Is the cognitive function of older patients affected by antihypertensive treatment? Results from 54 months of the Medical Research Council's treatment trial of hypertension in older adults

Martin J Prince, Anne S Bird, Robert A Blizard, Anthony H Mann

See editorial and p 805

Abstract

***Objective*—To establish whether initiation of treatment with diuretic or β blocker is associated over 54 months with change in cognitive function.**

***Design*—A cognitive substudy, nested within a randomised, placebo controlled, single blind trial.**

***Setting*—226 general practices from the Medical Research Council's general practice research framework.**

***Subjects*—A subset of 2584 subjects sequentially recruited from among the 4396 participants aged 65-74 in the trial of treatment of hypertension in older adults. The 4396 subjects were randomised to receive diuretic, β blocker, or placebo. Subjects had mean systolic pressures of 160-209 mm Hg and mean diastolic pressures <115 mm Hg during an eight week run in.**

***Outcome measures*—The rate of change in paired associate learning test (PALT) and trail making test part A (TMT) scores (administered at entry and at 1, 9, 21, and 54 months) over time.**

***Results*—There was no difference in the mean learning test coefficients (rate of change of score over time) between the three treatments: diuretic −0·31 (95% confidence interval −0·23 to −0·39), β blocker −0·33 (−0·25 to −0·41), placebo −0·30, (−0·24 to −0·36). There was also no difference in the mean trail making coefficients (rate of change in time taken to complete over time) between the three groups: diuretic −2·73 (95% confidence interval −3·57 to −1·88), β blocker −2·08 (−3·29 to −0·87), placebo −3·01, (−3·69 to −2·32). A less conservative protocol analysis confirmed this negative finding.**

***Conclusion*—Treating moderate hypertension in older people is unlikely to influence, for better or for worse, subsequent cognitive function.**

Section of Epidemiology and General Practice, Institute of Psychiatry, London SE5 8AF
Martin J Prince, *lecturer in psychiatry*
Anthony H Mann, *professor of epidemiological psychiatry*

Royal Free Hospital, London NW3 2QG
Anne S Bird, *consultant psychiatrist*

Academic Department of Psychiatry, Royal Free Hospital, London NW3 2QG
Robert A Blizard, *lecturer in statistics*

Correspondence to:
Dr Prince.

BMJ 1996;312:801-5

Introduction

Until recently antihypertensive treatment was commonly withheld from older people because of two widely held opinions—namely, that high blood pressure was a healthy adaption to arteriosclerotic rigidity and that lowering blood pressure was fraught with complications. In 1989 a popular textbook of family medicine[1] talked of high blood pressure in older people having "a different significance from high blood pressure in the young . . . A high blood pressure in the aged might actually have survival value." It went on to warn that hypotensive drugs were "more likely to produce postural hypotension and confusion in the aged." The first of these views is no longer tenable. In the past 15 years four randomised placebo controlled trials have established that treating moderate hypertension in older adults reduces cardiovascular and cerebrovascular morbidity and mortality.[2-5] The second view, that antihypertensive treatment may be associated with unacceptable complications, in particular cognitive impairment, may deter physicians from initiating treatment in older subjects. This reluctance may have important adverse consequences on public health; the largest reduction in cardiovascular mortality in the 1980s has been among those aged 75 years and over.[6]

The Framingham study reported a modest inverse association between mean blood pressure over five years and cognitive function measured 12 to 15 years later.[7,8] It was most evident among subjects who had not been treated with antihypertensive medication.[7] Of course the existence of a relation between untreated hypertension and cognitive impairment need not imply that lowering blood pressure with drugs will confer benefit. Indeed, studies have suggested that too large a reduction in blood pressure may be associated with increased vascular morbidity.[9] Farmer *et al* cited two studies that reported on patients with hypertension who were treated rather than untreated; two that reported poorer performance; and five that found no difference.[8,10] In these studies the cognitive outcome may have been affected by factors influencing the decision to treat, such as the age of the subject, the degree of hypertension, and severity of vascular pathology. For this reason the balance of cognitive risks and benefits for older hypertensive subjects on antihypertensive treatment is best studied in a randomised controlled trial.

The Medical Research Council trial of treatment of hypertension in older adults compared the effects of a diuretic drug and a β blocker with placebo in a randomised, placebo controlled, single blind design.[5] In a cognitive substudy we investigated the effects of the initiation of antihypertensive treatment and of lowering blood pressure on the cognitive performance of trial participants. We wanted to establish whether there is any medium term benefit or disadvantage for cognitive function associated with antihypertensive treatment for older people with moderate hypertension.

