Papers

Temporal relation between depression and cognitive impairment in old age: prospective population based study

David J Vinkers, Jacobijn Gussekloo, Max L Stek, Rudi G J Westendorp, Roos C van der Mast

Abstract

Objective To examine the temporal relation between depression and cognitive impairment in old age.
Design Prospective, population based study with four years of follow up.
Setting City of Leiden, the Netherlands.
Participants 500 people aged 85 years at recruitment.
Main outcome measures Annual assessments of depressive symptoms (15 item geriatric depression scale), global cognitive function (mini-mental state examination), attention (Stroop test), processing speed (letter digit coding test), and immediate and delayed recall (12 word learning test).
Results At 85 years old, participants' depressive symptoms and cognitive impairment were highly significantly correlated ($P < 0.001$). During follow up, an accelerated annual increase of depressive symptoms was associated with impaired attention (0.08 points (95% confidence interval 0.01 to 0.16)), immediate recall (0.17 points (0.09 to 0.25)), and delayed recall (0.10 points (0.02 to 0.18)) at baseline. In contrast, depressive symptoms at baseline were not related to an accelerated cognitive decline during follow up ($P > 0.05$).
Conclusion Care givers should be aware of the development of depressive symptoms when cognitive impairment is present. However, the presence of depression only does not increase the risk of cognitive decline.

Introduction

Depression and cognitive impairment are among the most important mental health problems in elderly people. Both conditions have severe consequences, including diminished quality of life, functional decline, increased use of services, and high mortality.[1] Late onset depression and cognitive impairment often occur together, suggesting a close association between them.[2–4] It is not known, however, whether depression leads to cognitive decline or vice versa.[4 5]

Clinical practice and research evidence suggest that depression precedes cognitive decline in old age.[5–10] However, inferring a relationship is hampered because most studies on this topic examined only the association between depression and the subsequent development of cognitive impairment.[6–14] As depression may be an early sign rather than an independent risk factor for cognitive impairment, the temporal relation between depression and cognitive impairment in old age remains unclear.

We followed up 500 elderly people living in the community with annual assessments of depressive symptoms and cognitive function in order to determine their temporal relation.

Participants and methods

Participants

The Leiden 85-plus study is a prospective, population based study of all 85 year old inhabitants of Leiden. Between 1 September 1997 and 1 September 1999, 599 participants were enrolled (response rate 87%). They were visited annually from the age of 85 to 89 years at their home for face to face interviews, and all gave their informed consent to participate.[15] For the present analysis, we included the 500 participants (83%) without severe cognitive impairment at baseline (mini-mental state examination score ≥ 19 points).

Cognitive function

We assessed

- Global cognitive function with the mini-mental state examination[16]—scores range from 0 to 30 points, with lower scores indicating impaired cognitive functioning
- Attention with the third chart of the 40 item Stroop test—time needed to name the ink colour of incongruously printed names of colours, with higher scores indicating poorer attention
- Processing speed with the letter digit coding test—total number of correct digits assigned to letters according to a code key in 60 seconds, with lower scores indicating a slower speed
- Immediate and delayed recall with the 12 word learning test—12 pictures are presented to the participant, who is then asked to recall them. Outcome for immediate recall is the total number of words correctly recalled immediately after each procedure; outcome for delayed recall is the number correctly recalled after 20 minutes. Lower scores indicate impaired memory.

Depressive symptoms

We assessed depressive symptoms with the 15 item geriatric depression scale (GDS-15).[17]

This is the abridged version of an article that was posted on bmj.com on 2 September 2004: http://bmj.com/cgi/doi/10.1136/bmj.38216.604664.DE

See also Clinical review p 895

Section of Gerontology and Geriatrics, Department of General Internal Medicine, Leiden University Medical Centre, PO Box 9600, 2300 RC Leiden, Netherlands
David J Vinkers *research associate*
Jacobijn Gussekloo *senior lecturer*
Max L Stek *senior lecturer*
Rudi G J Westendorp *professor*
Department of Psychiatry, Leiden University Medical Centre, Netherlands
Roos C van der Mast *senior lecturer*
Correspondence to: D J Vinkers
d.j.vinkers@lumc.nl

