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A SCAN-SADS Comparison Study of Psychotic Subjects and Their First-Degree Relatives

Anne Farmer[1], Paul Cosyns[2], Marion Leboyer[3], Wolfgang Maier[4], Ole Mors[5], Matthew Sargeant[6], Paul Bebbington[7], and Peter McGuffin[1]

[1]Department of Psychological Medicine, University of Wales College of Medicine, Heath Park, Cardiff CF4 4XN, Wales, UK
[2]Universitaire Instelling Antwerpen, Universiteitsplein1, B-2610 Wilrjik-Antwerpen, Belgium
[3]Hospital de la Salpetriere, Bd de L'Hopital, 75013 Paris, France
[4]Department of Psychiatry, University of Mainz, Untere Zahlbacher Strasse 8, W-6500 Mainz, Germany
[5]Institute of Psychiatric Demography, Psychiatric Hospital in Aarhus, Skovagervej 2, 8240 Risskov, Denmark
[6]St. Tydfil's Hospital, Merthyr Tydfil, Wales, UK
[7]MRC Social Psychiatry Unit, Institute of Psychiatry, De Crespigny Park, Denmark Hill, London, UK

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Summary. Two diagnostic interviews, the Schedule for Affective Disorders and Schizophrenia (lifetime version) (SADS-LA) and the Schedule for the Clinical Assessment of Neuropsychiatry (SCAN) were compared for main diagnoses and for their acceptibility to psychotic subjects and their psychiatrically well relatives. Broad agreement for DSM-III, DSM-III-R and draft ICD-10 diagnoses was good, although there were areas of disagreement between the two interviews which are discussed.

Key words: SADS – SCAN – Diagnosis – Comparison – Genetic research

Introduction

The European Science Foundation (ESF) Network on the Molecular Neurobiology of Mental Illness (MNMI) was set up in 1987 to explore the feasibility of a coordinated programme to map the whole human genome for linkage markers for schizophrenia and affective disorder in order to identify the genes conferring susceptibility to these illnesses. During the Network phase, broad agreement was established on diagnostic instruments, molecular genetic approaches and methods of data storage and analysis. Subsequently, an ESF scientific programme on MNMI was established in 1990. This paper describes part of the evaluation of diagnostic instruments in the Network phase.

At a workshop of the Network held in Crete in April 1988, the standardisation of diagnostic procedures was discussed, and the consensus agreement of 38 scientists from 17 countries was that two semi-structured psychiatric interviews should receive preliminary approval and assessment. These were the Schedule for Affective Disorders and Schizophrenia lifetime version (SADS-LA) (Endicott and Spitzer 1978; Mannuza et al. 1986) and the Present-State-Examination-10th-edition (PSE-10) component of the Schedule for the Clinical Assessment in Neuropsychiatry (SCAN) (Wing et al. 1990). As these interviews are quite different in style and content, it was considered essential that comparison and reliability studies should be carried out to examine the diagnoses produced via each interview. The SADS provides a semi-structured clinical interview that was first published in 1978 and subsequently a lifetime version was introduced (SADS-L) (Mannuzza et al. 1986). The questions are designed to elicit the individual operationalised items included in the Research Diagnostic Criteria (Spitzer et al. 1978) for affective disorder and schizophrenia. Additional questions were added by us to the interview to enable the rater also to make DSM-III diagnoses.

The SCAN system of assessment has a rather different historical basis and nosological approach; it includes the PSE-10 and field trials have recently been undertaken in 11 countries with the support of the World Health Organisation. The PSE-10 "core" of SCAN is based on clinical "cross-examination" which aims to discover the presence or absence of a comprehensive list of symptoms and their degree of severity. Although the order and form of questioning is suggested, the interviewer may depart from this in order to follow leads provided by the respondent. While earlier versions of the PSE were limited to a 1-month timeframe, a SCAN interview allows the interviewer to choose which period to focus on. Unlike the SADS-L interview which is hand-scored by the interviewer, SCAN has a computerised scoring programme (CATEGO5) which enables DSM-III-R and International Classification of Diseases 10th Edition (May 1990 draft) diagnoses to be assigned. Thus, the two interviews provide rather different approaches to the clinical examination, although both may be used to apply DSM-III clinical criteria. Previous work

Correspondence to: Anne Farmer

comparing two different diagnostic interviews, the PSE (9th edition) and the Composite International Diagnostic Interview (CIDI) (Robins et al. 1988) has shown that, although individual item-by-item reliability is poor, reliability for overall diagnosis achieves satisfactory and statistically significant agreement (Farmer et al. 1987). In addition, satisfactory reliability for lifetime-ever disorder has also been demonstrated (Keller et al. 1981).

