ARIC Manuscript Proposal # 1858

PC Reviewed: 10/11/11  Status: A  Priority: 2
SC Reviewed: ________  Status: _____  Priority: ____

1.a. Full Title: Midlife occupation and cognitive decline: the ARIC study

b. Abbreviated Title (Length 26 characters): Occupation and cognition

2. Writing Group:
Writing group members: Mehul Patel, Rebecca Gottesman, Thomas Mosley, Andrea Christman, Ola Selnes, Josef Coresh, A. Richey Sharrett

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

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3. Timeline:

We expect to complete the manuscript less than 12 months after approval.

4. Rationale:

Cognitive, or brain, reserve is a theoretical property of the central nervous system characterized by the capacity to preserve cognitive performance in the presence of brain disease, like Alzheimer’s Disease or vascular dementia. Factors that have these effects, such as education, occupational complexity, and mental activities (e.g. crossword
puzzles), might influence either the level of cognitive performance or the rate of cognitive decline.

A recent systematic review presents convincing evidence for the protective effects of higher education, more complex occupation, and more stimulating mental activities (individually and combined) on rate of cognitive decline [1]. Still, results are difficult to compare between studies since there is significant heterogeneity in the way cognitive performance is tested. Furthermore, while education is generally defined in terms of years of school completed, various occupational classifications and status scores are used as proxies for the intellectual complexity of occupations. Studies of the independent effect of occupation on cognitive decline have produced mixed results, with either insignificant or a minimally significant benefit of higher occupation [2-6], except for a recent study that found a greater decline in the high occupation group [7]. Discrepancies in reported findings can be attributed not only to differences in occupation and cognitive performance measures but also in the covariates adjusted for in analyses.

We aim to estimate the association of midlife occupation with baseline level of cognitive performance and cognitive decline later in life in the Atherosclerosis Risk in Communities (ARIC) cohort, adjusting for education and other relevant covariates. The ARIC study offers an ideal setting given the detailed education and occupation data that were collected at baseline and cognitive function testing covering a range of cognition domains that was conducted at multiple follow-up visits. Furthermore, the ARIC study is one of the largest population-based studies of white and black, men and women in the US.

5. Main Hypothesis/Study Questions:

Main Hypothesis: Higher occupational status at midlife is associated with increased levels of baseline cognitive performance and decreased cognitive decline later in life

Primary Aim: Estimate the association of participant’s occupational status (1987-89) with baseline levels and declines in cognitive test scores (Delayed Word Recall, DWR; Digit Substitution, DSS; Word Fluency, WF) from 1990-92 to 2004-06, adjusting for educational attainment and other relevant covariates

Secondary Aim: Estimate the joint effect of occupation and education on baseline levels and declines in cognitive test scores

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
The ARIC cohort consists of 15,792 white and black, men and women ages 45–64 years at the onset of the study (1987-89). The proposed study will include follow-up through Visit 4 (1996-98) for cohort participants and through the Brain/Carotid MRI visits (2004-06) for the subsample selected for those studies. For the analysis, we will restrict to individuals of white and black race because of insufficient numbers of other races. Participants with missing occupation information will be excluded.

Additional Exclusions

We will exclude participants with a neurologic disorder that could affect cognitive performance – stroke/TIA, multiple sclerosis, Parkinson’s disease, dementia, brain tumor, or surgery or radiation therapy involving skull or brain. Also, participants who did not undergo cognitive testing on at least two separate visits will be excluded from the analysis of cognitive decline.

Exposure: Occupation

For the purposes of this analysis, occupation will be defined in two ways: a categorical occupation classification and a continuous occupational status score. Based on each participant’s report of his/her current employment status and most recent occupation, we will code participant’s occupation into the six Census summary groupings, which are based on the 1977 Standard Occupational Classification (shown in ARIC Cohort Procedures Manual 2a Visit 1 Appendix III), and additional groups will be created for “retired” and “homemaker” employment status. Table 1 displays the distribution of occupation groups by gender. We hypothesize that the highest status group (i.e. managerial and professional specialty occupation) will be associated with the highest baseline cognitive function and the lowest cognitive decline.

