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Gender differences in schizophrenia in three cultures

Results of the WHO collaborative study on psychiatric disability

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Summary. As part of a systematic research project on the influence of gender factors on age at onset, symptomatology, and course of schizophrenia, data on gender differences in age at onset and symptomatology of schizophrenia from the WHO Collaborative Study "On Assessment and Reduction of Psychiatric Disability" were compared between seven research centres of three different cultural regions. Results on age at onset of five European centres confirmed the well known fact of an earlier onset in men. The earlier onset in women seen in Khartoum and Ankara could be attributed to patient selection because male/female differences in age at onset and male/female ratios in the various samples covary. In the Islamic centres no relevant gender differences in real age at onset and in symptomatology could be detected as probable causes of earlier hospitalisation of women. Major gender differences in symptomatology were found in the Balkan centres of Sofia and Zagreb with a high prevalence of delusional symptoms in women and depression in men. In Western Europe centres, nuclear schizophrenic symptoms were equally prevalent in either sex, while nonspecific symptoms like irritability and tiredness (more frequent in women) and maladaptive illness behaviours like alcohol abuse and social withdrawal (more frequent in men) differed between the sexes. Explanatory hypotheses and the implications of these results are discussed.

Gender differences in age at onset, symptomatology, and course of schizophrenia are being systematically studied in an extensive research project at the Central Institute of Mental Health (Häfner et al. 1989; Häfner et al. 1991 a). The analysis of gender differences, the development of explanatory hypotheses and their testing is carried out on all levels relevant to this issue: Biological factors like family history, obstetric complications, or the female menstrual cycle in humans and the effect of estrogens on dopamine induced behaviours in animal models (Häfner et al. 1991 c) are studied, as well as social factors (e.g., life events).

A prospective longitudinal study includes variables related to the early course of the disease, illness and coping behaviours by analysing a large sample of first admitted schizophrenic patients. A significant difference in age at onset between the sexes was found for both broad and narrow definitions of schizophrenic disorders. The distribution of age at onset indicated an earlier onset in men with a peak in the mid-twenties and progressive decline in older age. The age distribution in women, in contrast, showed a later peak, and a substantial additional peak after 45 (Häfner et al. 1991 b).

The transnational stability of gender differences in schizophrenia was tested by comparing the comprehensive and representative case register data from Denmark and Mannheim based on first admissions, where by the same results on age at onset were found (Riecher et al. 1991). In order to extend this transnational comparison, we studied data from 6 more countries collected in the "WHO Collaborative Study on Assessment and Reduction of Psychiatric Disability" (Jablensky et al. 1980).

Up to the present, nearly all studies that included gender comparisons in onset and symptomatology of schizophrenia have been carried out in the industrialised countries (Angermeyer and Kühn 1988). Among the few studies from developing countries are reports from South East Asia (Tsoi and Cheng 1979; Buhrich and Haq 1980) and Ghana (Sikanartey and Eaton 1984) indicating a similar delay in first hospitalisation in women as in the Western world. Weiner and Marvit (1977), however, reported a reversed gender pattern in Philippinos included in their multiethnic sample of Hawaiian schizophrenic patients. In an Indian sample of 245 men and 141 women no gender difference in age at first admission was found (Verghese et al. 1985). The underrepresentation of women in this sample – compared with the equal life time morbid risk for schizophrenia demonstrated in controlled studies (Häfner et al. 1991 a) – shows the influence of selection factors in this study. A selection-free, full assessment of all schizophrenic patients in a defined catchment area therefore becomes an important prerequisite for unbiased results.

Table 1. Sex distribution and drop-out rates in the subsamples[a]

Centre	Total	Male	Female	M/F-Ratio	Drop-out rates (%)
Groningen	82	43	39	1.1	14.5
Mannheim	70	41	29	1.4	3.0
Zurich	70	32	38	0.8	[b]
Zagreb	32	7	25	0.3	55.9
Sofia	115	55	60	0.9	46.6
Ankara	70	44	26	1.7	22.9
Khartoum	71	55	16	3.4	45.1
Total	510	277	233	1.2	28.6

[a] Ten patients of the original sample could not be classified according to age screening criteria.
[b] Zurich did not participate in the follow-up.

