RESEARCH ARTICLE

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Late life depression: a comparison of risk factors and symptoms according to age of onset in community dwelling older adults

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Background: It has been reported that late onset depression is more frequently associated with acquired organic pathology and that patients are less likely to report a family history of depression. Differences in phenomenology according to age of onset have been described although these have not been consistently replicated. The majority of these studies have been in hospital populations. The aim of this study is to address this question in a sample of community dwelling older adults.

Methods: 89 subjects with GMS-AGECAT depression were identified from a sample of 1231 community dwelling adults aged 65 years and over. Subjects were analysed across a range of aetiological and phenomenological variables according to age of onset of first depressive episode.

Results: Subjects with late onset depression (≥ 60) were significantly less likely to report a family history of depression, were less likely to report previous hospitalisation for depression and had greater cognitive impairment. Late onset subjects were also less likely to report feelings of guilt or thoughts that life was not worth living in the previous month.

Conclusion: While we found that patients with late onset depression differed from early onset patients according to certain aetiological risk factors, we did not find a distinctive profile of depressive symptomatology which might be considered clinically useful at an individual level. These findings are consistent with studies based in hospital populations. Copyright © 2009 John Wiley & Sons, Ltd.

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Introduction

Depressive symptoms are a significant cause of morbidity and mortality in community dwelling older adults (Blazer, 2003). A previous systematic review of community based studies (subjects $\geq$55 years) reported an average prevalence of 1.8% for major depression while all depressive syndromes considered clinically relevant reached a prevalence of 13.5% (Beekman *et al.*, 1999). The variables implicated in the aetiology of late life depression are many and include factors relating to psychosocial adversity, increased medical comorbidity, neurological abnormalities and genetic vulnerability (Blazer, 2003). There is also a growing understanding of the complex bidirectional relationship between depression and vascular disease with ongoing exploration of possible neuroendocrine and inflammatory mediators (Teper and O'Brien, 2008). It has been proposed that patients with first onset of depressive episode in later life include a large subgroup of patients with acquired organic pathology (Alexopoulos, 2005). Late onset depression has been

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associated with abnormalities on neurological evaluation (Baldwin *et al*., 2005), stuctural brain changes and an increase in subcortical vascular pathology (Baldwin, 2005, Teper and O'Brien, 2008). Patients with late onset depression have also been reported to have increased carotid intima-media thickness which is a marker of systemic atherosclerosis (Smith *et al*., 2009). It has been proposed that such patients may vary in terms of clinical presentation, course of illness and response to treatment according to underlying aetiopathology. Specifically, patients with a *vascular* subtype of depressive illness have been reported to display decreased negative cognitions, more psychomotor retardation, increased apathy, dysexecutive features on neurocognitive evaluation and have a poorer response to treatment (Alexopoulos *et al*., 1997a) (Alexopoulos *et al*., 2002). These distinctions in clinical presentation have not been replicated by all investigators while others have suggested that such symptoms may be too non-specific to be diagnostically useful (Baldwin, 2005). It has also been hypothesised that earlier age of onset of first depressive episode may be a marker of greater genetic vulnerability (Brodaty *et al*., 2001). Indeed the association between earlier age of onset and a postive family history of depression has been replicated in a number of studies although this has not been universally found (Brodaty *et al*., 2001, Baldwin and Tomenson, 1995, Conwell *et al*., 1989). It has equally been reported that patients with later age of onset have an increased familial risk of vascular disease suggesting an alternate genetic pathway to depression in later life (Kendler *et al*., 2009). Investigators have reported an excess of personality disorders, particularly cluster C, in subjects with early onset depression (Camus *et al*., 1997, Fava *et al*., 1996) while in one study, members of this group reported an increased frequency of dysfunctional maternal relationships (Brodaty *et al*., 2001). The issue of whether late *versus* early onset depression differ according to phenomemological characteristics is yet more controversial. Certain investigators have reported that patients with early onset depression have increased anxiety symptoms, (Baldwin and Tomenson, 1995, Baldwin *et al*., 2005) increased guilt (Conwell *et al*., 1989) and less apathy (Krishnan *et al*., 1995) while others have failed to find any notable association (Brodaty *et al*., 2001). The majority of studies which have examined age of onset of depressive disorder in relation to phenomenological and aetiological variables have either included patients who self-presented to primary care or were referred for specialist treatment. To the best of our knowledge, only a small number of studies have examined these hypotheses in community-based samples (Janssen *et al*., 2006, van Ojen *et al*., 1995b, Corruble *et al*., 2008). Given that a minority of patients with depression in the community are referred to secondary care and that such patients tend to have more severe and enduring illness means that findings from hospital samples may not necessarily generalise to community populations (Eustace *et al*., 2001). In addition, it is possible that patients who manifest depressive symptoms such as increased apathy may be less likely to present for treatment and are thus excluded from opportunistic samples. The aims of this study, therefore are, to examine the distribution of aetiologic and phenomenologic variables as they apply to patients living in the community according to age of onset of first depressive episode.