Method

Details of the trial of treatment of hypertension in older adults[5] and a report of the first nine months of the substudy[11] have already been published. Details of the subjects and methods relevant to this analysis are summarised in the box.

MEASURES OF COGNITIVE FUNCTION USED IN THE SUBSTUDY

A package of tests was constructed to test aspects of brain function at entry to the trial and at 1, 9, 21, and 54 months thereafter. Memory and attention are reported to be the cognitive domains most affected by raised blood pressure.[7,12,13] Two measures were chosen

The Medical Research Council trial of the treatment of hypertension in older people[5]

Subjects

Screened volunteers: 4396
Period: 1982-9
Inclusion criteria:
- Systolic pressure 160-209 mm Hg and mean diastolic pressure < 115 mm Hg during eight week run in
- Age 65-74 years

Exclusion criteria:
- Taking antihypertensive medication
- Cardiac failure, angina, diabetes, asthma or other serious disease
- Myocardial infarction or cardiovascular accident in previous 3 months

Method

Setting: 226 general practices from the MRC research framework
Design: Randomised, placebo controlled, single blind trial
Randomisation:
- Placebo (50%)
- Atenolol 50 mg daily (25%)
- Hydrochlorothiazide 25 mg plus amiloride 2·5 mg daily (25%) (all medication adjusted and supplemented to keep blood pressure within target range)

Baseline measures:
- Systolic and diastolic blood pressure at entry, and annually for 5 years
- Smoking habit on entry to the MRC trial (ex-smokers not distinguished from non-smokers)

Outcome

End points:
- Strokes
- Coronary events
- All cardiovascular events
- Deaths from all causes

Mean follow up: 5·8 years
Results: Significant reduction in strokes, coronary events, and all cardiovascular events in diuretic but not β blocker group

The cognitive substudy to the Medical Research Council trial[5]

Subjects

The first 2680 recruits for the MRC trial; 29 refused, 2651 agreed

Recruitment: 1983-5
Inclusion criteria:
Completion of main outcome cognitive test measures (PALT and TMT) at entry or 1 month, and at least one further follow up
Exclusion criteria: None
Final numbers qualifying:
- PALT analysis 2567
- TMT analysis 2584

Method

Design: A comparison of change in cognitive performance over time, nested within a randomised, controlled trial
Measures of cognitive function (at entry, 1, 9, 21, and 54 months):
- Paired associate learning test (PALT)[14]
- Trail making test A (TMT)[16]

Intelligence measures (entry only):
- Raven's progressive matrices parts A and B (RM)[21]
- New adult reading test (NART)[20]

Other measures: Self-care-D[22]—a validated brief, self completed depression rating scale
All administered by an appropriately trained MRC research nurse attached to each practice

Outcome

Outcome measures:
- Rate of change in PALT over time (PALT coefficient)
- Rate of change in time taken to complete TMT over time (TMT coefficient)

Follow up: 54 months
Results: Preliminary analysis of the first nine months of the study suggested no effect on cognitive performance[11]

to detect any change. Firstly, we used the paired associate learning test (PALT).[14] This tests the capacity to recall the second half of a pair of words cued by the first half of the couplet therefore examining one component of cognitive function—semantic memory. Memory testing, however, is a core component of many general tests of cognitive function, and the learning test correlates well with brief tests of broader cognitive function such as the abbreviated mental test score and the psychogeriatric assessment schedule.[15]

Secondly, we used the trail making test (TMT) part A[16] to test attention, concentration, and psychomotor function. Subjects are timed while they join consecutive numbers, arranged at random. There is evidence from magnetic resonance scanning studies that this test should be sensitive to early change in cognitive function related to hypertensive arteriopathy.[17-19]

At entry to the trial only, we used two measures of intelligence: the new adult reading test (NART)[20]—a stable measure of premorbid intelligence—and Raven's matrices parts A and B[21]—tests of non-verbal intelligence sensitive to age related cognitive decline. The scores from the learning test and the trail making test at entry and at 1, 9, 21, and 54 months were converted into summary measures for each subject to reflect changes in their scores over time. The summary measures (PALT coefficient and TMT coefficient) were calculated as the slope of the regression lines derived by regressing the cognitive test scores on time for each subject. In the regression calculation time values of 1, 2, 3, 4, and 5 were assigned respectively to the cognitive test scores at entry and 1, 9, 21, and 54 months as doing so led to a better linear fit for the regressions than using the actual time in months (see results).

