Appearance of depression in later life

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Chapter 2

Phenomenology of depression in older compared with younger adults: meta-analysis

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Abstract

Background

Late-life depression may differ form early-life depression in its phenomenology.

Aims

To investigate the effect of age on the phenomenology of major depression.

Method

A systematic search was conducted in Pubmed, Embase and PsycINFO for all studies examining the relation between age and phenomenology of major depression, according to the RDC, DSM and ICD criteria. Studies were included only if the age groups were compared at the single-item level using the 17-, 21- or 24-item versions of the Hamilton Rating Scale for Depression; a meta-analysis was done for each item of the 17 item scale.

Results

Eleven papers met the inclusion criteria. Older depressed adults, compared to younger depressed adults, demonstrated more agitation, hypochondriasis and general as well as gastrointestinal somatic symptoms, but less guilt and loss of sexual interest.

Conclusions

The phenomenology of late-life depression differs only in part from that of early-life depression. Major depression in older people may have a more somatic presentation, whereas feelings of guilt and loss of sexual function may be more prevalent in younger people.

Introduction

Late-life depression is a common psychiatric disorder at old age. It often has a poor long-term prognosis more frequently showing a chronic course and a higher relapse rate compared to depression at younger age.[1] In addition, late-life depression is linked to more medical co-morbidity (e.g. cognitive impairment and cardiovascular diseases) and a high risk of mortality.[2-4] A different phenomenology has been suggested for late-life compared to early-life depression. Possible reasons for a different presentation of late-life depression are the overlap of somatic symptoms of depression and physical disease in old age, and socio-cultural factors such as the minimal expression of sadness in the current cohort of old people not used to complaining about depressed mood.[5] Also, age-related biological and psychological factors may underlie a different phenomenology of late-life and early-life depression. In 3 narrative reviews insufficient evidence was found to support a different presentation of depression in older people.[5-7] However, conceptual and methodological limitations of the reviewed studies, and the inherent subjectivity and bias proneness of narrative reviews, might have played a role in this conclusion. Therefore, this meta-analysis of studies examines the phenomenology of depression at the single-item level of the Hamilton Rating Scale for Depression (HRSD), also known as the Hamilton Depression Rating Scale (HDRS) or abbreviated to HAM-D.

Methods

Study selection

A systematic literature search was performed in PubMed, EMBASE and PsycINFO. The following (key)words were used: depress*, depressive, major depression, dysthymic disorder, geriatric patients, geriatric psychiatry, elder*, elderly, geriatric, aged, old age, old, oldest old, middle aged, adult, adults, early onset, late onset, onset age, age of onset, age at onset, phenomenol*, symptom*, clinical presentation, clinical features, atypical, melanchol* and dimension*. These were combined with the Medical Subject Headings (MeSH) depression, depressive disorder, signs and symptoms and age factors. The search was run on the 18 July 2011. No limitations in the search strategy were inserted. Reference lists from all relevant literature were hand searched for additional relevant articles overlooked by the database search. Then, titles and abstracts of the articles were screened to identify possible relevant articles. Finally, the remaining articles were full-text reviewed (by J.H.) with respect to our inclusion and exclusion criteria. In case of doubt, articles were discussed in a consensus meeting with three authors (J.H., R.K., R.M.).

Studies were excluded if no comparison was made between old age and younger age regarding the phenomenology of major depression; if studies did not present primary data (e.g. letters, comments and reviews were excluded); and if the study population consisted mainly of persons with bipolar disorder, schizoaffective disorder or dementia.

Samples could be drawn from an in-patient, out-patient, primary healthcare or general population. As depression is a heterogeneous disorder irrespective of age, strict diagnostic criteria were used. Participants had to be diagnosed with major depression according to either the RDC, ICD-9, ICD-10, DSM-III, DSM-III-R or DSM-IV criteria. The cut-off age for late-life depression had to be defined between 50 and 70 years or, alternatively, correlation coefficients between age and item scores had to be presented. To increase homogeneity, we only included studies in which symptoms of depression were measured using the HAM-D and both age groups were compared at the single-item level for the HAM-D-17, HAM-D-21 or HAM-D-24. Furthermore, the HAM-D is the most commonly used observer-rated and validated instrument for rating depression in both younger and older adults.[8] Where articles reported data on overlapping cohorts, the studies with the largest sample size or with the most complete information were included.