BMJ 2004;329:881–3

Table 1 Cross sectional correlation of depressive symptoms* with various measures of cognitive function in 500 people aged 85 years living in the community

Cognitive function test	Pearson's correlation coefficient (*r*)	P value
Global cognitive function	−0.296	<0.001
Attention	0.182	<0.001
Processing speed	−0.238	<0.001
Immediate recall	−0.194	<0.001
Delayed recall	−0.182	<0.001

*Depressive symptoms assessed with the 15 item geriatric depression scale (GDS-15).

Table 2 Impact of cognitive function at baseline on depressive symptoms from age 85 to 89 years in 334 people living in the community without depressive symptoms at baseline (GDS-15 score ≤2 points). Impact is additional annual increase of depressive symptoms score per SD of cognitive function test score at baseline (2.65 for global cognitive function, 31.59 for attention, 7.08 for processing, 5.72 for immediate recall, and 2.74 for delayed recall)

Cognitive function test	Additional annual increase of GDS-15 score (SE)	P value
Global cognitive function	−0.06 (0.04)	0.17
Attention	0.08 (0.04)	0.05
Processing speed	−0.03 (0.04)	0.42
Immediate recall	−0.17 (0.04)	0.01
Delayed recall	−0.10 (0.04)	0.02

Associations were assessed by separate linear mixed models adjusted for sex and educational level. GDS-15 score increased highly significantly over time in all models (P<0.001).
GDS-15=15 item geriatric depression scale.

Table 3 Impact of depressive symptoms at baseline (GDS-15 score) on cognitive decline from age 85 to 89 years in 415 people living in the community without cognitive impairment at baseline (MMSE score ≥24 points). Impact is additional annual impact on cognitive function per SD of mean GDS-15 score at baseline (2.11)

Cognitive function test	Additional annual impact on cognitive function score (SE)	P value
Global cognitive function	−0.01 (0.04)	0.79
Attention	−0.49 (0.38)	0.20
Processing speed	−0.09 (0.06)	0.14
Immediate recall	−0.08 (0.07)	0.21
Delayed recall	0.001 (0.03)	0.97

Associations were assessed by separate linear mixed models adjusted for sex and educational level. All measures of cognitive function showed highly significant decline over time (P<0.001).
GDS-15=15 item geriatric depression scale.
MMSE=mini-mental state examination.

Statistical analysis

We estimated the cross sectional correlation between depressive symptoms and cognitive function with Pearson's correlation coefficient. To assess the temporal relation between depression and cognitive function, we used separate linear mixed models adjusted for sex and level of education. We examined the impact of cognitive function at baseline on the course of depressive symptoms, restricting the analysis to participants without significant depressive symptoms at baseline (geriatric depression scale score ≤ 2 points). We examined the impact of depressive symptoms at baseline on the course of cognitive function, restricting the analysis to participants without serious cognitive impairment at baseline (mini-mental state exam score ≥ 24).

Results

During 1459 person-years of follow up (mean per person, 2.9 years), 39 people (8%) refused to participate in the repeated annual measurements, most of them at the first follow up visit. Of the 334 participants without significant depressive symptoms at baseline (geriatric depression scale score ≤ 2 points), 97 (29%) died and 28 (8%) declined to participate during follow up. Of the 415 non-demented participants at baseline (mini-mental state examination score ≥ 24 points), 124 (30%) died and 32 (8%) declined to participate during follow up.

Of the 500 participants, 184 (37%) were men, 303 (61%) had only a low level of education (≤ 6 years of schooling), 334 (67%) had no significant depressive symptoms (geriatric depression scale score ≤ 2 points), and 415 (83%) had no serious cognitive impairment (mini-mental state exam score ≥ 24 points).

At baseline, depressive symptoms were significantly correlated with lower scores for global cognitive function, attention, processing speed, and immediate and delayed recall and with higher test scores for attention (indicating reduced attention) (table 1).

