Clinically defined vascular depression in the general population

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ABSTRACT

Background. Vascular depression is regarded as a subtype of depression, especially in, but not entirely restricted to, the elderly, characterized by a specific clinical presentation and an association with (cerebro)vascular risk and disease. It could have major implications for treatment if subjects at risk for such a depression could be easily identified by their clinical presentation in general practice.

Method. We studied the symptom profile of depression in subjects with and without vascular risk factors in two large Dutch community-based studies, the Rotterdam Study and the Amsterdam Study of the Elderly (AMSTEL).

Results. We could not confirm the specific symptom profile in depressed subjects with vascular risk factors in either of the two cohorts. Depressed subjects with vascular risk factors showed more loss of energy and more physical disability than those without vascular risk factors. However, presumed specific symptoms of vascular depression, namely psychomotor retardation and anhedonia, were not significantly associated with any of the vascular risk indicators. Loss of energy was significantly associated with myocardial infarction and peripheral arterial disease.

Conclusions. In these two large community-based studies we identified some differences between vascular and non-vascular depressed subjects but found no evidence for a specific symptom profile of vascular depression as previously defined.

INTRODUCTION

The vascular depression hypothesis states that, especially in the elderly, a subtype of depressive disorder exists that is caused by vascular brain disease. This hypothesis is a very old one. Around 1900, the German psychiatrist Gaupp described 'atherosclerotic depression' (Gaupp, 1905). The concept was revitalized by Krishnan

and Alexopoulos and colleagues in the 1990s (Alexopoulos *et al.* 1997*a, b*; Krishnan *et al.* 1997), boosted by the development of new imaging techniques. Krishnan *et al.* coined the entity 'MRI defined vascular depression', with the vascular lesions on magnetic resonance imaging (MRI) as the obligatory finding. Besides the vascular characteristics, this group of patients could be recognized by a specific symptom profile of the depression. According to Alexopoulos *et al.*, the characteristics of this vascular depression include more pronounced

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psychomotor retardation, greater overall cognitive impairment and physical disability, fewer feelings of guilt and greater lack of insight. The MRI-defined vascular depression group of Krishnan *et al.* showed a similar picture; the subjects in his study were older, had a later age of depression-onset and showed more anhedonia and physical disability. Furthermore, in this study the non-psychotic symptoms prevailed whereas a family history of mental illness was less common. Both studies were conducted in hospital-based settings, which limits generalization to the general population. The concept of vascular depression has been challenged by several others, who found no specific association of cerebrovascular risk factors and depression subtypes in a primary care setting (Lyness *et al.* 1999; Licht-Strunk *et al.* 2004). The clinical importance of recognizing vascular depression as a subtype of affective disorder in primary care would be enhanced if it were possible to identify patients by simple tests or procedures, such as through specific symptoms or risk profiles. The recognition of such a specific subtype of depression could be of major importance in predicting the course of illness and the effect of medication and other therapeutic interventions. In the present study, we aimed to assess these phenomenological characteristics of depressed subjects with and without vascular disease in the general population. We thereby tested the hypothesis that subjects with a vascular risk would show more anhedonia and psychomotor retardation, and less feelings of guilt. Furthermore, we expected these vascular depressed subjects to show more physical disability.

METHOD

Subjects and procedures

Subjects were recruited from two large samples of community dwelling elderly adults: the Amsterdam Study of the Elderly (AMSTEL) and the Rotterdam Study. The AMSTEL is a prospective study that assesses mental health problems, medical diagnoses and demographic characteristics. The sampling and data collection procedures have been described elsewhere (Schoevers *et al.* 2000). In brief, the population base for AMSTEL included non-institutional individuals in the age range 65–84 years who lived in the city of Amsterdam. The profile of the study sample corresponded to the non-institutionalized Amsterdam population in terms of age and gender. Sample procedures and response rates have been described elsewhere (Launer *et al.* 1994). For this study, data on 4051 subjects were used. They were interviewed during home visits by lay interviewers who were specially trained using video sessions and were regularly supervised. Information on psychiatric symptoms, demographic and medical status, previous history and family history was gathered.