ANALYSIS

We carried out two analyses. An intention to treat analysis dealt with subjects only according to their initial trial randomisation; subsequent changes in medication were ignored. A less conservative protocol analysis further subdivided subjects into nine treatment protocols according to whether they remained on their randomised allocation throughout the 54 months of the study or needed treatment with another antihypertensive agent to lower their blood pressure into the target range or had stopped their randomised medication (whether or not they required additional medication).

To assess the adequacy of the randomisation for the subset of trial participants used in the cognitive substudy the means of the initial trial characteristics were compared for those randomised to placebo, diuretic, and β blocker by using one way analysis of variance. Next, the mean learning test and trail making test coefficients for the three treatment groups were compared by using analysis of variance with adjustment for any non-randomly distributed characteristics. As the benefits of randomisation were lost in the protocol analysis the means and coefficients for each of the nine treatment protocols were compared by using analysis of variance with age, sex, trail making or learning test score (as appropriate) at entry, reading score (NART), Raven's matrices score, and entry self care D depression score entered as covariates, all of which were independently associated with both the learning and trail making coefficients. To illustrate the treatment effect on blood pressure the mean fall in systolic blood pressure (the difference between the systolic blood pressure at entry and the mean of subsequent measures) was compared across the three randomised groups and the nine protocols.

Results

Table 1 summarises the general characteristics of the sample by initial randomisation.

Loss to follow up—For the trail making test 551 subjects (21% of the sample) recorded the maximum five data points, 1582 (61%) four or more, and 2263

(88%) recorded at least three. The figures for the paired associate learning test, administered during the same session, were very similar. During the course of the 54 month cognitive substudy 192 subjects (8%) died. Of these only 77 (3%) died during the first 21 months. If we grouped the subjects into three by mortality —death before 21 months, death between 21 and 54 months, and survival to the end of the study—we found no relation between either the cognitive test scores recorded at entry, the summary learning or trail making coefficients, systolic blood pressure at entry, or age and mortality during the trial. Smokers were less likely to survive to the end of the trial: 30% of those who died during the trial smoked compared with 20% of those surviving to 54 months (χ^2 12·5; P=0·0004). By stratifying the sample by the number of data points recorded and excluding subjects who died during the course of the study we found a relation between loss to follow up for reasons other than death and several baseline measures (table 2). Those who completed the study were younger and less depressed at entry to the trial with less impaired entry scores on the learning test, trail making, and Raven's matrices. There was no relation between the score on the reading test and loss to follow up.

Changes in learning and trail making scores over time—In the estimation of the learning and trail making coefficients the time points were taken as ordinal values 0, 1, 2, 3, and 4 as this provided a better approximation to a straight line than using exact time points. Mean (SD) learning test scores deteriorated from 17·0 (1·7) at entry to the trial to 16·3 (2·2) at 54 months (table 3). The mean learning test coefficient was −0·30 (95% confidence interval −0·27 to −0·35; range −8·0 to 9·0). Lower scores indicated greater impairment, hence the more negative the coefficient the greater the deterioration in test performance over time. The distribution had a pronounced central tendency with most subjects recording similar learning test scores at each data point. The mean of the times taken to complete the trail making test actually improved steadily from 60·5 seconds at entry to 51·9 seconds at 54 months. The mean trail making coefficient was −2·71 (−1·3 to −3·8; −145 to 195). This distribution also had a strong central tendency. Shorter times to complete the test indicated better performance; hence the less negative the coefficient the less the improvement in performance over time.

Intention to treat analysis—The first row of table 3 shows that there was no difference in the mean learning test or trail making coefficients between the three randomised allocations. Inclusion as a covariate of entry systolic blood pressure (the only baseline characteristic non-randomly distributed between the three treatment arms) did not modify this result.

Protocol analysis—Table 3 also shows the breakdown of the sample by initial randomisation and subsequent course of treatment, together with the effect of initial randomisation and subsequent treatment on the mean fall in systolic blood pressure over the 54 months of the trial. The fall in blood pressure was greater for subjects randomised to active treatment groups than for those randomised to placebo. This treatment effect was largest among subjects who completed the study on their original randomisation. Table 3 also gives the mean learning test and trail making coefficients for each of the nine possible treatment protocols. These have been adjusted for the independent predictors of the two coefficients. Despite the treatment effect on blood pressure, there was no evidence of significant heterogeneity in the cognitive outcome between treatment groups.