Mean scores and standard deviations as well as frequencies of the 17 items of the HAM-D-17 for all HAM-D scales, mean total HAM-D scores (and standard deviations), and number of participants were extracted from the articles. Form studies reporting frequencies of high- or low-severity scores on individual HAM-D items, as well as presence of the item, the frequency of any presence at all was extracted. Correlations were extracted when articles provided only correlations between age and single-item scores. When only subsets of the 17 HAM-D items were presented, the authors of more recent studies (published after 1995) were contacted and requested to provide missing data. Where mean scores or correlations were presented separately for men and women or for early-onset and late-onset late-life depression, these were transformed into one weighted combined mean score (SD) or correlation coefficients using appropriate formula.

Quality assessment

Quality assessment of observational studies in meta-analyses is not usual and there is no consensus regarding the method used.[9,10] In the present study, the quality of the included studies was assessed by two authors (J.H., E.G.) using a checklist with the following 5 criteria: (a) both age groups were selected from the same source population; (b) population characteristics and inclusion and exclusion criteria were described; (c) (semi)structured diagnostic instruments were used; (d) difference in overall disease severity between younger and older patients controlled for, or no statistically significant difference in depression severity reported; and (e) a complete set of 17 HAM-D items was usable or transformable for

meta-analysis. For two criteria weighting was applied, resulting in quality criteria a through c being coded as 0 or 1, and criteria d and e as 0, 1 or 2 points, and these criteria were summed to yield a sum score ranging from 0 to 8 points. If no information was provided as to whether a specific quality criterion was met, it was coded as 0 points. The cut-off for high or low quality was defined at a score of 5 or more, based on the 60% cut-off point commonly used in quality assessments.[11] Discrepancies between the reviewers were resolved through discussion (J.H., E.G.).

Statistical analyses

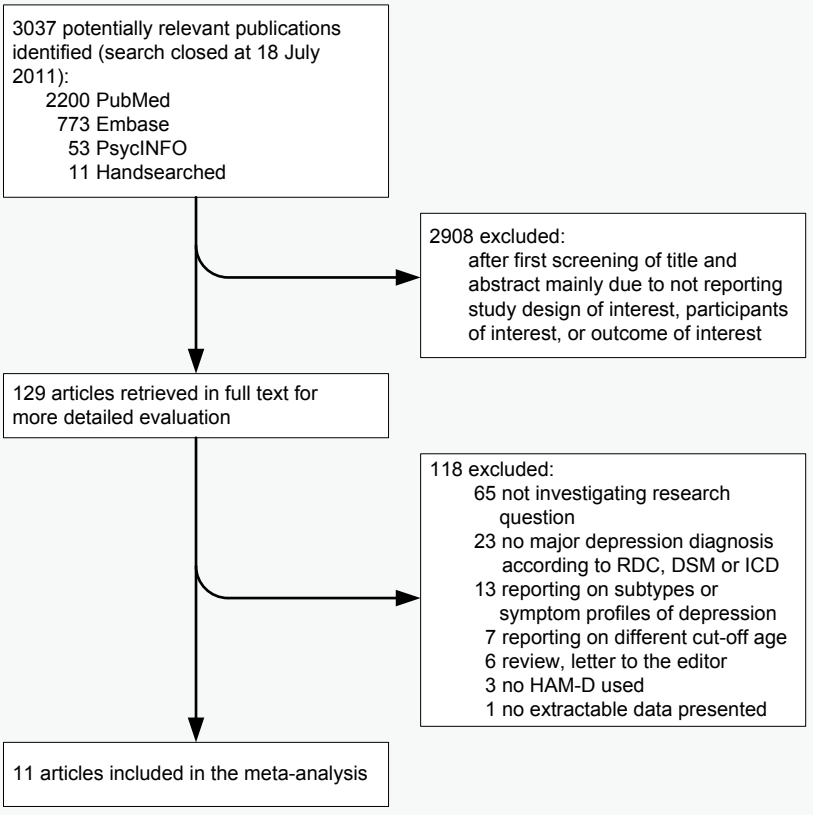
Data management, calculation of effect sizes and quantitative data synthesis were performed using the Comprehensive Meta-Analysis software version 2.0.021 (www.meta-analysis.com). Odds ratios were calculated for each HAM-D-17 item separately and were used for all mean comparisons. A higher odds ratio means that the particular HAM-D item showed higher prevalence rates and/or higher severity in older *v*. younger patients. Because considerable heterogeneity was expected, all analyses were performed with the random-effects model that reduces the risk of a type I error (as fixed models typically result in narrower confidence intervals). To assess heterogeneity between the studies we calculated the I^2, which is an indicator of heterogeneity in percentages, and used a value ≥50% to indicate meaningful heterogeneity.[12] In addition, *Q* statistics were calculated. A statistically significant *Q* rejects the null hypothesis of homogeneity and indicates a heterogeneous distribution of effect sizes between studies, meaning that systematic differences, possibly influencing the results, are present. For each HAM-D-17 item two summary estimates were calculated: an estimate based on the studies with usable data (see Fig. 2); and an estimate based on the studies with a quality score of ≥5 points, to estimate the effect of bias and potential confounding. A p-value below 0.01 was considered statistically significant, because of multiple testing for every HAM-D item.

