Recent publications using the NACC Database

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Data requests and publications

Using NACC data

Type	Number of requests by year						
	2009	2010	2011	2012	2013	2014	2015
Data files*	55	85	217	174	204	229	216
Tables*	39	106	133	85	51	48	41

*Includes updating files with most recent data, adding variables, other adjustments, etc.

>450 published manuscripts and abstracts to date

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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)

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Example Genetic Studies

Using NACC data

- Nelson PT et al. **Reassessment of risk genotypes (GRN, TMEM106B, and ABCC9 variants) associated with hippocampal sclerosis of aging pathology.** J Neuropathol Exp Neurol,74:75-84,2015.

- Serrano-Pozo A. et al. **APOEε2 is associated with milder clinical and pathological Alzheimer disease.** Ann Neurol. 2015 Jun;77(6):917-29.

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Examples studies looking beyond AD

Using NACC data

- Crary JF et al. **Primary age-related tauopathy (PART): a common pathology associated with human aging.** Acta Neuropathol, 128:755-766, 2014.

- Deutsch MB et al. **Interactions between traumatic brain injury and frontotemporal degeneration.** Dement Geriatr Cogn Disord. 2015;39(3-4):143-53.

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

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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.

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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

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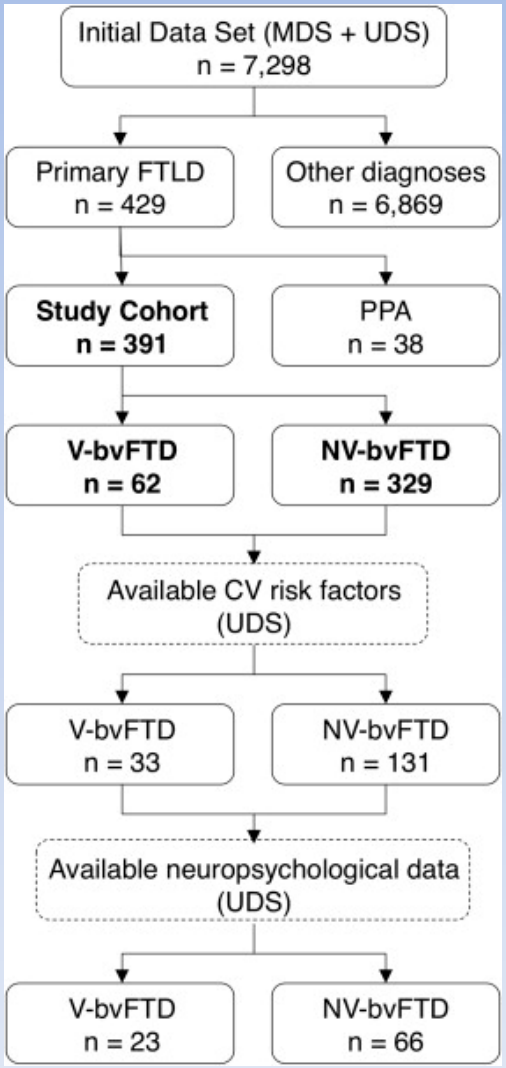
Study Definitions

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

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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)

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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%)

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Neuropathological Findings

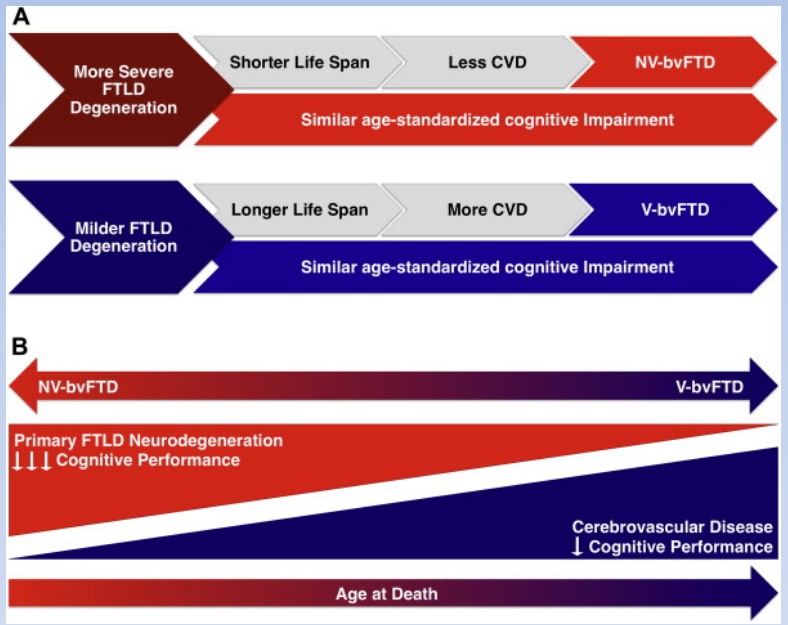
Torralva and Sposato et al

- 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



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Example 2

Barnes J, Dickerson BC, Frost C, Jiskoot LC, Wolk D, van der Flier WM. **Alzheimer's disease first symptoms are age dependent: Evidence from the NACC data set.** Alzheimer's & Dementia, available online 24 April 2015.