Table 1—*Means (95% confidence intervals) and proportions (%) of baseline characteristics by randomisation in hypertension treatment trial*

Characteristic	Diuretic (n=633)	β Blocker (n=640)	Placebo (n=1311)
Age	70·4 (70·2 to 70·6)	70·3 (70·1 to 70·5)	70·3 (70·1 to 70·4)
Proportion of men (%)	42%	42%	42%
Short care depression score at entry	2·0 (1·8 to 2·2)	2·0 (1·8 to 2·2)	1·9 (1·8 to 2·0)
Score on new adult reading test	31·1 (30·2 to 31·9)	30·8 (29·9 to 31·6)	31·4 (30·8 to 32·0)
Score on Raven's matrices	15·3 (15·0 to 15·7)	15·4 (15·1 to 15·7)	15·4 (15·2 to 15·6)
Paired associate learning test score at entry	17·0 (16·9 to 17·1)	17·0 (16·8 to 17·1)	17·0 (16·9 to 17·1)
Trail making test score at entry	59·9 (57·7 to 62·1)	59·9 (57·7 to 62·0)	61·0 (59·3 to 62·8)
Systolic blood pressure (mm Hg) at entry	184·9 (183·9 to 185·9)	184·2 (183·2 to 185·2)	183·5 (182·8 to 184·2)
Diastolic blood pressure (mm Hg) at entry	90·3 (89·4 to 91·2)	90·7 (89·9 to 91·6)	90·5 (89·9 to 91·2)

Discussion

This study prospectively assessed cognitive status in a large sample of older adults randomised to diuretic, β blocker, or placebo treatment groups. This was an ideal opportunity to investigate the relation between treatment of moderately raised blood pressure and cognition. The finding of no association between hypertensive treatment and cognitive outcome over 54 months is reassuring. The benefits of treatment with thiazide diuretic have been shown by the Medical Research Council's trial of the treatment of hypertension in older adults.[5] Fears regarding adverse effects on cognition are not borne out in this analysis and need not influence clinicians in their decision to initiate antihypertensive treatment in an older patient.

There was a substantial attrition from the trial cohort. Little of this could be attributed to death. Subjects who failed to complete the study were older than those who completed it and showed impairment of current cognitive function (as measured by the paired associate learning test, the trail making test, and Raven's matrices) but not of premorbid function as measured by the new adult reading test at entry to the study. This would support the view that subclinical

Table 2—*Characteristics of sample (means and 95% confidence intervals) by number of recorded data points. Subjects dying during course of trial are excluded*

	Trail making test data points					
Characteristic	2 (n=265)	3 (n=589)	4 (n=988)	5 (n=550)	F value	P value
Age	70·3 (70·0 ro 70·6)	70·5 (70·3 to 70·7)	70·3 (70·1 to 70·4)	70·1 (69·8 to 70·3)	2·7	0·045
Raven's matrices	14·9 (14·3 to 15·4)	15·2 (14·9 to 15·6)	15·3 (15·1 to 15·6)	15·7 (15·4 to 16·1)	2·7	0·045
Paired associate learning test score at entry	16·6 (16·3 to 16·8)	16·9 (16·8 to 17·1)	17·0 (16·9 to 17·1)	17·1 (17·0 to 17·3)	7·5	0·0001
Trail making test score at entry	63·8 (59·8 to 67·9)	62·2 (59·7 to 64·7)	59·1 (57·3 to 60·9)	59·2 (56·8 to 61·7)	2·6	0·050
Self care depression score at entry	2·5 (2·1 to 2·8)	2·0 (1·8 to 2·2)	1·9 (1·8 to 2·0)	1·8 (1·6 to 2·0)	5·5	0·0009
Learning test coefficient (adjusted for entry score)	−0·32	−0·28	−0·34	−0·28	0·7	0·56
Trail making coefficient (adjusted for entry score)	−3·8	−3·7	−2·7	−2·2	3·9	0·009

Table 3—*Mean fall in systolic blood pressures* (in mm Hg) trail making and learning test coefficients by initial randomisation and course of subsequent treatment*

