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Mania in the elderly

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A retrospective study of 92 patients admitted with mania, aged over 65 years of age, found that 26% had no prior history of affective illness; 30% had previously only experienced depression, and half of these had at least three episodes of depression before the first manic illness. Patients with a family history of affective disorders had a significantly earlier age of onset of illness. There was evidence of cerebral organic impairment in 24% of the patients, and this group had a significantly later age of onset of illness. Prognosis was good, with only 8% still in hospital at six months. Half of the patients were started on lithium prophylaxis, but this did not significantly alter the number of readmissions. A quarter of those started on lithium developed evidence of lithium toxicity.

Whereas depression in elderly patients is acknowledged to be common, mania has been considered a rare condition (Perris, 1966; Loranger & Levine, 1978). This view is not supported by two studies which have used Department of Health statistics to investigate the age at which patients were admitted to hospital with their first manic illness. Both Spicer *et al* (1973) and Eagles & Whalley (1985) found an increase in the inception rate for mania with advancing age. This was particularly marked after the age of 75 years.

Shulman & Post (1980) studied 67 elderly bipolar patients. Forty-two of these had initially presented with depression and more than half of this latter group had three or more depressions before developing mania, often many years after the first illness.

There is general agreement that for both unipolar and bipolar disorder late-onset patients have a lower incidence of family history of affective illness, although definitions of a late-onset case have varied from 20 to 50 years of age (Hopkinson, 1964; James, 1977; Baron *et al*, 1981; Glassner & Haldipur, 1983).

There has been recent interest in the concept of secondary mania, and Krauthammer & Klermann (1978) comprehensively reviewed the literature concerning mania as a secondary illness. In single case reports mania has been described secondary to L-dopa, procyclidine and steroid medications, to infections such as influenza, Q fever and St Louis Type A encephalitis, and to space-occupying lesions such as meningioma, subarachnoid haemorrhage and metastases, these latter usually occurring in the non-dominant hemisphere (Oppler, 1950; Glaser, 1953; Ryback & Schwab, 1971; Steinberg *et al*, 1972; Schwartz, 1974; Weisart & Hendrie, 1977; Jamieson & Wells, 1979; Cohen & Niska, 1980; Coid & Strang, 1982).

In elderly patients with bipolar disorder, Shulman & Post (1980) found some evidence of cerebral organic disorder in 16 out of 67 patients (24%) with conditions such as cerebrovascular accident (CVA), trauma and Guillain-Barré syndrome. Only three patients had dementia. The authors suggested that organic factors may precipitate mania in some elderly patients.

Lithium treatment has been found to be effective in the elderly (Angst *et al*, 1970; Himmelhoch *et al*, 1980). However, the latter study found that elderly patients with neurological deficit responded poorly and suffered a high incidence of lithium toxicity. Murray *et al* (1983) found that between the fourth and eighth decade there was a 34% reduction in the lithium dosage required to give the same plasma level.

The prognosis for elderly manic patients has only been described in studies which take affective illness as a whole. There appears to have been an improvement in the last few decades. Roth (1955) found that 52% of admissions with affective psychosis were discharged at six months; whereas Blessed & Wilson (1982) described 80% discharged by six months and Christie (1982) reported 91% discharged.

The present study examines various aspects of mania in the elderly such as prior history, prognosis, and lithium treatment. Two-tailed tests are used to compare differences between groups.

The hypothesis that late age of onset is associated with less family history and more organic impairment is examined using one-tailed tests.