Results

Selected studies

The search yielded 3037 articles, including 2200 in PubMed, 773 in Embase, 53 in PsycINFO and 11 hand-searched articles. Exclusion of duplicates and irrelevant references after a first screening of the titles and abstracts left 129 potentially relevant articles for further evaluation (Fig. 1). Most articles were excluded because they did not report the outcome of interest (65 studies), mainly as follows: comparing the phenomenology of early onset *v*. late onset late-life depression (20 studies), or examining neurocognitive function rather than

Figure 1. Flow chart of study selection.



depressive symptomatology in relation with age (14 studies). Of the 23 excluded articles not concerning a diagnosis of major depression, 21 reported on depressive symptoms, one reported on minor depression and one on dysthymic disorder.

Finally, 11 articles were included in this meta-analysis comparing early and late-life major depression. Because some articles did not present all individual items of the HAM-D, three sets of authors were contacted.[13-16] In one case we received the unreported HAM-D items.[13] In the second case,[14,15] the authors were also asked whether two different articles presented data on the same study population. Although our question was not answered we extracted the data, choosing the article with the largest study population. As the HAM-D items 'weight loss' and 'anxiety' were not presented in this larger study, we extracted these data from the article with the smaller sample size.[14,15] Data from a third article by this group were

Table 1. Characteristics of the 11 included studies.

