

Gender Differences in Age at Onset of Schizophrenia

An Overview

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Summary. We present the results of a review of the literature concerning gender differences in age at the onset of schizophrenia. In view of the very consistent finding that the first admission to hospital for schizophrenia occurs on average earlier in men than in women we examined the question whether this is due to the fact that the psychosis manifests itself earlier in men or that the period between first manifestation and admission to hospital is shorter than in women. By means of a metaanalytic approach we then looked for evidence for the existence of local or temporal variations in the degree of gender difference. Lastly, we dealt with the question whether gender differences in age of onset can be observed in other functional psychoses.

Key words: Schizophrenia – Gender differences – Age at onset – Age at first hospitalization – Meta-analysis

Introduction

Many years ago in his classical textbook of psychiatry Kraepelin (1909–1915) published data suggesting that men develop schizophrenia at a younger age than women. As early as 1934 Braatoy emphasized that the gender-dependent variation in age of onset was a problem calling for urgent investigation. Despite the important etiological implications this area was long ignored in schizophrenia research (Slater and Cowie 1971; Samuels 1979) and only recently has there been growing interest in it (Lewine 1981; Seeman 1982; Häfner 1987). We thus considered it was time to examine the empirical evidence for this phenomenon in a more systematic way.

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In particular we addressed the following questions:

- How consistent are the findings indicating that first admission to hospital occurs earlier in male schizophrenic patients than in female patients?
- Can the gender difference also be demonstrated using age-specific incidence rates?
- How strong is the evidence that the actual onset of schizophrenic disorder is earlier in men?
- Do temporal or cultural factors affect the amount of gender difference?
- Is the gender difference in age of onset specific for schizophrenia or can it also be observed in other functional psychoses?

The paper is based on a systematic review of the literature. To locate and collect the relevant papers a MEDLARS search of all publications on gender differences in schizophrenia, regardless of language, was carried out. We also screened the major psychiatric journals published in English and German during the last 20 years¹. Finally, we searched through all major monographs on schizophrenia in English or German published during the same period of time.

¹ The following psychiatric journals published in English were searched: American Journal of Psychiatry; Archives of General Psychiatry; Journal of Nervous and Mental Disease; American Journal of Orthopsychiatry; Schizophrenia Bulletin; Canadian Journal of Psychiatry; British Journal of Psychiatry; Acta Psychiatrica Scandinavica; Social Psychiatry. In addition the following psychiatric journals published in German were included into our literature survey: Nervenarzt; Archiv für Psychiatrie und Nervenkrankheiten; Fortschritte der Neurologie und Psychiatrie; Pharmacopsychiatry (formerly Pharmako-Psychiatrie); Psychiatrische Praxis; Psychiatrie Neurologie Medizinische Psychologie; Schweizer Archiv für Neurologie, Neurochirurgie und Psychiatrie; Psychiatria clinica (formerly Monatsschrift für Psychiatrie und Neurologie; Psychiatria et Neurologia); Confinia Psychiatrica; Wiener Zeitschrift für Nervenheilkunde

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Table 1. Overview of studies on gender differences of date of first hospitalization for schizophrenia (studies published until 1983 are included)