Preliminary analyses of data from the WHO Collaborative Study on "Determinants of Outcome of Severe Mental Disorders" (Sartorius et al. 1986) showed peaks in the distribution of the age at first admission for schizophrenia before age 24 in six centres for males and in two centres for females (Jablensky 1987). A detailed cross-sectional analysis of these data is here carried out by our group.

Although not specifically designed to study gender differences, transnational and transcultural WHO studies may add to our knowledge about gender differences discovered in a single country. They may be interpreted as exploratory studies, and hence help to discern relevant information, factors resulting in contrary effects, artefacts, or real differences in age distribution of onset of schizophrenia between the sexes. The cross-cultural comparison may help to generate hypotheses on the relative influence of biological and socio-cultural factors on schizophrenia. Because of the lack of transnational studies carried out with the same instruments and design in different countries, data of multi-centre WHO studies have to be considered valuable sources of information on this important issue.

Method

The "WHO Collaborative Study on the Assessment and Reduction of Psychiatric Disability" was carried out from 1976 to 1980 with participation of seven centres: Groningen, Mannheim, Zurich, Sofia, Zagreb, Khartoum, Ankara. The intention was to assess series of 70 patients, each selected in the seven catchment areas on the basis of specific screening criteria, using the "Present State Examination", PSE 9 (Wing et al. 1974) and two instruments especially designed for this study, the "Psychological Impairments Rating Scale" PIRS (Biehl et al. 1989a, b), and the "Disability Assessment Schedule", DAS (WHO 1988), to evaluate the patients' observed behaviour during interview, especially interaction skills, and their social functioning in various fields of social life.

Screening criteria for the study were: age 15–44; residence in a defined catchment area; absence of organic brain disease, severe mental retardation, severe sensory deficits, alcohol or drug dependence; onset of symptomatology dating not more than 24 months prior to the screening; and a clinical diagnosis of schizophrenia, paranoid or unspecified psychosis (ICD-9 295, 297, 298.3, 298.4, 298.8, 298.9).

The number of the male and female patients participating in the seven centres and the drop-out rates at follow-ups are reported in Table 1.

In order to minimize centre-specific biases, (e.g., imbalances in male/female ratio) data on symptomatology were pooled, making up three cultural regions: Western Europe (Groningen, Mannheim, Zurich), Balkan (Sofia, Zagreb), Islamic region (Ankara, Khartoum). This strategy also led to a reduction of the complexity of the data set and fostered more substantive testing of explanatory hypotheses.

The WHO study also provided data on the course of the disease during the two years following first admission. Due to the wide range of drop-out rates in these one- and two-year-follow-ups between the centres, centre- or even region-specific gender analyses were not appropriate. In order to explore gender differences in the course of schizophrenia in a multinational sample ($n = 313$), the whole follow-up data set was pooled. The comparison of patients remaining in the follow-up with drop-outs found no differences in clinical diagnostic and sex distribution. Drop-outs, however, were significantly ($P < 0.05$) older than patients assessed in the follow-ups (27,10 vs. 25,14 yrs). χ^2-statistics were applied to test the gender differences in symptomatology and course.

Results

Gender differences in age at onset in seven centres: Screening criteria of the WHO study excluded all patients with an onset of symptomatology dating back more than 24 months from the admission to the centre. The first occurrence of psychotic symptoms, however, was not definitely assessed or reliably reported. Age at onset of schizophrenia, therefore, had to be defined as age at admission to centre (i.e., age at inclusion into the sample).