Method

A computer search was made of all in-patients aged 65 years and over who were admitted to the Royal Edinburgh and Victoria Hospitals over a ten-year period (1972–81) with a diagnosis of mania. Their case notes were reviewed and patients were included in the study only if they satisfied Feighner's criteria (Feighner *et al*, 1972) for the diagnosis of mania. Further details were elicited from the case notes with regard to the following areas:

(a) index admission (the first admission with mania after the age of 65) and also previous and subsequent episodes of affective illness
(b) lithium treatment and, in particular, evidence of lithium toxicity
(c) family history of affective illness
(d) evidence of cerebral organic impairment; this was only recorded if it fell into one of the following categories:
  (i) disease known to be associated with cerebral pathology, e.g. Parkinson's disease
  (ii) presence of gross cerebral pathology, e.g. CVA occurring during the admission or not more than six months preceding it
  (iii) presence of disorganised cerebral function such as *grand mal* epilepsy or coma, provided this occurred during the admission or in the week preceding it
  (iv) presence of persisting cognitive deficit such as confusion, and short-term memory impairment provided this persisted throughout the admission and did not resolve as the mania responded to treatment.

Results

Index admission data

A total of 92 cases were found, comprising 63 female and 29 male, a ratio of 2.17 : 1. The age range was from 65 to 82, with a mean of 70.3 years. The average length of index admission was 5.4 weeks. Only five patients failed to be discharged from hospital: these all remained as in-patients with chronic relapsing mania until their deaths, which occurred from 2 to 13 years later.

Of those who were discharged, only two had admissions which approached six months in length. Thus, 85 out of 92 patients were discharged by six months.

Previous history of affective illness

Twenty-four of the patients (26%) had no previous history of affective illness. Twelve had previous episodes of mania and 29 had experienced only episodes of depression prior to the index admission.

The mean age of onset of affective illness was 57 years (range 16–82). There was no significant difference relating either to sex or whether the first episode of illness was mania or depression.

In the 29 patients who had experienced only episodes of depression previously, the mean latency period to the first manic illness was 16 years. Fourteen of these patients had experienced three or more episodes of depression prior to their first mania.

Follow-up and readmission data

Eight patients had no follow-up and the remainder had from one month to ten years, with a mean of 3.2 years.

During the follow-up period 47 patients (51%) required readmission, with a total of 117 readmissions between them.

TABLE I
Number of readmissions with affective illness

Number of readmissions (0–10)	*Patients with no previous history (n = 24)*	*Patients with history of affective illness (n = 63)*
0	13	27
1	9	17
2	1	8
3	0	0
4	1	3
5+	0	8

Mann–Whitney U test: $Z = 1.619$ (corrected for ties), $P = 0.1$.

Table I compares the number of readmissions in patients with and without a prior history of affective illness. It can be seen there is no overall significant difference between these groups, although it is noteworthy that those patients with a previous history appear more likely to have a large number of readmissions.

Fifteen patients (16%) had died within two years of discharge.

Lithium treatment

Lithium treatment was commenced in the five chronic in-patients, with no evidence of benefit. Forty-three of the remaining 87 patients were started on lithium prophylaxis. Of these, 19 patients had no readmissions, 14 had one readmission, and the group as a whole had 47 readmissions (mean number per patient, 1.1; mean length of time readmitted, 2.3 months).

Of the 44 patients not started on lithium, 21 had no readmissions, 13 had one readmission, and the group together had 69 readmissions (mean number per patient, 1.6; mean length of time readmitted, 3.0 months).

There were no significant differences in readmissions between the two groups (Mann–Whitney U test, $Z = 0.236$, $P = 0.41$).

One patient developed a goitre while taking lithium, and eleven patients developed lithium toxicity. In nine of the cases, symptoms of lithium toxicity were present and lithium levels ranging from 1.4 mmol/l to 2.6 mmol/l were documented. In the other two cases symptoms of tremor, vomiting and ataxia were present. These resolved on stopping lithium, but lithium levels were not recorded.

Five lithium-toxic patients required admission with symptoms of acute confusional state.

Family history

Eighty-three patients had sufficient details in their case notes for a decision to be made as to whether a family history of affective illness was present or absent, and 22 patients had a positive family history. Seven patients had two first-degree relatives affected and the remainder only had one.