An accelerated annual increase of depressive symptoms during follow up was associated with impaired attention, poorer immediate recall, and poorer delayed recall at baseline (table 2). However, depressive symptoms at baseline were not associated with an accelerated cognitive decline during follow up (table 3).

Discussion

Depressive symptoms and cognitive impairment were highly significantly correlated cross sectionally, showing that they do co-occur in old age. Crucially, we found that cognitive impairment at baseline was associated with an accelerated increase of depressive symptoms, whereas depressive symptoms at baseline were not related to an accelerated cognitive decline. Thus our data show that cognitive impairment preceded the onset of depressive symptoms but not vice versa.

How does cognitive impairment lead to depression in old age?

We found specifically that impairment of attention and memory preceded the development of depressive symptoms. The awareness of cognitive decline may cause depression as a psychological reaction to the loss of cognitive functioning. Indeed, memory complaints in old age may be an early sign of dementia and, as such, upset elderly people.[18] Thus, adequate functioning of attention and memory may be especially important to elderly people, explaining why their loss is associated with an accelerated increase of depressive symptoms. A common aetiology or sharing of risk factors is less likely to explain the association between depression and cognitive impairment. In that case, we would have expected that depressive symptoms precede cognitive decline also.

Comparison with other studies

Inferring causality in the relation between depression and cognitive impairment in old age has been hampered by the fact that most studies have examined only one direction of this relation. Some studies found that depression is a risk factor for the development of cognitive decline,[6–10] whereas others could not confirm this finding.[11–14] Examination of both directions of the relation between depression and cognitive impairment shows that depression in old age is a concomitant phenomenon of already existing cognitive impairment rather than an independent risk factor. Our findings, based on various measures of cognitive function instead of a dichotomous end point, are in line with those from a large population based study in people

Depression and cognitive impairment often occur together in old age

The temporal relation between depression and cognitive impairment is unclear

Impairment of attention or memory in old age precedes the development of depressive symptoms

Presence of depressive symptoms, however, is not related to accelerated cognitive decline

aged 65 and older showing that depression is an early manifestation rather than a predictor of Alzheimer's disease.[19] Thus, in elderly people the presence of depressive symptoms does not mean that they are at increased risk of cognitive decline.

Conclusions

We found that cognitive decline preceded depression in old age—specifically impairment of attention or memory preceded the development of depressive symptoms. Depression seems to be a concomitant symptom of cognitive impairment rather than an independent risk factor. Therefore, care givers should pay special attention to early detection and treatment of depressive symptoms in elderly people with cognitive impairment.

Contributors: See bmj.com

Funding: This study was funded by unrestricted grants from the Netherlands Organisation of Scientific Research (ZonMw) and the Dutch Ministry of Health, Welfare, and Sports.

Competing interests: None declared.

Ethical approval: The medical ethics committee of Leiden University Medical Centre approved the study.