The aim of the Rotterdam Study is to investigate determinants of chronic and disabling diseases. The study was started in 1990, when all inhabitants aged 55 years and above in Ommoord, a district of Rotterdam, The Netherlands, were invited to participate. Sampling procedures and response rates have also been described elsewhere (Hofman *et al.* 1991). In this paper, data on 4603 subjects are used from the second follow-up survey in 1997 to 1999. In this survey assessment of depressive symptoms and a subsequent psychiatric work-up in persons who screened positive for depression was added to the study protocol. In addition, the total cohort is continuously being monitored for major morbidity and mortality through linkage of general practitioner and municipality records. Both studies were approved by the local medical ethics committee and written informed consent was obtained from all participants.

Psychiatric evaluation (Fig. 1)

In the AMSTEL, diagnoses of dementia and depression were made according to the Geriatric Mental State – Automated Geriatric Examination for Computer Assisted Taxonomy (GMS-AGECAT) system (Copeland *et al.* 1986, 1988). The Dutch language version has proven reliability for epidemiological work in replication studies (Hooijer *et al.* 1991). Cognitive status was also assessed by the Mini-Mental State Examination (MMSE) score (Folstein *et al.* 1975). 'Depressive caseness' (i.e. depression warranting intervention as defined by psychiatrists) was defined as a GMS-AGECAT level 3 or higher.

In the Rotterdam Study diagnosis of depression was assessed by a two-step procedure.
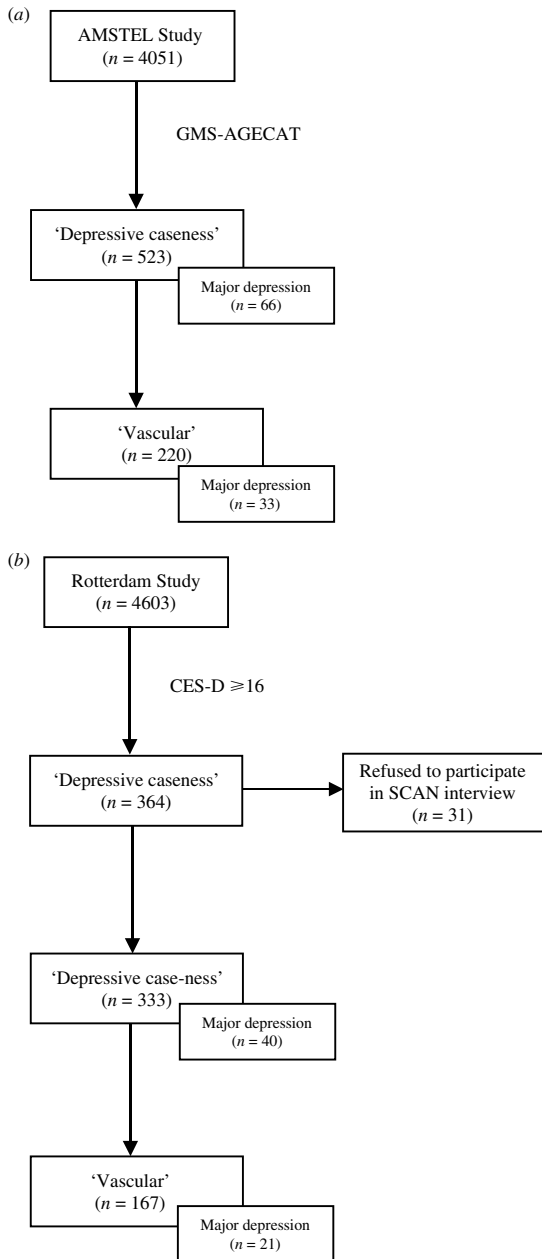
FIG. 1. Flow diagrams of (*a*) the AMSTEL and (*b*) the Rotterdam Study.

