



THE EFFECT OF INCREASINGLY STRINGENT DIAGNOSTIC CRITERIA ON SEX DIFFERENCES IN SCHIZOPHRENIA

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Sex differences in premorbid function and symptomatology were examined as increasingly stringent criteria for schizophrenia were applied to 182 male and 139 female psychotic patients. The male/female ratio rose from 1.6 among those meeting the CATEGO 'broad' criteria for schizophrenia to 3.7 among those satisfying *DSM-III* criteria. Of 76 women meeting the former criteria, 53 were excluded by the latter, the majority rediagnosed as affective or schizo-affective psychosis. Consequently, although women meeting CATEGO 'broad' criteria showed more affective and fewer typical schizophrenic symptoms than their male counterparts, these differences were abolished by *DSM-III* criteria. Among CATEGO 'broad' schizophrenics, men were more likely than women to have received special education, and had shown worse childhood social adjustment and worse adult social achievement than women. These differences disappeared among *DSM-III* schizophrenics, but women continued to have fewer premorbid schizoid and schizotypal traits, a greater likelihood of marriage, and a later age of onset.

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Gender differences have been reported in schizophrenia throughout this century.^{1,2} Bardenstein and McGlashan,³ who examined some 40 variables for gender differences, concluded that male schizophrenic patients experience more negative symptoms, such as affective flattening, poverty of content of thought, and lack of volition, while women are more likely to suffer from affective symptoms. In 1994 Hafner and colleagues⁴ found more depressive symptoms and sexual delusions in

women than men in a sample of first admissions with an international classification of diseases (ICD) diagnosis of schizophrenia. A number of studies report that male schizophrenics are characterised by poorer premorbid function and an earlier age of onset than their female counterparts.^{5,6}

Several studies⁷⁻⁸ have suggested that while the incidence of broadly defined schizophrenia is roughly equal in males and females, the incidence of the disorder when narrowly defined is greater among men than women, i.e. the more rigorous the diagnostic criteria for schizophrenia, the higher the male/female ratio among those meeting the criteria. What is not clear is whether the use of rigorous criteria abolishes the sex differences in symptom profile and premorbid function.

We therefore set out to establish whether premorbid and symptomatic differences between male and female schizophrenics remain stable when increasingly stringent criteria are used to define the disorder.

METHODS

Patients

The patient sample has been described in detail in several previous papers.⁹⁻¹¹ Briefly, the probands were patients aged 16 - 70 years who were admitted to three South London hospitals with delusions, hallucinations or thought disorder in the absence of organic pathology.

Assessment procedure

The patients were interviewed using the Present State Examination.¹² The CATEGO programme collapses the 140 PSE symptoms into 38 syndromes. These include: nuclear syndrome (NS), incoherent speech (IS), residual syndrome (RS), auditory hallucinations (AH), affective flattening (AF), slowness of activity and speech (SL), self-neglect (NG), depressive delusions (DD), simple depression (SD), special features of depression (ED), hypomania (HM), overactivity (OV), persecution (PE), reference (RE), grandiosity (GR), sexual and fantastic delusions (SF), visual hallucinations (VH), olfactory hallucinations (OH), nonspecific psychosis (NP), obsessionality (ON), generalised anxiety (GA), situational anxiety (SA), hysteria (HY) and agitation (AG).

Diagnostic categorisations were made according to the CATEGO computer programme,¹² the research diagnostic criteria (RDC) of Spitzer *et al.*¹³ and *DSM-III*.¹⁴ Details of the diagnostic procedures are given by Jones *et al.*⁹ Definitions of schizophrenia were ranked in the following order of increasing stringency: (i) CATEGO classes N, P & O; (ii) RDC schizophrenia; and (iii) *DSM-III* schizophrenia.

These criteria could be applied to the sample either independently or sequentially. This rank order was chosen *a priori* according to published evidence. Classes N, P and O of CATEGO provide a 'broad' definition of schizophrenia.^{15,16}

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Castle *et al.*⁵ found the incidence of *DSM-III* schizophrenia to be almost half that diagnosed according to the RDC, and the studies of sex ratios and diagnostic stringency that we aimed to replicate⁶⁻⁸ all used a similar rank order of criteria.

Age at first psychiatric contact was taken as an indication of the onset of psychosis. Socio-demographic data, including marital status, occupation and schooling, were also collected. An estimate of premorbid verbal IQ was obtained using the National Adult Reading Test¹⁷ or the vocabulary subscale of the Wechsler Adult Intelligence Scale (WAIS).¹⁸

Socio-economic status at birth, defined by paternal social class, and best-ever social status achieved by the patient, were assessed according to the Goldthorpe and Hope¹⁹ classification.

