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Research report

Early and late onset depression in old age: different aetiologies, same phenomenology

Henry Brodaty[a,b,*], Georgina Luscombe[a,b], Gordon Parker[a], Kay Wilhelm[a,c], Ian Hickie[d], Marie-Paule Austin[e,f], Philip Mitchell[a,f]

[a]*School of Psychiatry, University of New South Wales, Sydney, Australia*
[b]*Academic Department for Old Age Psychiatry, Prince of Wales Hospital, McNevin Dickson Building, Prince of Wales Hospital, Avoca St., Randwick, Sydney, NSW 2031, Australia*
[c]*Liaison Psychiatry and GP Shared Care Liaison Units, St. Vincent's Hospital, Sydney, Australia*
[d]*Academic Department of Psychiatry and Mental Health Evaluation Team, St. George Hospital and Community Health Service, Sydney, Australia*
[e]*Liaison Psychiatry, Prince of Wales Hospital, Sydney, Australia*
[f]*Mood Disorders Unit, Prince of Wales Hospital, Sydney, Australia*

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Abstract

Background: Phenomenological differences between older patients with early onset (EO; onset of first major depressive episode before 60 years) and late onset (LO) depression have been inconsistent but, if real, may reflect differences in aetiology. We aimed to compare aetiological factors, phenomenology and cognitive function in older patients with depression by age of onset. *Methods*: Subjects were all patients ≥ 60 years old ($n = 73$) from 407 consecutive attenders to a Mood Disorders Unit, diagnosed with DSM-III-R Major Depressive Episode, at or close to the nadir of their episode. Putative risk factors were assessed by structured interview. Psychological morbidity and depressive symptoms were assessed by the 21-item Hamilton Rating Scale for Depression, CORE rating of psychomotor disturbance, Newcastle Endogeneity Scale, Zung Depression Scale and General Health Questionnaire. Cognition was assessed by tests of memory, attention, executive function and motor speed. *Results*: Personality abnormalities, a family history of psychiatric illness and dysfunctional past maternal relationships were significantly more common in EO depression. The two age of onset groups were essentially similar in terms of depressive sub-type and severity, phenomenology, history of previous episode, and in neuropsychological performance. *Limitations*: Use of self-report data, moderate sample size, sample not age-matched, tertiary referral patients. *Conclusions*: EO and LO depression are similar phenotypically, but differ aetiologically. The pursuit of mechanisms which predispose depressive episodes may be heuristically more valuable than further investigation of individual depressive features in distinguishing early from late onset depression.

Keywords: Age at onset; Early-onset; Major depression; Aetiology; Phenomenology

*Corresponding author. Tel.: +61-2-9382-3759; fax: +61-2-9382-3762.
E-mail address: h.brodaty@unsw.edu.au (H. Brodaty).

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1. Introduction

Investigation of depression in old age continues to evoke interest (Ruegg et al., 1988; Blazer et al., 1987; Musetti et al., 1989; Brodaty et al., 1991; Krishnan, 1991; Baldwin, 1994; Reynolds et al., 1998), in particular comparisons of early onset (EO), usually before 60 years of age, and late onset (LO) depression (Lyness et al., 1995; Baldwin, 1995; Baldwin and Tomenson, 1995; Krishnan et al., 1995; Brodaty et al., 1991; Steingart and Herrman, 1991; Holroyd and Duryee, 1997; Papassotiropoulos et al., 1999).

The only well replicated differences between EO and LO late-life depression have been aetiological, in particular a lower rate of family history of mood disorder in persons with LO depression (Hopkinson, 1964; Post, 1968; Mendlewicz, 1976; Conwell et al., 1989; Brodaty et al., 1991; Baldwin, 1994, 1995), suggesting a greater genetic influence in EO depression. Findings have been less clear about pre-morbid personality disturbances (Post, 1978; Bergmann, 1978; Burvill et al., 1989; Brodaty et al., 1991; Abrams et al., 1994; Fava et al., 1996; Camus et al., 1997) and physical illness (Roth and Kay, 1956; Baldwin and Tomenson, 1995; Baldwin, 1990; Conwell et al., 1989; Greenwald and Kramer-Ginsberg, 1988; Burvill et al., 1989; Brodaty et al., 1991; Lyness et al., 1995; Holroyd and Duryee, 1997).

