ARIC Manuscript Proposal #734

PC Reviewed: 08/29/00	**Status: A**	**Priority: 2**
SC Reviewed: 10/03/00	**Status: A**	**Priority: 2**

1a. Full Title: "Blood pressure over time and changes in cognitive function"
 b. Abbreviated Title (Length 26 characters): Blood pressure & cognitive function

2. Writing Group: (list individual with lead responsibility first)

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3. Timeline:

      The first manuscript is expected in 4-6 months.

4. Rationale:

Because hypertension leads to end-organ damage, it is reasonable to postulate that neuropsychological deficits resulting from brain damage may occur as a consequence of high blood pressure levels (1-3). Psychomotor speed, visual constructive ability, learning, memory and executive ability seem to be particularly vulnerable to increases in blood pressure (4). Cognitive decline as measured over 10 years using the Wechsler Adult Intelligence test (WAIS) was found to be more marked for hypertensive patients with cardiovascular disease than for normotensive subjects in relatively good health (4). A prospective relationship between systolic and diastolic levels and dementia was demonstrated in a cohort aged 79-85 years (5). Based on a

review of 34 papers, Anstey & Christensen suggested that hypertension, low educational level, and markers of cardiovascular health, should be considered as risk factors for poor cognitive performance (6). In a recent analysis from the ARIC cohort study, Knopman et al reported independent effects of both hypertension and diabetes on cognitive decline (7). In addition, in the Framingham study, an important interaction was found between hypertension and diabetes in relation to visual memory impairment (8). No cognitive function effects were, however, observed in studies evaluating the effect of anti-hypertensive therapy (9-12).

In Knopman et al's study (7), only predictors at baseline (2nd clinic visit) were considered. No studies have been done heretofore examining the relationship of cognitive function changes to blood pressure changes, or the predictive values of prevalent vs. incident hypertension on age-related cognitive declines. The availability of blood pressure and cognitive data for ARIC's visits 2 and 4 provides an opportunity to investigate these relationships while simultaneously considering time-dependent confounding variables.

5.   Main hypotheses/ Study questions

The analyses aim at examining the relationships between visit 2 to visit 4 changes in blood pressure and changes in cognitive function, with adjustment for time changes in the level of confounding variables.

6.   Data (variables, time window, source, inclusions/exclusions):

Visit 2 and visit 4 data are necessary to examine the study questions. Blood pressure change is the main exposure variable, and average cognitive change, the main outcome variable. In addition to the use of blood pressure as a continuous variable, the following normotension/hypertension categories will be considered:

Hypertension in:		
Visit 2	Visit 4	Category
No	No	Normotension
Yes	No	Controlled hypertension
No	Yes	Incident hypertension
Yes	Yes	Prevalent Hypertension

These categories of hypertension will be defined using ARIC standard definitions.
Cognitive changes will be based on the average [visit 4 minus visit 2] differences, and will be assessed separately for each of the tests used in ARIC (Delayed Word Recall, WAIS Digit Simbol Subtest, and Word Fluency).

Covariates include age, gender, race/center, diabetes, education, health status, total plasma cholesterol and fractions, plasma fibrinogen, vital exhaustion, BMI, and carotid IMT. Education,

health status and fibrinogen are available only for visit 1. Vital exhaustion was evaluated only in visit 2. The other continuous variables will be categorized in quintiles of visit 4 - visit 2 changes. Exclusions include history of stroke or TIA, and use of medications affecting the CNS.

Statistical Power Considerations:

The statistical power of the study (table below) was calculated taking in account the Pearson correlation for each pair of cognitive test in both visits (Ancova Method: Stata-vs, 6.0) and the 4 categories of the main exposure variable taking in account an alpha value=0.05. The mean cognitive changes (visit4 *minus* visit2) and standard deviations were considered in each category of hypertension: The overall mean cognitive changes, based on the women population[1] were respectively: DWR (-0.13) ; DSS/W-R (-2,61); and WF (-0,53).

Hypertension in: Visit 2 Visit 4		DWR	DSS/W-R	WF
No*	No*	Statistical Power		
Yes	No	0.41	0.98	0.04
No	Yes	0.82	0.79	0.25
Yes	Yes	0.90	1.00	0.99

* Reference Category

7.a. Will the data be used for non-CVD analysis in this manuscript?   ____ Yes _✔_ No

  b. If Yes, is the author aware that the file ICTDER01 must be used to exclude persons with a value RES_OTH = "CVD Research" for non-DNA analysis, and for DNA analysis RES_DNA = "CVD Research" would be used?   ____Yes____No
  (This file ICTDER01 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored sample use for research.)

8.a. Will the DNA data be used in this manuscript?   ____ Yes _✔_ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER01 must be used to exclude those with value RES_DNA = "No use/storage DNA"?   ____ Yes ____ No

References

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[1]"Prospective Assessment of Estrogen Replacement Therapy and Cognitive Functionning"-ARIC MS#:700

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3.   Biessels GL. Cerebral complications of diabetes: clinical findings and pathogenetic mechanisms. Neth J Med 1999; 54(2): 35-45.

4.   Elias MF. Effects of chronic hypertension on cognitive functioning. Geriatrics 1998; Suppl 1: S49-52.

5.   Skoog I; Lernfelt B; Landahl S; Palmertz B; Andreasson LA; Nilsson L; Persson G; Odén A; Svanborg A. 15-year longitudinal study of blood pressure and dementia. Lancet 1996;347: 1141-45.

6.   Anstey K; Christensen H. Education, Activity, Health, Blood Pressure and apolipoprotein E as predictors of cognitive change in old age: A Review. Gerontology 2000; 46(3):163-77.

7.   Knopman D; Boland L; Mosley T; Howard G; Liao Duanping; Skklo, M et al. Cardiovascular risk factors and cognitive decline in middle aged adults: The Atherosclerosis Risk in Communities Study. Am J Epidemiol 2000. In Press.

8.   Stewart R; Liolitsa D. Type 2 diabetes mellitus, cognitive impairment and dementia. Diabet Med 1999; 16(2); 93-112.

9.   Tedesco MA; Ratti G; Mennella S; Manzo G; Grieco M; Rainone AC; Iarussi D; Iacono A. Comparison of losartan and hydrochlorothiazide on cognitive function and quality of life in hypertensive patients. Am J Hypertens 1999; 12(11 Pt 1): 1130-34.

10.   Nilsson P; Gullberg G; Ekesbo R; Von Schenck H; Gustafson L. No impaired cognitive function in treated patients withh muil-moderate hypertension compared to normotensive controls. Blood press 1998; 7(4): 209-13.

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