

# Late-Onset Schizophrenia: An Overview

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## Abstract

Onset of schizophrenia after the age of 40 has been a controversial topic. We reviewed more than 30 publications (mainly from Europe) on this subject. Many of the studies had methodological shortcomings, including problems in precisely dating the onset of schizophrenia. Nonetheless, it appears that a certain proportion of patients present for the first time with diagnosable schizophrenia after age 40. Late-onset schizophrenia is characterized by **paranoid symptomatology**, a high female:male ratio, an elevated prevalence of hearing loss and ocular pathology, schizoid or paranoid traits in premorbid personality, a tendency toward chronicity, and symptomatic improvement with neuroleptics. Family studies suggest that the prevalence of schizophrenia in relatives of late-onset schizophrenic probands is higher than that in the general population, but lower than that in relatives of earlier-onset schizophrenic probands. We believe that late-onset schizophrenia is a valid entity (or group of entities). Studies of the course, biological associations, neuropsychological performance, and pharmacological characterization of late-onset schizophrenia are warranted.

I got the starting point of the line of thought which in 1896 led to dementia praecox being regarded as a distinct disease, on the one hand, from the overpowering impression of the states of dementia quite similar to each other which developed from the most varied initial clinical symptoms, on the other hand from the experience connected with the observations of Hecker that these peculiar dementias seemed to stand in

near relation to the period of youth. . . . It has since been found that the assumptions upon which the name chosen (dementia praecox) rested are at least doubtful. As will have to be explained more in detail later, the possibility cannot in the present state of our knowledge be disputed, that a certain number of cases of dementia praecox attain to complete and permanent recovery, and also the relations to the period of youth do not appear to be without exception.—*Emil Kraepelin* (1919/1971, pp. 3–4).

The onset of schizophrenia in mid to late life has been a controversial issue. Kraepelin (1919/1971) used the term "dementia praecox" to describe a state characterized by ". . . a peculiar destruction of the internal connections of the psychic personality" with the predominant effects in the "emotional and volitional spheres of mental life" (p. 3). He observed that most of these peculiar dementias developed during youth. As suggested by the quote above, however, Kraepelin did go on to question the appropriateness of the term "dementia praecox" for describing this illness since all cases did not result in a permanent dementia (a term he used for loss of volition over thinking, feeling, and acting) nor was the onset found to be restricted to adolescence and young adulthood. Yet, Kraepelin often included patients with predominantly paranoid symptoms starting after early adult life under the category "paraphrenia." Followup studies of Kraepelin's paraphrenic cases by Mayer (1921) and Mayer-Gross (1932) found,

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however, that many of those patients had a course of illness similar to that of patients Kraepelin had called dementia praecox.

Confusion over terms such as late-onset schizophrenia, paraphrenia, late paraphrenia, and paranoid states has persisted to this date. It is intriguing that, in spite of a number of European (especially German and British) investigations reporting that about 20 percent of schizophrenic patients have onset of symptoms after age 40 (see table 1), American researchers have been relatively uninterested in the entity of late-onset schizophrenia or paraphrenia.<sup>1</sup>

One possible reason may be the historical tendency to diagnose such patients as having affective or organic disorders (Roth and Morrissey 1952). Recently, *DSM-III* (American Psychiatric Association 1980) recommended exclusion of the diagnosis of schizophrenia if symptoms started after age 45. This age cutoff was not based on any published hard data. To correct this problem and to allow for a possible diagnosis of schizophrenia developing after the age of 44, the *DSM-III Revised* (American Psychiatric Association 1987) has introduced the category of late-onset schizophrenia.

If schizophrenia does occur in later life, recognition of this entity is important for clinical as well as research purposes. Clinically, the prevalence, symptomatology, course, and prognosis of late-onset

schizophrenia must be evaluated in order to diagnose and provide appropriate treatment for this patient population. Such data will also serve as a basis for further studies into the etiology and pathogenesis of this condition.

The purpose of this article is to review the available literature on late-onset schizophrenia/paraphrenia critically so as to obtain at least tentative impressions about its prevalence and clinical characteristics. We hope that such an overview will help generate interest in studies of patients who develop schizophrenic symptoms late in life.

### Chronology of the Development of Terminology for Late-Onset Schizophrenia

Historically, the onset of a psychotic illness in late life not secondary to an organic or affective disorder has been referred to as late-onset schizophrenia, paraphrenia, late paraphrenia, or involuntal psychotic reaction. The terminology has been used differently by different investigators resulting in considerable confusion. Below is a listing of some major milestones in this area.

*Guislain (19th Century)*: The term "paraphrenia" was used in the early part of the 19th century by Guislain, who employed it synonymously with a clinical syndrome then known as "folly"; the latter is roughly the equivalent to today's schizophrenia (Hinsie and Campbell 1974).

*Kraepelin (1919/1971)*: Kraepelin used the term "dementia praecox" to describe an illness with onset usually in youth resulting in chronic deterioration of the mental processes responsible for emotion and volition. He also

used the term "paraphrenia" to describe a group of cases that had many points in common with dementia praecox but with lesser disturbance of emotion and volition. Kraepelin classified paraphrenia into four groups: paraphrenia systematica, paraphrenia expansiva, paraphrenia confabulans, and paraphrenia phantastica.

Paraphrenia systematica was described as an extremely insidious development of a progressive delusion of persecution. Later, ideas of exaltation, ideas of reference, and auditory hallucinations appeared. The capacity to work was preserved for a long time. Sixty percent of Kraepelin's patients were males. Over half the patients had onset of symptoms between ages 30 and 40, and a little more than 20 percent between ages 40 and 50. Only isolated cases began before the 25th or after the 50th year.

Paraphrenia expansiva was described as "exuberant megalomania with predominately exalted mood and slight excitement" (p. 3). Hallucinations appeared fairly early. Later, delusions became somewhat more nonsensical and more disconnected. There was a lack of judgment, a certain incoherence, superficiality of emotions, and weakness of volition but no "disintegration of the psychic personality." Unlike mania, the course was chronic. Almost all of Kraepelin's patients were women. The onset of symptoms in 75 percent of the patients was between 30 and 50 years of age. One patient had onset of symptoms at age 64 without any signs of senile dementia.

Paraphrenia confabulans was characterized by delusions of persecution and exaltation.

