: with the BFNE and BDI-II scores as independent variables (n = 105).

Independent variable	Un-standardized Coefficients	t value	p value	95% CI
BFNE	0.09	2.01	0.048	0.001-0.18
BDI-II	0.19	4.03	< 0.001	0.09-0.28

12.7.4 The relationship between the fear of negative evaluation and each of the 6 factors of the PDI-21

Spearman rank correlation coefficients were calculated in order to examine the association between the fear of negative evaluation and each of the 6 factors of the PDI-21 that had been suggested by Preti and his colleagues (Preti, Sardu, & Piga, 2007)(Table 17). In the student sample, the BFNE was mildly related to factors 1: schizophrenia (Spearman's $r = 0.32$, $p < 0.001$), 2: paranoid (Spearman's $r = 0.32$, $p < 0.001$), 3: psychotic depression (Spearman's $r = 0.36$, $p < 0.001$), 4: manic bipolar (Spearman's $r = 0.22$, $p = 0.001$) and 5: paranormal beliefs (Spearman's $r = 0.25$, $p < 0.001$) (Table 17). Alternatively, in the patient sample, the BFNE was moderately related to factor 3: psychotic depression (Spearman's $r = 0.44$, $p < 0.001$), and was mildly associated with factors 1: schizophrenia (Spearman's $r = 0.30$, $p = 0.002$), 2: paranoid (Spearman's $r = 0.37$, $p < 0.001$), 4: manic bipolar (Spearman's $r = 0.20$, $p = 0.036$) and 5: paranormal beliefs (Spearman's $r = 0.33$, $p = 0.001$).

Table 17: Spearman's correlation coefficients (two-tailed probabilities) between the fear of negative evaluation from others and the 6 factors of the PDI-21.

	Student sample	Patient sample
Factor 1: schizophrenia	0.32 (p < 0.001, n = 227)	0.30 (p = 0.002, n = 106)
Factor 2: paranoid	0.32 (p < 0.001, n = 229)	0.37 (p < 0.001, n = 106)
Factor 3: psychotic depression	0.36 (p < 0.001, n = 229)	0.44 (p < 0.001, n = 106)
Factor 4: manic bipolar	0.22 (p = 0.001, n = 232)	0.20 (p = 0.036, n = 106)
Factor 5: paranormal beliefs	0.25 (p < 0.001, n = 229)	0.33 (p = 0.001, n = 106)
Factor 6: mystic delusions	0.07 (p = 0.296, n = 230)	0.08 (p = 0.430, n = 106)

12.8 Conclusion

The association between the FNE and delusional ideations was significant, both in the non-clinical sample and in patients with schizophrenia, even after depression was controlled as a confounding factor. These results indicate that the FNE is associated with the development of delusions and is clinically significant. Indeed, FNE may be a key target for CBT in schizophrenia, with it being used to reduce delusional symptoms. Moreover, FNE could also be a suitable candidate as an external validator which can be used to establish the construct validity of the illness's sub-types. A more detailed discussion of the results presented herein is contained in Chapter 18 ("Discussion").

Chapter 13: Psychometric Evaluation of the English and Japanese Versions of the SCIPS

13.1 Overview

As described in Chapter 10 ("Method") and Chapter 11 ("Development of the English and Japanese Versions of the SCIPS"), both versions of the SCIPS tool were developed as a way of classifying patients with schizophrenia into 4 sub-groups: drug related, traumatic, anxiety and stress sensitivity. It was, then, necessary to validate the developed interview, before its use in clinical or research settings. Indeed, and in general, a structured or semi-structured interview cannot be valuable if it has low inter-rater reliability, concurrent validity, diagnostic sensitivity, or specificity. In this chapter, these psychometric properties of the SCIPS (both the English and Japanese versions) were evaluated. In this process, cut-off points for a number of the items which were involved in the differentiation between the anxiety and stress sensitivity sub-types were treated as a variable. Then, the most appropriate cut-off point was determined by assigning 5 values (1-5) to it and comparing their impact on the psychometric properties of the test.

13.2 Aims of this study

The aims of this study are as follows;

1. To establish the inter-rater reliability and concurrent validity of a SCIPS diagnosis (in both its English and Japanese versions).

2. To determine the best diagnostic criteria for making a distinction between the anxiety and stress sensitivity sub-types.

3. To evaluate the sensitivity and specificity of a SCIPS diagnosis (in both its English and Japanese versions).

13.3 Procedure

Participant recruitment

The procedure for the recruitment of the participants and the descriptive data about them are described in Chapter 10 (see section 10.9, "Procedure"; also see Figure 1 and 2, and Tables 10 and 11).

13.4 Sample size

There is no formal method for the sample size calculation of kappa statistics. Therefore, 2 experts (an epidemiologist and a statistician) were consulted, with it being initially agreed that samples containing a minimum of 20 individuals were needed to use kappa coefficients to evaluate the inter-rater reliability and concurrent validity of a SCIPS diagnosis. In order to assess the diagnostic sensitivity and specificity thereof, sub-groups with the highest achievable validity were determined for the largest possible number of participants who were recruited for the other study, which is presented in Chapter 15 ("Construct Validity of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types: A Preliminary Study in the UK") and Chapter 16 ("Construct Validity of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types: A Study with a Larger Sample in Japan"). Explanations of how to determine the sub-groups with the highest achievable validity can be found in Chapter 10 (see section 10.7, "Determination of the sub-groups with the highest achievable validity").

13.5 Results

13.5.1 Omission of item 2-1 from the SCIPS

Although we had assumed that most patients with schizophrenia experienced changes in work or school performance before the first episode thereof, we discovered that many of our sample answered 'no deterioration had happened' or 'cannot remember' for item 2-1 of the SCIPS interview (see Appendix A). For instance, the interviewers rated 'no deterioration' for 5 participants and 'impossible to rate because the participant could not remember' for 4 others of the 42 people recruited for the UK project. Similarly, in the Japanese sample, the interviewers rated 'no deterioration' for 29 respondents and 'impossible to rate because the participant could not remember' for 2 others among the sample of 107. This meant that the ratings of these 9 participants (21.4%) in the UK and 31 (29.0%) in Japan for this item had to be treated as 'missing', because they would make very little contribution to the differentiation between the anxiety and stress sensitivity sub-types. Moreover, the kappa coefficient for item 2-1 was low in the English version

(kappa coefficient = 0.22, 95%CI = 0.02-0.43) (see Table 21), and as a consequence, we ultimately decided to omit this item from the SCIPS.

13.5.2 The best diagnostic criteria for making a distinction between the anxiety and stress sensitivity sub-types (English version)

The diagnostic criteria for the anxiety and stress sensitivity sub-types were determined as described in Chapter 11 (see section 11.8, "Basic concept of the diagnostic criteria for the SCIPS sub-groups"). Values ranging from 1 to 5 were assigned to the cut-off point for (A) (number of items which had to be rated as '1' for the diagnosis of the anxiety sub-type), and the kappa coefficients for inter-rater reliability and concurrent validity were calculated for each cut-off point (Table 18). Both inter-rater reliability (kappa coefficient = 0.93, 95%CI = 0.66-1.20, agreement ratio = 95.0%) and concurrent validity (kappa coefficient = 0.73, 95%CI = 0.47-1.00, agreement ratio = 76.2%) were greatest when the cut-off point was 3. Table 19 presents cross tables that were used for the calculation of the inter-rater reliability and concurrent validity of the SCIPS diagnosis for the participants in the UK with this optimum cut-off point. In the second interview, the sub-type could not be determined for one of the participants because he could not give enough information about the timing of his use of stimulants/ hallucinogens.

Table 18: Inter-rater reliability and concurrent validity of the SCIPS diagnosis calculated with 5 cut-off points.

Cut-off point	Kappa coefficient for inter-rater reliability (95%CI)	Kappa coefficient for concurrent validity (95%CI)
1	0.82 (0.49-1.15)	0.45 (0.20-0.71)
2	0.79 (0.52-1.06)	0.52 (0.26-0.78)
3	0.93 (0.66-1.20)	0.73 (0.47-1.00)
4	0.86 (0.59-1.13)	0.61 (0.35-0.86)
5	0.85 (0.57-1.13)	0.54 (0.30-0.79)

Table 19: Cross tables used for the calculation of the inter-rater reliability and concurrent validity of the SCIPS diagnosis for the participants in the UK.

For the inter-rater reliability

		2nd SCIPS diagnosis					
		Drug related	Traumatic	Anxiety	Stress sensitivity	Subtype not determined	Total
1st SCIPS diagnosis	Drug related	6	0	0	0	1	7
	Traumatic	0	1	0	0	0	1
	Anxiety	0	0	6	0	0	6
	Stress sensitivity	0	0	0	6	0	6
	Total	6	1	6	6	1	20

For the concurrent validity

		Diagnosis with highest achievable validity				
		Drug related	Traumatic	Anxiety	Stress sensitivity	Total
1st SCIPS diagnosis	Drug related	6	0	0	1	7
	Traumatic	0	2	0	0	2
	Anxiety	0	0	4	1	5
	Stress sensitivity	1	0	1	5	7
	Total	7	2	5	7	21

13.5.3 Inter-rater reliability and concurrent validity of a diagnosis made with the Japanese version of the SCIPS

Kappa coefficients for the inter-rater reliability and concurrent validity of the sub-types determined with the Japanese version of the SCIPS were 0.73 (95%CI = 0.49-0.97, agreement ratio = 82.9%, n = 35) and 0.83 (95%CI = 0.65-1.00, agreement ratio = 92.1%, n = 88) respectively. The diagnostic criteria determined with the English version, as described above (cut-off point = 3), were used to make a diagnosis. Table 20 presents cross tables that were used for the calculation of the inter-rater reliability and concurrent validity of the SCIPS diagnosis for the participants in Japan.

Table 20: Cross tables used for the calculation of the inter-rater reliability and concurrent validity of the SCIPS diagnosis for the participants in Japan.

For inter-rater reliability

		2nd SCIPS diagnosis				
		Drug related	Traumatic	Anxiety	Stress sensitivity	Total
1st SCIPS diagnosis	Drug related	4	0	0	0	4
	Traumatic	0	0	0	0	0
	Anxiety	0	0	13	1	14
	Stress sensitivity	0	0	3	12	17
	Total	4	14	16	13	35

For concurrent validity

		Diagnosis with highest achievable validity				
		Drug related	Traumatic	Anxiety	Stress sensitivity	Total
1st SCIPS diagnosis	Drug related	4	0	0	0	4
	Traumatic	0	1	0	0	1
	Anxiety	0	0	19	2	21
	Stress sensitivity	0	0	5	57	62
	Total	4	1	24	59	88

13.5.4 Inter-rater reliability of the ratings for each item of the SCIPS

The kappa coefficients were calculated (Table 21) for the ratings produced by 2 independent raters for each item in the SCIPS.

Table 21: Kappa coefficients (95%CI) of the ratings for each item of the SCIPS provided by 2 independent raters (English and Japanese versions).

Item	English version (n = 20)	Japanese version (n = 35)
1-1. Age at 1st episode	0.89 (0.45-1.32)	0.88 (0.55-1.21)
1-2. Mode of onset	0.47 (0.18-0.75)	0.13 (-0.19-0.44)
1-3. Triggers	1.00 (0.56-1.44)	0.72 (0.38-1.05)
2-1. Deterioration in performance prior to onset	0.22 (0.02-0.43)	0.43 (0.21-0.65)
2-2. Social relationships since early adolescence	0.57 (0.14-1.00)	0.28 (-0.04-0.59)
2-3. Pre-morbid close relationships	0.50 (0.12-0.88)	0.71 (0.38-1.04)
3-1. Precipitating use of hallucinogens	0.89 (0.49-1.30)	1.00 (0.67-1.33)
3-2. Traumatic experience	0.90 (0.46-1.33)	0.55 (0.25-0.84)
3-3. Borderline personality disorder	N/A	N/A

The ratings for item 3-3 in the first interviews using the SCID-II were commonly used for the inter-rater reliability of the two SCIPS diagnoses.

13.5.5 Sensitivity and specificity of the SCIPS diagnosis in the UK

Table 22 sets out the sensitivity and specificity of the SCIPS diagnosis for each of the 4 sub-types of schizophrenia in the UK. A 2 x 2 table for each sub-type that was used to calculate sensitivity and specificity is presented in Table 23.

Table 22: Sensitivity and specificity of the SCIPS diagnosis for participants in the UK (n = 21).

Sub-type	Sensitivity (95% CI)	Specificity (95% CI)
Drug related	0.86 (0.60-1.12)	0.93 (0.79-1.06)
Traumatic	1.00 (1.00-1.00)	1.00 (1.00-1.00)
Anxiety	0.80 (0.45-1.15)	0.94 (0.82-1.06)
Stress sensitivity	0.86 (0.67-1.04)	0.71 (0.38-1.05)

Table 23: The 2x2 tables used for the calculation of the sensitivity and specificity of the SCIPS diagnosis for participants in the UK (n = 21).

Drug related sub-group

		Diagnosis with the highest achievable validity		
		Positive	Negative	Total
SCIPS diagnosis	Positive	6	1	7
	Negative	1	13	14
	Total	7	14	21

Traumatic sub-group

		Diagnosis with the highest achievable validity		
		Positive	Negative	Total
SCIPS diagnosis	Positive	2	0	2
	Negative	0	19	19
	Total	2	19	21

Anxiety sub-group

		Diagnosis with the highest achievable validity		
		Positive	Negative	Total
SCIPS diagnosis	Positive	4	1	5
	Negative	1	15	16
	Total	5	16	21

Stress sensitivity sub-group

		Diagnosis with the highest achievable validity		
		Positive	Negative	Total
SCIPS diagnosis	Positive	12	2	14
	Negative	2	5	7
	Total	14	7	21

13.5.6 Sensitivity and specificity of the SCIPS diagnosis in Japan

Table 24 sets out the sensitivity and specificity of the SCIPS diagnoses for each of the 4 sub-groups in Japan. A 2x2 table which was used to calculate these elements for each sub-type is presented in Table 25.

Table 24: Sensitivity and specificity of the SCIPS diagnosis for participants in Japan (n = 88).

Sub-type	Sensitivity (95% CI)	Specificity (95% CI)
Drug related	1.00 (1.00-1.00)	1.00 (1.00-1.00)
Traumatic	1.00 (1.00-1.00)	1.00 (1.00-1.00)
Anxiety	0.79 (0.63-0.95)	0.97 (0.93-1.01)
Stress sensitivity	0.97 (0.92-1.01)	0.83 (0.69-0.97)

Table 25: 2x2 tables used for the calculation of sensitivity and specificity of the SCIPS diagnosis for participants in Japan.

Drug related sub-group

		Diagnosis with the highest achievable validity		
		Positive	Negative	Total
SCIPS diagnosis	Positive	4	0	4
	Negative	0	84	84
	Total	4	84	88

Traumatic sub-group

		Diagnosis with the highest achievable validity		
		Positive	Negative	Total
SCIPS diagnosis	Positive	1	0	1
	Negative	0	87	87
	Total	1	87	88

Anxiety sub-group

		Diagnosis with the highest achievable validity		
		Positive	Negative	Total
SCIPS diagnosis	Positive	19	2	21
	Negative	5	62	67
	Total	24	64	88

Stress sensitivity sub-group

		Diagnosis with the highest achievable validity		
		Positive	Negative	Total
SCIPS diagnosis	Positive	57	5	62
	Negative	2	24	26
	Total	59	29	88

13.6 Conclusion

Psychometric properties, namely inter-rater reliability and concurrent validity, were examined and established for the SCIPS (English and Japanese versions) in this study. Furthermore, the SCIPS diagnoses for patients with schizophrenia revealed high sensitivity and specificity. Indeed, these results confirmed that the SCIPS can be used for further investigation of the validation of the classification scheme which has been adopted therein. A more detailed discussion about the results presented in this chapter is contained in Chapter 18 ("Discussion").

Chapter 14: Six Month Stability of the SCIPS Diagnosis: A Longitudinal Study in Japan

14.1 Overview

As described in Chapter 3 ("Arguments on the Classification of Schizophrenia"), the instability of the diagnoses has been suggested as a reason why the utility of the sub-types defined by the DSM and ICD systems is reduced. It is, therefore, valuable to establish the stability of a new classification system over time. In this chapter, the results of a prospective follow-up study, which was conducted to establish the stability of the sub-types discussed herein, are described. Indeed, if it is proved that the sub-types determined with the SCIPS do not change over time, this classification scheme could be regarded as being more significant. On the other hand, any classification system that is unstable over time would be less useful. Accordingly, and in order to establish the stability of the sub-type diagnoses, the SCIPS interview was carried out twice on 2 different days, with an interval of at least 6 months between them. The results of this study are discussed in this chapter.

14.2 Aims of this study

The aim of this study is to examine whether the sub-types determined with the SCIPS change over a period of 6 months.

14.3 Procedure

Participant recruitment

The procedure for the recruitment of participants and the descriptive data about them are described in Chapter 10 (see section 10.9, "Procedure"; also see Figure 2 and Table 11).

14.4 Sample size

There is no formal method for sample size calculation for kappa statistics. We, therefore, consulted 2 experts (an epidemiologist and a statistician), with it being agreed initially that samples comprising a minimum of 20 individuals were needed to use kappa coefficients to evaluate the longitudinal stability of the SCIPS diagnoses.

14.5 Results

14.5.1 Participant demographics: prevalence of the sub-types according to the follow-up SCIPS interview

Table 26 sets out the prevalence of the sub-types according to the follow-up SCIPS interviews for the stability study.

Table 26: Prevalence of the sub-types according to the SCIPS follow-up interviews.

Drug related	2 (4.6%)
Traumatic	0 (0.0%)
Anxiety	10 (23.3%)
Stress sensitivity	31 (72.1%)
Not determined	0 (0.0%)

14.5.2 Six month stability of the SCIPS diagnosis

Of the 43 patients, 37 (86.0%) remained in the same sub-group and stable over the 6 month period. The kappa coefficient for the stability of the determined SCIPS diagnoses was 0.69 (95%CI = 0.46-0.92, n = 43). In particular, both (100.0%) of the 2 patients diagnosed with the drug related sub-type in the first assessment remained in the same sub-group over the 6 month period. 8 (75.0%) of the 12 diagnosed with the anxiety sub-type were also stable, while diagnoses of 4 (25.0%) changed to the stress sensitivity sub-group. On the other hand, 27 (93.1%) of the 29 with the stress sensitivity sub-type remained in the same sub-group, while 2 (6.9%) moved to the anxiety category.

14.6 Conclusion

This part of the study revealed that the SCIPS diagnoses for 3 of the 4 sub-types, namely drug related, anxiety and stress sensitivity, were stable over a period of at least 6 months. A more detailed discussion of the results in this chapter is contained in Chapter 18 ("Discussion").

Chapter 15: Construct Validity of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types: A Preliminary Study in the UK

15.1 Overview

Although the conceptualisation of the 4 sub-types of schizophrenia has already been developed, it still requires validation. Indeed, its construct validity, including prognostic quality, has not been established. In this chapter, the results of a cross-sectional study, which was conducted to establish the construct validity of the categories, anxiety and stress sensitivity, are set out. This research involved the evaluation of the difference in the levels of potential external validators, as discussed in Chapter 1 ("Classification in Psychiatry"). There were 3 such validators, namely negative and positive evaluative beliefs, the fear of negative evaluation from others (FNE) and depression (see Chapter 8, "Potential External Validators of the Sub-types in the Current Study"). These variables were compared between the anxiety and stress sensitivity sub-groups. The work was divided into 2 stages, a preliminary study in the UK (in which negative and positive evaluative beliefs and FNE were employed as external validators) and a study with a larger sample in Japan (in which negative and positive evaluative beliefs, FNE and depression were compared between the sub-types). The data about the SCIPS diagnoses that was obtained in the first assessment was used in this study, and the results are discussed in this chapter.

15.2 Aims of this study

The aims of this study are to examine 2 primary and 1 secondary hypotheses which are described below:

Primary hypotheses:

1. Patients with the stress sensitivity sub-type of schizophrenia have higher levels of negative evaluative beliefs (negative-self and negative-others) than those in the anxiety sub-group.

2. Patients with the stress sensitivity sub-type of schizophrenia have lower levels of positive evaluative beliefs (positive-self and positive-others) than those in the anxiety sub-group.

Secondary hypothesis:

Individuals in the stress sensitivity sub-group have a higher fear of negative evaluation from others than those in the anxiety sub-group.

15.3 Procedure

Participant recruitment

The procedure for the recruitment of participants and the descriptive data about them are described in Chapter 10 (see section 10.9, "Procedure"; also see Figure 1 and Table 10).

15.4 Measures

The Brief Core Schema Scale (BCSS) (Fowler et al., 2006)

The Brief Fear of Negative Evaluation Scale (BFNE) (Collins et al., 2005)

Details of the scales are provided in Chapter 10 (see section 10.8, "Measures").

15.5 Sample size

The available information was not enough to enable us to calculate what sample size was needed to detect significant differences between the anxiety and stress sensitivity sub-types with regard to the BCSS and FNE scores. Accordingly, it was initially agreed that a pilot study should be carried out with a sample of a minimum of 40 individuals. We expected that this research would provide important information with which to calculate the appropriate sample size for a larger study of this same issue.

15.6 Results

15.6.1 Prevalence of the sub-types

According to the first SCIPS interview using the determined diagnostic criteria, the numbers of participants in the 4 sub-groups were as follows: 13 (31.0%) drug related, 2 (4.8%) traumatic, 10 (23.8%) anxiety and 15 (35.7%) stress sensitivity. The sub-types could not be determined for 2 of the participants because 1 of them did not complete the interview and the other could not give enough information about the timing of his use of stimulants/ hallucinogens.

15.6.2 Distribution of the BCSS and BFNE scores in the sample in the UK

As set out in Figures 4 and 5, the 4 scores in the BCSS scale, and the total score of the BFNE, did not reveal a pattern of normal distribution. Accordingly, the Mann-Whitney U Test, (a type of non-parametric test for 2 independent samples), was conducted to assess the differences between the 2 sub-groups. Table 27 presents the mean scores and the median for the variables assessed in this study.

Table 27: The mean scores and the median for the variables assessed in this study (the UK sample).

Variables	Mean scores (SD)	Median (IQR)
NS-BCSS (n = 40)	4.85 (5.02)	3.50 (1.00-6.00)
PS-BCSS (n = 40)	9.63 (7.01)	8.50 (3.00-15.75)
NO-BCSS (n = 40)	7.78 (6.50)	7.00 (3.00-12.00)
PO-BCSS (n = 40)	10.33 (6.39)	10.00 (5.25-15.00)
BFNE (n = 42)	25.26 (11.76)	23.00 (17.00-33.25)

NS-BCSS: BCSS score which represents beliefs about negative-self;
PS-BCSS: BCSS score which represents beliefs about positive-self;
NO-BCSS: BCSS score which represents beliefs about negative-others;
PO-BCSS: BCSS score which represents beliefs about positive-others.

Figure 4: Distribution of BCSS scores in the UK sample.
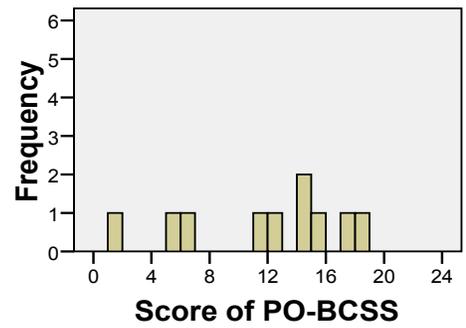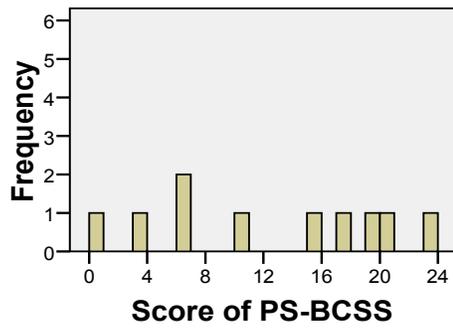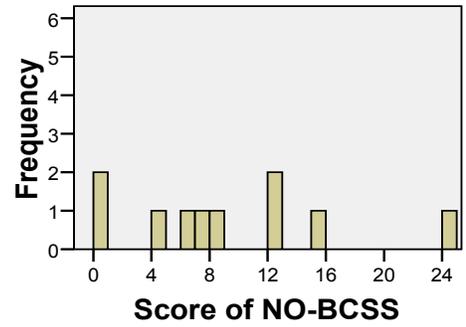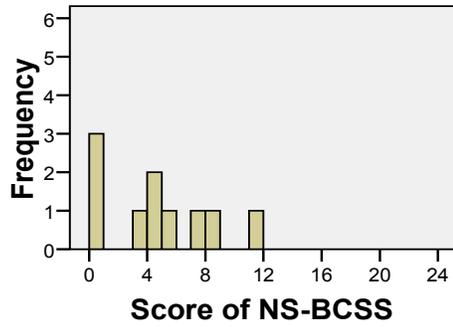
Anxiety sub-type

Figure 4 continued.

