ARIC Manuscript Proposal # 1119r

1.a. Full Title: MRI predictors of global and domain specific cognitive function at 10 years follow-up: the ARIC MRI Study

b. Abbreviated Title (Length 26 characters): MRI & Cognitive Decline

2. Writing Group: Writing group members: Laura Coker, Tom Mosley, Diane Catellier, David Knopman, Dean Shibata, Jonathan Burdette

I, the first author, confirm that all coauthors have given their approval for this manuscript proposal. ___LHC ____ [please confirm with your initials electronically or in writing]

First Author: Laura H. Coker, PhD
Address: Department of Public Health Sciences
Wake Forest University School of Medicine
1 Medical Center Blvd.
Winston-Salem, NC, 27157
Phone: 336-716-3324 Fax: 336-716-7554
Email: lcoker@wfubmc.edu

Corresponding/senior author (if different from first author correspondence will sent to both the first & the corresponding author):
Address:
Phone: Fax:
Email:

3. Timeline: Analysis will begin following approval of Publications Committee

4. Rationale:

Dementia is a major US public health problem which is increasing due to aging of the population ((Brookmeyer et al., 1998). Cognitive decline and dementia are important sources of patient dependency and morbidity and physical and financial burden to the family and society. There is a critical need to know who is at greatest risk of developing cognitive decline and dementia. And because the diagnosis of dementia is often preceded by gradual cognitive decline, or a “preclinical phase” (Elias et al, 2000), identifying predictors of cognitive decline may assist in forecasting the patterns of decline. MRI provides a sensitive, noninvasive method for detecting cerebral structural changes associated with cognitive functioning. Formal neuropsychological testing provides a sensitive way to measure the both global and domain-specific cognitive functions.

In a cross-sectional analysis from the large, community-based ARIC study, Mosley et al., 2005 reported that high ventricular grade on cerebral MRI was associated with significantly lower scores on the Delayed Word Recall Test (DWRT) (a measure of verbal learning and memory), the
Digit Symbol Substitution Test (DSST) (attention, concentration and psychomotor speed), and greater risk of impaired scores (i.e. < 10th percentile) on the DWRT. Coexisting white matter hyperintensities and silent infarcts were associated with lower scores on all cognitive tests and greater risk of impaired functioning on the DSST and Word Fluency Test (executive functioning). The presence of two or more high-grade abnormalities was associated with increased risk of impaired functioning on all cognitive tests, independent of multiple covariates and silent infarcts. Using longitudinal analyses from the Rotterdam Scan Study, Vermeer et al (2003) reported silent infarctions on MRI predicted an increased risk of dementia and a steeper decline in cognitive function on 3.6 years follow-up in men and women aged 60-90; and Prins et al. (2005) reported periventricular white matter lesions, brain infarcts, and generalized cerebral atrophy on MRI were associated with a steeper rate of decline in cognitive functioning on average follow-up of 5.2 years. Furthermore, these structural brain changes were associated with declines in specific cognitive domains of information processing speed and executive function.

The purpose of this study is to evaluate the associations between structural cerebral findings on MRI and global and domain specific cognitive functioning (verbal memory, concentration and psychomotor speed, verbal fluency, and executive functioning) 10 years later in a community-dwelling cohort of older men and women enrolled in the ARIC MRI Study.

References


5. Main Hypotheses/Study Questions:
Do prevalent structural findings on cerebral MRI predict significant declines in global and specific cognitive functions (memory, attention/concentration and psychomotor speed, and executive function) at 10-years follow-up?

We hypothesize that the strongest and most consistent relationships with brain abnormalities will be found for measures of cognitive functions that represent processing speed and executive functioning.