'depressive cases'. This cut-off had a very high sensitivity for major depression in another Dutch study in the elderly (Beekman *et al.* 1997). In a second step, screen-positive subjects had a psychiatric work-up. Of the 4603 subjects, 364 (7·9%) were screened positive as measured by the CES-D. Of these, 31 refused further participation and the psychiatric work-up was performed in the remaining participants (Table 1, *n* = 333). They were studied with the Dutch version of the Present State Examination, a semi-structured psychiatric interview included in the Schedules for Clinical Assessment in Neuropsychiatry (SCAN; WHO, 1997). All interviews were conducted by one of two experienced clinicians. Depressive disorders were classified according to the DSM-IV (APA, 1994) criteria by using the GMS (AMSTEL) and SCAN scores (Rotterdam Study). If subjects had either 'depressed mood' or 'loss of interest or pleasure', and a total of five or more of the nine DSM-IV depression symptoms, they were classified as having major depression. Subjects who had either 'depressed mood' or 'loss of interest or pleasure' and a total of at least two but no more than four depression symptoms were classified as having minor depression. According to the profiles found by Forsell, Janzing and colleagues, for each individual the following measures of depression were computed for both study groups (AMSTEL and Rotterdam) after the extended psychiatric work-up by counting the positively rated criteria (Forsell *et al.* 1993; Janzing *et al.* 1999):

- *Mood symptoms*: dysphoria, appetite disturbance, feelings of guilt and thoughts of death.
- *Motivational symptoms*: loss of interest, psychomotor retardation, loss of energy and thinking or concentration disturbance.

The total number of depressive symptoms was calculated by counting all positively rated criteria.

Finally, in the Rotterdam Study, we dichotomized subjects according to the presence of some of the typical symptoms of 'vascular depression' that were reported in the literature: anhedonia, psychomotor retardation and loss of energy (Alexopoulos *et al.* 1997*a*; Krishnan *et al.* 1997).

First, participants completed the Dutch version of the Center for Epidemiological Studies Depression Scale (CES-D) during the home interview. We used a score of 16 as a cut-off to indicate depressive symptoms and in our further analysis we have used this group as

Table 1. *Demographic and clinical characteristics of elderly patients with presumed vascular and non-vascular depressive disorder in both Rotterdam and AMSTEL study groups*

| | Rotterdam Study | | | | | AMSTEL | | | | |
| | Vascular (n=167) | | Non-vascular (n=166) | | | Vascular (n=220) | | Non-vascular (n=303) | | |
	Mean	S.D.	Mean	S.D.	p value	Mean	S.D.	Mean	S.D.	p value
Age (years)	76·5	7·2	73·9	7·6	0·001	75·5	5·7	75·9	5·6	0·36
Sex (% female)	68		82		0·006	73		90		<0·001
ADL	2·0	0·7	1·8	0·7	0·014	11·0	1·6	11·3	1·5	0·08
I-ADL	21·1	4·7	22·4	4·5	0·011	12·8	3·9	13·5	3·6	0·04
MMSE	26·4	3·0	26·9	3·0	0·18	25·8	4·3	26·0	4·2	0·48
Hamilton score	7·9	5·0	7·5	4·9	0·45	—	—	—	—	—
Diagnosis of major depression	21		19		0·60	33		33		0·99
Diagnosis of minor depression	17		21		0·47	10		11		0·81
Total number of depressive symptoms	2·0	2·2	1·9	2·0	0·81	3·0	1·8	2·8	1·7	0·21
Total number of mood symptoms	0·9	1·1	0·8	1·0	0·27	1·3	1·0	1·2	1·0	0·44
Total number of motivation symptoms	1·1	1·2	1·1	1·2	0·79	1·7	1·2	1·5	1·2	0·23

AMSTEL, the Amsterdam Study of the Elderly; S.D., standard deviation; ADL, Activities of Daily Living; I-ADL, Instrumental Activities of Daily Living; MMSE, Mini-Mental State Examination; GMS-AGECAT, Geriatric Mental State – Automated Geriatric Examination for Computer Assisted Taxonomy; CES-D, Center for Epidemiological Studies Depression Scale.

Depressive caseness is defined as a CES-D score >16 (the Rotterdam Study) or GMS-AGECAT level 3 or higher (AMSTEL).

Vascular risk

In the original study by Alexopoulos *et al.* (1997*a*), vascular risk was defined according to the score on the Cumulative Illness Rating Scale (CIRS; Miller *et al.* 1992). The original CIRS consisted of multiple organ-specific categories, but for the vascular depression categorization only the vascular subscale was used by Alexopoulos *et al.* We classified our subjects from both the AMSTEL and the Rotterdam Study into groups of persons with a high or low cardiovascular risk profile (a 'vascular' and a 'non-vascular' group). When subjects had a score equal to or greater than 1 on the CIRS they were assigned to the vascular group. Because with the CIRS subjects with severe and mild vascular risk were all assigned to the same group, we have also divided our sample into (*a*) a group of patients without any vascular risk factor, (*b*) a group of patients with vascular risk factors but no apparent vascular disease and (*c*) a group of patients with evident vascular disease. As this more detailed subdivision had no influence on the results, we have used only the original categorization using the CIRS.