| Investigators | Time period | Country | Numbe of patie | | | alization | | |
|------------------------------|--------------------|-------------|-------------------|-----------------|----------------|-----------|---------------------------------|--|
| | | | M | F | Mean or median | | Odds ratio ≤ 25 years/ | |
| | | | IVI | Г | M | F | ≤ 23 years ≤ 30 years | |
| Pollock (1926) | 1912–18 | USA | 4735 | 4333 | 30.6 | 36.4 | 1.89/2.12 | |
| , , | 1922 | | 8950 | 6576 | | | 1.53/1.61 | |
| White (1926) | 1920 | USA | | | | | /2.08 | |
| Dahlberg and Stenberg (1931) | 1903-29 | Sweden | 641 | 821 | | | 2.39/2.25 | |
| Braatoy (1934) | 1926-29 | Norway | 1231 | 1061 | | | 1.37/1.81 | |
| Rosanoff et al. (1934) | 1932-33 | USA | 1482 | 1360 | | | /2.04ª | |
| Malzberg (1935) | 1929-31 | USA | 4163 | 3376 | 31.8 | 36.5 | 2.04/2.16 | |
| Faris and Dunham (1939) | 1922-31 | USA | 3916 | 3337 | | | 1.58/1.58 | |
| Rennie (1939) | 1913-23 | USA | 198 | 258 | | | /1.46 | |
| Malzberg (1949) | 1939-41 | USA | 5699 | 5605 | | | 1.41/1.37 | |
| Malzberg (1955) | 1919-21 | USA | | | 30.1 | 35.7 | | |
| | 1929-31 | | | | 31.6 | 35.9 | | |
| | 1939-41 | | | | 33.6 | 31.3 | | |
| | 1949-51 | | 8300 | 8517 | 31.2 | 33.9 | 1.69/1.71 | |
| Israel and Johnson (1956) | 1913-22 | USA | 330 | 300 | | | /1.97 | |
| , , | 1923-32 | | 276 | 299 | | | /2.10 | |
| | 1933-42 | | 656 | 609 | | | /1.63 | |
| | 1943-52 | | 791 | 993 | | | /1.04 | |
| Lapouse et al. (1956) | 1949-51 | USA | | | 30.7 | 33.5 | | |
| Shepherd (1957) | 1931-33 | UK | 38 | 41 | | | 1.68/ | |
| Z(() | 1945–47 | | 27 | 31 | | | 1.49/ | |
| Hardt (1959) | 1935-44 | USA | | | | | 1.14/ | |
| Lehrman (1960) | 1943–44 | USA | 1189 | 1752 | | | 1.34/1.23 | |
| Walker (1961) | ? | USA | 253 | 34 | 26 | 29 | 2.11/2.22 | |
| Garrone (1962) | 1901–50 | Switzerland | 1397 | 2043 | | | 1.76/1.97 | |
| Auch (1962) | 1924–33 | Germany | 1512 | 1866 | 29.7 | 32.8 | 1.31/1.55 | |
| 71ucii (1902) | 1949–58 | Commany | 652 | 1152 | 28.4 | 35.2 | 2.74/2.87 | |
| Lucas et al. (1962) | 1958 | UK | 196 | 209 | 28.7 | 33.6 | 20, 0,210, | |
| Farina et al. (1963) | 1949-54 | USA | 60 | 52 ^b | 29.6 | 28.7 | | |
| Tarilla et al. (1903) | 1747-54 | 00/1 | 23 | 33° | 29.0 | 29.5 | | |
| Helgason (1964) | _ | Iceland | 11 | 19 | 27.0 | 27.5 | /3.19 | |
| Brown et al. (1966) | 1956 | UK | 55 | 56 | 33 | 40 | 1.33/1.82 | |
| Noreik and Odegard (1967) | 1926-30 | Norway | 33 | 50 | 28.2 | 32.3 | 1.55/1.62 | |
| Note ik and Odegard (1907) | 1931–35 | Noiway | | | 29.1 | 32.6 | | |
| | 1931-33 | | | | 28.5 | 31.7 | | |
| | 1941–45 | | | | 28.5 | 32.1 | | |
| | 1946-50 | | | | 29.3 | 33.6 | | |
| | 1951-55 | | | | 30.6 | 35.3 | | |
| | 1956–60 | | | | 30.9 | 35.7 | | |
| Hurley and Conwell (1967) | 1960 | USA | 81 | 114 | 50.7 | 33.7 | 2.28/ | |
| Hurley and Conwell (1907) | 1954 | USA | 1471 | 1617 | | | 1.68/ | |
| | 1934 | | 1564 | 1969 | | | 1.97/ | |
| | 1960 | | 488 | 666 | | | 1.70/ | |
| | 1900 | | 263 | 306 | | | 1.43/ | |
| | 1954 | | 263 167 | 154 | | | 1.49/ | |
| | 1704 | | 186 | 257 | | | 0.99/ | |
| | 1960 | | 560 | 622 | | | 1.91/ | |
| | 1300 | | 2033 | 2303 | | | 1.85/ | |
| A abas (1067) | 1950/1960 | Finland | 2033 72 | 128 | | | 1.05/ | |
| Achté (1967) | 1220/1300 | 1 Illianu | 32 | 65 | | | 2.88/3.43 | |
| Lewine (1980) | | | 32 22 | 36 | | | 1.89/3.73 | |
| Aghté and Ang (1967) | 1950-52 | Finland | 154 | 121 | 29.7 | 31.7 | 1.07/3.13 | |
| Achté and Apo (1967) | 1950-52 1957-59 | FIIIIailU | 159 | 121 | 32. | 34. | | |

Table 1 (continued)

| Investigators | Time period | Country | Number | | Age of | first hospi | talization |
|-----------------------------|--------------|-------------|------------------|------------------|----------------|-------------|---------------------------|
| | | | of patie | | Mean or median | | Odds ratio |
| | | | M | F | M | F | ≤ 25 years/ ≤ 30 years |
| Pollack et al. (1968) | 1960-61 | USA | 39 | 42 | | | /1.49 |
| Walsh (1969) | 1962 | Ireland | 136 | 150 | | | /3.15 |
| Soskis et al. (1969) | ? | USA | | | ? | ? | |
| Lindelius (1970) | 1900-10 | Sweden | 104 | 103 | 31.9 | 36.3 | 1.28/1.71 |
| Forrest and Hay (1972) | 1966-68 | UK | 160 | 180 | | | /2.15 |
| | | | 41 | 49 | | | /3.96 |
| | | | 52 | 56 | | | /1.95 |
| | | | 67 | 75 | | | /1.99 |
| Lassenius et al. (1973) | 1944–46 | Sweden | 40 | 33 | 29.2 | 33.9 | |
| | 1955-56 | | 46 | 33 | 31.0 | 37.2 | |
| | 1959-60 | | 26 | 22 | 31.1 | 35.0 | |
| | 1944–46 | | 63 | 41 | 28.7 | 28.4 | |
| | 1955–56 | | 54 | 33 | 30.2 | 34.0 | |
| | 1959–60 | | 39 | 23 | 30.8 | 36.4 | |
| Flor-Henry (1974) | 1960 | UK | 3347 | 2667 | | | /1.62 |
| Hartmann and Meyer (1974a) | 1969 | FRG | 1429 | 1775 | 29.2 | 36.2 | /1.62 |
| Hartmann and Müller (1974b) | 1967–70 | FRG | 31 | 68 | ? | ? | |
| McCabe (1975) | 1967/68 | Denmark | 136 | 113 | 36.5 | 47.7 | 2.66/2.85 |
| v. Trostorff (1975) | | GDR | 165 | 148 | 28.2 | 34.8 | |
| | | | 89 | 102 | 27.9 | 36.1 | |
| Ciompi and Müller (1976) | -63 | Switzerland | 92 | 197 ^d | | | 3.15/ |
| Bland et al. (1976) | 1963 | Canada | 51 | 40 | | | /1.30 |
| Bland (1977) | 1972 | Canada | 3196 | 2868 | 29.3 | 34.7 | /2.32 |
| Weiner and Marvit (1977) | 1962-63 | USA | 746 ^e | | 30.9 | 33.7 | |
| | | | 303 ^f | | 34.3 | 37.1 | |
| | | | 205g | | 32.3 | 33.1 | |
| | | | 175 ^h | | 43.2 | 36.2 | |
| | | | 122 ⁱ | | 33.6 | 34.1 | |
| Nyman (1978) | 1964–67 | Sweden | 40 | 21 ^k | 24.0 | 22.0 | |
| | | | 32 | 22^{1} | 23.0 | 21.5 | |
| Bland and Orn (1978) | 1963 | Canada | 22 | 21 | 34.5 | 30.6 | 0.56/1.12 |
| Tsoi and Chen (1979) | 1975 | Singapore | 367 | 265 | | | /1.63 |
| Babigian (1980) | 1970 | USA | 122 | 96 ^m | | | 2.54/ |
| a (1000) | 10=0 =1 | | 14 | 18 ⁿ | | | 1.57/ |
| Gam (1980) | 1970-71 | Denmark | 203 | 116 | 25.8 | 36.4 | /3.67 |
| Schwarz et al. (1980) | 1978 | FRG | 41 | 29 | | | 1.64/ |
| Buhrich and Haq (1980) | 1977–78 | Malaysia | 279 | 145° | | | /1.25 |
| | | | 310 | 227 ⁱ | | | /1.66 |
| F. 1 17 (4004) | 1044 =01 | *** | 129 | 104 ^p | | | /1.17 |
| Zigler and Levine (1981) | 1964–72/ | USA | 30 | 30 | 24.6 | 29.4 | |
| T (1004) | 1966–72 | | 30 | 30 | 32.4 | 37.6 | |
| Lewine et al. (1981) | ? | USA | 25 | 27 ^q | | | 7.90/ |
| | | | 29 | 17 | | | 4.07/ |
| | | | 24 | 15 | | | 7.60/ |
| A | 1072 70 | EDG | 16 | 9 | | | 24.50/ |
| Angermeyer et al. (1982) | 1973–78 | FRG | 40 | 31 | | | /1.43 |
| Salokangas (1983) | 1965–67/1969 | Finland | 82 | 93 ^r | | | 1.91/ |
| Hilger et al. (1983) | 1949-50 | FRG | 62 | 120 | | | /3.27 |
| | 1965–67 | | 82 | 145 | | | /2.57 |

