

8 Mania

Ken Shulman

Classification • Epidemiology • Aetiology • Age of onset and clinical course • Clinical presentation • Management • Prognosis • Conclusion

Mania occurring in later life has come under closer scrutiny in recent years. As a result, important issues related to the classification and the neurobiological basis of affective illness have become clearer.

Classification

Historical context

Kraepelin (1921) established the separateness of affective disorders from other major psychoses by developing the concept of manic-depressive illness. This was a unitary concept combining mania and depression. It was not until the 1960s that the bipolar-unipolar dichotomy was postulated (Perris, 1966). Despite preliminary evidence of support, recent thinking has shifted away from the notion that manic disorders are fundamentally different from unipolar depression. Indeed, the study of elderly bipolars reveals that many of them 'convert' from a unipolar depressive pattern after many years and multiple depressive episodes (Shulman & Post, 1980; Snowden, 1991).

Spectrum of affective disorders

Akiskal *et al* (1983), noted that young people with depression, followed prospectively for 3–6 years, developed mania in about 20% of cases. Moreover, it is difficult clinically to determine when a picture of mild pressure of speech or disinhibition, following treatment of major depression, represents a 'true' hypomania. Therefore, the idea of a spectrum of affective disorders was developed in which a hierarchy of different patterns of illness is described (Akiskal, 1983). These range from milder expressions, such as cyclothymia and dysthymia, to unipolar major depression, bipolar II (with mild hypomania) and bipolar I (full-blown manic episodes). Tsuang *et al* (1985) suggest a "threshold hypothesis" in which mania is a more severe form of affective disorder, requiring lower levels of stress to precipitate a decompensation.

Mixed affective states

To emphasise the blurring of manic and depressive phases, Clothier *et al* (1992) described the condition of 'dysphoric mania', a mixed affective state. Kraepelin (1921) has already provided a classification of six sub-types of 'mixed' affective states. These are: depressive/anxious mania, excited depression, mania with poverty of thought, manic stupor, depression with flight of ideas and inhibited mania. Careful and systematic clinical observations in young and old patients force us to reconsider our fundamental view of mania and its relationship to depression.

ICD-10

ICD-10 (World Health Organization, 1992) considers mood disorders as a spectrum, with mania and severe depression at opposite ends. Mood disorders are divided into: manic episode, bipolar affective disorder, depressive episode, recurrent depressive disorder and persistent mood disorders. Bipolar affective disorder is characterised by repeated episodes of mood disturbance, at least one of which is mania or hypomania, and one of which is depression. Manic episodes are divided into hypomania, mania without psychotic symptoms, and mania with psychotic symptoms (Box 8.1).

Epidemiology

Data regarding the incidence and prevalence of mania in old age show opposite trends. The incidence, as measured by first admission rates to

**Box 8.1 Summary of the ICD-10 criteria for a manic episode
(World Health Organization, 1992)**

Without psychotic symptoms:

- Elevated mood or irritability
- Increased energy and overactivity
- Pressure of speech
- Decreased sleep
- Social disinhibition
- Poor attention and marked distractibility
- Grandiose or over-optimistic ideas
- Extravagant schemes and over spending
- Aggressive or amorous episodes

With psychotic symptoms; as above and:

- Severe and sustained excitement
- Flight of ideas
- Mood congruent delusions or hallucinations

hospital, increases with age even in the extremes of old age (Eagles & Whalley, 1985). However, the community prevalence decreases with age (Weissman *et al*, 1988). One-year prevalence rates are 0.1% in over 65s (Box 8.2) and 1.4% in the 18- to 44-year-old age group. This prompts the question 'where have all the young bipolars gone?'. This is addressed later in this chapter.

The prevalence of mania on psychogeriatric in-patient units has been reviewed by Yassa *et al* (1988) and Shulman *et al* (1992). Over the course of a year, an average unit can expect to treat eight patients suffering from mania severe enough to require hospitalisation. This represents 12% of all affective disorders treated on specialised geriatric psychiatry units. The gender ratio of elderly manic patients shows a female preponderance, with a ratio of about two to one.

Aetiology

Genetics

Affective disorders are known to have a marked genetic predisposition (Goodwin & Jamison, 1984). Bipolar disorders have usually been considered to have a stronger genetic component than depression (Gershon *et al*, 1975). However, Tsuang *et al* (1985) could find no difference in risk for affective disorder between the relatives of younger bipolar and unipolar probands. This led to the conclusion that both phenotypes share a common aetiological pool including environmental, psychological, biological and genetic factors.