<sup>1</sup> There are some notable recent exceptions, including studies by Rabins et al. (1984) and Miller et al. (1986) and reviews by Bridge and Wyatt (1980a, 1980b), Gold (1984), and Volavka (1985).

Pseudomemories (i.e., "memories" of impossible events, such as having fought in a war two centuries ago) occurred as well as megalomania. The mood was happy, yet later became irritable, morose, or indifferent. Many patients also heard voices over the course of the illness, and the delusions became more nonsensical and incoherent. Both sexes were equally represented. The age of onset was evenly distributed between the 20th and 50th years.

Paraphrenia phantastica was described as being characterized by highly extraordinary, disconnected, and changing delusions. There were ideas of persecution, auditory hallucinations, delusions of personal influence, and pseudomemories. The mood was somewhat exalted or indifferent, but sometimes gloomy or strained. The patients were sometimes inclined to violence. Speech was characterized by neologisms or silly plays on words. Many sentences were incomprehensible. The course was progressive, and the speech became more confused and disconnected. Males predominated, accounting for 60 to 70 percent of the cases. Twenty-five percent of the cases had onset after age 40.

There is a great overlap between these clinical pictures of paraphrenia and those of different patients with dementia praecox. Although Kraepelin stressed an absence of personality disintegration in the first two subtypes of paraphrenia (*systematica* and *expansiva*), he also reported that some patients with dementia praecox (especially paranoid type) also did not have marked deterioration of functioning. Indeed, followup studies of Kraepelin's paraphrenic patients by other investigators found that a number

of them resembled those with dementia praecox (Mayer 1921; Mayer-Gross 1932).

*Bleuler (1943)*: Bleuler described late schizophrenia as having onset after age 40 with symptoms not very different from those of early-onset schizophrenia. Bleuler excluded psychotic symptoms caused by pathologic brain disturbances or amnesic syndrome.

*DSM-I (American Psychiatric Association 1952)*: Involuntional psychotic reaction was a classification for psychotic reactions occurring in the involuntional period, with some cases characterized chiefly by depression and others by paranoid ideas. The course was usually long and symptoms included anxiety, intractable insomnia, guilt, agitation, somatic concerns, and sometimes delusions. It was pointed out that differentiation from other psychotic reactions with onset in this age group was difficult and patients were not to be included in this category merely because of their age.

*Kay and Roth (1950's and 1960's)*: During the 1950's and early 1960's, Kay and Roth investigated late-onset paranoid psychosis. Their definitions of paraphrenia and late paraphrenia evolved over this time period suggest that their differentiation of paraphrenia from late-onset paranoid schizophrenia was blurred. Roth and Morrissey (1952) described 12 schizophrenic patients with onset of symptoms after age 60 characterized by prominent "paraphrenic delusions" occurring in the setting of a well-preserved personality and "usually associated with the passivity feelings or other volitional disturbances and hallucinations in clear consciousness pathognomonic of schizophrenia."

Hopkins and Roth (1953) used

the term "paraphrenia" to describe those in whom a well-organized system of paranoid delusions, usually with auditory hallucinations, existed in the setting of a well-preserved personality and affective response.

Roth (1955) believed that in the majority of paraphrenic patients the illness began after age 60. He noted that "the clinical picture has many similarities to the paranoid illness described by Kraepelin under the heading of paraphrenia (later shown to be a relatively late form of schizophrenia)," and used the name "late paraphrenia" for this group in place of schizophrenia.

Kay and Roth (1961) used late paraphrenia to describe a paranoid symptom complex with no signs of organic dementia or confusion. From the content of the delusions and hallucinations, the illness was judged not to be a primary affective disorder. The patients had "more or less well-marked schizophrenic symptoms," with a small proportion having no hallucinations. The investigators were able to divide the late paraphrenic patients into three groups.

Group 1—Twenty percent of the late paraphrenic cases had abnormal personalities before the onset of the paranoid psychoses. Hallucinations were absent. The age of admission was often over 75. Delusions were confined to theft, poisoning, or ill treatment by people in contact with them. The symptoms appeared to be an extension of longstanding personality traits.

Group 2—Twenty-five percent of the late paraphrenic patients were in this group in which the delusions were said to be somewhat understandable in the light of their circumstances or to have

followed prolonged social isolation.

Group 3—The majority (55 percent) of late paraphrenic patients had symptoms that could not be attributed either to social stressors or to long-term personality disorders. These patients were considered to have “endogenous” paraphrenia.

*Leonhard (1959)*: In his classification of schizophrenia, Leonhard used the term “paraphrenia” to refer to all paranoid schizophrenics without distinction as to the age of onset. Other German authors also used the term in this manner (*Fish 1960*).

*Post (1966)*: Post classified patients who were suffering from paranoid symptoms that appeared for the first time after age 50 and were unrelated to affective illness into three categories, according to symptoms: paranoid hallucinosis, schizophreniform syndrome, and schizophrenic syndrome.

In “paranoid hallucinosis,” auditory hallucinations were the only type of psychotic experience associated with delusions of persecution. The “schizophreniform syndrome” was characterized by paranoid experiences that were somewhat more understandable or psychodynamically more comprehensible. Patients labeled as having “schizophrenic syndrome” had Schneiderian first rank symptoms. Post felt that patients who met criteria for this last category would clearly be diagnosed as having paranoid schizophrenia or paraphrenia by psychiatrists of different schools. After a 3-year followup, Post was unable to discover any clear etiological differences among the three syndromes and concluded that they were merely three different symptom clusters arranged along a continuum.

*DSM-II (American Psychiatric Association 1968)*: *DSM-II* did not have an age cutoff for making the diagnosis of schizophrenia. It described a paranoid psychosis characterized by delusion formation with onset in the involutional period as involutional paranoid state (involutional paraphrenia). The latter was distinguished from schizophrenia by the absence of conspicuous thought disorder typical of schizophrenia.

*Feighner et al. (1972)*: The Feighner research criteria for schizophrenia required that three of five items had to be present to make a definite diagnosis. One of these five items was onset before age 40.

*RDC (1978)*: The Research Diagnostic Criteria (*Spitzer et al. 1978*) had no age specifications for schizophrenia.

*ICD-9 (World Health Organization 1978)*: The ninth version of the International Classification of Diseases did not have an age cutoff for schizophrenia. It defined paraphrenia as paranoid psychosis with conspicuous hallucinations, often in several modalities. Affective symptoms and disordered thinking, if present, did not dominate the clinical picture and the personality was well preserved.