Initial randomisation	Diuretic	β Blocker	Placebo	F value	P value
Intention to treat analysis					
No of subjects	633	640	1311		
Mean fall in blood pressure	33·5 (32·2 to 34·9)	30·9 (29·5 to 32·2)	16·4 (15·4 to 17·4)	267	<0·0001
Trail making coefficient	−2·73 (−3·57 to −1·88)	−2·08 (−3·29 to −0·87)	−3·01 (−3·69 to −2·32)	1·10	0·33
Learning test coefficient	−0·31 (−0·23 to −0·39)	−0·33 (−0·25 to −0·41)	−0·30 (−0·24 to −0·36)	0·14	0·86
Late protocol					
Completed study on randomised allocation. No additional antihypertensive agent needed:					
No of subjects	236	134	622		
Mean fall in blood pressure	39·3 (37·5 to 41·1)	31·5 (28·9 to 34·1)	14·7 (13·4 to 15·9)	242	<0·0001
Trail making coefficient†	−2·54	−2·51	−2·46	0·02	0·98
Learning test coefficient†	−0·25	−0·23	−0·29	0·49	0·61
Remained on randomised allocation, but needed additional antihypertensive agent:					
No of subjects	127	172	18		
Mean fall in blood pressure	30·6 (28·1 to 33·1)	33·3 (30·9 to 35·7)	16·4 (6·8 to 26·1)	9·78	0·0001
Trail making coefficient†	−2·31	−1·72	−3·50	0·64	0·53
Learning test coefficient†	−0·32	−0·34	−0·15	0·47	0·63
Off randomised allocation for part of trial, whether or not needing additional antihypertensive agent:					
No of subjects	270	334	671		
Mean fall in blood pressure	29·3 (27·1 to 31·5)	29·0 (27·1 to 31·1)	18·3 (16·7 to 19·8)	50·0	<0·0001
Trail making coefficient†	−3·36	−2·96	−2·95	0·12	0·89
Learning test coefficient†	−0·30	−0·34	−0·36	0·28	0·76

*Difference between systolic blood pressure at entry and mean of subsequent measures.
†Adjusted for age, sex, Raven's matrices score, new adult reading test score, entry learning test or trail making score (as appropriate), and entry self care depression score.

cognitive decline on recruitment was a factor in determining later drop out. Non-completion was also related to randomisation (table 2) in that subjects randomised to atenolol were more likely to be off medication for at least part of the study. It is doubtful, however, that loss to follow up will have influenced our results unduly. Inclusion of subjects with only two learning test or trail making values has meant that an outcome measure was available for 96% of trial subjects. Summary outcome measures based on fewer data points will be measured with more error, but this error is likely to be random. Inclusion of subjects with incomplete follow up therefore seemed to be the lesser of two evils. In any event, restriction of the analysis to those subjects who had completed the trial did not alter the result.

This analysis does not provide any evidence for a cognitive benefit from antihypertensive treatment. Even restriction of the analysis to those subjects who had completed the study and remained on their randomised medication throughout (thereby maximising the treatment effect on mean systolic blood pressure) did not reveal any difference in cognitive outcome between the placebo and active treatment groups. This result does not, however, prove that treating hypertension cannot benefit cognitive function in older adults. Though the learning test and trail making test should be sensitive to relatively small degrees of cognitive deterioration and should cover the cognitive domains most likely to be affected by hypertension more detailed cognitive testing may have revealed a treatment effect. The 54 month follow up period may have been too short to detect a difference between treated and untreated groups. In the Framingham cohort historical[7] rather than concurrent[10] blood pressure records were associated with cognitive impairment. Alternatively the subjects in this trial, who were 65 years or older at entry, may have been exposed to raised blood pressure for too long to benefit from this intervention.

Key messages

- There has been a tendency in the past to withhold antihypertensive drugs from older people
- Studies have shown that treating hypertension in older adults reduces cardiovascular mortality and morbidity
- Treating moderate hypertension with either diuretic or β blocker does not seem to influence cognitive function
- Concerns about damaging cognition should not deter doctors from treating hypertension in older patients
- Age should no longer be a factor in the decision to initiate antihypertensive treatment

We thank the MRC Working Party and the MRC Epidemiology and Medical Care Unit (director—Professor T Meade, study coordinator—Dr J Connelly, statistician—P Brennan), the MRC general practice framework general practitioners and research nurses (coordinator Mrs W Browne), and Mrs I Godstone.

Funding: Dr Prince holds a clinical training fellowship in epidemiology funded by the Wellcome Trust.

Conflict of interest: None.