Studies of first degree relatives of elderly manic probands have found a quarter to a half are affected (Glasser & Rabins, 1984; Stone, 1989; Broadhead & Jacoby, 1990; Snowden, 1991; Shulman *et al*, 1992). The relatively high yield of positive family history may reflect the longer periods of exposure in the parents, siblings and children of elderly probands who present with mania. Earlier age of onset is associated with a positive family history (Stone, 1989), while the presence of coarse neurological disorders has a lower genetic predisposition (Snowdon, 1991; Shulman *et al*, 1992). In the Shulman *et al* (1992) study, the elderly people with mania with neurological disorders had a significantly lower family history than those without. None the less, the prevalence of affective illness in first degree relatives was still 32%.

Box 8.2 Epidemiology of mania in older patients

Average age at onset 55 years

Female to male ratio 2:1

One year community prevalence 0.1%

Proportion of in-patient affective patients 12%

Brain disease

All studies that have systematically assessed the prevalence of cerebral-organic disorders in elderly people with mania have found a significant association between brain disease and mania (Table 8.1). Depending on the rigorousness of the search (i.e. whether by case notes, neurological examination, imaging or cognitive testing), the prevalence of organic brain disorders in patients with mania ranges from 20–40%. In the two studies where a consistent methodology was applied, the proportion of neurological disorders was closer to 40% (Broadhead & Jacoby, 1990; Shulman *et al*, 1992). Broadhead & Jacoby (1990) used computerised tomography scans, a Kendrick battery and a clinical assessment. They found a significant increase in cortical atrophy and an increase in cognitive impairment on the Kendrick. However, clinical assessment did not confirm the presence of dementia, a finding similar to other studies (Shulman & Post, 1980; Shulman *et al*, 1992). Consistent with the concept of secondary mania as defined by Krauthammer & Klerman (1978), 20% of the elderly people with mania had their first manic attack in close temporal proximity to a cerebral disorder, while this was not evident in any of the young people with mania.

There appears to be a trend for the secondary mania subgroup to have mania as the first affective episode (Broadhead & Jacoby, 1990; Shulman *et al*, 1992). As noted earlier, there is also a trend for the secondary manias to have a lower genetic predisposition. However, many of these patients do have a positive family history for affective disorder.

The brain diseases are heterogeneous in nature, without any consistent localising pattern according to the available data. Cerebrovascular disorders, chronic alcoholism and head injury appear most common (Shulman *et al*, 1992). Secondary mania has been systematically reviewed by Strakowski *et al* (1994), who concluded that lesions tend to involve right-sided brain structures. Similarly, Robinson *et al* (1988) found an association between right-sided stroke and mania. Silent cerebral infarctions have been noted more often in late-onset mania than matched elderly depressives (Fujikawa *et al*, 1995). Similarly, Kobayashi *et al* (1991)

Table 8.1 Aetiology

	Associations
Genetic	Earlier age of onset Absence of neurological damage
Brain disease	Cerebrovascular disease Chronic alcohol misuse Head injury Right-sided lesions

showed an increased incidence of silent cerebral infarctions with age among patients with mania.

Anecdotal case reports of cerebrovascular disease associated with mania have accumulated in recent years (Shulman, 1993). Neuroimaging studies have confirmed an increase in subcortical hyperintensities, presumably reflecting cerebrovascular pathology in old age (McDonald *et al*, 1991). Alzheimer's disease does not seem to be associated with mania in late-life. No more than the expected proportion in the population seem to progress to a full-blown dementia following a manic episode.

Summary of aetiology

Evidence suggests that there is a significant neurological substrate for mania in old age. In some elderly patients that vulnerability is manifested by earlier depressions that 'switch' to mania after a prolonged latency. In a second subgroup, coarse neurological disorders play a prominent role in producing a syndrome of 'secondary mania', and genetic factors are less important. None the less, it is uncertain why this relatively small group of patients present a different clinical picture to the vast majority of elderly patients who suffer neurological insults. New neuroimaging techniques such as the positron emission tomography, single photon emission tomography and magnetic resonance imaging scanners (see Chapter 12) may offer further insights into the nature of the cerebral changes associated with mania.

Age of onset and clinical course

On average, elderly people with mania have an onset of affective disorder in their late 40s. The onset of mania is later, at a mean age of about 55 years. However, the incidence figures reveal manic cases occurring for the first time, well into their 80s. For about half of elderly people with mania their first affective episode is depression (Shulman & Post, 1980; Broadhead & Jacoby, 1990; Snowden, 1991). In this subgroup, an average of 16 years elapsed before mania became manifest, often preceded by repeated episodes of depression. This group tends not to suffer from coarse neurological disorders, which suggests that an 'ageing factor' may 'convert' affectively predisposed individuals to a manic presentation.

General adult studies of hospitalised patients with mania find an age of onset of about 30 years (Goodwin & Jamison, 1984; Tohen *et al*, 1990). The Epidemiologic Catchment Area (ECA) study using a community sample showed a very early onset, at a mean of 21 years (Weissman *et al*, 1988). In marked contrast, very few elderly people with mania have become manic before the age of 40 years (Shulman & Post, 1980; Snowden, 1991). Available evidence points to two possible explanations.

The first is that the disorder beginning early in life eventually burns out after an initial clustering of affective episodes (Winokur, 1975).

The second explanation, supported by Snowden (1991), suggests that premature death may be partly responsible. Goodwin & Jamison (1984) found a mortality among bipolars more than twice that of the general population, and half of these patients died before the age of 70. Long-term follow-up of bipolars shows higher suicide rates (Tsuang, 1978) and excess mortality (Weeke & Vaeth, 1986). Because prospective follow-up studies of 40–50 years are impractical, the best approach may be to prospectively study a large cohort of early-onset, middle-aged people with mania.

Clinical presentation

Earlier anecdotal observations suggested that mixed affective disorders were more common in elderly people with mania, as described in Kraepelin's "mixed states", such as dysphoric mania (Shulman & Post, 1980). Systematic analyses of the clinical features of elderly patients with mania, however, show no significant differences from younger bipolars (Broadhead & Jacoby, 1990), except that young people with mania have a more severe form of the disorder, as measured by a standardised rating scale. Therefore, one should expect the usual range of symptoms as described by Glasser & Rabins (1984) including: decreased sleep, physical hyperactivity, flight of ideas, thought disorder, overspending, grandiose delusions, irritability and hypersexuality (Box 8.1).

Management

Unfortunately, little systematic data are available regarding the treatment of mania in old age. Clinical reports suggest that lithium retains an important role but is associated with an increased incidence of neurotoxicity (Himmelhoch *et al*, 1980; Stone, 1989) (Table 8.2). Altered renal excretion and distribution, result in a prolonged half-life (Hardy *et al*, 1987) and require much lower doses, in the range of 150–600 mg per day. A mean dose of 300–450 mg per day should achieve blood levels of about 0.5 mmol/l (Shulman *et al*, 1987). More work is needed to confirm these reports and establish the range of dosage and blood levels necessary for effective and safe treatment in old age.

The anticonvulsants carbamazepine and valproate are now widely used in the management of mania (McElroy *et al*, 1992) but little is known of their use in old age. McFarland *et al* (1990) provide an anecdotal series of cases, suggesting that valproate is a useful adjunct to lithium in the management of refractory, elderly patients with mania. Kando *et al* (1996) found valproate to be well tolerated and efficacious in a retrospective

Table 8.2 Drug treatment of mania

	Treatment
Lithium	Plasma levels approximately 0.5 mmol/l Be aware of risk of toxicity
Carbamazepine	Risk of neurotoxicity
Valproate	Possible adjunct to lithium Risk of neurotoxicity

chart review of elderly patients suffering from an affective disorder. Concerns regarding neurotoxicity, however, suggest a cautious approach to the addition of these medications.

Prognosis

Studies have examined the outcome of mania in old age. Shulman *et al* (1992) used a retrospective cohort method to determine survival in elderly people with mania and an age- and gender-matched group of elderly people with depression. After an average follow-up period of six years (range 3–10 years), 50% of the patients with mania had died compared with only 20% of the unipolar patients with depression. This suggests that mania may have a poorer prognosis and represent a more severe disruption of central nervous system function. Interestingly, only one patient in the cohort of 100 was known to have committed suicide.

Dhingra & Rabins (1991) followed up elderly people with mania for 5–7 years (Table 8.3) and found that 34% had died. At follow-up, 32% of the patients with mania had experienced significant cognitive decline, as measured by a score of less than 24 on the Mini-Mental State Examination. However of those alive, 72% were symptom free and 80% were living independently. They concluded that the prognosis for mania in old age has improved considerably compared to that of the previous generation, reported by Roth (1955).

Table 8.3 Outcome after 5–7 year follow-up (adapted from Dhingra & Rabins, 1991)

	(<i>n</i> =38)
Symptom free	72% ¹
Living independently	80% ¹
Cognitive decline	32% ¹
Died	34%

1. Per cent of those surviving

Conclusion

Late-onset mania appears to be fundamentally different from early-onset mania in terms of clinical course, outcome and its association with coarse cerebral disorders. However, the clinical presentation is similar. The high mortality of patients with mania is of concern, and may mean that mania results from a more severe disruption of central nervous system. However, newer technologies and treatments offer hope for improved understanding and management of this important syndrome.

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