*DSM-III (American Psychiatric Association 1980)*: *DSM-III* did not recognize paraphrenia or involutional paranoid disorder as diagnoses. To make the diagnosis of schizophrenia, the onset of symptoms *must be* before age 45. *DSM-III* included a separate category of “paranoid disorders” to refer to persistent persecutory delusions without prominent hallucinations or any of the major symptoms (criterion A) of schizophrenia. There was no age

restriction for diagnosing paranoid disorders.

*DSM-III-R (American Psychiatric Association 1987)*: The *DSM-III-R* Advisory Group recognized the need to allow a diagnosis of schizophrenia presenting for the first time after the age of 44. Accordingly, the revised version of *DSM-III* has specified “late onset” if the disturbance, including the prodromal phase, develops after age 45.

Thus, it is clear that there is no consensus about terminology for schizophrenic symptoms appearing for the first time after 40 or 45 years of life. Even worse, the classification systems used by different researchers have employed arbitrary distinctions or cutoffs, with poor data base. For instance, the differentiation between paraphrenia and paranoid schizophrenia is not based on the results of long-term studies comparing these two entities. *Roth (1955)* and *Post (1966)*, who used the term paraphrenia, could not find any clear differences between paraphrenia and schizophrenia.

Below we will attempt to review the available data on late-onset schizophrenia.

### Studies of Late-Onset Schizophrenia

A review of the literature was done to look at the prevalence, gender ratio, clinical descriptions, and family studies of late-onset schizophrenia. We found articles published from 1913 to 1986. Most of the studies were European. The studies were obtained by using the *Index Medicus* and *Med-Search*. Cross-references from these articles were also used to obtain other original articles. In

addition, references from books on geriatric psychiatry were used. Articles written in a language other than English were translated.

Before examining the findings of the studies themselves, we will consider the generic and specific limitations of clinical investigations into late-onset schizophrenia.

1. There is a conceptual bias due to the terminology used, leading to circular thinking. The restriction placed by *DSM-III* (American Psychiatric Association 1980) on the age of onset of schizophrenia prevents clinicians from even considering schizophrenia in patients with onset of psychosis after age 44. Hence an analysis of chart diagnoses since 1980 is not likely to reveal the true prevalence of late-onset schizophrenia. Such data could then be used to support the "conceptual basis" of the original diagnostic criterion. Similarly, the results of family studies of schizophrenia would be expected to be biased by restricting the risk period to < 45 years.

In an ongoing investigation, we have so far studied 15 patients who met *DSM-III-R* criteria for late-onset schizophrenia (Jeste et al. 1987). Previously, most of the patients had been diagnosed, using *DSM-III*, as having either "atypical psychosis" or "paranoid disorder."

2. Defining the age of onset of schizophrenia is difficult for several reasons. The onset of symptoms is usually insidious and therefore hard to pinpoint to a specific time. Premorbid schizoid or paranoid personality traits further complicate determining the precise age of onset. Most patients do not have insight into the early symptoms of their illness. In elderly patients, there

may be age-associated memory problems that make it difficult to recall previous psychiatric history as well as a lack of contemporaries to substantiate the patient's psychiatric history.

3. There are problems in following late-onset schizophrenic patients over time: (a) There may be social isolation from a combination of schizophrenia and old age with a loss of important friends, family members, and spouses, so that there are fewer concerned people to help ensure psychiatric followup. (b) Medical illnesses and even death interfere with evaluation of the course, treatment response, and prognosis of the schizophrenic illness. (c) Sensory deficits may complicate the symptomatology as well as interfere with driving, making it difficult for patients to keep appointments. (d) Following the patient's retirement, financial problems may limit access to medical care.

4. There may be a tendency to attribute paranoid symptoms in older patients to other causes such as (a) organic mental syndromes including medication-induced mental status changes, (b) affective disorders, or (c) sensory deficits.

5. Symptoms of late-onset schizophrenia may be mixed with age-related difficulties in learning and recent memory.

6. Research protocols for schizophrenia typically exclude older patients, due to clinical as well as human subjects considerations.

7. It is probable that late-onset schizophrenia is not a homogeneous entity, but a combination of several different (and partly overlapping) subtypes. Separating these subtypes from one another

may need a detailed assessment of relevant clinical and biological variables.

### Critique of Published Studies

The published studies on late-onset schizophrenia have frequently been fraught with important methodological and other problems.

**Material.** 1. Post (1966) attributed low estimates of late-onset schizophrenia in some studies to difficulties in identifying such patients in the general population, even when evaluated by experienced psychiatrists. For example, he cited a study done by Kay et al. (1964) in which no patients meeting Roth's criteria for late paraphrenia were found among 309 persons over age 65 in Newcastle. Yet, a survey revealed that there were at least eight paraphrenic patients from that population who had been in institutions or mental hospitals. Post believed from his conversations with welfare workers that several other reports of low prevalence were underestimates. Post also gave an example of a family setting where mental illness was not discovered in an elderly man until after his death when a diary was discovered in which nothing but paranoid experiences had been recorded.

2. Most of the early investigations were not conducted with the goal of studying late-onset schizophrenia. Rather, they were surveys either of schizophrenia in different age groups or of psychosis in the elderly. Hence they often neglected to give pertinent details of important variables, such as gender distribution (e.g., Kraepelin 1919/1971;

Robertson and Mason-Browne 1953; Fish 1958, 1960; Herbert and Jacobson 1967) or level of education (no studies gave this information).

3. Many studies that attempted to evaluate the prevalence of late-onset schizophrenia either among schizophrenic patients from various age groups or among elderly psychiatric patients were not true prevalence surveys. Their denominator population usually consisted of series of unselected patients (instead of, say, all the schizophrenic patients from a specific catchment area).

4. Some investigators did not include appropriate control groups. For example, family studies of late-onset schizophrenic patients often failed to include age-comparable normal controls and patients with onset of schizophrenia at a younger age from similar populations (Kay and Roth 1961; Post 1966; Herbert and Jacobson 1967; Larson and Nyman 1970; Huber et al. 1975; Rabins et al. 1984).

**Methods.** 1. Many studies did not mention the criteria used for diagnosing schizophrenia, affective disorders, or organic mental syndromes (Robertson and Mason-Browne 1953; Kay and Roth 1961; Retterstøl 1966; Larson and Nyman 1970).