Maternal interview

In a subsample of 197 patients whose mothers were available, premorbid functioning was assessed using the maternal interview for premorbid schizoid and schizotypal traits (PSST) and the interview for premorbid social adjustment (PSA). The PSA is rated for two age periods, namely 5 - 11 years (PSA1) and 12 - 16 years (PSA2). We described the interviews in detail in earlier papers; in our hands the inter-rater reliability was good.^{20,21}

Statistical analyses

We used chi-square tests for the categorical variables and *t*-tests for continuous variables. Where appropriate, non-parametric tests such as the Mann-Whitney *U*-test were used after testing for distribution.

RESULTS

Sample description

There were 182 male and 139 female patients in the sample. The mean age (SD) at interview was 29 (9.4) years for men and 36.5 (13.4) years for women, with a 95% CI (4.7, 10.1). Women had a significantly higher age at first psychiatric contact than men, and were more likely to have been married (Table I).

Table I. Patient characteristics in the total sample

	Men (N = 182)	Women (N = 139)	Significance (P-value)*
Mean age (yrs) (SD)	29 (9.4)	36.5 (13.8)	0.001
Mean age at first contact (yrs)	23 (7.6)	27.4 (11.2)	0.001
Number of patients who never married	143	67	0.001
Number of patients with special education	29	7	0.003
Mean IQ score (SD)	103.5 (13.6)	101.3 (14.2)	NS

* 2-tailed *t*-test.

Women had also achieved a higher social status than men (Mann-Whitney *U*-test *Z* score = -2.3, *P* = 0.02).

There were no significant differences between the sexes in terms of either paternal social class at time of patient's birth, or ethnicity. There was no significant overall difference in intelligence between men and women. However, 29 men but only 7 women had needed special education, and those patients who needed special education had a significantly lower IQ (*t* = 2.96, *P* = 0.003). Premorbid functioning (PSA1 and PSA2) and premorbid schizoid and schizotypal characteristics (PSST) did not differ between men and women when all diagnostic categories were analysed together.

Diagnosis and gender

The different diagnostic systems classified varying numbers of the total 321 subjects as schizophrenic (Table II): 198 patients met the CATEGO 'broad' criteria (N, P and O), and 165 met RDC criteria. The *DSM-III* criteria were the narrowest, classifying only 135 subjects as schizophrenic. Among the 76 women who met the broad CATEGO criteria for schizophrenia, only 29 received a *DSM-III* diagnosis of schizophrenia, while 21 were reclassified as having an affective disorder and 8 as having schizo-affective disorder.

Table II. Sex ratio in cases meeting increasingly stringent diagnostic criteria for schizophrenia

	Men	Women	M/F ratio
Total sample (N = 321)	182	139	1.3
CATEGO N, P, O (N = 198)	122	76	1.6
CATEGO N (N = 169)	106	63	1.7
RDC schizophrenia (N = 165)	116	49	2.3
<i>DSM-III</i> schizophrenia (N = 135)	106	29	3.7

As predicted, the narrower the criteria for schizophrenia, the higher was the male/female ratio (Table II); this rose from 1.3:1 in the total sample and 1.6:1 for those meeting broad CATEGO criteria, to 3.7:1 among those considered schizophrenic according to *DSM-III*.

Premorbid characteristics

We then examined what happened to the differences between men and women when increasingly stringent diagnostic criteria for schizophrenia were used (Table III). No matter which diagnostic criteria we used, there were no significant differences between men and women in terms of paternal social class, ethnicity or IQ. On the other hand, women remained significantly more likely to have married, even among those who met the most stringent criteria. Similarly, no matter the criteria used, women had a greater age at first



Table III. Comparison of men and women with a schizophrenic illness defined by increasingly stringent criteria

Diagnostic criteria	CATEGO N, P, O	RDC	DSM-III
	N = 198	N = 165	N = 135
Mean age*	t = 5.18 P = 0.001	t = 5.74 P = 0.001	t = 2.65 P = 0.01†
Mean age at first contact*	t = 4.27 P = 0.001	t = 5.67 P = 0.001	t = 2.39 P = 0.02†
Number of patients that never married	$\chi^2 = 20.37$ P = 0.001	$\chi^2 = 23.22$ P = 0.001	$\chi^2 = 14.07$ P = 0.001
Number of patients with special education	$\chi^2 = 8.31$ P = 0.003	$\chi^2 = 3.24$ P = 0.07	$\chi^2 = 1.56$ P = 0.21
PSST*	t = 3.41 P = 0.001	t = 2.89† P = 0.006	t = 2.18 P = 0.033
PSA1*	t = 2.84 P = 0.006†	t = 1.80† P = 0.082	t = 1.35 P = 0.191†
PSA2*	t = 1.41 P = 0.164†	t = 0.28† P = 0.78	t = 0.87 P = 0.394†
Best-ever social achievement	M-W U-test Z = -1.9 P = 0.05	M-W U-test Z = -3.5 P = 0.001	M-W U-test Z = 0.5 P = 0.58

* All P-values 2-tailed.