Study	Assessment instrument, Criterion	Population	Sample size, n			Age, years						Exclusion Criteria	HAM-D score: mean (SD)			
						Mean age			Cut-off age	Mean age at onset						
			EL	LL	All	EL	LL	All		EL	LL		EL	LL	All	Q[a]
Brown *et al* (1984)	SADS, RDC	IP	28	63	91	39	64		50	34	60	Bipolar disorder, schizophrenia, schizoaffective disorder, secondary depression	32.0 (7.5)	31.3 (7.8)		7
Small *et al* (1986)	NR, DSM-III	OP	38	39	77	35	67		55			Psychosis, actively suicidal	22.1 (5.0)	22.7 (6.1)		4
Brodaty *et al* (1991)	Semi-structured interview, DSM-III	IP/OP	181	61	242	37	69		60			Primary diagnosis of alcohol or drug abuse, not fluent in English, insufficient cognition	18.8 (7.6)	21.2 (9.6)		5
Koenig *et al* (1993)	DIS, RDC	Medical IP	26	44	70				<40-70+[b]			NR				5
Wallace *et al* (1995)	Structured interview, DSM-III	IP			257			39				Medical or pharmacological condition that might invalidate dexamethasone suppression test				5
Brodaty *et al* (1997)	Structured interview, DSM-III-R	OP	208	77	285	38	69		60			Bipolar disorder, depression secondary to organic disorder, diagnosis other than major depression episode	20.8 (6.5)	25.2 (7.1)		5
Stage *et al* (2001)	Structured interview DSM-III/III-R/IV	IP	228	233	461			55	55			Other mental or neurological disorders, acute infections, pregnancy, severe systemic diseases			23.1 (4.4)	6
Tan *et al* (2001)	Structured interview, DSM-IV	IP/OP	28	42	70	38	73		60	35	69	Neurological disorder, dementia, mute	23.8 (5.2)	26.5 (6.3)		8
Brodaty *et al* (2005)	Structured interviews, DSM-III-R/IV	IP/OP	242	40	282				60			Depression secondary to physical illness or substance abuse	19.1 (6.5)	22.2 (8.0)		5
Shahpesandy (2005)	NR, ICD-10	NR	60	46	106	45	71		65			NR				1
Gournellis *et al* (2010)	SCID-IV, DSM-IV	IP	30	69	99	45	70		60	45	56	MMSE<23, depression secondary to somatic condition, non-psychotic depression	29.3 (5.7)	30.3 (6.0)		8
All studies					2011											

DIS, Diagnostic Interview Schedule; EL, Early-Life Depression; HAM-D, Hamilton Rating Scale for Depression; IP, in-patient; LL, late-life depression; MMSE, Mini-Mental State Examination; NR, not reported; OP, out-patient; RDC, Research Diagnostic Criteria; SADS, Schedule for Affective Disorders and Schizophrenia; SCID, Structured Clinical Interview for DSM-IV Axis I Disorders.

a. Quality assessment score.
b. Participants were aged <40 or >70 years.

also included in this meta-analysis because the study population was without any doubt a different group.[17] In the third case, the author was unobtainable for further information concerning not reported or not transformable HAM-D scores and methodological issues.[16] For this latter article, Z scores and p-value statistics were used for the reported HAM-D items.

Late-life depression v. early-life depression

Table 1 presents the characteristics of the included studies; the total number of patients was 2011. On average, older patients had significantly more severe depression (seven studies with standardized difference in means: 0.33, 95% CI 0.13-0.52, p=0.001).[13-15,17-20] However, four studies did not report the overall HAM-D severity scores for older and younger patients.[16,21-23] In fact, depression severity was particularly higher in older patients in the three studies of Brodaty *et al.*[14,15,17] Apart from this, another study included a population with psychotic depression only,[13] in which both age groups were severely affected. Small *et al* reported only on guilt.[19] With regard to quality assessment, we rated 9 articles[13-15,17,18,20-23] as being of high quality and 2 articles[16,19] as being of lower quality.

Figure 2 presents the pooled odds ratios for the relation between age and symptoms of depression according to the HAM-D-17. Random effect modelling, with a 95% confidence interval (CI) and p<0.01, showed that older people with major depression, compared to younger people, demonstrated more agitation (OR=1.84, 95% CI 1.39-4.45, p<0.001), general

Figure 2. Forest plot of overall odds ratios (and their 95% confidence intervals as the extremes of the diamonds) comparing early-life and late-life occurrence of every HAM-D-17 item in a random-effects meta-analysis of 11 studies, ordered according to the magnitude of the effect size. Red diamonds indicate the items more prevalent and/or severe in older patients, and the blue diamonds the items more prevalent and/or severe in younger patients.