Stress sensitivity sub-type
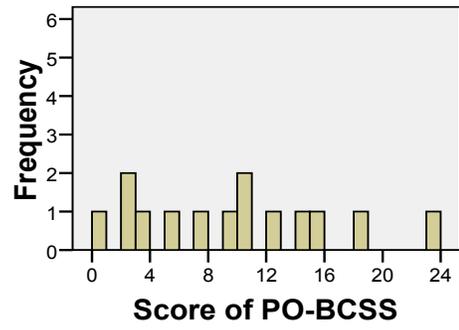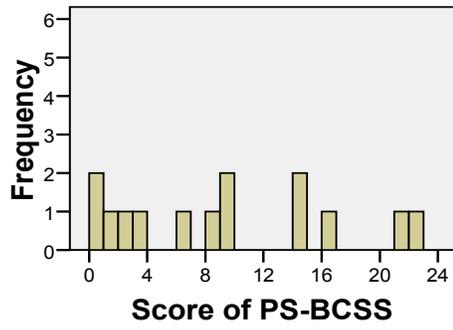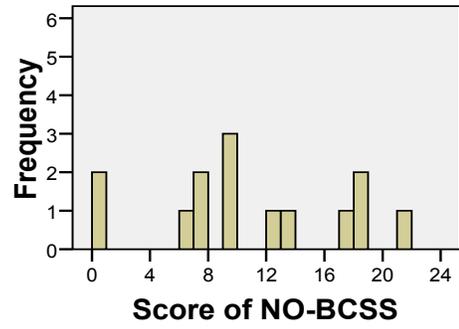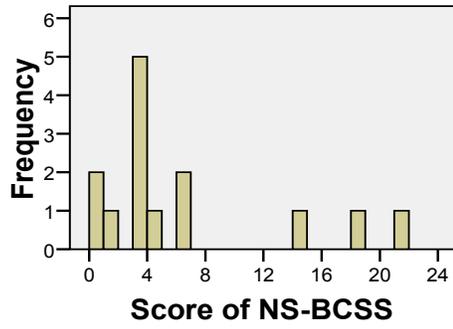
Figure 5: Distribution of BFNE scores in the UK sample.
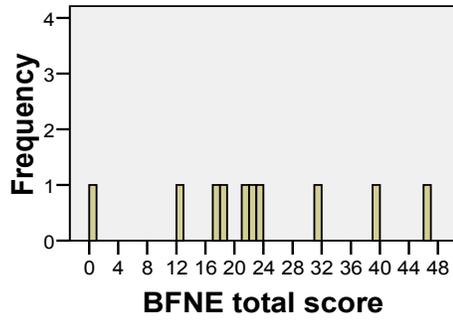
Anxiety sub-type

Stress sensitivity sub-type
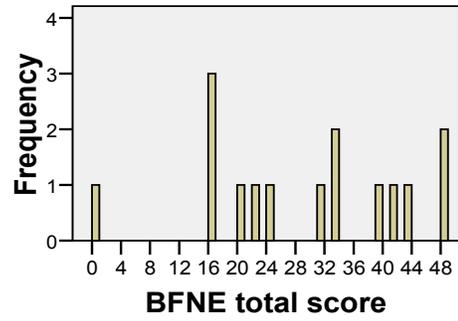
15.6.3 Differences in the BCSS and BFNE scores between the anxiety and stress sensitivity sub-types

The p values for the differences (Mann-Whitney U Test) between the scores for the negative-self, positive-self, negative-others, and positive-others evaluative beliefs were 0.882 (anxiety < stress sensitivity), 0.333 (anxiety > stress sensitivity), 0.427 (anxiety < stress sensitivity), and 0.348 (anxiety > stress sensitivity) respectively. On the other hand, the p value for the discrepancy between the BFNE scores was 0.317 (anxiety < stress sensitivity). Although these differences were not statistically significant, some trends were demonstrated in terms of the distinctions between the anxiety and stress sensitivity categories. For example, the FNE and the positive-self evaluative belief scores appeared higher in the stress sensitivity sub-type. Furthermore, the discrepancy in the BFNE scores between these 2 classifications seemed to be detected with statistical significance in a larger sample.

15.7   Conclusion

Although they were not statistically significant, some appreciable trends were found in the differences in the level of evaluative beliefs and FNE, which were consistent with our hypotheses. Conducting a study to examine if these distinctions were confirmed in a larger sample, therefore, seemed worthwhile, and was subsequently planned and carried out. The results are described in Chapter 16 ("Construct Validity of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types: A Study with a Larger Sample in Japan"). A more detailed discussion of the findings presented in this chapter is contained in Chapter 18 ("Discussion").

Chapter 16: Construct Validity of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types: A Study with a Larger Sample in Japan

16.1   Overview

Although some differences between the anxiety and stress sensitivity sub-types were suggested in the preliminary study described in Chapter 15 ("Construct Validity of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types: A Preliminary Study in the UK"), these were not statistically significant, and the construct validity of these 2 sub-groups was not established. In particular, the levels of fear of negative evaluation from others (FNE) and positive-self evaluative belief appeared to be higher in the stress sensitivity sub-type than in the anxiety sub-group, although the p values for these differences were greater than 0.05. In order to establish the validity of these categories, the levels of FNE and negative and positive evaluative beliefs were compared again in a larger sample in Japan. Difference in the extent of depression between the sub-groups was also examined in this sample. Furthermore, an additional analysis was conducted to examine if there was any association between the SCIPS and DSM sub-types. The data about the SCIPS diagnoses that was obtained in the first assessment was used in this study, and the results are discussed in this chapter.

16.2   Aims of this study

The aims of this research were essentially the same as in the preliminary study which is described in Chapter 15 ("Construct Validity of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types: A Preliminary Study in the UK"). However, when the hypotheses examined in this chapter were proposed, the results of the preliminary piece of work were taken into consideration, and modifications were made on the basis of what had been learnt. Accordingly, the aims of this study were to examine 1 primary, 4 secondary and 1 additional hypotheses as described below:

Primary hypothesis:

The stress sensitivity sub-group reveals a greater fear of negative evaluation from others than those in the anxiety sub-group.

Secondary hypotheses:

1. Patients with the stress sensitivity sub-type reveal higher levels of negative evaluative belief (negative-self and negative-others) than those in the anxiety sub-group.

2. Patients with the stress sensitivity sub-type reveal lower levels of positive evaluative belief (positive-self and positive-others) than those in the anxiety sub-group.

3. Patients with the stress sensitivity sub-type reveal higher levels of depression than those in the anxiety sub-group.

4. Same as the primary hypothesis and secondary hypotheses 1 to 3, which were listed above, but when patients with a diagnosis of both schizoaffective disorder and schizophrenia are included.

A hypothesis which was examined in an additional analysis states that there is no association between the SCIPS and DSM sub-types.

16.3   Procedure

Participant recruitment

The descriptive data of the participants, as well as the procedure for their recruitment, are described in Chapter 10 (see section 10.9, "Procedure"; also see Figure 2 and Table 11).

16.4   Measures

The Brief Fear of Negative Evaluation Scale (BFNE) (Collins et al., 2005)

The Brief Core Schema Scale (BCSS) (Fowler et al., 2006)

Beck Depression Inventory II (BDI-II) (Beck, Steer, & Brown, 1996)

Details of the scales are provided in Chapter 10 (see section 10.8, "Measures").

16.5 Sample size

We calculated the necessary sample size for detecting a significant difference in FNE equal to that found in the preliminary study in the UK with a two-sided test at the 5% level and with a power of 80%. It was calculated based on the description in Cohen (Cohen, 1988) and using the nQuery advisor 7.0, and the results of the preliminary study in the UK were utilised for this purpose. It was, therefore, initially agreed that samples comprising a minimum of 100 individuals were needed to make any comparisons.

16.6 Results

16.6.1 Prevalence of the sub-types

The numbers of participants in the 4 sub-groups diagnosed with the SCIPS were as follows: 5 (4.7%) drug related, 1 (0.9%) traumatic, 26 (24.3%) anxiety and 75 (70.1%) stress sensitivity. Sub-types could not be determined for 10 of the 117 participants, because they pulled out of the project at the very beginning of the assessment and did not complete any of the questionnaires or the interview, including the SCIPS.

16.6.2 Distribution of the BCSS and BFNE scores in the sample in Japan

As shown in Figures 6 to 8, the scores in the BFNE, BCSS and BDI-II scales did not reveal a pattern of normal distribution. Thus, a Mann-Whitney U Test, (a kind of non-parametric test for 2 independent samples), was conducted to assess the differences between the 2 sub-groups. Table 28 presents the mean scores and the median for the variables assessed in this study.

Table 28: The mean scores and the median for the variables assessed in this study (the Japanese sample).

Variables	Mean scores (SD)	Median (IQR)
BFNE (n = 107)	17.55 (10.14)	17.00 (9.00-24.00)
NS-BCSS (n = 105)	6.34 (4.14)	6.00 (3.00-9.00)
PS-BCSS (n = 106)	5.49 (5.07)	4.00 (1.00-8.25)
NO-BCSS (n = 105)	2.60 (3.12)	1.00 (0.00-4.00)
PO-BCSS (n = 104)	9.10 (5.93)	8.00 (4.25-12.00)
BDI-II (n = 105)	14.03 (10.07)	13.00 (6.50-19.00)

NS-BCSS: BCSS score which represents beliefs about negative-self;
PS-BCSS: BCSS score which represents beliefs about positive-self;
NO-BCSS: BCSS score which represents beliefs about negative-others;
PO-BCSS: BCSS score which represents beliefs about positive-others.

Figure 6: Distribution of BFNE scores in the Japanese sample.
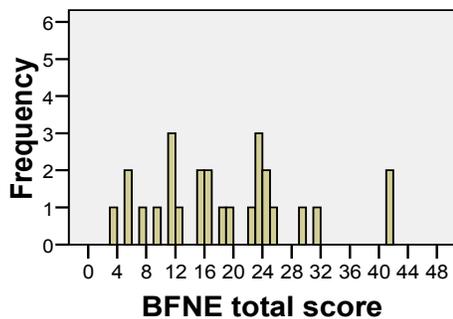
Anxiety sub-type

Stress sensitivity sub-type
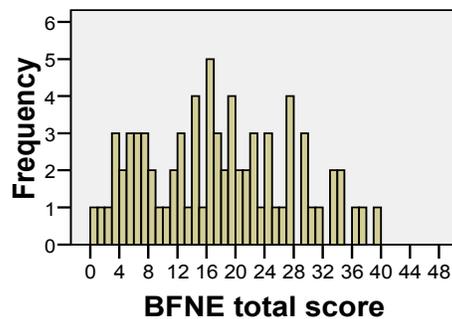
Figure 7: Distribution of BCSS scores in the Japanese sample.

Anxiety sub-type

Score of NS-BCSS

Score of NO-BCSS

Score of PS-BCSS

Score of PO-BCSS
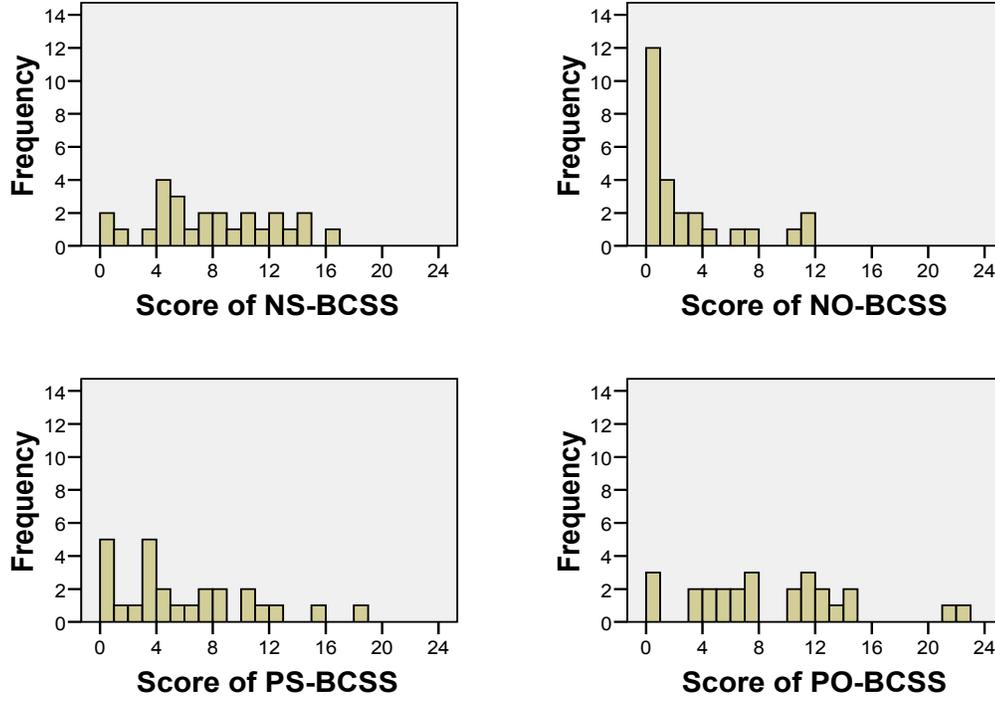
Figure 7 continued.

Stress sensitivity sub-type
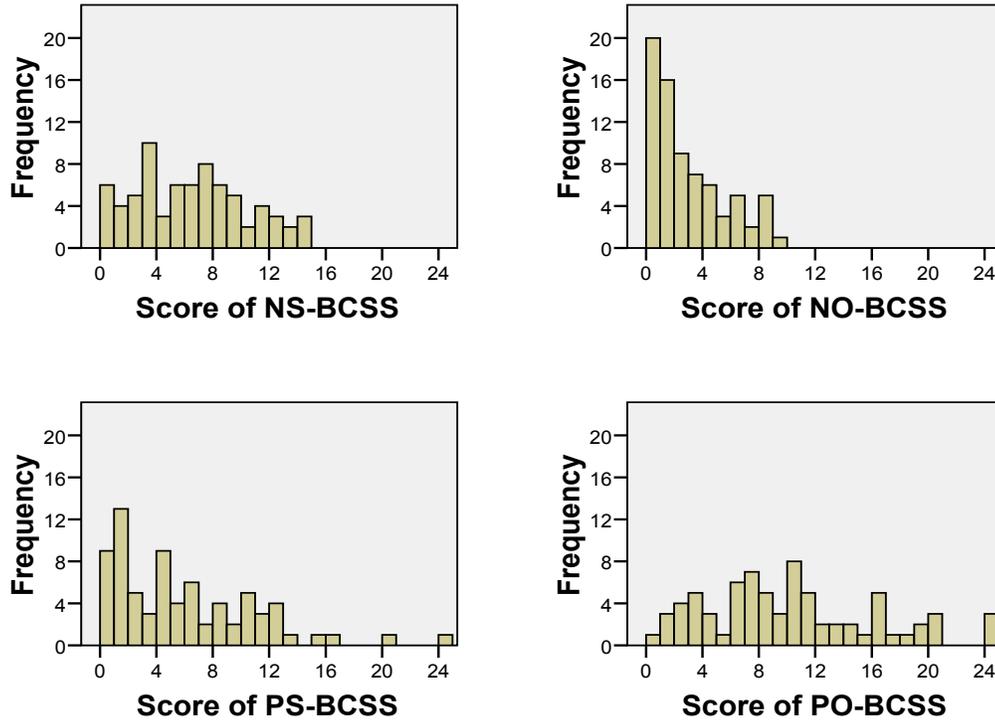
Figure 8: Distribution of BDI-II scores in the Japanese sample.
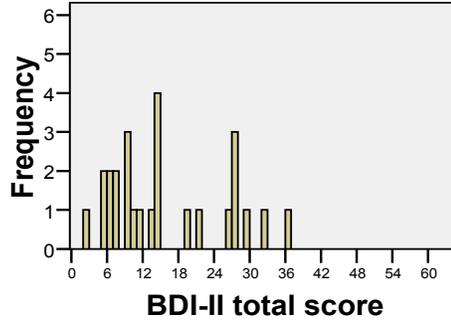
Anxiety sub-type

Stress sensitivity sub-type
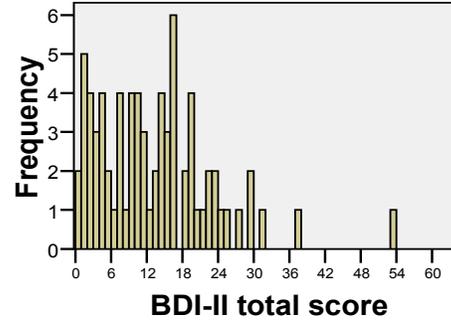
16.6.3 Differences in the BFNE, BCSS and BDI-II scores between the anxiety and the stress sensitivity sub-types

The p value for the differences (Mann-Whitney U Test) in the BFNE score was 0.678 (anxiety > stress sensitivity). On the other hand, the p values for the differences in the scores for the evaluative beliefs: negative-self, negative-others, positive-self, and positive-others were 0.182 (anxiety > stress sensitivity), 0.981 (anxiety < stress sensitivity), 0.246 (anxiety < stress sensitivity), and 0.401 (anxiety < stress sensitivity) respectively. In addition, the p value for the difference in the BDI-II score was 0.260 (anxiety > stress sensitivity). These differences were not statistically significant, and all of the hypotheses in this study were rejected. Indeed, even the difference in the BFNE score, which was suggested in the preliminary study, could not be detected. Possible reasons for these results are discussed in Chapter 18 ("Discussions").

When the participants with a diagnosis of schizoaffective disorder were included in the analysis, the p value for the differences (Mann-Whitney U Test) in the BFNE score was 0.707 (anxiety > stress sensitivity). On the other hand, the p values for the differences in the scores for the evaluative beliefs: negative-self, negative-others, positive-self, and positive-others were 0.104 (anxiety > stress sensitivity), 0.322 (anxiety < stress sensitivity), 0.893 (anxiety > stress sensitivity), and 0.388 (anxiety < stress sensitivity) respectively. In addition, the p value for the difference in the BDI-II score was 0.133 (anxiety > stress sensitivity). These differences were also not statistically significant.

16.6.4 Comparison of the SCIPS and the DSM sub-types of schizophrenia

A cross table for the comparison of the SCIPS and the DSM sub-types of schizophrenia is presented in Table 29. It was impossible to conduct a Chi square test with this table to examine the association between the SCIPS and DSM sub-types, because at least 5 participants are needed in each cell of the table for the analysis. Accordingly, the anxiety and stress sensitivity categories of the SCIPS were chosen for the comparison and four 2x2 tables for each of the DSM sub-types were prepared (Table 30). These 2 particular sub-groups were chosen for this purpose because there may be an overlap in the concepts

behind them, and differentiating between them, thus, seemed to be especially important, as discussed in Chapter 10 (see section 10.1, "Justification for the present study"). Thereafter, a Chi square test or Fisher's exact test was conducted using each of the 4 tables. No significant association was detected between the distinction of the two SCIPS sub-groups and any of the DSM sub-types (Table 31). Neither of the 2 statistical tests could not be conducted for the catatonic sub-group, because none of the participants were diagnosed with the sub-type.

Table 29: Comparison of the SCIPS and the DSM sub-types of schizophrenia.

| | DSM IV subtypes | | | | | |
	Paranoid	Disorganised	Catatonic	Undifferentiated	Residual	Total
SCIPS Sub-types						
Drug related	3	0	0	0	2	5
Traumatic	1	0	0	0	0	1
Anxiety	13	0	0	2	11	26
Stress sensitivity	40	1	0	3	31	75
Total	57	1	0	5	44	107

Table 30: Comparison of the distinction of the anxiety and stress sensitivity sub-groups, and each of the DSM sub-types of schizophrenia.

Paranoid sub-type

		DSM-IV paranoid sub-type		
		Positive	Negative	Total
SCIPS diagnosis	Anxiety	13	13	26
	Stress sensitivity	40	35	75
	Total	53	48	101

Disorganised sub-type

		DSM-IV disorganised sub-type		
		Positive	Negative	Total
SCIPS diagnosis	Anxiety	0	26	26
	Stress sensitivity	1	74	75
	Total	1	100	101

Catatonic sub-type

		DSM-IV catatonic sub-type		
		Positive	Negative	Total
SCIPS diagnosis	Anxiety	0	26	26
	Stress sensitivity	0	75	75
	Total	0	101	101

Undifferentiated sub-type

		DSM-IV undifferentiated sub-type		
		Positive	Negative	Total
SCIPS diagnosis	Anxiety	2	24	26
	Stress sensitivity	3	72	75
	Total	5	96	101

Residual sub-type

		DSM-IV residual sub-type		
		Positive	Negative	Total
SCIPS diagnosis	Anxiety	11	15	26
	Stress sensitivity	31	44	75
	Total	42	59	101

Table 31: Association between the SCIPS and the DSM sub-types (df = 1).

DSM sub-type	Statistical test	χ^2	P value
Paranoid	Chi square test	0.086	0.769
Disorganised	Fisher's exact test	N/A	1.000
Catatonic	N/A	N/A	N/A
Undifferentiated	Fisher's exact test	N/A	0.601
Residual	Chi square test	0.008	0.931

16.7 Conclusion

No significant difference was shown in the evaluative beliefs and the FNE between the anxiety and stress sensitivity sub-types. That is to say, the trends found in the preliminary study in the UK were not reproduced in a statistically significant manner in Japan. Thus, all the hypotheses proposed were not approved in this study. In addition, no association was suggested between the SCIPS and DSM sub-types, and the discriminant validity was indicated for the distinction between the anxiety and stress sensitivity sub-types. A more detailed discussion on the results presented in this chapter is given in Chapter 18 ("Discussion").

Chapter 17: Predictive Value of the Conceptualisation of the Anxiety and Stress sensitivity Sub-types

17.1 Overview

Predictive value, or prognostic quality, is one of the main components which must be established to prove the construct validity of a classification system. It is, therefore, also important to establish the predictive value of the 4 sub-types. In this chapter, the results of a retrospective cohort study, which was conducted to establish the prognostic quality of the anxiety and stress sensitivity categories, are presented. Indeed, if it is revealed that the distinction between these 2 sub-groups could predict the difference in some clinically meaningful variables, such as clinical outcomes or future social functioning, it would be considered to be more significant. On the other hand, a classification system that has no predictive value may be less useful. Accordingly, in order to establish the predictive value of the sub-types, clinical outcomes in relation to hospitalization and the history of self harming were compared. The data about the SCIPS diagnosis that was obtained in the first assessment was used in this study, and the results are discussed in this chapter.

17.2 Aims of this study

The aims of this study are to examine 1 primary and 3 secondary hypotheses, as set out below:

Primary hypothesis:

Patients with the stress sensitivity sub-type of schizophrenia stay in hospital longer than those with the anxiety sub-type over a period of 3 years after the date of their first admission with the illness.

Secondary hypotheses:

1. The duration of the first hospitalization with schizophrenia is longer in those with the stress sensitivity sub-type than it is for those with the anxiety sub-type.

2. Patients with the anxiety sub-type have a higher risk of self harming than those with the stress sensitivity sub-type.

3. Same as the primary hypothesis and secondary hypotheses 1 and 2, which were listed above, but when patients with a diagnosis of both schizoaffective disorder and schizophrenia are included.

17.3   Procedure

17.3.1 Participant recruitment

The descriptive data of the participants, as well as the procedure for their recruitment, is set out in Chapter 10 (see section 10.9, "Procedure"; also see Figure 2 and Table 11).

17.3.2 Data collection

As described in Chapter 10 (see section 10.8, "Measures"), 2 variables for the hospitalization comparison, namely variable 1 "total time spent in hospital during the period of 3 years after the date of their first admission" and variable 2 "duration of the first hospitalization" were obtained from the participants' case notes. In addition, information about earlier self harming was collected as a part of the SCID-II interview used for making diagnosis of borderline personality disorder in the first assessment. Of the 107 patients who completed the SCIPS interview, 56 provided information about variable 1 (52.3%), while data about variable 2 was available for 65 of them (60.7%). Six patients (5.6%) had not experienced hospitalization, 36 (33.6%) did not have enough information in their case notes, and 9 (8.4%) had been hospitalized for the first time in the last 3 years (and so variable 1 was not applicable). None but one (0.9%) was in their first hospitalization, when they were recruited for the study. Variable 1 was provided for this participant, because he had been hospitalized for more than 3 years. In addition, variable 2 of the patient was calculated by subtracting his first admission date from the current date and included in the analysis. Of the 56 for whom variable 1 did apply, 10 were diagnosed as having the anxiety sub-type (17.9%), 43 were in the stress sensitivity group (76.8%) and 3 were in the drug related category (5.4%). Of the 65 patients for whom variable 2 was available, 11 were diagnosed with the anxiety sub-type (16.9%), 49 with the stress sensitivity variant (75.4%) and 5 with the drug related condition (7.7%). None of the participants who provided information for variables 1 or 2 were diagnosed as

belonging to the traumatic sub-group. All of the 107 people who completed the SCIPS interview gave details about self harming. Of them, 64 (59.8%) self harmed after the onset of their first psychotic episode, while 43 (40.2%) did not.

17.4   Sample size

The available information was not enough to enable us to calculate what sample size was needed to detect significant differences between the anxiety and stress sensitivity sub-types with regard to the variables which were selected for the comparison in this part of the study. Accordingly, it was initially agreed that a pilot study should be carried out with the same sample, which had been recruited for the assessment of the construct validity of the SCIPS diagnosis in Japan (see Chapter 16, "Construct Validity of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types: A Study with a Larger Sample in Japan", and Figure 2).