In addition, vascular risk was studied more extensively in the Rotterdam Study. Of the screen-positive (CES-D) subjects (*n*=333) who participated in the home interview, 246 came to the research centre for non-invasive assessments of atherosclerosis. The 87 subjects with no assessment of atherosclerosis were on average older (79 *v.* 74 years) and had more depressive symptoms [total number of depressive symptoms 3·2 (S.D.=2·3) *v.* 2·5 (S.D.=2·0), overall total number 2·7 (S.D.=2·1)]. There was no difference in gender between the participants and non-participants (female: 78% *v.* 74%).

We measured atherosclerosis non-invasively with four established methods: the ankle-brachial blood pressure index, intima–media thickness in the common carotid arteries, the presence of plaques in the carotid arteries, and aortic atherosclerosis. These measures assess extra-coronary atherosclerosis at different locations in the body. All measures are strongly associated with incident cerebrovascular and coronary artery disease (Witteman *et al.* 1986; McKenna *et al.* 1991; Hollander *et al.* 2002). Details of these assessments are outlined in an earlier publication (Tiemeier *et al.* 2004).

Other measurements

In both studies some extra variables were assessed by similar methods. Age, sex, education,

cognitive function, cigarette smoking, blood pressure, diabetes mellitus, history of myocardial infarction and/or stroke, total cholesterol level, body mass index and use of antidepressant medication were all taken into account. Education was dichotomized into low (primary school or less) or high education. Level of handicap was measured with the Activities of Daily Living (ADL) scale (Katz *et al.* 1963) and the Instrumental Activities of Daily Living (IADL) scale (Lawton & Brody, 1969). Depression severity was measured only in the Rotterdam Study, with the Hamilton Depression Rating Scale (HAMD; Hamilton, 1960). Cigarette smoking was coded into categories of current, former or never smoker. History of myocardial infarction or stroke was only considered positive when it was verified by a physician. Total cholesterol level was assessed only in the Rotterdam Study and was analysed in fasting blood samples by an automatic enzymatic procedure. Body mass index was calculated using the Quetelet method (weight in kilograms divided by the square of height in metres) and was only measured in the Rotterdam Study. Information on antidepressant medication was obtained in the home interviews and in the Rotterdam Study it was secured by a cabinet check.

Statistical analysis

For statistical analysis we used SPSS version 12.0 (SPSS Inc., Chicago, IL, USA). χ^2 analysis was used to compare categorical variables and the independent samples *t* test to compare continuous variables. Prevalence of major and minor depression was established for the vascular and non-vascular groups, and the mean total number of depressive symptoms and also the specific mean number of mood and motivation symptoms were counted. The prevalence of all individual depressive symptoms was calculated for both the vascular and non-vascular groups. In the Rotterdam Study, the prevalence of vascular risk factors was calculated for subgroups of patients with specific depression symptoms, which supposedly would be more prevalent in 'vascular depression': anhedonia and psychomotor retardation. In this group, a subsequent logistic regression analysis was carried out controlling for confounding effects of age, sex, level of education and use of antidepressant medication.

RESULTS

General characteristics of the study groups (Table 1)

In the AMSTEL we identified a total of 523 subjects who fulfilled the diagnosis of depressive disorder according to the AGECAT system ('depressive caseness'). Two-hundred and twenty of these fulfilled vascular criteria (42%). The vascular subgroup differed from the non-vascular in that there were more males ($\chi^2 = 21.910$, df 1, $p < 0.001$) and they had lower scores on the I-ADL measure ($t = 63.292$, df 1, $p = 0.04$). In the Rotterdam Study, we identified 333 subjects with a cut-off score on the CES-D $\geqslant 16$ ('depressive caseness'). Of these, 167 fulfilled vascular criteria (50%). In this group the subjects in the vascular subgroup were older ($t = 577.086$, df 1, $p < 0.001$), there were more males ($\chi^2 = 7.656$, df 1, $p = 0.006$), and they had had more impairments on ADL ($t = 3.406$, df 1, $p = 0.014$) and I-ADL scores ($t = 137.761$, df 1, $p = 0.011$).

