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## A Comparative Study of 470 Cases of Early-Onset and Late-Onset Schizophrenia

ROBERT HOWARD, DAVID CASTLE, SIMON WESSELY and ROBIN MURRAY

The presence or absence of 22 schizophrenic symptoms was recorded with the age at onset of illness in 470 patients with non-affective, non-organic psychoses. Positive and negative formal thought disorder, affective symptoms, inappropriate affect, delusions of grandiosity or passivity, primary delusions other than delusional perception, and thought insertion and withdrawal were all more common in early-onset cases (age at onset 44 years or less;  $n = 336$ ). Persecutory delusions with and without hallucinations, organised delusions, and third-person, running commentary and accusatory or abusive auditory hallucinations were all more common in late-onset cases (age at onset 45 years or more;  $n = 134$ ). There was no difference between cases of early and late onset in the prevalence of delusions of reference, bizarre delusions, delusional perception, or lack of insight. We conclude that although there are clinical similarities between cases of schizophrenia with early and late onset, there are sufficient differences between them to suggest that they are not phenotypically homogeneous.

Both Kraepelin (1904) and Bleuler (1911) observed that the relatively rare schizophrenic patients who had a late age of onset resembled those with early onset. Kraepelin, using a narrow concept of dementia praecox and specifically excluding paraphrenia, found that 5.6% of 1054 schizophrenic patients had an age of onset greater than 40 years (Kraepelin, 1913, 1919). Later workers found higher rates: 16% of Carl Schneider's 889 subjects (Kolle, 1931); 18% of 182 patients (Kolle, 1931); 15% of schizophrenic patients (Bleuler, 1943); 31% of 101 elderly schizophrenic patients (Mueller, 1959); and 21% of 100 chronic patients (Fish, 1960).

Since the late 1950s, the European literature on schizophrenia and schizophrenia-like illnesses with a late onset has been dominated by the diagnosis of late paraphrenia (Roth, 1955; Kay & Roth, 1961; Post, 1966; Grahame, 1984; Holden, 1987). Debate has raged as to whether late paraphrenia represents cases of late-onset schizophrenia with an age of onset of over 60 years (Fish, 1960; Kay & Roth, 1961; Grahame, 1984), or a variety of disorders within which only a proportion of patients satisfy diagnostic criteria for schizophrenia (Post, 1966; Holden, 1987). Late paraphrenia is certainly more common than late-onset schizophrenia was reported to be by the classical European psychiatrists. A study in a single catchment area has shown the incidence of late paraphrenia to be between 17 and 26 per 100 000 per year (Holden, 1987). In comparison, schizophrenia with such late onset was classically considered rare. In only 0.2% of Kraepelin's 1054 cases of schizophrenia did the illness begin after the age of 60 years (Kraepelin, 1913). Bleuler (1943) specifically

searched for cases with late onset, but could only find five that had begun after the age of 60 years.

The North American view until the revision of DSM-III (DSM-III-R; American Psychiatric Association, 1987) was that onset after the age of 44 precluded a diagnosis of schizophrenia (American Psychiatric Association, 1980). Repeated reports of patients who were clinically indistinguishable from schizophrenic patients, but whose age at onset had been greater than the arbitrary limit of 45 years set by DSM-III, led to a call for the diagnostic criteria to be changed so as to accommodate such patients within the diagnosis of schizophrenia (Rabins *et al.*, 1984; Gold, 1984; Volavka, 1985; Harris & Jeste, 1988). Since the inclusion of late-onset schizophrenia in DSM-III-R, there have been few attempts to compare the clinical features of late-onset cases of schizophrenia with their earlier-onset counterparts. Any attempt to understand whether they are two conditions, or the expressions of a unitary condition affected by age, should logically begin with a comparison of their clinical features.