Mean age of onset varies from 22,9 yrs (Ankara) up to 27,1 yrs (Zagreb) in men and from 19,4 yrs (Khartoum) to 29,4 yrs (Zagreb) in women (Fig. 1).

MANOVA revealed highly significant main effects of sex and centre on age of onset ($F(612,48) = 12.41, P < 0.001$

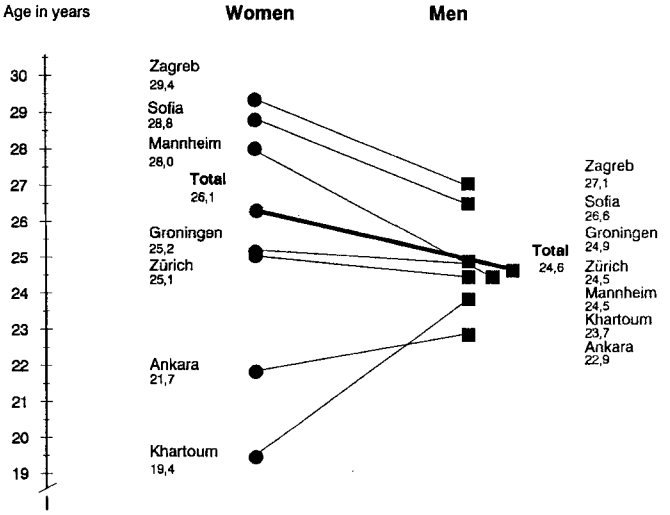

Fig. 1. Mean ages of onset in the centres ($n = 510$)

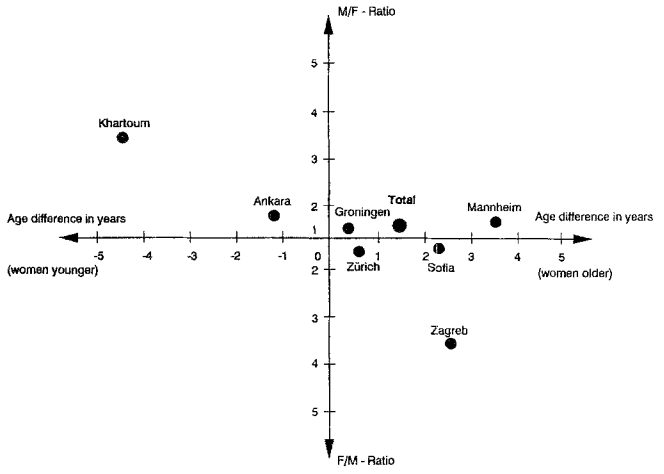

Fig. 2. Interrelation between gender difference in mean age of onset and gender ratio in the subsamples ($n = 510$)

and $F\,(522,02) = 11.51$, $P < 0.001$) and a significant interaction of sex and centre ($F(119,99) = 2.75, P < 0.05$).

Gender differences in age at onset and male/female-ratios in the centres' sample seem to be related (Fig. 2).

Similar results were found whether narrow or broad definitions of schizophrenia (S +, or S, P, O according to PSE-CATEGO) were applied.

Gender differences in symptomatology in three cultures: Gender differences in symptomatology show different patterns in Western Europe, Balkan and Islamic countries. In Western European centres (Table 2) among the nuclear psychotic symptoms only hallucinations differed in frequency between the sexes, but this symptom was only assessed in about half of the sample. Substantial gender differences could be detected in accessory symptoms like worrying, tiredness, or irritability (more frequent in women) and on social behaviours (more often disturbed in men).

The most significant gender differences could be detected in the Balkan centres, where men were more likely to be severely depressed, while the nuclear psychotic syndrome (i.e. the Schneiderian first rank symptoms) was more common in women (Table 3). In Islamic countries, few gender differences were found, although there was a higher incidence of general anxiety, morbid jealousy and self-depreciation in women (Table 4).

Gender differences in the course in the pooled sample: One- and two-year follow-ups indicate gender differences in affective symptoms and social behaviours with a higher incidence of blunted affect, social withdrawal, alcohol abuse, and self-neglect in men and more signs of situational and free-floating anxiety, and depersonalisation or derealisation in women. Women are more often affected by diagnostic shifts to paranoid or neurotic disorders (i.e. ICD-9 297 or ICD-9 300).

Discussion

Gender differences in age at onset of schizophrenia were found in a large representative sample of German patients (Häfner et al. 1991 a) and were corroborated in the comprehensive Danish case register data (Riecher et al. 1991). In order to test the hypothesis that these gender differences not only exist in two culturally quite similar countries, but in other regions of the world as well, a re-analysis of data from multicentre WHO studies was thought to be useful.

Before the hypothesis can be verified or falsified with the WHO data, artefacts (especially selection errors), confounding variables, and alternative explanations have to be excluded. Inclusion criteria can be major causes of selection biases. In the WHO Disability Study, the selection criterion of a maximum age of 44 – in accordance with DSM-III – outrules an important section of late onset schizophrenia with specific relevance to gender differences (Häfner et al. 1991 a). The criterion of a maximum duration of 12 to 24 months of symptomatology prior to inclusion excludes another group of patients with a longer period of incipient schizophrenia. In addition, due to different inclusion criteria for symptomatology and preclinical course in the 7 centres, a rather heterogenous sample was assessed – another possible source of methodological error.

Differences in the utilization of psychiatric services between centres and between the sexes also lead to a bias in sample composition. Considering the equal life-time morbidity risk for schizophrenia in both sexes (Häfner et al. 1989; Häfner et al. 1991 a) male/female ratios in representative samples would be expected to be close to 1.0 (in samples with a maximum age of 44 years slightly higher).

Table 2. Gender differences in symptomatology in Western European centres ($n = 223$)

	% of male cases	% of female cases	No. of cases assessed	P
More frequent in men				
Neologisms	6.9	2.0	220	*
Alcohol abuse	9.6	1.0	220	*
Disturbed hetero-sexual role behaviour	82.5	63.6	124	*
Serious impaired work performance	77.6	48.0	127	**
Social withdrawal	69.2	55.1	205	*
More frequent in women				
Depersonalisation	17.9	29.9	209	*
Pseudo- or true hallucinations	33.8	50.8	138	*
Visual hallucinations	9.8	25.9	129	*
Painful worrying	21.8	31.9	204	*
Tiredness	43.3	55.5	210	*
Obsessional cleanliness and similar rituals	0.9	6.1	210	*
Hypomanic affect	4.3	15.1	222	*
Flight of ideas	1.8	9.4	222	*
Histrionic behaviour	5.0	16.1	222	*
Lability of mood	5.2	16.4	219	*
Irritability (CATEGO)	11.2	20.5	223	**

* $P < 0.05$; ** $P < 0.01$

Table 3. Gender differences in symptomatology in Balkan centres ($n = 156$)

	% of male cases	% of female cases	No. of cases assessed	P
More frequent in men				
Primary anxiety or depression	53.9	18.0	87	**
Morning depression	40.7	19.3	89	*
Early waking	25.8	9.2	96	*
Pathological guilt	20.0	5.9	98	*
Tiredness	40.4	21.8	139	*
Hypochondriasis	21.6	9.2	138	*
Obsessional checking and repeating	11.5	2.4	138	*
More frequent in women				
Primary delusions	18.5	31.0	109	**
Delusional mood	13.5	24.4	138	*
Delusions of control	2.7	21.9	110	*
Delusions of assistance	0.0	22.0	108	*
Delusion of grandiose abilities	14.3	23.6	107	*
Derealisation	20.0	39.0	127	*
Thought broadcast	9.7	21.1	102	*
Incongruency of affect	7.6	18.6	139	*
Nuclear syndrome (CATEGO)	24.2	48.4	155	**
Depersonalisation (CATEGO)	21.0	41.9	155	*
Hysteria (CATEGO)	1.6	16.1	155	**
Irritability (CATEGO)	3.2	19.4	155	**
Residual syndrome (CATEGO)	4.8	16.1	155	*
Doubtful interview (CATEGO)	31.6	49.5	155	*

