ARIC Manuscript Proposal #762

PC Reviewed: 01/16/01 **Status: A** **Priority: 1**
SC Reviewed: 01/30/01 **Status: A** **Priority: 1**

1a. Full Title: "Prospective Assessment of Cognitive Functioning and Stroke Incidence"
b. Abbreviated Title (Length 26 characters): Cognitive Function & Stroke

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:

Cerebrovascular risk factors, such as diabetes, hypertension, and hypercholesterolemia, are known to result in silent brain infarcts or white matter lesions, with a consequent decline in cognitive functioning. (1-5). Based on MR angiographies, Uehara demonstrated in multivariate models that age and hyperlipidemia were independent predictors for cervical carotid artery stenoses, whereas age and hypertension predicted intracranial stenosis (6). In addition to aging, experimental and epidemiological studies have supported the role of the microvascular system in the development of cognitive disorders (7-8). Although clinically diagnosed strokes have been related to cognitive impairment, Leys et al. raised the possibility of the occurrence of vascular dementia (VaD) without

stroke, and the clinical relevance of silent infarcts in the development of VaD (9). In a population-based cohort of 1551 subjects with no clinical history or signs of stroke Zhu et al. found that subjects with mild dementia had a higher risk of developing stroke (RR=2.6; 95% CI, 1.2-5.7) (10). These authors underlined the importance of cognitive impairment as a manifestation of clinically unrecognized stroke, which in turn would increase the risk of a subsequent stroke (10). Cognitive impairment as a predictor of stroke incidence was suggested by Ferrucci et al., who found an increased incidence in those with low and intermediate cognitive impairment levels, compared with those having a normal performance in the Short Portable Mental Status Questionnaire (SPMSQ). An adjusted relative risk of 2.2 (95% CI, 1.2-3.8) for stroke was found in individuals with cognitive function severely impaired (11). The availability of cognitive function test results in ARIC's visit 2, as well as the subsequent stroke incidence provide an opportunity to investigate these relationships considering simultaneously the confounding by cardiovascular risk factors.

5. Main hypotheses/ Study questions

The analysis aims at evaluating if the cognitive functioning scores taken in visit 2 (DWR; DSS/WAIS-R and WF) predict clinically diagnosed stroke incidence, after adjusting for the cardiovascular risk factors.

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

ARIC Visit 2 data are necessary to examine the main exposure variable (cognitive function scores) and covariates. The stroke incidence (outcome) will be based on the dataset available through 1997. Covariates include age, gender, education, race, health status, hypertension, diabetes, smoke, BMI, plasma fibrinogen, carotid IMT, plasma cholesterol and fractions, and vital exhaustion. As education, health status and plasma fibrinogen are only available for visit 1, values for these variables are those for visit 1. Exclusion criteria include history of stroke or TIA before visit 2, and use of medications affecting the CNS. Mean values of the test results will be calculated for individuals developing and those not developing incident strokes. Cox proportional hazards model will be used to take time to event into account.

Statistical Power Considerations:

The statistical power of the study was estimated based on the comparison of the means and standard deviations between individuals developing and those not developing stroke, and an alpha value = 0.05 (Stata vs, 6.0) (12). A preliminary analysis of cognitive function test results for individuals with and without stroke is shown in the table below. Although these results do not take into consideration the exclusion criteria, they indicate that the study's power will be sufficient to test the main hypothesis.

Cog. Test	N	Mean	Std.Dev.	Power
Stroke=0				
DWR	13862	6.6 (a)	1.5	
DSS-WAIS-R	13823	44.8 (b)	14.1	
WF	13846	33.2 (c)	12.5	
Stroke=1				
DWR	339	5.8 (**a**)	1.7	>0.99*
DSS-WAIS-R	331	34.0 (**b**)	14.7	>0.99**
WF	335	28.3 (**c**)	13.0	>0.99***

* (**a**) compared with (a)
** (**b**) comapred with (b)
***(**c**) compared with (c)

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 ICTDER02 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 (Not Applicable)
(This file ICTDER02 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 (Not Applicable)

References

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