HAM-D-17 item	Statistics for each study					Sample size		Odds ratio and 95% confidence interval
	Odds ratio	Lower limit	Upper limit	Z value	P value	N studies	N participants	
Hypochondriasis	3.132	2.240	4.378	6.679	< 0.001	9	1678	
Somatic–general	2.007	1.382	2.916	3.657	< 0.001	7	1154	
Agitation	1.842	1.388	2.445	4.229	< 0.001	6	1048	
Somatic–gastrointestinal	1.580	1.266	1.971	4.052	< 0.001	7	1154	
Weight loss	1.554	0.989	2.441	1.914	0.056	7	1333	
Insomnia–late	1.513	1.082	2.117	2.417	0.016	7	1154	
Anxiety–somatic	1.476	1.023	2.129	2.079	0.038	8	1439	
Loss of insight	1.305	0.858	1.984	1.243	0.214	7	1154	
Retardation	1.157	0.585	2.288	0.418	0.676	7	1154	
Work and activity	1.145	0.664	1.975	0.487	0.626	7	1154	
Insomnia–middle	1.141	0.833	1.564	0.824	0.410	7	1154	
Anxiety–psychic	1.127	0.779	1.630	0.636	0.525	7	1333	
Insomnia–early	1.125	0.887	1.427	0.972	0.331	6	1048	
Depressed mood	0.921	0.555	1.529	–0.318	0.750	7	1154	
Guilt	0.524	0.424	0.646	–6.020	< 0.001	9	1473	
Sexual interest	0.512	0.373	0.703	–4.138	< 0.001	7	1154	
Suicidality	0.450	0.213	0.952	–2.088	0.037	6	1048	

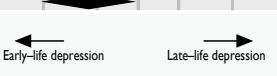
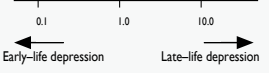


Figure 3. Forest plot for the 6 statistically significant HAM-D-17 items ($P<0.01$) for the comparison between early-life and late-life depression.

