

# Schizophrenia and delusional disorders with onset in later life

## Esquizofrenia e transtornos delirantes com início na terceira idade

Anne Hassett

University of Melbourne, North Western Aged Persons Mental Health Program, Australia

**Abstract** Schizophrenia-spectrum illness is most commonly associated with an onset in early adulthood. When non-affective psychotic symptoms emerge for the first time in later life, the clinical presentation has both similarities and differences with earlier-onset syndromes. This situation has resulted in continuing debate about the nosological status of late-onset psychosis, and whether there are particular risk factors associated with this late-life peak in incidence. Although early cognitive decline is frequently identified in these patients, studies, to date, have not established if there is a relationship with the dementing illnesses of old age. Sensory impairment, social isolation, and a family history of schizophrenia have been associated with late-onset psychosis, but appear to exert a nonspecific influence on vulnerability. While diagnostic issues remain unresolved, clinicians need to formulate treatment strategies that most appropriately address the constellation of symptoms in the clinical presentation of their psychotic elderly patients.

**Keywords** Schizophrenia. Psychotic disorders. Psychoses. Cognition. Social isolation. Aged.

**Resumo** *Transtornos mentais do espectro da esquizofrenia são comumente associados a início na primeira fase da vida adulta. Quando sintomas psicóticos não-afetivos emergem pela primeira vez em fases tardias da vida, a apresentação clínica tem semelhanças e diferenças em relação às síndromes de início precoce. Essa situação resultou em debate contínuo sobre o status nosológico da psicose de início tardio e sobre se há fatores de risco associados a esse pico de incidência na terceira idade. Embora déficits cognitivos precoces sejam frequentemente identificados entre esses pacientes, ainda não foi possível estabelecer se problemas cognitivos estão associados a um quadro demencial dos idosos. Comprometimento sensorial, isolamento social e história familiar de esquizofrenia têm sido associados à psicose de início tardio, mas esses fatores de risco parecem exercer um papel não-específico sobre a vulnerabilidade. Ainda que as questões sobre o diagnóstico mais adequado para esses quadros clínicos permaneçam não resolvidas, os psiquiatras precisam formular estratégias de tratamento que levem em consideração a complexa constelação de sintomas da apresentação clínica de pacientes idosos psicóticos.*

**Descritores** *Esquizofrenia. Transtornos psicóticos. Psicoses. Cognição. Isolamento social. Idoso.*

### Introduction

The emergence of psychotic symptoms for the first time in later life poses a diagnostic challenge for clinicians assessing and treating elderly persons with mental illness. In these situations clinicians are frequently confronted with comorbidity issues relating to cognitive deficits, affective symptomatology, and physical illness. Most commonly, late-onset delusions and hallucinations are associated with dementing and affective disorders; however, in a small but

substantial number of cases these symptoms arise de novo. Whether schizophrenia or delusional disorder can be diagnosed in these situations has been the subject of considerable debate since Roth<sup>1</sup> first proposed that 'late paraphrenia' was a variant of schizophrenia unique to late life. The following discussion will examine issues relevant to this debate, and the resulting implications for the management of elderly psychotic patients. As the nomenclature for psychotic states arising in later life has been a contentious point, the

term 'late-onset psychosis' will be used to designate psychotic symptoms arising in later life when the primary diagnosis is neither dementia nor an affective disorder.

### **Epidemiology, diagnostic issues and possible risk factors**

Problems with case ascertainment have bedevilled the investigation of the prevalence of psychotic symptomatology among the elderly population. There is now a general consensus that significant under-reporting of paranoid ideation is likely because elderly psychotic individuals are often socially isolated and suspicious about revealing their concerns.<sup>2</sup> This issue was highlighted by Christenson and Blazer who found that, whilst 4% of an elderly community-dwelling sample had persecutory delusions, less than half of these individuals were receiving any psychiatric care.<sup>3</sup> In their review of 15 population-based studies of late-onset psychosis, Henderson & Kay<sup>4</sup> reported prevalence rates from 0.1% to 8.9%. More recent surveys by Henderson et al,<sup>5</sup> and Forsell & Henderson,<sup>6</sup> found rates of 5.7% and 6.3% respectively. Sample selection, particularly relating to age cut-off, inclusion of comorbid cognitive impairment, response rate and assessment methodology, are obvious factors which influence the variance noted in these studies.