Table 1. Distribution of occupational groups by gender, ARIC Visit 1 (1987-89)

<table>
<thead>
<tr>
<th>Derived Occupation Groups</th>
<th>Men, n</th>
<th>Women, n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Census Summary Groupings*</td>
<td></td>
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</tr>
<tr>
<td>Managerial and Professional Specialty Occupations</td>
<td>1,903</td>
<td>1,607</td>
</tr>
<tr>
<td>Technical, Sales, and Administrative Support Occupations</td>
<td>1,053</td>
<td>2,059</td>
</tr>
<tr>
<td>Service Occupations</td>
<td>353</td>
<td>1,339</td>
</tr>
<tr>
<td>Farming, Forestry, and Fishing Occupations</td>
<td>100</td>
<td>17</td>
</tr>
<tr>
<td>Precision Production, Craft, and Repair Occupations</td>
<td>1,100</td>
<td>151</td>
</tr>
<tr>
<td>Operators, Fabricators, and Laborers</td>
<td>970</td>
<td>598</td>
</tr>
<tr>
<td>Homemakers</td>
<td>15</td>
<td>1,546</td>
</tr>
<tr>
<td>Retired</td>
<td>1,567</td>
<td>949</td>
</tr>
<tr>
<td>missing/never worked</td>
<td>21</td>
<td>444</td>
</tr>
</tbody>
</table>

*Based on 1977 Standard Occupational Classification

Since occupational summary groups can be heterogeneous with respect to type of job, we will also characterize occupation using a socioeconomic status (SES) score. The Nam-Powers occupational status score (ranging from 0 to 100) ranks by the median education and median income of the persons employed in that occupation for each decennial US Census since 1940 [8]. While there are several such scores to consider, we chose Nam-Powers since it has been created for the 1980 Census and can be readily coded from the available data in ARIC. Furthermore, a previous study found a strong association between cognitive impairment and low SES, as measured by the Nam-Powers
occupation score [9]. Finally, although occupational status scores are mainly a measure of social standing, we feel the Nam-Powers score is a reasonable, yet limited, proxy for occupational complexity. We hypothesize that an increase in Nam-Powers occupational status score will be associated with a higher baseline cognitive function and a lower cognitive decline.

Outcome: Cognitive Performance and Decline

Cognition performance was measured with three tests, Delayed Word Recall (DWR), Digit Substitution (DSS), and Word Fluency (WF), at ARIC Visits 2-4 and Brain/Carotid MRI visits (Table 2). The same protocols were used at all visits. Cognitive test score will be set to missing if the participant was taking CNS-altering medications (anxiolytics, antipsychotics, hypnotics/sedatives, anticonvulsants, and dementia drugs or nootropics) since these drugs may have affected cognitive performance. Baseline levels of cognitive function will be determined by Visit 2 cognitive test scores. Cognitive decline will be defined as a decrease in test scores over 6 or 15 years, depending on the final cognitive testing visit.

Table 2. Number of ARIC participants administered cognitive tests by visit

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Examined, N</td>
<td>14,327</td>
<td>12,873</td>
<td>11,620</td>
<td>1,130</td>
<td>2,058</td>
</tr>
<tr>
<td>Cognitive testing, N</td>
<td>14,201</td>
<td>1,920*</td>
<td>11,343</td>
<td>1,130</td>
<td>1,943</td>
</tr>
</tbody>
</table>

*cognitive tests only administered to participants in Forsyth and Jackson who had cerebral MRI scans

Relevant Covariates

Demographic variables will include age, gender, and race X center. Education level, defined as years of school completed, will be treated as a potential confounder. To test effect measure modification by education, categories of less than high school, high school or equivalent (GED/vocational school), and more than high school will be used. Other relevant covariates will include smoking, diabetes, hypertension, blood pressure-lowering medications, history of CAD, and APOE genotype. Covariates believed to affect both occupation and cognitive decline will be treated as potential confounders. Carotid intima-media thickness (measured by ultrasound) will be included because Carotid MRI participants were sampled based on these values.

Statistical Analysis

Cognitive test scores will be analyzed individually and combined using linear mixed models. To estimate associations between cognitive decline and occupation, we will use a random-effects linear model for repeated test measures within individuals. Separate analyses will be conducted for the cohort participants with only two cognitive testing visits (Visits 2 + 4) and for the subsample that underwent testing on multiple visits over a 15-year period. Models with occupational categories will be gender-stratified since a much larger proportion of female participants were homemakers (19%) compared to males. The main regression models will include demographic variables and education. We will not adjust for baseline test scores when modeling cognitive decline because baseline adjustment can introduce bias if the baseline level is predicted by the exposure [10]. In this case, participant’s occupation may have an effect on his/her baseline (Visit 2)
cognitive function. To assess joint effects, we will fit models with interaction terms between occupational status score and education level.

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 ICTDER03 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.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)?

MS 1742 Education and cognitive change from 1990-92 to 2004-06 (First author: Gottesman)

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? ___x__ Yes _____ No
Brain MRI (Mosley)

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.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


