National Alzheimer’s Coordinating Center

Standardized data collection and collaborative research
August 24, 2007  Austin, Texas

NACC is supported by The National Institute on Aging (U01 AG16976)

and is located at the University of Washington’s School of Public Health and Community Medicine
Enhancing Research Collaboration Through a Common Database for NIA Alzheimer's Disease Centers

What's New

- NIA Sponsored Research Opportunity Click here
- Instructions for preparing annual ADC Progress Reports for NIA Click here
- NIH Policy on Enhancing Public Access to Archived Publications Resulting from NIH-Funded Research

The National Alzheimer's Coordinating Center (NACC) was established by the National Institute on Aging (U01 AG016976) in 1999 to facilitate collaborative research among the 29 NIA-funded Alzheimer's Disease Centers (ADCs) nationwide. NACC developed and maintains a large relational database of standardized clinical and neuropathological research data collected from each ADC, and this database provides a valuable resource for both exploratory and explanatory Alzheimer's disease research.
Milestones in the NIA ADC data collection program

- **1984**: First ADCs funded
- **1984-1997**: Data discussions among ADCs leading to minimum data set
- **1999**: NACC Begins!!
- **1997**: NACC MDS and NP data
- **2002**: Clinical Task Force
- **2005**: NACC UDS
The NACC Database Structure

UDS Data

Minimum Data

Neuropath Data

Centers Data

Collaborative Data

Other AD Data
Database features

• Seamless integration of data sets
• Website design improvements
• Data Input/Output enhancements
• Working with the ADC personnel to provide numbers, projects and productivity
Minimum Data Set
Evolution >> Revolution

• ~ 60 data elements to characterize subjects enrolled at ADCs
  – Cross-sectional not longitudinal
• Gateway for research:
  – Additional detailed data available only at specific request and negotiation with ADC
• Standardized data **reporting**, not **collection**
  – Data mapping by data managers
• Clinical leaders and Directors improve data quality
Neuropathology data expansion 2001

- Neuropathologists determine and define data elements—Key to success
- NACC implements database
  - Linked to MDS
- Routine and continuous data collection
  - Retrospective data completed and submitted by neuropathologists
- Neuropathological – clinical studies
Uniform Data Set (UDS)

- Clinical Task Force formed by NIA 2002 (John Morris, chair)
  - Described clinical evaluation
  - “Informant” participation required
  - Standardized data collection (not just standard reporting per MDS);
- Longitudinal data collection
- NACC relational database and web interface input and output
- Potential future expansion for specific disease subtypes
Mission
To develop an expanded, standardized dataset on ADC subjects to improve clinical assessment and diagnosis, provide data in support of current projects, and stimulate research.

Uniform Data Set collection will:
• serve as a unique research resource for:
  – natural history studies (MCI transition; rare disorders)
  – comorbidities
  – variability across ethnic groups, geographic region
• provide phenotypic descriptions to identify multiplex families (Genetics Initiative) and resource for GWAS
Members

Helena Chui (USC)
Jeffrey Cummings (UCLA)
Charles DeCarli (UCD)
Steven Ferris (NYU)
Norman Foster (U Michigan)
Douglas Galasko (UCSD)
Neill Graff-Radford (Mayo Clinic)
John Morris (Wash U) - Chair
Elaine Peskind (U of Washington)
Sandra Weintraub (Northwestern)
*Dan Mungas (UCDavis)
*Joe Hesse (UCSF)

Affiliates

NACC
Walter Kukull

ADC Genetics Initiative
Richard Mayeux

NIA
Creighton Phelps
Neil Buckholtz
Nina Silverberg
Marcelle Morrison-Bogorad
UDS Forms: types of data

• Forms for Initial Visit Packet
  – “A” forms: Demographics and history
  – “B” forms: Clinical evaluation
  – “C” form: Neuropsychological battery
  – “D” form: Clinical Diagnoses
  – “E” form: Lab specimen and imaging taken

• The Guidebook
  – Operational definitions and Criteria
  – References to original articles
  – Appendix: Cognitive test procedures; other diagnostic criteria
UDS Forms (2)

- Paper and electronic forms
  - Available through website
- Data Submission System
  - Individual subject or “file” entry system direct through the web; encrypted
  - Includes multi-level error checks
UDS Forms (3)