The age of onset of illness was uncertain in one patient. In the remaining 82 patients, those with a family history

TABLE II
Age at onset of affective illness and its relationship to family history

	Patients with no family history	*Patients with a family history*
Patients aged <30 at onset	1	2
Patients aged 30–39 at onset	4	3
Patients aged 40–49 at onset	7	3
Patients aged 50–59 at onset	14	7
Patients aged 60–69 at onset	16	6
Patients aged 70+ at onset	18	1
Age at onset		
Mean	60.4	53.1
Median	63	55

$t = 2.10$, d.f. = 80, $P < 0.025$.

had a significantly earlier age of onset. Table II gives further details.

Cerebral organic impairment

Persisting clinical evidence of cerebral organic impairment was found in 22 of the 92 patients. Fourteen patients had memory impairment, usually a specific short-term memory loss, and six of this group also had persisting disorientation and confusion. CT scans were performed on three patients and in each case they confirmed generalised cortical atrophy. During the follow-up period only three of the fourteen went on to develop dementia of a moderate to severe degree.

The remaining eight patients with cerebral organic impairment had a variety of more specific conditions. One of these had Parkinson's disease and another an intention tremor and facial dyskinesia. Two patients had a CVA, one of these, on the right side, occurring four months prior to the index admission, and the other, affecting the left internal capsule, developing in the second week of the admission. Three patients who were not previously epileptic had *grand mal* seizures: in one case this occurred on the day before admission and in the other two during the admission; one of the latter cases also had slurred speech and facial dyskinesia and the other had CT-scan evidence of dilated third and lateral ventricles. The eighth patient became disorientated, confused and semi-comatose during the index admission; this resolved with no definite diagnosis being made.

Three of these eight cases had no previous history of affective illness and would satisfy Krauthammer & Klermann's (1978) criteria for secondary mania.

The age of onset of affective illness in those patients with cerebral organic impairment was found to be significantly later than in the remaining patients. Details are given in Table III. Only two patients with cerebral organic impairment also had a family history of affective illness.

TABLE III
Age at onset of affective illness and its relationship to cerebral organic impairment

	Patients with no cerebral impairment (n = 70)	*Patients with cerebral impairment (n = 21)*
Patients aged <30 at onset	3	2
Patients aged 30–39 at onset	7	0
Patients aged 40–49 at onset	13	1
Patients aged 50–59 at onset	19	4
Patients aged 60–69 at onset	15	8
Patients aged 70+ at onset	13	6
Age at onset		
Mean	56.0	61.0
Median	55.5	67

Mann–Whitney U test: $Z = 1.946$, $P = 0.026$.

The patients with cerebral organic impairment did not differ significantly from the remaining patients on any of the following parameters: clinical features of mania, number of readmissions, response to lithium, or percentage dying within a two-year follow-up.

Discussion

The mean age of onset of affective illness was 58 years: this contrasts strikingly with the results of other workers (Carlson *et al*, 1977; Baron *et al*, 1981), who have found a mean age of onset of less than 30 years.

Shulman & Post (1980), who also studied an elderly cohort, found a later age of onset of 49 years. It may be, as Winokur (1975) has suggested, that a proportion of affective illness 'burns out' with age, so is not included in an elderly sample.

One-quarter of the patients in this study first became ill after the age of 65, and both Spicer *et al* (1973) and Eagles & Whalley (1985) found a raised inception rate for mania with increasing age, particularly after 75 years. As the elderly population increases in the next decade it seems likely that there will be more manic patients requiring resources from psychogeriatric services.

Fourteen out of 29 patients (48%) with a previous history solely of depression had at least three episodes before the index admission with mania. Exactly the

same percentage was found by Shulman & Post (1980), although they found a mean latency period of 10 years to the first manic episode, compared with 16 years in the present study. These findings contrast with Perris's (1966) figure of 16% for patients who 'convert' to bipolar after three episodes of depression. One reason for this difference is that patients who remained unipolar were not included in the present study. It is striking, however, that some of the present cohort of patients would have been wrongly classified for a long period of time.

