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Brief communication

Cardiovascular risk and memory in non-demented elderly women

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Abstract

Objective: To determine whether cardiovascular (CV) risk is associated with subtle memory deficits in non-demented, healthy older women with a family history of Alzheimer disease (AD).
Methods: Baseline data of 375 participants from a randomized, double-blind placebo-controlled primary prevention trial to test the efficacy of hormone replacement therapy in delaying AD and cognitive decline were analyzed. All subjects were women over 65 with a family history of AD who had normal cognition and no active heart disease at baseline. A baseline memory composite score was calculated, consisting of immediate and delayed recall of verbal and nonverbal material. Multiple linear regression was performed to examine the association of relative CV risk with memory functioning; age, ethnicity and education level were included as covariates.
Results: Mean baseline memory composite score was significantly higher in those with low relative CHD risk than those with high relative CHD risk.
Conclusion: These findings suggest that subtle elevation of CHD risk may negatively affect memory functioning even in otherwise healthy, non-demented older women without a history of heart disease.
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Keywords: Cognitive aging; Memory; Neuropsychological assessment; Cardiac

1. Introduction

Vascular risk factors may play a role in memory dysfunction and progression to dementia (Bergmann and Sano, 2006; Rosano and Newman, 2006). Studies have shown inconsistent evidence for an association between poorer cognitive performance in the non-demented elderly and individual cardiovascular risk factors (Bergmann and Sano, 2006; Elias et al., 2004; Luchsinger et al., 2005; Rosano and Newman, 2006). About 25% of Americans have at least three cardiovascular risk factors (Malik et al., 2004), and in the Cardiovascular Health Study, 60% of subjects 65 or over had at least two risk factors and over 10% had four or more (McNeill et al., 2006). The cumulative burden of vascular disease may have an important effect on cognition similar to that seen in coronary heart disease (CHD) (Rosano and Newman, 2006). Previous studies suggest that higher vascular risk may contribute to poorer cognitive status. Clustering of vascular risk factors has been associated with an increased risk of Alzheimer disease (AD) (Luchsinger et al., 2005), and in the Framingham Offspring Study, dementia and stroke-free subjects with higher cerebrovascular risk had lower cognitive performance (Elias et al., 2004). We examined whether higher CHD risk is associated with cognitive deficits in non-demented, healthy elderly women with a family history of AD.

2. Methods

We examined baseline data from a multicenter trial for the primary prevention trial of AD and memory loss in 477

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Table 1
Baseline characteristics of the entire cohort and each CHD risk group

Variables	Entire ($n = 375$)	Low risk ($n = 170$)	High risk ($n = 205$)	p[a]
Relative CHD risk	1.37 (0.75)	0.80 (0.22)	1.85 (0.69)	<0.001
CHD risk components				
Age (year)	72.7 (5.3)	72.2 (5.0)	73.1 (5.4)	0.077
LDL (mg/dL)	140.4 (36.9)	128.9 (32.5)	150.0 (37.7)	<0.001
TC (mg/dL)	223.7 (39.2)	218.2 (35.8)	228.2 (41.4)	0.014
HDL (mg/dL)	56.7 (16.2)	66.7 (13.8)	48.4 (13.0)	<0.001
Systolic BP (mm Hg)	133.8 (17.8)	124.5 (15.3)	141.6 (15.9)	<0.001
Diastolic BP (mm Hg)	78.1 (9.7)	74.9 (9.2)	80.7 (9.4)	<0.001
Diabetes mellitus, *n* (%)	26 (6.9)	2 (1.2)	24 (11.7)	<0.001
Smoking, *n* (%)	23 (6.1)	6 (3.5)	17 (8.3)	0.056
Additional variables				
Mean educational level (year)	14.2 (3.2)	14.9 (3.1)	13.7 (3.1)	<0.001
Ethnicity, non-Caucasian, *n* (%)	73 (19.5)	25 (14.7)	48 (23.4)	0.034
Beck Depression Inventory[†]	4.3 (3.6)	4.1 (3.7)	4.6 (3.5)	0.193
APOE ε4 carrier, *n* (%)[†]	116 (32.4)	50 (30.3)	66 (34.2)	0.433
MMSE (0–30)	28.9 (1.4)	29.1 (1.3)	28.7 (1.5)	0.005
SRT Immediate Recall (0–72)	46.5 (8.7)	47.9 (8.7)	45.3 (8.6)	0.005
SRT Delayed Recall (0–12)	7.5 (2.3)	7.8 (2.3)	7.2 (2.3)	0.020
VRT Immediate Recall (0–41)	29.9 (7.3)	31.2 (7.0)	28.8 (7.4)	0.001
VRT Delayed Recall (0–41)	23.0 (9.8)	24.6 (9.8)	21.7 (9.5)	0.004
Memory Composite (0–166)	106.8 (22.0)	111.4 (21.4)	103.0 (21.7)	<0.001