17.5   Results

17.5.1 Distribution of the 2 variables related to hospitalization

As shown in Figure 9, the 2 variables: total time [the number of days] spent in hospital over a period of 3 years after the date of first admission; and the duration [the number of days] of the first hospitalization, were not normally distributed. Accordingly, a Mann-Whitney U Test was conducted to assess the differences between the 2 sub-groups. The median for variables 1 and 2 was 278.5 (IQR = 146.5-577.3) and 137.0 (IQR = 67.5-290.5) respectively.

Figure 9: Distribution of the 2 variables related to hospitalization.
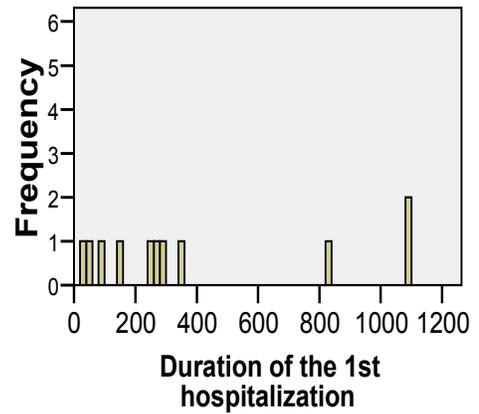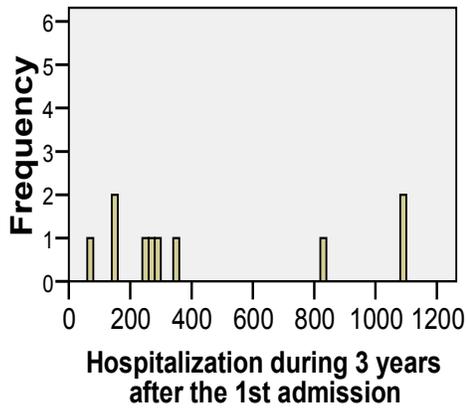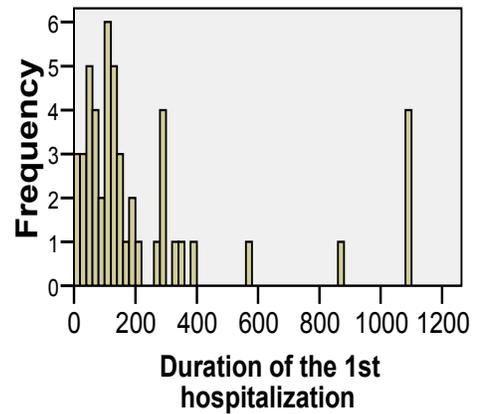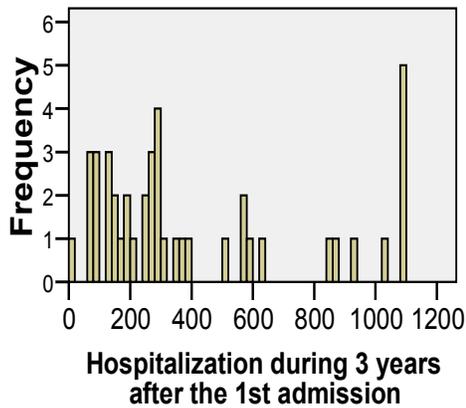
NB.
1. In terms of the time unit used in this figure, the number of days was presented for the two variables.

2. In the graphs for the 1st hospitalization (in the right-hand column on this page), a duration of the 1st hospitalization of longer than 1080 days (3 years) was counted as 1080.

17.5.2 Differences in the 2 variables concerning hospitalization between the anxiety and stress sensitivity sub-types

The p value for the discrepancies in variable 1: "total time spent in the hospital over a period of 3 years after the date of 1st admission" and variable 2 "duration of 1st hospitalization" were 0.811 (anxiety > stress sensitivity) and 0.141 (anxiety > stress sensitivity) respectively. These differences were not statistically significant and the primary hypothesis of this study was, therefore, rejected. Furthermore, these trends were contrary to the a priori expectations. Similar results were reproduced, even after cases with deviated levels of variables (variable 1 > 400 for the analysis of "total time spent in hospital over a period of 3 years after the date of 1st admission" and variable 2 > 400 for the analysis of "duration of 1st hospitalization") were excluded. Possible reasons for these results are discussed in Chapter 18 ("Discussions").

When the participants with a diagnosis of schizoaffective disorder were included in the analysis, the p value for the discrepancies in variable 1 and variable 2 were 0.811 (anxiety > stress sensitivity) and 0.249 (anxiety > stress sensitivity) respectively. These differences were also not statistically significant.

17.5.3 Differences in the risk of self harming between the anxiety and stress sensitivity sub-types

A Chi square test was conducted, and revealed that the differences in the risk of self harming between the anxiety and stress sensitivity sub-types was not statistically significant ($p = 0.110$). Relative risk (RR) for self harming was 1.50 (anxiety > stress sensitivity, 95%CI = 0.61-3.69), which was also not statistically significant (Table 32).

Table 32: 2x2 Table used for the evaluation of the differences in the risk of self harming between the anxiety and stress sensitivity sub-types (patients with schizophrenia).

		History of self harming		
		Positive	Negative	Total
SCIPS diagnosis	Anxiety sub-type	14	12	26
	Stress sensitivity sub-type	27	48	75
	Total	41	60	101

When the participants with a diagnosis of schizoaffective disorder were included in the analysis, the difference in the risk of self harming between the 2 sub-types was revealed to be statistically significant by the Chi square test (p = 0.044). The RR for self harming was 1.59 (anxiety > stress sensitivity, 95%CI = 0.66-3.81) which was not statistically significant (Table 33).

Table 33: 2x2 Table used for the evaluation of the differences in the risk of self harming between the anxiety and stress sensitivity sub-types (patients with schizophrenia and schizoaffective disorder).

		History of self harming		
		Positive	Negative	Total
SCIPS diagnosis	Anxiety sub-type	17	12	29
	Stress sensitivity sub-type	28	48	76
	Total	45	60	105

17.5.4 Differences in demographics as confounding factors between the anxiety and stress sensitivity sub-types

In order to assess the influence of demographic parameters (i.e., age, sex, in or out-patient, and years after the age of onset of the first psychotic episode) as confounding factors (Table 34), the 2 sub-types were compared. Participants with a diagnosis of schizoaffective disorder were included in the analysis, and a Chi square test was conducted for gender in each of the 2 sub-categories, while Mann-Whitney U Test was carried out for the other 2 parameters. No statistically significant differences were found in terms of gender ($\chi^2 = 1.6$, df = 1, p = 0.204, n = 105) (Table 35), proportion of outpatients ($\chi^2 = 2.2$, df = 1, p = 0.141, n = 105) (Table 36), and years since the age of

onset (p = 0.662). However, the differences in age between the 2 groups were statistically significant (anxiety > stress sensitivity, p = 0.003).

Table 34: Participant demographics in the 2 sub-groups (patients with schizophrenia and schizoaffective disorder in Japan).

	Anxiety sub-type (n = 29)	Stress sensitivity sub-type (n = 76)
Mean age (SD)	50.5 (8.9)	42.3 (12.6)
Median age (IQR)	53.0 (42.0-58.0)	40.5 (32.0-53.8)
Male, No. (%)	16 (55.2)	52 (68.4)
Outpatients, No. (%)	25 (86.2)	72 (94.7)
Mean years after the age of onset (SD)	20.0 (9.9)	19.3 (12.6)
Median years after the age of onset (IQR)	20.0 (11.0-28.5)	18.0 (10.0-29.0)

Table 35: 2x2 Table used for the evaluation of the differences in sexuality between the anxiety and stress sensitivity sub-types (patients with schizophrenia and schizoaffective disorder).

		Sex		
		Male	Female	Total
SCIPS diagnosis	Anxiety sub-type	16	13	29
	Stress sensitivity sub-type	52	24	76
	Total	68	37	105

Table 36: 2x2 Table used for the evaluation of differences in proportion of outpatients between the anxiety and stress sensitivity sub-type (patients with schizophrenia and schizoaffective disorder).

		Outpatients	Inpatients	Total
SCIPS diagnosis	Anxiety sub-type	25	4	29
	Stress sensitivity sub-type	72	4	76
	Total	97	8	105

17.6   Conclusion

No differences were found between the anxiety and stress sensitivity sub-types in the total time spent in hospital over a period of 3 years after the date of the first admission (variable 1) and the duration of the first hospitalization (variable 2). In addition, in terms of the risk of self harming, no statistically significant differences were found between these 2 sub-types, and the RR for self harming was also not statistically significant. Nevertheless, when the participants with a diagnosis of schizoaffective disorder were included, and a Chi square test was conducted again, a statistically significant difference was found in the risk of self-harm between the anxiety and stress sensitivity categories. Possible interpretations of these results are discussed in Chapter 18 ("Discussions").

Chapter 18: Discussion

18.1   Overview

This discussion begins with a brief overview of the main findings of this thesis, and the demographics of the study's samples are also considered. Since the results should be interpreted on the basis of the research's methodological limitations, its strengths and weaknesses are discussed in so far as they relate to the properties of the SCIPS assessment tool, the study's design and measurement selection. The key findings are then examined in terms of the relevant literature, and clinical implications are considered. Finally, suggestions for future research are highlighted.

In this study, the SCIPS was developed as a way of sub-grouping patients with schizophrenia into 4 sub-categories (Chapter 11, "Development of the English and Japanese versions of the SCIPS"). The psychometric properties of the tool were then evaluated (Chapter 13, "Psychometric Evaluation of the English and Japanese versions of the SCIPS"). Kappa statistics were used to assess reliability, while both they and sensitivity and specificity were used to test validity. In this process, the optimum cut-off point for differentiation between the anxiety and stress sensitivity sub-types of the illness were determined. When the optimum cut-off point was used to make a distinction, both the English and Japanese versions of the SCIPS revealed high inter-rater and test-retest reliability, as well as high concurrent validity.

In preparation for the assessment of the construct validity of the differentiation between the anxiety and stress sensitivity sub-types, the FNE was revealed to be associated with delusional thinking, and could, thus, be used as an external evaluator for classification purposes (Chapter 12, "Relationship between the Fear of Negative Evaluation from Others and Delusions"). This part of the study used a cross-sectional design for both the non-clinical and the patient samples.

Thereafter, prospective research was conducted to establish the longitudinal stability of the sub-groups determined with the SCIPS. This part of the study revealed that the SCIPS

diagnoses for 2 of the 4 sub-types, namely drug related and stress sensitivity, were stable over a period of at least 6 months, though the stability of those for anxiety sub-type was not satisfactory.

The scores of the selected psychometric scales (the BCSS and the BFNE for the UK sample, and the BCSS, BFNE and BDI-II for the Japanese sample) were compared between the anxiety and stress sensitivity categories, but no significant differences were found (Chapter 15, "Construct Validity of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types: A Preliminary Study in the UK", and Chapter 16, "Construct Validity of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types: A Study with a Larger Sample in Japan"). In addition, in terms of the relationship between the SCIPS and DSM sub-types, no significant association was detected between the distinction of the two SCIPS sub-groups, namely the anxiety and stress sensitivity sub-types, and any of the DSM sub-types. A cross-sectional design was used for this part of the study.

A preliminary analysis of retrospective cohort data, which explored the differences between the anxiety and stress sensitivity sub-types in relation to hospitalization and the risk of self harming, was also conducted. Two variables, namely: 1) total time spent in hospital over a period of 3 years after the date of first admission and 2) duration of the first hospitalization, were compared between these 2 groups. Differences between them in terms of the risk of self harming were also examined. However, once again, no statistically supported differentiation was found, although when patients with a diagnosis of both schizoaffective disorder and schizophrenia were included in the analysis, the difference in the risk of self harming was revealed to be statistically significant by the Chi-square test.

18.2   Is the sample used for the studies in this thesis representative of patients with schizophrenia?

Subjects were recruited from psychiatric outpatient clinics and psychiatric hospitals in an adult community mental health service in the UK, and, in Japan, from psychiatric

hospitals which function like these community mental health teams. Accordingly, the patients included in the research were expected to be representative of those who are diagnosed with schizophrenia through the community mental health services in both countries.

Our patient samples in the UK (χ^2 = 7.5, df = 1, p = 0.006, n = 42) and Japan (χ^2 = 5.3, df = 1, p = 0.021, n = 117) included more males than females, which is consistent with previously published studies (Lewine, Burbach, & Meltzer, 1984; Thornicroft et al., 2004). Moreover, the demographics in terms of marital status were similar to those previously reported (Thornicroft et al., 2004); of the individuals who participated in this particular study and had diagnoses of schizophrenia (n = 404), 57% were men, 65% were single, and 17% were married.

Other studies have suggested that there are no significant differences between males and females in terms of the prevalence of schizophrenia (Bhugra, 2005), and it is, indeed, still a matter of debate whether the proportion of men with the illness is greater than that in the female population. However, the fact that the percentage of men with schizophrenia in the samples in the current study is higher than in the general population, may be explained by the influence of sampling bias. As described in Chapter 10 "Method", patients who might be suitable participants in the research were nominated by their consultants (see sections 10.9.1, "Recruitment of participants in the UK" and 10.9.4, "Recruitment of participants in Japan"), meaning that not all of those diagnosed with schizophrenia at these institutions were recruited. Accordingly, it is possible that this process may have caused some imbalance in the proportion of males and females in the sample.

Alternatively, the differences in the male/female split might also be related to 2 other factors. Firstly, the high number of men in the drug related sub-type may have increased the proportion of male patients in the sample. Indeed, in the UK, all of those put into this sub-group (n = 13) were men, and, if they were excluded from the analysis, the difference between the numbers of male and female participants was not statistically significant (χ^2

= 1.8, df = 1, p = 0.145, n = 29). Similarly, in the sample in Japan, 4 of the 5 patients in the drug related sub-group were male (80.0%), and if they had been excluded from the analysis, the difference between the numbers of male and female participants was, again, not significant (χ^2 = 3.6, df = 1, p = 0.058, n = 112).

Secondly, the difference in the expression of schizophrenia between men and women might have caused some discrepancy. Evidence from a large body of literature demonstrates that the modal age at onset for men is between 18 and 25 years, whereas it is between 25 and the mid-30s for women (American Psychiatric Association, 2000). This means that the age at onset in the former gender is lower than in the latter. Consequently, at least in theory, if the lifetime prevalence of schizophrenia is the same in males and females, and this statistic is compared over the same range of ages, the presence of the illness may be greater in men than in women.

Whatever the circumstances, the influence of sampling bias should always be carefully considered when the results in the present study are interpreted. For instance, patients who were either mentally unstable, or were reluctant to participate in the research, would have been excluded by their consultants. In other words, those whose ability to communicate was grossly impaired, or who had limited insight into their condition, were not included in the sample, which may have affected the representative nature thereof.

Accordingly, so far as the psychometric properties of the SCIPS are concerned, although acceptable inter-rater reliability and concurrent validity were indicated in 2 different settings (i.e., the UK and Japan), the tool's reliability and validity could have been enhanced if interviews has also been conducted with patients whose communication levels were impaired and with those who had limited insight into their mental health (this topic will be discussed in greater detail below).

18.3   Strengths and weaknesses of the SCIPS
The English version of the SCIPS was developed as a way of sub-grouping patients with schizophrenia into 4 sub-types: drug related, traumatic, anxiety and stress sensitivity, and

was revealed to have high face validity. The optimum cut-off point for differentiation between the latter 2 sub-groups was also determined in order to achieve the best inter-rater reliability and concurrent validity, meaning that a SCIPS diagnosis obtained with these diagnostic criteria did have acceptable levels thereof. The test-retest reliability of the diagnosis was also established. As a consequence, this interview tool is able to be used effectively in both research and clinical settings.

The Japanese version of the SCIPS was also established with high face validity. To prepare this test, the English example was translated into Japanese, and a back translation procedure was utilised, as described in Chapter 11 (see section 11.3, "Preparation of the Japanese version of the SCIPS"). Four psychiatrists who had extensive clinical experience with the diagnosis and treatment of schizophrenia, and could understand Japanese, reviewed that version, and the face validity of the interview was, ultimately, confirmed. The psychometric properties of this Japanese version were, then, tested, as had occurred with the English document. Inter-rater and test-retest reliability, concurrent validity, and the sensitivity and specificity of a diagnosis with this Japanese version of the tool were revealed to be acceptable.

The determination of a SCIPS diagnosis was based equally on age and mode of onset, pre-morbid adjustment, and aetiology, such as drug-misuse and traumatic experience. A high level of stability is to be expected with this system, because these properties cannot change after the onset of the disease. At the same time, significant predictive value is also anticipated, because the factors used for classification purposes have been revealed to predict the clinical outcome of schizophrenia or psychosis (Chapter 4, "Psychosocial Factors and Psychosis").

However, as set out in Table 21 (Chapter 13, "Psychometric Evaluation of the English and Japanese Versions of the SCIPS"), the inter-rater reliability of some of the items in the tool (i.e., items 1-2, 2-2 and 2-3 of the English version and items 1-2 and 2-2 of the Japanese version) was comparatively low. Ambiguity about what was being asked and rated may have been the cause of this. Accordingly, the reliability of these items could be

improved by providing a more detailed description of the information required for the assessment of each of these elements. We, therefore, plan to make some further refinements, with the aim of improving the reliability of the SCIPS diagnoses.

In a process of exploring the cause of the low inter-rater reliability for each of the items, it was noticed that one interviewer included the second or later psychotic episodes for the assessment of the mode of onset (item 1-2) in Japan. That is to say, the period taken for the development of schizophrenia until the peak of the whole course of the illness was rated as a mode of onset for some of the participants, though this item aimed to assess the interval between the start and the peak of the first psychotic episode. Accordingly, a specific explanation will be additionally given in the SCIPS to emphasise that item 1-2 should be rated with regard to the first psychotic episode.

Although the SCIPS assessment tool may be useful in both research and clinical settings, and may well also improve the reliability of the classification scheme, it is still debatable whether it would be applicable to all patients with schizophrenia. Indeed, most of the participants in the present study were outpatients, and all of them agreed to be interviewed twice. Accordingly, conducting the interview with those who are in hospital with relatively severe conditions and/or reluctant to talk about their situations may be more difficult. Consequently, further investigation might be appropriate to establish the reliability and validity of the SCIPS in a broader spectrum of patients with the illness, including individuals whose communication levels were impaired and with those who had limited insight into their mental health.

Moreover, there may be a limitation in accuracy of the sub-types determined with the highest achievable validity in this study. Information from the case notes might have been imprecise to some extent and led to incorrect sub-grouping of the participants. In other words, the sub-groups determined with the SCIPS might have been more valid for some of the participants than those with the highest achievable validity used in the assessment of the concurrent validity. This may have reduced the magnitude of coincidence between the former and the latter (kappa coefficient = 0.73 in the UK and = 0.83 in Japan, for the concurrent validity), though the level thereof was still acceptable.

There are 6 other problems which may decrease the validity of the SCIPS' diagnoses. Firstly, the stressful life events listed in the SRRSQ may not cover all of the patients' relevant experiences. In other words, some significant and stressful events might be ignored in the process of making diagnosis with the SCIPS. Nevertheless, the SRRSQ is a well established scale, and has been widely used in clinical research (Abel et al., 1999; Lynch et al., 2005). Consequently, in order to achieve high reliability for the diagnoses in the current study, only the events included in the SRRSQ were rated as being stressful. However, in clinical terms in particular, life experiences which are not listed in this tool could also be rated as 'stressful' if it is apparent that they preceded the onset of a patient's first psychotic episode and caused significant upset.

Secondly, childhood traumatic experiences are assessed with a single question, and no account was taken of duration, or the severity of the abuse, in item 3.2. This may decrease the validity, and even the reliability, of an assessment of this item. However, questions about early childhood trauma may cause a great amount of stress in individuals who have had such experiences, and it is important for such questions to be addressed with minimum upset being brought about in a respondent. Moreover, it is also essential to maintain the clinical utility of the SCIPS by minimising the number of questions therein and total time taken for the interview. It was therefore decided not to include additional questions in the instrument relating to the childhood trauma.

Thirdly, the influence of recall bias may have an impact on the validity of a diagnosis. Patients might not be able to correctly remember all of the information which is required, and may even give incorrect answers to the questions included in the SCIPS interview. This could lead to a misdiagnosis of the sub-types of schizophrenia. For instance, and in so far as we discussed this issue with all of the raters who interviewed the patients in this present study, a few of the participants (2 in the UK and around 5 in Japan) had difficulty in reporting the chronology of the start of their psychotic symptoms and their use of illicit drugs.

Fourthly, the conceptualisation of psychosis that emerged herein, and upon which this work is based, is on a vulnerability-stress continuum, which may lead to there being some difficulty in differentiating between the groups. This was particularly apparent with the anxiety and stress sensitivity categories, but refinement of the criteria did make allocation thereto both possible and reliable.

Fifthly, it is questionable whether the drug related sub-group is homogeneous. The substances listed in the diagnostic criteria have a number of different characteristics in terms of their impact on patients. For example, in one study, cannabis use was revealed to be associated with greater pre-morbid adjustment, while the use of stimulants or hallucinogens was not (Arndt et al., 1992). These drugs do, however, have at least 1 common feature - they all appear to be able to induce psychotic symptoms (Angrist et al., 1974; Arndt et al., 1992). Furthermore, specific psychosocial interventions, which broadly target substance misuse in people with psychosis, have been developed and shown to be effective (Haddock et al., 2003; James et al., 2004; Wright et al., 2008). Nevertheless, sub-classification according to which kinds of drugs a patient uses might need to be considered in the future. The potential overlap between the traumatic and drug related groups may also need further exploration, although it did not emerge as a significant complicating factor in this study.

Sixthly, the SCIPS diagnostic criteria do not allow for the co-existence of the anxiety or stress sensitivity classifications with any other sub-types. Though a hierarchical system is employed and the co-existence of the sub-types is not allowed in the current criteria, occurrence of such a situation should be taken into consideration in reality. Therefore, in the future, modified diagnostic criteria, in which the anxiety and stress sensitivity sub-types could exist with other sub-groups, might have to be provided.

In conclusion, the SCIPS is a promising tool with which to sub-group patients with schizophrenia according to this recently developed classification scheme. The semi-structured interview achieves acceptable inter-rater and test-retest reliability, and

concurrent validity. Accordingly, it can now be used to test the validity of the classification itself.

18.4 Strengths and weaknesses of the methodology: general issues

18.4.1 Application of the SCIPS for evaluating the stability and construct validity of the classification scheme

As discussed above, and with acceptable inter-rater reliability and concurrent validity, the SCIPS was developed as an instrument with which to sub-group patients with schizophrenia. Then, in order to evaluate the stability and construct validity of the classification scheme, the present study employed the tool to determine the sub-types of the participants' illnesses. Thus, sufficient reproducibility and concurrent validity was expected, at least in terms of the sub-categories used herein.

Nevertheless, the SCIPS does have limitations, as discussed above (see section 18.3, "Strengths and weaknesses of the SCIPS"), and these must be borne in mind whenever the interview element thereof is used in clinical or research settings.

18.4.2 Selection of psychometric scales

The use of standardized self-reporting questionnaires is one of the major strengths of this study. All of these have been previously used in psychotic disorders' research and are available in both English and Japanese. All of them (both the English and Japanese versions) have good psychometric properties, and are of a reasonable length, meaning that they could be used as a part of the assessment process in this work.

There is, however, a major problem with regard to the use of these questionnaires for the evaluation of the construct validity of the sub-types of schizophrenia. The BFNE, BCSS, PDI-21 and BDI-II scores of patients with the illness can change within a few months or a year, apparently in conjunction with alterations in their symptomatology. This means that these scales might not be suitable for assessing the construct validity of the sub-types, which are expected to be stable. Indeed, some of the participants told their interviewers

that their scores on these questionnaires had changed over time, and asked about which period they should base their answers upon. We, therefore, instructed people in the patients sample in the UK and Japan to respond to these self-report scales based upon how they had been feeling over a specified period prior to taking the tests (i.e., 1 month for the BFNE, BCSS and PDI-21, and 2 weeks for the BDI-II). Accordingly, when the protocol was prepared for this study, the importance of using questionnaires which were more stable over time should have been considered.

18.4.3 Limitations of cross-sectional study design

Although the cross-sectional study design is useful for highlighting an association between 2 or more factors, it cannot demonstrate causal relationships between them. Indeed, it is almost impossible to deduce which factor is the cause of the illness, and which is the consequence, even when the link between them is revealed to be statistically significant. This limitation is discussed in detail below with regard to the study about the relationship between the fear of negative evaluation from others and delusions.

18.4.4 An issue relating to multiple comparisons

A number of hypotheses were tested in the present study. That is to say, in a number of situations, one sample was used for not less than two comparisons in the analysis. Consequently, probability of finding a significant difference just by chance (a Type I error) would have become higher (Altman, 1991). Accordingly, the results, especially the statistically significant ones, from the comparisons made in this thesis should be interpreted cautiously.