In both studies, no differences were found in the prevalence of major or minor depressive disorders, nor were there any differences in total number of depressive symptoms or number of mood or motivation symptoms.

Clinical profile of vascular and non-vascular depressive cases

The prevalence of DSM-IV depressive symptoms in both the vascular and non-vascular depressed cases of both community studies is shown in Table 2. Both in the AMSTEL and the Rotterdam Study subjects in the vascular subgroup showed more loss of energy (AMSTEL: $\chi^2 = 4.138$, df 1, $p = 0.04$; Rotterdam Study: $\chi^2 = 4.709$, df 1, $p = 0.03$). In the AMSTEL, subjects in the vascular subgroup also showed more appetite disturbance ($\chi^2 = 4.558$, df 1, $p = 0.03$).

Vascular risk profile in patients with predominant 'vascular depression' symptoms

In Table 3, the vascular risk profile of subjects of the Rotterdam Study with and without the supposed specific vascular depressive symptoms

Table 2. *Prevalence of individual symptoms of depression in vascular and non-vascular depressed cases*

	Rotterdam Study			AMSTEL		
DSM-IV mood item	Vascular ($n=167$) (%)	Non-vascular ($n=166$) (%)	p value*	Vascular ($n=220$) (%)	Non-vascular ($n=303$) (%)	p value*
Depressed mood	38	33	0·32	51	51	0·96
Loss of interest	37	39	0·70	25	23	0·48
Appetite disturbance	18	14	0·31	20	13	0·03
Sleep disturbance	73	71	0·69	51	57	0·20
Psychomotor retardation	20	25	0·28	32	32	0·90
Loss of energy	39	28	0·03	59	51	0·04
Feelings of guilt	6	7	0·65	11	11	0·99
Thinking/concentration	14	13	0·86	48	47	0·90
Thoughts of death	26	31	0·35	48	48	0·94

AMSTEL, the Amsterdam Study of the Elderly; GMS-AGECAT, Geriatric Mental State – Automated Geriatric Examination for Computer Assisted Taxonomy; CES-D, Center for Epidemiological Studies Depression Scale.

Depressive caseness is defined as CES-D score >16 (Rotterdam) or GMS-AGECAT level 3 or higher (AMSTEL).

* χ^2 (Pearson); analysis by logistic regression adjusting for age, sex, ADL and I-ADL in the Rotterdam Study, and for sex and I-ADL in AMSTEL.

is shown. All three symptom groups were more severely depressed and more cognitively disturbed. Subjects with anhedonia used more antidepressant medication than those without anhedonia ($\chi^2=10\cdot105$, df 1, $p=0\cdot001$). Subjects with loss of energy more often had peripheral arterial disease than those without loss of energy ($\chi^2=5\cdot241$, df 1, $p=0\cdot022$). No other associations were found. Subgroups of subjects with anhedonia, psychomotor retardation or loss of energy showed similar levels of depression, as measured with the HAMD, and also similar levels of cognitive functioning, as measured with the MMSE.

DISCUSSION

We found no evidence for a specific symptom profile of depression in subjects with vascular risk factors, as previously proposed by Alexopoulos and Krishnan and co-workers, in two large population-based cohorts. This finding is in line with an earlier study on the vascular depression hypothesis in the community (Licht-Strunk *et al.* 2004). In agreement with that study, we found that depressed persons with an increased vascular risk showed more loss of energy in both cohorts, and in one of our cohorts this vascular depressed group also showed more appetite disturbance. The other presumed specific symptoms of vascular depression, especially anhedonia and

psychomotor disturbance, were not more prevalent in the vascular than in the non-vascular subjects in either of the two cohorts. In a *post hoc* analysis we used a more extensive set of vascular risk measures in the Rotterdam Study. We found no relationship between the presumed specific symptoms of vascular depression, anhedonia and psychomotor retardation, other than that subjects with psychomotor retardation were more 'current smokers'. The symptom 'loss of energy' was particularly associated with myocardial infarction and peripheral arterial disease.