1 McWhinney IR. *A textbook of family medicine.* New York: Oxford University Press, 1989.
2 Hypertension Detection and Follow-up Program Co-operative Group. Five year findings of the hypertension detection and follow-up program. II. Mortality by race, sex and age. *JAMA* 1979;242:2572-7.
3 The Australian Therapeutic Trial in Mild Hypertension. The Management Committee. Treatment of mild hypertension in the elderly. *Med J Aust* 1981;2:398-402.
4 SHEP Cooperative Research Group. Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. *JAMA* 1991;265:3255-64.
5 MRC Working Party. Medical Research Council trial of treatment of hypertension in older adults: principal results. *BMJ* 1992;304:405-12.
6 National Center for Health Statistics. *Health, United States, 1990.* Hyattsville, Maryland: Public Health Service, 1991:85. (DHSS publication no (PHS) 91-1232.)
7 Elias MF, Wolf PA, D'Agostino RB, Cobb J, White LR. Untreated blood pressure is inversely related to cognitive functioning: the Framingham study. *Am J Epidemiol* 1993;138:353-64.
8 Farmer ME, Kittner SJ, Abbott RD, Wolz MM, Wolf PA, White LR. Longitudinally measured blood pressure, antihypertensive medication use, and cognitive performance: the Framingham study. *J Clin Epidemiol* 1990;43:475-80.
9 Farnett L, Mulrow CD, Linn WD, Lucey CR, Tuley MR. The J-curve phenomenon and the treatment of hypertension: is there a point beyond which the treatment of hypertension is dangerous? *JAMA* 1991;265:489-95.
10 Farmer ME, White LR, Abbott RD, Kittner SJ, Kaplan E, Wolz MM, *et al.* Blood pressure and cognitive performance. The Framingham study. *Am J Epidemiol* 1987;126:1103-14.
11 Bird AS, Blizard RA, Mann AH. Treating hypertension in the older person: an evaluation of the association of blood pressure level and its reduction with cognitive performance. *J Hypertens* 1990;8:147-52.
12 Wilkie F, Eisdorfer C. Intelligence and blood pressure in the aged. *Science* 1971;172:959-62.

13 Waldstein SR, Ryan CM, Manuck SB. Learning and memory function in men with untreated blood pressure elevation. *J Consult Clin Psychol* 1991;59: 513-7.
14 Inglis J. A paired-associate learning test for use with elderly psychiatric patients. *Journal of Mental Science* 1959;105:440-3.
15 Little A, Hemsley D, Bergmann K, Volans J, Levy R. Comparison of the sensitivity of three instruments for the detection of cognitive decline in elderly living at home. *Br J Psychiatry* 1987;150:808-14.
16 Reitan RM. Validity of the trail making test as an indication of organic brain damage. *Perceptual Motor Skills* 1959;8:271-6.
17 van Swieten JC, Geyskes GG, Derix MMA. Hypertension in the elderly is associated with white matter lesions and cognitive decline. *Ann Neurol* 1991;30:825-30.
18 Breteler MM, van Amerongen NM, van Swieten JC, Claus JJ, Grobbee DE, van Gijn J, *et al.* Cognitive correlates of ventricular enlargement and cerebral white matter lesions on magnetic resonance imaging. The Rotterdam study. *Stroke* 1994;25:1109-15.
19 Schmidt R, Fazekas F, Offenbacher H, Dusek T, Zach E, Reinhart B, *et al.* Neuropsychologic correlates of MRI white matter hyperintensities: a study of 150 normal volunteers. *Neurology* 1993;43:2490-4.
20 Nelson H, O'Connell A. Dementia. The estimation of pre-morbid intelligence levels using the new adult reading test. *Cortex* 1978;14:234-44.
21 Raven JC. Matrix tests. *Mental Health* 1940;1:10-8.
22 Bird AS, Macdonald AJD, Mann AH, Philpott MP. Preliminary experience with the self-care-D: a self-rating depression questionnaire for use with the elderly. *International Journal of Geriatric Psychiatry* 1987;2:31-8.