18.5   Discussion of specific issues arising out of each study in this thesis: interpretation of the results and their clinical implications

18.5.1 Relationship between the fear of negative evaluation from others and delusions

As described in Chapter 12 ("Relationship between the Fear of Negative Evaluation from Others and Delusions"), the present study demonstrated the association between FNE and delusional ideation in a non-clinical population. Martin & Penn's earlier research (2001), which similarly revealed the relationship between FNE and sub-clinical paranoid ideations in a non-clinical population, was therefore replicated herein with the non-clinical sample in Japan.

A similar link between FNE and delusional ideations was also demonstrated in this study, in patients with schizophrenia. In fact, the BFNE and PDI-21 scores were mildly associated with each other.

Accordingly, although the influence of selection bias should be considered carefully, it can be concluded that the association between FNE and delusional thinking is a universal phenomenon, which is independent of where a person is from and whether or not he has schizophrenia. Indeed, a similar relationship was also found in the patients who were recruited in the UK for the study herein (Spearman's $r = 0.51$, 95%CI = 0.24-0.71, p = 0.001, n = 40).

The linear regression analyses in both the non-clinical and clinical samples revealed that the relationships between FNE and delusional ideations were not confounded by depression, one of the key factors contributing to the development of psychotic symptoms (Drake et al., 2004; Freeman & Garety, 2003; Hafner et al., 2005; Iqbal et al., 2000; Krabbendam et al., 2005; Smith et al., 2006).

Although the PDI-21 and BFNE scores seem to be higher in the student sample than in the patient sample (Table 12), these scores cannot be compared directly between the two

groups because of the reason described in Chapter 10 (see section 10.9.8, "Data collection and the assessment process").

These results lead us to conclude that FNE is clinically significant in terms of the development of delusions in patients with schizophrenia. However, these findings could be interpreted in one of two ways: 1. a high FNE is causal, and contributes to the development, maintenance or exaggeration of delusions; 2. a high FNE is a consequence, with delusions leading to an increase in this fear.

A high FNE could be a causal factor in the development, maintenance or elevation of delusional ideations, and may, therefore, be a potential target for both the psychological and pharmacological treatment of patients with delusions. CBT is a psychological therapy which may be able to control FNE, and we are currently in the process of developing a version which targets it specifically. Similarly, in terms of the pharmacological treatment of FNE in patients with delusions, psychotropic drugs which can reduce this symptom might be used for patients with schizophrenia. Antidepressants, such as selective serotonin reuptake inhibitors (SSRIs) may be candidates, although the specific effect thereof on reducing FNE remains to be demonstrated.

Even if high FNE is a consequence of delusions, it would still be a potential variable which could have an impact on the estimation of the severity thereof. In other words, even when a direct evaluation of delusions is difficult, FNE might still be assessed and used as a sensitive proxy indicator. Indeed, it is often the case that patients with schizophrenia demonstrate poor insight into, and decline to talk about, their delusions, thus making it difficult to directly evaluate the severity of this psychotic symptom. In such a circumstance, patients may feel more comfortable in talking about their FNE than their delusions. Moreover, a high FNE could be a maintaining factor, and may, thus, be a target for psychological or pharmacological intervention.

There are 2 main limitations in the present study.

Firstly, the research employed a cross-sectional design, and it is therefore impossible to demonstrate a causal relationship between FNE and delusional ideations. In other words, we do not know from our results whether a high FNE leads to the development of delusions, or vice versa. Therefore, it is still unclear if either a reduction in FNE contributes to any improvement in the severity of delusions during a course of treatment, or if it is a suitable target for relevant psychotherapy. The implications for future research into the establishment of this causal relationship are discussed below (see section 18.7.1, "Assessment of the causal relationship between the fear of negative evaluation from others and delusions").

Secondly, the observed associations could be explained by content overlap between a number of the items in the BFNE and the PDI-21. For example, item 15 in the latter ("Do you ever feel that people look at you oddly because of your appearance?") overlaps with what is asked in the BFNE. Moreover, individuals who answer 'Yes' to item 4 of the PDI-21 ("Do you ever feel as if you are being persecuted in some way?") would naturally be concerned about negative evaluation from others. Yet, this overlap cannot explain away all of the associations between the BFNE and 5 of the 6 factors of the PDI-21 (see Table 17). For instance, factors 1: schizophrenia, 4: manic bipolar and 5: paranormal beliefs did not include any items whose content seemed to display a similarity, and yet they were still significantly associated with the BFNE in both the non-clinical and clinical samples.

In conclusion, while also controlling for the effect of depression, the present study demonstrated the association between FNE and delusional thinking, both in the non-clinical population and in patients with schizophrenia. It is possible that this link is a universal phenomenon, which is independent of where the person is from and whether or not he has the illness. Indeed, it was suggested in our research that FNE is clinically significant in terms of the psychopathology of delusions, and may well, therefore, be a potential target for both psychological and pharmacological treatments for patients with these symptoms. Finally, FNE might also be a good indicator of the severity of delusions, especially when their direct assessment is difficult.

18.5.2 Six month stability of the SCIPS diagnoses

As described in Chapter 14 ("Six Month Stability of the SCIPS Diagnosis: A
Longitudinal Study in Japan"), the study herein suggested that 2 of the sub-types of
schizophrenia (drug related, anxiety and stress sensitivity) determined with the SCIPS
were stable over a period of 6 months, though the stability of those for anxiety sub-type
was not satisfactory.

This instability of the sub-group was considered to be caused by inaccuracy of the
information collected in the SCIPS interview. At least in theory, the factors assessed in
the interview never change after the onset of psychosis, as discussed in Chapter 10 (see
section 10.1, "Justification for the present study"). Therefore, main cause of the
discrepancy between the 2 diagnoses with the interval could be the change of the ratings
for any of these factors, which cannot occur theoretically. Accordingly, improvement of
the stability could be achieved by collecting and using more accurate information for the
SCIPS diagnosis. In other words, information from case notes or carers in addition to that
from patients themselves can be used to improve the stability, as well as test-retest
reliability, of the diagnosis.

This research was prospective in nature, and the categories were determined by
interviewing the participants twice at 2 different times, with an interval of at least 6
months between them. Unfortunately, there was only 1 patient in the traumatic sub-group
in the sample, and this individual could not be followed up in the stability assessment.

These results empirically support the theoretical expectation that our classification
scheme would provide acceptably stable diagnoses of the sub-types of schizophrenia, as
described in Chapter 10 (see section 10.1, "Justification for the present study"). Such
stability may well be a major strength of the classification system because, as described
in Chapter 3 ("Arguments on the Classification of Schizophrenia"), the instability of
diagnoses has been suggested as a reason for reducing the usefulness of the sub-types of
the illness that are defined by the DSM and ICD schemes.

Nevertheless, because its sample size is comparatively small, it is debatable whether the results of the current study can be generalised. In fact, our sample contained no patients in the traumatic category and only 2 in the drug related sub-group. In order to resolve this problem, a piece of work which adopts the same procedure as the research herein, but with a larger sample, including patients with the traumatic sub-type of schizophrenia, should be conducted. In addition, the follow up period in our study (6 months) is relatively brief, and stability in the longer term should also be explored in further work. The prevalence of the traumatic sub-type in the Japanese sample is similar to that expected from the results in earlier studies. No definite (0.0%), but 2 probable (3.2%), cases of borderline personality disorder among 63 patients with schizophrenia were reported in research conducted by Keshavan and his colleagues (Keshavan et al., 2005). In another piece of work, 1 (2.5%) of 40 individuals with the illness had a pre-morbid diagnosis of borderline personality disorder (Rodriguez Solano & Gonzβlez De Chβvez, 2000). However, other studies have recruited significant numbers of such patients in the UK (Kingdon et al, submitted).

There could be 3 explanations for this discrepancy. Firstly, some form of bias, including selection bias, may have caused the increase in the proportion of patients with the traumatic sub-type in other research. For instance, the prevalence of this category might be higher among patients from specific psychiatric units (e.g., forensic units). Secondly, issues about the reliability and validity of diagnostic procedures should also be considered. Even when the SCID is used to identify borderline personality disorder, the inter-rater reliability and concurrent validity of the diagnosis is not ideal. Indeed, it was reported that the former was comparatively low for diagnoses made by use of the Structured Interview for DSM-III-R Personality (SCID-II for DSM-III-R) (kappa coefficient = 0.58, to differentiate between patients with and without a personality disorder) (Pilkonis et al., 1995). In addition, in the same study, and in terms of the concurrent validity of the diagnosis, the kappa coefficient for the level of agreement between the SCID-II interview and the consensus diagnosis of whether there is a personality disorder or not was 0.37 (Pilkonis et al., 1995).

18.5.3 Construct validity of the distinction between the anxiety and stress sensitivity sub-types

Despite our attempts to establish construct validity of the differentiation between the anxiety and stress sensitivity sub-types, no statistically significant differences were found between these 2 groups in terms of the scores of the selected psychometric scales.

As discussed above (see section 18.4.2, "Selection of psychometric scales"), a possible reason for the absence of these distinctions is that the scores of the patients with schizophrenia sometimes changed over a period of a few months or longer, apparently in conjunction with alterations in their symptomatology. Indeed, the BFNE, BCSS and BDI-II scores may not be constant over time, or even suitable for comparison between categories that are expected to be stable.

It is, thus, important to identify psychometric scales which can both assess the properties that will not change over time, and differentiate between the anxiety and stress sensitivity sub-types. The construct validity of these sub-groups could, then, be established by using these psychometric scales. New criteria for the identification thereof are discussed below (see section 18.7.2, "Further evaluation of the construct validity of the distinction between the anxiety and stress sensitivity sub-types with the minimum influence of selection bias" and Table 37).

With regard to the comparison of the SCIPS and the DSM sub-types, no association was suggested between these two classification schemes and the discriminant validity was indicated for the distinction between the anxiety and stress sensitivity sub-types (see section 16.6.4, "Comparison of the SCIPS and the DSM sub-types of schizophrenia"). Indeed, this result can be well explained by the premise that the approach employed in the SCIPS is different from that in the DSM, as described in Chapter 4 (see section 4.6, "A concept of clinical sub-groups integrating psychosocial factors"). However, there are 2 major problems in this study. Firstly, both the SCIPS and DSM sub-types were determined for each participant by one interviewer and this might be a cause of bias.

Secondly, it is debatable if the diagnoses of the DSM sub-groups are valid enough. It seems difficult to collect sufficient information for a diagnosis of the DSM sub-types in only one interview with a participant, even when supplementing data are provided by psychiatric staff who is responsible for the patient (see section 10.8.5, "DSM sub-types"). Indeed, there is limited support for the concurrent validity of a diagnosis of the sub-types of schizophrenia according to the DSM-IV. Despite an extensive literature search, no article was found in which diagnoses of the sub-types according to the SCID, or the DSM-IV diagnostic criteria, were compared with the gold standard diagnoses thereof.

18.5.4 Predictive value of the distinction between the anxiety and stress sensitivity sub-types

Despite attempts to establish the predictive quality of the differentiation between the anxiety and stress sensitivity categories of schizophrenia, no statistically significant difference was found between these 2 sub-groups with regard to the variables selected for this study.

Sampling bias in relation to the severity of patients' conditions may have influenced the results. Most of the participants in Japan were recruited from day care units, and were experiencing a chronic clinical course. This meant that those who had a better clinical outcome and, therefore, did not need the continuous use of the mental health services, were not approached for this study. If patients in the anxiety sub-group had demonstrated better clinical results, and had, thus, required less regular access to treatment than those in the stress sensitivity category, this study may have included relatively severe cases of the former and mild cases of the latter. If this had happened, it might have been difficult to detect the differences which exist between these 2 sub-types in representative cases with schizophrenia.

When participants with a diagnosis of schizoaffective disorder were included alongside those with schizophrenia, and a Chi square test was conducted, the patients with the anxiety sub-type not only had a higher risk of self harming than those in the stress

sensitivity sub-group, but this difference was statistically significant. This finding is consistent with the results of the work carried out by Pompili and his colleagues (2007), which revealed that schizophrenic patients with a good pre-morbid function are more likely to commit suicide. According to the diagnostic criteria, those with the anxiety form of the illness would have better pre-morbid functioning than those with the stress sensitivity sub-type.

No statistically significant difference was found in terms of gender and status as outpatients between the 2 sub-types in our sample. These 2 variables did, therefore, not seem to be confounding factors causing an apparent difference in the risk of self-harm between the 2 categories. In terms of the age of the participants, the median age of those in the anxiety sub-group was higher than those with the stress sensitivity sub-type of the disease, and this difference was statistically significant. Consequently, this distinction may have caused the difference in the factor relating to the risk of self-harm. However, because there was no significant difference between these 2 groups in the number of years since the age of onset of the first psychotic episode, the increased risk of self-harm could not simply be explained by an increase in the length of time that a patient had suffered from schizophrenia or schizoaffective disorder.

In any event, although the result obtained with the Chi square test was statistically significant, the RR indicated that the difference in the risk of self harming between the 2 sub-types was not. Accordingly, the evidence is not strong enough to conclude that patients with the anxiety form of schizophrenia are more likely to harm themselves than those in the stress sensitivity sub-group.

Moreover, the influence of selection bias in these circumstances should also be taken into consideration. If relatively severe cases of the anxiety sub-type had been selectively recruited for the study, as discussed above, the difference in the risk of self harming between these 2 sub-groups might have been exaggerated. In other words, we may have detected a difference which did not really exist in representative cases of schizophrenia and schizoaffective disorder. In addition, the reinclusion of the patients with

162

schizoaffective disorder into the analyses might be another cause of bias. Especially, this process could increase the risk of type I errors, or false positives, caused by multiple comparisons, as discussed above (see section 18.4.4, "An issue relating to multiple comparisons").

18.6   Implications for clinical practice of the SCIPS and the newly established sub-grouping scheme

18.6.1 General issues

Antipsychotic medication and psychosocial interventions can be used together to substantially improve the likelihood of recovery from the symptoms of schizophrenia for many sufferers. However, there are 2 major problems, which have a negative impact on such treatment. Firstly, the term schizophrenia is itself associated with a major degree of stigma. Indeed, it has consistently proved difficult to use with many patients, who reject it either on the basis of the associations that it now has with aggressive behaviour and a deteriorating clinical course, or because they do not consider themselves to be unwell (British Psychological Society, 2000).

Secondly, patients with a diagnosis of schizophrenia tend to be socially excluded (Kingdon et al., 2006) by the general population. Health promotion campaigns have had a marginal impact (Crisp et al., 2004), and concerns about the danger posed by those suffering from the disease have, if anything, become cemented in the public's imagination (Department of Health, 2003). This is not simply due to a lack of knowledge, because campaigns to promote a biological model of schizophrenia have been successful in conveying this message. However, they may also have had the paradoxical effect of increasing social distancing (Angermeyer & Matschinger, 2005).

In such a situation, our previous study (Kingdon et al., 2008a) suggested that using the terminology related to the 4 sub-groups of the illness significantly reduced the negative perceptions of medical students about those who suffer from the 'group of schizophrenias'. Moreover, the terms for the sub-types, namely drug related, traumatic,

anxiety and stress sensitivity, might also be more acceptable to patients (Kingdon et al., 2008b). The SCIPS would both provide strong empirical support for the classification scheme, and enable the dissemination of these terms, as well as the destigmatisation of people diagnosed with the disorder.

Furthermore, in terms of its clinical application, the SCIPS might provide both clinicians and patients with a clear and broad understanding of the condition. In fact, consideration of the rating for each item in the SCIPS assessment would help all relevant parties to have a more comprehensive overview of an individual's specific disorder. Moreover, sub-grouping each patient according to the SCIPS would be helpful in the creation of an appropriate treatment plan. Indeed, it has been proposed that consideration of a patient's sub-category of the illness, as well as all of the information gathered by the SCIPS, would be useful in enabling CBT to be targeted more effectively (Kingdon & Turkington, 2005).

18.6.2 Application of the sub-types to patients with a diagnosis of psychotic disorders other than schizophrenia

There is general agreement that patients who meet the criteria for schizophrenia, according to current versions of the DSM or ICD, are a very diverse group (Myin-Germeys, Delespaul, & van Os, 2005; van Os, 2009), and there can be an overlap with bipolar disorder. A conference on 'Deconstructing Psychosis' held by the DSM-V prelude project (Allardyce et al., 2007; Kraemer, Shrout, & Rubio-Stipec, 2007; Regier, 2007) recently included a recommendation that a broad psychosis spectrum should replace the current categories (First, 2007). This kind of approach is neither absolutely new nor unconventional, because patients with schizophrenia and other psychotic disorders (e.g., schizoaffective disorder and delusional disorder) have not been distinguished in a number of previously published articles (Barnes et al., 2008; Doering et al., 1998; Walshe et al., 2007). For instance, individuals with schizoaffective disorder and schizophrenia were recruited and assigned to the same group in a number of randomised controlled trials which evaluated the effectiveness of antipsychotics (Leucht et al., 2009; Meltzer et al., 2008; Robinson et al., 2006; Sikich et al., 2008). Furthermore, in most of

these studies (Robinson et al., 2006; Sikich et al., 2008), the differences in the different diagnostic categories were not considered. Thus, although further work is required to conclude that such an approach really is valuable, it may be clinically relevant to define a broad psychosis group in which patients with schizophrenia, schizoaffective disorder and delusional disorder are included, before then sub-grouping them into the 4 sub-categories. In these circumstances, the SCIPS may then be used to categorise patients belonging to this broad psychosis group.

18.7   Implications for future research; building on the present study

18.7.1 Assessment of the causal relationship between the fear of negative evaluation from others and delusions

As discussed above (see section 18.5.1, "Relationship between the fear of negative evaluation from others and delusions"), it is important to demonstrate that there is a causal relationship between the FNE and delusional ideations. It is still questionable whether a reduction in the former symptom is either a suitable target for psychotherapy, or would contribute to any improvement over the course of treatment in the delusions that a patient is suffering from. A prospective experimental study which examines the effectiveness of CBT in the reduction of FNE in patients with delusions may, therefore, be valuable. Subsequently, if there is a reduction in FNE after CBT, which is then followed by an improvement in the extent of the delusions experienced by patients with psychotic disorders, a high FNE would have been proved to contribute to the development and/ or maintenance of this symptom. Accordingly, a randomised controlled study could be set up to compare the effects on the reduction in delusions of CBT and a control treatment. Although it is unclear if the FNE is a successful target for psychological intervention, it has been demonstrated that group cognitive behavioural therapy for social anxiety disorder has been effective in patients with schizophrenia, and did reduce their FNE (Kingsep, Nathan, & Castle, 2003).

18.7.2 Further evaluation of the construct validity of the distinction between the anxiety and stress sensitivity sub-types with the minimum influence of selection bias

As discussed above (see sections 18.5.3, "Construct validity of the distinction between the anxiety and stress sensitivity sub-types" and 18.5.4, "Predictive value of the distinction between the anxiety and stress sensitivity sub-types"), the risk of selection bias and the use of psychometric variables which might change over time are 2 of the major problems in the present study. Accordingly, further research into the evaluation of construct validity in which these problems are dealt with could be planned.

Firstly, with regard to the risk of selection bias, patients who are representative of both the anxiety and stress sensitivity sub-types of schizophrenia should be recruited. To do so, one possible procedure would be to approach such individuals at the time of either their first presentation at a psychiatric outpatient clinic, or at their first assessment by the community mental health service. This would enable us to contact all patients at about the time of the onset of their psychosis and to avoid selectively recruiting those with comparatively severe conditions. Early intervention teams, which are part of the mental health services available in the UK, are a promising resource. The difficulty of such an approach is that it would take a significant period of time to recruit a sufficient number of participants, because the annual incidence of schizophrenia is low, in the range of 0.5 to 5.0 per 10000 people (American Psychiatric Association, 2000). For instance, a source of patients covering between 200, 000 and 2 million of the general population would be expected to provide approximately 100 individuals who have experienced a first episode of schizophrenia. Even if such a resource could be found, it would take at least a year to recruit this number of participants.

Secondly, in relation to the psychometric variables which are stable over time, a further search for other such potential factors would be required. The new criteria, which consist of the 5 items listed in Table 37, could be used to identify candidates for these validators. Items 1 to 4 are the same as those listed in the criteria employed for the present study (see

166

section 8.2, "Criteria for the identification of the candidates to be validators", and Table 9).

Table 37: The new criteria for the identification of potential validators.

1. A variable which is not included in the SCIPS.

2. A variable which is expected to differ among the sub-types.

3. A variable which is suggested as being associated with the intensity of psychotic symptoms (e.g., delusions and hallucinations).

4. A variable which is indicated as being a target for cognitive behavioural therapy (CBT).

5. A variable which is stable over time.

Pre and/or co-morbid diagnoses of schizoid personality disorder, which are revealed with the DSM diagnostic system (American Psychiatric Association, 2000), might be an option and able to differentiate between the anxiety and stress sensitivity sub-types. Patients in the latter sub-group, may be more likely to have a pre or/ and co-morbid diagnosis of schizoid personality disorder than those with the anxiety form thereof. However, the diagnostic criteria for both this personality disorder and the stress sensitivity category do overlap to some extent (i.e., both criteria include poor social relationships as an item). Thus, this variable would not fulfill item 1) of the criteria for the validators.

Another possibility would be to use psychometric questionnaires for the assessment of temperament, which may differ between sub-types and is expected to be stable over a long period of time. This variable may also be a target for CBT. One study (Hori et al., 2008) suggested that patients with schizophrenia had a unique personality profile when assessed with the Temperament and Character Inventory (TCI). This research also demonstrated that personality dimensions were moderately associated with the symptom dimensions assessed by the Positive and Negative Syndrome Scale (PANSS) (Hori et al., 2008). However, in the same study, male patients were revealed to experience an even greater change in personality than females when both groups were compared to healthy

individuals, and instability of temperament is implicated in this finding. In addition, a further study, which also used the TCI (Fresan et al., 2007), suggested that novelty seeking and reduced cooperation, as character dimensions, were risk factors for violent behaviour in schizophrenic patients.

Instruments for cognitive assessment might also be used to validate the classification. Although the level of cognitive functioning would not be stable over a long period of time, this variable might differ among the sub-types. Moreover, cognitive impairment might be a target for CBT. In fact, in one study (Brazo et al., 2002), it was suggested that schizophrenia could be characterised by heterogeneous cognitive dysfunctions. In this piece of work (Brazo et al., 2002), executive/attentional function and episodic memory were explored by conducting neuropsychological tests on individuals suffering from schizophrenia. These included the modified card sorting test (de Zubicaray et al., 1998; Nelson, 1976), the trail making test (Lezak, 1995), the Stroop colour-word test (Jensen & Rohwer, Jr., 1966; van der Elst et al., 2006) and the California verbal learning test (Hawkins & Wexler, 1999; Woods et al., 2006). Then, the differences in the 2 modals of cognitive functions, determined with the schedule for the deficit syndrome (Brazo et al., 2002), was revealed among the sub-types. In order to test the cognition of patients with schizophrenia, brief assessment tools were also developed. For instance, the Brief Assessment of Cognition in Schizophrenia (BACS) and the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) were developed to analyse the cognitive levels of patients with the illness. Moreover, the psychometric properties and ease of use of these tests were demonstrated as being satisfactory (Chianetta et al., 2008).

18.7.3 Evaluation of the construct validity of the classification system including the drug related and traumatic sub-types

In this present study, the construct validity of the distinction between the anxiety and stress sensitivity sub-types were examined by exploring the potential differences between these categories. These 2 sub-groups were chosen for this assessment because there might be an overlap between the concepts behind them, and because the differentiation between

them also seemed to be particularly important. However, the establishment of the construct validity of the other 2 categories – drug related and traumatic – is still important, and they have yet to be confirmed.

Thus, in order to establish the construct validity of the classification system, including all of the 4 sub-types, another study should be conducted. The psychometric variables and procedure for recruiting subjects, which were discussed in the previous section, could be used therein, and if the early intervention teams can be a source of participants, as discussed above, the sample should be large enough to include a sufficient number of patients in the traumatic sub-group. This is because the prevalence of this sub-type among individuals with schizophrenia is comparatively low, and is not expected to exceed 5% (see section 18.5.2, "Six month stability of the SCIPS diagnosis").

18.8 Development of treatment interventions

The overarching aim of this work was to explore whether clinically relevant sub-groups could be differentiated across the wide range of schizophrenia presentations seen in routine clinical practice. It is argued that this type of sub-grouping system should be simple and practical to use, and should highlight aspects of clinical presentation that, if addressed in treatment, may facilitate improved outcomes. Given this, future work could usefully focus on developing the links between the sub-types and treatment interventions. Initial work could involve defining the key components of treatment for patients presenting in each of the 4 sub-groups; a task that may involve conducting a number of case series. Treatments for those with the drug related sub-type could concentrate on controlling their drug misuse (e.g., as Haddock and colleagues (2003) have attempted). On the other hand, interventions for those with the traumatic sub-type may best focus more intensively on borderline personality issues and coping with early traumatic experiences. When clinicians plan treatment for patients with the anxiety sub-type, greater consideration may have to be given to the risk of self harming. In contrast, help for those in the stress sensitivity category could focus more heavily on therapeutic engagement and inter-personal functioning. In these circumstances, it would be valuable

to standardise these treatment approaches for each of the 4 sub-types, and then evaluate if they work better than the services currently offered to each group.