a Cut-off point 35 years
 b Recovered patients, age 17–40 years
 c Nonrecovered patients, age 17–40 years
 d Only patients of Swiss nationality born 1873–1897
 e Japanese
 f Caucasian

g Part Hawaiian
h Filipino
Chinese
Regressive schizophrenia
Nonregressive schizophrenia
White patients

ⁿ Nonwhite patients

[°] Malay

^p Indian

^q Age 15-55 years ^r Age 15-45 years

Gender Differences in Age at First Admission for Schizophrenia

Many studies have been published reporting data on gender differences in age at first admission for schizophrenia. Altogether, we found 53 studies, the first dating from 1926. In Table 1 data from all these studies are listed. Due to the differing information provided by the authors either mean/median age for male and female patients at first admission is given or the odds ratio calculated from the odds in favor of first admission below age 25 (or 30, depending on the age groups used in the reports) for both men and women. Values above 1 indicate that the risk of being hospitalized below age 25 (or 30) is greater for men than for women. Conversely, values below 1 indicate a higher risk of first admission below this cut-off age for women².

The results of our review were highly consistent. Apart from very few exceptions (Malzberg 1955; Farina et al. 1963; Lassenius et al. 1973; Nyman 1978; Bland and Orn 1978) male schizophrenic patients were first admitted on average earlier than female patients. The maximum difference between the sexes was 11.2 years (McCabe 1975); the difference most often reported was 4–5 years.

Gender Differences in Age-Specific Incidence Rates for Schizophrenia

One could argue that different age profiles in the general population might be responsible for the gender differences observed in the studies which we have so far quoted, since they were all based on absolute numbers of cases. In Table 2 we have therefore compiled all the studies which reported age-specific rates for first admission broken down according to gender. The ratio between the rates for males and females was calculated for each age group separately. A value over 1 means that the rate of first admission is higher for men than for women. In 20 out of 28 studies the highest ratio was found in the age groups under 25. In only 3 studies was it above the 30-year limit. This proves that even when taking the reference population into account, men were admitted to hospital for schizophrenia earlier than women.

odds ratio =
$$\frac{a}{b} \frac{d}{c}$$

where a = number of males age \leq 25 years (or \leq 30 years) b = number of males age > 25 years (or > 30 years)

 $c = number of females age \le 25 years (or \le 30 years)$

d = number of females age > 25 years (or > 30 years)

Gender Differences in Age of Onset of Schizophrenia

The fact that first admission occurs earlier in male schizophrenic patients than in female does not necessarily mean that the actual onset of the illness also occurs earlier. It could well be that the first manifestation of the illness occurs at the same age in both sexes but that the time elapsing between onset and first admission is shorter in males than in females. If this is so the following three factors could play a part:

- gender differences in type of onset and symptomatology of schizophrenia;
- differing illness behavior in the two sexes;
- differences in the response of the environment to the psychosis according to sex of the patient.

The gender difference in age at first admission may be due to a more acute onset of the disorder which in women may develop rather insidiously and therefore be recognized relatively late. However, empirical data do not support this explanation as an acute onset has so far been observed more often in female patients than in male patients (Bleuler 1972; Huber et al. 1979).