HAM-D-17 item	Sample size	Statistics for each study					Odds ratio and 95% confidence interval
	N	Odds ratio	Lower limit	Upper limit	*Z* value	*P* value	
Hypochondriasis							
Brown *et al* (1984)	91	2.250	0.995	5.089	1.948	0.051	
Brodaty *et al* (1991)	242	5.398	2.824	10.318	5.101	< 0.001	
Koenig *et al* (1993)	70	1.020	0.322	3.231	0.034	0.973	
Wallace *et al* (1995)	257	2.688	1.693	4.269	4.192	< 0.001	
Stage *et al* (2001)	461	2.018	1.439	2.830	4.066	< 0.001	
Tan *et al* (2001)	70	7.497	2.960	18.989	4.249	< 0.001	
Shahpesandy (2005)	106	3.336	1.594	6.978	3.198	0.001	
Brodaty *et al* (2005)	282	5.127	2.353	11.172	4.113	< 0.001	
Gournellis *et al* (2010)	99	3.447	1.555	7.643	3.046	0.002	
Overall	**1678**	**3.132**	**2.240**	**4.378**	**6.679**	**< 0.001**	
Somatic–general							
Brown *et al* (1984)	91	1.000	0.446	2.242	0.000	1.000	
Koenig *et al* (1993)	70	1.508	0.411	5.538	0.619	0.536	
Wallace *et al* (1995)	257	1.516	0.968	2.376	1.817	0.069	
Tan *et al* (2001)	70	6.824	2.709	17.188	4.074	< 0.001	
Stage *et al* (2001)	461	1.870	1.335	2.619	3.638	< 0.001	
Shahpesandy (2005)	106	3.336	1.594	6.978	3.198	0.001	
Gournellis *et al* (2010)	99	1.734	0.794	3.788	1.381	0.167	
Overall	**1154**	**2.007**	**1.382**	**2.916**	**3.657**	**< 0.001**	
Agitation							
Brown *et al* (1984)	91	2.562	1.130	5.812	2.252	0.024	
Koenig *et al* (1993)	70	1.128	0.425	2.990	0.242	0.809	
Wallace *et al* (1995)	257	1.683	1.072	2.641	2.263	0.024	
Stage *et al* (2001)	461	2.097	1.494	2.943	4.280	< 0.001	
Tan *et al* (2001)	70	3.272	1.345	7.963	2.613	0.009	
Gournellis *et al* (2010)	99	0.978	0.449	2.128	–0.057	0.955	
Overall	**1048**	**1.842**	**1.388**	**2.445**	**4.229**	**< 0.001**	
Somatic–gastrointestinal							
Brown *et al* (1984)	91	1.296	0.577	2.908	0.628	0.530	
Koenig *et al* (1993)	70	13.255	0.657	267.586	1.686	0.092	
Wallace *et al* (1995)	257	1.472	0.940	2.306	1.689	0.091	
Stage *et al* (2001)	461	1.494	1.070	2.087	2.354	0.019	
Tan *et al* (2001)	70	1.103	0.463	2.626	0.222	0.825	
Shahpesandy (2005)	106	2.457	1.194	5.057	2.441	0.015	
Gournellis *et al* (2010)	99	2.216	1.010	4.860	1.986	0.047	
Overall	**1154**	**1.580**	**1.266**	**1.971**	**4.052**	**< 0.001**	
Guilt							
Brown *et al* (1984)	91	0.713	0.317	1.600	–0.821	0.412	
Small *et al* (1987)	77	0.403	0.141	1.151	–1.697	0.090	
Brodaty *et al* (1991)	242	0.967	0.521	1.795	–0.107	0.915	
Koenig *et al* (1993)	70	0.545	0.154	1.933	–0.939	0.348	
Wallace *et al* (1995)	257	0.446	0.283	0.705	–3.458	0.001	
Stage *et al* (2001)	461	0.477	0.340	0.669	–4.280	< 0.001	
Tan *et al* (2001)	70	2.842	0.301	26.862	0.911	0.362	
Shahpesandy (2005)	106	0.403	0.196	0.829	–2.468	0.014	
Gournellis *et al* (2010)	99	0.482	0.220	1.055	–1.826	0.068	
Overall	**1473**	**0.524**	**0.424**	**0.646**	**–6.020**	**< 0.001**	
Sexual interest							
Brown *et al* (1984)	91	0.322	0.141	0.734	–2.696	0.007	
Koenig *et al* (1993)	70	0.211	0.073	0.609	–2.875	0.004	
Wallace *et al* (1995)	257	0.588	0.374	0.922	–2.311	0.021	
Stage *et al* (2001)	461	0.804	0.576	1.122	–1.284	0.199	
Tan *et al* (2001)	70	0.452	0.188	1.087	–1.773	0.076	
Shahpesandy (2005)	106	0.470	0.230	0.961	–2.070	0.038	
Gournellis *et al* (2010)	99	0.455	0.208	0.998	–1.964	0.050	
Overall	**1154**	**0.512**	**0.373**	**0.703**	**–4.138**	**< 0.001**	



(OR=2.01, 95% CI 1.38-2.92, p<0.001) and gastrointestinal somatic symptoms (OR=1.58, 95% CI 1.27-1.97, p<0.001) and hypochondriasis (OR=3.13, 95% CI 2.24-4.38, p<0.001), but less guilt (OR=0.52, 95% CI 0.42-0.65, p<0.001) and less loss of sexual interest (OR=0.51, 95% CI 0.37-0.70, p<0.001) (Fig. 3). A sensitivity analysis of the 9 articles of high quality revealed that the significant differences persisted for all 6 HAM-D-17 items.[13-15,17,18,20-23] Another sensitivity analysis excluding studies with more severe depression in older people *v.* younger people revealed similar results.[14,15,17] Again, removing the study with patients with psychotic depression only,[13] did not notably affect the sizes of the odds ratios, although these were no longer significant for loss of sexual interest and general and gastro-intestinal somatic symptoms.

Heterogeneity between studies was not significant for the items agitation (Q=6.44, p=0.26), gastrointestinal (Q=5.17, p=0.52) somatic symptoms, guilt (Q=8.10, p=0.43) and loss of sexual interest (Q=10.12, p=0.12), suggesting a homogeneous distribution of effect sizes between the studies. However, for the items hypochondriasis (Q=17.90, p=0.02) and general somatic symptoms (Q=13.17, p=0.04) the I^2 value was just above the 50%, which has a minor effect as we used random-effect models. No study was identified as a consistent outlier for most of the 17 HAM-D items.

