

# Increased rate of psychosis and psychomotor change in depression with age<sup>1</sup>

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## ABSTRACT

**Background.** We examined the phenomenology of depression in younger (< 60 years old) versus older (≥ 60 years) subjects and, more specifically, the interaction between age and psychomotor disturbance associated with depression.

**Method.** Two hundred and eighty-five patients with a DSM-III-R diagnosis of unipolar major depression referred to a mood disorders unit were assessed using the CORE rating scale, a sign-based system for defining melancholia. Subjects were also assessed using the Hamilton Rating Scale for Depression, Zung Depression Scale, Newcastle Endogenous Depression Inventory and the General Health Questionnaire.

**Results.** The total CORE score (and each of its subscales) was found to interact with age. Rates of psychotic and melancholic depression increased with age. Elderly depressives suffered more severe depression (higher HRSD scores), appetite loss and weight loss. Level of psychomotor disturbance and rates of psychosis did not differ between those elderly subjects with an early onset (before the age of 60 years) and those with a late onset (at or after 60 years) of depression.

**Conclusions.** There appear to be robust phenomenological differences in depression between older and younger subjects. The association between age and psychomotor change may assist our understanding of the neurobiology of depression.

## INTRODUCTION

The interaction of age and depression remains controversial. Some studies comparing older and younger patients have reported features such as withdrawal, apathy, lack of interest, lack of drive, suicidality and guilt to be over-represented in the elderly (Zung, 1965; APA, 1968; Brown *et al.* 1984; Ruegg *et al.* 1988), others have found little or no difference (Gurland, 1976; Blazer *et al.* 1987; Musetti *et al.* 1989). These inconsistencies may be explained by sampling differences and, more importantly, by the failure of researchers to analyse their data according to subcategories of depression (Brown

*et al.* 1984; Burvill *et al.* 1989; Musetti *et al.* 1989; Brodaty *et al.* 1991).

We have confirmed the importance of psychomotor disturbance (PMD) in defining the melancholic subtype of depression. Motor phenomena have long been held to be integral to melancholia (Parker & Brotchie, 1992; Mitchell *et al.* 1996; Parker *et al.* 1996a) and may even precede emotional phenomena (Mitchell *et al.* 1996). The essential motoric features of PMD are generally considered to be retardation, defined as being characterized by poverty of associations, impaired insight, slowed movement and speech, reduced speech, immobility of face and body and self-preoccupation; and agitation defined by features of motor restlessness reflecting inner mental perturbation, viz: 'persistent, excessive or inappropriate motor activity... manifested by a clear inability to sit or stay still', and by 'typically slow rubbing, pacing,

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writhing movements' (Parker & Brotchie, 1992). We developed a clinician-rated evaluation of PMD, the CORE instrument, which we have tested and refined (Parker *et al.* 1990, 1991, 1993; Hadzi-Pavlovic *et al.* 1993; Parker & Hadzi-Pavlovic, 1993). The CORE instrument assesses, in depressed patients, the central constructs of PMD as observable signs rather than as self-reported subjective symptoms (Parker *et al.* 1990; Parker & Brotchie, 1992).

In an earlier study of the comparative phenomenology of late-life depression, we analysed data sets for several subcategories of depression in a cohort with pure unipolar major depression (Brodaty *et al.* 1991). Of 242 consecutive patients with unipolar DSM-III defined major depressive episode, the 61 elderly (aged 60 years or more) patients had modestly, but significantly, more severe depression, as measured by the Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960), substantially higher Newcastle Endogenous Depression Inventory scores (Carney *et al.* 1965) and higher PMD scores on CORE-I, the first version of the rating instrument (Parker *et al.* 1990). Older depressives were more likely to be delusional and agitated and to have marked loss of appetite (Brodaty *et al.* 1991). Psychosis occurred in no patient under the age of 40 years, 16% of those 40–59 years old and 33% ( $N = 20$ ) of the older patients. Marked agitation occurred in 4% of the young, 15% of the middle-aged and 28% of the elderly depressives. Re-analysis of results after exclusion of patients with psychotic depression again found an over-representation of agitation in older patients indicating that this finding was not merely an effect of psychosis. Psychomotor retardation, as rated by HRSD, and age were not significantly associated.