In clinical samples Barclay & Almeida<sup>7</sup> have highlighted the nosological issues which contribute to a continuing lack of clarity in classifying psychotic disorders in late life. Reviewing recent studies of the area they noted that little progress had been made, although a recent International Consensus Statement<sup>8</sup> had attempted to address inconsistencies in nomenclature and age cut-offs. This group proposed that a nosological separation could be made between late-onset schizophrenia (onset between 40 and 60 years) and very-late-onset-schizophrenia-like psychosis (onset after 60 years). Implicit in this subtyping is the notion that, with increasing age, the syndromal presentation of psychosis is more likely to vary from younger age groups. As Barclay & Almeida<sup>7</sup> concluded, the utility of this approach has yet to be tested; however, it would appear to more appropriately reflect the 'real life' situation with which clinicians are faced in assessing elderly psychotic patients.

The evidence for possible risk factors contributing to psychosis developing for the first time in later life has been extensively reviewed by Almeida et al.<sup>9</sup> Family history studies suggest that, while hereditary factors are present, they are less influential than in earlier-onset schizophrenia.<sup>2,10</sup> These studies are, however, methodologically problematic as late-onset patients often have few remaining relatives, and/or have lost contact with those who are still alive.<sup>11,12</sup> Further, females have been noted to exceed males in late-onset psychosis samples by six- to ten-fold.<sup>10,13,14</sup> This gender imbalance is not fully explained by the greater longevity of women, and is at variance with the much closer female-to-male ratio in early-onset schizophrenia.<sup>10</sup> The anti-dopaminergic effect of oestrogen has been postulated as conferring some protection for premenopausal women who are genetically predisposed to developing schizophrenia.<sup>15,16</sup> Häfner et al<sup>15</sup> have suggested,

therefore, that oestrogens may modulate both the age distribution of onset, and symptom severity in women, but not in men. According to this hypothesis, the presence of oestrogen should potentially delay the onset of psychosis in vulnerable women, or attenuate symptom severity in women with an early onset of illness, at least until after the menopause. Taking up this issue, Howard et al.<sup>17</sup> pointed out that there is frequently a time lag of several decades between the menopause and the late-life peak for psychosis. These authors proposed that falling oestrogen levels per se were unlikely to determine symptom onset, but that the significance of oestrogen withdrawal in postmenopausal females may lie in a subsequent increased vulnerability to cerebrovascular disease, which could be a risk factor for late-onset psychosis.

The role of brain degenerative processes in late-onset psychosis has been investigated in a number of studies.<sup>18-20</sup> Brain imaging studies have looked for focal structural abnormalities, comparing late-onset with earlier-onset psychosis cases, as well as cases of clear-cut dementia. Although abnormalities have been noted in late-onset psychosis, these changes have been subtle and generally similar to those found in patients with illness onset in earlier life.<sup>19,20</sup> Sachdev et al<sup>20</sup> reported larger ventricles in both early- and late-onset cases, as compared with controls. These authors did find that the late-onset cases had more signal hyperintensities than the early-onset cases and controls, particularly in the periventricular regions. They concluded that the aetiological significance of these changes was uncertain as they are also found in healthy elderly individuals. On the other hand, when only older patients are examined, i.e., over 65 years, there does appear to be increasing diversity in clinical presentation.<sup>21,22</sup> Examining the pattern of cognitive deficits and psychotic symptomatology in 47 patients with 'late paraphrenia', Almeida et al<sup>21</sup> concluded that, at least, a subgroup of these patients may be in the early phase of a dementing process. In addition, the growing literature on the psychiatric complications of dementing disorders has identified that delusions (and less frequently hallucinations) occur in 50% or more of cases, usually fluctuating over time.<sup>23,24</sup> At a clinical level, there appears to be a spectrum of late-onset presentations with both psychotic symptoms and cognitive deficits, but the course and outcome of each is not consistently related.<sup>25</sup> This complex interweaving of symptomatology requires a longitudinal perspective of a patient's illness trajectory which may not be available to the clinician undertaking a cross-sectional assessment of a psychotic elderly individual.