In the literature there are some suggestions that the illness produces a different symptomatology in men than in women. A number of authors report that a phenomenon which they name role reversal takes place (Al-Issa 1982). In this process men are thought to become more passive, apathetic, and socially withdrawn while women, in contrast, become more impulsive, outgoing, and domineering (Ellison and Hamilton 1949; Cheek 1964; Rogler and Hollingshead 1965; Weich 1968; McClelland and Watt 1968; Bienert 1976; Nyman 1978; Ludewig 1984; Goldstein 1986). It is also considered that women more often develop paranoid symptoms (Berner et al. 1969; Forrest and Hay 1971; Nyman 1978; Floru et al. 1979; Vollmoeller 1983) and men, on the other hand, religious delusions and delusions of grandeur (Pauleikoff 1954; Steinebrunner and Scharfetter 1976; Nyman 1978; Floru et al. 1979; Fujimori 1981). At first sight it seems unlikely that these differences do affect the age at first admission. More relevant could be the fact that male schizophrenics like men in general tend to display more aggressive behavior than female patients, which could result in male patients being noticed and eliciting sanctions from their environment earlier (Shumakov et al. 1975; Shader et al. 1977; Diebold and Engel 1977; Inamdar et al. 1982; Gebhardt and Pietzcker 1985). A similar effect could be that not only criminal behavior but also alcohol and drug abuse occur more frequently in male patients than in female³.

² The odds ratio was obtained using the following formula (Last 1983):

³ Unpublished results from a study of first admitted schizophrenic patients carried out in Hannover (FRG)

Table 2. Overview of studies on gender differences of date of first hospitalization for schizophrenia providing age-specific rates (studies published until 1983 are included)

| Investigators | Population studied | Time period of study | 15- 20- 19 24 | | 0- 35- 4 39 | 40- 44 | | 50– 55– 54 59 | 60– 64 |
|------------------------------|-----------------------|----------------------------|------------------|---------------|-----------------|-----------|--------|------------------|-----------|
| Pollock (1926) | USA | 1912–18 | 1.67 <u>1.88</u> | 1.36 1 | .07 0.75 | 0.54 | 0.43 (| 0.31 0.40 |) |
| Dahlberg and Stenberg (1931) | Sweden | 1903-29 | 1.60 <u>1.65</u> | 0.99 0 | .76 0.67 | 0.47 | 0.50 | 0.44 0.20 | 6 0.67 |
| Braatoy (1934) | Norway | 1926-29 | 1.22 1.61 | <u>1.90</u> | 1.16 | 0.7 | 70 | 0.65 | 0.89 |
| Landis and Page (1938) | USA | 1933 | 1.47 <u>1.86</u> | 1.49 1 | .21 0.90 | 0.80 | 0.83 | 0.62 0.59 | 0.74 |
| Odegaard (1946) | Norway | 1926-35 | 1.00 1.24 | 1.54 <u>1</u> | <u>.56</u> 1.45 | 1.31 | 1.23 | 1.14 1.13 | 1.10 |
| Malzberg (1955) | New York State/ | 1919-31 | 2.43 2.58 | 1.97 1 | .45 0.97 | 0.64 | 0.47 | 0.35 0.28 | 3 0.65 |
| | USA | | <u>2.15</u> 2.13 | 1.73 1 | .34 1.20 | 0.99 | 0.67 | 0.60 0.43 | 5 0.58 |
| | | | 1.20 1.45 | 1.19 1 | .08 0.85 | 1.25 | 0.79 | 0.77 0.69 | 0.53 |
| | | | 1.23 <u>1.68</u> | 1.23 0 | .92 0.82 | 0.87 | 0.75 | 0.76 0.73 | 0.67 |
| Shepherd (1957) | County of | 1931-33 | <u>1.29</u> | | 1.04 | | | 0.57 | |
| | Buckinghamshire | 1945-47 | <u>1.27</u> | | 1.00 | | | | |
| Locke et al. (1958) | Ohio State/USA | 1948-52 | <u>1.13</u> | 0.75 | 0. | .73 | 0.72 | 2 (| 0.30 |
| | | | <u>1.12</u> | 0.75 | 0. | .63 | 0.79 |) (| 0.66 |
| | | | 0.86 | 0.76 | <u>0.</u> | 98 | 0.84 | 1 (| 0.57 |
| | | | <u>1.40</u> | 0.80 | 0. | 93 | 1.03 | 3 | 1.29 |
| Hardt (1959) | Syracuse/USA | 1935-44 | 1.34 | 1.68 | 1. | .14 | 0.6 | 1 (| 0.42 |
| Walsh (1969) | Dublin/Ireland | 1962 | <u>1</u> | <u>.84</u> | 1.06 | 0.7 | 73 | 0.43 | 1.12 |
| Walsh and Walsh (1970) | Ireland | 1964 | 1.18 <u>1.49</u> | 1.30 | 1. | .47 | 0.90 | 5 1.1 | 1 0.67 |
| Slater and Cowie (1971) | England and Wales | 1952-60 | 1.19 <u>1.47</u> | 1.22 | 0. | 94 | 0.58 | 3 (| 0.48 |
| McCabe (1975) | Denmark | 1967-68 | 1.68 | 1.65 2 | .40 1.69 | 0.47 | 1.18 | 0.37 0.30 | 0.47 |
| Bland et al. (1976) | S. Alberta/Canada | 1963 | <u>1.93</u> 1 | .37 | 1.23 | 0.8 | 84 | 0.64 | |
| | England and Wales | 1960 | 1.10 <u>1.62</u> | 1.15 | 0. | .92 | 0.6 | L (| 0.50 |
| Bland (1977) | Canada | 1972 | 1.50 <u>1</u> | <u>.71</u> | 0.87 | 0.6 | 67 | 0.50 | 0.54 |
| Bland and Orn (1978) | S. Alberta/Canada | 1963 | 1.35 | <u>2.33</u> | 1.47 | 1.45 | 0.93 | | |
| Tsoi and Chen (1979) | Singapore | 1975 | <u>1</u> | <u>.70</u> | 0.91 | 1.0 | 05 | 1.16 | 0.75 |
| Babigian (1980) | Monroe County/ | 1970 | 2.34 | 0.95 | 0. | .82 | 1.00 |) (| 0.69 |
| | USA | | <u>1.27</u> | 0.39 | 0. | .71 | 1.0 | L | |
| Dayton (1980) | Massachusetts/USA | 1917-33 | <u>1</u> | .58 | 0.93 | 0.5 | 57 | 0.40 | 0.46 |