The comparative studies that are reported in the literature are few in number and mostly pre-date operationalised diagnostic procedure. Bleuler (1943) studied 126 schizophrenic patients with an age at onset of 40 years or greater, and reported only a slight variance in phenomenological features compared with patients having early onset. In late-onset cases the symptoms were milder, there was less affective flattening, and formal thought disorder was less likely. Fish (1960) observed that the clinical picture in early-onset cases did not differ from that in late-onset ones, but believed that with increasing

age at onset, schizophrenia took on a more 'paraphrenic' form. Authors who have compared late paraphrenia with schizophrenia of an early onset have commented on the phenomenological similarities between them (Kay & Roth, 1961; Grahame, 1984), but have not always considered them to be the same illness (Post, 1966; Holden, 1987).

Choosing 45 years, rather than 60 years, as the lower age limit for late-onset schizophrenia is more likely to yield late-onset cases that are aetiologically and clinically closer to more 'typical' earlier-onset schizophrenia. The effects of general medical conditions, organic brain disorders, and sensory impairment are all thought to contribute to the generation of psychotic symptoms in the over-60s, and these factors would tend to obscure similarities between cases with early and late onset. For this reason alone, comparisons that have divided patients into early and late onset using DSM-III-R criteria would be expected to reveal similarities that are not seen between late paraphrenics and early-onset schizophrenics.

Pearlson *et al* (1989) reviewed the charts of 54 schizophrenic patients with an age at onset of greater than 44 years and compared them with the charts of 54 young and 22 elderly patients with early-onset schizophrenia. Phenomenological similarities were found to outweigh the differences between early- and late-onset cases. Nevertheless, patients with late-onset schizophrenia were more likely to have visual, tactile, and olfactory hallucinations, persecutory delusions, and premorbid schizoid personality traits. They were less likely to have thought disorder or affective flattening. Late-onset patients were found to respond well to neuroleptics, and have a good prognosis.

To our knowledge, no previous study has compared the phenomenology of late- and early-onset schizophrenia in a representative catchment-area sample of patients. The current study sought to investigate issues of phenomenology in late-onset ( $n=134$ ) and early-onset ( $n=336$ ), non-affective psychotic patients in a representative first-contact catchment-area sample of such patients on the Camberwell Cumulative Psychiatric Register (Wing & Hailey, 1972) over 20 years. Selection bias in terms of age at onset or illness severity was thus excluded. The hypothesis under test was that late-onset schizophrenia (age of onset >44 years) is not the same illness as early-onset schizophrenia. The two conditions may differ in terms of their aetiology, clinical presentation, natural history, and treatment response (reviewed by Castle & Howard, 1992). This study investigates whether they differ in

phenomenology. A brief preliminary report of the analyses on early- and late-onset patients is given elsewhere (Howard *et al*, 1993).

### Method

The methodology of this study is detailed elsewhere (Castle *et al*, 1991). Essentially, we assessed all first-contact, non-affective, non-organic psychotic patients on the Camberwell Cumulative Psychiatric Register (Wing & Hailey, 1972). This broad group included patients with a register diagnosis of schizophrenia (equivalent ICD-9 codes 295.0-9 (World Health Organization, 1978)), including schizoaffective type (ICD-9 295.7), as well as 'paraphrenia' (ICD-9 297.2) and 'other non-organic psychosis' (ICD-9 298.1-9). The Operational Criteria Checklist for Psychotic Illness (OPCRIT; McGuffin *et al*, 1991) was completed for all patients. The OPCRIT is based on phenomenological descriptions in the Present State Examination (Wing *et al*, 1974), is designed to be completed from case records, and covers a range of operational definitions of schizophrenia. The OPCRIT provides explicit guidelines for the rating of phenomenological symptoms. Two independent workers (DC and SW) rated the case records. Inter-rater reliability was assessed on a random subset of 50 case records, which were rated by both workers. The value of kappa for diagnoses of schizophrenia was 0.82 using Research Diagnostic Criteria (RDC; Spitzer *et al*, 1978) and 0.76 using DSM-III.