Discussion

The results of this meta-analysis show a partly different phenomenology of late-life depression compared with early-life depression. Older people with major depression demonstrated more agitation, general and gastrointestinal somatic symptoms and hypochondriasis, but less guilt and less loss of sexual interest, compared with younger people with major depression. The difference between the two groups did not reach statistical significance for late insomnia, somatic anxiety and suicidality, which might be due to the small numbers of subjects (type II error). In general, these results indicate that major depression in older people may have a more somatic presentation, whereas feelings of guilt and loss of sexual function may be symptoms that are more specific for depression at a younger age.

Our results are largely consistent with some earlier studies examining this subject in a different way than comparison at the single-item level of HAM-D. For example, older people with major depression were found more likely to have somatic symptoms and less likely to have guilt, suicidal and cognitive symptoms.[24] Another study found that older people were more likely to have agitation and late insomnia,[25] whereas younger people were more likely to have increased appetite, weight gain and decreased libido. Similarly, in a study examining exclusively psychotic depression,[26] an increase of agitation and a decrease of suicidality

and guilt was found in old age compared with younger age. Husain *et al* used the 30-item Inventory of Depressive Symptomatology - Clinician Rated and found clinically meaningful differences.[27] In their study, older people with non-psychotic major depression had more gastrointestinal symptoms and middle and late insomnia, less irritability and hypersomnia, and were less likely to hold negative cognitions of the self or the future. Others, [28-30] however, found no differences in the phenomenology of late-life and early-life depression. For instance, no differences in symptomatology of major depression were found in an inpatient psychiatric population using the Duke Depression Evaluation Schedule for the Elderly.[31] In addition, Corruble *et al*,[32] using the Montgomery-Äsberg Depression Rating Scale (MADRS), found similar results in a comparison of the phenomenology of major depression at age ≥60 years *v.* <60 years. In a sensitivity analysis we added the seven items that roughly corresponded to the HAM-D items, which did not lead to different conclusions (data not shown). In three reviews without quantitative data analysis it was argued that no clinically relevant differences were found.[5-7] However, although the studies in these earlier narrative reviews almost overlap with our studies, some recent articles were not included. Also, these differences in interpretation may relate to the advantages of a meta-analysis over a narrative review that is more prone to subjectivity and bias. Remarkably, in contrast to earlier studies, we did not find differences between older and younger age in the HAM-D items 'loss of insight', 'work and activity' and 'psychomotor retardation', which are closely related to the concept of apathy.[33-35] Also, in spite of what has been suggested by others,[5,36,37] no difference was found in depressed mood.

The question arises whether age-related factors modify the presentation of depression or just lead to overlap of somatic symptoms of depression and medical illness, both complicating the diagnosis of late-life depression. For example, not only decrease of sexual desire and sexual function with ageing, but also the lack of a living partner, might explain our finding that older patients had less sexual dysfunction caused by depression compared with younger patients.[38] The expression of more somatic symptoms and less guilt in older patients might be explained by the tendency of the current cohort of older people to express somatic instead of psychological complaints.[39] Alternatively, it might be that the phenomenology of late-life depression is related to specific risk factors; for instance, in the oldest old people, psychomotor retardation and loss of energy were associated with vascular or neurodegenerative risk factors whereas symptoms such as thoughts of death, as well as sleep and appetite disturbances, were more strongly related to an inflammatory risk factor.[40] However, another study on this subject reported conflicting results.[41] Besides, it is difficult to distinguish apathy and cognitive impairment as distinct clinical entities from depression at old age because of overlap of symptoms. Again, it follows that depression may have been overestimated in these studies, suggesting a different phenomenology based on

wrong assumptions.[42,43]