Comparisons of phenomenology in EO and LO depression in late life have been inconsistent (Krishnan et al., 1995; Baldwin, 1994). Patients with EO depression may experience *more* guilt (Brown et al., 1984; Conwell et al., 1989) but *less* generalised anxiety (Post, 1962; Brown et al., 1984; Meyers and Greenberg, 1986), hypochondriasis (Brodaty et al., 1991; Meyers and Mei-Tel, 1985; Meyers and Greenberg, 1986; Post, 1962; Brown et al., 1984), apathy or loss of interest (Krishnan et al., 1995), delusions or psychosis (Alexopoulos et al., 1988). These results have not always been replicated (Post, 1962; Greenwald and Kramer-Ginsberg, 1988; Musetti et al., 1989; Hopkinson, 1964; Nelson et al., 1989; Winokur et al., 1980; Carroll, 1991).

There is some evidence for greater cognitive impairment in persons with LO depression (Cole and Hicking, 1976; Steingart and Herrman, 1991, Davies et al., 1978; Burvill et al., 1989; Lesser et al., 1996; Salloway et al., 1996), but this is inconsistent possibly because of sampling differences. Of ten studies which looked at the association between age of onset and Mini-Mental State Examination (MMSE; Folstein et al., 1975) scores, seven found no significant association (Alexopoulos et al., 1984; Greenwald and Kramer-Ginsberg, 1988; Abrams et al., 1994; Baldwin and Tomenson, 1995, Lyness et al., 1995; Holroyd and Duryee, 1997; Palsson et al., 1999), one reported equivocal results (Burvill et al., 1989), one found a relationship between poor MMSE scores and depression in elderly patients without a psychiatric history (i.e. LO illness) (Van Ojen et al., 1995) and one found a negative association between MMSE score and age of initial depressive symptom onset (Steingart and Herrman, 1991). Cole and Hicking (1976) reported a higher prevalence of LO depression in subjects with comorbid minor organic signs, defined as partial impairment in recent memory, orientation and registration. The four studies that described a link between greater age of onset and cognitive impairment postulated that cerebral degeneration or cerebrovascular disease may be a causal factor in LO depression (Steingart and Herrman, 1991; Van Ojen et al., 1995; Salloway et al., 1996; Lesser et al., 1996).

Limitations to previous work have included sample restrictions, such as only using inpatients (Greenwald and Kramer-Ginsberg, 1988; Lyness et al., 1995), absence of strict diagnostic criteria (Post, 1962) and use of different ages to divide late from early onset (Greenwald and Kramer-Ginsberg, 1988; Krishnan et al., 1995; Lyness et al., 1995). These limitations, combined with the above inconsistencies in findings, led us to re-examine predisposing and phenomenological factors in EO and LO late-life depression.

In an earlier study, we focussed on psychomotor retardation and agitation as key constructs defining melancholia (Brodaty et al., 1991; Parker et al., 1994; Parker and Brotchie, 1992; Parker and Hadzi-Pavlovic, 1996). We now used a refined version of a clinician-rated measure of the *signs* of psychomotor disturbance (PMD) — to quantify the degree of agitation and retardation, which has demonstrable validity and reliability (Parker and Hadzi-Pavlovic, 1996). The CORE comprises three clinically meaningful and factorially independent sub-scales: *non-*

interactiveness, agitation and *retardation*. Additionally, apart from three studies (Davies et al., 1978; Lesser et al., 1996; Salloway et al., 1996), previous investigators have either neglected or only used single omnibus instruments such as the MMSE (which is not a very sensitive indicator of executive function) to compare neuropsychological performance in patients with EO and LO depression. The present study examines a fresh cohort of subjects with no overlap with our previous sample (Brodaty et al., 1991). We included measures of reaction time, frontal lobe function, attention and memory as patients with LO depression appear to have poorer performance in executive function cognitive domains (Lesser et al., 1996; Salloway et al., 1996).

Based on the literature and our previous work, we had three hypotheses: (i) that there would be differences in predisposing factors, and specifically, that family history of mood disorder as well as personality abnormalities would be more common in persons with EO depression; (ii) the phenomenology of depression would be similar in EO and LO groups; and (iii) patients with LO depression would perform more poorly on neuropsychological tests.

2. Method

2.1. The sample

The sample was derived from a new cohort of 407 consecutive attenders (both inpatients and outpatients) to the Mood Disorders Unit at a Sydney teaching hospital. The study had institutional ethics committee approval. Most of the data were obtained as part of the clinical interview; where extra information was required, written informed consent was obtained from patients. From previous experience, about one quarter of patients were referred by general practitioners, about one half by psychiatrists and the remainder from other sources (Brodaty et al., 1993). Diagnoses, based on DSM-III-R criteria, were derived from structured interviews (Brodaty et al., 1987) using diagnostic algorithms (Brodaty et al., 1991), and then confirmed by at least two Mood Disorders Unit clinicians all of whom were experienced psychiatrists.

