ARIC Manuscript Proposal #3432

PC Reviewed: 7/9/19  Status: _____  Priority: 2
SC Reviewed: _________  Status: _____  Priority: _____

1.a. Full Title: Objectively measured physical activity and MRI cortical volume

b. Abbreviated Title (Length 26 characters): physical activity, MRI volume

2. Writing Group:
   Writing group members: Laura Skow, Adam Spira, Rebecca Gottesman, A. Richey Sharrett, Jennifer Schrack, others welcome.

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

First author: Laura F. Skow, BA
Address: Welch Center for Prevention, Epidemiology, and Clinical Research
Department of Epidemiology
Johns Hopkins University,
2024 E. Monument Street,
Baltimore, MD 21287

Phone: 630-743-3651
E-mail: lskow1@jhu.edu

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).
Name: Jennifer A. Schrack, PhD, MS
Address: Center on Aging and Health
Department of Epidemiology,
Johns Hopkins University,
615 N. Wolfe Street, E7144
Baltimore, MD 21205

Phone: 410-502-9328
E-mail: jschrac1@jhu.edu

3. Timeline: Analysis to begin immediately, manuscript to be completed over the following 6 months.
4. Rationale:

The association between physical activity and cognitive performance in older age has been well established. Studies connecting physical activity to brain structure and function are heterogeneous and largely rely on questionnaires and other self-report measures of physical activity, which are powerful tools but are also subjective and open to recall issues. The following will focus on only literature concerning objective measures of physical activity and brain structure and function.

Objectively-measured physical activity has also been linked with increased brain MRI volume, particularly in the prefrontal and hippocampal regions (1), but results are inconsistent as to which measure of physical activity is used and which brain region is associated. However, among participants with mild cognitive impairment, moderate-to-vigorous physical activity (2), and moderate physical activity (3) but light or total physical activity was associated with larger hippocampal volume and less brain atrophy respectively. However, among non-demented participants in the Framingham Offspring cohort, total physical activity corresponded to increased brain volume (4). In non-demented adults, total activity and grey and hippocampal brain volume are similarly linked, but only among adults over the age of sixty-five (5).

Other studies of hippocampal volume demonstrate a similar trend of increased volume by physical activity (6, 7), and the reverse association (8), but even among studies all using objective physical activity measures, there is heterogeneity. Assigned physical activity intervention increases left hippocampal volume (9), which supports physical activity as a promising area of research for improving brain structure in older adults, but more research is needed to clarify what kind of physical activity.

Accelerometry-measured physical activity provides promising granularity in physical activity volume, intensity, and patterns beyond previous metrics, including fragmentation (10). This analysis proposes to use accelerometry-based objective physical activity measures of total activity, activity intensity, and activity trends to evaluate the association between physical activity and brain MRI measures in the ARIC-PET-Sleep data.

(References at end.)

5. Main Hypothesis/Study Questions:

In this small, cross-sectional pilot study, we propose to assess the association between objective accelerometry-based, free-wear physical activity and brain function and structure by assessing:

1. Total physical activity amount.
   a. Hypothesis 1: Higher amounts of physical activity will be associated with larger cortical volume and smaller ventricle space.
2. Physical activity intensity.
   a. Hypothesis 2: Higher intensity physical activity will be associated with larger cortical volume and smaller ventricle space.

   a. Hypothesis 3: A greater degree of activity fragmentation (i.e. with activity broken into more, smaller bouts) will have smaller cortical volume and larger ventricle space.

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).

Study Population:

Inclusions: Participants who have available MRI and accelerometry at the Washington County ARIC PET-Sleep study.

Exclusions: Participants with fewer than three days of valid accelerometry data or with other missing covariate will be excluded from the analysis.

Exposure

Physical activity measures will be derived from the raw accelerometry data, which tracks movement magnitude and direction along three axes (X-, Y-, and Z-axis).

   a. Total physical activity time: Average minutes per day with movement vectors in excess of the threshold for baseline motion, according to established standard.

   b. Physical activity intensities: Using the vector summary measures, cut-offs will be marked to differentiate ‘light’, ‘moderate’, and ‘vigorous’ physical activity signals, according to established standard.

   c. Physical activity patterns: The fragmentation index uses the number of bouts of activity in excess of the baseline threshold and the length of those bouts of activity to quantify how segmented a participant’s usual physical activity is.

AIC, BIC, adjusted $R^2$, and other selection criteria will be used to select the most appropriate physical activity summary measures using the raw data.

Outcomes

Based on the available MRI data, we propose to look at the following:
1. Cortical volume  
2. Ventricle volume  
3. (DTI (FA and MD) and WMH volume)

**Covariates**

Proposed covariates, given data availability, are age, sex, ApoE4 (0, 1+), body mass index, blood pressure medication use, smoking, alcohol use, blood pressure, and cardiovascular comorbidities (e.g. diabetes, coronary heart disease, stroke, heart failure).

**Statistical Analysis:**

Proposed analysis includes but is not limited to a multivariable linear regression of the association between each PA measure and MRI brain volume and function.

For each PA measure, two models are proposed.

- Model 1: Adjusted for age, sex, ApoE4 and intracranial volume.
- Model 2: Adjusted for Model 1 and body mass index, medication use, smoking, alcohol use, blood pressure, and cardiovascular comorbidities (e.g. diabetes, coronary heart disease, stroke, heart failure).

**7.a. Will the data be used for non-CVD analysis in this manuscript?**  
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___ 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?**  
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___ 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?**  
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___ Yes ___ x__ No

**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”?**  
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___ 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.cscencer.edu/ARIC/search.php](http://www.cscencer.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)?**

#3035 – Palta; leisure-time PA and MRI
#3349 – Palta; leisure-time PA and brain amyloid

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* ____________ )
   ___ 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/](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/](http://publicaccess.nih.gov/) are posted in [http://www.cscc.unc.edu/aric/index.php](http://www.cscc.unc.edu/aric/index.php) under Publications, Policies & Forms.**

[http://publicaccess.nih.gov/submit_process_journals.htm](http://publicaccess.nih.gov/submit_process_journals.htm) shows you which journals automatically upload articles to Pubmed central.

13. **Per Data Use Agreement Addendum for the Use of Linked ARIC CMS Data, approved manuscripts using linked ARIC CMS data shall be submitted by the Coordinating Center to CMS for informational purposes prior to publication.**

Approved manuscripts should be sent to Pingping Wu at CC, at pingping_wu@unc.edu. I will be using CMS data in my manuscript ____ Yes __x__ No.

References:


