ARIC Manuscript Proposal #2729

PC Reviewed: 4/12/16  Status: A  Priority: 2
SC Reviewed: _________  Status: _____  Priority: ____

1.a. Full Title: Neurocognitive correlates of mobility: ARIC-NCS

b. Abbreviated Title (Length 26 characters): Neurocognitive correlates of mobility.

2. Writing Group:
   B. Gwen Windham, Seth Lirette, Jonathan Tingle, Susumu Mori, Kirby G Parker, Melinda Power, Cliff Jack, Steve Kritchevsky, Michael E. Griswold, Thomas H. Mosley
   Others welcome

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

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ARIC author to be contacted if there are questions about the manuscript and the first author does not respond or cannot be located (this must be an ARIC investigator).

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3. Timeline: Writing and analysis to begin immediately. Abstract submission to GSA 03/2016.

4. Rationale:
Mobility impairments affect 1/3 of older adults, are associated with falls, disability, institutionalization, premature mortality\textsuperscript{1-5} and are costly.\textsuperscript{6} The brain is emerging as an important contributor to aging-related mobility decline, and abnormalities in brain structure may modify responses to gait rehabilitation strategies.\textsuperscript{7} Therefore, understanding neural contributors to gait may yield targeted therapies for gait disturbances.

Prior studies have shown that white matter hyperintensities (WMH), atrophy, infarcts,\textsuperscript{8,9} and executive function (EF)\textsuperscript{10,11} are associated with poor gait. Gait is a complicated process that relies on bilateral cortical input to process and integrate motor, sensory, cognitive and other signals that ultimately lead to efficient and safe mobility. White matter tracts through the corpus callosum (CC) facilitate intracerebral communication yet limited studies have examined the relationship of CC structure with gait. Studies suggesting microstructural integrity of WM in the CC is associated with gait tend to be limited by sample size,\textsuperscript{12} lack of important confounders,\textsuperscript{12,13} or assessments in selected populations.\textsuperscript{13} Therefore, the relationship of gait with CC microstructural integrity of the CC is poorly understood.

The current study will examine relations of anterior and posterior CC (aCC, pCC) microstructural integrity using diffusion tensor imaging (DTI) to usual gait speed in community-dwelling older adults, independent of structural brain measures, EF, and comorbidities. Elucidating subtle changes in brain structure that are linked to gait impairments may identify preclinical abnormalities in the aging brain that impact mobility. Furthermore, defining the joint effects of structural and cognitive contributions to gait may inform targeted interventions useful in gait rehabilitation.

5. Main Hypothesis/Study Questions:
DTI measures in the CC will be associated with poorer lower extremity performance measures, such as slower walking speed and balance in older persons independent of WMH and infarcts.

6. Design and analysis (study design, inclusion/exclusion, outcome and other variables of interest with specific reference to the time of their collection, summary of data analysis, and any anticipated methodologic limitations or challenges if present).

DESIGN: cross sectional.

Exclusions:
Missing data for MRI variables.

Outcomes:
SPPB and components (gait speed, chair stands, balance)

Main predictor variables:
Visit 5 MRI variables:
- FA and MD in periventricular regions and CC
- Infarcts
- WMH
- Atrophy
- Total brain volume

**Covariates:**
The following covariates will be used to examine adjusted regression models: age, BMI, sex, race, site, diabetes, systolic blood pressure, diastolic blood pressure, antihypertensive medications, heart disease and heart failure.

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 ICTDER03 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 ICTDER 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 __X__ No

8.b. If yes, is the author aware that either DNA data distributed by the Coordinating Center must be used, or the file ICTDER03 must be used to exclude those with value RES_DNA = “No use/storage DNA”? _____ 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 publications lists under the Study Members Area of the web site at: http://www.csc.c.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)?

MS 2383 Lifes simple 7 relationship with Late Life Physical Function
MS 2551 Midlife and late life vascular risk factors and white matter integrity assessed using diffusion tensor imaging: the ARIC-NCS study

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
   ___ A. primarily the result of an ancillary study (list number* 2008.06)
   ___ 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.edu/aric/forms/

12a. 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 date of the approval, the manuscript proposal will expire.

12b. The NIH instituted a Public Access Policy in April, 2008 which ensures that the public has access to the published results of NIH funded research. It is your responsibility to upload manuscripts to PUBMED Central whenever the journal does not and be in compliance with this policy. Four files about the public access policy from http://publicaccess.nih.gov/ are posted in http://www.cscc.unc.edu/aric/index.php, under Publications, Policies & Forms. http://publicaccess.nih.gov/submit_process_journals.htm shows you which journals automatically upload articles to PubMed central.

References


7. Nadkarni NK, Perera S, Studenski SA, Rosano C, Aizenstein HJ, VanSwearingen JM. Callosal Hyperintensities and Gait Speed Gain From Two Types of Mobility Interventions in Older Adults. Archives of physical medicine and rehabilitation. 2015;96(6):1154-1157.