2. A number of studies were based on retrospective chart reviews (Kay and Roth 1961; Larson and Nyman 1970; Rabins et al. 1984) or on assessments done by clinicians other than the investigators (Angst et al. 1973; Bland 1977).

3. As noted earlier, there has been considerable confusion in the terminology used by different

authors; e.g., the term "late onset" has been used to connote onset after age 40, 45, 60, or 65.

4. Followup periods were variable. Some patients were followed for only several months (Herbert and Jacobson 1967), while others were followed for 10 to 30 years. Kraepelin's paraphrenic cases were followed by Mayer (1921) and Mayer-Gross (1932). Other long-term followups were done by Kay and Roth (1961), Post (1966), and Bleuler (1972).

5. Investigations into specific areas such as sensory loss are especially difficult to evaluate. Studies looking at sensory loss in late-onset schizophrenic patients often did not give their methods of evaluating the sensory loss (Kay and Roth 1961; Herbert and Jacobson 1967).

6. Most investigations did not describe treatment response, neuropsychological performance, or any major biological parameter.

It should be stressed in defense of the studies in table 1, however, that clinical research into a number of other psychiatric disorders during the same time period was methodologically similar—i.e., it focused on clinical descriptions instead of on controlled studies of specific disorders. Furthermore, when we reanalyzed the published data to take into account relevant variables, we found more similarities than differences in the results with respect to late-onset schizophrenia.

**Epidemiology.** Table 1 lists studies that looked at certain epidemiological aspects of late-onset schizophrenia in relatively large populations of patients. (Patients said to have late-onset

paraphrenia have been included in the category of late-onset schizophrenia.) We excluded case reports.

**Prevalence.** As stated earlier, a major drawback in many investigations of the prevalence of late-onset schizophrenia was that the case samples came from a series of unselected patients. Hence, in the discussion below, we have preferred the term "proportion" to "prevalence." Eight studies reported on the occurrence of late onset (generally defined as onset after age 40) among schizophrenic patients from various age groups (Kolle 1931 [who included two different populations of patients]; Fish 1958; Retterstøl 1966; Larson and Nyman 1970; Bleuler 1972; Huber et al. 1975; Bland 1977). The weighted mean proportion (weighted by sample size) of late-onset schizophrenia in these eight studies was 23.5 percent with the range being 15.4 percent (Retterstøl 1966) to 32.0 percent (Larson and Nyman 1970). Kraepelin (1919) and Schulz (1933) specifically excluded paraphrenic patients from their populations with dementia praecox. The mean proportion of late-onset schizophrenia in these two reports was only 5.6 percent. As discussed earlier, however, the distinction between paraphrenia and schizophrenia is unclear.

Robertson and Mason-Browne (1953), Müller (1959), and Larson and Nyman (1970) examined the proportion of late-onset schizophrenia among elderly schizophrenic populations. The mean was 31.0 percent. The remaining investigations included either surveys of all elderly psychiatric patients or only late-onset schizophrenic patients.

**Table 1. Studies of late-onset schizophrenia**

Author	Patient population	Total	Diagnostic criteria	n with late onset	Distribution of age of onset			Female:male	Comments
					Age	n	n		
Kraepelin (1919/1971)	Patients with diagnosis of dementia praecox excluding paraphrenia	1,054	Paraphrenia—paranoia & hallucinations, later age of onset, no progression to dementia, no affective blunting or thought disorder	61	41-45 46-50 51-55 56-60	35 13 11 2	Predominance of women	Kraepelin stated that at least 40% of patients diagnosed as paraphrenia would progress to dementia praecox	
Mayer (1921)	Followup of Kraepelin's paraphrenic patients	78	Kraepelin's definition of paraphrenia	78	?	?	?	>40% developed course of dementia praecox	
Kolle (1931)	Schizophrenic patients	889	Schizophrenia—Schneider's first-rank symptoms	142	41-60 >60	88 54	?		
Kolle (1931)	Schizophrenic patients	182	Schizophrenia—Schneider's first-rank symptoms	33	41-60 >60	33 0	?		
Schulz (1933)	Schizophrenic patients, excluding paraphrenia	660	Late-onset schizophrenia—onset after 40	35	?	?	?		
Bleuler (1943, 1972)	Late-onset schizophrenic patients	730	Late-onset schizophrenia—onset after 40, not secondary to organic pathology	130	40-44 45-49 50-54 55-60 >60	45 43 21 16 5	1.9:1	Drop in incidence of late-onset schizophrenia over age 60, according to Bleuler, was due to choosing an involutional diagnosis in preference to paraphrenic or schizophrenic diagnosis	
Lehler (1950)	Psychiatric inpatients over age 65	355	Late-onset schizophrenia—onset after 40	30	?	?	?	In those with onset after 65, 14 of 18 cases of late-onset schizophrenia misdiagnosed as arteriosclerotic or senile dementia	
Robertson & Mason Browne (1953)	Female patients over 60, hospitalized between 1946 and 1951, with paraphrenia or schizophrenia	23	Not stated	3	All had age >60		All women		

Table 1. Studies of late-onset schizophrenia—Continued

Author	Patient population	Total	Diagnostic criteria	n with late onset	Distribution of age of onset		Female: male	Comments
					Age	n		
Fish (1958)	Female chronic schizophrenic patients from all wards of a mental hospital except geriatric ward	110	Schizophrenia with onset after 40	22	40-49 50-59 >60	13 9 1	All women	Fish felt that the number with late-onset schizophrenia may have been underestimated due to exclusion of geriatric wards. Clinical picture did not differ from patients with onset before age 40
Müller (1959)	101 elderly patients with schizophrenia	101	Schizophrenia with onset after 40	34	41-60 >60	29 5	?	
Fish (1960)	All hospitalized psychiatric patients over 60	264	Schizophrenia with onset over 40	16	>50 51-59 61-71	5 4 7	?	No distinctive clinical picture
Kay & Roth (Roth 1955; Kay & Roth 1961; Kay 1963)	Hospitalized patients with late paraphrenia. Authors examined 42 patients & reviewed 57 patients' charts	99	Late paraphrenia—paranoid symptoms with complex delusions & occasional hallucinations not secondary to organic or affective disorder, age of onset >60	99	All had onset after age 60		7:1	Paraphrenics constituted 10% of all admissions over age 60. Authors concluded that schizophrenia in old age manifested as paraphrenia
Stjögren (1964)	Swedish mental hospital patients over age 70, with "functional" psychiatric disorders	649	Late paraphrenia, as per Kay & Roth (1961)	202	?		?	
Reitersjöel (1966)	84 paranoid schizophrenic patients	84	Late-onset schizophrenia—onset after 40	13	40-49 >50	10 3	?	
Herbert & Jacobson (1967)	All hospitalized patients age >65 examined & followed for several months	47	Late paraphrenia: age >65 on admission, systemized delusions with or without hallucinations in clear consciousness. Onset <55, senous dementia & chronic schizophrenia excluded	47	(Age at admission) 65-69 70-74 75-79 80-84 85+	9 11 13 10 4	45:2	Most had personality traits that could be grouped as either paranoid or schizoid. Only 4 considered cheerful, social & warm
Larson & Nyman (1970)	All schizophrenic males admitted to a mental ward &	153	Late-onset schizophrenia—age of onset >40 Chart review	49	41-50 51-60 61-70	28 16 3	All men	