Methods

The sample

Data were collected as part of a study on mental disorders among the community dwelling elderly which was ongoing in Dublin during the years 1993–1999. Recruitment and methods have previously been described (Kirby *et al*., 1997). In brief, a convenience sample of community dwelling adults aged 65 and over, was recruited from the registers of seven general practices located within the catchment area of St James's Hospital, Dublin. One thousand two hundred and thirty one subjects completed interviews with the GMS-AGECAT system and ALPHA minimum data set. The age and gender of the sample was similar to that of the elderly Dublin population according to 1991 census data (Kirby *et al*., 1997). One hundred and sixteen (9.4%) patients were identified as having case level depressive symptoms of whom 102 had additional data regarding age of onset and symptoms. Patients with a known history of cerebrovascular disease, case-level organic symptoms, neurological disorder or a history of bipolar illness or schizophrenia were excluded. Thirteen subjects were excluded either because of a history of cerebrovascular accident ($n = 9$), parkinson's disease ($n = 2$) or case level organic symptoms ($n = 2$). The remaining sample of 89 subjects comprised of 34 with early onset (< 60) and 55 with late onset (≥ 60) depression.

Measures

Diagnostic assessments were completed using the geriatric mental state interview (GMS) which is a semi-

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structured interview designed to assess organic and functional psychiatric disorders in the elderly. The interview was administered by trained interviewers (a doctor or research nurse) in the subject's home and the data collected were applied to the automated geriatric examination for computer assisted taxonomy (AGECAT) package to generate standardised diagnoses. According to this system each subject is awarded a score (0-5) for each of eight diagnostic clusters (organic brain syndrome, schizophrenia, mania, depression, obsessional neurosis, hypochondriasis, phobia and anxiety) which represents the level of diagnostic confidence for each syndrome. Scores of 3 or above on a diagnostic cluster have been shown to equate well with what psychiatrists would ordinarily rate as a case (Copeland *et al*., 1986). GMS-AGECAT generated diagnoses have been compared to those derived from DSM III criteria and have demonstrated good agreement for cases of depression against combined major depression and dysthymia (Copeland *et al.*, 1990). Data regarding individual depressive symptoms were extracted from the geriatric mental state examination and comorbid anxiety was assessed according to AGECAT generated diagnostic scores.

Sociodemographic data were collected using the minimum data set devised for the ageing in liverpool: health aspects (ALPHA) study (Saunders *et al*., 1993). Social network type was identified through the use of a social network instrument which describes five types of social network (Wenger, 1997). Subjects were dichotomised according to membership of a social network considered to be higher (*family dependent, local self-contained, private restricted*) or lower risk (*locally integrated, wider community-focussed*). Educational attainment was assessed by recording the number of years spent in formal education and socio-economic group according to occupational status. A modified version of the list of threatening events was used to identify serious life events in the preceeding 2 years (Brugha and Cragg, 1990). Patient reported chronic medical conditions and current medication were recorded on a checklist within the ALPHA data set. Cerebrovascular risk factors were defined as currently treated diabetes, hypertension, hypercholesterolaemia, atrial fibrillation or ischaemic heart disease. Subjects were dichotomised according to the presence of one or more risk factors. Global severity of illness was measured using an observer rated global illness severity scale which rated health status from excellent to severely impaired on a scale from 1 to 6. Subjects were asked if there were days when their usual activities were restricted by disability. Subjects were questioned regarding the age of first onset of depression and whether any first degree relatives had a history of depression. A history of previous hospitalisation for depression or electroconvulsive treatment was also collected by self-report. Cognitive testing was conducted using the the mini-mental state examination (Folstein *et al*., 1975).

Statistical analyses

A cut-point of 60 years was used to distinguish between early and late onset depression. This cut-point was chosen for consistency with previous studies on this topic (Brodaty *et al*., 2001) (Krishnan *et al*., 1995). Univariate and multivariate tests were applied as appropriate. Summary statistics and univariate analyses for the two groups are presented in Table 1. The groups were also assessed for phenomenological differences according to responses to individual items in the GMS which assessed for the presence or absence of symptoms over the preceeding month (Table 2). Pearson's χ^2 test was used for categorical data and Student's *t*-test for continuous data. A nominal significance level of $\alpha = 0.05$ was used. The variables examined are not independent and no formal correction for multiple testing was applied in this analysis. Variables found to be significant were subsequently entered into a multivariate analysis to identify independent association with late onset.

Results

Eighty-nine subjects met inclusion criteria and consisted of 34 with early onset (< 60) and 55 with late onset (≥ 60) depression. The mean age of onset was 35.3 (SD 13.8) and 67.8 (SD 7.3) respectively. There were no between group differences in age, gender, life events, education, socio-economic group, psychotropic medication use or severity of depressive symptoms (see Table 1). Subjects with late onset depression were, however, less likely to report a family history of depression, had lower scores on mini mental state examination and were less likely to report previous hospitalisation for depression. The association between later age of onset and cognition remained significant when age, gender and education were adjusted for in a logistic regression analysis (OR 0.75 95% CI 0.59–0.93, $p < 0.01$). Previous hospitalisation remained significant following adjustment for age, gender, current depression severity, socio-economic group, disability, life events and social network in a logistic regression analysis (OR 0.17 95% CI 0.043–0.691, $p < 0.012$).

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Table 1 Distribution of risk factors for depression and sociodemographic characteristics

Characteristic	Early *n* (%) ($n = 34$)	Late *n* (%) ($n = 55$)	χ^2/t	*df*	*p*	*p** (*adjusted*)
Age, mean (SD)	71.68 (5.04)	73.35 (5.91)	87	0.175		
Gender						
Female	26 (76.5%)	36 (65.5%)	1.21	1	0.27	
Male	8 (23.5%)	19 (34.5%)				
Married	14 (41.2%)	27 (49.1%)	0.53	1	0.47	
Bereavement	17 (50%)	32 (58.2%)	0.37	1	0.54	
Total life events, mean (SD)	1.18 (0.7)	1.31 (0.8)	0.7	86	0.49	
Social network (> risk)	16 (47.1%)	24 (43.6%)	0.99	1	0.752	
SE Group (4/5)	27 (79.4%)	35 (63.6%)	2.14	1	0.14	
Family history (depression)	14 (41.2%)	10 (18.2%)	5.64	1	0.018	0.021
MMSE, mean (SD)	26.8 (2.67)	25.6 (3.02)	2.05	86	0.044	0.01
Years education, mean(SD)	14.7 (1.59)	14.58 (1.23)	0.29	83	0.771	
Chronic illness, mean (SD)	0.74 (0.79)	0.95 (0.85)	−1.17	87	0.25	
Illness severity, mean (SD)	3.15 (0.78)	3.27 (0.89)	0.68	87	0.501	
Cerebrovascular risks (≥1)	15 (44.1%)	26 (47.3%)	0.08	1	0.77	
Disability	20 (58.8%)	35 (63.6%)	0.21	1	0.65	
Depression severity						
Dn3	22 (64.7%)	39 (70.9%)	0.37	1	0.54	
Dn4	5 (14.7%)	8 (14.6%)	0.00	1	0.983	
Dp3/4	7 (20.6%)	8 (14.6%)	0.55	1	0.46	
Previous ECT	3 (8.8%)	3 (5.5%)	0.379	1	0.538	
Depression Hospitalisation	10 (29.4%)	5 (9.1%)	6.19	1	0.013	0.012
Antipsychotic medication	2 (5.9%)	2 (3.6%)	0.247	1	0.619	
Antidepressant medication	10 (29.4%)	10 (18.2%)	1.52	1	0.217	
Benzodiazepine medication	19 (53.9%)	28 (50.9%)	0.209	1	0.648	

*Adjusted *p*-value following multivariate analysis.

Family history remained significantly associated following adjustment for age, gender and education (OR 0.3 95% CI 0.11–0.84, $p < 0.021$). Late onset subjects were also less likely to report feelings that life was not worth living in the previous month or to endorse symptoms of excessive guilt. Cognition and previous hospitalisation, which were found to be significant in the first analysis, were entered into a logistic regression model with the above phenomenologic findings. Both thoughts that life was not worth living (OR 0.31 95% CI 0.12–0.86, $p < 0.024$) and excessive guilt (OR 0.19 95% CI 0.052–0.68, $p < 0.011$) remained significantly less frequent in patients with late onset depression.

Table 2 Distribution of depressive symptoms

Symptoms	Early *n*(%)	Late *n*(%)	χ^2	*df*	*p*	*p* (*adjusted*)*
Depressed mood	26 (76.5%)	47 (85.5%)	1.15	1	0.284	
Diurnal mood variation	22 (64.7%)	37 (67.3%)	0.06	1	0.803	
Decreased appetite	6 (17.6%)	13 (23.6%)	0.45	1	0.503	
Excessive guilt	12 (35.3%)	4 (7.3%)	10.91	1	0.001	0.011
Decreased confidence	3 (8.8%)	8 (14.6%)	0.64	1	0.43	
Hopelessness	14 (41.2%)	24 (43.6%)	0.05	1	0.82	
Life not worth living	23 (67.6%)	25 (45.5%)	4.17	1	0.041	0.024
Ever suicidal/death wish	18 (52.9%)	18 (32.7%)	3.56	1	0.059	
Suicide attempt/plan	2 (5.9%)	2 (3.6%)	0.247	1	0.619	
Lack of energy	17 (50%)	29 (52.7%)	0.063	1	0.80	
Apathy	7 (20.6%)	18 (32.7%)	1.53	1	0.216	
Decreased sleep	18 (52.9%)	23 (41.8%)	1.05	1	0.306	
Excessive worry	21 (61.8%)	33 (60%)	0.023	1	0.868	
Slowing of thoughts	14 (41.2%)	28 (50.9%)	0.79	1	0.372	
Slowing of movements	27 (79.4%)	49 (89.1%)	1.58	1	0.21	
Comorbid anxiety (≥ An3)	12 (35.3%)	10 (18.2%)	3.306	1	0.069	

*Adjusted *p*-value following multivariate analysis.

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Discussion

One of the stengths of this study is that interviews were carried out by experienced clinicians utilising a recognised and validated diagnostic procedure. The study subjects were identified in the course of a large naturalistic study of the community dwelling elderly and subjects with a history of stroke, neurological disorder or complicating psychiatric diagnoses such as schizophrenia or bipolar disorder were excluded. In addition we were able to measure and adjust for a range of potentially confounding sociodemographic and treatment related factors. One of the limitations is that age of first onset of depression was collected retrospectively and as such is subject to the recall bias of elderly depressed subjects. It is known that patients frequently tend to undervalue or forget past episodes of depression and there is some evidence that older respondents may systematically increase the age of onset of their symptoms (Kruijshaar *et al*., 2005, Prusoff *et al*., 1988). It is also possible that type II errors may have arisen given the small number of subjects under study.

There are nonetheless a number of interesting findings in this sample of community dwelling older adults. We found that subjects with late onset depression were significantly less likely to report a positive family history of depression and to have lower scores on mini mental state examination. The finding of an association between earlier age of onset and a positive family history of depression is probably one of the more consistently replicated findings in this area (Brodaty *et al*., 2001, Baldwin and Tomenson, 1995, Conwell *et al*., 1989). The finding of increased cognitive impairment in subjects with late onset depression has also been reported by other investigators (Salloway *et al*., 1996, Lesser *et al*., 1996) although a large number of studies have not demonstrated this finding (Brodaty *et al*., 2001, Baldwin and Tomenson, 1995). Specifically, with regard to studies based in the community dwelling elderly, one study using similar methodology found an association between later age of onset and cognitive impairment (van Ojen *et al*., 1995a) while another found no significant association after adjustment for confounders (Janssen *et al*., 2006). It has been argued that differences in selection processes and methodology may account for some of this variability in research findings (Brodaty *et al*., 2001). Differing neurocognitive profiles have been described in *amyloid-associated* and *vascular* depression (Sun *et al*., 2008, Alexopoulos *et al*., 2002). In addition, the relationship between depression and cognition is complex with increasing evidence for a bidirectional relationship (Steffens *et al*., 2006). In this study we did not find any significant association between the presence of cerebrovascular risk factors and later age of onset. This may be attributable to the fact that cognition was relatively well preserved in this sample of community dwelling older adults.

We did find that subjects with early onset depression were more likely to report previous hospitalisation for depression although they did not differ otherwise in terms of current severity of depressive symptoms, current psychotropic medication or history of treatment with electroconvulsive therapy. Unfortunately, however, the interpretation of this finding is limited by the absence of additional information regarding number and severity of previous depressive episodes. The finding of increased thoughts of guilt and feelings that life was not worth living with a trend towards ever being suicidal or having a death wish in early onset subjects might be interpreted as consistent with a history of more severe depressive illness requiring hospitalisation. It is noteworthy that a 3-year follow-up of depression in the same population found that a positive family history of depression was a predictor of relapse and persistent symptoms. Earlier age of onset was also noted to be associated with poor outcomes in those with a positive family history (Denihan *et al*., 2000). It has previously been reported that older adults with early onset depression have a worse prognosis (Brodaty *et al*., 1993) while conversely others have reported that late onset depression was a predictor of chronicity (Alexopoulos *et al*., 1996, Conwell *et al*., 1989). It has also been reported that specific subgroups of patients with acquired neuropathology such as severe deep white matter lesions have been found to have poorer outcomes (O'Brien *et al*., 1998). More recently an analysis of 3896 subjects enrolled in the sequenced treatment alternatives to relieve depression (STAR*D study) reported that earlier ages at onset were associated with having a family history of depression, more recurrent and more severe episodes, more suicide attempts, higher levels of medical comorbidity and increased social disruption (Zisook *et al*., 2007). It is possible that aetiological heterogeneity in the samples under study may account for some of the variability in findings and that an analysis by age of onset alone may be too simplistic to accurately define the aetiopathology and illness trajectory for particular patient subgroups. It is also important to note that two randomised controlled trials have reported no difference in treatment outcomes accord-

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ing to the age of onset although one did report a slower speed to remission in early onset cases (Reynolds *et al.*, 1998, Kozel *et al.*, 2008).

The finding of increased negative cognitions such as increased feelings of guilt in subjects with early onset depression is one which has been found in a number of studies (Corruble *et al.*, 2008, Conwell *et al.*, 1989). These findings however, have not been consistently replicated and those who have found small phenomenological differences have concluded that the findings were too modest or too non-specific to be of clinical utility at an individual level (Corruble *et al.*, 2008, Brodaty *et al.*, 2001). It is also noteworthy that we did not find significant differences in other symptoms which might ordinarily be considered part of a complex of negative cognitions such as depressed mood, decreased confidence and expressions of hopelessness. Early onset subjects did not report previous suicidal planning or attempts significantly more frequently than late onset subjects although this was an infrequent occurrence in the sample overall. We also did not replicate differences which other authors have reported such as increased apathy and psychomotor retardation (Krishnan *et al.*, 1995, Alexopoulos *et al.*, 1997a, Alexopoulos *et al.*, 1997b) in subjects with late onset depression. These features have been particularly associated with cerebrovascular pathology which was likely under-represented in this largely cognitively intact sample of community dwelling elderly.

In conclusion, in this community dwelling population of older adults with depression, we found that early and late onset groups differed significantly according to the family history of depression and cognition consistent with the proposition that these groups may pursue differing aetiological pathways towards the depressive phenotype. While we did find significant differences in guilt and feeling that life was not worth living, we did not find any clear profile of depressive symptomatology which might be considered clinically useful in terms of distinguishing patients with late onset depression from those with earlier or more familial forms of the disease. This is consistent with findings from studies based in hospital populations. Future studies may benefit from the use of novel and emerging disease biomarkers to extend existing knowledge in this area. The complex and multifactorial nature of depression in later life mandates the clinician to consider all possible competing and contributory aetiological mechanisms towards pursuit of a successful outcome in each patient.

Key points

- We examined differences in phenomenology and risk factors for depression according to the age of onset in a sample of community dwelling older adults.
- Subjects with late onset depression were significantly less likely to report a family history of depression and had greater cognitive impairment.
- Variability in aetiological factors by age of onset did not define a distinctive symptom profile which might be considered clinically useful at an individual level. This is consistent with findings from studies based in hospital populations.

Conflict of interest

None known.

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