Of the 103 patients aged ≥ 60 years, 30 were excluded: three who did not have a diagnosis of depression, 12 with bipolar mood disorder (in order to focus on unipolar depression), two with a definite or suspected organic mood disorder, four with a known history of cerebrovascular disease and nine whose depression had already improved substantially. We excluded patients who had improved or were improving in order to obtain a more accurate picture of phenomenology and extent of psychomotor disturbance. Determination that the patient had not yet improved substantially proved straightforward as patients had a mean duration of depression of 69.1 weeks (S.D. 78.1). Patients with dementia, neurological disease such as Parkinson's disease or secondary depression were excluded. Sub-clinical cerebrovascular disease detected subsequently on magnetic resonance imaging (MRI) was not an exclusionary criterion. All assessors were blind to the hypotheses to be tested.

Age of onset of depression was defined as the age when the patient received their first diagnosis of major depressive episode. For the purposes of this study, major depression diagnosed before the age of 60 was labelled early onset (EO) and major depression diagnosed at the age of 60 or older was termed late onset (LO).

2.2. Instruments

Patient assessment was the same as described previously (Brodaty et al., 1991), except for the incorporation of new structured questions to derive DSM-III-R diagnoses, and use of the CORE instrument (Parker and Hadzi-Pavlovic, 1996). Assessment also included the clinician-rated 21-item Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) and Newcastle Endogeneity Scale (Carney et al., 1965), as well as two self-report measures, the 30-item General Health Questionnaire (GHQ; Goldberg, 1972) and the Zung Depression Scale (Zung, 1965). From the HRSD we also created intrapsychic and somatic sub-scale scores (Troisi et al., 1996), by dividing the first 17 items of the HRSD into psychological symptoms (HAMPSY): depressed mood, feelings of guilt, suicidal ideation and psychic anxiety; and somatic symptoms and signs (HAMSOM): work and interests, loss of libido, gastrointestinal symptoms, loss of weight, early, middle and

late insomnia, general somatic symptoms, somatic anxiety, hypochondriasis, retardation and agitation. These sub-scales have been developed for use in patients with dementia and depression but we reasoned that they had good face validity. Also, when we attempted a factor analysis of the 21-item version of the HRSD we obtained an eight factor solution that explained 69% of the variance but was not clinically interpretable.

Adequacy of pre-morbid personality was assessed by Unit clinicians on the basis of history and, where available, reports from informants or other clinicians, on a five-point scale using defined anchor points (available from the authors) to rate: healthy adaptation = 1, minor abnormal personality traits = 2, abnormal personality traits = 3, severely abnormal personality traits = 4, and (DSM-III-R defined) personality disorder = 5. For example, abnormal personality traits (= 3) were identified as *personality traits which cause the patient distress but do not interfere with normal functioning; the patient has healthy interpersonal relationships and normal social functioning*. Abnormal personality traits were coded according to DSM-III-R descriptors and rated as present or prominent. In addition, occurrence of physical impairment was rated as: 0 = no physical symptoms, 1 = mild physical symptoms causing no impairment, 2 = mild physical symptoms plus some impairment or moderate physical symptoms, and 3 = severe symptoms and/or severely impaired function.

Occupational status was rated according to the seven-point Congalton status ranking list of occupations in Australia (Congalton, 1969), and then dichotomised (1–4 as higher and 5–7 as lower status).

A mini-battery of neuropsychological tests for memory, frontal lobe function and psychomotor speed was administered to 51 (66%) patients at intake. This comprised the Controlled Oral Word Association Test (COWAT), a measure of word fluency (Spreen and Benton, 1969); the Symbol Digit Modalities Test (SDMT), a measure of psychomotor speed, attention and concentration (Smith, 1982); the Wechsler Memory Scale Associate Learning subtest, a measure of verbal learning (AL; Wechsler, 1945); the Trail Making Test (part A), a test of speed for visual search, attention and motor function (Reitan, 1958); and simple and complex reaction times — respectively measuring both psychomotor speed and choice or decision speed (Huppert, 1987). The test variables used in analysis included the total number of allowable words reported for the three stimulus letters in the COWAT, the total number of correct symbol substitutions during a 90-second period for the SDMT, raw AL scores calculated as credits on easy associations divided by two, plus the credits on the hard associations, total time in seconds to complete Trail Making Test part A, and total reaction times for both simple and complex reactions.