• Standardized data collection
  – Uniform clinical assessments
  – Longitudinal follow-up
• “The Task Force recommends that the UDS be administered as a standard protocol…”
• Linked to MDS and NP data
  – MDS collection phased out
## UDS Data Submission System

**Sample Center**

Select the UDS ID to Edit:

- JLH001
- JLH002
- JLH003
- 1
- 2

[Edit]
Database Design Features

- Oracle back end
- SAS front end
- Automated data element dictionary
- Form version control
- Automated error checks
- And lots of other cool and clever things
Everything’s easy, once you understand the mechanism...
The NACC Database
04/2007 “Data Freeze”

<table>
<thead>
<tr>
<th></th>
<th><strong>UDS</strong></th>
<th><strong>MDS</strong></th>
<th><strong>NP</strong></th>
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<td></td>
<td>- Initial</td>
<td>8,899</td>
<td>9,626</td>
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<td>- Follow - Up</td>
<td>821</td>
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<td>- UDS / MDS Subjects</td>
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## Demographics

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<th>Race</th>
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<td>7,413</td>
<td>62,231</td>
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<td>African American</td>
<td>1,113</td>
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<td>Asian/Pacific Islander</td>
<td>115</td>
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<table>
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<td>Male</td>
<td>3,794</td>
<td>30,374</td>
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<tr>
<td>Female</td>
<td>5,105</td>
<td>45,171</td>
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</table>
## Cognitive Status

<table>
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<tr>
<th>Clinical Dx group</th>
<th>UDS</th>
<th>MDS</th>
<th>NP</th>
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<tr>
<td>Normal</td>
<td>3,437</td>
<td>12,614</td>
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<tr>
<td>MCI</td>
<td>1,779</td>
<td>8,379*</td>
<td>485</td>
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<tr>
<td>Demented</td>
<td>3,388</td>
<td>47,631</td>
<td>7,851</td>
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<tr>
<td>Other</td>
<td>295</td>
<td>6,921</td>
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</table>

* “Questionable Dementia” which includes MCI and other categories.
<table>
<thead>
<tr>
<th>Clinical Diagnosis</th>
<th>UDS</th>
<th>MDS</th>
<th>NP</th>
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</thead>
<tbody>
<tr>
<td>Alzheimer’s Disease</td>
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<td>- Probable</td>
<td>2,420</td>
<td>30,268</td>
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<td>- Possible</td>
<td>432</td>
<td>8,298</td>
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<td>DLB</td>
<td>272</td>
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<td>Vascular Dementia</td>
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<td>2,230</td>
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<td>FTLD (FTD or PPA)</td>
<td>337</td>
<td>1,879</td>
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</table>
# MCI Categories

*(after Petersen et al)*

<table>
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<th>Subgroup</th>
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<td><strong>Amnestic</strong></td>
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<tr>
<td>- Single Domain</td>
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<td>- Multiple Domain</td>
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<td><strong>Non-Amnestic</strong></td>
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<tr>
<td>- Single Domain</td>
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<tr>
<td>- Multiple Domain</td>
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<tr>
<td><strong>Impaired</strong></td>
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<tr>
<td>- Not MCI</td>
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</tbody>
</table>
Research readiness

• Data Quality assurance and control
  – Expansion and improvement of capabilities
  – Constant scrutiny by control freaks
• Research
  – The Topic System
  – NACC-funded and other Projects
    • Large and small NACC projects
  – Statistical support
  – Methodological development
Click on “Investigators/researchers”
Then on “UDS research ideas”

Enhancing Research Collaboration Through a Common Database for NIA Alzheimer’s Disease Centers

Staking a Claim to a UDS Research Idea

Research with UDS data is encouraged. The process described below is intended to:

- Promote high-quality research with UDS data
- Avoid wasted effort if a potential project’s data needs cannot be met adequately with UDS data
- Coordinate the efforts of multiple users, so that two or more investigators do not unknowingly pursue projects with substantially overlapping aims
The process...