Another relevant fact would be that so-called atypical schizophrenic syndromes appear to occur more frequently in women than in men (Tsuang et al. 1976). Women also display affective disturbances and types of delusion typical for affective psychosis more frequently than men (Pauleikoff 1954; Lucas et al. 1962; Steinebrunner and Scharfetter 1976; Diebold and Engel 1977; Floru et al. 1979; Rudden et al. 1983; Vollmoeller 1983; Westermeyer and Harrow 1983; Gebhardt and Pietzcker 1985; Goldstein 1986). This could result in women being first alloted a diagnosis other than schizophrenia and only receiving this label later.

Not only are the intrinsic characteristics of the illness such as type and intensity of symptoms important with regard to the time of first admission but also a number of social factors, in particular the illness be-

havior of patients and of their relatives, that is the perception and interpretation of the psychological disturbances and the behavioral reactions deamed appropriate to them (Mechanic 1986). We are not aware of any investigations into differences in the way schizophrenic patients of different sexes perceive the illness. In general it seems that women have a lower threshold of perception for emotional disturbances and are also more ready to recognize the psychological nature of difficulties and problems (Mechanic 1982). This would at first sight lead one to believe that women should come into contact with psychiatry earlier than men. Acting against this however is the fact that the relatives of female schizophrenic patients seem to notice psychological disturbances in them less and also to be slower in seeking help from social or psychiatric services (Clausen et al. 1982;

Table 3. Overview of studies on gender differences of date of onset of schizophrenia (studies published until 1983 are included)

| Investigators | Time period | Country | Numb | | Age at onset | | | |
|------------------------------------|----------------------------------|-------------|-------------|------------------|--------------|------------|----------------------------------|--|
| | | | of patients | | Mean | Odds ratio | | |
| | | | M | F | M | F | M/F ≤ 25 years/ ≤ 30 years | |
| Kraepelin (1909–1915) | ? | Germany | 625 | 449 | | | 1.57/1.71 | |
| Bleuler (1911) | ? | Switzerland | 6 | 18 | | | 1.69/2.15 | |
| Strömgren (1935) | | Germany | 365 | 293 | | | 1.57/2.01 | |
| Langfeldt (1937) | 1926-29 | Norway | 46 | 54 | | | /3.92 | |
| Rennie (1939) | 1913-23 | USA | 198 | 258 | | | /1.44 | |
| Achté (1961) | 1933-35/ | Finland | 64 | 60° | | | 1.46/1.19 | |
| | 1953-55 | | 22 | 35 ^b | | | 4.00/1.56 | |
| Noreik and Odegaard (1967) | 1931-35 | Norway | ? | ? | 28.3 | 32.2 | | |
| <u> </u> | 1951-55 | · | | | 26.9 | 32.7 | | |
| Walker (1961) | | India | 89 | 49 | 24 | 26 | 1.50/2.38 | |
| Auch (1962) | 1946-50 | FRG | 294 | 486 | 27.3 | 29.9 | 2.10/2.08 | |
| ` , | 1952-56 | | | | 26.8 | 34.5 | 3.30/5.20 | |
| Helgason (1964) | _ | Iceland | 14 | 22 | 26.6 | 30.4 | 6.30/1.19 | |
| Raskin and Golob (1966) | ? | USA | 72 | 66° | ? | ? | | |
| Achté (1967) | | Finland | 32 | 65 ^d | | | 3.61/4.89 | |
| Lewine (1980) | | | 22 | 36 ^e | | | 1.89/4.76 | |
| Hartmann and Meyer (1969) | 1964 | FRG | 648 | 725 | 26.9 | 31.9 | 21057 1170 | |
| Noreik (1970) | 1938–59 | Norway | 457 | 324 | 20.5 | 0117 | /2.08 | |
| Lindelius (1970) | 1900-10 | Sweden | 104 | 133 | 27.1 | 32.3 | 1.82/2.58 | |
| Murakami (1970) | 1951/ | Japan | 225 | 191 | 27.1 | 32.3 | 1.25/1.63 | |
| Marakann (1770) | 1958–59/ 1965–66 | Japan | 223 | 171 | | | 1.23/1.03 | |
| Bleuler (1972) | 1942-43 | Switzerland | 100 | 108 | | | /1.59 | |
| Dube and Kumar (1972) | ? | India | 38 | 26 | | | 2.10/ | |
| Hinterhuber (1973) | 1930/1933/ 1935/1937/ 1940 | Austria | 70 | 87 | | | /1.72 | |
| Angst et al. (1973) | ? | ? | 82 | 114 ^f | 25 | 26 | | |
| Aligst Ct al. (1973) | • | • | 103 | 184 ^g | 29 | 37 | | |
| | | | 66 | 154 ^h | 24 | 29 | | |
| Hartmann and Meyer (1974) | 1969 | FRG | 1775 | 1429 | 26.7 | 32.0 | 3.42/ | |
| Liberman (1974) | 1910–64 | USSR | | 021 | 20.6 | 26.8 | 3. IL | |
| Vogel and Vliegen (1975) | 1960–69 | FRG | 91 | 70 | 26.5 | 29.1 | | |
| Khramelashvili and Liberman (1976) | ? | USSR | 295 | 620 ⁱ | 20.3 | 27.1 | 1.29/1.28 | |
| Nystrup (1976) | 1953/1962 | Denmark | 283 | 223 | | | /1.74 | |
| Sharikow (1977) | ? | USSR | 561 | 822 | | | /2.25 | |
| Diebold and Engel (1977) | ? | FRG | 30 | 30 ⁱ | 22.5 | 23.1 | | |
| - , , | | | 30 | 30 ^g | 24.9 | 30.9 | | |
| Nyman (1978) | 1964-67 | Sweden | 39 | 16 ^k | 20.2 | 21.8 | 1.76/ | |
| • | | | 32 | 22^{1} | 17.8 | 17.2 | 0.97/ | |
| Shmaonova and Liberman (1979) | ? | USSR | ? | ? | | | 2.20g/ | |
| Sharikow et al. (1979) | ? | USSR | ? | ? | | | 2.51 ^m / | |
| Shmaonova and Liberman (1979) | ? | USSR | 1151 | 397 | | | 3.06 ^m / 0.76/ | |
| Huber et al. (1979) | 1945-59 | FRG | 209 | 293 | | | /2.17 ⁿ | |
| () | | | 857 | 1632 | | | /1.91° /2.68° | |
| Gerard (1980) | 1917/18 | Poland | 1 | 74 | 24.7 | 26.9 | | |
| • | 1927/28 | | | 83 | 25.6 | 23.3 | | |
| | 1937/38 | | | 87 | 26.9 | 26.6 | | |
| | 1948 | | | 91 | 27.1 | 28.1 | | |
| | 1958 | | | 20 | 24.4 | 27.1 | | |
| | 1967/68 | | | 40 | 24.5 | 29.4 | | |