				71-80	2	
Angst et al. (1973)	born between 1881 & 1900 709 schizophrenics from 7 institutions in 5 countries	709	Schizophrenia with onset after 40	?	Of the paranoid group (number not stated), onset ages 41-50 64% >50 36%	?
Huber et al. (1975)	644 schizophrenics admitted to a hospital between 1945 & 1959	644	Late-onset schizophrenia—criteria same as Bleuler's. Also included Schneider's first-rank symptoms. Average years of followup: 17.8	110	84 23 3	1.8:1
Bland (1977)	6,064 first admissions for schizophrenia	6,064	ICD-8	1,555	878 467 155 47 8	5:3
Blessed & Wilson (1982)	All patients over 65 admitted to hospital in 1976. Chart review	320	Late paraphrenia, as per Roth (1955)	28	11 17	6:1
Rabins et al. (1984)	35 patients with late paraphrenia (2.7% of admissions over age 44). 25 late paraphrenics studied prospectively; charts of other 10 reviewed	35	Late paraphrenia as defined by Kay & Roth (1961), except for age of onset >44 years	35	16 19	10.7:1

**Distribution of Age of Onset:**

Ten studies (Kolle 1931 [who included two different populations of patients]; Fish 1958, 1960; Müller 1959; Larson and Nyman 1970; Bleuler 1972; Huber et al. 1975; Bland 1977; Rabins et al. 1984) reported on the differences in proportion of schizophrenia with age of onset before and after age 60. When the numbers from these reports are combined, the weighted mean proportion of late-onset (usually after 40) schizophrenia before age 60 is 86 percent and that after age 60 is 14 percent.

A further breakdown of the distribution of age of onset of schizophrenia is possible on the basis of data from Bleuler (1972), Fish (1958, 1960), Larson and Nyman (1970), Huber et al. (1975), and Bland (1977). In these five investigations, the weighted mean proportion of late-onset schizophrenia in the fifth decade of life was 57.5 percent, that in the sixth decade 30.2 percent, and after age 60 it was 12.3 percent.

Thus, in the studies reviewed, approximately 13 percent of all schizophrenic patients had onset of symptoms in the fifth decade, 7 percent in the sixth decade, and 3 percent thereafter. These proportions may appear to be much greater than those in the common clinical experience. The reasons are probably twofold. The above-mentioned reports may have exaggerated the prevalence of late-onset schizophrenia, partly because of difficulties in precisely dating the onset of schizophrenia—i.e., some of the so-called late-onset patients might have had schizophrenic symptoms since earlier in life. On the other hand, it is highly likely that schizophrenia tends to be under-

diagnosed in patients with late onset of psychotic symptoms because of various factors discussed previously. Well-designed prospective investigations are needed to establish the exact incidence and prevalence of late-onset schizophrenia. Nonetheless, it is fair to suggest that onset of schizophrenia after age 40 is far from rare.

**Gender Difference.** Without exception, all the studies that included both male and female patients with late-onset schizophrenia reported a predominance of women (table 1). The lowest female:male ratio was 1.9:1 (Bleuler 1943, 1972), and the highest ratio was 45:2 (Herbert and Jacobson 1967). The study by Bland (1977) suggested that the female:male ratio increased with an increase in age at first hospitalization for schizophrenia. This is in contrast to the consistently higher treated incidence rates for early-onset schizophrenia in males than in females, particularly between the ages of 15 and 34 (Babigian 1985).

It is very unlikely that the small difference (of about 2 years) in the mean longevity of men and women provides an adequate explanation for the female predominance in late-onset schizophrenia. Seeman (1982) gives several alternative hypotheses: (1) There may be two forms of schizophrenia—a juvenile-onset form with a higher incidence in men, and a late-onset form with a higher incidence in women. (2) There is commonly an accumulation of nonspecific stressors that mainly affect males during adolescence. (3) There may be specific biological protective factors in the female, such as relatively bilateral representation of left-hemisphere functions or relative dopaminergic

inhibition by estrogens. Careful research into this important area is necessary.

**Family Studies.** Some specific difficulties are encountered in studying the families of late-onset schizophrenic patients. For example, migration of family members may make it difficult to locate and evaluate them. It is not often easy to find contemporaries to provide information about family members. The risk period for possible development of a late-onset schizophrenic disorder is long, requiring that family members ideally be followed until death. If death occurs earlier in life, there is no way to determine if a schizophrenic disorder would have developed. There are also difficulties in the diagnosis of late-onset schizophrenia in relatives without personal and careful evaluation. As mentioned earlier, such patients frequently carry a diagnosis other than schizophrenia.

Table 2 summarizes family studies of probands with late-onset schizophrenia. The study by Funding (1961) was excluded because schizophrenic patients were not separated from affective disorder patients among their late-onset psychotic probands. Two limitations of most of these studies are that they did not describe their method of identifying family members; nor did they give the number of family members on whom information was not available (e.g., due to death at a young age or migration).

**Findings.** Four studies (Bleuler 1943; Kay and Roth 1961; Herbert and Jacobson 1967; Larson and Nyman 1970) looked at the overall prevalence of schizophrenia in siblings of probands. With the exception of Larson and Nyman (1970), they also included parents

of late-onset schizophrenic probands. The combined mean prevalence was 7.2 percent in siblings and 2.9 percent in parents. Huber et al. (1975) and Rokhlina (1975) looked at the prevalence of schizophrenia among all relatives. The mean prevalence was 15.1 percent. Rokhlina (1975) found a 10.8 percent prevalence of schizophrenia in relatives of late-onset schizophrenic patients compared with a 17.7 percent prevalence in relatives of early-onset schizophrenic patients. Affective disorders were rare in relatives of late-onset schizophrenic patients (Huber et al. 1975; Rokhlina 1975; Rabins et al. 1984), except in the studies by Klages (1961) and Post (1966).