(Accepted 5 December 1995)

Low blood pressure and dementia in elderly people: the Kungsholmen project

Zhenchao Guo, Matti Viitanen, Laura Fratiglioni, Bengt Winblad

See editorial and p 801

Abstract

***Objective*—To examine the relation between blood pressure and dementia in elderly people.**

***Design*—Cross sectional, population based study.**

***Setting*—Kungsholmen district of Stockholm, Sweden.**

***Subjects*—1642 subjects aged 75-101 years.**

***Main outcome measures*—Prevalence and adjusted odds ratio of dementia by blood pressure.**

***Results*—People with systolic pressure ≤140 mm Hg were more often diagnosed as demented than those with systolic pressure >140 mm Hg: odds ratios (95% confidence interval) adjusted for age, sex, and education were 2·98 (2·17 to 4·08) for all dementias, 2·91 (1·93 to 4·38) for Alzheimer's disease, 2·00 (1·09 to 3·65) for vascular dementia, and 5·07 (2·65 to 9·70) for other dementias. Similar results were seen in subjects with diastolic pressure ≤75 mm Hg compared with those with higher diastolic pressure. When severity and duration of dementia were taken into account, only moderate and severe dementia were found to be significantly related to relatively low blood pressure, and the association was stronger in subjects with longer disease duration. Use of hypotensive drugs and comorbidity with cardiovascular disease did not modify the results for all dementias, Alzheimer's disease, and other dementias but slightly reduced the association between vascular dementia and diastolic blood pressure.**

***Conclusions*—Both systolic and diastolic blood pressure were inversely related to prevalence of dementia in elderly people. We think that relatively low blood pressure is probably a complication of the dementia process, particularly Alzheimer's disease, although it is possible that low blood pressure may predispose a subpopulation to developing dementia.**

Stockholm Gerontology Research Center and Department of Geriatric Medicine, Karolinska Institute, Dalagatan 9-11, S-113 82 Stockholm, Sweden
Zhenchao Guo, *guest researcher*
Matti Viitanen, *associate professor of geriatric medicine*
Laura Fratiglioni, *senior researcher*
Bengt Winblad, *professor of geriatric medicine*

Correspondence to:
Dr Guo.

BMJ 1996;312:805-8

Introduction

Blood pressure may be related to dementia in different ways. High blood pressure is recognised as the most powerful risk factor for cerebrovascular disease.[1] Since cerebrovascular disease is the main cause of vascular dementia,[2] it is generally believed that high blood pressure is also the most important risk factor for vascular dementia.[3] But this widely accepted view lacks direct evidence from population studies.[4] On the other hand, clinical observations have shown that episodes of hypotension can result in cerebral hypoperfusion, which may play a causative role in the development of dementia.[5,6] Furthermore, recent studies have observed that patients with Alzheimer's disease had lower arterial blood pressures than people without dementia,[7,8] suggesting that blood pressure decreases during the course of Alzheimer's disease.[9] None of these hypotheses for the relation between blood pressure and dementia is supported by strong evidence. Further investigations, especially population studies, are necessary.

The aim of this study was to examine whether blood pressure is a determinant of the prevalence of dementia in a community based population of people aged 75 and over.

Subjects and methods

DATA COLLECTION

This report is based on cross sectional data from the Kungsholmen project—a longitudinal study of aging and dementia targeting all the inhabitants of the Kungsholmen district of Stockholm who were aged 75 or more on 1 October 1987.[10] Of the eligible subjects, 1810 (77%) participated in the initial survey. Cases of dementia were detected by means of a two phase process: a screening phase and a clinical examination phase. Dementia was defined according to the diagnostic criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, third edition, revised.[11] Details of the clinical examination and diagnostic procedure are given elsewhere.[12,13] Severity of dementia was determined according to the clinical dementia rating scale,[14] with some modifications.[15] The age when symptoms of dementia first appeared was estimated from information given by an informant, and the duration of the disease was the difference between the date when symptoms started and the date of the screening test.

Arterial blood pressure (systolic Korotkoff phase I and diastolic phase V) was measured with a mercury sphygmomanometer and with the subject sitting after having rested for five minutes. Subjects' educational levels were based on formal schooling and were divided into two categories in the analyses (<8 years and ≥8 years). Subjects were considered to be taking a drug if it had been used at any time in the two weeks before the interview. All drugs that potentially could be used for lowering blood pressure (anatomical therapeutic chemical (ATC) classification system,[16] codes C02, C03, and C07) were recorded as hypotensive drugs. If subjects were unable to provide reliable information an informant (relative, carer, or others) was required.

Information on the subjects' medical history was obtained from the computerised inpatient register, which covers all hospitals in the area of Stockholm. Cardiovascular disease (coronary heart disease, cardiac dysrythmia, heart failure, and stroke) was treated as a possible confounder.