Sensory impairment, especially hearing loss, has been proposed in a number of studies as a possible aetiological factor in the emergence of late-onset psychotic symptoms, although caution is required in drawing any conclusions from these findings.<sup>13,26,27</sup> Firstly, samples were usually drawn from 'convenience' populations of patients, and subject numbers were relatively small. The prevalence rates of hearing impairment obtained in this way may not be representative of the broader population of late-onset psychotic individuals,

many of whom remain untreated.<sup>10</sup> Secondly, epidemiological surveys have demonstrated that more than 50% of elderly persons have some degree of hearing impairment, the majority of whom do not develop psychopathology.<sup>28</sup> Consequently, it is difficult to determine the particular relationship between such a commonly occurring problem in the elderly, and late-onset psychosis, which has a much lower base rate. Nevertheless, several authors<sup>26-28</sup> have postulated that sensory deficits, particularly hearing loss, may exert an influence as a risk factor for late-onset psychosis by reinforcing a pre-existing tendency to social isolation or withdrawal. From this perspective, hearing loss by itself would be considered relatively nonspecific as a risk factor, but one that may have an additive effect with other risk factors, e.g., genetic vulnerability, in the genesis of late-onset psychosis.

Social isolation has been cited as a factor that may predispose a vulnerable elderly person to psychosis in late life, particularly persecutory ideation.<sup>14,29</sup> Paranoid or schizoid personality features have been described in these patients, but such retrospective assessment of premorbid adjustment is problematic as psychotic symptoms may have been present for several years. Howard & Levy<sup>30</sup> highlighted this methodological difficulty in their investigation of personality traits in 25 'late paraphrenia' patients. They concluded that paranoid features were likely to be overestimated if patients were psychotic at the time of assessment. Nevertheless, from an interactive perspective, social isolation, like sensory impairment, might be a factor that could expedite the development of psychotic symptoms in elderly individuals who were already 'vulnerable' because of their personality style. Weeks,<sup>31</sup> reviewing concepts of 'loneliness' and its relationship to social isolation in old age, identified that isolated elderly persons were particularly at risk of developing faulty self-attributions which could lead to negative interpretations of the actions and intentions of others. On the other hand, psychotic elderly individuals may also become more socially isolated and withdrawn as a consequence of their illness.<sup>32</sup> As Henderson & Kay<sup>4</sup> concluded in their review of the functional psychoses of late-onset, the mechanism by which social isolation appears to have an association with these states still remains to be clarified.

### Clinical presentation

Studies have consistently found that, while patients who develop schizophrenia-spectrum illness late in life have similar positive symptoms to patients with an earlier onset of illness, they are less likely to exhibit negative symptoms or thought disorder.<sup>13,33</sup> Further, the absence of a 'disorganisation' dimension, commonly associated with a poorer prognosis in schizophrenia, was a major factor in Roth's<sup>1</sup> proposal that a schizophrenia-like syndrome emerging in old age should be differentiated as 'late paraphrenia'. Roth's intention was to emphasize that these elderly patients did not deteriorate over time like many early-onset patients. Expanding on this issue, Häfner et al<sup>15</sup> suggested that, when psychotic symptoms emerge for the first time in later life, the person's more mature

coping abilities and established personality style might have an ameliorating influence on thought disorder and the frequency of negative symptoms.