Table 3 (continued)

| Investigators | Time period | Country | Number of patients | | Age at onset | | | |
|-------------------------------|-------------|---------|--------------------|-----------------|--------------|-----------|----------------------------------|--|
| | | | | | Mean | or median | Odds ratio | |
| | | | M | F | M | F | M/F ≤ 25 years/ ≤ 30 years | |
| Shmaonova and Liberman (1980) | ? | USSR | 1195 | 2266 | | | /1.96 | |
| Bellodi et al. (1982) | ? | Italy | 59 | 33 ^p | 20.4 | 20.8 | | |
| , | | | 22 | 12 ^q | 20.9 | 27.8 | | |
| | | | 34 | 38 ^r | 28.9 | 32.5 | | |
| Rzewuska and Angst (1982) | 1973-77 | Poland | 25 | 25 ^g | 24.7 | 27.4 | | |
| | 22.2 // | | 25 | 25 ^h | 24.9 | 25.7 | | |

^a Typical schizophrenia, age under 35 years

Warren 1983). Taking into account the fact that the first contact of schizophrenic patients with psychiatric services usually takes place on the instigation of third persons, often the relatives, the latter phenomenon could well be the more important (Hornstra and Udell 1974).

In view of the role differences existing between the sexes in industrial societies we can assume that male patients are more in danger of failing to fulfill the roles expected of them (Tudor et al. 1977). The social control exerted on them is likely to be stricter and the tolerance shown to them with regard to abnormal behavior less. There is therefore a greater probability of their being noticed as abnormal and consequent earlier admission to a psychiatric hospital. In addition it seems that there is more stigma attached to schizophrenia in men than in women (Phillips 1964; Stumme 1975; Farina et al. 1978) and this would also negatively influence their chances of being able to stay in the community.

On the basis of these theoretical considerations it seems quite plausible that the difference in age at first admission between the sexes can be explained by the fact that women are able to remain outside hospital for longer after the first appearance of schizophrenic symptoms. The results of empirical investigations which are at present available do not, however,

agree with this assumption. On the other hand they suggest that men really do show first symptoms of schizophrenia earlier than women. In our search of the literature we discovered 36 papers giving data on the onset of schizophrenia in men and women. With 3 exceptions (Nyman 1978; Gerard 1980; Shmaonova and Liberman 1979) all of these came to the conclusion that the schizophrenic disturbance appears earlier in men than in women (Table 2). This difference seems to be particularly obvious with regard to the paranoid type of schizophrenia (Angst et al. 1973; Diebold and Engel 1977; Bellodi et al. 1982; Rzewuska and Angst 1982). The validity of the studies is however reduced by a methodological problem: in most cases the authors gave no operational definition of onset of illness and when they attempted to do this their definition was usually inprecise and did not conform to modern diagnostic criteria. Only in the study of Bellodi et al. (1982) the date of onset was defined as the time when the patient first met RDC criteria for definite schizophrenia. Another problem is that, with only 2 exceptions, they were clinical investigations giving no indication of the true incidence. It is therefore important to note that 2 field studies which exist (Helgason 1964; Dube and Kumar 1972) also confirmed that the onset of illness is earlier in men than in women.

^b Schizophreniform psychosis, age under 35 years

c Age 16-45 years

d Typical schizophrenia

Schizophreniform psychosis

Catatonic schizophrenia

g Paranoid schizophrenia

^h Schizoaffective psychosis

ⁱ Nonparanoid schizophrenia

k Regressive schizophrenia

¹ Nonregressive schizophrenia

m Cut-off point 20 years

ⁿ First manifestation of prodromal or psychotic symptoms

o First manifestation of psychosis

^p Hebephrenics

q Mixed

^r Paranoids

Another important argument against the hypothesis that the younger age of men at first admission is accounted for by a shorter period between onset and first admission is given by studies in which the time of onset and of first admission are dealt with. Of the 14 investigations with relevant data 10 showed no significant sex difference in the period between onset and first admission (Pollock 1926; Rennie 1939; Lehrman 1960; Dunham 1965; Achté and Apo 1967; Achté 1967; Lindelius 1970; Gerard 1980; Lewine et al. 1981; Rotstein 1982). Only 2 reported a shorter period in men (Hartmann and Meyer 1969; Huber et al. 1979), 2 studies even showed a shorter period in women (Nyman 1978; Gam 1980).