18.9   Final conclusions

Most of the studies which explore the classification of schizophrenia have focused on sub-grouping this mental disorder according to the symptom profiles of patients. The current research, however, made a novel attempt to sub-group a heterogeneous sample of individuals with the illness on the basis of psychosocial factors which would be relevant to treatment interventions and clinical outcome. A semi-structured interview, which we named SCIPS, was developed to sub-group patients into 4 categories, and its reliability and concurrent validity were established. The 6 month stability of SCIPS diagnoses of the drug related, anxiety and stress sensitivity sub-types was also indicated through a longitudinal study. A preliminary analysis provided little evidence of construct validity, though a comparison between the SCIPS and DSM sub-types indicated the discriminant validity of the differentiation between the anxiety and stress sensitivity sub-groups. The risk of self harming was, however, suggested as being associated with a distinction between these two categories – the anxiety and stress sensitivity – when the SCIPS was applied to a broader range of psychosis, including schizophrenia and schizoaffective disorder. Further investigations should be carried out into co-morbidity, clinical course and the outcomes for patients in each of the sub-groups. In the process of identifying candidate variables for the assessment of the construct validity of the sub-types, an association between FNE and delusional thinking was also demonstrated in both the non-clinical population and patients with schizophrenia.

Appendix A: Semi-Structured Clinical Interview for Psychosis Sub-groups (SCIPS).

Semi-Structured Clinical Interview for Psychosis Sub-groups (SCIPS)

Instructions:

This interview is for use with patients with Schizophrenia, Persistent Delusional Disorders, Induced Delusional Disorder and Schizoaffective Disorders diagnosed with ICD-10[1], or Schizophrenia, Schizoaffective Disorder, Delusional Disorder, and Shared Psychotic Disorder diagnosed with DSM-IV[2].

This interview is semi-structured, and the interviewer may use additional questions and prompts to collect the required information.

In order to sub-group a patient, the **"SCIPS Interview"** is completed first. Then, the **"Rating Sheet for the SCIPS"** is completed according to the results of the interview. Finally, the **"Diagnostic Criteria for the SCIPS sub-groups"** is used to sub-group the patient. Whenever an interviewer finds a difficulty in rating, **Appendix 3, "The Diagnostic Guidelines for Psychosis Sub-types",** can be referred to clarify what should be rated for each item.

---

[1] ICD-10: International Classification of Diseases 10th edition, World Health Organization.

[2] DSM-IV: Diagnostic and Statistical Manual for Mental Disorders 4th edition, American Psychiatric Association.

SCIPS Interview

1. Onset of psychosis

Identify the initial psychotic symptom(s) experienced in the first psychotic episode and when they occurred[3]:

…………………………………………………………………………………………………
………………………………………………………………………………………

1-1   Age at 1st episode
Ask:
How old were you when you first experienced psychotic symptoms (e.g., voices, paranoia)?   ……**yrs**
RATE: 0 Under 30 / 1 30 or over

1-2   Mode of onset
Ask:
How long did it take from when you first noticed that something was wrong with you to the peak of your first episode?   **………yrs……….mths**
(Prompt: *Did your first psychotic episode develop quickly - within 1 month, or did it build up gradually, taking more than 1 month?*)

RATE: 0 Equal to or more than 1 mth / 1 less than 1 mth

1-3   Triggers
Show the Social Readjustment Rating Scale and Questionnaire (Appendix 1) to the patient.
Ask:
Was there any particular event that made you upset or stressed in the 3 months before the symptoms started? Please identify the event(s) in the list, if any.

- If no event was experienced, or the life change unit of the life event (which is shown in the list) is less than 40:

RATE: 0 No, or minor, life event, and go to item 2-1.

- If the life change unit of the life event is equal to or more than 40:

Ask:
Did it happen within 3 months of the onset of your psychotic symptoms? **(Yes / No)**
Was there any change in your sleeping pattern just after the event? **(Yes / No)**
If No to either or both of above,   RATE: 0 No, or minor, life event
If Yes to both of above,   RATE: 1 Stressful life event

---

[3] Use information from clinical records or family interviews if available and necessary.

2. Social Functioning

2-1   Change in work or school performance before the first episode
Prompt:
I would like to ask about your performance change during the period before you developed symptoms/problems.
Ask:
During this period did your work or school performance change?
Did you find that you could do less work than before? **(Yes / No)**
Did you find that you did your work slower than before? **(Yes / No)**
If No to both of above, RATE: 2 No performance change and go to item 2-2
If Yes to any of above, **Ask:**
When did the change in your school/work performance start? Did it start within 6 months, or was it more than 6 months before you first experienced the [psychotic] symptoms you have described
RATE: 0 change started within 6 mths of onset of first episode
1. The change started at or more than 6 mths before onset of first episode

2-2   Social relationships since early adolescence
Prompt:
Now I would like to ask you about your early teens, meaning when you were aged between 12 and 15.
Ask:
i) Did you stay by yourself almost every day, or did you often get together with friends at, or after, school? Were you withdrawn or isolated, or did you get together with friends frequently?
>   1.   **Withdrawn or isolated**
>   2.   **Getting together with friends frequently**
If rating is 2, RATE: 1 Moderate or good social relationships and go to item 2-3.

Ask:
ii) After that period in your later teens/early 20s, did you become more sociable? Were you still withdrawn or isolated, or did you start to get together with friends frequently?
>   1.   **Still withdrawn or isolated**
>   2.   **Becoming sociable and getting together with friends frequently**

If rating is 1, RATE: 0 Poor social relationships
If rating is 2, RATE: 1 Moderate or good social relationships

2-3   Pre-morbid close relationships
Ask:
What was your marital status when you first became ill?[4]
>   Single   ☐
>   Married   ☐

---
[4] Please note that all the questions in this item concern social relationships before the patient became ill.

Divorced ☐
Widowed ☐

If answer is other than single, RATE: Pre-morbid close relationship: 1 Yes and go to item 3-1.

Ask:
Had you ever had someone you would describe as a boy or girlfriend? **(Yes / No)**
If No, RATE: Pre-morbid close relationship: 0 No and go to item 3-1.

Ask:
Had you dated a girl/boyfriend constantly (more than once a week on average) for more than 6 months? **(Yes / No)**
Had you ever lived with a partner for more than 1 month? **(Yes / No)**

If Yes to either question, RATE: Pre-morbid close relationship: 1 Yes
If No to both, RATE: Pre-morbid close relationship: 0 No

3. *Factors Related to Psychosis*

3-1 Usage of illicit drugs and their association with psychotic symptoms

Ask:
Have you ever used any kinds of illegal drugs? **(Yes / No)**
If No (confirmed by other information sources, if possible),
RATE: Precipitating use of stimulants/hallucinogens: 0 No and go to item 3-2.

Ask:
What kind of drugs have you used?
Stimulants/Hallucinogens:

Amphetamine **(Yes / No)**
Cocaine **(Yes / No)**
LSD **(Yes / No)**
Ecstasy **(Yes / No)**
Cannabis **(Yes / No)**
Others[5] **(Yes: Name of the drug(s)?** /No)

If a patient has not used any of the stimulants/hallucinogens listed above,
RATE: Precipitating use of hallucinogens: 1 No, and go to item 3-2.

Ask:
Were you taking them in the 2 weeks before the psychotic symptoms started?
(Yes / No)

If No, RATE: Precipitating use of hallucinogens: 0 No
If Yes, RATE: Precipitating use of hallucinogens: 1 Yes

3-2 Existence of early traumatic experience
Prompt:
Childhood traumatic experiences are often associated with mental health problems.
Ask:
Is it alright for me to ask you if you have had any such experiences? **(Yes / No)**

If No, RATE: Traumatic experience: 0 Not discussed.
If Yes, proceed:

Ask:
Do you believe that you were emotionally or sexually abused in your childhood (under 18)? **(Yes/ No)**
If No, RATE: Traumatic experience: 1 No, and go to item 3-3.

---

[5] If the patient has used any other kind of drugs which are proved to cause psychotic symptoms (e.g. diethylpropion), record their names here.

If Yes, RATE: Traumatic experience: 2 Yes

Ask:
Have you discussed it with your care manager/psychiatrist/therapist?
If Yes, no action necessary.
If No, ask:
Would you like me to pass what you have said onto your care manager/psychiatrist/therapist?

3-3   Borderline personality disorder
Diagnose according to whether patient meets DSM-IV criteria (See Appendix 2)

RATE: Diagnosis of borderline personality disorder: 0 No / 1 Yes

YK/DK   **1st November 2008**

Rating Sheet for the SCIPS

1-1. Age at 1st episode?

0. Under 30
1. 30 or over

1-2. Mode of onset?

0. Equal to or more than 1 month
1. Less than 1 month

1-3. Triggers?

0. No, or minor, life event
1. Stressful life event

2-2. Social relationships since early adolescence?

0. Poor
1. Moderate or good

2-3. Pre-morbid close relationships?

0. No
1. Yes

Scores for differentiation between the anxiety and the stress sensitivity sub-groups	
(A) Number of items which are rated as '1' (in items 1-1, 1-2, 1-3, 2-2 and 2-3) (0-5)	
(B) Number of items which are rated as '0' (in items 1-1, 1-2, 1-3, 2-2 and 2-3) (0-5)	

3-1. Precipitating use of hallucinogens?

0. No
1. Yes

3-2. Traumatic experience?

0. Not discussed
1. No
2. Yes

3-3. Borderline personality disorder? (Diagnosed with DSM-IV)

0. No
1. Yes

Diagnostic Criteria for SCIPS Sub-groups

- **Diagnostic criteria for the drug related and traumatic sub-groups**

If Yes for 3-1: precipitating use of hallucinogens,
SUB-GROUP: 1. Drug related;

If Yes for both 3-2: traumatic experience and 3-3: borderline personality disorder,
SUB-GROUP: 2. Traumatic;

If the patient is sub-grouped as being drug related and/ or traumatic, stop here.

If No for 3-1 and either of 3-2 or 3-3,
go to "Diagnostic criteria for the anxiety and the stress sensitivity sub-groups".

- **Diagnostic criteria for the anxiety and the stress sensitivity sub-groups**

If (A) Number of items which are rated as '1' shown in the table: "Scores for the differentiation between the anxiety and the stress sensitivity sub-groups" is equal to or more than 3,
SUB-GROUP: 3. Anxiety;

If (B) Number of items which are rated as '0' shown in the table: "Scores for differentiation between the anxiety sub-group and the stress sensitivity sub-group" is equal to or more than 3,
SUB-GROUP: 4. Stress sensitivity.

[Note: where items cannot be scored, or adequate information is not available, it may not be possible to determine sub-types.]

Appendix 1: The Social Readjustment Rating Scale and Questionnaire (Life Change Unit >= 40).

Life Experience	Life Change Units
Death of spouse	100
Divorce	73
Marital separation	65
Jail term	63
Death of close family member	63
Personal injury or illness	53
Marriage	50
Fired at work	47
Marital reconciliation	45
Retirement	45
Change in health of family member	44
Pregnancy	40
Sex difficulties	39
Gain of new family member	39
Business readjustment	39
Change in financial state	38
Death of close friend	37
Change to different line of work	36
Change in number of arguments with spouse	35
Large mortgage	31
Foreclosure of mortgage or loan	30
Change in responsibilities at work	29
Son or daughter leaving home	29
Trouble with in-laws	29
Outstanding personal achievement	28
Wife begins or stops work	26
Begin or end school	26
Change in living conditions	25
Revision of personal habits	24
Trouble with boss	23
Change in work hours or conditions	20
Change in residence	20
Change in schools	20
Change in recreation	19
Change in church activities	19
Change in social activities	18
Small loan	17
Change in sleeping habit	16
Change in number of family get-togethers	15
Change in eating habits	15
Vacation	13

Christmas	**12**
Minor violation of the law	**11**

Appendix 2: Diagnostic Criteria for Borderline Personality Disorder in DSM-IV.

A pervasive pattern of instability of interpersonal relationships, self-image, and affects, and marked impulsivity beginning by early adulthood and present in a variety of contexts, as indicated by 5 (or more) of the following:

(1) Frantic efforts to avoid real or imagined abandonment. Note: do not include suicidal or self-mutilating behaviour covered in Criterion 5.
(2) A pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation.
(3) Identity disturbance: markedly and persistently unstable self-image or sense of self.
(4) Impulsivity in at least two areas that are potentially self-damaging (e.g., spending, sex, substance abuse, reckless driving, binge eating). Note: do not include suicidal or self-mutilating behaviour covered in Criterion 5.
(5) Recurrent suicidal behaviour, gestures, or threats, or self-mutilating behaviour
(6) Affective instability due to a marked reactivity of mood (e.g., intense episodic dysphoria, irritability, or anxiety usually lasting a few hours and only rarely more than a few days).
(7) Chronic feelings of emptiness
(8) Inappropriate, intense anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, recurrent physical fights)
(9) Transient, stress-related paranoid ideation or severe dissociative symptoms

Appendix 3: Diagnostic Guidelines for Psychosis Sub-types

Drug Related Psychosis

Core characteristics
The person has used at least 1 of the stimulants/ hallucinogens which are listed below in the 2 weeks before the onset of psychotic symptoms.

List of hallucinogens:

Amphetamine, cocaine, LSD, ecstasy, cannabis, others[6]

Supporting characteristics
Age of onset:
- Usually in their teens or 20s.

Mode of onset:[7]
- Either acute or insidious.

Lifetime pattern of social interaction:
- Individuals with this sub-type are relatively sociable, having many friends at school and may have partners or spouses.

Symptom pattern:
- Symptom patterns tend to be diverse.
- Negative symptoms tend to be less prominent with this sub-type.

Traumatic Psychosis

Core Characteristics
The person meets the criteria for co-morbid borderline personality disorder and has experienced childhood sexual or emotional abuse.

Supporting characteristics
Age of onset:
- Usually in their teens or 20s.

Mode of onset:
- Either acute or insidious.

Lifetime pattern of social interaction:
- Individuals with this sub-type have chaotic relationships with others (e.g., severe conflict with their families, unstable sexual relationships with many boy/girlfriends).

---

[6] Any other kinds of drugs which are proved to cause psychotic symptoms (e.g., diethylpropion) can be included.

[7] Mode of onset is defined as the period between the first reported symptom or noticeable behavioural change and the patient's subjective peak of the first episode. In this case, 'acute' onset means less than 1 month, while 'insidious' onset means equal to or more than 1 month.

Symptom pattern:

- Abusive hallucinations (auditory or visual) are frequent.

Anxiety Psychosis

Core characteristics
The person has had good peer relationships in early adolescence and usually developed close relationships with a partner or spouse.

Supporting characteristics
Age of onset:

- Usually in their 30s or older.

Mode of onset:

- Acute.
- Individuals have experienced stressful life events which have immediately preceded psychotic symptoms within 3 months.
- Lifetime pattern of social interaction:
- Individuals with this sub-type are relatively sociable, having friends at school and partners or spouses in adulthood.

Symptom pattern:

- Delusions, especially systematized (well organized) delusions, are generally prominent.
- Hallucinations (auditory, visual, or with other modals) can occur but are less prominent.
- Negative symptoms tend to be less prominent with this sub-type.

Stress Sensitivity Psychosis

Core characteristics
The person is more stress sensitive[8] and less sociable.

Supporting characteristics
Age of onset:

- Usually in their teens or early 20s.

Mode of onset:

- Insidious.

Lifetime pattern of social interaction:

- Individuals with this sub-type are less sociable, having few friends in their childhood and adolescence, and they do not have partners or spouses prior to developing symptoms.

Symptom pattern:

---

[8] 'Stress sensitive' means that emotional reactivity is high to daily life stress, or 'daily hassles' (Myin-Germeys et al., 2001; Myin-Germeys & van Os, 2007).

- Negative symptoms are prominent, even in the first episode.
- A diverse range of positive symptoms occur.

Appendix B: An example of a systematic review record.

Scales for Evaluative beliefs/ Self-Esteem.

Measure, author and year	Aims/ Subscales	Psychometrics	Used in the schizophrenia/psychosis field	Item/Lang	Practice
Brief Core Schema Scale (BCSS)(Fowler et al., 2006)	**Aim** Designed to assess core beliefs about the self and others. **Subscales** Four scores that represents beliefs about negative-self, negative-others, positive-self, and positive-others are obtained.	Cronbach's alpha in non-clinical (and clinical) samples Negative-self: 0.78 (0.79) Positive-self: 0.86 (0.84) Negative-others: 0.88 (0.84) Positive-others: 0.88 (0.87) Test-retest reliability (Pearson's *r*) in non-clinical sample Negative-self: 0.84 Positive-self: 0.82 Negative-others: 0.70 Positive-others: 0.72	Yes - Negative evaluative beliefs about self were shown to be associated with persecutory delusions even after the confounding effects of depression and low self-esteem were controlled (Smith et al., 2006).	24 (6 for each subscale) English Japanese	Possible

186

	Aim / Subscales	Reliability	Validity	Items / Language	Japanese version
Evaluative Beliefs Scale (EBS) (Chadwick, Trower, & Dagnan, 1999)	**Aim** Used to assess self-evaluative beliefs about self and others. **Subscales** Three subscales for self-evaluation (Self-Self), evaluations of other people (Self-Other) and beliefs about how other people evaluate the respondents (Other-Self).	Cronbach's alpha Self-Self: 0.90 Self-Other: 0.92 Other-Self: 0.86	Yes – A relationship Other-Self evaluative beliefs and sealing-over coping strategy in patients with schizophrenia or related disorders (Tait, Birchwood, & Trower, 2004).	18 (6 for each subscale) English	Possible But Japanese version not available
Young Schema Questionnaire Short form (YSQ-S) (Young, 1998)	**Aim** Developed to assess 15 core beliefs about the self and others. **Subscales** 15 scores for core beliefs (unconditional, schema- level cognitions about oneself, others and the world)	Cronbach's alpha in clinical sample (patients with eating disorder) > 0.80 for all 15 scales.	No	75 English	Possible But Japanese version not available and not used in the field of schizophrenia/ psychosis.

187

Instrument	Aim / Subscales	Reliability		Number of items / Language	Japanese version
Beck Self-Esteem Scale (BSE) (Beck et al., 2001)	**Aim** Designed to assess evaluative beliefs about self and others. **Subscales** Two subscales for self-evaluation (Self Scale), evaluations of other people (Other Scale)	Cronbach's alpha in clinical sample (psychiatric outpatients) Self Scale: 0.94 Other Scale: 0.95	No	18 English	Possible But Japanese version not available and not used in the field of schizophrenia/ psychosis.
Rosenberg Self-Esteem Scale (SES) (Rosenberg, 1979)	**Aim** Designed to assess global self-esteem.	A Guttman scale coefficient of reproducibility: 0.92 Correlations for test-retest reliability (two-weeks): 0.85 and 0.88, in two independent studies.	Yes Self-esteem assessed using this scale were demonstrated to be associated with positive symptoms in patients with non-affective psychosis (Smith et al., 2006).	10 English Japanese	Possible But at least two kinds of Japanese version exist and their psychometrics are uncertain.
Coopersmith Self-Esteem Inventory (SEI) (Coopersmith, 1967)	**Aim** Designed to assess global self-esteem.	Not reported.	No	25 English	Possible But Japanese version not available and not used in the field of schizophrenia/ psychosis.

Appendix C: The 21-item Peters Delusions Inventory (PDI-21).

Appendix

P.D.I.-21

This questionnaire is designed to measure beliefs and vivid mental experiences. We believe that they are much more common than has previously been supposed, and that most people have had some such experiences during their lives. Please answer the following questions as honestly as you can. There are no right or wrong answers, and there are no trick questions.

Please note that we are NOT interested in experiences people may have had when under the influence of drugs.

IT IS IMPORTANT THAT YOU ANSWER *ALL* QUESTIONS.

For the questions you answer YES to, we are interested in
(a) how distressing these beliefs or experiences are
(b) how often you think about them; and
(c) how true you believe them to be.
On the right hand side of the page we would like you to circle the number which corresponds most closely to how distressing this belief is, how often you think about it, and how much you believe that it is true.
If you answer NO please move on to the next question

Example

189

1) Do you ever feel as if people seem to drop hints about you or say things with a double meaning ?

NO   YES ——▶

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

2) Do you ever feel as if things in magazines or on TV were written especially for you ?

NO   YES ——▶

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

3) Do you ever feel as if some people are not what they seem to be ?

NO   YES ——▶

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

4) Do you ever feel as if you are being persecuted in some way ?

NO   YES ——▶

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

5) Do you ever feel as if there is a conspiracy against you ?

NO   YES ——▶

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

6) Do you ever feel as if you are, or destined to be someone very important ?

NO   YES ⟶

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

7) Do you ever feel that you are a very special or unusual person ?

NO   YES ⟶

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

8) Do you ever feel that you are especially close to God ?

NO   YES ⟶

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

9) Do you ever think people can communicate telepathically ?

NO   YES ⟶

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

10) Do you ever feel as if electrical devices such as computers can influence the way you think ?

NO   YES ⟶

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

11) Do you ever feel as if you have been chosen by God in some way ?

NO   YES

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

12) Do you believe in the power of witchcraft, voodoo or the occult ?

NO   YES

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

13) Are you often worried that your partner may be unfaithful ?

NO   YES

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

14) Do you ever feel that you have sinned more than the average person ?

NO   YES

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

15) Do you ever feel that people look at you oddly because of your appearance ?

NO   YES

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

16) Do you ever feel as if you had no thoughts in your head at all ?

NO   YES

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

17) Do you ever feel as if the world is about to end ?

NO   YES

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

18) Do your thoughts ever feel alien to you in some way ?

NO   YES

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

19) Have your thoughts ever been so vivid that you were worried other people would hear them ?

NO   YES

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

20) Do you ever feel as if your own thoughts were being echoed back to you ?

NO   YES

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

21) Do you ever feel as if you are a robot or zombie without a will of your own ?

NO   YES

(please circle)

Not at all distressing				Very distressing
1	2	3	4	5
Hardly ever think about it				Think about it all the time
1	2	3	4	5
Don't believe it's true				Believe it is absolutely true
1	2	3	4	5

Appendix D: The Brief Core Schema Scale (BCSS).

The Brief Core Schema Scales: beliefs about self and others

This questionnaire lists beliefs that people can hold about themselves and other people. Please indicate whether you hold each belief (NO or YES). If you hold the belief then please indicate how strongly you hold it by circling a number (1-4). Try to judge the beliefs on how you have generally, over time, viewed yourself and others. Do not spend too long on each belief. There are no right or wrong answers and the first response to each belief is often the most accurate.

				Believe it slightly ↓	Believe it moderately ↓	Believe it very much ↓	Believe it totally ↓
MYSELF							
I am unloved	NO	YES	→	1	2	3	4
I am worthless	NO	YES	→	1	2	3	4
I am weak	NO	YES	→	1	2	3	4
I am vulnerable	NO	YES	→	1	2	3	4
I am bad	NO	YES	→	1	2	3	4
I am a failure	NO	YES	→	1	2	3	4
I am respected	NO	YES	→	1	2	3	4
I am valuable	NO	YES	→	1	2	3	4
I am talented	NO	YES	→	1	2	3	4
I am successful	NO	YES	→	1	2	3	4
I am good	NO	YES	→	1	2	3	4
I am interesting	NO	YES	→	1	2	3	4
OTHER PEOPLE							
Other people are hostile	NO	YES	→	1	2	3	4
Other people are harsh	NO	YES	→	1	2	3	4
Other people are unforgiving	NO	YES	→	1	2	3	4
Other people are bad	NO	YES	→	1	2	3	4
Other people are devious	NO	YES	→	1	2	3	4
Other people are nasty	NO	YES	→	1	2	3	4
Other people are fair	NO	YES	→	1	2	3	4
Other people are good	NO	YES	→	1	2	3	4
Other people are trustworthy	NO	YES	→	1	2	3	4
Other people are accepting	NO	YES	→	1	2	3	4
Other people are supportive	NO	YES	→	1	2	3	4
Other people are truthful	NO	YES	→	1	2	3	4

Appendix E: The Brief Fear of Negative Evaluation Scale (BFNE).

Brief Fear of Negative Evaluation Scale
Leary (1983)

Read each of the following statements carefully and indicate how characteristic it is of you according to the following scale:

1 Not at all characteristic of me
2 Slightly characteristic of me
3 Moderately characteristic of me
4 Very characteristic of me
5 Extremely characteristic of me

_____ 1. I worry about what other people will think of me even when I know it doesn't make any difference.

_____ 2. I am unconcerned even if I know people are forming an unfavorable impression of me.

_____ 3. I am frequently afraid of other people noticing my shortcomings.

_____ 4. I rarely worry about what kind of impression I am making on someone.

_____ 5. I am afraid others will not approve of me.

_____ 6. I am afraid that people will find fault with me.

_____ 7. Other people's opinions of me do not bother me.

_____ 8. When I am talking to someone, I worry about what they may be thinking about me.

_____ 9. I am usually worried about what kind of impression I make.

_____ 10. If I know someone is judging me, it has little effect on me.

_____ 11. Sometimes I think I am too concerned with what other people think of me.

_____ 12. I often worry that I will say or do the wrong things.

From: Leary, M. R. (1983). A brief version of the Fear of Negative Evaluation Scale. *Personality and Social Psychology Bulletin, 9,* 371-376.