While there was a trend for CORE-I scores to increase with age in the non-psychotic depressives, a weakness of CORE-I was its lack of agitation items and its heavy weighting to psychomotor retardation (Brodaty *et al.* 1991). Accordingly, we developed a revised instrument to rate psychomotor disturbance in depression, CORE-II, which has been validated by several methods (Parker *et al.* 1994, 1996*b*; Hickie, 1996; Hickie *et al.* 1996; Mitchell *et al.* 1996) and which comprises three clinically meaningful and factorially independent subscales (Parker *et al.* 1993). The items for non-interactiveness

(which relates to the functioning of cognitive processing domains which, when impaired in the context of a depression, may lead to diagnosis of 'pseudo-dementia') comprise non-interactiveness, non-reactivity, shortened verbal responses, inattentiveness, poverty of associations and impaired spontaneity of talk. Agitation items are facial apprehension, facial agitation, motor agitation, verbal stereotypy and stereotyped movements. Retardation items are facial immobility, postural slumping, delay in responding verbally, immobility, slowed speed of movement, delay in motor activity and slowing of speech rate (Parker *et al.* 1993). All items are rated on a four point scale where 0 = sign not present or normal, 1 = slight, 2 = moderate and 3 = severe or marked.

The present study of a further 285 consecutive in- and out-patients with a DSM-III-R defined (APA, 1987) unipolar major depressive episode focused on the interaction of age with scores on CORE-II (called CORE hereafter) and its subscales. We hypothesized that with older age, patients with a major depressive episode would exhibit higher rates of psychosis, greater levels of psychomotor disturbance – in particular, more severe agitation, and more frequent loss of appetite, but that the rate of psychosis and the levels of psychomotor disturbance in the elderly would not vary by age of onset.

## METHOD

### The sample

A second sample of in- and out-patients, separate from that reported in our earlier paper (Brodaty *et al.* 1991), was derived from 407 consecutive attenders to the Mood Disorders Unit at a Sydney teaching hospital, of whom approximately half were referred by general practitioners and half by psychiatrists (Brodaty *et al.* 1993). Usual reasons for referral are for a second opinion (70%), help with management (24%) or handing the case over (6%; Eysers *et al.* 1996). Diagnoses, using clinical and DSM-III-R criteria, were derived from structured interviews using diagnostic algorithms and were confirmed by at least two Mood Disorders Unit clinicians. We excluded 122 patients: 69 because they did not have a diagnosis of depression or their depression was not at its nadir, 44 with bipolar affective disorder, six with diagnoses other than

major depressive episode, and three with a definite or suspected organic affective disorder. It was reasoned that as clinical observations of patients who were recovering from their depression would not accurately capture the extent of PMD, it was desirable to perform our analyses only on patients who were in or near to the depth of their depression. Patients with depression judged clinically to be secondary to organic disorders, in particular Parkinson's disease, were excluded.

As psychotic depression was much more common in older depressives and, in case psychosis and PMD were related, we repeated our analyses for the following DSM-III-R defined diagnostic subgroups of unipolar major depression: psychotic depression alone; non-psychotic melancholic depression; the combination of psychotic and melancholic depressions (i.e. all DSM-III-R melancholics); non-melancholics; and combined melancholic and non-melancholic depressions which excluded those with psychosis.

#### Instruments

Patient assessment was identical to that described previously (Brodaty *et al.* 1991) except for the use of the later version of the DSM and the CORE instrument. This revised CORE instrument has a high inter-rater reliability, with an intra-class correlation of 0.87 (Hadzi-Pavlovic *et al.* 1993). Assessment included the clinician-rated 21-item Hamilton Rating Scale for Depression (HRSD; Hamilton, 1960) and Newcastle Endogenous Depression Inventory (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). Physical impairment was rated globally by clinicians on a four point scale: 0 = none, 1 = mild physical symptoms causing no impairment, 2 = mild physical symptoms with impairment, or moderate symptoms and 3 = severe symptoms and/or severely impaired function (e.g. chronic pain, unable to do housework).

