ARIC Manuscript Proposal #3405

1.a. Full Title: Prevalence of Disproportionately Enlarged Subarachnoid Space Hydrocephalus (DESH) in Study Group Populations

b. Abbreviated Title (Length 26 characters): DESH prevalence

2. Writing Group:
   Writing group members: Petrice Cogswell, David Knopman, Cliff Jack, Jeff Gunter, David Jones, Jonathan Graff-Radford

I, the first author, confirm that all the coauthors have given their approval for this manuscript proposal. __PMC

First author: Petrice Cogswell
Address: 200 First St SW, Rochester, MN 55905

Phone: 507-284-0440 Fax: 
E-mail: cogswell.petrice@mayo.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: David Knopman
   Address: 200 First St SW, Rochester, MN 55905

Phone: 507-266-4106 Fax: 
E-mail: knopman@mayo.edu

3. Timeline: Study will be a cross-sectional study performed June-August 2019 on currently available data.

4. Rationale: It has recently been recognized that alterations in cerebrospinal fluid dynamics is more common than previously recognized and that it is far more than the oft-disparaged diagnosis of normal pressure hydrocephalus. The Mayo group has two publications in re-review that are examining the relationship of alterations in ventricular size and sulcal anatomy with
cognition. The first is one looking at associations of ventricular volume to gait and cognition in persons with a full biomarker profile to exclude Alzheimer disease. The second is based on observations that enlarged ventricles are often associated with alterations in sulcal width over the convexities. It is this latter issue that is the subject of this analysis. The radiological finding Disproportionately Enlarged Subarachnoid Hydrocephalus (DESH) has been shown to be an indicator of shunt responsive hydrocephalus in the Japanese population. An algorithm has been derived by Jeff Gunter, a co-author, to automatically identity the DESH imaging signature from 3D T1-weighted MRI. The algorithm referred to as Computational DESH (CDESH) identified the DESH imaging phenotype in 6% of the Mayo Clinic Study of Aging (MCSA) population, agnostic of clinical data. We point out that CDESH is purely based on imaging whereas a formal DESH diagnosis under the Japanese NPH guidelines is predicated on the existence of clinical hydrocephalus symptom in concert with imaging. Features included in the creation of the CDESH score include tightness of sulci at the high convexity and along the midline of the brain in concert with ventriculomegaly and enlarged Sylvian fissures. CDESH may co-exist in study group populations for diseases such as Alzheimer Disease, possibly confounding clinical characterization and assessment of treatment response. We will generate CDESH scores for the ARIC cohort and compare ARIC with ADNI, MCSA and other study cohorts.

5. Main Hypothesis/Study Questions: The purposes of this work are to (i) assess the prevalence of CDESH in the ARIC population as well as other study groups and (ii) compare clinical characteristics of CDESH vs non-CDESH patients in each study group.

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).
This is a cross-sectional study of subjects ages 45-89 years who were previously enrolled in the ARIC, MCSA, or ADNI studies and have undergone diagnostic quality 3D T1-weighting MR imaging. Exclusion criteria are minimal, requiring only successful image processing of acceptable quality images. The CDESH algorithm generates a continuous pattern matching score to which a threshold may be applied providing a discrete CDESH positivity output. Outcomes will be prevalence of CDESH across the cohorts, comparison of continuous CDESH score across cohorts, and comparison of demographics and clinical characteristics between the CDESH positive and negative groups. The ARIC scans are resident in the Jack Imaging Laboratory at Mayo. We will be requesting basic demographic, cognitive cardiovascular risk data and APOE genotype on participants whose scans are used in the analysis. We would request those variables from the visit in which the scan was obtained, and in the case of cardiovascular data, from ARIC visit 1. Ideally, it would be convenient to draw this data from the set used for Knopman et al. Midlife vascular risk factors…. ALz Dem 14:1406, 2018; ARIC MS# 2120b.

7.a. Will the data be used for non-CVD analysis in this manuscript? _XXX_ Yes  ___ 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? _XX_ 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? _XX_ Yes _____ No - APOE genotype only

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”? _XX_ 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/mantrack/maintain/search/dtSearch.html

_____ XXX_ Yes _______ No

The only 3 manuscripts that came up in my search were Schneider Neurology March 2019, Knopman Neurology 2011 (#1553) and Mosley Neurology 2005 (#314), all of which Knopman was a co-author on, and he can vouch that they are unrelated to the current request.

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)? There are none

11.a. Is this manuscript proposal associated with any ARIC ancillary studies or use any ancillary study data? _XXX_ Yes _____ No ➔ This will use ARIC NCS data

11.b. If yes, is the proposal

_____ A. primarily the result of an ancillary study (list number* 2008.06_ARIC NCS)

_____ 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 https://www2.cscc.unc.edu/aric/approved-ancillary-studies

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.csec.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.