Date:

Name: _____ Marital Status: _____ Age: _____ Sex: _____
Occupation: _____ Education: _____

Instructions: This questionnaire consists of 21 groups of statements. Please read each group of statements carefully, and then pick out the **one statement** in each group that best describes the way you have been feeling during the **past two weeks, including today**. Circle the number beside the statement you have picked. If several statements in the group seem to apply equally well, circle the highest number for that group. Be sure that you do not choose more than one statement for any group, including Item 16 (Changes in Sleeping Pattern) or Item 18 (Changes in Appetite).

1. Sadness
0   I do not feel sad.
1   I feel sad much of the time.
2   I am sad all the time.
3   I am so sad or unhappy that I can't stand it.

2. Pessimism
0   I am not discouraged about my future.
1   I feel more discouraged about my future than I used to be.
2   I do not expect things to work out for me.
3   I feel my future is hopeless and will only get worse.

3. Past Failure
0   I do not feel like a failure.
1   I have failed more than I should have.
2   As I look back, I see a lot of failures.
3   I feel I am a total failure as a person.

4. Loss of Pleasure
0   I get as much pleasure as I ever did from the things I enjoy.
1   I don't enjoy things as much as I used to.
2   I get very little pleasure from the things I used to enjoy.
3   I can't get any pleasure from the things I used to enjoy.

5. Guilty Feelings
0   I don't feel particularly guilty.
1   I feel guilty over many things I have done or should have done.
2   I feel quite guilty most of the time.
3   I feel guilty all of the time.

6. Punishment Feelings
0   I don't feel I am being punished.
1   I feel I may be punished.
2   I expect to be punished.
3   I feel I am being punished.

7. Self-Dislike
0   I feel the same about myself as ever.
1   I have lost confidence in myself.
2   I am disappointed in myself.
3   I dislike myself.

8. Self-Criticalness
0   I don't criticize or blame myself more than usual.
1   I am more critical of myself than I used to be.
2   I criticize myself for all of my faults.
3   I blame myself for everything bad that happens.

9. Suicidal Thoughts or Wishes
0   I don't have any thoughts of killing myself.
1   I have thoughts of killing myself, but I would not carry them out.
2   I would like to kill myself.
3   I would kill myself if I had the chance.

10. Crying
0   I don't cry anymore than I used to.
1   I cry more than I used to.
2   I cry over every little thing.
3   I feel like crying, but I can't.

Subtotal Page 1 _____

Continued on Back

0154018392

11. Agitation

0   I am no more restless or wound up than usual.

1   I feel more restless or wound up than usual.

2   I am so restless or agitated that it's hard to stay still.

3   I am so restless or agitated that I have to keep moving or doing something.

12. Loss of Interest

0   I have not lost interest in other people or activities.

1   I am less interested in other people or things than before.

2   I have lost most of my interest in other people or things.

3   It's hard to get interested in anything.

13. Indecisiveness

0   I make decisions about as well as ever.

1   I find it more difficult to make decisions than usual.

2   I have much greater difficulty in making decisions than I used to.

3   I have trouble making any decisions.

14. Worthlessness

0   I do not feel I am worthless.

1   I don't consider myself as worthwhile and useful as I used to.

2   I feel more worthless as compared to other people.

3   I feel utterly worthless.

15. Loss of Energy

0   I have as much energy as ever.

1   I have less energy than I used to have.

2   I don't have enough energy to do very much.

3   I don't have enough energy to do anything.

16. Changes in Sleeping Pattern

0   I have not experienced any change in my sleeping pattern.

1a   I sleep somewhat more than usual.

1b   I sleep somewhat less than usual.

2a   I sleep a lot more than usual.

2b   I sleep a lot less than usual.

3a   I sleep most of the day.

3b   I wake up 1–2 hours early and can't get back to sleep.

17. Irritability

0   I am no more irritable than usual.

1   I am more irritable than usual.

2   I am much more irritable than usual.

3   I am irritable all the time.

18. Changes in Appetite

0   I have not experienced any change in my appetite.

1a   My appetite is somewhat less than usual.

1b   My appetite is somewhat greater than usual.

2a   My appetite is much less than before.

2b   My appetite is much greater than usual.

3a   I have no appetite at all.

3b   I crave food all the time.

19. Concentration Difficulty

0   I can concentrate as well as ever.

1   I can't concentrate as well as usual.

2   It's hard to keep my mind on anything for very long.

3   I find I can't concentrate on anything.

20. Tiredness or Fatigue

0   I am no more tired or fatigued than usual.

1   I get more tired or fatigued more easily than usual.

2   I am too tired or fatigued to do a lot of the things I used to do.

3   I am too tired or fatigued to do most of the things I used to do.

21. Loss of Interest in Sex

0   I have not noticed any recent change in my interest in sex.

1   I am less interested in sex than I used to be.

2   I am much less interested in sex now.

3   I have lost interest in sex completely.

21 22 23 24 25 26 27 28 29 30 A B C D E

_____ Subtotal Page 2

_____ Subtotal Page 1

_____ Total Score

Appendix G: Patient information sheet.

University of Southampton

School of Medicine
Community Clinical
Sciences Research Division

Department of Mental Health
University of Southampton
Royal South Hants Hospital
Brintons Terrace
Southampton SO14 0YG
United Kingdom

Tel +44 023 80825054/80825191
Fax +44 02380234243
E-mail dgk@soton .ac.uk

Prof. David Kingdon, MD MRCPsych
Professor of Mental Health Care Delivery

PATIENT INFORMATION SHEET   14 September 2007

Study Title: Developing a Semi-structured Clinical Interview for Psychosis Subgroups (SCIPS)

RESEARCHERS: Dr. Yoshihiro Kinoshita, Prof. David Kingdon
ETHICS NUMBER: 07/H0501/72
VERSION: 2

1. **Invitation paragraph**
You are being asked if you would agree to take part in a research study. Before you decide about this, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Thank you for reading this.

2. **What is the purpose of the study?**
The purpose of the study is to know whether a newly developed interview tool – SCIPS- is helpful for understanding the situation of people who have been given a diagnosis of schizophrenia or a similar diagnosis. Understanding this better may help you and mental health staff make choices about treatment and could improve the treatments available.

3. **What will I be asked about?**
You will be asked about your symptoms and thoughts you get. You will be helped to fill in some questionnaires about these and also about past experiences. The questions you will be asked are similar to those generally asked within mental health services. You do not have to answer any questions that you don't want to and can stop the interview at any time.

4. **Why have I been chosen?**
We have asked your consultant if we can approach you to ask you to take part and your consultant having considered this, they have given consent. We are now asking you if you agree to participate in an interview with the doctor doing this research.

5. **Do I have to agree?**
No, it is up to you to decide whether or not you take part. If you do decide to, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw that consent at any time and without giving a reason. If you do so, you will be asked if you consent to the information that you have already supplied being included in the study or not. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

6. **What will happen to me if I take part?**
The researcher will meet with you and ask a number of questions and help you fill in some questionnaires. It will probably take about 1 hour in one or two occasions but you will be free to stop at any time and, if you agree, do the remainder of the interview later. If you agree, the interview will be audiotaped for the purposes of this research study which require that it is listened to, by another research psychiatrist. The audiotape will be destroyed at the end of the period specified by the Research Ethics Comittee.

7. **What do they have to do?**

This just involves answering questions and filling in questionnaires. If you don't want to answer any question, you do not have to do so. Your care would not be affected in any way by this.

8. **What are the possible disadvantages and risks of taking part?**

This is an interview and questionnaire study so there are no significant risks or disadvantages of participating. If you should get distressed, tell the researcher who has instructions in how best to reduce this and who will contact his supervisor and make sure that your care coordinator, consultant and GP are made aware of this.

9. **What are the possible benefits of taking part?**

We hope that this study will help you. However, this cannot be guaranteed. The information we get from this study may help us to treat future patients with schizophrenia better.

10. **What if something goes wrong?**

If you should have any complaints about this study, these will be documented by the researcher and passed to the Complaints Officer, Hampshire Partnership Trust, Tatchbury Mount, Southampton or you can write to them directly yourself.

11. **Will my taking part in this study be kept confidential?**

All information which is collected about you during the course of the research will be kept strictly confidential. Any information about you will have your name and address removed so that you cannot be recognised from it.'

12. **What will happen to the results of the research study?**

The results of the research will be submitted for publication to scientific journals and may be presented at conferences when the study is finished within the next two years. A copy of the published results will be available at that time from Professor Kingdon. You will not be identified in any report/publication.

13. **Who is organising and funding the research?**

Hampshire Partnership Trust are sponsoring and funding the research.

14. **Who has reviewed the study?**

Isle of Wight, Portsmouth & South East Hampshire Research Ethics Committee has reviewed the study.

15. **Contact for Further Information**

If you would like more information now or in the future, please contact Professor Kingdon (023 80825045).

Thank you for your help.

You will be given a copy of the information sheet and a signed consent form to keep.

Appendix H: Patient consent form.

University
of Southampton

School of Medicine
Community Clinical
Sciences Research Division

Department of Mental Health
University of Southampton
Royal South Hants Hospital
Brintons Terrace
Southampton SO14 0YG
United Kingdom

Tel +44 023 80825054/80825191
Fax +44 02380234243
E-mail dgk@soton .ac.uk

Prof. David Kingdon, MD MRCPsych
Professor of Mental Health Care Delivery

PATIENT CONSENT FORM   3 August 2007

Study: ***Developing a Semi-structured Clnical Interview for Psychosis Subgroups***

RESEARCHERS: Dr. Yoshihiro Kinoshita, Prof. David Kingdon
ETHICS NUMBER: 07/H0501/72
Version: 1

Please tick box:

(1) I confirm that I have read and understand the information sheet - dated 03/08/07 - for the above study and have had the opportunity to ask questions.

☐

(2) I understand that my participation is voluntary and that I am free to withdraw at any time, without giving reason, and without my medical care or rights being affected.

☐

(3) I understand that sections of any of my medical notes may be looked at by the researchers or responsible individuals from regulatory authorities where it is relevant to my taking part in the research. I give my permission for these individuals to have access to my records.

☐

(4) I agree to take part in the above study.

☐

(5) I agree to audiotaping of the interview for the purposes of this research project.

☐

_____   _____ _____
Name of Patient   *Date*   *Signature*

_____   _____ _____
Researcher   *Date*   *Signature*

P.I.N. for this trial: _____ 1 for patient, 1 for researcher, 1 to be kept with hospital notes

Appendix I: Construct validity of the traumatic sub-type with broader conceptualization.

1. Overview

Though, according to the SCIPS diagnostic criteria, patients with traumatic sub-type should have childhood trauma and satisfy diagnostic criteria for borderline personality disorder, conceptualisation of this sub-type might be expanded by including those who have been traumatised in childhood but not diagnosed with borderline personality disorder. In order to examine the construct validity of the traumatic sub-group with this wider conceptualisation, those whose rating for item 3-2 "traumatic experience" was positive were put into the traumatic category and the data collected in the UK and Japan were re-analysed. In these analyses, negative and positive evaluative beliefs and FNE were employed as external validators. Furthermore, in order to establish the predictive value of the conceptualisation, clinical outcomes in relation to hospitalization and the history of self harming which were assessed in Chpater 17 ("Predictive Value of the Conceptualisation of the Anxiety and Stress Sensitivity Sub-types") were compared between the traumatic and non-traumatic sub-types in the Japanese patients.

1. Aims of this study

The aims of this study are to examine 2 primary and 4 secondary hypotheses which are described below:

Primary hypotheses:

1. Patients with the traumatic sub-type of schizophrenia have higher levels of negative evaluative beliefs (negative-self and negative-others) than those without the sub-type.

2. Patients with the traumatic sub-type have a higher risk of self harming than those without the sub-type.

Secondary hypotheses:

1. Patients with the traumatic sub-type of schizophrenia have lower levels of positive evaluative beliefs (positive-self and positive-others) than those without the sub-type.

2. Individuals in the traumatic sub-group have a higher fear of negative evaluation from others than those in other sub-groups.

3. Patients with the traumatic sub-type reveal higher levels of depression than those without the sub-type.

4. Patients with the traumatic sub-type of schizophrenia stay in hospital shorter than those without the sub-type over a period of 3 years after the date of their first admission with the illness.

5. The duration of the first hospitalization with schizophrenia is shorter in those with the traumatic sub-type than it is for those without the sub-type.

3. Measures

The Brief Core Schema Scale (BCSS) (Fowler et al., 2006)

The Brief Fear of Negative Evaluation Scale (BFNE) (Collins et al., 2005)

Beck Depression Inventory II (BDI-II) (Beck, Steer, & Brown, 1996)

Details of the scales are provided in Chapter 10 (see section 10.8, "Measures").

4. Results

Prevalence of the sub-types

According to the ratings for item 3-2 in first SCIPS interview, the participants were categorized into the traumatic (i.e., patients who have been traumatised) and non-traumatic (i.e., patients who have been traumatised) sub-types. Table A-1 presents the numbers of individuals in the traumatic and non-traumatic subtypes in the UK and Japanese samples. The sub-types could not be determined for 3 of the participants in the UK because 1 of them did not complete the interview and the other 2 could not give enough information about their childhood trauma. By including those who have been traumatised in childhood but not diagnosed with borderline personality disorder into the conceptualisation of the traumatic sub-type, the number of participants in this category

changed from 2 (4.8%) to 14 (33.3%) in the UK sample, while in the Japanese sample, it changed from 1 (0.9%) to 22 (20.6%).

Table A-1: Numbers (%) of participants in the traumatic and non-traumatic sub-types.

Sub-type	The UK (n = 42)	Japan (n = 107)
Traumatic	14 (33.3)	22 (20.6)
Non-traumatic	25 (59.5)	85 (79.4)
No information	3 (7.1)	0 (0)

Differences in the BCSS, BFNE and BDI-II scores between the traumatic and non-traumatic sub-types

In the UK sample:

The p values for the differences (Mann-Whitney U Test; This method was chosen because the scores showed non-normal distribution) between the scores for the negative-self, positive-self, negative-others, and positive-others evaluative beliefs were 0.120 (traumatic > non-traumatic), 0.463 (traumatic < non-traumatic), 0.076 (traumatic > non-traumatic), and 0.917 (traumatic < non-traumatic) respectively. On the other hand, the p value for the discrepancy between the BFNE scores was 0.592 (traumatic > non-traumatic). These differences were not statistically significant.

In the Japanese sample:

The p values for the differences (Mann-Whitney U Test; This method was chosen because the scores showed non-normal distribution) between the scores for the negative-self, positive-self, negative-others, and positive-others evaluative beliefs were 0.554 (traumatic > non-traumatic), 0.166 (traumatic > non-traumatic), 0.023 (traumatic > non-traumatic), and 0.225 (traumatic < non-traumatic) respectively. On the other hand, the p value for the discrepancy between the BFNE scores was 0.994 (traumatic < non-traumatic). In addition, the p value for the difference in the BDI-II score was 0.389 (traumatic > non-traumatic). Only the difference in negative-others evaluative beliefs was statistically significant.

Differences in the 2 variables concerning hospitalization between the anxiety and stress sensitivity sub-types

The p value for the discrepancies (Mann-Whitney U Test; This method was chosen because the scores showed non-normal distribution) in variable 1: "total time spent in the hospital over a period of 3 years after the date of 1st admission" and variable 2 "duration of 1st hospitalization" were 0.803 (traumatic < non-traumatic) and 0.280 (traumatic < non-traumatic) respectively. These differences were not statistically significant.

Differences in the risk of self harming between the anxiety and stress sensitivity sub-types

A Chi square test was conducted, and revealed that the differences in the risk of self harming between the anxiety and stress sensitivity sub-types was not statistically significant (p = 0.938). RR for self harming was 1.02 (traumatic > non-traumatic, 95%CI = 0.58-1.80), which was also not statistically significant (Table A-2).

Table A-2: 2x2 Table used for the evaluation of the differences in the risk of self harming between the traumatic and non-traumatic sub-types.

	History of self harming		
	Positive	Negative	Total
Traumatic sub-type	9	13	22
Non-traumatic sub-type	34	51	85
Total	43	64	107

5. Discussion

A statistically significant difference was found in the negative-others evaluative beliefs between the traumatic and non-traumatic categories in the Japanese sample. Also in the UK sample, patients with the traumatic sub-type had higher negative-others evaluative beliefs than those without the sub-type, though the difference was not statistically significant. No difference was found between the traumatic and non-traumatic sub-types in other variables which were examined in the analyses.

It is reasonable that those who have been traumatised or offended by others have higher negative evaluative beliefs for others. When clinicians plan treatment for patients with

childhood trauma, greater consideration may have to be given to this type of schema. Schema modification technique in CBT might be especially useful for this group of patients.

There are 2 main limitations with the present study. Firstly, as discussed in Chapter 18 (see section 18.3 "Strengths and weaknesses of the SCIPS"), childhood traumatic experiences were assessed with a single question, and no account was taken of duration, or the severity of the abuse, in item 3.2 of the SCIPS. This may decrease the validity, and even the reliability, of the diagnosis used in this analysis. Secondly, this analysis was a secondary one of the collected data and the risk of type I errors, or false positives, caused by multiple comparisons should be taken into consideration.

References

Abel, G. A., Chen, X., Boden-Albala, B., & Sacco, R. L. 1999, "Social readjustment and ischemic stroke: lack of an association in a multiethnic population", *Neuroepidemiology*, vol. 18, no. 1, pp. 22-31.

Abi-Dargham, A. 2004, "Do we still believe in the dopamine hypothesis? New data bring new evidence.", *International Journal of Neuropsychopharmacology*, vol. 7, p. Suppl-5.

Addington, J. & Duchak, V. 1997, "Reasons for substance use in schizophrenia", *Acta Psychiatrica Scandinavica*, vol. 96, no. 5, pp. 329-333.

Alda, M., Zvolsky, P., Dvorakova, M., & Papezova, H. 1991, "Study of chronic schizophrenics with positive and negative family histories of psychosis", *Acta Psychiatrica Scandinavica*, vol. 83, no. 5, pp. 334-337.

Allardyce, J., Gaebel, W., Zielasek, J., & van Os, J. 2007, "Deconstructing Psychosis conference February 2006: the validity of schizophrenia and alternative approaches to the classification of psychosis", *Schizophrenia Bulletin*, vol. 33, no. 4, pp. 863-867.

Altman, D. G. 1991, *Practical Statistics for Medical Research* Chapman & Hall/CRC, London.

American Psychiatric Association 1952, *Diagnostic and Statistical Manual of Mental Disorders 1st edition (DSM-I)* Washington D.C.

American Psychiatric Association 1968, *Diagnostic and Statistical Manual of Mental Disorders 2nd edition (DSM-II)* Washington D.C.

American Psychiatric Association 1980, *Diagnostic and Statistical Manual of Mental Disorders 3rd edition (DSM-III)* Washington D.C.

American Psychiatric Association 2000, *Diagnostic and Statistical Manual for Mental Disorders 4th edition (DSM-IV)* American Psychiatric Association, Arlington.

Andreasen, N. C. & Olsen, S. 1982, "Negative v positive schizophrenia. Definition and validation", *Archives of General Psychiatry.39(7):789-94*.

Angermeyer, M. C. & Matschinger, H. 2003, "Public beliefs about schizophrenia and depression: similarities and differences", *Social Psychiatry & Psychiatric Epidemiology*, vol. 38, no. 9, pp. 526-534.

Angermeyer, M. C. & Matschinger, H. 2005, "Causal beliefs and attitudes to people with schizophrenia. Trend analysis based on data from two population surveys in Germany.", *British Journal of Psychiatry*, vol. 186, pp. 331-334.

Angrist, B., Sathananthan, G., Wilk, S., & Gershon, S. 1974, "Amphetamine psychosis: behavioral and biochemical aspects", *Journal of Psychiatric Research*, vol. 11, pp. 13-23.

Angrist, B. M. & Gershon, S. 1970, "The phenomenology of experimentally induced amphetamine psychosis--preliminary observations", *Biological Psychiatry*, vol. 2, no. 2, pp. 95-107.

Arndt, S., Tyrrell, G., Flaum, M., & Andreasen, N. C. 1992, "Comorbidity of substance abuse and schizophrenia: the role of pre-morbid adjustment", *Psychological Medicine*, vol. 22, no. 2, pp. 379-388.

Bailer, J., Brauer, W., & Rey, E. R. 1996, "Premorbid adjustment as predictor of outcome in schizophrenia: results of a prospective study", *Acta Psychiatrica Scandinavica*, vol. 93, no. 5, pp. 368-377.

Barnes, T. R., Leeson, V. C., Mutsatsa, S. H., Watt, H. C., Hutton, S. B., & Joyce, E. M. 2008, "Duration of untreated psychosis and social function: 1-year follow-up study of first-episode schizophrenia", *British Journal of Psychiatry*, vol. 193, no. 3, pp. 203-209.

Barrowclough, C., Haddock, G., Tarrier, N., Lewis, S. W., Moring, J., O'Brien, R., Schofield, N., & McGovern, J. 2001, "Randomized controlled trial of motivational interviewing, cognitive behavior therapy, and family intervention for patients with comorbid schizophrenia and substance use disorders", *American Journal of Psychiatry.158(10):1706-13*.

Bebbington, P. E., Bhugra, D., Brugha, T., Singleton, N., Farrell, M., Jenkins, R., Lewis, G., & Meltzer, H. 2004, "Psychosis, victimisation and childhood disadvantage: evidence from the second British National Survey of Psychiatric Morbidity", *British Journal of Psychiatry*, vol. 185:220-6, 2004 Sep., pp. 220-226.

Beck, A. T. 1976, *Cognitive Therapy and the Emotional Disorders.* IUP, New York.

Beck, A. T., Brown, G. K., Steer, R. A., Kuyken, W., & Grisham, J. 2001, "Psychometric properties of the Beck Self-Esteem Scales", *Behaviour Research & Therapy*, vol. 39, no. 1, pp. 115-124.

Beck, A. T., Steer, R. A., & Brown, G. K. 1996, *BDI-II Manual* The Psychological Corporation, San Antonia.

Bernstein, D. P., Ahluvalia, T., Pogge, D., & Handelsman, L. 1997, "Validity of the Childhood Trauma Questionnaire in an adolescent psychiatric population", *Journal of the American Academy of Child & Adolescent Psychiatry*, vol. 36, no. 3, pp. 340-348.

Berrettini, W. H. 2000, "Are schizophrenic and bipolar disorders related? A review of family and molecular studies.", *Biological Psychiatry*, vol. 48, no. 6, pp. 531-538.

Bhugra, D. 2005, "The Global Prevalence of Schizophrenia", *PLoS Med*, vol. 2, no. 5, p. e151.

Blashfield, R. K. 1984, "Kraepelin and His Influence on Modern Classification," in *The Classification of Psychopathology*, Plenum Press, New York, pp. 3-24.

Bleuler, E. 1911, *Dementia Praecox or the Group of Schizophrenias* International Universities Press, New York.

Boks, M. P., Leask, S., Vermunt, J. K., & Kahn, R. S. 2007, "The structure of psychosis revisited: the role of mood symptoms", *Schizophrenia Research*, vol. 93, no. 1-3, pp. 178-185.

Boydell, J., van Os, J., McKenzie, K., Allardyce, J., Goel, R., McCreadie, R. G., & Murray, R. M. 2001, "Incidence of schizophrenia in ethnic minorities in London: ecological study into interactions with environment", *BMJ*, vol. 323, no. 7325, pp. 1336-1338.

Brady, K. T., Lydiard, R. B., Malcolm, R., & Ballenger, J. C. 1991, "Cocaine-induced psychosis", *Journal of Clinical Psychiatry*, vol. 52, no. 12, pp. 509-512.

Brazo, P., Marie, R. M., Halbecq, I., Benali, K., Segard, L., Delamillieure, P., Langlois-Thery, S., van der Elst, A., Thibaut, F., Petit, M., & Dollfus, S. 2002, "Cognitive patterns in subtypes of schizophrenia", *European Psychiatry: the Journal of the Association of European Psychiatrists.17(3):155-62*.

British Psychological Society 2000, *Recent advances in understanding mental illness and psychotic experiences* British Psychological Society, Leicester.

Brown, G. W. & Birley, J. L. 1968, "Crises and life changes and the onset of schizophrenia", *Journal of Health & Social Behavior*, vol. 9, no. 3, pp. 203-214.

Calinoiu, I. & McClellan, J. 2004, "Diagnostic interviews.", *Current Psychiatry Reports.6(2):88-95*.

Cannon-Spoor, H. E., Potkin, S. G., & Wyatt, R. J. 1982, "Measurement of premorbid adjustment in chronic schizophrenia", *Schizophrenia Bulletin*, vol. 8, no. 3, pp. 470-484.

Cantor-Graae, E. 2007, "The contribution of social factors to the development of schizophrenia: a review of recent findings.", *Canadian Journal of Psychiatry - Revue Canadienne de Psychiatrie*, vol. 52, no. 5, pp. 277-286.