The data on the age of onset of illness in schizophrenic relatives of late-onset schizophrenic probands are sparse. According to Bleuler (1943), such probands have comparable numbers of relatives with early- and late-onset schizophrenia.

The results of family studies of late-onset schizophrenia, despite their limitations, may be compared to those of schizophrenia in general. According to Weiner (1985), the risk of schizophrenia in siblings of schizophrenic probands in different studies ranges from 3 percent to 14 percent, while that in parents is 0.2 percent to 12 percent. Thus, it appears that the prevalence of schizophrenia in the first-degree relatives of late-onset schizophrenic probands is greater than that in the general population, but lower than that in the first-degree relatives of earlier-onset schizophrenic patients.

### **Other Characteristics of Late-Onset Schizophrenia**

**Main Symptoms.** According to

most studies, the symptoms of late-onset schizophrenia are similar to those of earlier-onset schizophrenia, especially the paranoid type. Fish (1960) noted that the clinical picture of 23 middle-aged and elderly schizophrenic patients did not differ from the clinical picture in patients with onset before age 40. In

seven out of nine patients with onset between 50 and 59 years, auditory hallucinations were a prominent feature.

Kay and Roth (1961) reported that delusions were more or less systematized and "fantastic." They were usually persecutory, but also exotic, hypochondriacal, or grandiose. In 28 percent of the

cases, feelings of mental or physical influence were found. Auditory hallucinations developed in 75 percent of the cases. Visual, tactile, and olfactory hallucinations also occurred. Incoherence of talk and even neologisms were seen in cases of long duration. Verbosity, circumstantiality, or irrelevance was found in about 30 percent of

**Table 2. Family studies of late-onset schizophrenic patients**

Investigators	Number of probands	Prevalence of schizophrenia in first-degree relatives	Prevalence of other psychiatric disorders in family	Risk of late-onset schizophrenia
Bleuler (1943)	65	9.8% in sibs; 4.4% in parents (6 of 24 affected relatives had "probable schizophrenia")	?	9 relatives had late-onset (& 15 early-onset) schizophrenia
Kay (1959); Kay & Roth (1961)	99 (including 57 from Sweden & 42 from U.K.)	Risk for schizophrenia between ages 18 & 50: 2.1% in parents 4.9% in sibs 6.3% in children (of 57 Swedish probands)	?	8 relatives of 99 late-onset schizophrenic probands (but only 2 relatives of 200 affective disorder patients)
Klages (1961)	53	8 first-degree relatives	7 depressives	
Herbert & Jacobson (1967)	45 women	2.2% in parents 2.3% in sibs	6 fathers psychopathic 2 alcoholic	Risk much greater in female than male relatives
Larson & Nyman (1970)	153 male schizophrenic patients (including 49 with late-onset)	Overall risk in sibs 11.6% 16 out of 64 schizophrenic sibs developed symptoms after 40	?	
Huber et al. (1975)	110	19.4% among all relatives	None with affective disorders	
Rokhlina (1975)	65	10.8% in relatives of late-onset schizophrenics & 17.7% in relatives of early-onset schizophrenics	2% relatives of late-onset & 6.6% of early-onset schizophrenics had affective psychoses	
Post (1966)	93	5 relatives with schizophrenia (including 2 with late onset)	16 affective disorders; 27 personality disorders & alcoholism; 8 organic disorders (including epilepsy)	
Rabins et al. (1984)	35	5 probands (vs. 3 of 35 depressed controls) had a family history of schizophrenia	No probands (vs. 12 of 35 depressed controls) had family history of affective disorder	

the cases. Some emotional blunting, mild incongruity, or euphoria was quite common in chronic patients. Kay and Roth (1961) felt that over time the clinical picture became indistinguishable from that seen in chronic schizophrenia. In 25 percent of cases, marked fluctuations in behavior continued for years. Sometimes, the illness eventually became "burnt out," leaving residual defects.

Post (1966) found that 60 percent of his 65 treated patients had "depressive admixtures." In longstanding cases, negative symptoms similar to those of other forms of schizophrenia were common.

Robins et al. (1984) observed that the symptoms in paraphrenic patients were similar to those suffered by patients diagnosed as having schizophrenia. Of the 35 paraphrenic patients, 24 suffered from hallucinations and 22 had Schneiderian first-rank symptoms. These numbers were significantly higher than those for affective disorder controls. Of 35 patients, 21 met the *DSM-III* criteria for schizophrenia, and 11 for schizophreniform disorder if the criterion requiring onset before age 45 was disregarded.

In our (Jeste et al. 1987) pilot study of 15 patients who met *DSM-III-R* criteria for late-onset schizophrenia, 14 patients were noted to have paranoid delusions while 6 patients also had auditory hallucinations.

**Sensory Deficits.** Auditory and visual deficits have been noted by English investigators in a sizable portion of the paraphrenic population. Cooper (1976) reviewed the literature concerning the relationship between deafness and psychiatric disorders in general. He concluded that the prevalence

of schizophrenia in the prelingually deaf was not significantly different from that in the normal population, whereas the postlingually deaf were overrepresented among samples of patients suffering from paranoid psychoses in later life. The following studies specifically looked at sensory deficits in the patients with late-onset paranoid psychosis.

Kay and Roth (1961) studied 42 patients with late paraphrenia from a British hospital and 57 comparable patients from a Swedish hospital. Visual defects were found in approximately 15 percent of cases, about half of those being severe. According to the authors, this percentage did not differ significantly from that in control groups of comparable age. (The control group was not clearly defined; it probably included affective disorder patients.) Some impairment of hearing was found in 40 percent of the British patients; in 15 percent, it was of marked degree. In Sweden only the most severe cases of hearing loss had been recorded, and their prevalence was 16 percent. The frequency in patients with affective disorders, on the average 3 years younger, was only 7 percent. The presence of visual or hearing loss did not seem to modify the symptomatology of paraphrenia greatly. Kay and Roth (1961) considered that deafness, along with abnormalities of personality and loss of many relatives, contributed to more social isolation in the paraphrenic population than in affective disorder patients. (The method of assessing visual and hearing loss was not stated.)