The following study was therfore carried out to examine how comparable SADS and SCAN are in producing a diagnostic classification for use in family-linkage studies. The subjects included those who had affective psychosis or schizophrenia and their first-degree relatives, the majority of whom were symptom free. Thus, the general acceptibility of both interviews to the psychiatrically ill group and their well relatives was also evaluated.

Subjects and Methods

Five of the centres participating in the ESF Programme took part in the interview comparison studies. These were Aarhus (Denmark), Antwerp (Belgium), Cardiff (Wales), Mainz (Germany) and Paris (France). Participants at the Crete workshop were trained in the use of SADS during a 2-day training session in English by ML, PC and WM. Training tapes were made available to individual centres to train other raters locally.

A 4-day training course was given by PB in the SCAN in English in Paris during October 1988. Translations and back-translations of both interviews were undertaken where necessary, and subjects and their relatives were interviewed in their own language.

Each site was asked to interview at least ten subjects, selecting psychotic probands and their first degree relatives from genetically informative families. It was hoped that each centre would include approximately 20% subjects who were psychiatrically well relatives, so that the general acceptability of the interview to those without psychiatric illness could be assessed. This proportion of well relatives (20%) was estimated to compare approximately with those without psychopathology who would be interviewed in the main study. Order of interviewing (whether SCAN or SADS was carried out first) was decided, so that each interview was presented first 50% of the time; but this depended also on the availability of the interviewers at each site.

Two different raters in each site, who were trained in the use of SCAN and SADS, carried out the interviews within the same week, blind to the status of the subject (whether proband or relative) and to each other's findings. A "lifetime-ever" timeframe for rating psychopathology was taken and interviewers were asked to use the interview to make DSM-III diagnoses. In addition, SCAN interviews were sent to London for scoring on CATEGO5. The computerised scoring programme produces DSM-III-R and draft ICD-10 categories.

Results

Sixty-two psychotic patients and their first-degree relatives were interviewed using SADS and SCAN in the five sites as follows; Aarhus: 11 patients, 1 relative; Antwerp: 9 patients, 7 relatives; Cardiff: 10 patients, 2 relatives; Mainz: 10 patients, 2 relatives; Paris: 10 patients. The combined data consisted of 25 male and 37 female subjects (mean age 42.9 years, SD 14 years, range 18–74 years). There was no significant difference between the

Table 1. SCAN-SADS-LA comparison study. Cross-tabulation of combined sites data. Main clinical diagnoses derived from each interview. SADS–DSM-III clinical diagnoses

	ODx	Anxiety disorders 300	Affective disorders 296	Schizophrenic disorders 295	
ODx	7_2 2_3 2_5		1_5		
	11	0	1	0	12
SCAN					
300		2_1 2_2 3_4	1_4		
	0	7	1	0	8
Clinical DSM-III					
296	1_3		5_1 6_2 9_3 6_4	2_1	
	1	0	6_5 32	2	35
295/298			2_5	3_1 1_2 1_5	
	0	0	2	5	7
	12	7	36	7	62

Chi-square 128.870, $df = 9$, significance < 0.001, contingency coefficient 0.822, Pearson's 0.897

Sites (n of subjects): 1 = Aarhus (12), 2 = Antwerp (16), 3 = Cardiff (12), 4 = Paris (10), 5 = Mainz (12)

Kappa = 0.814, observed agreement: 90%, expected agreement: 39%

Table 2. SCAN-SADS-LA comparison study. Cross-tabulation of combined sites data. SADS clinical DSM-III diagnoses and CATEGOS5-derived ICD-10 main diagnoses (lifetime-ever)