6. Data (variables, time window, source, inclusions/exclusions): Visit 3 MRI data (1993-1994); visit 3 and visit 5 cognitive data; visit 3 covariates. Specifically:
Inclusions: ARIC Visit 3. Participants age 55 years and older from the Forsyth and Jackson study sites willing to undergo a cerebral MRI at the Visit 3 Examination. ARIC Brain Follow-up Visit, 2002-2005. Participants enrolled in the ARIC Follow-up Study willing to complete a battery of cognitive tests

Exclusions: Previous surgery for an aneurysm in the brain; metal fragments in the eyes, brain, or spinal cord; valvular prosthesis, cardiac pacemaker, cochlear implant, spinal cord stimulator, or other internal electrical device; pregnancy; and occupations associated with exposure to metal fragments.

Excluded From Analysis: Center not Jackson or Forsyth, and race not Black or White

1. white matter grade
2. ventricular grade
3. sulcal size
4. silent infarcts

ARIC Brain MRI Follow-up Visit (2002-2005) Cognitive Data:
1. Delayed Word Recall Test – A measure of verbal learning
2. Digit Symbol Substitution Test – A measure of attention, concentration, and psychomotor speed
3. Trail Fluency Test – A measure of frontal lobe/executive function
4. Trailmaking Tests A & B – Measures of attention/concentration, psychomotor speed, and executive function
5. Stroop Color- Measures of reading ability (word score), naming (color score), and executive functioning (the word-color interference)
6. Modified Mini Mental State Examination with delayed recall – A screening test of global cognitive functioning.
7. Animal Naming – A measure of verbal fluency
8. Finger Tapping Test – A measure of psychomotor speed showing lateral differences

Other variables:
Visit 1: gender, education
Visit 3: Cognitive function: (cnfb1, cnfb2, cnfb4)
Medications with CNS effects
Age, (v3age31), fasting blood sugar (glusiu31), history of diabetes (diabts32), smoking status (cursmk31, forsmk31, evrsmk31, cigt31), hypertension status incl. antihypertensive meds (hypert35), IMT (mnc45_1s), BMI (bmi31), drinking status and alcohol intake (drnk31 ethanl34), lipid variables (total chol, HDL, LDL, triglycerides), blood pressure (sbpb31 sbpb32)
Ancillary data: APOE-E4 status
Incident data: incident stroke

A series of linear models will be fit. Initially, we will simply examine the effect of a single MRI variable on mean V3-V5 change in cognitive function (for the first 3 cognitive variables that were measured at both V3 and V5) controlling for age, race/center, sex, and education level. Alternatively, we will fit a mixed model to estimate the effect of the MRI variable on the rate of change (slope) in cognitive function over the V3-V5 period.
7.a. Will the data be used for non-CVD analysis in this manuscript?  __Yes  _X_ No

   b. If Yes, is the author aware that the file ICTDER02 must be used to exclude persons with a value RES_OTH=”VCD Research” for non-DNA analysis, and for DNA analysis RES_DNA= “CVD Research” would be used? _____Yes _____No
   (This file ICTDER02 has been distributed to ARIC PIs, and contains the responses to consent updates related to stored samples use for research.)

8a. Will the DNA data be used in this manuscript?  _X_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 ICTDER02 must be used to exclude those with value RES_DNA=”No use/storage DNA”?  __X__Yes  _____No

9. The lead author of this manuscript proposal has reviewed the list of existing ARIC Study manuscript proposals and has found no overlap between this proposal and previously approved manuscript proposals either published or still in active status. ARIC Investigators have access to the publication lists under the Study Members Area of the web site at:
http://www.cscc.unc.edu/ARIC/search/php

   __X__ Yes  _____No

10. What are the most related manuscript proposals in ARIC (authors are encouraged to contact lead authors of these proposals for comments on the new proposal or collaboration)?

   ARIC # 314  Mosley Neurology 2005

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data?  _X___Yes  ____No

11.b. If yes, is the proposal
   __X_ A. primarily the result of an ancillary study (list number* 1999.01)
   _____ B. primarily based on ARIC data with ancillary data playing a minor role  (usually control variables; list number(s)* _______ _______ _______)

*ancillary studies are listed by number at http://www/cscc.unc/aric/forms/

12. Manuscript preparation is expected to be completed in one to three years. If a manuscript is not submitted for ARIC review at the end of the 3-years from the data of the approval, the manuscript proposal will expire