2.3. Statistical methods

All age of onset group comparisons of continuous data were analysed using Student's *t*-tests. The duration of episode variable was normalised using a logarithmic transformation for significant positive skew. The depression variables were also analysed by means of analysis of covariance (ANCOVA), covarying for age. For the CORE and its sub-scale scores, the analyses covaried for both age and use of anti-psychotic medication (we wished to control for any possible effect of medication on psychomotor disturbance). Group comparisons of categorical data were analysed using χ^2 tests with Yates continuity correction for all 2×2 tables. The neuropsychological test scores were analysed using analysis of covariance (ANCOVA), with age, gender, anti-psychotic medication use and education as covariates. Alpha was set at 0.05 except in the case of multiple comparisons where a Bonferroni adjustment was applied. Data were analysed using SPSS for Windows V6.0 (Norussis, 1993).

As psychomotor disturbance appears distinctly severe in psychotic depression (Parker et al., 1996), we repeated key analyses using the combined DSM-III-R defined diagnostic sub-groups of melancholia and non-melancholia (ie. excluding those with psychosis).

3. Results

3.1. Demographic and diagnostic details

The sample comprised 73 patients aged between 60 and 88 years. There were 35 patients with early onset (ie. onset before age 60) and 38 with late onset

(i.e. onset at or after age 60) major depression, with 77.1 and 89.5%, respectively, being inpatients ($\chi^2 = 1.22$, df = 1, ns). The average age of patients was 68.4 years (S.D. 7.0), the LO group being significantly older (EO: mean 65.5, S.D. 4.2; LO: mean 71.1 years, S.D. 8.0; $t = -3.83$, df = 57.2, $P < 0.001$). There were 25 males and 48 females, with the gender distribution for the age of onset groups being almost identical ($\chi^2 = 0.00$, df = 1, ns). Just over half (53.4%) of the sample were married, 28.8% were widowed, 9.6% were separated or divorced and the remaining 8.2% had never married. There were significant differences in marital status between the two groups, with 17.1% of the EO group divorced or separated compared with only 2.6% of the LO group ($\chi^2 = 7.98$, df = 3, $P < 0.05$). Marital status (married/widowed versus single/divorced/separated) was not associated with previous occurrence of depression ($\chi^2 = 0.004$, df = 1, ns) or duration of current episode ($t = 0.10$, df = 71, ns) (Numbers were too small to repeat these analyses for EO and LO depressives separately). The proportion of people with EO depression affirming an ongoing dysfunctional relationship with their spouse or intimate was just over double that of those with LO depression, however this difference was not significant (EO: 25.7%, $n = 9$, LO: 13.2%, $n = 5$; $\chi^2 = 1.13$, df = 1, ns). The two groups did not differ significantly in terms of either years of education (mean = 9.1 years, S.D. 2.7; $t = -0.37$, df = 70, ns) nor dichotomised occupational status (23.6% or 17/72 belonging to the higher category; $\chi^2 = 0.07$, df = 1, ns).

Depressive diagnostic sub-types — psychotic, non-psychotic melancholic and non-melancholic — were equally represented in the EO and LO groups ($\chi^2 = 0.43$, df = 2, ns). Twenty-one (60.0%) of the EO and 25 (65.8%) of the LO patients were diagnosed with non-psychotic melancholia, 11 (31.4%) of the EO group and 11 (28.9%) of the LO group with psychotic melancholia, and three (8.6%) of the EO group and two (5.3%) of the LO group with non-melancholic depression.

The current episode of depression had lasted 82.2 weeks (S.D. 90.5) on average for the EO group and 57.1 weeks (S.D. 63.4) for the LO group. This was not a significant difference ($t = 0.92$, df = 71, $P = 0.36$).

3.2. Medications

At the time of interview, five (14.3%) EO and seven (18.4%) LO subjects were taking anti-psychotic medications ($\chi^2 = 0.03$, df = 1, ns) of similar average doses in chlorpromazine equivalents (EO mean = 211.0, S.D. = 172.8; LO mean = 242.9, S.D. = 133.6; $t = -0.36$, df = 10, ns). Over half the sample (57.5%) were taking anti-depressants or mood stabilising drugs, with no differences in usage between the age of onset groups (EO = 62.9%, LO = 52.6%; $\chi^2 = 0.42$, df = 1, ns).

3.3. Family history and personality

The proportion of EO patients with a family history of psychiatric illness was significantly higher than in LO patients (EO: 54.3%; LO: 28.9%; $\chi^2 = 4.83$, df = 1, $P < 0.05$). The proportion of EO patients with a history of a first-degree relative experiencing psychotic, bipolar or endogenous depression involving hospitalisation or other treatment was almost double that of LO patients, but this difference did not reach significance (EO: 28.6%, $n = 10$; LO: 15.8%, $n = 6$; $\chi^2 = 1.07$, df = 1, ns). Patients with EO depression were four times more likely to affirm having a generally dysfunctional (uncaring, distant, overprotective) mother than LO patients (EO: 42.9%, $n = 15$; LO: 10.5%, $n = 4$; $\chi^2 = 8.28$, df = 1, $P < 0.01$). About one-third of EO patients (34.3%) affirmed having a generally dysfunctional father, compared with approximately one-tenth of LO patients (10.5%), however this difference was not significant after Bonferroni correction ($\chi^2 = 4.70$, df = 1, $P = 0.03$).