The patients were analysed in two groups according to age at onset (early onset 44 years or younger, late onset 45 years or older). Illness onset was defined as "the earliest age at which medical advice was sought for psychiatric reasons or at which symptoms began to cause subjective distress or impair functioning". Analyses were performed using the  $\chi^2$  statistical test.

### Results

Rateable notes were available on 470 patients (90% of the total). The patients for whom notes were missing did not differ significantly from the rest in terms of sex or age distribution. Of the 470 subjects, 336 had onset of illness at age 44 years or less, and 134 at age 45 years or over. The early-onset group contained 141 women (42.0%), and the late-onset group 90 women (67.2%).

Research Diagnostic Criteria for a diagnosis of schizophrenia were satisfied by 63% of the early-onset patients, and 83% of the late-onset patients. The mean age at onset was 41 years for women and 31 years for men. Distributions of age at onset for male and female patients are shown in Figure 1.

The only symptom which was distributed significantly differently between men and women was the presence of predominant affective features. In the early-onset group, affective symptoms were present in 35% of women, but in only 11% of men ( $P<0.01$ ). Affective symptoms were rarer in later-onset cases, but there were no significant differences between the sexes in this group (7% of men and 9% of women).

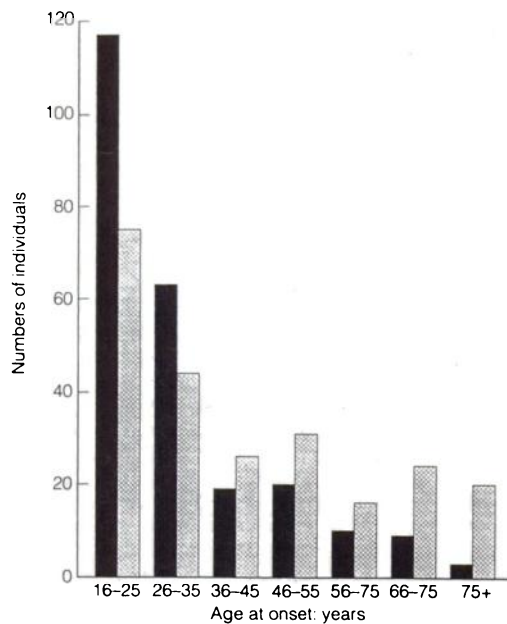


Fig. 1 Age distribution for onset of illness in men and women (■ men, ▨ women).

The investigated symptoms were divided into three classes: those more common in the early-onset group, those more common in the late-onset group, and those no more common in either patient group. Table 1 shows the prevalences of those symptoms under investigation that were more common in the early-onset and late-onset groups. Symptoms which were no more common in either group were delusional perception, bizarre delusions, and delusions of reference.

### Discussion

This study has certain advantages over extant work in the field. The sample size was large and all non-affective, non-organic psychotics were assessed, thus precluding bias from the use of any one set of operational criteria for schizophrenia, or any age-at-onset bias. The sample was based on a catchment area, and all first-contact patients were assessed; thus there was no bias arising from referral to a specialist centre, or from stay in hospital. Although retrospective case-note studies have their limitations, the quality of the Joint Hospitals' case-notes (Bethlem Royal Hospital and the Maudsley Hospital) is high, and descriptive phenomenology is particularly carefully documented in them.

An important limitation to the study is the fact that neither those psychiatrists writing in the case-notes, nor the current authors who were examining them, were blind to the age of illness onset of the

Table 1  
Prevalence of symptoms more common in early-onset and late-onset patients

