Application of the ATN Framework in African Americans and Caucasians

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Non-FDA approved/ Off-label applications will be discussed.

Are there racial differences in AD between AA and Caucasians in the US?

Prevalence of dementia: 2-4x higher in AA's

- AD dementia
- Vascular dementia
- Other dementia
- Faster progression? Or later presentation / delayed diagnosis?

Confounds

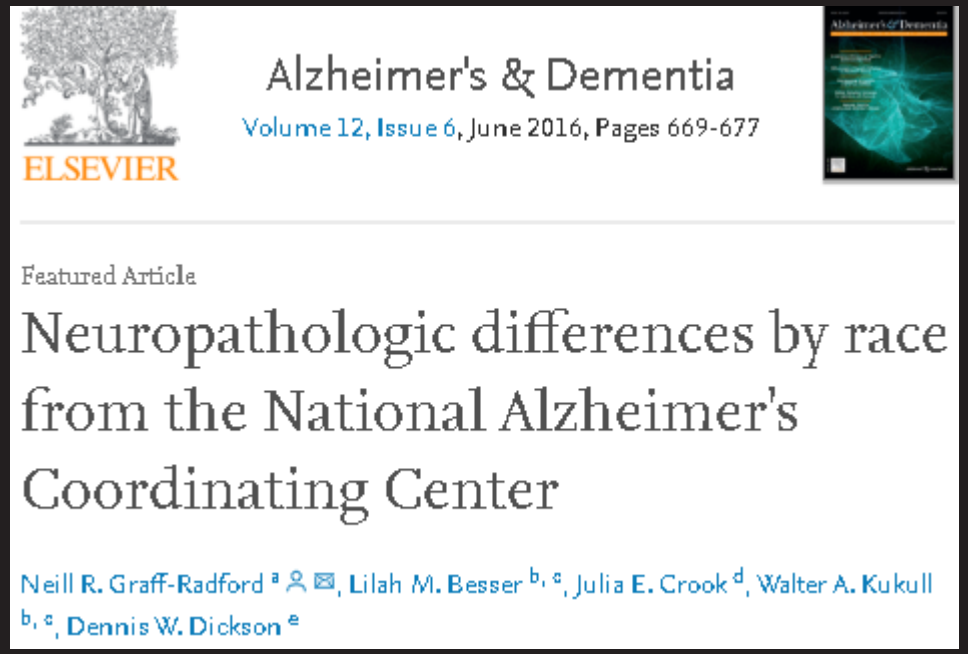
- Cultural differences
- Levels of participation in research
- Health disparities, including vascular risk factors
  - Diabetes
  - Hypertension
- Economic disparities
- Educational disparities

What are the genetic differences?

- APOE4
- ABCA7
- Both genes are hypothesized to result in increased amyloid burden and may account for increased rates of AD dementia in AA cohorts

- Within the US, overall the genetics are more similar than different

What does autopsy data tell us?



ELSEVIER

Alzheimer's & Dementia

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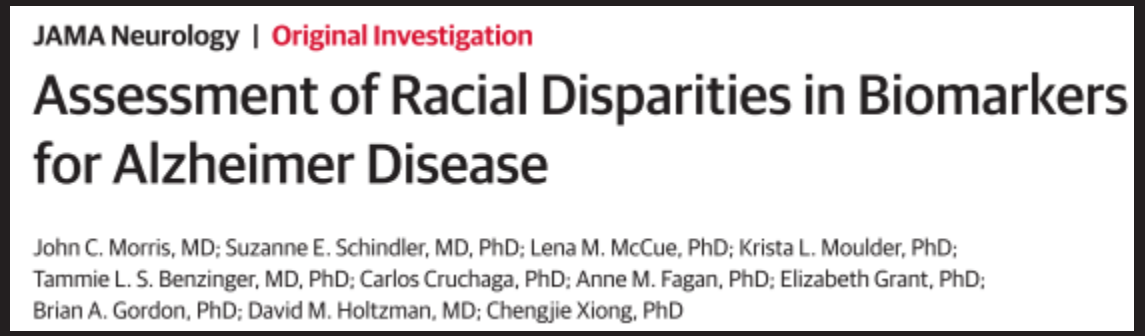
Featured Article

Neuropathologic differences by race from the National Alzheimer's Coordinating Center