#### Statistical methods

The distribution of subjects to age groups within the different diagnostic categories was analysed using the chi-square test (with Yates' correction). We used Spearman's rank-order correlation ( $r_s$ ),

a non-parametric procedure, to examine the effect of age (as a non-normally distributed continuous variable) on CORE and the subscale scores. After determining a significant correlation, we used Student's *t* tests to compare those subjects < 60 years and  $\geq$  60 years on total CORE and CORE subscale scores. The age of 60 years is the most commonly used age in the literature to split younger *versus* older subjects (Burvill *et al.* 1989; Abas *et al.* 1990; Brodaty *et al.* 1991; Baldwin, 1994; Tarbuck & Paykel, 1995; Devanand *et al.* 1996). These bivariate age comparisons were made for two reasons: (i) the study was a partial replication of previous work which used this cut-point; and (ii) it was more interesting clinically to obtain rates for the two age groups. Comparisons between older and younger subjects on other measures of depression, endogeneity, psychological morbidity and duration of illness were made using the distribution-free Mann-Whitney Rank Sum test since all variables were skewed. Analysis of phenomenological differences between the older and younger depressives was with the chi-square test (with Yates' correction), and alpha was adjusted for multiple comparisons using a Bonferroni correction. An analysis of covariance was used to examine the ability of CORE score to discriminate between melancholic and non-melancholic depressives after the effect of age had been removed. The level of significance was set at 0.05, except for corrected alphas for the multiple phenomenological comparisons, and all tests were, conservatively, two-tailed.

## RESULTS

### Demographic details and risk factors

The sample comprised 285 subjects, 155 (54.4%) in-patients and 130 (45.6%) out-patients. There were 208 subjects who were less than 60 years of age and 77 who were 60 years or older, of whom 36 had had their first episode of depression before the age of 60 – the early-onset or EO elderly depressives, and 41 had had their first onset when 60 years or older – the late-onset or LO elderly depressives. The average age of subjects under 60 years was 37.5 years (S.D. = 11.0) and for subjects 60 years and older was 68.6 (7.0). There were 103 males and 182 females, with the gender distribution for each age group being remarkably similar: 63.9% of younger

Table 1. *DSM-III-R diagnoses by age in subjects with unipolar major depressive episode*

Depressive subtype*	Subjects				All subjects			
	< 40 years		40–59 years		< 60 years		≥ 60	
	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%	<i>N</i>	%
Psychotic	3	3	6	7	9	4	25	32
Melancholic	35	29	46	52	81	39	47	61
Non-melancholic	81	68	37	41	118	57	5	7
Whole group	119	100	89	100	208	100	77	100

\* Categories are mutually exclusive: melancholic subtype here excludes psychotic depression.

subjects were female, compared with 63.6% of the older subjects. Older subjects had received significantly less education (mean of 9.0 years, s.d. = 2.6) than younger subjects (12.0 years, s.d. = 3.4;  $t = 6.91$ ,  $df = 281$ ,  $P < 0.001$ ). Occupational status did not differ significantly between the age groups, with 14.9% of the younger group belonging to the high category as compared with 9.2% of the older group. When demographic variables for the elderly were compared by age of onset of depression, they were all similar except for mean age: as expected, LO subjects were older.

We confirmed that older patients with depression were less likely than younger ones (< 60 years) to have a family history of a depressed parent (10.5% v. 36.7%,  $\chi^2 = 17.03$ ,  $df = 1$ ,  $P < 0.001$ ). Physical impairment, as rated globally by a clinician, was significantly more common in older than younger depressives (35.1% v. 12.5%,  $\chi^2 = 17.44$ ,  $df = 1$ ,  $P < 0.01$ ). Subjective reports of feeling physically unwell were similar in younger and older depressives.

### Diagnosis

Psychosis was over-represented in older patients (see Table 1), occurring in a third of those 60 years and older, and was almost absent in those younger than 40 years ( $\chi^2 = 43.22$ ,  $df = 2$ ,  $P < 0.001$ ). There was no significant difference in the proportions of psychotic depressives in the younger (< 40 years) and middle-aged (40–59 years) groups ( $\chi^2 = 1.29$ ,  $df = 1$ , NS). Melancholia was more common in the older depressives and correspondingly non-melancholia more common in those younger than 60 years ( $\chi^2 = 55.78$ ,  $df = 1$ ,  $P < 0.001$ ). There were significantly fewer non-melancholic depressives in the

middle-aged group than in the young ( $\chi^2 = 13.50$ ,  $df = 1$ ,  $P < 0.001$ ).

### Depression severity

Older depressives were more severely depressed (see Table 2) according to the clinician-rated HRSD, the Newcastle Endogenous Depression Inventory and the CORE, but not on the self-rated Zung or GHQ. The differences in Newcastle and CORE scores remained significant after the exclusion of the patients with psychotic depression, and when only the melancholics were studied. The Zung did not reveal any difference in severity of depression by age.

