Recent publications using the NACC Database

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# Data requests and publications

Using NACC data

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<th>Type</th>
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*Includes updating files with most recent data, adding variables, other adjustments, etc.

>450 published manuscripts and abstracts to date
Research proposals using NACC data

Example topics in the last year:

• Preclinical and prodromal disease
• Non-AD dementias
• Minority populations (e.g., African Americans, Hispanics)
• Genetics, APOE e4 and e2 studies
• Imaging data and MRI studies
• Methodology (e.g., machine learning)
Example Genetic Studies

Using NACC data


Examples studies looking beyond AD
Using NACC data


• Wyman-Chick KA & Scott BJ. Development of Clinical Dementia Rating Scale Cutoff Scores for Patients with Parkinson's Disease. Movement disorders, in press 2015.
Example 1

Torralva T, Sposato LA, Riccio PM, Gleichgerrcht E, Roca M, Toledo JB, Trojanowski JQ, Kukull WA, Manes F, Hachinski V.

Role of brain infarcts in behavioral variant frontotemporal dementia: Clinicopathological characterization in the National Alzheimer's Coordinating Center database.

Neurobiology of Aging, available online 3 July 2015.
Background & Aims
Torralva and Sposato et al

Background:

• bvFTD diagnosis typically ruled out if cerebrovascular disease (CVD)

• Prior studies of FTD often exclude those with brain infarcts on imaging

Study aim:

• To characterize and compare bvFTD subjects with CVD at autopsy and bvFTD subjects with no CVD at autopsy
Study Definitions
Torralva and Sposato et al

- Inclusion criteria:
  - Primary NP diagnosis of FTLD
  - No aphasic FTD symptoms

- Diagnosis groups:
  - V-bvFTD: With CVD
  - NV-bvFTD: No CVD
Methods
Torralva and Sposato et al

CVD defined as at least one:

• Gross infarct, lacunar infarct, microinfarct, or hemorrhage

Methods:

• Unadjusted statistical comparisons of demographics, diagnosis before death, vascular risk factors, CDR, and neuropsychological tests
  
  – Neuropsychological test scores normalized for age and sex (calculated z-scores)
Clinical Findings

Torralva and Sposato et al

- Compared to NV-bvFTD group, V-bvFTD group:
  - Had an average 9 years older age of onset
  - Scored better on Trail Making Part B and Animals list, last visit before death

- Regardless of CVD, subjects had improved cognition and functional status with increasing age

- DLB more frequent in V-bvFTD (8.1%) versus NV-bvFTD (1.5%)
Neuropathological Findings
Torralva and Sposato et al

- No differences in non-CVD neuropathology in two groups, except:
  - PART-AGD was 3 times more frequent in V-bvFTD (29%) than NV-bvFTD (11%)
Conclusions
Torralva and Sposato et al

- Severe primary FTLD neurodegeneration as cause of worse cognition at younger ages
- V-bvFTD: Slower neurodegeneration; more time to develop vascular risk factors/CVD
- Coexisting CVD should not prevent the diagnosis of bvFTD
Example 2

Background: While episodic memory loss is often first AD symptom, some subjects first experience impairment in other domains such as visuospatial, executive function, or language.

Study aim: Examine presentation age and first symptoms among subjects diagnosed with AD

Sample: 7,815 with probable/possible AD dementia at Initial Visit
Research Question 1
Barnes et al

Compared to older ages, do those at younger ages more often experience non-memory symptoms first?

- Memory as first symptoms: 74% among <60 year olds, 92% among ≥70 year olds
- For 10 year decrease in age, 1.7 times more likely to present with non-memory symptom first.
- Odds of judgment/problem solving; language; and visuospatial problems as first symptom increases with younger age.
Research Question 2
Barnes et al

Are behavioral symptoms more common at younger ages?

- Apathy: most common first behavioral symptom
- Odds of depression increased with younger age
- Odds of psychosis/no behavioral symptom increased with older age
Research Question 3
Barnes et al

Do neuropsychological test scores differ based on age of first presentation?

• Outcome: UDS neuropsychological test battery
  – Younger age associated with increased difficulty with MMSE pentagon and Digit Span tests.
  – For the rest of the UDS battery, older age associated with worse performance.
Conclusions
Barnes et al

• Heterogeneity in first symptoms experienced in AD patients
• Non-cognitive and behavioral symptoms are more common among those experiencing first symptoms at younger ages
• Difficulty with MMSE pentagon at younger ages consistent with previous findings, visual presentation of AD
Example 3

Background, Aim, and Sample
Masters et al

**Background:** Few studies have examined the development of behavioral and functional symptoms before AD dementia onset.

**Study aim:** Characterize time course of noncognitive symptoms preceding AD dementia, as captured on FAQ, GDS, NPI-Q.

**Sample:** Subjects with global CDR=0 at Initial Visit

- n = 1,218 developed CDR>0 at follow-up
- n = 1,198 subjects maintained CDR=0 throughout follow-up
  - Frequency matched by APOE e4, age, education, and length of follow-up
Methods
Barnes et al

- Survival analyses: Kaplan-Meier survival curves and Cox proportional hazards models

- Compared time to development of noncognitive symptoms among those who develop CDR>0 versus those who maintain CDR=0

- Outcome: time from initial assessment to first visit when a noncognitive symptom was endorsed on FAQ, GDS, NPI-Q

- Controlled for age, sex, education, race, APOE e4
NPI-Q Symptoms
Barnes et al

• Order of symptom occurrence similar for those maintaining CDR=0 and those later developing CDR>0
  – Night behaviors, irritability, depression occurred sooner than other symptoms

• Time to develop each NPI-Q symptom was generally sooner for the group later developing CDR>0.

• Both groups rarely had elation, euphoria, hallucinations
FAQ Symptoms

Barnes et al

• Time to develop most FAQ symptoms significantly different between the two groups

• FAQ symptoms:
  – Not often present among those maintaining CDR=0
  – More frequent among those developing CDR>0

• First developed difficulties with paying bills, current events, preparing meals, traveling, and remembering appointments.
GDS Symptoms
Barnes et al

- Time to develop most of the GDS symptoms significantly different between the two groups
- Two groups experienced same types of GDS symptoms:
  - Do not feel full of energy
  - Dropped activities and interests
  - Prefer to stay at home
- Rest of GDS symptoms rarely reported in either group
Conclusions

Barnes et al

• Found many noncognitive symptoms during preclinical disease, among those who later develop CDR>0.

• Future work needed to determine if specific noncognitive symptoms exhibited in preclinical disease are associated with distinct AD subtypes.
Conclusions

• Provided examples of recently published papers using NACC database
• A large variety of new studies can be done with NACC database as more data come available on:
  – Longer follow-up among those who start out with normal cognition
  – Non-AD dementias or mixed dementias
  – New neuropathological criteria in NP v10 form
  – Imaging / MRI
  – UDS 3 data