Do Temporal or Cultural Factors Affect the Amount of Gender Difference in Age of Onset or of First Admission?

In the hope of being able to determine how important social factors are in causing the gender difference in age of onset of schizophrenic disturbance we looked for possible variations in this difference related to differences in time at or region in which the investigation took place. For this purpose we carried out a metaanalysis. We could not, however, use all the studies listed in Tables 1 and 3 since the information given was too heterogeneous. We limited ourselves to those investigations which gave data on cases/admissions per age group. We also took 30 years of age as the cut-off point which allowed us to include the largest number of studies in our analysis. In order to investigate time-related trends we grouped the studies into those carried out before 1945 and those carried out after this date. To test regional differences we grouped the studies according to area of origin as follows: Central Europe, Scandinavia, United Kingdom, Ireland, USSR, North America, and Southeast Asia.

The quality of the data did not permit us to use the procedure developed by Smith et al. (1980) for the metaanalysis of quantitative data. Instead we used the following procedure: the results of the individual studies were arranged in fourfold tables, showing the number of male and female patients in each age group. These data were then combined statistically using the Mantel-Haenszel statistic (Mantel and Haenszel 1959; Mantel 1963; Fleiss 1981). In essence, this statistical method estimates the overall difference between both sexes, adjusting for the heterogeneity of study findings. For the groups made up according to region and time period we computed a mean effect size which indicated the difference between the percentage of men and women. The consistency of the effects was tested by means of the χ^2 test. The χ^2 was broken down into two components, the first representing the similarity of effects, the second being a measure of the significance of the mean effect size. We could thus check the homogeneity of the effects in each group and at the same time estimate the mean effect size (\overline{d}) for each group. Lastly we tested the influence of regional and temporal factors on the effects applying an analysis of variance to the weighted differences in the percentages of both sexes (Hedges and Olkin 1985) (a detailed description of the statistical procedure is available on request).

Table 4 gives the values for χ^2 and the mean effect sizes \overline{d} for the different areas. The χ^2 values were highly significant for all areas, the lowest value being calculated for Southeast Asia.

The largest effect sizes were observed in the Central European and Scandinavian groups, both for date of onset and date of first admission. Analysis of variance showed clearly that the region influenced

| Table 4. | Gender | differences of | date of | onset/first | hospitalization | in v | arious | geographical areas |
|----------|--------|----------------|---------|-------------|-----------------|------|--------|--------------------|
| | | | | | | | | |

| Area | Criterion | Comparisons (N) | Males ≤30 | (<i>N</i>) > 30 | Females ≤30 | (N) >30 | χ ² (MH) | đ |
|----------------|-----------------------|-----------------|--------------|-------------------|-------------|------------|------------------------|------|
| Central Europe | Onset | 8 | 2040 | 760 | 1930 | 1907 | 270.60 | 0.87 |
| | First hospitalization | 6 | 1979 | 1781 | 2040 | 3661 | 238.31 | 0.67 |
| Scandinavia | Onset | 6 | 488 | 205 | 346 | 336 | 61.61 | 0.77 |
| | First hospitalization | 7 | 1373 | 985 | 929 | 1399 | 148.30 | 0.72 |
| UK/Ireland | First hospitalization | 4 | 2147 | 1416 | 1504 | 1684 | 111.90 | 0.52 |
| USSR | Onset | 3 | 1490 | 613 | 2280 | 1495 | 73.73 | 0.50 |
| North America | First hospitalization | 18 | 29261 | 25208 | 19465 | 28994 | 1968.67 | 0.56 |
| Southeast Asia | First hospitalization | 4 | 701 | 404 | 395 | 346 | 16.38 | 0.40 |

 0.97^{a}

 0.63^{b}

| Time period | Criterion | Comparisons (N) | Males ≤30 | (N) >30 | Females ≤30 | (N) >30 | χ ² (MH) | đ |
|-------------|-----------------------|-----------------|--------------|------------|-------------|------------|------------------------|------------|
| Before 1945 | Onset | 9 | 1485 | 417 | 1061 | 709 | 78.82 | 0.67ª |
| | First hospitalization | 17 | 25121 | 22372 | 16996 | 26225 | 1674.87 | 0.55^{b} |

1575

10225

604

7275

1657

7284

Table 5. Gender differences of date of onset/first hospitalization during different time periods

7

20

Onset

First hospitalization

After 1945

the effect size both with regard to onset of illness $(F_{2.754} = 145.42, P = 0.000)$ and date of first hospitalization $(F_{4.7635} = 248.47, P = 0.000)$. It is of course still an open question whether gender differences are really smaller in Southeast Asia or whether this result is due to differences in diagnostic systems. In this respect it is interesting to note that Weiner and Marvit (1977) in Hawaii demonstrated the expected gender difference in whites but not in Filipinos. The final answer to the question whether gender differences as regards time of onset of illness and first admission are smaller in developing countries could result from the analysis of the data of the WHO Collaborative Study on Determinants of Outcome of Severe Mental Disorders (Sartorius et al. 1986).

In our investigation into possible time trends with regard to gender differences in age at onset of illness we were concerned to avoid confusion with regional variations and therefore we selected only those studies originating in Central Europe and Scandinavia. As shown in Table 5 comparison of the time before and after 1945 showed a definite increase in effect size ($F_{1.637} = 279.01$, P = 0.000). The results of three studies in which the age at onset was determined in the same place in the 1930s and in the 1950s agreed with one another, showing an increase in gender difference (Noreik and Odegaard 1967; Achté 1961; Gerard 1980). However, the changes could be due to changes in diagnostic habits.