Cantor-Graae, E. & Pedersen, C. B. 2007, "Risk of schizophrenia in second-generation immigrants: a Danish population-based cohort study", *Psychological Medicine*, vol. 37, no. 4, pp. 485-494.

Cantor-Graae, E. & Selten, J. P. 2005, "Schizophrenia and migration: a meta-analysis and review.", *American Journal of Psychiatry*, vol. 162, no. 1, pp. 12-24.

Chadwick, P., Trower, P., & Dagnan, D. 1999, "Measuring Negative Person Evaluations: The Evaluative Beliefs Scale", *Cognitive Therapy and Research*, vol. 23, no. 5, pp. 549-559.

Chambers, R. A., Krystal, J. H., & Self, D. W. 2001, "A neurobiological basis for substance abuse comorbidity in schizophrenia.", *Biological Psychiatry*, vol. 50, no. 2, pp. 71-83.

Chianetta, J. M., Lefebvre, M., LeBlanc, R., & Grignon, S. 2008, "Comparative psychometric properties of the BACS and RBANS in patients with schizophrenia and schizoaffective disorder", *Schizophrenia Research*, vol. 105, no. 1-3, pp. 86-94.

Cohen, J. 1988, in *Statistical Power Analysis for the Behavioral Sciences*, 2nd edn, Lawrence Erlbaum, Hillsdale, p. 102.

Collins, K. A., Westra, H. A., Dozois, D. J., & Stewart, S. H. 2005, "The validity of the brief version of the Fear of Negative Evaluation Scale", *Journal of Anxiety Disorders*, vol. 19, no. 3, pp. 345-359.

Coopersmith, S. 1967, *The antecedents of self esteem.* W. H. Freeman, San Francisco.

Crisp, A., Gelder, M., Goddard, E., & Meltzer, H. 2004, "Stigmatization of people with mental illnesses: a follow-up study within the Changing Minds campaign of the Royal College of Psychiatrists", *World Psychiatry*, vol. 4, no. 2, pp. 106-113.

Crow, T. J. 1985, "The two-syndrome concept: origins and current status", *Schizophrenia Bulletin.11(3):471-86.*

Cullberg, J. 2003, "Stressful life events preceding the first onset of psychosis. An explorative study", *Nordic Journal of Psychiatry*, vol. 57, no. 3, pp. 209-214.

D'Souza, D. C., bi-Saab, W. M., Madonick, S., Forselius-Bielen, K., Doersch, A., Braley, G., Gueorguieva, R., Cooper, T. B., & Krystal, J. H. 2005, "Delta-9-tetrahydrocannabinol effects in schizophrenia: implications for cognition, psychosis, and addiction", *Biological Psychiatry*, vol. 57, no. 6, pp. 594-608.

de Zubicaray, G. I., Smith, G. A., Chalk, J. B., & Semple, J. 1998, "The Modified Card Sorting Test: test-retest stability and relationships with demographic variables in a healthy older adult sample", *British Journal of Clinical Psychology*, vol. 37, no. Pt 4, pp. 457-466.

Deister, A. & Marneros, A. 1993, "Long-term stability of subtypes in schizophrenic disorders: a comparison of four diagnostic systems", *European Archives of Psychiatry & Clinical Neuroscience*, vol. 242, no. 4, pp. 184-190.

Department of Health 2003, *National Statistics*, http://www.dh.gov.uk/assetRoot/04/07/91/16/04079116.pdf .

DeQuardo, J. R., Carpenter, C. F., & Tandon, R. 1994, "Patterns of substance abuse in schizophrenia: nature and significance", *Journal of Psychiatric Research*, vol. 28, no. 3, pp. 267-275.

Dernovsek, M. Z. & Tavcar, R. 1999, "Age at onset of schizophrenia and neuroleptic dosage", *Social Psychiatry & Psychiatric Epidemiology*, vol. 34, no. 12, pp. 622-626.

Dixon, L. 1999, "Dual diagnosis of substance abuse in schizophrenia: prevalence and impact on outcomes.", *Schizophrenia Research.35 Suppl:S93-100*.

Dixon, L., Haas, G., Weiden, P. J., Sweeney, J., & Frances, A. J. 1991, "Drug abuse in schizophrenic patients: clinical correlates and reasons for use", *American Journal of Psychiatry*, vol. 148, no. 2, pp. 224-230.

Doering, S., Muller, E., Kopcke, W., Pietzcker, A., Gaebel, W., Linden, M., Muller, P., Muller-Spahn, F., Tegeler, J., & Schussler, G. 1998, "Predictors of relapse and rehospitalization in schizophrenia and schizoaffective disorder", *Schizophrenia Bulletin.24(1):87-98*.

Dowson, J. H., Sussams, P., Grounds, A. T., & Taylor, J. 2000, "Associations of self-reported past "psychotic" phenomena with features of personality disorders", *Comprehensive Psychiatry*, vol. 41, no. 1, pp. 42-48.

Drake, R. E., Osher, F. C., Noordsy, D. L., Hurlbut, S. C., Teague, G. B., & Beaudett, M. S. 1990, "Diagnosis of alcohol use disorders in schizophrenia", *Schizophrenia Bulletin.16(1):57-67*.

Drake, R. J., Pickles, A., Bentall, R. P., Kinderman, P., Haddock, G., Tarrier, N., & Lewis, S. W. 2004, "The evolution of insight, paranoia and depression during early schizophrenia", *Psychological Medicine*, vol. 34, no. 2, pp. 285-292.

Dudley, R., Siitarinen, J., James, I., & Dodgson, G. 2009, "What do people with psychosis think caused their psychosis? A Q methodology study.", *Behavioural and Cognitive Psychotherapy*, vol. 37, no. 1, pp. 11-24.

Eaton, W. W., Mortensen, P. B., Herrman, H., Freeman, H., Bilker, W., Burgess, P., & Wooff, K. 1992, "Long-term course of hospitalization for schizophrenia: Part I. Risk for rehospitalization", *Schizophrenia Bulletin*, vol. 18, no. 2, pp. 217-228.

Endler, N. S., Parker, J. D., Bagby, R. M., & Cox, B. J. 1991, "Multidimensionality of state and trait anxiety: Factor structure of the Endler Multidimensional Anxiety Scales.", *Journal of Personality and Social Psychology*, vol. 60, no. 6, pp. 919-926.

Falloon, I. R. H. 1984, "Stress and schizophrenia," in *Schizophrenia*, S. R. Hirsch, ed., Henston, London, p. 31.

Fenigstein, A. & Vanable, P. A. 1992, "Paranoia and self-consciousness", *Journal of Personality & Social Psychology*, vol. 62, no. 1, pp. 129-138.

Fenton, W. S. & McGlashan, T. H. 1991a, "Natural history of schizophrenia subtypes. I. Longitudinal study of paranoid, hebephrenic, and undifferentiated schizophrenia", *Archives of General Psychiatry*, vol. 48, no. 11, pp. 969-977.

Fenton, W. S. & McGlashan, T. H. 1991b, "Natural history of schizophrenia subtypes. II. Positive and negative symptoms and long-term course", *Archives of General Psychiatry*, vol. 48, no. 11, pp. 978-986.

Fergusson, D. M., Horwood, L. J., & Ridder, E. M. 2005, "Tests of causal linkages between cannabis use and psychotic symptoms.", *Addiction.100(3):354-66*.

First, M. B. 2007, *Deconstructing psychosis*, http://dsm5.org/conference5.cfm..

First, M. B. & Gibbon, M. 2004, "The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II).," in *Comprehensive handbook of psychological assessment, Vol. 2: Personality assessment.*, vol. 2 M. J. Hilsenroth & D. L. Segal, eds., John Wiley & Sons, Inc, NJ, US, pp. 134-143.

Fowler, D., Freeman, D., Smith, B., Kuipers, E., Bebbington, P., Bashforth, H., Coker, S., Hodgekins, J., Gracie, A., Dunn, G., & Garety, P. 2006, "The Brief Core Schema Scales (BCSS): psychometric properties and associations with paranoia and grandiosity in non-clinical and psychosis samples", *Psychological Medicine*, vol. 36, no. 6, pp. 749-759.

Fowler, I. L., Carr, V. J., Carter, N. T., & Lewin, T. J. 1998, "Patterns of current and lifetime substance use in schizophrenia", *Schizophrenia Bulletin*, vol. 24, no. 3, pp. 443-455.

Freeman, D. & Garety, P. A. 2003, "Connecting neurosis and psychosis: the direct influence of emotion on delusions and hallucinations.", *Behaviour Research & Therapy*, vol. 41, no. 8, pp. 923-947.

Fresan, A., Apiquian, R., Nicolini, H., & Cervantes, J. J. 2007, "Temperament and character in violent schizophrenic patients", *Schizophrenia Research*, vol. 94, no. 1-3, pp. 74-80.

Gilbert, P. 1992, *Depression: The evolution of Powerlessness* Erlbaum, London.

Goldberg, T. E. & Weinberger, D. R. 1995, "A case against subtyping in schizophrenia.", *Schizophrenia Research.17(2):147-52*.

Green, A. I. 2005, "Schizophrenia and comorbid substance use disorder: effects of antipsychotics.", *Journal of Clinical Psychiatry.66 Suppl 6:21-6*.

Green, A. I., Zimmet, S. V., Strous, R. D., & Schildkraut, J. J. 1999, "Clozapine for comorbid substance use disorder and schizophrenia: do patients with schizophrenia have a reward-deficiency syndrome that can be ameliorated by clozapine?.", *Harvard Review of Psychiatry*, vol. 6, no. 6, pp. 287-296.

Gupta, S., Rajaprabhakaran, R., Arndt, S., Flaum, M., & Andreasen, N. C. 1995, "Premorbid adjustment as a predictor of phenomenological and neurobiological indices in schizophrenia", *Schizophrenia Research*, vol. 16, no. 3, pp. 189-197.

Haddock, G., Barrowclough, C., Tarrier, N., Moring, J., O'Brien, R., Schofield, N., Quinn, J., Palmer, S., Davies, L., Lowens, I., McGovern, J., & Lewis, S. 2003, "Cognitive-behavioural therapy and motivational intervention for schizophrenia and substance misuse. 18-month outcomes of a randomised controlled trial.", *British Journal of Psychiatry*, vol. 183, pp. 418-426.

Hafner, H., Maurer, K., Trendler, G., an der, H. W., Schmidt, M., & Konnecke, R. 2005, "Schizophrenia and depression: challenging the paradigm of two separate diseases--a controlled study of schizophrenia, depression and healthy controls", *Schizophrenia Research*, vol. 77, no. 1, pp. 11-24.

Hafner, H. & Nowotny, B. 1995, "Epidemiology of early-onset schizophrenia", *European Archives of Psychiatry & Clinical Neuroscience*, vol. 245, no. 2, pp. 80-92.

Hambrecht, M. & Hafner, H. 1996, "Substance abuse and the onset of schizophrenia", *Biological Psychiatry.40(11):1155-63*.

Harrison, G., Croudace, T., Mason, P., Glazebrook, C., & Medley, I. 1996, "Predicting the long-term outcome of schizophrenia", *Psychological Medicine*, vol. 26, no. 4, pp. 697-705.

Hawkins, K. A. & Wexler, B. E. 1999, "California Verbal Learning Test practice effects in a schizophrenia sample", *Schizophrenia Research*, vol. 39, no. 1, pp. 73-78.

Hawley, L. L., Ringo Ho, M. H., Zuroff, D. C., & Blatt, S. J. 2007, "Stress reactivity following brief treatment for depression: differential effects of psychotherapy and medication", *Journal of Consulting & Clinical Psychology*, vol. 75, no. 2, pp. 244-256.

Hawton, K., Sutton, L., Haw, C., Sinclair, J., & Deeks, J. J. 2005, "Schizophrenia and suicide: systematic review of risk factors.", *British Journal of Psychiatry*, vol. 187, pp. 9-20.

Helzer, J. E. 1983, "Standardized interviews in psychiatry.", *Psychiatric Developments.1(2):161-78*.

Hollis, C. 2003, "Developmental precursors of child- and adolescent-onset schizophrenia and affective psychoses: diagnostic specificity and continuity with symptom dimensions", *British Journal of Psychiatry*, vol. 182, pp. 37-44.

Holmes, T. H. & Rahe, R. H. 1967, "The Social Readjustment Rating Scale", *Journal of Psychosomatic Research*, vol. 11, no. 2, pp. 213-218.

Hori, H., Noguchi, H., Hashimoto, R., Nakabayashi, T., Saitoh, O., Murray, R. M., Okabe, S., & Kunugi, H. 2008, "Personality in schizophrenia assessed with the Temperament and Character Inventory (TCI)", *Psychiatry Research*, vol. 160, no. 2, pp. 175-183.

Howard, R., Rabins, P. V., Seeman, M. V., & Jeste, D. V. 2000, "Late-onset schizophrenia and very-late-onset schizophrenia-like psychosis: an international consensus. The International Late-Onset Schizophrenia Group.", *American Journal of Psychiatry*, vol. 157, no. 2, pp. 172-178.

Hurd, H. M. 1881, "A plea for systematic therapeutical, clinical and statistical study", *Journal of Insanity*, vol. 38, pp. 16-31.

Iqbal, Z., Birchwood, M., Chadwick, P., & Trower, P. 2000, "Cognitive approach to depression and suicidal thinking in psychosis. 2. Testing the validity of a social ranking model", *British Journal of Psychiatry*, vol. 177, pp. 522-528.

Ishikawa, R., Sasaki, K., & Fukui, I. 1992, "Standardization of Japanese version of FNE and SADS.", *Koudou Ryouhou Kenkyu (Jap J Behav Ther)*, vol. 18, pp. 10-17.

James, W., Preston, N. J., Koh, G., Spencer, C., Kisely, S. R., & Castle, D. J. 2004, "A group intervention which assists patients with dual diagnosis reduce their drug use: a randomized controlled trial.", *Psychological Medicine.34(6):983-90*.

Janssen, I., Krabbendam, L., Bak, M., Hanssen, M., Vollebergh, W., de, G. R., & van Os, J. 2004, "Childhood abuse as a risk factor for psychotic experiences", *Acta Psychiatrica Scandinavica*, vol. 109, no. 1, pp. 38-45.

Jaspers, K. 1959, "The synthesis of disease entities (Nosology)," in *General Psychopathology*, vol. 2 The Johns Hopkins Press, London, pp. 564-616.

Jensen, A. R. & Rohwer, W. D., Jr. 1966, "The Stroop color-word test: a review.", *Acta Psychologica*, vol. 25, no. 1, pp. 36-93.

John, E. R., Prichep, L. S., & Easton, P. 1994, "Standardized varimax descriptors of event related potentials: evaluation of psychiatric patients", *Psychiatry Research*, vol. 55, no. 1, pp. 13-40.

John, E. R., Prichep, L. S., Winterer, G., Herrmann, W. M., diMichele, F., Halper, J., Bolwig, T. G., & Cancro, R. 2007, "Electrophysiological subtypes of psychotic states.", *Acta Psychiatrica Scandinavica*, vol. 116, no. 1, pp. 17-35.

Jorgensen, P. 1985, "Long-term course of acute reactive paranoid psychosis. A follow-up study", *Acta Psychiatrica Scandinavica*, vol. 71, no. 1, pp. 30-37.

Jorgensen, P., Bennedsen, B., Christensen, J., & Hyllested, A. 1997, "Acute and transient psychotic disorder: a 1-year follow-up study", *Acta Psychiatrica Scandinavica*, vol. 96, no. 2, pp. 150-154.

Kay, S. R. & Singh, M. M. 1989, "The positive-negative distinction in drug-free schizophrenic patients. Stability, response to neuroleptics, and prognostic significance", *Archives of General Psychiatry*, vol. 46, no. 8, pp. 711-718.

Kelley, M. E., Gilbertson, M., Mouton, A., & van Kammen, D. P. 1992, "Deterioration in premorbid functioning in schizophrenia: a developmental model of negative symptoms in drug-free patients", *American Journal of Psychiatry*, vol. 149, no. 11, pp. 1543-1548.

Kendell, R. E. 1989, "Clinical validity.", *Psychological Medicine*, vol. 19, no. 1, pp. 45-55.

Kendell, R. M. D. & Jablensky, A. M. D. 2003, "Distinguishing Between the Validity and Utility of Psychiatric Diagnoses.", *American Journal of Psychiatry*, vol. 160, no. 1, pp. 4-12.

Kendler, K. S. 1980, "The nosologic validity of paranoia (simple delusional disorder). A review", *Archives of General Psychiatry*, vol. 37, no. 6, pp. 699-706.

Kendler, K. S., Gruenberg, A. M., & Tsuang, M. T. 1984, "Outcome of schizophrenic subtypes defined by four diagnostic systems", *Archives of General Psychiatry*, vol. 41, no. 2, pp. 149-154.

Kendler, K. S., Gruenberg, A. M., & Tsuang, M. T. 1985, "Subtype stability in schizophrenia", *American Journal of Psychiatry.142(7):827-32*.

Kendler, K. S., McGuire, M., Gruenberg, A. M., & Walsh, D. 1994, "Outcome and family study of the subtypes of schizophrenia in the west of Ireland", *American Journal of Psychiatry*, vol. 151, no. 6, pp. 849-856.

Kendler, K. S. & Tsuang, M. T. 1988, "Outcome and familial psychopathology in schizophrenia.", *Archives of General Psychiatry*, vol. 45, no. 4, pp. 338-346.

Keshavan, M. S., Duggal, H. S., Veeragandham, G., McLaughlin, N. M., Montrose, D. M., Haas, G. L., & Schooler, N. R. 2005, "Personality dimensions in first-episode psychoses", *American Journal of Psychiatry*, vol. 162, no. 1, pp. 102-109.

Khazaal, Y., Favrod, J., Libbrecht, J., Finot, S. C., Azoulay, S., Benzakin, L., Oury-Delamotte, M., Follack, C., & Pomini, V. 2006, "A card game for the treatment of delusional ideas: a naturalistic pilot trial", *BMC Psychiatry*, vol. 6, p. 48.

Kilcommons, A. M. & Morrison, A. P. 2005, "Relationships between trauma and psychosis: an exploration of cognitive and dissociative factors", *Acta Psychiatrica Scandinavica*, vol. 112, no. 5, pp. 351-359.

Kingdon, D., Vincent, S., Vincent, S., Kinoshita, Y., & Turkington, D. 2008a, "Destigmatising schizophrenia - does changing terminology reduce negative attitudes?", *Psychiatric Bulletin*, vol. 32, pp. 419-422.

Kingdon, D., Gibson, A., Kinoshita, Y., Turkington, D., Rathod, S., & Morrison, A. 2008b, "Acceptable terminology and subgroups in schizophrenia: an exploratory study", *Social Psychiatry & Psychiatric Epidemiology*, vol. 43, no. 3, pp. 239-243.

Kingdon, D., Ramon, S., Perkins, R., & Morris, D. 2006, *Social inclusion for psychiatrists*, NIMHE & Royal College of Psychiatrists, London.

Kingdon, D. G., Kinoshita, Y., Naeem, F., Swelam, M., Hansen, L., Vincent, S., & Rathod, S. 2007, "Schizophrenia can and should be renamed.", *BMJ*, vol. 334, no. 7587, pp. 221-222.

Kingdon, D. G. & Turkington, D. 1994, *Cognitive-behavioral therapy of schizophrenia* Guilford Press, New York.

Kingdon, D. G. & Turkington, D. 2005, *Cognitive therapy of schizophrenia.* Guilford Press, New York.

Kingsep, P., Nathan, P., & Castle, D. 2003, "Cognitive behavioural group treatment for social anxiety in schizophrenia", *Schizophrenia Research.63(1-2):121-9*.

Kirkpatrick, B., Buchanan, R. W., McKenney, P. D., Alphs, L. D., & Carpenter, W. T., Jr. 1989, "The Schedule for the Deficit syndrome: an instrument for research in schizophrenia", *Psychiatry Research.30(2):119-23*.

Kirkpatrick, B. M., Buchanan, R. W. M., Ross, D. E. M., & Carpenter, W. T. J. 2001, "A Separate Disease Within the Syndrome of Schizophrenia.", *Archives of General Psychiatry*, vol. 58, no. 2, pp. 165-171.

Kojima, M., Furukawa, T. A., Takahashi, H., Kawai, M., Nagaya, T., & Tokudome, S. 2002, "Cross-cultural validation of the Beck Depression Inventory-II in Japan", *Psychiatry Research*, vol. 110, no. 3, pp. 291-299.

Krabbendam, L., Myin-Germeys, I., Hanssen, M., De, G. R., Vollebergh, W., Bak, M., & van Os, J. 2005, "Development of depressed mood predicts onset of psychotic disorder in individuals who report hallucinatory experiences", *British Journal of Clinical Psychology*, vol. 44, no. Pt:1, pp. 1-25.

Kraemer, H. C., Shrout, P. E., & Rubio-Stipec, M. 2007, "Developing the diagnostic and statistical manual V: what will "statistical" mean in DSM-V?", *Social Psychiatry & Psychiatric Epidemiology*, vol. 42, no. 4, pp. 259-267.

Kraepelin, E. 1919, *Dementia Praecox and Paraphrenia* E. & S. Livingstone, Edinburgh.

Krausz, M. & Muller-Thomsen, T. 1993, "Schizophrenia with onset in adolescence: an 11-year followup", *Schizophrenia Bulletin*, vol. 19, no. 4, pp. 831-841.

Landabaso, M. A., Iraurgi, I., Jimenez-Lerma, J. M., Calle, R., Sanz, J., & Gutierrez-Fraile, M. 2002, "Ecstasy-induced psychotic disorder: six-month follow-up study", *European Addiction Research*, vol. 8, no. 3, pp. 133-140.

Larsen, T. K., Friis, S., Haahr, U., Johannessen, J. O., Melle, I., Opjordsmoen, S., Rund, B. R., Simonsen, E., Vaglum, P. V., & McGlashan, T. H. 2004, "Premorbid adjustment in first-episode non-affective psychosis: distinct patterns of pre-onset course", *British Journal of Psychiatry*, vol. 185:108-15, 2004 Aug., pp. 108-115.

Larsen, T. K., McGlashan, T. H., Johannessen, J. O., & Vibe-Hansen, L. 1996, "First-episode schizophrenia: II. Premorbid patterns by gender", *Schizophrenia Bulletin*, vol. 22, no. 2, pp. 257-269.

Leary, M. R. 1983, "A brief version of the Fear of Negative Evaluation Scale", *Personality and Social Psychology Bulletin*, vol. 9, no. 3, pp. 371-375.

Leucht, S., Komossa, K., Rummel-Kluge, C., Corves, C., Hunger, H., Schmid, F., Asenjo, L. C., Schwarz, S., & Davis, J. M. 2009, "A meta-analysis of head-to-head comparisons of second-generation antipsychotics in the treatment of schizophrenia", *American Journal of Psychiatry*, vol. 166, no. 2, pp. 152-163.

Lewine, R., Burbach, D., & Meltzer, H. Y. 1984, "Effect of diagnostic criteria on the ratio of male to female schizophrenic patients", *American Journal of Psychiatry*, vol. 141, no. 1, pp. 84-87.

Lezak, M. D. 1995, *Neuropsychological Assessment*, 3rd edn, Oxford University Press, New York.

Liddle, P. F. & Barnes, T. R. 1990, "Syndromes of chronic schizophrenia", *The British Journal of Psychiatry*, vol. 157, no. 4, pp. 558-561.

Lieberman, J. A., Kane, J. M., & Alvir, J. 1987, "Provocative tests with psychostimulant drugs in schizophrenia", *Psychopharmacology*, vol. 91, no. 4, pp. 415-433.

Luoma, S., Hakko, H., Ollinen, T., Jarvelin, M. R., & Lindeman, S. 2008, "Association between age at onset and clinical features of schizophrenia: the Northern Finland 1966 birth cohort study", *European Psychiatry: the Journal of the Association of European Psychiatrists*, vol. 23, no. 5, pp. 331-335.

Lynch, D. J., McGrady, A., Alvarez, E., & Forman, J. 2005, "Recent life changes and medical utilization in an academic family practice", *Journal of Nervous & Mental Disease*, vol. 193, no. 9, pp. 633-635.

Lysaker, P., Bell, M., Beam-Goulet, J., & Milstein, R. 1994, "Relationship of positive and negative symptoms to cocaine abuse in schizophrenia", *Journal of Nervous & Mental Disease*, vol. 182, no. 2, pp. 109-112.

Magri, C., Gardella, R., Barlati, S. D., Valsecchi, P., Sacchetti, E., & Barlati, S. 2007, "Mitochondrial DNA haplogroups and age at onset of schizophrenia", *American Journal of Medical Genetics*, vol. Part, no. 4, pp. 496-501.

Malla, A. K., Cortese, L., Shaw, T. S., & Ginsberg, B. 1990, "Life events and relapse in schizophrenia. A one year prospective study", *Social Psychiatry & Psychiatric Epidemiology*, vol. 25, no. 4, pp. 221-224.

Marneros, A., Pillmann, F., Haring, A., Balzuweit, S., & Bloink, R. 2003, "What is schizophrenic in acute and transient psychotic disorder?", *Schizophrenia Bulletin*, vol. 29, no. 2, pp. 311-323.