This association of vascular risk and loss of energy was also found by Licht-Strunk *et al.* (2004) and, in addition, as in our study, depressed subjects with vascular risk showed more disability as measured with ADL and I-ADL scales. Sato *et al.* (1999) suggested that the functional consequences of cerebrovascular disease may be the causal pathway by which basal ganglia and non-basal ganglia lesions are associated with depressive symptomatology.

Numerous studies have been conducted on the subject of vascular depression. They address the relationship of vascular lesions in the brain and depression, a specific symptom profile of vascular depression or the age of onset as a specific marker of (vascular) depression. The vast amount of literature on this topic illustrates the ongoing debate around the vascular depression concept. Level of caseness, depression

Table 3. *Vascular risk characteristics of subjects with and without anhedonia, psychomotor retardation or loss of energy in the Rotterdam Study*

	No anhedonia (n=159)	Anhedonia (n=87)	No psychomotor retardation (n=196)	Psychomotor retardation (n=50)	No loss of energy (n=172)	Loss of energy (n=74)
Age, mean (s.d.), years	73·8 (6·9)	73·8 (7·1)	73·9 (7·1)	73·5 (6·4)	73·5 (7·0)	74·5 (6·8)
Sex, % female	76	71	75	72	73	77
Primary education only, %	61	56	60	57	58	61
MMSE-score, mean (s.d.)	27·1 (2·6)	26·2 (3·4)*	27·0 (2·8)	26·0 (3·4)*	27·2 (2·2)	25·9 (4·1)**
Hamilton-score, mean (s.d.)	5·4 (3·4)	11·4 (4·7)**	6·9 (4·9)	9·8 (4·1)**	6·0 (3·6)	11·0 (5·5)**
History of stroke, %	6	8	8	2	7	7
History of MI, %	9	12	11	6	9	19**
Smoking						
Current smoker, %	18	23	17	28**	20	19
Ex-smoker, %	42	41	44	38	43	42
Antidepressant medication, %	6	20*	11	12	9	16
Blood pressure, mean (s.d.), mmHg						
Diastolic	72 (11)	74 (13)	72 (11)	76 (13)	74 (12)	71 (12)
Systolic	142 (21)	140 (26)	140 (22)	144 (27)	142 (21)	139 (27)
Total cholesterol, mean (s.d.) mmol/l	5·8 (0·9)	5·9 (1·0)	5·8 (0·9)	5·9 (1·1)	5·9 (1·0)	5·7 (0·8)
Body mass index, mean (s.d.)	27·1 (4·0)	26·7 (3·9)	26·9 (3·8)	27·0 (4·6)	27·0 (4·0)	27·0 (4·1)
Diabetes mellitus, %	12	6	11	6	10	10
Common carotid intima–media thickness, mean (s.d.), mm	0·88 (0·16)	0·90 (0·16)	0·88 (0·15)	0·91 (0·17)	0·88 (0·15)	0·88 (0·17)
Peripheral arterial disease,[a] %	23	22	24	15	18	31**
Carotid plaques, %						
None	29	28	28	28	28	29
Mild	17	18	16	21	16	19
Moderate	33	35	35	28	35	31
Severe	22	20	21	23	21	21
Aortic calcifications, %						
None	18	16	18	15	17	16
Mild	30	33	32	27	29	34
Moderate	28	17	22	34	29	15
Severe	25	34	29	24	25	34

MI, myocardial infarction; MMSE, Mini-Mental State Examination; s.d., standard deviation.

Continuous variables were analysed by analysis of covariance using the *t* test, and categorical variables by logistic regression, adjusted for age, sex, Hamilton and MMSE scores when appropriate.

Numbers of aortic calcifications were 212 in all three groups, 237 for carotid plaques. Group percentages did not differ significantly from the total group that was screened and no correlation was found between severity of aortic calcification or carotid plaques in any of three groups (Spearman's ρ).

[a] Defined as an ankle-brachial blood pressure index below 0·9.

* $p < 0.05$, ** $p < 0.001$.

diagnosis and referral bias are the major factors that affect findings and conclusions of different studies. In our study, as in other community studies, a certain restriction of range was encountered. Compared to clinical samples our subjects were less severely depressed.