- **View** the topic list or think of a topic on your own
- **Talk to NACC** about data/feasibility;
- **Submit** a ~2 pp. description for the Publications Committee to officially “claim” topic;
- After Pubs “claiming” approval, a NACC liason will be named to help with analytic issues;
- **NACC will create a data file for you**;
- **Do** analysis; write paper [NACC helps, prn];
- **Submit** final draft paper to Pubs Comm.
## THEME 1: Description of UDS clinical population and subgroups of interest

<table>
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<th>WORKING TITLE</th>
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<td>Establish Norms and Identify new Groups</td>
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<td>Neuropsychological Test Scores</td>
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<tr>
<td>Description of UDS MCI, pre-MCI, and Control Subjects</td>
<td>Available</td>
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<tr>
<td>Establish Norms and Compare with Other Published Norms</td>
<td>Available</td>
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<tr>
<td>Age of onset</td>
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<tr>
<td>Hachinski Scale scores</td>
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<tr>
<td>Variations across Centers</td>
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<tr>
<td>Compare UDS to other AD Data Sets</td>
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<td>Rapidly Progressive AD (Part 1)</td>
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<td>Factors associated with early and late evaluation for dementia</td>
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<td>Sex differences in early symptoms of dementia</td>
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<tr>
<td></td>
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<td>301</td>
<td>Diagnostic Accuracy</td>
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<td>302</td>
<td>Correlation between clinical and neuropath diagnosis</td>
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<td>311</td>
<td>Improving neuropath diagnosis</td>
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<tr>
<td>312</td>
<td>Detecting dementia: CDR vs Neuropsych Test Battery</td>
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<td>321</td>
<td>Consensus versus Single clinician diagnosis</td>
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<td>322</td>
<td>Self-reported History versus Informant Report</td>
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<tr>
<td>331</td>
<td>Reliability of Diagnosis</td>
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<td>341</td>
<td>Stability of dementia diagnosis</td>
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<td>342</td>
<td>Stability of MCI diagnosis</td>
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<td>351</td>
<td>Initial presentation of cognitive dysfunction</td>
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<tr>
<td>361</td>
<td>Analysis of FAQ data</td>
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</tbody>
</table>
Facilitating GWAS: Emergent Scientific Efforts

- Neuropathology specimens
- Case and Control specimens
- Inclusion of prospective studies
- Large sets for gene discovery and replication (>20,000 subjects?!) 
- Rapidly changing technology increases the likelihood of finding new genes
GAB2 Alleles Modify Alzheimer’s Risk in APOE ε4 Carriers

Eric M. Reiman, 1,2,3,17,18* Jennifer A. Webster, 1,17,18 Amanda J. Myers, 4,5,18 John Hardy, 5,6 Travis Dunckley, 1,17 Victoria L. Zismann, 1,17 Keta D. Joshipura, 1,17 John V. Pearson, 1,17 Diane Hu-Lince, 1,17 Matthew J. Huentelman, 1,17 David W. Craig, 1,17 Keith D. Coon, 1,7,17 Winnie S. Liang, 1,17 RiLee H. Herbert, 1,17 Thomas Beach, 8,17 Kristen C. Rohrer, 5 Alice S. Zhao, 5 Doris Leung, 5 Leslie Bryden, 5 Lauren Marlowe, 5 Mona Kaleem, 5 Diego Mastroeni, 8 Andrew Grover, 8,17 Christopher B. Heward, 9 Rivka Ravid, 10 Joseph Rogers, 8,17 Michael L. Hutton, 11 Stacey Melquist, 11 Ron C. Petersen, 12 Gene E. Alexander, 13,17 Richard J. Caselli, 14,17 Walter Kukull, 16 Andreas Papassotiropoulos, 1,15 and Dietrich A. Stephan 1,2,17,*
Faculty and staff

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  – Mary Lovely
  – Maggie Connor

• Methods Group
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  – Andrew Zhou
  – Nate Mercaldo
  – Bill Lee
  – Yueh-Yun Chi
  – Erin Ramos (emeritus)

• Data Group
  – Duane Beekly (chair)
  – Mary Jacka
  – Joylee Wu
  – Janene Hubbard
  – Woody Dietrich
  – Bill Lee
  – Erin Ramos

• Q/A-Q/C Comm
  – Tom Koepsell (Chair)
  – And the usual suspects