### Phenomenology

We found that the elderly had significantly higher rates of hallucinations, appetite loss (any or marked), weight loss, hypochondriasis (any or marked) and marked guilt (see Table 3). Except for hypochondriasis ( $\chi^2 = 5.78$ ,  $df = 1$ , NS) and marked guilt ( $\chi^2 = 2.66$ ,  $df = 1$ , NS), these findings were also confirmed when psychotic patients were excluded.

### Psychomotor disturbance

Total CORE scores increased with age ( $r_s = 0.44$ ,  $N = 285$ ,  $P < 0.001$ ), being greatest in the elderly (subjects ≥ 60 years, mean = 15.3, s.d. = 9.9; subjects < 60 years, mean = 5.0, s.d. = 6.0;  $t = -10.73$ ,  $df = 283$ ,  $P < 0.001$ ), with most of the increase occurring in the melancholic depressives (mean = 12.7, s.d. = 8.3 v. 6.7, 6.2;  $t = -4.65$ ,  $df = 126$ ,  $P < 0.001$ ). The comparison did not reach significance in the psychotic depressives presumably because of a ceiling effect, with scores high in both age groups (mean = 22.7, s.d. = 8.6 v. 19.4, 7.6), and because there

Table 2. Characteristics of depression and psychological distress by age

Measure*	Subjects				Analysis		
	< 60 years		≥ 60 years		z	df†	P
	Mean	s.d.	Mean	s.d.			
HRSD, mean (s.d.)	20.8	(6.5)	25.2	(7.1)	-4.70	284	0.000
Newcastle	1.8	(2.6)	6.1	(2.8)	-9.40	284	0.000
Zung	58.2	(7.8)	56.5	(8.8)	-1.65	257	0.100
GHQ	24.3	(6.8)	22.8	(7.5)	-1.29	253	0.198
Episode duration (wks)‡	83.1	(87.1)	68.0	(76.6)	-1.20	284	0.232

\* See text for depression measure abbreviations.

† df differs for Zung and GHQ because of missing data.

‡ Range of episode duration was 2-250+ weeks for all subjects.

Table 3. Depressive phenomenology of adult subjects and elderly subjects

Symptoms*	Subjects				Analysis	
	< 60 years (N = 208)		≥ 60 years (N = 77)		$\chi^2$ (df = 1)†	P‡
	N	%	N	%		
Delusions	8	3.8	23	29.9	36.62	0.000
Hallucinations	1	0.5	7	9.1	12.28	0.001
Appetite loss						
Any	129	62.0	62	80.5	7.88	0.003
Marked	72	34.6	47	61.0	15.07	0.000
Weight loss§	82	39.4	55	71.4	21.80	0.000
Weight gain	54	26.0	11	14.3	3.71	0.054
Hypersomnia	40	19.2	9	11.7	1.75	0.186
Suicidal plans	80	38.5	17	22.1	6.01	0.014
Insomnia						
Early	113	54.3	44	57.1	0.08	0.772
Middle	116	55.8	49	63.6	1.12	0.289
Late	80	38.5	43	55.8	6.23	0.013
Anxiety - psychic§						
Any	199	95.7	69	89.6	2.68	0.086
Marked	166	79.8	64	83.1	0.21	0.646
Anxiety - somatic§						
Any	160	76.9	60	77.9	0.00	0.984
Marked	117	56.3	44	57.1	0.00	1.000
Guilt§						
Any	135	64.9	51	66.2	0.00	0.945
Marked	8	3.8	13	16.9	12.15	0.000
Hypochondriasis§						
Any	69	33.2	45	58.4	13.92	0.000
Marked	33	15.9	31	40.3	17.83	0.000

\* Unmarked variables were rated from the Mood Disorders Unit structured interview.

† All values are Yates' corrected.

‡ Using a Bonferroni adjustment,  $\alpha = 0.0026$ .