Although none of the sample was diagnosed with a personality disorder, only one (2.9%) of the EO patients was given a personality rating of healthy adaptation, compared with 17 (45.9%; one LO subject with missing data) of the LO patients ($\chi^2 = 24.52$, df = 3, $P < 0.001$). Dependent personality traits were present or prominent in 68.5% ($n = 24$) of the EO patients, compared with 32.4% (12) LO patients ($\chi^2 = 9.40$, df = 2, $P < 0.01$). Six EO patients were rated as having passive aggressive personality traits present, compared with only one of the LO patients ($\chi^2 = 4.66$, df = 1, $P = 0.03$, ns after Bonferroni correction). Obsessive compulsive personality traits were rated as present or prominent in

45.7% of the EO group, compared with 37.8% of the LO group, not a significant difference ($\chi^2 = 3.53$, df = 2, ns). Avoidant personality traits were rated as present or prominent in 40.0% of the EO group and 21.6% of the LO group, again a non-significant difference ($\chi^2 = 3.04$, df = 2, ns).

3.4. Physical health and functioning

There were no significant differences in the clinicians' ratings of physical health between EO and LO subjects ($\chi^2 = 1.27$, df = 3, ns). There were similar rates of a history of cardiovascular disease in the two groups (EO: 17.6%, $n = 6/34$; LO: 21.1%, $n = 8$; $\chi^2 = 0.15$, df = 2, ns). When cerebrovascular disease was categorised as absent or possible, there were no significant differences between the EO and LO groups (possible: 5/29 EO, 8/38 LO patients; $\chi^2 = 0.15$, df = 1, ns). (Patients with definite cerebrovascular disease ratings were excluded from the sample).

3.5. Depression severity measures

There were no significant differences between EO and LO patients in depression severity (HRSD or Zung), endogeneity (Newcastle Endogeneity scale) or psychological morbidity (GHQ), nor when age was used as a covariate. Severity scores in the two groups were also similar when patients with psychotic depression were excluded (again, because of significant age differences between the groups, analyses were repeated with age as a covariate) (Table 1).

3.6. Phenomenology

Importantly, the two groups had similar total CORE (EO: mean 13.6, S.D. 10.2, LO: 15.8, 9.2) and sub-scale CORE scores. Results were similar when age was used as a covariate. However, when only the subjects with non-psychotic depression were included in the analysis, total CORE scores tended to be higher in the LO group (EO: mean 9.3, S.D. 8.3; LO: 13.9, 8.3; Table 1); although sub-scale scores did not differ significantly. Similar results were obtained when CORE scores were reanalysed using ANCOVA to covary for anti-psychotic medication use, as well as for age.

As regards other phenomenological comparisons, 'marked' hypochondriasis (HRSD item >2) was significantly more prevalent in the LO group. When

Table 1
Measures of psychological morbidity by age of onset groups for all subjects and for non-psychotic subjects only

Measure[a]	Score				Comparison (ANCOVA)[d]			
	Early onset ($n = 35$)		Late onset ($n = 38$)		All subjects (df = 1, 72)[e]		Non-psychotic subjects (df = 1, 50)[f]	
	Mean	S.D.	Mean	S.D.	*F*	*P*	*F*	*P*
HRSD	25.0	8.0	24.9	6.5	0.31	0.58	1.21	0.28
HAMPSY	8.4	3.0	7.6	3.0	0.03	0.86	0.71	0.50
HAMSOM	14.6	5.2	15.2	4.4	0.47	0.50	1.12	0.29
Zung[b]	57.0	7.9	55.3	9.4	0.01	0.94	0.34	0.56
Newcastle	5.7	3.3	6.5	2.4	0.53	0.47	0.59	0.45
GHQ[c]	21.4	8.0	23.7	7.1	2.11	0.15	2.68	0.11
CORE	13.6	10.2	15.8	9.2	1.46	0.23	2.73	0.11
CORE sub-scales								
Agitation	3.9	3.5	4.0	3.2	0.27	0.61	2.55	0.12
Retardation	4.2	3.7	5.5	4.0	1.99	0.16	1.69	0.20
Non-interactiveness	5.5	4.3	6.3	4.2	1.14	0.29	1.62	0.21