Lithium was used in the initial treatment of mania in one-fifth of the cases and for prophylaxis in a half. This latter group did not differ significantly in the number or length of readmissions from the patients not started on lithium, although since the patients were not randomly allocated for lithium treatment no firm conclusions about its efficacy can be drawn. The majority of studies showing the value of lithium prophylaxis have had a lower mean age of patient (Angst *et al*, 1970; Coppen *et al*, 1971), but Shulman & Post (1980) gained a "strong impression of the usefulness of lithium in bipolar patients aged 60 years and over". Also Himmelhoch *et al* (1980) found that the majority of 81 elderly bipolar patients responded well to lithium, the exceptions being 17 patients with cerebral organic impairment, who were not only poor responders but more likely to develop lithium toxicity.

In the present study, cerebral organic impairment had no effect on either response to lithium or toxicity. The type of impairment appears to be different, however, with Himmelhoch *et al* identifying 12 patients with extrapyramidal symptoms who were all included in the group of 19 patients who developed chronic mania. This contrasts with two patients with extrapyramidal symptoms and only five who developed chronic mania in this study.

A quarter of the 45 patients started on lithium developed lithium toxicity with lithium levels of 1.4–2.6 mmol/l, and five of these required admission with an acute confusional state. This is a considerably greater percentage than the 13% with lithium toxicity described by Roose *et al* (1979) in 31 patients over the age of 60.

Murray *et al* (1983) found a 34% reduction with advanced age in the lithium dosage required to produce a therapeutic level. The present study underlines the need for careful monitoring of lithium levels in this age group, even in those without antecedent cerebral damage.

It is now well documented that early onset of affective illness is associated with an increased genetic component, as demonstrated by family history (Hopkinson & Ley, 1969; Baron *et al*, 1981) and Smeraldi *et al* (1983) have suggested that age of onset is an index of penetrance variability. Different workers have used different ages between 20 and 50 years to divide early- and late-onset cases, however. In the present study a progressive decrease in family history with advancing age of onset was noted, with the biggest decrease after 70 years.

With increasing evidence that first episodes of mania can occur in advanced old age it may be necessary to reconsider the age before which a patient should be thought of as an early-onset case. The present findings support the suggestion made by Shulman & Post (1980) that 50 years rather than 20 or 30 might be more appropriate in this respect.

Another finding in common with Shulman & Post is that 24% of the patients had evidence of cerebral organic impairment. There was also an excess of male patients (31%) compared with female (22%), but in contrast with the results of Shulman & Post this did not reach statistical difference.

Although 14 patients had generalised cortical atrophy, only three of the 92 patients went on to develop well-documented dementia over the follow-up period. It now seems clear that in elderly patients with either unipolar or bipolar affective disorder there is a normal incidence of dementia (i.e. they develop dementia no more than one would expect by chance) (Kay *et al*, 1955; Shulman & Post, 1980; Baldwin & Jolley, 1986).

Eight patients had more specific localised evidence of cerebral dysfunction, and three of these had no previous history of affective disorder and would satisfy Krauthammer & Klermann's (1978) criteria for secondary mania.

The patients with organic impairment had a significantly later age of onset of illness and only two of them had a family history of illness. This supports the hypothesis that there may be two overlapping populations who suffer from mania: those with a genetic component as evidenced by family history, who develop the illness early in life; and those with no (or a smaller) genetic component, who are precipitated into illness by cerebral organic impairment in later life.

Tsuang *et al* (1985) proposed a common-aetiology model for affective illness with a lower threshold for depression and a higher threshold for mania. This would be consistent with the present result that the mean latency from first depression to first mania was 16 years. Also, only five of the 22 patients with cerebral organic impairment had a prior history of mania, eight having no previous history and nine having experienced only episodes of depression. In some of these cases it may be that organic factors occurring in old age caused them to exceed

the higher threshold and develop a manic illness for the first time.

The link between organicity and onset of illness is less clear-cut in this group of patients than in the three cases of secondary mania, but it is a much larger group and it seems likely that in elderly manic patients the role of organic impairment as part of a multifactorial aetiology will be increasingly recognised.

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