§ Items from the HRSD (any = 0 v. 1-4; marked = 0-2 v. 3, 4).

were few younger psychotic subjects. Similarly the lack of a difference between age groups in their CORE scores in the non-melancholic subjects was affected by floor effects, with both younger and older non-melancholics having low scores (mean = 3.2, s.d. = 3.5 v. 2.7, 3.1), and by the presence of only a handful of old non-

melancholics. The strong interaction of CORE and age in the melancholics ( $r_s = 0.36$ ,  $N = 128$ ,  $P < 0.001$ ) was preserved when combined with either the non-melancholic ( $r_s = 0.35$ ,  $N = 251$ ,  $P < 0.001$ ) or psychotic depressives ( $r_s = 0.39$ ,  $N = 162$ ,  $P < 0.001$ ). There were no significant differences in total CORE scores between young

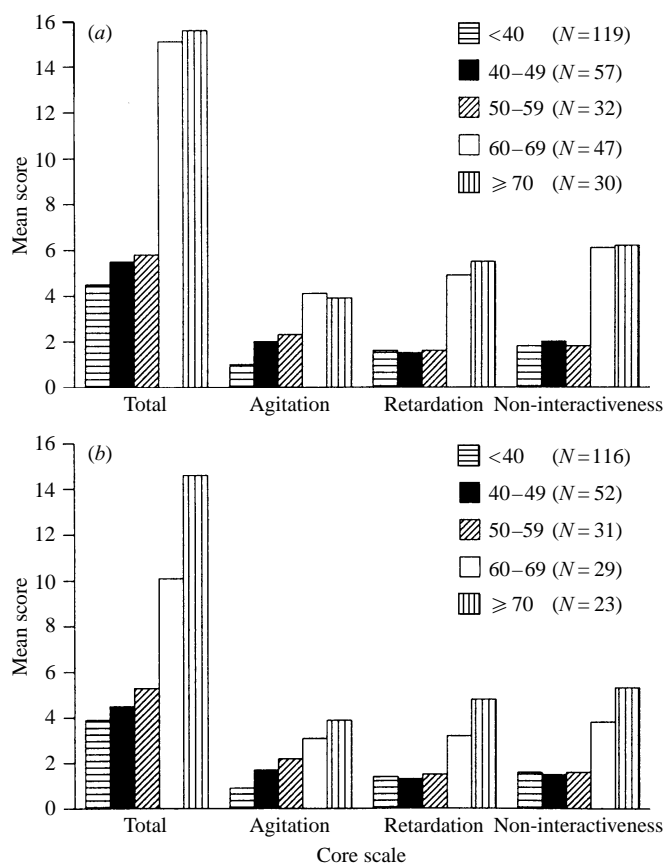


FIG. 1. Mean total CORE and subscale scores by decade: (a) all subjects with unipolar major depression ( $N = 285$ ); and (b) all subjects with unipolar non-psychotic major depression ( $N = 251$ ).

and middle-aged depressives. There appeared to be a 'dose effect' of age on CORE, which is more apparent when viewed by decades (Fig. 1a), even when patients with psychotic depression were excluded (Fig. 1b).

Examination of the separate CORE subscales (agitation, retardation and non-interactiveness) revealed no difference from the total CORE score analyses in terms of their relationship with age and diagnosis.

We now reversed the procedure in order to determine whether the diagnostic capacity of the CORE was merely a result of its association with age. After co-varying for age, the total CORE score still discriminated significantly between melancholic and non-melancholic depressives ( $F = 42.6$ ,  $df = 1$ ,  $282$ ,  $P < 0.001$ ). When the reversed analysis was repeated for the three

subscale scores the results did not differ from that for the total CORE score.

#### Age of onset and recurrence

In EO and LO subjects, depressive diagnostic subtypes were equally represented ( $\chi^2 = 0.45$ ,  $df = 2$ , NS) and total CORE (EO, mean = 14.0, s.d. = 10.3; LO, 16.5, 9.4;  $t = -1.12$ ,  $df = 75$ , NS) and subscale scores were similar. Subjects with first episode ( $N = 106$ ) and those who had experienced previous episodes ( $N = 179$ ) had similar total CORE and subscale scores. Similarly, neither the CORE nor subscale scores correlated significantly with the number of episodes ( $r_s$  from  $-0.02$  to  $0.04$ ,  $N = 283$ ), even when those subjects with psychotic depression were removed from the analysis ( $r_s$  from  $-0.05$  to  $0.03$ ,  $N = 249$ ).

## DISCUSSION

We concede that the study may be limited by a reliance on a clinical sample and because the sample was partly comprised of psychotic or very severely depressed in-patients whose histories may conceivably be somewhat unreliable. However, the nature of the sample also allowed for rigorous diagnostic assessment and facilitated the analysis by subtype of depression. It is possible that such a sample may have introduced a systematic age bias, given that elderly depressed patients tend to have a more severe illness when presenting to hospital (Brodaty *et al.* 1991; Larson *et al.* 1991). However, we note the proportions of non-melancholic depression and severity decreased with age, even among subjects younger than 60 years, in whom such a selection bias is far less likely. Further, referral patterns were similar for the three age groups.