[a] HRSD = 21-item Hamilton Rating Scale for Depression; HAMPSY = total of 17-item Hamilton Rating Scale for Depression items reflecting psychological symptoms, HAMSOM = those reflecting somatic symptoms; Zung = Zung Depression Scale; Newcastle = Newcastle Endogeneity Scale; GHQ = 30-item General Health Questionnaire; CORE = measure of psychomotor disturbance. [b] $n = 29$ for EO and 31 for LO subjects. [c] $n = 31$ for EO and 28 for LO subjects. [d] Analysis of covariance allowing for age (and for both age and anti-psychotic medication for the CORE sub-scales). [e] Zung: df = 1, 59; GHQ: df = 1, 58. [f] Zung: df = 1, 42; GHQ: df = 1, 42.

the data were reanalysed excluding subjects with psychotic depression, 'marked' hypochondriasis was present in one-third of the LO group, and none of the EO group, however this difference was not significant after Bonferroni correction. There were no significant differences on any of the other HRSD items. Data are presented in Table 2 for items of particular interest.

We also compared EO and LO patients on Hamilton sub-scale scores (HAMPSY and HAMSOM). Scores on the HAMPSY were slightly higher and on the HAMSOM slightly lower in EO patients, however these differences were not significant after covarying for age (Table 1). The same results were found when the patients with psychotic depression were removed from the analysis.

3.7. Neuropsychological tests

No significant differences were found between the age of onset groups on any of the tests of neuropsychological performance after allowing for the effects of age, gender, education and anti-psychotic medication use by ANCOVA (Table 3). Using appropriately adjusted normative scores for the COWAT, SDMT and reaction time tests (i.e. age and either education or gender adjusted depending upon test), we explored the data to see if either group contained a particularly poorly performing subgroup, defined conservatively as greater than or equal to two S.D.s worse than the normative data. There did not appear to be any differences in the proportions of impaired performers between the groups on any of these tests (23.1–31.6% in the EO group and 21.4–45.5% in the LO group).

3.8. Recurrence versus first episode of depression

Of the 23 patients experiencing their first episode of depression, 21 had LO and two, both with prolonged episodes, had onset before the age of sixty. Of the 50 patients with recurrent depression, 33 had EO. There were no significant differences in age, years of education or diagnostic type between those patients with or without previous episodes of depression (respectively: $t = 0.04$, df = 71, ns; $t = 0.54$, df = 70, ns; $\chi^2 = 4.01$, df = 2, ns). Severity of psychological morbidity/depression did not differ between patients having a first or recurrent episode. We repeated the phenomenological comparisons for

Table 2
Phenomenological comparisons between the EO and LO groups for all subjects and non-psychotic subjects only

Measure	Proportion of group with feature present		Comparison					
	% Early onset ($n = 35$)	% Late Onset ($n = 38$)	All subjects			Non-psychotic subjects		
			χ^2	df	P[b]	χ^2	df	P[c]
Delusions	28.6	28.9	0.00	1	1.00	N/A	–	–
Guilt								
Any	68.6	63.2	0.06	1	0.81	0.00	1	0.96
Marked[a]	20.0	15.8	0.03	1	0.87	1.18	1	0.28
Hypochondriasis								
Any	45.7	65.8	2.22	1	0.14	0.95	1	0.33
Marked	5.7	39.5	9.81	1	0.002	7.56	1	0.006[d]
Loss of interest								
Any	100.0	94.7	0.43	1	0.51	0.41	1	0.52
Marked	57.1	57.9	0.00	1	1.00	0.00	1	1.00
Anxiety (psychic)								
Any	91.4	86.8	0.06	1	0.80	0.02	1	0.89
Marked	60.0	39.5	2.30	1	0.13	0.46	1	0.50
Anxiety (somatic)								
Any	85.7	68.4	2.16	1	0.14	0.58	1	0.45
Marked	20.0	18.4	0.00	1	1.00	0.02	1	0.88

[a] 'Marked' means HRSD item scores dichotomised into 0–2 vs. 3–4. [b] Bonferroni adjusted $\alpha = 0.0045$. [c] Bonferroni adjusted $\alpha = 0.005$. [d] Not significant after Bonferroni adjustment.