	ODx	Anxiety disorders 300	Affective disorders 296	Schizophrenic disorders 295	
ODx	7_2 2_3 2_5		1_4 2_5		
	11	0	3	0	14
SCAN					
F4/F1		1_1 2_2	1_5		
	0	3	1	0	4
CATEGOS5-derived ICD-10					
F3		1_1 3_4	3_1 6_2 8_3 5_4	2_1	
	0	4	4_5 26	2	32
F2	1_3		2_1 1_3 1_4	3_1 1_2 1_5	
	1	0	2_5 6	5	12
	12	7	36	7	62

Chi-square 70.088, *df* = 9, significance < 0.001, contingency coefficient 0.728, Pearson's 0.778
Sites (*n* of subjects): 1 = Aarhus (12), 2 = Antwerp (16), 3 = Cardiff (12), 4 = Paris (10), 5 = Mainz (12)
Kappa = 0.563, observed agreement: 73%, expected agreement: 37%

Table 3. SCAN-SADS-LA comparison study. Cross-tabulation of combined sites data. SADS clinical DSM-III diagnoses and CATEGOS5-derived DSM-III main diagnoses (lifetime-ever).
SADS–DSM-III clinical diagnosis

	ODx	Anxiety disorders 300	Affective disorders 296	Schizophrenic disorders 295	
ODx	7_2 2_3 2_5		2_4 2_5	1_1	
	11	0	4	1	16
SCAN					
300		2_2 2_4	1_2 2_3 1_4		
	0	4	1_5 5	0	9
CATEGO-derived DSM-III-R					
296	1_3	2_1 1_4	5_1 5_2 6_3 4_4	2_1	
	1	3	5_5 25	2	31
295/298			1_3 1_5	2_1 1_2 1_5	
	0	0	2	4	6
	12	7	36	7	62

Chi-square 63.249, *df* = 9, significance < 0.001, contingency coefficient 0.711, Pearson's 0.739
Sites (*n* of subjects): 1 = Aarhus (12), 2 = Antwerp (16), 3 = Cardiff (12), 4 = Paris (10), 5 = Mainz (12)
Kappa = 0.541, observed agreement: 71%, expected agreement: 37%

ages of male and female subjects (all sites) and no significant age difference across sites. In total 50 subjects were patients (mean age 43.76, range 18–74 years) and 12 subjects (19%) were psychiatrically well first degree relatives (mean age 39 years, range 27–59 years). Both interviews were acceptable to patients and relatives in all sites since all agreed to participated in the interviewing until completion. The sole exception was one patient in Cardiff whose SADS interview had to be abandoned because of its length.

Table 1 shows a cross-tabulation of the main clinical DSM-III diagnoses derived from the two interviews. Comparisons are made for broad diagnostic groups namely 295 and 297 (Schizophrenic and other non-affective psychoses), 296 (affective disorders), 300 (anxiety states and substance misuse) and "no diagnosis". The strength of association as reflected in the contingency coefficient was satisfactory (0.822) and this was highly significant ($P < 0.001$). Chi-square tests were significant (chi-square 128.870, $df = 9$, $P < 0.001$), and kappa was 0.814 (observed agreement 89%, expected agreement 39%, $P < 0.001$).

Table 2 compares the SADS DSM-III clinical diagnosis with the draft ICD-10 categories derived from CATEGO5. Once again broad diagnostic groups are shown. ICD-10 F2 is considered equivalent to 295–297, F3 is equivalent to 296, F4 is equivalent to 300 in DSM-III. The exception is that F1 (alcohol misuse) is equivalent to 303 in DSM-III. Again the strength of association as measured by the contingency coefficient was good (0.728) and the level of agreement was highly significant ($P < 0.001$). Chi-square tests were also significant (chi-square = 70.088, $df = 9$, $P < 0.001$), and kappa was 0.563 (observed agreement 73%, expected agreement 37%, $P < 0.001$).

Table 3 compares the SADS DSM-III clinical diagnoses with the DSM-III-R diagnoses derived from CATEGO5. As in Table 1, broad diagnostic groupings are compared. The strength of association as measured by the contingency coefficient was good (0.711) and the level of agreement highly significant ($P < 0.001$). Chi-square tests were significant (chi-square = 63.249, $df = 9$, $P < 0.001$), and kappa was 0.541 (observed agreement 71%, expected agreement 37%, $P < 0.001$).