† t-test for unequal variance according to Levene's test for equality of variance.

psychiatric contact and a greater current age. Although the best ever achieved social status was higher for women than men in those meeting CATEGO broad and RDC diagnostic criteria, no such difference was found between men and women who met *DSM-III* criteria.

The difference in terms of special education disappeared among those meeting RDC and *DSM-III* criteria. Premorbid personality, as measured by PSST, was more deviant in men irrespective of diagnostic criteria. However, the gender difference in premorbid social adjustment that was found among those meeting broader criteria disappeared when more restrictive criteria were applied.

Syndromes and gender

We then examined sex differences in individual PSE/CATEGO syndromes. Among those fulfilling broad CATEGO criteria for schizophrenia, women ($N = 76$) were significantly more likely to suffer from depressive delusions, general anxiety and hypomanic syndrome, whereas men ($N = 122$) were significantly more likely to suffer from incoherence of speech and nuclear syndrome. Among those fulfilling RDC criteria for schizophrenia, women ($N = 49$) remained significantly more likely to suffer from depressive delusions ($\chi^2 = 4.5$, $P < 0.03$), delusions of reference ($\chi^2 = 6.7$, $P < 0.009$), sexual and fantastic delusions ($\chi^2 = 10.8$, $P < 0.001$) and olfactory hallucinations ($\chi^2 = 10$, $P < 0.001$); again they were less likely than men to show incoherence of speech ($\chi^2 = 8.6$, $P < 0.003$). Among those who

met *DSM-III* criteria for schizophrenia, no syndromal differences were found between men and women.

DISCUSSION

We have confirmed previous reports that men with psychosis are more likely than women with psychosis to be diagnosed as schizophrenic when restrictive criteria are employed that exclude patients with affective features (*DSM-III* and RDC) and emphasise chronicity (*DSM-III*). The ratio of men to women with schizophrenia increased from 1.6 with CATEGO broad criteria to 3.7 with *DSM-III* criteria. Although our results concern patients on both their first admission and readmissions, they are similar to those from epidemiological studies of first-episode patients, for example from our local district of Camberwell.⁶

The sex differences in syndrome profile that we found when employing broader criteria (i.e. essentially more affective symptoms among women and more typical and negative symptoms among men) are similar to those described by Hafner *et al.*⁴

The phenomenological differences noted above disappeared when *DSM-III* criteria were used because the narrower criteria excluded those patients, largely women, who had affective symptoms and who were less chronic. The majority of excluded women received a diagnosis of affective or schizo-affective disorder.

When broad CATEGO criteria were used, women were less likely to have needed special education, had shown better premorbid social adjustment, and had achieved higher social status than men. These three differences were abolished by the application of *DSM-III* criteria, but some premorbid differences remained. Women meeting the narrow criteria still had a later age of onset, were more likely to have married, and had exhibited fewer schizoid and schizotypal traits as children.

Rössler *et al.*²² have shown changes in symptom profile in schizophrenic female patients during the menstrual cycle and have claimed that oestrogen protects against schizophrenic symptoms. Their group has hypothesised that oestrogens also account for the age of onset distribution in women, with women being over-represented in the late-onset group, i.e. after menopause.^{4,23} We could not test this hypothesis because our sample was biased towards a younger age group. However even using the most stringent criteria, age of onset was higher in women.

There is increasing evidence from human and animal studies that sexual hormones not only influence receptor function during adult life but also play an important role during brain development *in utero*. Testosterone has been implicated in influencing brain development during gestation and in the first 5 years of life.²⁴ Its secretion begins in the human male fetus as



early as week 12 through week 18, and appears to affect neuronal circuitry by controlling the rate of growth of certain steroid-sensitive cells.²⁵ The resultant differential brain development in men and women has been proposed as one explanation for the higher frequency of developmental disorder in the former, in particular reading difficulties.²⁶ It has been suggested²⁷ that the slower growth of the left hemisphere in males may be one reason why men subject to early environmental hazards are more prone to long-term neurological dysfunction,²⁸ as well as to a range of neurodevelopmental disorders.²⁹

We cannot exclude the possibility that the differences we found between men and women who met *DSM-III* criteria for schizophrenia are simply common differences between men and women. For instance, women tend to marry earlier than men. Similarly, our finding that men are more likely to show evidence of premorbid schizotypal traits is not specific to schizophrenic patients. Raine³⁰ has described a similar phenomenon in a non-clinical sample; men were more likely to have negative schizotypal traits comparable to the traits that we assessed with the PSST.¹⁹

It is clear that studies examining sex differences in schizophrenia are hopelessly confounded by the stringency of the diagnostic criteria employed. We believe that although they are unfashionable, broader criteria for schizophrenia, such as CATEGO classes N, P and O, remain useful. Until the concept of schizophrenia has been better validated³¹ we cannot tell whether broader or narrower criteria better reflect biological reality.

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