Neill R. Graff-Radford [a], Lilah M. Besser [b, c], Julia E. Crook [d], Walter A. Kukull [b, c], Dennis W. Dickson [e]

- NACC 2005-2015
- 2500 Caucasians, 110 AA
- AA had higher
  - Cognitive impairment
  - ApeE4 allele
  - Hypertension
  - Braak stage and CERAD score
  - Infarcts, hemorrhages

Application of the A-T-N framework to a large cohort of community volunteers



JAMA Neurology | Original Investigation

Assessment of Racial Disparities in Biomarkers for Alzheimer Disease

John C. Morris, MD; Suzanne E. Schindler, MD, PhD; Lena M. McCue, PhD; Krista L. Moulder, PhD; Tammie L. S. Benzinger, MD, PhD; Carlos Cruchaga, PhD; Anne M. Fagan, PhD; Elizabeth Grant, PhD; Brian A. Gordon, PhD; David M. Holtzman, MD; Chengjie Xiong, PhD

- 1255 participants/ 173 AA
- Amyloid
  - PiB PET SUVR –NO DIFFERENCE
  - CSF Aβ42 –NO DIFFERENCE
- Tauopathy
  - Lower CSF tau (p- and t-) with a race by ApoE4 interaction
- Neurodegeneration
  - Differences in hippocampal volumes (mild) associated with + family history
- Vascular
  - Clinical MRI read + for infarction – NO DIFFERENCE

Application of the A-T-N to a hospital-based cohort

- 81 cognitively normal participants admitted to Barnes-Jewish Hospital for acute stroke, age 65 and older
- 52% AA
- 2:1 age, gender, and racially matched controls from community sample
- Volumetric MRI, PiB PET, MMSE, Family history, HgbA1c, BMI

Application of the A-T-N to a hospital-based cohort

A:Amyloid PET

- Acute stroke cohort had similar rates of PiB positivity (24%) compared to the community based volunteers
- No racial differences

Application of the A-T-N to a hospital-based cohort

N:Neurodegeneration

- No differences in hippocampal volume by race or stroke

Application of the A-T-N to a hospital-based cohort

ApoE4

- Highest in the AA's with stroke
- (Other studies report overall ~15% in the general population)

One or two APOE s, n (%)	**AA**	**Caucasian**	
Stroke, No	38 (46.3)	33 (42.3)	0.6078
Stroke, Yes	22 (59.5)	11 (29.7)	**0.0114**

Application of the A-T-N to a hospital-based cohort

Racial differences in vascular risk

- HgbA1c – no difference
- BMI – higher in AA community volunteers
- Hypertension – no difference

- (HgbA1c and BP > with stroke, but not different by race)

Increased # of lacunar infarcts in AA with stroke compared to Caucasians with stroke dg

Application of the A-T-N to a hospital-based cohort

- Higher incidence of microbleeds in AAs compared to Caucasians
- True for both stroke and community samples
- Overall, 15% of AA's had 5 or more microbleeds **which would exclude them from many clinical trials for AD therapeutics**

Conclusions from the hospital-based study

- Both AA's and Caucasians presenting for inpatient stroke admission, in comparison to healthy community volunteers, had
  - Higher blood pressure
  - Lower education
- The rate of amyloid positivity was ~24% regardless of race or recruitment source
- Racial differences were found for
  - ApoE4+ (60% of the AAs with stroke)
  - Number of lacunar infarcts (higher in AAs with stroke)
  - Number of microbleeds (higher in AAs both with and without stroke)

Limitations (& strengths) of using the hospital-based cohort

- Small sample sizes
- Lack of a measure of tauopathy
- Recruitment from a hospital-based setting
  - Increased AA participation from 14% to 52%
  - High drop out rates, insufficient data to statistically evaluate rates of conversion to dementia
- Co-pathology
  - More “real world” complexity of co-morbidities

What future studies are needed?

- In order to increase participation in research, barriers need to be identified
- Education and outreach are critical, for both researchers and study participants
- We need to redesign the research studies
- *In this analysis, 15% of AA's over age 65 would potentially be excluded from clinical trials in AD based on presence of microbleeds*

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Data sharing – www.oasis-brains.org
& DIAN.wustl.edu

Postdocs, students, potential collaborators welcome!
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