1 Macdonald AJD. Mental health in old age. *BMJ* 1997;315:413-7.
2 Migliorelli R, Teson A, Sabe L, Petracchi M, Leiguarda R, Starkstein SE. Prevalence and correlates of dysthymia and major depression among patients with Alzheimer's disease. Am J Psychiatry 1995;152:37-44.
3 Zubenko GS, Zubenko WN, McPherson S, Spoor E, Marin DB, Farlow MR, et al. A collaborative study of the emergence and clinical features of the major depressive syndrome of Alzheimer's disease. *Am J Psychiatry* 2003;160:857-66.
4 Jorm AF. History of depression as a risk factor for dementia: an updated review. *Aust N Z J Psychiatry* 2001;35:776-81.
5 Schweitzer I, Tuckwell V, O'Brien J, Ames D. Is late onset depression a prodrome to dementia ? *Int J Geriatr Psychiatry* 2002;17:997-1005.
6 Devanand DP, Sano M, Tang M-X, Taylor S, Gurland BJ, Wilder D, et al. Depressed mood and the incidence of Alzheimer's disease in the elderly living in the community. *Arch Gen Psychiatry* 1996;53:175-82.
7 Yaffe K, Blackwell T, Gore R, Sands L, Reus V, Browner WS. Depressive symptoms and cognitive decline in nondemented elderly women. *Arch Gen Psychiatry* 1999;56:425-30.
8 Paterniti S, Verider-Taillerfer M-H, Dufouil C, Alpérovitch A. Depressive symptoms and cognitive decline in elderly people. *Br J Psychiatry* 2002;181:406-10.
9 Green RC, Cupples LA, Kurz A, Auerbach S, Go R, Sadovnick D, et al. Depression as a risk factor for Alzheimer disease. *Arch Neurol* 2003;60:753-9.
10 Wilson RS, Mendes de Leon CF, Bennett DA, Bienias JL, Evans DA. Depressive symptoms and cognitive decline in a community population of older persons. *J Neurol Neurosurg Psychiatry* 2004;75:126-9.
11 Dufouil C, Fuhrer R, Dartigues J-F, Alpérovitch A. Longitudinal analysis of the association between depressive symptomatology and cognitive deterioration. *Am J Epidemiol* 1996;144:634-1.
12 Henderson AS, Korten AE, Jacomb PA, Jorm AF, Rodgers B, Jacomb P, et al. The course of depression in the elderly: a longitudinal community-based study in Australia. *Psychol Med* 1997;27:119-29.
13 Cervilla JA, Prince M, Joels S, Mann A. Does depression predict cognitive outcome 9 to 12 years later? Evidence from a prospective study of elderly hypertensives. *Psychol Med* 2000;30:1017-23.
14 Broday H, Luscombe G, Anstey KJ, Cramsie J, Andrews G, Peisah C. Neuropsychological performance and dementia in depressed patients after 25-year follow-up: a controlled study. *Psychol Med* 2003;33:1263-75.
15 Bootsma-van der Wiel A, van Exel E, de Craen AJM, Gussekloo J, Lagaay AM, Knook DL, et al. A high response is not essential to prevent selection bias: results from the Leiden 85-plus study. *J Clin Epidemiol* 2002;55:1119-25.
16 Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189-98.
17 Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M, et al. Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res* 1982;1:37-49.
18 Jonker C, Geerlings MI, Schmand B. Are memory complaints predictive for dementia? A review of clinical and population-based studies. *Int J Geriatr Psychiatry* 2000;15:983-91.
19 Chen P, Ganguli M, Mulsant BH, DeKosky ST. The temporal relationship between depressive symptoms and dementia. *Arch Gen Psychiatry* 1999;56:261-6.

(Accepted 19 July 2004)

doi 10.1136/bmj.38216.604664.DE

Issues in the reporting of epidemiological studies: a survey of recent practice

Stuart J Pocock, Timothy J Collier, Kimberly J Dandreo, Bianca L de Stavola, Marlene B Goldman, Leslie A Kalish, Linda E Kasten, Valerie A McCormack

Abstract

Objectives To review current practice in the analysis and reporting of epidemiological research and to identify limitations.

Design Examination of articles published in January 2001 that investigated associations between risk factors/exposure variables and disease events/measures in individuals.

Setting Eligible English language journals including all major epidemiological journals, all major general medical journals, and the two leading journals in cardiovascular disease and cancer.

Main outcome measure Each article was evaluated with a standard proforma.

Results We found 73 articles in observational epidemiology; most were either cohort or case-control studies. Most studies looked at cancer and cardiovascular disease, even after we excluded specialty journals. Quantitative exposure variables predominated, which were mostly analysed as ordered categories but with little consistency or explanation regarding choice of categories. Sample selection, participant refusal, and data quality received insufficient attention in many articles. Statistical analyses commonly used odds ratios (38 articles) and

Department of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, London WC1E 7HT
Stuart J Pocock *professor*
Timothy J Collier *lecturer*
Bianca L de Stavola *reader*
Valerie A McCormack *lecturer*

continued over

This is the abridged version of an article that was posted on bmj.com on 6 October 2004: http://bmj.com/cgi/doi/10.1136/bmj.38250.571088.55

BMJ 2004;329:883–7