Post (1966) found that deafness was present in 25 percent of 72 elderly paranoid disorder patients, compared to only 11 percent of elderly depressives. The method

used to assess hearing loss was not specified.

Herbert and Jacobson (1967) studied 45 late-paraphrenic patients and found moderate to severe visual loss in one or both eyes in 47 percent of the patients. In 12 cases (27 percent), critical visual defects in both eyes were present. Forty percent of the patients had moderate to severe auditory loss. No controls were used in this study.

Cooper and Porter (1975) examined the association between ocular pathology and functional psychoses in 54 paranoid and 57 affective elderly patients. Appreciable ocular pathology was found in 30 paranoid and 21 affective disorder patients. Significantly more cataracts were detected among the paranoid patients than among the affective disorder patients.

Cooper and Curry (1976) studied 27 paranoid and 18 affective disorder patients who were deaf before the onset of their psychosis. A significant association emerged between paranoid illness and bilateral conductive deafness which had an earlier age of onset, longer duration, and greater severity than the forms of sensorineural deafness found in affective disorder patients.

In sum, there is some suggestive evidence for a higher-than-normal prevalence of visual and, especially, auditory deficits in late-onset schizophrenic patients. Important methodological problems in the published studies make it difficult, however, to draw any etiopathological inferences.

**Abnormal Personality Traits.** Abnormal personalities were noted in the late-paraphrenic population by the following

groups of investigators.

Kay and Roth (1961) reported that paraphrenic patients without hallucinations (20 percent of the total patient sample) had longstanding personality abnormalities that interfered with interpersonal relationships. The onset of psychosis in these patients was difficult to date, and relatives tended to regard it as a caricature of the premorbid personality. Another third were described as explosive or sensitive. In 45 percent of the cases, the personality traits found were predominantly of paranoid and schizoid type (jealousy, suspiciousness, arrogance, egocentricity, emotional coldness, and extreme solitariness). The authors concluded that abnormalities of personality were present in a large proportion of the patients and were probably related to the frequent failure to marry, the low fertility, and the social isolation.

Herbert and Jacobson (1967) excluded from their paraphrenic category patients with premorbid personality traits that had been disabling enough to prevent them from coping with their environment. Out of 45 patients with late paraphrenia so diagnosed, only 4 were considered to have been lacking abnormal personality traits. The others were mostly schizoid or paranoid.

Kay and Roth (1961) and Herbert and Jacobson (1967) reported that a large number of their paraphrenic patients were unmarried and childless. These investigators did not provide data on age-matched controls, however.

Rabins et al. (1984) found that 10 of 35 paraphrenic patients were married, compared to 17 of 35 age- and sex-matched affective disorder controls. These researchers also noted that 22 of 35

paraphrenic patients, compared with 28 of 35 affective disorder controls, had children. Neither of these differences was significant.

**Brain Lesions.** Miller et al. (1986) found evidence of an "occult" neurological disorder in five late-onset schizophrenic/paraphrenic patients. We (Jeste et al. 1987) have been studying late-onset schizophrenic patients with a neuropsychological battery and magnetic resonance imaging (MRI). Our preliminary results suggest that a subset of these patients has neuropsychological impairment and structural brain abnormalities on MRI, while another subset is normal (for age) on neuropsychological performance and MRI scans.

**Course and Prognosis.** All four investigations of the course and prognosis of late-onset schizophrenia concluded that the course tended to be chronic, and prognosis unfavorable. Kay and Roth (1961) found prognosis to be poor. In Graylingwell, recovery was reported to be very rare. All but 4 of the 24 cases known to be alive after 5 years were still hospitalized. Of the 14 deaths, only 2 took place after discharge and neither of these patients was discharged under supervision. About half the remaining lifespan was spent in mental hospitals or similar institutions. Post (1966) reported that life expectancy was normal, but prognosis with regard to loss of symptoms was poor. Herbert and Jacobson (1967) found that prognosis in their 45 late-paraphrenic patients was poor and the course was chronic. Of the 45 patients admitted, 29 were discharged. Fourteen of these were readmitted, but eight were discharged again after a short

stay. Within 1 year, two patients were readmitted and, within 2 years, one more patient was readmitted. Of the 16 patients who remained in the hospital, 10 were over age 75 and showed intellectual deterioration. There were eight deaths (length of followup is not given). Fish (1960) was able to discharge only 3 of 110 senile schizophrenic patients between 6 and 12 months after admission. One patient had relapsed, one was lost to followup, and another patient claimed that she was doing well in a letter to the author, which he felt was not very reliable information.

**Treatment.** Only a few recent studies of late-onset schizophrenia have looked at the treatment response of these patients. Janzarik (1957), as cited by Post (1966), studied 50 elderly schizophrenic patients with onset of symptoms after age 60 and noted that electroconvulsive therapy (ECT) and medications (chlorpromazine was mentioned in one case; other medications used were not specified) produced temporary remissions. Kay and Roth (1961) reported temporary remissions occurring spontaneously, with ECT or with "tranquilizers" (these were not identified) in about 25 percent of the patients treated at Graylingwell. Twelve of 43 patients received ECT; seven of them improved and were discharged. On followup, only one patient remained symptom free. The authors felt that the small number of patients considered appropriate for ECT and the poor response to it were further evidence that late paraphrenia was not a primary affective disorder.

Post (1966) followed 93 late-onset schizophrenic patients who were

divided into two groups according to phenothiazine treatment. Twenty-two patients had received either no neuroleptic treatment or inadequate dosage. Only one of these patients had remission during the 16-month followup period. Seventy-one patients received at least short-term adequate treatment, usually with trifluoperazine (10–30 mg/day) or thioridazine (50–400 mg/day). Six of these patients had no response, 22 had moderate improvement, and 43 had complete remission. Sixty-five patients were followed for 12–41 months. Twenty-two patients remained free of all psychotic symptoms after initial treatment; 25 patients had symptoms for periods of varying length; and 18 remained psychotic throughout the followup period, though in most cases there was some improvement.