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Aims and Sample

Barnes et al

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

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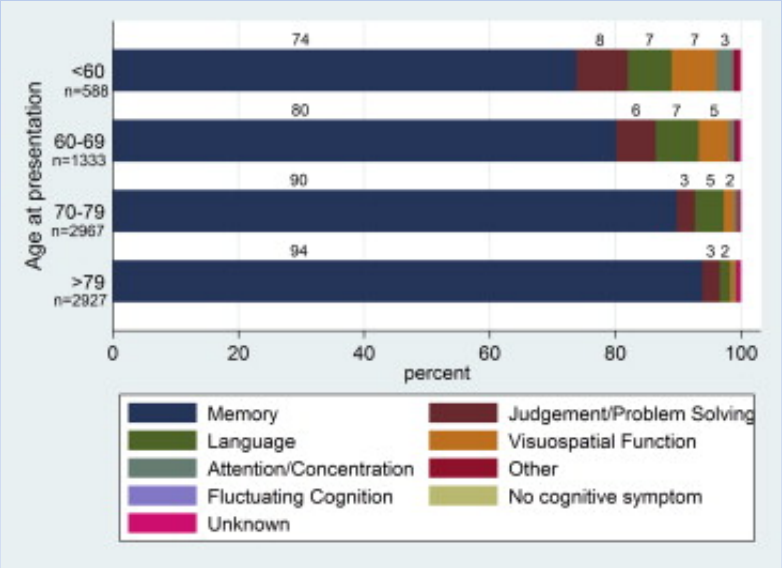
Research Question 1

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.



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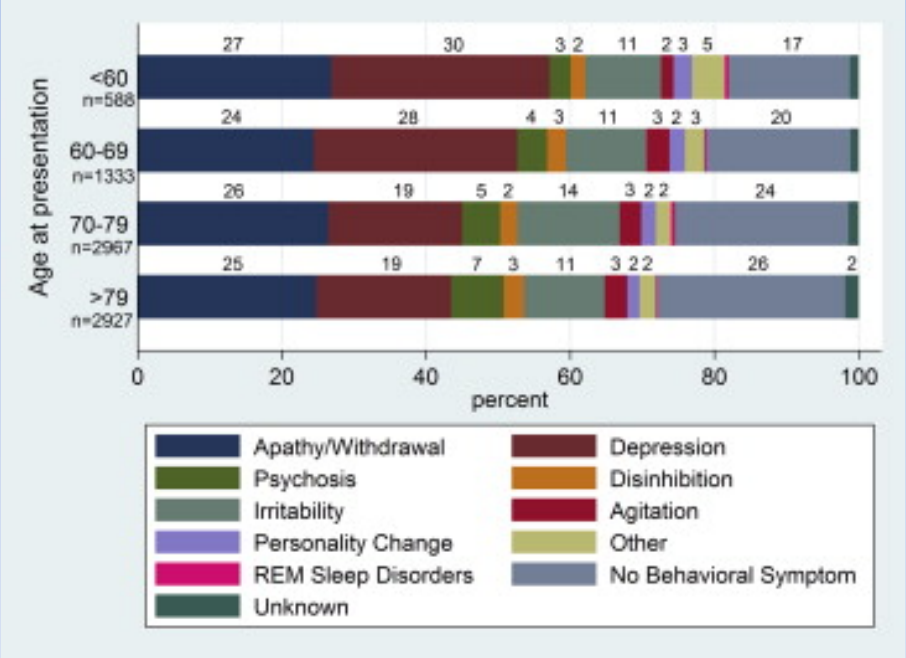
Research Question 2

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



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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.

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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

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Example 3

Masters MC, Morris JC, Roe CM. **“Noncognitive” symptoms of early Alzheimer’s Disease: A longitudinal analysis.** Neurology 2015, 84(6):617-22.

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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

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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

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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.

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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

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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.

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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

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