	Percentage of patients		P value
	Early onset (n = 336)	Late onset (n = 134)	
<i>Symptoms more common in early-onset patients</i>			
Positive formal thought disorder	27.4	10.4	0.005
Negative formal thought disorder	11.0	2.2	0.01
Inappropriate affect	17.8	4.4	0.005
Restricted affect	13.1	3.7	0.01
Passivity delusions	29.5	17.2	0.05
Catatonia	8.0	2.2	0.05
Primary delusions other than delusional perception	13.7	4.4	0.025
Thought insertion	15.2	7.5	0.05
Thought withdrawal	12.5	2.4	0.005
Grandiose delusions	24.1	14.9	0.05
<i>Symptoms more common in late-onset patients</i>			
Persecutory delusions	71.4	93.3	0.005
Organised delusions	19.6	54.5	0.005
Persecutory delusion with hallucinations	58.6	73.9	0.025
Third person auditory hallucinations	28.9	42.5	0.05
Accusatory or abusive voices	45.5	61.2	0.025
Running commentary	14.6	22.4	0.05

patients. Since traditionally (and particularly during the assessment period of 1965-84), late- and early-onset cases might have been expected to have different phenomenology, this might have been reflected in the material chosen for record. There is, sadly, no adequate way to control for, or eliminate, this potential area of historical bias.

Gender differences in the epidemiology of schizophrenia have recently been reviewed by Lewine (1988). He concluded that, while there is no consensus over whether or not the absolute rate of schizophrenia is higher in men, an earlier onset in men is consistently replicated. A fuller exposition of gender differences in the current Camberwell Case Register data set is provided elsewhere (Castle *et al*, 1993). Suffice it to say here that the preponderance of women in the late-onset group is consistent with earlier studies, although the sex imbalance is less marked than in some. Pearlson *et al* (1989) reported that 87% of their late-onset schizophrenic patients were women, while other workers have reported women:men ratios of 1.9:1 (Bleuler, 1943) to 22.5:1 (Herbert & Jacobson, 1967). Possible explanations for the female preponderance among late-onset schizophrenic patients (which far exceeds the preponderance of women among the elderly in the general population) are discussed elsewhere

(Harris & Jeste, 1988; Pearlson *et al*, 1989; Castle & Murray, 1991).

#### *First-rank symptoms of Schneider*

Pearlson *et al* (1989) established the presence of Schneiderian first-rank symptoms in 35% of their late-onset schizophrenic patients (age at onset > 44 years), not significantly different from the 40.9% in a control population of early-onset patients matched for current age. These percentages are lower than the more usual 40–60% incidence of first-rank symptoms reported in late paraphrenic patients (age at onset > 59 years) (Kay, 1972; Grahame, 1984; Holden, 1987) and in schizophrenic patients (Mellor, 1970; Carpenter *et al*, 1973). Regarding individual first-rank symptoms in our subjects, third-person and running-commentary auditory hallucinations were more common in the late-onset group. This is in accord with previous studies. Grahame (1984) found running-commentary (21%) and third-person (29%) auditory hallucinations to be more prevalent in his late paraphrenic patients (age at onset > 59 years) than reported in the studies of schizophrenic patients that he reviewed. He also reported that thought-insertion and withdrawal did not occur in late paraphrenia, but had been found in up to 47% of reviewed studies of schizophrenic patients. In our study, both thought insertion and withdrawal were less common in cases of later onset; thought insertion was particularly uncommon in this group.

Passivity experiences occurred with greater frequency among our late-onset cases. Grahame (1984), in his study of first-rank symptoms in late paraphrenia, found passivity phenomena to occur in 21% of such patients. A comparable number of early-onset schizophrenic patients in the studies he reviewed had this symptom.

#### *Thought disorder*

The comparative rarity of formal thought disorder among our late-onset cases is consistent with earlier reports (Bleuler, 1943; Kay & Roth, 1961). Pearlson *et al* (1989) found formal thought disorder in only 5.6% of late-onset schizophrenic patients, but 55% of elderly early-onset controls.