We also acknowledge that the presence of cerebrovascular disease may well have contributed to psychomotor changes in this sample. Unfortunately, due to restraints of the study, presence or absence of cerebrovascular disease was only systematically rated in those patients aged 60 years or more, and so we are not able to comment on the proportion of the total sample potentially affected. A further issue pertaining to the methodology of this study is that of measurement of depression in elderly subjects. In recognition of phenomenological differences with age, scales have been designed specifically for the measurement of depression in the elderly, e.g. the Geriatric Depression Scale (Yesavage *et al.* 1983 *a*). However, because we endeavoured to examine the phenomenology of depression across a wide age range, it was necessary to use measurement scales applicable to all ages, and both the HRSD and the Zung have been shown to be reliable and valid but less sensitive measures of depression in the elderly (Yesavage *et al.* 1983 *b*).

While earlier authors provided vivid descriptions of PMD in depressives (Kraepelin, 1921; Lewis, 1934), only little attention was paid to an examination of phenomenology by the age of patient or the age of onset of depression (Tait *et al.* 1957; Post, 1968). In this hospital-based sample of both younger and older depressives, psychosis and psychomotor disturbance (PMD)

increased independently with age. As before, psychosis occurred in approximately one in three elderly depressives (Brodaty *et al.* 1991). Older depressives had episodes which were more severe (as defined by the HRSD) than younger patients in both studies even when allowances were made for differences in diagnostic subtypes. Regarding other clinical features of depression, we confirmed a strong nexus with age and appetite loss. The over-representation of weight loss and objective physical impairment in elderly depressives, neither of which we examined previously, were new findings.

We now examine putative explanations for the increase in psychosis and psychomotor disturbance in older depressives. First, we do not consider that these findings are merely a consequence of a subgroup of late-onset elderly depressives inflating the results for the older depressive group. Late-onset older depressives appear phenotypically similar to early-onset older patients (Brodaty *et al.* 1991; Baldwin, 1994; Krishnan *et al.* 1995). Secondly, while repeated episodes could conceivably cause organic changes, e.g. through the effect of hypercortisolaemia (Sapolsky *et al.* 1988) or the effects of treatment, this was insufficient in itself to explain our findings as first episode depressives had similar clinical presentations and CORE scores as those with repeated episodes. Thirdly, we reject the possibility of a cohort effect: the age gradients demonstrated in Fig. 1 argue against this. Fourthly, given the gradient effect of psychomotor disturbance and psychosis with age, we consider as unlikely the possibility that our findings merely reflect referral artefact, i.e. the threshold for referral is lower for younger patients and only more difficult elderly patients are being referred, as it is improbable that such a bias would be operating for middle-aged patients.

A fifth explanation is more tenuous. If the prevalence of melancholia remains constant into late life but the numbers of patients with non-melancholic depression decrease, two consequences follow: a lower prevalence of depression overall, and a higher relative proportion of elderly depressives having a melancholic (and psychotic) subtype. There is strong evidence for a lower prevalence of depression in the elderly (Henderson, 1994; Wittchen *et al.* 1994). Could 'psychological immunization' (Henderson *et al.*

1972), maturation or increased resilience to adversity (Henderson, 1994), reduce an individual's propensity to depression over time, especially, we hypothesize, to non-melancholic depression? It is unclear whether this would be of sufficient magnitude to explain the higher proportions of depression with psychomotor features and psychosis in late life (Brodaty, 1996).

We conclude that the phenomenological differences in late-life depression appear to be real and robust, and suggest that they may be linked to pathoplastic effects of age on EO depression or to structural brain changes in LO depression. The reported associations between LO depression and cerebrovascular disease (Krishnan, 1991; Alexopoulos *et al.* 1993; Hickie *et al.* 1995), and the negative association between late-life depression and family history (Brodaty *et al.* 1991; Krishnan, 1991; Hickie *et al.* 1995), which was confirmed here, may be relevant. There is a pressing need for more studies that carefully correlate phenomenology of depression with neuropsychological and neuroimaging findings; to repeat such studies on these same patients when not depressed; and, in time, to obtain post-mortem neuropathology.

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