Several methods have been proposed to resolve the issue of overlap of somatic symptoms of depression and physical illness, complicating the diagnosis of late-life depression. For example, in an inclusive approach all somatic symptoms are included regardless of being primarily due to a medical illness, whereas in an exclusive approach somatic symptoms of depression are excluded and only psychological symptoms are counted for a diagnosis of depression. Next, in an aetiological approach a somatic symptom is only counted if not caused by a medical illness and in a substitutive approach the somatic symptoms are replaced by non-somatic alternatives.[44] Although the HAMD-17 is criticized for its use in patients with physical illness due to including too many somatic items, the use of this scale is even justified to diagnose post-stroke depression and depression in Parkinson's disease.[45,46] Moreover, some somatic symptoms were highly sensitive for post-stroke depression.[45]

Strenghts and limitations

The present study has some limitations. First, older patients had on average a higher level of severity of depression compared to younger patients, which may account for the slightly different phenomenology in older patients. Although statistically significant, these differences in depression severity were small and therefore not regarded as clinically relevant. In addition, sensitivity analysis excluding studies with significantly more severe depression in older people revealed similar results,[14,15,17] suggesting that our results are not likely explained by differences in depression severity. Alternatively, overlapping somatic symptoms of depression and co-morbid age-related physical disorders may explain the higher scores on depression severity scales in the older population. Second, we could not adjust for co-morbid physical disorders in older *v.* younger people. Lack of this information means that we cannot be certain if our findings are related to somatic co-morbidity. In fact, all but one study included in-patients, and perhaps older patients with a more somatic presentation were hospitalized more often than younger depressed patients in order to exclude an underlying somatic illness. In previous studies,[21,27] however, differences in the phenomenology of major depression persisted after adjustment for somatic comorbidity. One of these studies was included in our meta-analysis and used an inclusive approach for rating HAM-D items.[21] Third, as studies mainly reported on in-patients it follows that generalization of our findings to an out-patient or the general population is limited. Fourth, a conceptual limitation is the use of strict RDC, DSM and ICD diagnostic criteria for major depression and the HAM-D. Obviously, if distinctive features of late-life depression indeed exist, they would be missed if not included in the HAM-D. Moreover, if depression in older people presents with many symptoms that differ from the DSM or ICD criteria, then these patients might not be diagnosed as having depression and would not have been included

in these studies. Finally, this meta-analysis focused on comparing depression at older and younger age, irrespective of age of first onset. It follows that we did not address the question of whether the age at onset of the first depressive episode is related to a specific symptom profile of early- or late-onset late-life depression. However, the studies of Gournellis *et al* and Brodaty *et al* compared both early *v.* late-life depression and early onset *v.* late onset in late-life depression.[13-15] Gournellis *et al* found differences related to both age at onset and current age in which the group of older patients with early-onset depression had an in-between position concerning the extent of differences in hypochondrial ideation and gastrointestinal symptoms compared to a group of older patients with late-onset and a group of younger patients with early-onset depression.[13] In the studies of Brodaty *et al*,[14,15] differences were found related to current age only, but not for age at onset. Furthermore, as late-life depression probably encompasses patients with recurrent depressive episodes and treatment-refractory depression, it is possible that differences in the phenomenology between late-life and early-life depression might be more marked when studies only include patients with first episode depressive episodes. Ideally, these would be prospective cohort studies because recall bias of age at onset is one of the problems of such studies.[47] However, older patients with recurrent depressive episodes might also have a 'new onset' distinctive depressive episode, for example related to (vascular) changes in the ageing brain.

Strengths of this meta-analysis include the thorough search resulting in over 2000 patients from 11 studies, the quality of the review process, and the consistent findings across studies with generally low heterogeneity. Moreover, we are not aware of previous meta-analyses examining the relation between age and the phenomenology of major depression.

Clinical implications

In summary, the results of this study suggest only in part a different phenomenology of major depression in older people compared with younger adult patients. These findings are relevant for clinical practice, because we should be aware that major depression in older people may present in a more somatic way. This may help our understanding of the phenomenology of late-life depression related to certain risk factors and age at onset, in order to improve recognition and early detection, and refine prevention and treatment of depression in older people.

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