* $P < 0.05$; ** $P < 0.01$

Table 4. Gender differences in symptomatology in Islamic centres ($n = 141$)

	% of male cases	% of female cases	No. of cases assessed	P
More frequent in women				
Self-depreciation	27.6	44.7	125	*
Morbid jealousy	2.5	13.9	117	*
General anxiety (CATEGO)	39.4	64.3	141	*

* $P < 0.05$

In the WHO Disability Study's subsamples, however, male/female ratios vary from 0.3 to 3.4.

An underutilization of psychiatric services in the developing countries by women has been found in several studies (Katchadonrian and Racy 1969; Schwarz 1976; Sikanartey and Eaton 1984; Verghese et al. 1985; Ihezue et al. 1986). The artefact of female underrepresentation is caused by several factors: First, faced with the scarcity of psychiatric facilities in developing countries, women, due to their social status, have a poorer chance of receiving adequate care, while men's treatment is considered more important because they are the major earners of family income. Secondly, the social position of women is not located in the public but in the family, where they are also kept in times of illness longer than men. Women in developing countries more often see traditional healers, as Sikanartey and Eaton (1984) noticed in Ghana. (In the subsequent WHO study on "Determinants of Outcome" (Sartorius et al. 1986) contacts with traditional healers and similar agencies for case finding were therefore included as well as hospitalizations.) Thirdly, the participation of men in public life and the higher prevalence of acting out and maladaptive social behaviours in men also leads to more hospitalization of men.

Women seem to be much more affected by centre-specific selection criteria. This holds especially true for the Islamic centres where older women have a poor chance of being included in the study, while in the Balkan states, on the other hand, women needed to be older and more severely disturbed in order to be admitted. Due to these selection effects, data on first admissions of female schizophrenic patients are not only more variable but also less representative compared with studies where all schizophrenic patients in a certain catchment area are assessed.

In contrast, mean ages at first admission of men show a considerable convergence in all centres. As they have a high chance of admission, their pooled data can be considered close to representativeness.

In relation to symptomatology, gender differences in Western Europe are minor, considering the great number of symptoms assessed. Among the Schneiderian first rank symptoms, only hallucinations were reported as significantly different, but this symptom could only be assessed in about half of the sample. Significant differences in more frequent symptoms concerned additional characteristics of the disease like disturbed social behaviour (higher prevalence in men) and tiredness, worrying, other affective disturbances, and depersonalisation (more frequent in women). The outstanding gender differences in symptomatology seen in the Balkan centres are probably due to a longer (untreated) preclinical course of the disease in this subsample of oldest mean age, but the high portion of doubtful interviews ($^1/_3$ in Balkan men, $^1/_2$ in Balkan women) allows only tentative conclusions.

Concerning the course of the disease after hospitalization, the pooled data of all centres support the common notion that maladaptive social behaviours (inappropriate illness behaviours, negative symptoms) are more prevalent in men (Pogue-Geile and Harrow 1985; Häfner et al. 1991 a, b). The women's symptomatology in this phase is characterised by non-psychotic anxiety and irritability, derealisation and depersonalisation – features that might often result in diagnostic shifts to neurotic or affective disorders and might explain why spectrum disorders in some studies are more often diagnosed in women (Tsuang et al. 1976).

In summing up, the analyses support the findings of an earlier onset of schizophrenia in men and demonstrate the influence of selection criteria in developing countries, expecially on women's treatment. With the exception of the Balkan sample where patients were older, the gender dif-

ferences in symptomatology are minor. In the course of the disease, illness behaviours, and social and affective features may already differ between men and women in the first two years after first admission.

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