

ARIC Manuscript Proposal # 1088

PC Reviewed: 06/17/05

Status: A

Priority: 2

SC Reviewed: 06/17/05

Status: A

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1.a. Full Title: Physical Activity and Cerebral Abnormalities on MRI

b. Abbreviated Title (Length 26 characters): PA and MRI

2. Writing Group: Thomas Mosley (UMMC), Diane Catellier (UNC),
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3. Timeline:

Manuscript proposal to Publication's Committee:

June / 2005

Data analysis completed:

September / 2005

Completed manuscript to Publication's Committee:

December / 2005

4. Rationale:

Evidence from an increasing number of studies suggests that exercise and physical activity may protect the brain from stroke and functional decline. ARIC and other investigators have found that exercise and physical activity offer some protection against stroke. In ARIC, participants in the lowest quartiles of sport, leisure, and work scores had the highest incidence of ischemic stroke during follow-up.¹ A recent meta-analysis of physical activity and cardiovascular disease in women found that increasing physical activity decreased the risk of stroke in a dose-response

relationship.² In an 11-year follow-up of male physicians, exercise vigorous enough to work up a sweat was inversely related to stroke.³

Investigators have begun to look for evidence of a protective effect of exercise and physical activity on subclinical markers of neurodegenerative changes using brain imaging. Notably, Colcombe and colleagues⁴ examined change in brain tissue density (defined on MRI) across several brain regions in a sample of older adults with varying levels of aerobic fitness. Although declines in tissue densities were observed in all groups and correlated with age, tissue losses were significantly lower in participants with higher levels of cardiovascular fitness. These effects remained after controlling for potential confounding factors.

In ARIC, MRI-defined cerebral abnormalities have been shown to be associated with various CVD risk factors.⁵⁻⁸ Physical activity has typically not been examined directly but rather controlled for as a covariate. Howard et al.⁵ did examine the relationship between PA and silent infarction. No significant association was found. No attempt was made to distinguish between types of PA in this study. We are not aware of any studies of the association between physical activity and MRI findings that have examined sedentary behaviors such as television watching. Television watching could be related to subclinical brain changes as it competes for time spent in physically active leisure or through its association with poor eating habits and weight gain.^{9,10}

In the current study, we propose to examine the association between physical activity and subclinical cerebral abnormalities identified on MRI in the ARIC cohort.

5. Main Hypothesis/Study Questions:

Study Question 1: What is the relationship between physical activity and MRI-defined cerebral abnormalities?

Study Question 2: What is the relationship between sedentary time, defined as time watching television, and MRI-defined cerebral abnormalities?

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

The primary dependent variables of interest are infarct-like lesions (> 3mm, present/absent), white matter hyperintensities (\geq grade 3, present/absent), ventricular size (\geq grade 4, present/absent), and sulcal size (\geq grade 3, present/absent). Because of the potential for age, ethnicity, and sex to confound the relationship between the MRI variables and potential risk factors, all analyses will control for these factors.

The primary exposure variables will be physical activity measured by the ARIC Baecke scores (Sport, Work, and Leisure indexes).¹¹ Each index will be examined separately. The Work index will be examined with and without participants employed outside the home. We will also examine other classifications of participation in physical activity used by previous ARIC investigators as exposure measures, including “regular vigorous activity” (defined as participation in activities classified as high intensity for at least 1 hour per week for \geq 10 months

per year)¹ and responses to the individual questions on frequency of walking during leisure time and leisure time activity compared to peers.

For study question 2, the exposure variable will be time spent watching television from the Baecke instrument (i.e., During leisure time do you watch television never, seldom, sometimes, often, or very often?). In the primary analyses, we will compare participants who responded at V1 that they watched television often or very often with those who reported watching seldom or never.

Analyses will examine exposure to physical activity and television watching measured at Visit 1. A series of linear regression models will be fit, adjusting for potential confounder variables and stroke risk factors (described in Framingham and ARIC) in successive models. Model 1 will adjust for demographic variables (age, sex, race/center, years of education, and income). Model 2 will add behavioral risk factors (smoking, alcohol consumption, and BMI). Model 3 will add biological risk factors (hx of CHD, LVH, HTN, antihypertensive medication, diabetes, plasma fibrinogen, creatinine, von Willebrand factor).

Exclusions:

1. Missing physical activity scores at V1
2. History of stroke or TIA prior to V3
3. Incident stroke prior to V3
4. Race not black or white

In secondary analyses, we will utilize the additional information available from V3 on physical activity by comparing groups of participants who maintained or increased their sport or leisure activity from V1 to V3 with those whose physical activity declined. Increase will be defined as an increase of ≥ 0.25 units for sport or leisure scores; maintenance will be defined as scores within ± 0.25 units; decrease will be defined as decrease of ≥ -0.25 units from the baseline scores.¹²

It is acknowledged that the study design cannot rule out reverse causality, and we cannot be certain whether the MRI findings at V3 predated V1 (though this seems unlikely).

Determination of causality is perhaps most problematic for the secondary analyses (V1-V3 change in physical activity levels). This limitation will be acknowledged and discussed in the manuscript.

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

(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 ICTDER02 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.unc.edu/ARIC/search.php>

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)?

We are aware of no current proposals of the proposed analysis.

11. a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? 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.csc.unc.edu/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 date of the approval, the manuscript proposal will expire.

References

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