Table 3
Measures of neuropsychological function by age of onset groups

Neuropsychological tests[a]	Raw test scores						Comparison (ANCOVA)[c]		
	Early onset			Late onset					
	n[b]	Mean	S.D.	*n*	Mean	S.D.	*F*	df	*P*
COWAT	14	24.4	12.0	22	21.0	14.0	0.72	1, 34	0.40
AL	16	10.3	4.0	27	10.3	2.9	0.45	1, 41	0.51
SDMT	17	21.5	12.3	22	21.7	12.7	2.51	1, 38	0.12
Trails A	17	84.4	50.0	25	100.2	61.9	0.83	1, 40	0.37
Reaction time									
Simple	19	546.3	330.9	28	542.7	321.2	0.23	1, 45	0.63
Complex	18	945.9	334.7	26	962.9	292.3	0.31	1, 42	0.58

[a] Abbreviations in text. [b] Note *n* values for different tests vary due to missing data. [c] Analysis of covariance, allowing for age, gender, education and anti-psychotic medication. Note: one subject had missing data for years of education, thus df one less than expected.

the recurrence groups and found no significant differences.

4. Discussion

We suggest that this study has important strengths including: (i) a reasonably large cohort of patients with late-life depression; (ii) a prospective design; (iii) the use of a number of recognised assessment instruments; (iv) the rating of possible aetiological factors; (v) the use of a 'mini-battery' of neuropsychological tests; (vi) the derivation of sample from a mixed age cohort of secondary and tertiary referrals (thus avoiding the biases inherent in only assessing referrals to a psychogeriatric service); (vii) the restriction of depressive diagnoses to unipolar major depressive episode and repeating analyses with psychotic depressed patients excluded, ensuring greater homogeneity; (viii) the assessment of phenomenology only of patients at or near the nadir of their episode; and (ix) the re-examination of psychomotor disturbance after allowing for effects of antipsychotic medications.

There were several limitations to the study. First, the results may not be generalisable as patients tended to be difficult to treat patients and most were inpatients. Secondly, there were a large number of statistical comparisons, however we used Bonferroni corrections where applicable. Thirdly, type II errors may well have arisen because of the limited number of subjects. We plan to overcome this in future by combining several cohorts of elderly patients with depression. Fourthly, the measures of personality were non-standardised and information on family history and relationships was by self-report. Finally, age of onset was categorical rather than continuous. In support of this latter decision, this allows comparison with previous reports and in this sample we note that all but two EO cases were recurrent from much earlier in life indicating a clear demarcation between early and late onset depression.

As in our previous work, there were similarities between the two age of onset groups of patients with late-life depression in terms of diagnosis (approximately one-third of elderly subjects in both samples had psychotic depression), proportion of inpatients and measures of depressive severity (Brodaty et al., 1991). We also found that, in both studies, the LO subjects were older, requiring partialling out of age effects where appropriate.

In examining our first hypothesis, regarding aetiology, we confirmed a higher prevalence of a positive family psychiatric history and of moderately to severely abnormal personality traits in the EO subjects. As in the Burvill et al. (1989) study, we found no significant difference between the groups in obsessive personality traits, but by contrast we found a larger number of EO subjects with dependent traits. Others have also reported a greater prevalence of Cluster C personality disorders in persons with EO depression (Abrams et al., 1994; Fava et al., 1996; Camus et al., 1997). A post hoc analysis revealed that our finding was not a result of recurrence of

episodes, there being no significant difference in the prevalence of dependent traits between patients having their first and those having a recurrent episode ($\chi^2 = 1.83$, df = 2, ns).

As well as their personality disturbances, there were trends for the EO group to experience more discord in either marital or other intimate relationships (i.e. higher divorce rate and reports of intimate relationship dysfunction) and to affirm dysfunctional past relationships with their parents more often. Recurrence of depression and marital status were not associated. In this and in our earlier study there was a trend for more objective physical impairment in the LO group (Brodaty et al., 1991). Holroyd and Duryee (1997) reported greater medical morbidity in geriatric outpatients with earlier onset of depression, which they attributed to a longer exposure to depression.

With one exception we confirmed our second hypothesis, that phenomenology in late-life depression would not be distinguishable by age of onset. We did find hypochondriasis to be more prominent in the LO group, as have others (Meyers and Mei-Tel, 1985; Meyers and Greenberg, 1986; Post, 1962; Brown et al., 1984) but this was no longer the case after the exclusion of psychotic subjects from the analysis. Consistent with other reports (Greenwald and Kramer-Ginsberg, 1988; Brodaty et al., 1991; Krishnan et al., 1995; Nelson et al., 1989; Baldwin, 1995), there were no significant differences between the groups in the prevalence of delusions, guilt or anxiety (psychic or somatic).

In contrast to the work of Krishnan et al. (1995), we did not find more apathy or loss of interest in LO than in EO patients. This is possibly due to the use of different scales to assess presence of phenomenological features — we used HRSD items (which were constructed to measure severity rather than presence) while Krishnan et al. (1995) used the Duke Depression Evaluation Schedule (a diagnostic interview instrument) and a different age (50 years) to differentiate EO from LO depression.

Even though Krishnan et al. (1995) hypothesised that motor retardation would be more severe in LO depression because of a greater incidence of basal ganglia lesions in LO than EO depression, he failed to find support. We also found, as in our 1991 study, no difference between the groups in terms of motor retardation. Total CORE scores, as well as those for agitation, retardation and non-interactiveness subscales, were similar for the two groups. Baldwin and Tomenson (1995) found a trend for higher prevalence of HRSD-rated agitation ($P = 0.046$) in the EO group after adjusting for the age difference between age of onset groups.

We were unable to confirm our third hypothesis that the neuropsychological performance would be worse in patients with LO depression. Scores on tests assessing memory, attention, executive function and motor speed were similar for the two groups, even when allowances were made for age, gender, education and psychotropic use. We can suggest three possibilities for these similar results. Firstly, the 'noise' of depression impairing cognition may have obscured 'signals' of differential cognitive function. Cognitive impairment due to depression may have been too severe for any additional impairment to be detected. Secondly, both EO and LO depression might be associated with cognitive impairment but by different pathways e.g. persons with EO depression presumably have longer exposure to the possibly damaging/toxic effects of depression (Sapolsky et al., 1988; Siegel et al., 1989; Abas et al., 1990), and/or anti-depressant treatment, while the LO pathway to cognitive impairment may be via (age-related) structural cerebral damage (Brodaty, 1996). Dahabra et al. (1998) concluded that, whilst structural changes were greater in LO patients, cognitive impairment was equivocal and therefore independent of structural changes. By contrast, Salloway et al. (1996) found greater cognitive dysfunction in their LO group, and that cognitive ability was significantly correlated with extent of subcortical hyperintensities.

A third possibility, that the real difference between EO and LO patients consists of a subset of LO depressives with severe cognitive impairment, was not supported in this data set. We tested for this by comparing the proportion of subjects in each age of onset group performing two standard deviations or worse below the mean, and found them to be equivalent. However, it is possible that our neuropsychological testing was not sensitive enough to detect such impairment; that differential cognitive abilities may only become apparent after recovery from depression or that longitudinal follow-up might reveal different rates of decline to dementia (Alex-

opoulos et al., 1993; Hickie et al., 1995, 1997; Greenwald et al., 1997). Contrary to this hypothesis, Palsson et al. (1999) found the incidence of dementia after a 3-year follow-up of 85-year-olds was significantly higher in their EO group when compared with the never depressed controls, but no greater than in the LO group.

While different aetiological factors operate in EO and LO depression (Hopkinson, 1964; Post, 1968; Mendlewicz, 1976; Conwell et al., 1989; Burvill et al., 1989; Brodaty et al., 1991; Baldwin, 1993, 1994, 1995; Krishnan, 1991; Hickie et al., 1996), they appear to be similar regards proportions of diagnostic sub-types and clinical phenotype. Our results support the hypothesis that there are (at least) two pathways to depression, one functional and one structural. Krishnan (1993), amongst others (e.g. Hickie et al., 1995, 1996; Alexopoulos et al., 1993) proposed that EO depression may have an inherited biochemical aetiology, whereas LO depression may be associated with structural brain changes.

We examined vascular factors in EO and LO groups because of the association between late-life depression and subtle brain damage (as indicated by both subtle cognitive impairment and structural changes). Eighteen percent of this sample (13/72) were rated as having possible, sub-clinical cerebrovascular disease, however the proportion was not significantly different between the LO and the EO groups. Krishnan et al. (1995), investigating vascular risk factors such as hypertension, heart disease and stroke, found no difference between age of onset groups, whereas Baldwin and Tomenson (1995) found a positive association between vascular disease and late onset depression. Greenwald et al. (1997) did not demonstrate an association between structural brain changes and modified Hachinski score in their geriatric depression sample, but suggest several aetiological pathways may be involved in late-onset depression, namely vascular, neurodegenerative, combinations of these and metabolic factors. In the future, other risk factors for vascular disease, e.g. homocysteine levels and antiphospholipid antibodies (Maes et al., 1993) and genetic markers such as the apolipoprotein E4 allele (Davignon et al., 1988; Holmes et al., 1998; Ohara et al., 1999; Papassotiropoulos et al., 1999) deserve further investigation.

We hypothesise different aetiological paths to the depressive syndrome, more specifically early onset depression appears to have greater genetic (and personality) aetiological contributions, whereas late onset depression appears to be more driven by acquired pathology. Once expressed, the phenomenology is stereotyped. Evidence supporting this is the similarity in phenomenology seen in unipolar and bipolar melancholic depression during the depressed phase (Mitchell and Sengoz, 1996), and between psychotic and non-psychotic depression in late life (Baldwin, 1995).

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