The long-term outcome with regard to the number of patients spending greater than 25 percent of their time in the hospital differed similarly with treatment. The numbers were as follows: 7 of 19 patients without neuroleptic treatment, 4 of 16 patients given initial adequate treatment but not maintained on medication, and only 2 of 21 patients maintained on medication remained hospitalized greater than 25 percent of the time. Treatment also resulted in significant improvement in psychotic symptoms (compared to no treatment). Neuroleptics did not, however, produce an improvement equal to the premorbid level of social adjustment. They also had little effect on the development of insight in a majority of patients.

Herbert and Jacobson (1967) treated 38 patients diagnosed as having late paraphrenia with trifluoperazine. Pharmacotherapy

was considered “impressive” in controlling aggression and irritability, and therefore helped in promoting discharge and keeping patients out of the hospital. (The length of followup, symptoms that responded to medication, dosage, and length of treatment were not given.)

Rabins et al. (1984) reported that 35 patients with a diagnosis of late-onset schizophrenia or paraphrenia were treated with neuroleptics and psychosocial therapies. (The types of neuroleptic, dosage, and length of treatment were not given.) On discharge, 20 patients were symptom free, 10 symptomatic but improved, and 5 symptomatically unchanged. A 2-year followup was done on 14 patients over age 60. Four patients remained symptom free, six patients had relapses with symptom-free periods, and three patients had chronic symptoms. With the exception of one patient who had suffered a stroke, all patients were living at home. (Whether these patients over age 60 were continued on neuroleptics after discharge is not known.)

In summary, a sizable proportion of late-onset schizophrenic patients improved with neuroleptic treatment. Aspects such as type of neuroleptic, dosage, blood levels, side effects, and degree of improvement in specific symptoms have not been sufficiently investigated. Also, there have been no double-blind, controlled studies similar to those conducted in younger patients. Nonetheless, the clinical impression that a number of late-onset schizophrenic patients are helped by neuroleptics is comparable to the experience with younger schizophrenic patients.

## Clinical and Research Implications

There is little debate about the fact that schizophrenia-like symptoms can develop for the first time in middle and late adulthood. In some of these cases, the patients clearly have major affective disorders, organic mental syndromes, or paranoid disorders. The main question is whether a syndrome that may be called “schizophrenia” occurs with any regular frequency after age 40 (or 44). In this regard, two specific problems must be recognized: (1) The validity of psychiatric diagnoses is often more difficult to establish than that of most other medical diagnoses because of an absence of suitable laboratory procedures (Rosenhan 1973). (2) Schizophrenia is, in all probability, not a single disease but a syndrome with multiple subtypes (see Jeste et al. 1982).

The literature we have reviewed suggests that investigators have diagnosed new-onset schizophrenia or paraphrenia after age 40 in a sizable proportion of patients. Furthermore, a number of researchers have failed to find any distinctive differences in course of illness between schizophrenia and paraphrenia. Late-onset schizophrenia is characterized by paranoid symptomatology, premorbid personality traits of schizoid or paranoid type, a tendency toward chronicity, and symptomatic improvement with neuroleptics.

Spitzer and Williams (1985) have discussed certain relatively objective methods for demonstrating validity other than face validity (which requires only consensus among observers). These include (1) descriptive validity, in which the characteristic features are unique; (2) predictive

validity, in which followup studies indicate a homogeneous course, complications specific to that disorder, and a differential treatment response; and (3) construct validity in which a familial pattern, biological abnormality, or relationship to environmental variables helps to explain etiology of a disorder.

It will obviously be difficult to quantify the validity of late-onset schizophrenia, or even of the overall schizophrenic syndrome, using these criteria. Nevertheless, the general similarities between late-onset and early-onset schizophrenia (including the results of family studies) suggest that the late-onset form is probably no less valid than the early-onset variety. Whether late-onset and early-onset schizophrenia are distinct subtypes (biologically or otherwise) or are merely forms of the same schizophrenic spectrum differing in age is unclear.

A number of important questions related to late-onset schizophrenia remain unanswered. What are the factors that protect these patients from a schizophrenic breakdown until later in life? Why is there a high preponderance of women in this group? How do these patients compare with age- and education-matched normal controls as well as earlier-onset (18-44 years) schizophrenic patients in their neuropsychological performance, structural brain abnormalities, psychosocial stressors, and family constellation? The treatment-response patterns of the late-onset schizophrenic patients also deserve a special study. Several reports indicate that elderly subjects have significantly higher blood levels of neuroleptics than younger patients given similar dosages (Mårtensson and Roos 1973; Jeste et al. 1981;

Yesavage et al. 1982). Similarly, the risk of tardive dyskinesia has been noted to be higher in schizophrenic patients with later age of onset of psychosis. (Yassa et al. 1986; Waddington and Youssef 1986).

### Suggestions for Future Research

There is a great need for careful research into late-onset schizophrenia. Among the methodological improvements that might be made in this area are the following:

- To reduce confusion in terminology, a single set of diagnostic criteria should be used. We prefer the nomenclature in the *DSM-III-R* (American Psychiatric Association 1987), which offers an operational definition of late-onset schizophrenia. Terms such as paraphrenia, which have been employed inconsistently, should be avoided.

- Diagnostic assessment should give special consideration to ruling out major affective disorders, organic mental syndromes, and delusional (paranoid) disorders. This will entail obtaining detailed past and family history (of possible affective disorder), and use of appropriate laboratory evaluations (e.g., thyroid function tests) to exclude "organic" causes of late-onset psychosis.

- Special efforts need to be made to ascertain the age of onset of schizophrenia. A thorough review of past medical records and interviews of "significant others" are necessary to rule out the possibility of an undiagnosed schizophrenic disorder before age 45.

- Prevalence surveys of late-onset schizophrenia should include the entire predefined population base (e.g., all the

schizophrenic patients from a given catchment area).

- Prospective, long-term followup investigations are necessary to determine the course of the illness.

Hypothesis-oriented clinical, neuropsychological, and biological evaluations of this patient population are indicated.

- The likelihood that late-onset schizophrenia is not a homogeneous entity but is a syndrome with clinically and biologically relevant subtypes should be considered in research in this field.

- It is important to determine the relative risk:benefit ratio with neuroleptics (as well as other treatments) in late-onset schizophrenic patients.

- Appropriate control groups, such as normal subjects matched for age, gender, level of education, and socioeconomic status, and adult-onset (18-44 years) schizophrenic patients matched for severity of psychopathology, are essential for interpreting any observed "abnormalities" in late-onset schizophrenic patients.

Research into late-onset schizophrenia promises to improve our understanding of schizophrenia in general.

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