Systematised 'partition' delusions, first described by Roth,<sup>1</sup> have been particularly associated with late-onset psychosis. Pearlson et al.<sup>33</sup> defined these phenomena as "the delusion that people, gas, electricity, or some other force was entering their home through the walls from a neighbouring dwelling" (p. 1570). These authors found that this type of phenomenon was present in 48% of 54 late-onset subjects, compared to 14% of 54 early-onset subjects. Similarly, Howard et al<sup>34</sup> reported these phenomena in 68% of 50 'late paraphrenia' subjects, compared with 20% of 20 young schizophrenic subjects. These 'partition' delusions were usually persecutory in nature, i.e., the elderly person believing that the outside environment was hostile and posed a threat to their home. Social isolation has been cited as a possible predisposing factor for the development of these phenomena. Howard et al<sup>34</sup> have also suggested that the cognitive deficits noted in these patients may increase their vulnerability to paranoid misinterpretation of environmental cues.

Thus, when assessing an elderly psychotic patient who is not depressed or overtly dementing, the clinician is likely to be presented with a socially isolated elderly female who may have some hearing impairment, and elaborates a systematised persecutory delusional system that involves some threat to her home, i.e., 'partition delusions'.<sup>33</sup> Perceptual disturbance may or may not be present, thus accounting for both late-onset schizophrenia and delusional disorder being included within Roth's construct of 'late paraphrenia'. As well as auditory hallucinations, olfactory, tactile, visual and gustatory phenomena have also been noted in these patients, although there appears to be no direct correlation with specific sensory organ impairment.<sup>27,35</sup> Further, even though the patient may not fulfil criteria for dementia, the clinician is still likely to elicit a spectrum of cognitive deficits in these patients, the significance of which is becoming increasingly pertinent as new treatment options for cognitive impairment become available.

### Treatment and longitudinal course

Unfortunately, there have been few follow-up studies to guide the clinician treating a patient with late-onset psychosis in terms of prognostic indicators. It would seem reasonable to assume that those patients with greater cognitive deficits might be more at risk of subsequently developing dementia. Holden<sup>22</sup> found that a subgroup of patients with an onset of psychosis after 60 years, i.e., 'very-late-onset', had an 'organic' form of illness with a relatively poor outcome. In contrast, Naguib & Levy<sup>36</sup> found that, although cognitive deficits were noted in 47 'late paraphrenia' patients, even after a 3.7 year follow-up period these had still not progressed to a stage which would warrant a diagnosis of dementia. In terms of functional outcome, Häfner et al<sup>15</sup> suggested that developmental maturity in late-onset patients might account for less social decline than that experienced by younger psychotic patients. Of note, problems likely to be encountered in following up late-onset

patients include the compounding effect of comorbid medical illness on outcome evaluation, and social isolation which may adversely influence compliance and continued psychiatric monitoring.<sup>2</sup>

Antipsychotic medication has been the mainstay of treatment for late-onset as well as early-onset psychotic symptoms. In particular, the delusions and hallucinations which typically characterise the illness in elderly patients usually respond well to these agents. Further, as negative symptoms are infrequent, functioning between episodes of psychosis (usually precipitated by poor compliance with treatment) is usually not impaired.<sup>2</sup> Nevertheless, sensitivity to antipsychotic medication has been identified in a number of treatment studies of late-onset psychosis, and necessitates a cautious approach by the clinician in considering this treatment option.<sup>37-39</sup> Extrapyramidal and anticholinergic side-effects, and drug interactions, are more common than in younger patients, resulting in significant morbidity. In addition, the risk of tardive dyskinesia is markedly greater in elderly patients taking antipsychotic medication.<sup>39,40</sup> In a follow-up study of 266 older outpatients receiving less than an average of 150 mg chlorpromazine equivalents daily, Jeste et al<sup>40</sup> found that the cumulative incidence of tardive dyskinesia at the end of 1, 2 and 3 years was 26%, 52% and 60% respectively. Fortunately, the introduction of atypical antipsychotic agents, such as risperidone, olanzapine and quetiapine, has markedly reduced these iatrogenic consequences of treatment.<sup>39,41</sup> However, as depot preparations are not available for these agents, compliance remains a problem if follow-up is not assertive.