Discussion

The results show that both interviews are acceptable to the types of subjects who will be studied in the main genetic linkage and association studies, namely severely mentally ill patients with schizophrenia or major affective disorder and their first-degree relatives, some of whom will have no psychiatric illness. As only a small number of patients and relatives were interviewed at each site, the data were pooled for the main statistical comparisons, although the cross tabulations in Tables 1–3 do indicate how the individual sites rated their subjects. For the same reason, the data for relatives were pooled, especially as some sites had chosen a higher proportion of relatives to probands than others. Nineteen percent of the total sample were psychiatrically well relatives, which was in keeping with the original design.

The tables show that mainly patients with affective disorder diagnoses were interviewed; smaller percentages having anxiety disorders or schizophrenic psychoses. The agreement between interviews for main lifetime-ever diagnosis is good but not perfect. As we have described in the introduction, lack of complete concordance is not surprising. Although both interviews are designed to elicit broadly the same phenomena, the wording of individual questions and interview style is different. As might be expected, agreement is best when both interviews are used to derive the same operational criteria clinically, namely DSM-III rather than its approximate equivalent in the two main classification schemes, DSM-III-R and ICD-10. In terms of level of significance, next best agreement is between CATEGO derived ICD-10 and DSM-III. This is perhaps surprising, since the operational definitions in ICD-10 are closer to DSM-III-R than DSM-III. However, too many conclusions should not be drawn from this, as the samples is small and from multiple sites.

As Tables 1–3 show, similar differences are found in the present study. These may be due to the use of different interviews (SADS and SCAN), different operational definition (DSM-III, DSM-III-R or ICD-10), or different rating methods, i.e. comparing rater clinical judgement (DSM-III ratings from SADS and SCAN) and a computerised scoring method (DSM-III-R and ICD-10 from CATEGO5). Owing to the limitations mentioned above regarding the sample size and multiple sites, more detailed interpretation of our data would be inappropriate.

Although the overall level of agreement is high, there must be concern about the areas of disagreement between the interviews. In this study, all the tables show that the main differences are for affective disorder and non-affective psychosis [including schizophrenic and atypical psychosis (295/297)] and anxiety disorder or affective disorder (300/296) assignments. The differences are found for all three operational criteria. In genetic linkage and association studies it is desirable to identify a clear demarcation between those affected and those unaffected by the disorder under investigation within informative families. Depending how broadly the researcher defines affected status, family members with major depression (296) may sometimes be included within the range of schizophrenic disorders (295 or 297), and at other times would be excluded. The same is true for 300/296 diagnostic differences. This is a critical point because most genetic researchers might allow that severe depression in the relatives of a psychotic proband should be included in the affected category. However, few would include relatives in a 300 category as affected. Accurately deciding just which is correct may be vital. In genetic linkage studies in particular, misclassification errors in diagnostic assignment usually lead to failure in detecting linkage when it actually exists (false-negative) rather than demonstrating linkage where none is present (false-positive).

In a major international research collaboration such as the ESF Network on Molecular Neurobiology of

Mental Illness, consensus regarding the use of a single interview is clearly desirable but often extremely difficult to obtain. In the present collaboration, two diagostic interviews (SADS and SCAN) were finally agreed after lengthy consideration. Individual research teams have their own preferences and expertise with different interviews. In addition, as each participating centre is required to obtain local (national) funding for the main research activity, it may not be desirable for the Network to be too narrowly prescriptive regarding methodology. Clearly, broad principles can be outlined as desirable, but if rules for participating are too strict, some centres may have to cease collaborating if they become over constrained. In this case, inclusion of both SADS and SCAN enabled all centes to remain within the programme and provided a reasonable alternative to having only one interview. The diagnostic differences produced by SADS and SCAN when used to rate lifetime illness in the same subjects are small and in our view should be acceptable to the teams involved in the main research. However, the fact that some diagnostic differences will occur must be considered and allowed for in the subsequent data analysis. In view of this, all centres will have the additional safeguard of a simple computer-scored operational criteria (OPCRIT) checklist which will be used to facilitate a polydiagnostic approach (McGuffin et al. 1991).

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