#### *Negative symptoms*

Bleuler (1943) observed that affective flattening was less commonly encountered in late-onset schizophrenia (age at onset > 40 years), and the absence of this symptom as a characteristic of Kraepelin's paraphrenics was partly responsible for Roth's choice of the term 'late paraphrenia'. Pearlson *et al*

(1989) reported affective flattening in only 7.4% of late-onset patients, whereas it occurred in 22.7% of age-matched, early-onset patients. In our series, both inappropriate affect and affective symptoms were more common in early-onset patients. These findings are consistent with the idea that negative or 'deficit' symptoms are characteristic of an early-onset form of schizophrenia (Murray *et al*, 1992).

#### *Delusions*

Grandiose delusions were more common among our early-onset patients. In their comparative study of early-onset (age 44 or less) and late-onset (age 45 or more) schizophrenic patients, Pearlson *et al* (1989) found grandiose delusions to be present in 16.7% of late-onset patients and 31.8% of elderly early-onset patients. This result is in accord with our findings, but interestingly in their second control group (schizophrenic patients with an early age of onset who were still young), Pearlson *et al* found grandiose delusions present in only 5.6%. Thus, there appears to be a further association between current age and the presence of grandiose delusions which is independent of age at onset of symptoms.

Our finding that persecutory delusions are more common in patients with a late age of onset is again consistent with previously published studies. Such symptoms are characteristic of late paraphrenia (Post, 1966), and, in Pearlson *et al*'s (1989) comparison, they occurred in 92.6% of late-onset schizophrenics and 77.3% of elderly and 44.4% of young, early-onset patients. Pearlson *et al*'s use of a second early-onset control group, containing young patients, revealed that, as for grandiose delusions, there is an association between age and the expression of persecutory delusions, independent of age at illness onset.

Organised delusions were also, not unexpectedly, more common in our late-onset patients. A systematised complex of delusions is encountered commonly in late paraphrenia (Post, 1966), and in cases of paranoid schizophrenia.

In Pearlson *et al*'s (1989) study, there appeared to be an age-related bias towards a higher prevalence of delusions in general in the elderly, which was independent of age at onset of illness: delusions were present in 98.1% of the late-onset schizophrenic patients, 100% of the early-onset but elderly patients, but only 68.5% of the currently young early-onset patients.

In our series, five of the studied symptoms were equally prevalent in both early- and late-onset patients. Delusions of reference and bizarre delusions

might have been expected to be more common among our late-onset patients, since, as suggested above, the prevalence of delusions appears to rise with the patient's age.

Primary delusions other than delusional perception were more common in the early-onset patients. This is a novel observation. Delusional perception was rare in both groups, but there was no significant difference in the frequency of this symptom between the two groups of patients.

### Conclusions

This study of first-contact, non-affective, non-organic psychotic patients from a large catchment area has repeated many of the consistent findings of previous comparisons between early- and late-onset cases. Earlier authors have tended, however, to regard early- and late-onset forms of schizophrenia as the same disorder, concentrating on the similarities and ignoring the differences between them. Although there are undoubted similarities between the symptoms of early- and late-onset schizophrenia, there are also clear differences.

Convincing aetiological theories for late-onset schizophrenia are still awaited. It would be both speculative and simplistic, but tempting, to view such cases as neurodegenerative rather than neurodevelopmental. It may be that the effects of development and degeneration are combined in the development of late-onset schizophrenia, so that a compensated neurodevelopmental abnormality becomes unmasked by the loss of brain capacity with ageing or environmental cerebral insults.

Late-onset schizophrenia remains understudied. One reason for this is a widespread failure to recognise it as a condition apart from early-onset schizophrenia which, as such, is deserving of investigative attention. The current study has shown that it is possible on clinical grounds to recognise separate early- and late-onset schizophrenia syndromes. Further research into the epidemiology and phenomenology of such patients should seek to integrate findings with other factors pertaining to the aetiology of late-onset schizophrenia, such as family history (Bleuler, 1943; Kay & Roth, 1961; Herbert & Jacobson, 1967; Huber *et al*, 1975) and neuroimaging studies (Naguib & Levy, 1987; Miller *et al*, 1989; Brietner *et al*, 1990).

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