By using two large community-based studies we have tried to overcome the problem of referral bias. We followed the definition of vascular depression according to Alexopoulos *et al.*, by studying only subjects who fulfilled criteria for depression and combining this with scores on the CIRS. There were two differences with the earlier reports of Alexopoulos *et al.* First, we could not include the age-of-onset criterion. Although important from a theoretical point of view, this criterion is often ill-defined and difficult to apply in clinical and community studies. This concerns both the onset of depressive symptoms and the onset of vascular changes. Second, Alexopoulos *et al.* measured severity and difference in severity of various depressive

symptoms, whereas we have dichotomized them and looked at the difference in prevalence of specific depression symptoms in vascular and non-vascular subjects. The argument for this is that we consider that scoring on symptom severity will introduce more subjectivity than just counting the absence or presence of a certain item. For the Rotterdam subjects we have compared the vascular and non-vascular subjects on overall symptom severity and found no significant difference.

As our study did not support the reports in the literature on vascular depression and the probability that this could be caused by differences in level of caseness of both depression and vascular risk, we also analysed our study groups with different definitions of both depression and vascular risk. Regarding the diagnosis of depression, we applied various definitions including 'depressive caseness' (AGECAT/ AMSTEL), major and minor depression and special symptom profiles. None of these had a major effect on the results. We consider that for general practice our use of 'depressive caseness' (AMSTEL) and screen-positive subjects (CES-D ⩾16, Rotterdam Study) was more appropriate because it includes all persons who might consult their general practitioner with their depressive complaints. It should be noted that we thus included a fairly large number of subjects with 'subclinical depressive symptoms' not fulfilling criteria for depressive disorder according to the DSM-IV. Regarding the definition of vascular risk, the CIRS may not be sensitive enough for use in general practice. In both samples we found a high prevalence of 'vascular disease' using the CIRS definition. This figure, however, is in line with the nearly 50 % rate found by Alexopoulos *et al.* in their 1997 study. This high prevalence indicates that from a public health point of view, the concept of vascular depression is potentially a very relevant concept. It could be argued that the CIRS overestimates the number of vascular subjects, but our subdivision and reanalysis into two groups with or without vascular risk factors and a third group with evident vascular disease did not significantly change our main results. Moreover, the mean scores on the HAMD scale in each symptom group show that there are no major differences in depression severity between the three symptom groups.

Some authors have focused on the concept of apathy rather than on depression after stroke, stating that the vascular 'depression' concerns apathy rather than depression (Starkstein *et al.* 1993). Apathy is defined as the absence or lack of feeling, emotion, interest or concern that expresses itself in emotion, behaviour or social interaction (Marin, 1990). Others have focused on 'new' syndromes such as the depressive-executive dysfunction syndrome (DEDS), in which the core symptoms are psychomotor disturbances, loss of interest and a mild vegetative syndrome (Alexopoulos *et al.* 2002; Vataja *et al.* 2005). For further evaluation of the vascular depression concept, it might be useful to focus on apathy instead of fully developed depression to elucidate the complex relationship between vascular brain damage and depression-like symptoms.

Our results do not definitively disprove the specific symptom profile of vascular depression. A 'vascular' aetiology of depression is possibly associated with a more chronic course of the depressive disorder (Mast *et al.* 2004) and might be a predictor of poor response to antidepressant medication (Fujikawa *et al.* 1996). It is also associated with poor outcome, as indicated by higher levels of mortality, higher incidence of new vascular events and higher incidence of subsequent cognitive decline (Baldwin *et al.* 1993; Penninx *et al.* 1998, 2001; Pohjasvaara *et al.* 2002). What remains is the challenge to detect subjects with a vascular risk in the general population. The clinical features of these subjects are still ill-defined and not very specific. Better use of refined psychiatric tools with emphasis on dimensional rather than syndromal diagnosis could be of major importance in detecting special subgroups of subjects with depression, for example those with vascular damage of the brain. Furthermore, not only are vascular changes of importance in provoking depressive symptoms and signs in (elderly) subjects suffering a vascular burden but also external motivation for depression cannot be denied, and for psychiatry the challenge remains to come to a full understanding of biological and social determinants of behaviour and their interaction (Kandel, 1998). The primary care physician will have to be focused on detecting depression in elderly individuals and also on looking carefully for co-morbid vascular disease

that may underlie or perpetuate the depressive state.

DECLARATION OF INTEREST

None.

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