Rather less clear-cut results were found when gender differences and time of first admission at different periods were examined (Table 5). We performed a two-factor analysis of variance using the data from Europe and North America and this only showed a main effect with regard to the factor time (F = 177.03, P = 0.000). There was no significant interaction between place and time, indicating similar changes taking place in Europe and North America. Investigations carried out in the same place in different periods produced no consistent picture: some showed an increase in gender difference (Noreik and Odegaard 1967; Lassenius et al. 1973) others a reduc-

tion (Malzberg 1955; Israel and Johnson 1956; Hilger et al. 1983).

1742

9859

261.74

878.51

Are Gender Differences in Age at Onset Specific for Schizophrenia?

We were interested to find out whether similar gender differences in age at onset could also be observed in other functional psychoses. We therefore searched the literature for studies reporting relevant data for affective psychoses. There was a marked contrast to the state of affairs in schizophrenia. In most studies no gender differences were found as regards age at onset or age at first hospitalization. A breakdown of the diagnostic subgroups produced the following picture. The majority of studies on manic-depressive psychoses showed no significant gender difference in age at onset (Rehm 1919; Slater 1938; Auch 1962; Helgason 1964) or first hospitalization (Wertham 1929; White 1935; Hardt 1959; Flor-Henry 1974; McCabe 1975; Bland 1977). In a few studies an earlier onset or first admission was observed in women (Faris and Dunham 1939; Schulz 1951; Angst 1966). Earlier hospitalization of men was only reported by Angermeyer and Robra (1982). The results for bipolar affective disorder were also very consistent, all showing no significant gender differences in age at onset or first admission [Diebold and Engel 1977; Loranger and Lewine 1978; Rzewucka and Angst 1982; Peselow et al. 1982 (with the exception of bipolar II disorder where females were hospitalized earlier than males); Joyce 1984; Weissman et al. 1988]. As regards depressive psychosis results of some older clinical studies suggested an earlier onset in women (Jung 1952; Hertrich 1962; Matussek et al. 1965). Two more recent studies using SADS interviews and RDC criteria for unipolar disorder did not yield significant gender differences in age at onset (Klerman et al. 1985; Lewinsohn et al. 1986). The same conclusion can be drawn from two epidemiological studies providing population-based incidence rates (Hagnell et al. 1982; Weissman et al. 1988). No gender

^a Only Central Europe and Scandinavia

^b Europe and North America

differences were found for age at first hospitalization (Peselow et al. 1982).

There are only a few studies reporting data on gender differences of age of onset of schizoaffective psychosis. Their results suggested a somewhat similar pattern as has been observed in schizophrenia. Omata (1985) in a study carried out in Japan and in the Federal Republic of Germany found an earlier onset in men, and similar results were reported by Labhardt (1963). Rzewuska and Angst (1982), however, failed to demonstrate a gender difference. According to Forrest and Hay (1972) men are first admitted to hospital for schizoaffective psychosis earlier than women.

Possible Determinants of Gender Differences in Age at Onset of Schizophrenia

Our review of the literature yielded overwhelming evidence that male schizophrenic patients are in fact first admitted to hospital earlier than female patients. The same holds good for population-based admission rates. The data also strongly suggested that the onset of schizophrenic disorder occurs earlier in men than in women, although limitations of method have prevented this issue being settled definitely. There seems to be some variation with regard to culture and time, the gender differences being less in developing countries and in the time before 1945. This result runs against assumptions based on the popular notion of converging trends of gender roles in modern Western societies. The same gender differences in age at onset were not found in affective psychoses.

How can the gender difference in age of onset of schizophrenia be explained? At present, due to the lack of empirical research we can only speculate about possible causes. When looking for an explanation for this phenomenon we should remember that the prevalence of schizophrenia has been proved to be the same in both sexes (Dohrenwend and Dohrenwend 1976; Neugebauer et al. 1980). The variation in time of onset can therefore not be accounted for by a greater general vulnerability or a greater degree of social stress in men. In this case we would expect men to suffer from schizophrenia more frequently than women. Basically, there are two different explanations possible depending on whether schizophrenia is conceived of as a homogeneous diagnostic category or as a heterogeneous syndrome consisting of various subtypes - a view which seems to become increasingly accepted among researchers.

In the first case one would expect differences in the temporal distribution of factors influencing the development of schizophrenic disturbance. For example, the degree of vulnerability could be different in men and women at different stages of life. The estrogens could play a part, as they modulate the sensitivity of dopamine receptors, and as in older women the production of estrogens is reduced this could result in a higher risk of developing schizophrenic disorder (Lewine 1981; Seeman 1981). Some authors discuss the possibility that men are exposed to psychosocial stress earlier than women. They may well experience social obligations particularly relevant in the preschizophrenic individual, for instance to achieve autonomy, at an earlier age (Lewine 1981; Loranger 1984). Furthermore, tasks such as leaving home, obtaining a job, and competing with others seem to be especially associated with the manifestation of schizophrenic disorders in men, whereas childbirth and family conflict are associated with schizophrenia in women (Bleuler 1972). Of special interest are the results of an epidemiological study by Markush and Favero (1974) who observed more life changes in men under 35 than in women of the same age group. The rate of life changes did not differ between the ages 35 and 55. Above 55 years, it was higher for women than for men. The fact that women on average get married earlier than men could also play a role as this could indicate that in early adulthood women are more likely than men to have sufficient social support available to them.

Finally, considering schizophrenia as a heterogeneous syndrome consisting of various distinct disorders one could argue that a particular subtype characterized by an early onset (besides, maybe, other features like poor premorbid functioning and an unfavorable course) is overrepresented in men (Lewine 1981; Angermeyer et al. 1988).

The answer to the question which one of these explanations, or whether a combination of both, will hold true may be provided by a study which is currently under way at the Central Institute of Mental Health in Mannheim (Häfner 1985).

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