Martin, J. A. & Penn, D. L. 2001, "Social cognition and subclinical paranoid ideation", *British Journal of Clinical Psychology*, vol. 40, no. Pt:3, pp. 3-5.

McCabe, M. S. 1975, "Reactive psychoses, a clinical and genetic investigation", *Acta Psychiatrica Scandinavica, Supplementum*, vol. 259, pp. 1-133.

Meltzer, H. Y., Bobo, W. V., Roy, A., Jayathilake, K., Chen, Y., Ertugrul, A., nil Yagcioglu, A. E., & Small, J. G. 2008, "A randomized, double-blind comparison of clozapine and high-dose olanzapine in treatment-resistant patients with schizophrenia.", *Journal of Clinical Psychiatry*, vol. 69, no. 2, pp. 274-285.

Meltzer, H. Y., Rabinowitz, J., Lee, M. A., Cola, P. A., Ranjan, R., Findling, R. L., & Thompson, P. A. 1997, "Age at onset and gender of schizophrenic patients in relation to neuroleptic resistance", *American Journal of Psychiatry*, vol. 154, no. 4, pp. 475-482.

Miller, F. T., Abrams, T., Dulit, R., & Fyer, M. 1993, "Psychotic symptoms in patients with borderline personality disorder and concurrent axis I disorder", *Hospital & Community Psychiatry*, vol. 44, no. 1, pp. 59-61.

Morgan, C., bdul-Al, R., Lappin, J. M., Jones, P., Fearon, P., Leese, M., Croudace, T., Morgan, K., Dazzan, P., Craig, T., Leff, J., Murray, R., & AESOP Study Group 2006, "Clinical and social determinants of duration of untreated psychosis in the AESOP first-episode psychosis study", *British Journal of Psychiatry*, vol. 189:446-52, 2006 Nov., pp. 446-452.

Morgan, C. & Fisher, H. 2007, "Environment and schizophrenia: environmental factors in schizophrenia: childhood trauma - a critical review.", *Schizophrenia Bulletin*, vol. 33, no. 1, pp. 3-10.

Morgan, M. J. 2000, "Ecstasy (MDMA): a review of its possible persistent psychological effects.", *Psychopharmacology*, vol. 152, no. 3, pp. 230-248.

Morrison, A., Read, J., & Turkington, D. 2005, "Trauma and psychosis: theoretical and clinical implications", *Acta Psychiatrica Scandinavica*, vol. 112, no. 5, pp. 327-329.

Mueser, K. T., Goodman, L. B., Trumbetta, S. L., Rosenberg, S. D., Osher, C., Vidaver, R., Auciello, P., & Foy, D. W. 1998, "Trauma and posttraumatic stress disorder in severe mental illness", *Journal of Consulting & Clinical Psychology*, vol. 66, no. 3, pp. 493-499.

Mueser, K. T., Yarnold, P. R., Levinson, D. F., Singh, H., Bellack, A. S., Kee, K., Morrison, R. L., & Yadalam, K. G. 1990, "Prevalence of substance abuse in schizophrenia: demographic and clinical correlates", *Schizophrenia Bulletin*, vol. 16, no. 1, pp. 31-56.

Myin-Germeys, I., Delespaul, P., & van Os, J. 2005, "Behavioural sensitization to daily life stress in psychosis", *Psychological Medicine*, vol. 35, no. 5, pp. 733-741.

Myin-Germeys, I. & van Os, J. 2007, "Stress-reactivity in psychosis: evidence for an affective pathway to psychosis.", *Clinical Psychology Review*, vol. 27, no. 4, pp. 409-424.

Myin-Germeys, I., van Os, J., Schwartz, J. E., Stone, A. A., & Delespaul, P. A. 2001, "Emotional reactivity to daily life stress in psychosis", *Archives of General Psychiatry*, vol. 58, no. 12, pp. 1137-1144.

Negrete, J. C., Knapp, W. P., Douglas, D. E., & Smith, W. B. 1986, "Cannabis affects the severity of schizophrenic symptoms: results of a clinical survey", *Psychological Medicine*, vol. 16, no. 3, pp. 515-520.

Nelson, H. E. 1976, "A modified card sorting test sensitive to frontal lobe defects", *Cortex*, vol. 12, no. 4, pp. 313-324.

NIMH 1985, "Clinical Global Impressions (CGI) scale", *Psychopharmacol Bull*, vol. 21, pp. 839-843.

Norman, R. M. & Malla, A. K. 1991, "Subjective stress in schizophrenic patients", *Social Psychiatry & Psychiatric Epidemiology*, vol. 26, no. 5, pp. 212-216.

Nuechterlein, K. H. & Dawson, M. E. 1984, "A heuristic vulnerability/stress model of schizophrenic episodes", *Schizophrenia Bulletin.10(2):300-12*.

Nuechterlein, K. H., Dawson, M. E., Ventura, J., Gitlin, M., Subotnik, K. L., Snyder, K. S., Mintz, J., & Bartzokis, G. 1994, "The vulnerability/stress model of schizophrenic relapse: a longitudinal study", *Acta Psychiatrica Scandinavica, Supplementum.382:58-64*.

O'Connor, L. E., Berry, J. W., Weiss, J., & Gilbert, P. 2002, "Guilt, fear, submission, and empathy in depression", *Journal of Affective Disorders*, vol. 71, no. 1-3, pp. 19-27.

Peters, E., Joseph, S., Day, S., & Garety, P. 2004, "Measuring delusional ideation: the 21-item Peters et al. Delusions Inventory (PDI)", *Schizophrenia Bulletin*, vol. 30, no. 4, pp. 1005-1022.

Peters, E. R., Joseph, S. A., & Garety, P. A. 1999, "Measurement of delusional ideation in the normal population: introducing the PDI (Peters et al. Delusions Inventory)", *Schizophrenia Bulletin*, vol. 25, no. 3, pp. 553-576.

Pilkonis, P. A., Heape, C. L., Proietti, J. M., Clark, S. W., McDavid, J. D., & Pitts, T. E. 1995, "The Reliability and Validity of Two Structured Diagnostic Interviews for Personality Disorders", *Archives of General Psychiatry*, vol. 52, no. 12, pp. 1025-1033.

Pompili, M., Amador, X. F., Girardi, P., Harkavy-Friedman, J., Harrow, M., Kaplan, K., Krausz, M., Lester, D., Meltzer, H. Y., Modestin, J., Montross, L. P., Bo, M. P., Munk-Jorgensen, P., Nielsen, J., Nordentoft, M., Saarinen, P. I., Zisook, S., Wilson, S. T., & Tatarelli, R. 2007, "Suicide risk in schizophrenia: Learning from the past to change the future", *Annals of General Psychiatry.6, 2007.Article Number: 10.Date of Publication: 16 Mar 2007.*

Preti, A., Sardu, C., & Piga, A. 2007, "Mixed-handedness is associated with the reporting of psychotic-like beliefs in a non-clinical Italian sample", *Schizophrenia Research*, vol. 92, no. 1-3, pp. 15-23.

Rabinowitz, J., Harvey, P. D., Eerdekens, M., & Davidson, M. 2006, "Premorbid functioning and treatment response in recent-onset schizophrenia", *British Journal of Psychiatry*, vol. 189:31-5, 2006 Jul., pp. 31-35.

Rathod, S., Kingdon, D., Smith, P., & Turkington, D. 2005, "Insight into schizophrenia: The effects of cognitive behavioural therapy on the components of insight and association with sociodemographics--data on a previously published randomised controlled trial.", *Schizophrenia Research*, vol. 74, no. 2-3, pp. 211-219.

Read, J. & Argyle, N. 1999, "Hallucinations, delusions, and thought disorder among adult psychiatric inpatients with a history of child abuse.", *Psychiatric Services*, vol. 50, no. 11, pp. 1467-1472.

Read, J., van Os, J., Morrison, A. P., & Ross, C. A. 2005, "Childhood trauma, psychosis and schizophrenia: a literature review with theoretical and clinical implications.", *Acta Psychiatrica Scandinavica*, vol. 112, no. 5, pp. 330-350.

Rector, N. A., Seeman, M. V., & Segal, Z. V. 2003, "Cognitive therapy for schizophrenia: a preliminary randomized controlled trial", *Schizophrenia Research*, vol. 63, no. 1-2, pp. 1-11.

Regier, D. A. 2007, "Time for a fresh start? Rethinking psychosis in DSM-V", *Schizophrenia Bulletin*, vol. 33, no. 4, pp. 843-845.

Regier, D. A., Farmer, M. E., Rae, D. S., Locke, B. Z., Keith, S. J., Judd, L. L., & Goodwin, F. K. 1990, "Comorbidity of mental disorders with alcohol and other drug abuse. Results from the Epidemiologic Catchment Area (ECA) Study.", *JAMA*, vol. 264, no. 19, pp. 2511-2518.

Richardson SA, Dohrenwend BS, & Klein D 1965, *Interviewing Its Forms and Functions* Basic Books.

Robins, E. & Guze, S. B. 1970, "Establishment of diagnostic validity in psychiatric illness: its application to schizophrenia", *American Journal of Psychiatry*, vol. 126, no. 7, pp. 983-987.

Robinson, D. G., Woerner, M. G., Napolitano, B., Patel, R. C., Sevy, S. M., Gunduz-Bruce, H., Soto-Perello, J. M., Mendelowitz, A., Khadivi, A., Miller, R., McCormack, J., Lorell, B. S., Lesser, M. L., Schooler, N. R., & Kane, J. M. 2006, "Randomized comparison of olanzapine versus risperidone for the treatment of first-episode schizophrenia: 4-month outcomes", *American Journal of Psychiatry*, vol. 163, no. 12, pp. 2096-2102.

Rodebaugh, T. L., Woods, C. M., Thissen, D. M., Heimberg, R. G., Chambless, D. L., & Rapee, R. M. 2004, "More information from fewer questions: the factor structure and item properties of the original and brief fear of negative evaluation scale", *Psychological Assessment*, vol. 16, no. 2, pp. 169-181.

Rodriguez Solano & Gonzβlez De Chβvez, M. 2000, "Premorbid personality disorders in schizophrenia", *Schizophrenia Research*, vol. 44, no. 2, pp. 137-144.

Rosenberg, M. 1979, *Conceiving the self.* Basic Books, New York.

Rosenthal, R. N., Hellerstein, D. J., & Miner, C. R. 1994, "Positive and negative syndrome typology in schizophrenic patients with psychoactive substance use disorders", *Comprehensive Psychiatry*, vol. 35, no. 2, pp. 91-98.

Ross, C. A. & Joshi, S. 1992, "Schneiderian symptoms and childhood trauma in the general population", *Comprehensive Psychiatry*, vol. 33, no. 4, pp. 269-273.

Roy, M. A. & Crowe, R. R. 1994, "Validity of the familial and sporadic subtypes of schizophrenia.", *American Journal of Psychiatry.151(6):805-14.*

Rusch, N., Corrigan, P. W., Powell, K., Rajah, A., Olschewski, M., Wilkniss, S., & Batia, K. 2009, "A stress-coping model of mental illness stigma: II. Emotional stress responses, coping behavior and outcome", *Schizophrenia Research*, vol. 110, no. 1-3, pp. 65-71.

Sadock, B. J. & Sadock, V. A. 2000a, "Diagnosis and psychiatry: Examination of the psychiatric patient," in *Kaplan & Sadock's comprehensive textbook of psychiatry, Vols. 1 & 2*, 7th ed. edn, B. J. Sadock & V. A. Sadock, eds., Lippincott Williams & Wilkins Publishers, Philadelphia, PA, US, pp. 652-788.

Sadock, B. J. & Sadock, V. A. 2000b, "Schizophrenia," in *Kaplan & Sadock's comprehensive textbook of psychiatry, Vols. 1 & 2*, 7th ed. edn, B. J. Sadock & V. A. Sadock, eds., Lippincott Williams & Wilkins Publishers, Philadelphia, PA, US, pp. 1096-1231.

Salyers, M. P. & Mueser, K. T. 2001, "Social functioning, psychopathology, and medication side effects in relation to substance use and abuse in schizophrenia", *Schizophrenia Research.48(1):109-23*.

Sato, M. 2006, "Renaming schizophrenia: a Japanese perspective", *World Psychiatry*, vol. 5, no. 1, pp. 53-55.

Schafer, I., Harfst, T., Aderhold, V., Briken, P., Lehmann, M., Moritz, S., Read, J., & Naber, D. 2006, "Childhood trauma and dissociation in female patients with schizophrenia spectrum disorders: an exploratory study", *Journal of Nervous & Mental Disease*, vol. 194, no. 2, pp. 135-138.

Schlenker, B. R. & Leary, M. R. 1982, "Social anxiety and self-presentation: A conceptualization model.", *Psychological Bulletin*, vol. 92, no. 3, pp. 641-669.

Schneider, K. 1959, *Clinical Psychopathology*, 5th edn, Grune & Stratton, Oxford, England.

Schultz, S. K., Ho, B. C., & Andreasen, N. C. 2000, "Clinical features characterizing young-onset and intermediate-onset schizophrenia", *Journal of Neuropsychiatry & Clinical Neurosciences*, vol. 12, no. 4, pp. 502-505.

Schurhoff, F., Golmard, J. L., Szoke, A., Bellivier, F., Berthier, A., Meary, A., Rouillon, F., & Leboyer, M. 2004, "Admixture analysis of age at onset in schizophrenia", *Schizophrenia Research*, vol. 71, no. 1, pp. 35-41.

Sevy, S., Kay, S. R., Opler, L. A., & van Praag, H. M. 1990, "Significance of cocaine history in schizophrenia", *Journal of Nervous & Mental Disease*, vol. 178, no. 10, pp. 642-648.

Shaner, A., Roberts, L. J., Eckman, T. A., Racenstein, J. M., Tucker, D. E., Tsuang, J. W., & Mintz, J. 1998, "Sources of diagnostic uncertainty for chronically psychotic cocaine abusers", *Psychiatric Services.49(5):684-90*.

Sherer, M. A., Kumor, K. M., Cone, E. J., & Jaffe, J. H. 1988, "Suspiciousness induced by four-hour intravenous infusions of cocaine. Preliminary findings.", *Archives of General Psychiatry*, vol. 45, no. 7, pp. 673-677.

Shevlin, M., Dorahy, M., & Adamson, G. 2007, "Childhood traumas and hallucinations: an analysis of the National Comorbidity Survey", *Journal of Psychiatric Research*, vol. 41, no. 3-4, pp. 222-228.

Sikich, L., Frazier, J. A., McClellan, J., Findling, R. L., Vitiello, B., Ritz, L., Ambler, D., Puglia, M., Maloney, A. E., Michael, E., De, J. S., Slifka, K., Noyes, N., Hlastala, S., Pierson, L., McNamara, N. K., porto-Bedoya, D., Anderson, R., Hamer, R. M., & Lieberman, J. A. 2008, "Double-blind comparison of first- and second-generation antipsychotics in early-onset schizophrenia and schizo-affective disorder: findings from

the treatment of early-onset schizophrenia spectrum disorders (TEOSS) study.", *American Journal of Psychiatry*, vol. 165, no. 11, pp. 1420-1431.

Singh, S. P., Croudace, T., Amin, S., Kwiecinski, R., Medley, I., Jones, P. B., & Harrison, G. 2000, "Three-year outcome of first-episode psychoses in an established community psychiatric service", *British Journal of Psychiatry*, vol. 176, pp. 210-216.

Smith, B., Fowler, D. G., Freeman, D., Bebbington, P., Bashforth, H., Garety, P., Dunn, G., & Kuipers, E. 2006, "Emotion and psychosis: links between depression, self-esteem, negative schematic beliefs and delusions and hallucinations", *Schizophrenia Research*, vol. 86, no. 1-3, pp. 181-188.

SPSS Inc 2006, *Statistical Package for the Social Sciences, version 15 [Computer software]*, SPSS Inc, Chicago.

StataCorp 2005, *Stata 8 [Computer software]*.

Stephens, J. H., Shaffer, J. W., & Carpenter, W. T., Jr. 1982, "Reactive psychoses", *Journal of Nervous & Mental Disease*, vol. 170, no. 11, pp. 657-663.

Suda, K., Hayashi, N., & Hiraga, M. 2005, "Predicting features of later development of schizophrenia among patients with acute and transient psychotic disorder", *Psychiatry & Clinical Neurosciences*, vol. 59, no. 2, pp. 146-150.

Suzuki, H., Tsukamoto, C., Nakano, Y., Aoki, S., & Kuroda, S. 1998, "Delusions and hallucinations in patients with borderline personality disorder", *Psychiatry & Clinical Neurosciences*, vol. 52, no. 6, pp. 605-610.

Swoboda, H., Demal, U., Krautgartner, M., & Amering, M. 2003, "Heightened embarrassability discriminates between panic disorder patients with and without agoraphobia", *Journal of Behavior Therapy & Experimental Psychiatry*, vol. 34, no. 3-4, pp. 195-204.

Tait, L., Birchwood, M., & Trower, P. 2004, "Adapting to the challenge of psychosis: personal resilience and the use of sealing-over (avoidant) coping strategies", *British Journal of Psychiatry*, vol. 185, pp. 410-415.

Talamo, A., Centorrino, F., Tondo, L., Dimitri, A., Hennen, J., & Baldessarini, R. J. 2006, "Comorbid substance-use in schizophrenia: relation to positive and negative symptoms", *Schizophrenia Research*, vol. 86, no. 1-3, pp. 251-255.

Teasdale, J. D. & Barnard, P. J. 1993, *Affect, Cognition, and Change: Re-modeling Depressive Thought.* Lawrence Erlbaum Associates, Hove, UK.

Teasdale, J. D. & Cox, S. G. 2001, "Dysphoria: self-devaluative and affective components in recovered depressed patients and never depressed controls", *Psychological Medicine*, vol. 31, no. 7, pp. 1311-1316.

Teasdale, J. D. & Dent, J. 1987, "Cognitive vulnerability to depression: an investigation of two hypotheses", *British Journal of Clinical Psychology*, vol. 26, no. Pt 2, pp. 113-126.

Thornicroft, G., Tansella, M., Becker, T., Knapp, M., Leese, M., Schene, A., Vazquez-Barquero, J. L., & EPSILON Study Group 2004, "The personal impact of schizophrenia in Europe", *Schizophrenia Research*, vol. 69, no. 2-3, pp. 125-132.

Tsuang, M. T., Woolson, R. F., & Simpson, J. C. 1980, "The iowa structured psychiatric interview. Rationale, reliability, and validity", *Acta Psychiatrica Scandinavica, Supplementum.283:96p..*

Turner, H. 2007, *An Alternative Approach to Sub-grouping the Eating Disorder Population: New Potential for Improving Treatment Effectiveness?,* Fuculty of Medicine, Health and Biological Sciences, School of Medicine, University of Southampton.

van der Elst, W., van Boxtel, M. P., van Breukelen, G. J., & Jolles, J. 2006, "The Stroop color-word test: influence of age, sex, and education; and normative data for a large sample across the adult age range", *Assessment*, vol. 13, no. 1, pp. 62-79.

van Kampen, J. & Katz, M. 2001, "Persistent psychosis after a single ingestion of 'ecstasy'", *Psychosomatics*, vol. 42, no. 6, pp. 525-527.

van Os, J., Fahy, T. A., Bebbington, P., Jones, P., Wilkins, S., Sham, P., Russell, A., Gilvarry, K., Lewis, S., & Toone, B. 1994, "The influence of life events on the subsequent course of psychotic illness. A prospective follow-up of the Camberwell Collaborative Psychosis Study", *Psychological Medicine*, vol. 24, no. 2, pp. 503-513.

van Os, J., Verdoux, H., Maurice-Tison, S., Gay, B., Liraud, F., Salamon, R., & Bourgeois, M. 1999, "Self-reported psychosis-like symptoms and the continuum of psychosis", *Social Psychiatry & Psychiatric Epidemiology*, vol. 34, no. 9, pp. 459-463.

van Os, J. 2009, "A salience dysregulation syndrome", *The British Journal of Psychiatry*, vol. 194, no. 2, pp. 101-103.

Vardy, M. M. & Kay, S. R. 1983, "LSD psychosis or LSD-induced schizophrenia? A multimethod inquiry", *Archives of General Psychiatry*, vol. 40, no. 8, pp. 877-883.

Verdoux, H. & van Os, J. 2002, "Psychotic symptoms in non-clinical populations and the continuum of psychosis", *Schizophrenia Research*, vol. 54, no. 1-2, pp. 59-65.

Walsh, E., Buchanan, A., & Fahy, T. 2002, "Violence and schizophrenia: examining the evidence.", *British Journal of Psychiatry*, vol. 180, pp. 490-495.

Walshe, M., Taylor, M., Schulze, K., Bramon, E., Frangou, S., Stahl, D., Kravariti, E., Daly, E., Fearon, P., Murray, R. M., & McDonald, C. 2007, "Familial liability to schizophrenia and premorbid adjustment", *British Journal of Psychiatry*, vol. 191, pp. 260-261.

Watson, D. & Friend, R. 1969, "Measurement of social-evaluative anxiety", *Journal of Consulting & Clinical Psychology*, vol. 33, no. 4, pp. 448-457.

Weinberger, D. R. & Berman, K. F. 1996, "Prefrontal function in schizophrenia: confounds and controversies.", *Philosophical Transactions of the Royal Society of London - Series B: Biological Sciences*, vol. 351, no. 1346, pp. 1495-1503.

Wiersma, D., Nienhuis, F. J., Slooff, C. J., & Giel, R. 1998, "Natural course of schizophrenic disorders: a 15-year followup of a Dutch incidence cohort", *Schizophrenia Bulletin*, vol. 24, no. 1, pp. 75-85.

Wing, J. K., Cooper, J. E., & Sartorius, N. 1974, *Measurement and classification of psychiatric symptoms; An instruction manual for the PSE and Catego program* Cambridge University Press, Oxford.

Winton, E. C., Clark, D. M., & Edelmann, R. J. 1995, "Social anxiety, fear of negative evaluation and the detection of negative emotion in others", *Behaviour Research & Therapy*, vol. 33, no. 2, pp. 193-196.

Woods, S. P., Delis, D. C., Scott, J. C., Kramer, J. H., & Holdnack, J. A. 2006, "The California Verbal Learning Test--second edition: test-retest reliability, practice effects, and reliable change indices for the standard and alternate forms", *Archives of Clinical Neuropsychology*, vol. 21, no. 5, pp. 413-420.

World Health Organization 1948, *The Classification of Mental and Behavioural Disorders; Clinical Descriptions and Diagnostic Guidelines 6th edition (ICD-6).* World Health Organization, Geneva.

World Health Organization 1967, *The Classification of Mental and Behavioural Disorders; Clinical Descriptions and Diagnostic Guidelines 8th edition (ICD-8).* World Health Organization, Geneva.

World Health Organization 1977, *The Classification of Mental and Behavioural Disorders; Clinical Descriptions and Diagnostic Guidelines 9th edition (ICD-9).* World Health Organization, Geneva.

World Health Organization 1992, *The Classification of Mental and Behavioural Disorders; Clinical Descriptions and Diagnostic Guidelines 10th edition (ICD-10).* World Health Organization, Geneva.

Wright, J. H., Turkington, D., Kingdon, D. G., & Basco, M. R. 2008, *Cognitive-Behavior Therapy for Severe Mental Illness: An Illustrated Guide.* American Psychiatric Punlishing, Washington, DC.

Yamasaki, S., Tanaka, S., Morimoto, S., Yamasue, H., Iwanami, A., Iwasaki, S., Shibata, K., Asai, H., Tsujii, K., Furukawa, S., Kasai, K., Tanno, Y., & Kato, N. 2004, "Peters et al. Delusions Inventory Japanese version: Its reliability and validity.", *Rinsho-Seishin-Igaku*, vol. 33, no. 7, pp. 911-918.

Yamauchi, T., Sudo, A., & Tanno, Y. 2009, "Reliability and validity of the Japanese version of the Brief Core Schema Scales.", *Japanese Journal of Psychology*, vol. 79, no. 6, pp. 498-505.

Young, J. E. 1998, *The Young Schema Questionnaire - short form (YSQ-S) (on line)*. Cognitive Therapy Centre, New York.

Zammit, S., Allebeck, P., Andreasson, S., Lundberg, I., & Lewis, G. 2002, "Self reported cannabis use as a risk factor for schizophrenia in Swedish conscripts of 1969: historical cohort study.", *BMJ*, vol. 325, no. 7374, p. 1199.

Zammit, S., Moore, T. H. M., Lingford-Hughes, A., Barnes, T. R. E., Jones, P. B., Burke, M., & Lewis, G. 2008, "Effects of cannabis use on outcomes of psychotic disorders: systematic review", *The British Journal of Psychiatry*, vol. 193, no. 5, pp. 357-363.

Zubin, J. & Spring, B. 1977, "Vulnerability--a new view of schizophrenia", *Journal of Abnormal Psychology.86(2):103-26*.

Zuroff, D. C. & Blatt, S. J. 2006, "The therapeutic relationship in the brief treatment of depression: contributions to clinical improvement and enhanced adaptive capacities", *Journal of Consulting & Clinical Psychology*, vol. 74, no. 1, pp. 130-140.