CHD = coronary heart disease; LDL = low-density lipoprotein; TC = total cholesterol; HDL = high-density lipoprotein; BP = blood pressure; MMSE = Mini-Mental State Examination; SRT = Selective Reminding Test; VRT = Visual Reproduction Test.
[a] *t*-test or χ^2 test as appropriate.
[†] Data were not available for all subjects. Values are based on *n*'s as stated in the text.

non-demented women age 65 and older who have a family history of AD (Sano et al., 2008). All protocols were approved by each site's Institutional Review Board (IRB). Recruitment strategy was individualized to each site and pre-approved by its IRB. All subjects signed informed consent. The entry criteria were no memory complaints, normal scores on immediate and delayed verbal recall, a score less than 16 on the Beck Depression Inventory, no serious medical, neurological (including stroke or transient ischemic attack) or psychiatric conditions, and no use of cognitive enhancing or experimental drugs. The LDL-based approach of the Framingham algorithm was used to calculate absolute 10-year CHD risk (Wilson et al., 1998). Since CHD risk as compared to an age and gender-matched, low-risk subject is a more accurate estimate of CHD risk in the elderly, we then calculated each subject's relative CHD risk as per NHBLI guidelines (NHL, 2007). Since our population was skewed towards the healthy elderly, for purposes of comparison, subjects were divided into a low CHD risk group (those below the study population's median) and a high CHD risk group (those at or above the median); the median relative CHD risk was 1.125 or an absolute risk of 9%. Subjects were similarly dichotomized for each continuous CHD risk factor. Analyses focused on tests of memory, the pre-stated primary outcome of the original study, namely the Selective Reminding Test (SRT), which measures the acquisition of verbal material by asking subjects to learn a list of twelve unrelated items after six trials and testing retention after 15 min; the Visual Reproduction Test (VRT) for the Wechsler Memory Scale-Revised, which measures the acquisition of nonverbal material by asking subjects to draw five line drawings from memory and testing retention after 30 min; and the Mini-Mental State Examination (MMSE). The *a priori* primary outcome measure of the planned clinical trial, the memory composite score, was calculated as the sum of the immediate and delayed recall scores for SRT and VRT.

102 participants (21.3%) were excluded because they were on a lipid-lowering agent or antihypertensive ($n = 56$) or were missing relevant data ($n = 46$). Since the percentage of smokers was low (10.0%), the 145 subjects with unknown smoking status were assumed to be non-smokers and were evenly divided between both CHD risk groups. All statistical analyses were performed with our cohort of 375 subjects except for 1 subject missing a Beck Depression Inventory Score, 17 subjects missing *APOE* genotyping data, and 2 subjects missing MMSE scores. Comparisons between the CHD risk groups were done using *t*-test and χ^2 tests as appropriate. We then performed multiple linear regression analyses with each cognitive measure as the dependent variable and with CHD risk group or risk factor with age, ethnicity, education and *APOE* ε4 status as the covariates. The level of significance was $p < 0.05$. All statistical analyses were done using SPSS v. 15.0.

3. Results

375 subjects were available for analyses. Table 1 presents the clinical characteristics and cognitive measures at baseline

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