The greater availability of anticholinesterase agents, such as donepezil and rivastigmine, now presents the clinician managing a patient with late-onset psychosis with a further pharmacological treatment choice. As some degree of cognitive decline is frequently noted in association with the psychotic symptoms, the possibility of an early dementing illness in, at least, a subgroup of these patients, needs to be considered.<sup>7,9</sup> It is now accepted that the benefits of anticholinesterase inhibitors, which delay the progression of cognitive deterioration in the most common type of dementia, namely Alzheimer's Dementia (and possibly Lewy Body Dementia), are maximal if treatment is instituted early in the progression of the disease.<sup>42,43</sup> This situation poses a dilemma for the clinician as to whether to commence treatment with an antipsychotic agent, an anticholinesterase agent, or both. Now that studies have found that anticholinesterase inhibitors appear to have a beneficial effect on emotional and behavioural symptoms associated with dementia,<sup>44</sup> there is a greater imperative for the clinician to be able to distinguish those cases of late-onset psychosis that are likely to progress to dementia from those that are less likely.

Finally, while pharmacotherapy is the cornerstone of management for patients with late-onset psychosis, treating clinicians also need to be mindful that there may be intrapsychic benefits in the formation of delusions, in par-

ticular, for these individuals. Informing this notion is the concept of 'meaningfulness', neglected as a controversial and unmeasurable entity for empirical research in psychiatry.<sup>45,46</sup> Roberts<sup>45</sup> has proposed that delusional thinking might have an adaptive function in providing creative attributions of meaning to the experience of psychotic disintegration. This 'alternative reality' may allow the socially isolated elderly person to regain a sense of meaning, albeit distorted, in the face of perceived threatening and anomalous experiences. Removing psychotic symptoms, while necessary to enable the person to "rejoin the human community",<sup>47</sup> may leave them vulnerable to other forms of psychological decompensation, such as depression. In younger psychotic patients, findings from studies of the cognitive mechanisms involved in paranoid thinking are now being translated into effective cognitive-behavioural models of treatment.<sup>48-50</sup> Central to this approach is the development of a shared formulation with the patient of the genesis of the psychotic symptoms. In this way the meaning of the symptoms for the patient can be examined, together with the cognitive biases that underlie their formation. In conjunction with psychotropic medication, this psychotherapeutic approach has been demonstrated to attenuate psychotic symptoms, improve quality of life, and facilitate the recovering individual's sense of psychological integration.<sup>50</sup> Just as psychotherapeutic strategies have been modified for the treatment of depression and anxiety in the elderly,<sup>51</sup> it would seem timely to explore how this treatment modality might complement pharmacological interventions for elderly psychotic patients.

## Conclusion

Non-affective psychotic symptoms arising in later life continue to present the clinician with a diagnostic challenge. While many aspects of the clinical presentation are similar to earlier-onset schizophrenia-spectrum illness, both biological and psychosocial factors associated with the ageing process need to be incorporated in a framework for understanding and managing these patients. Although further studies are still required, it would appear that subtle cognitive deficits, social isolation, and sensory impairment might increase vulnerability to psychosis in genetically predisposed elderly individuals. The treating clinician, therefore, needs to take these factors into account in formulating appropriate treatment strategies. While antipsychotic medication remains the mainstay of management for these patients, anticholinesterase inhibitors may also represent a treatment option. In addition, from a psychotherapeutic perspective, cognitive-behavioural interventions developed for younger psychotic patients may be applicable in challenging the delusional beliefs of elderly psychotic patients. Most importantly, these patients need to be able to negotiate the final developmental stage of their lives without the distorted sense of meaning that these phenomena appear to provide for them.



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**Correspondence:** Anne Hassett

University of Melbourne, North Western Aged Persons Mental Health Program, Sunshine Campus  
176-190 Furlong Road – St Albans, Victoria 3021, Australia  
Tel.: (+61) (3) 8345-1335/ Fax: (+61) (3) 9366-8581 – E-mail: anne.hassett@mh.org.au

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