



Alzheimer's Biomarkers Consortium of Down Syndrome (ABC-DS)

AN OVERVIEW

(with material provided by Ben Handen & Nicole Schupf)

<https://www.nia.nih.gov/research/abc-ds>



Alzheimer's Biomarkers Consortium of Down Syndrome (ABC-DS)

- Two multi-site studies supported by NIA and NICHD
 - Neurodegeneration in Aging Down Syndrome (NiAD)
 - Alzheimer's Disease in Down Syndrome (ADDS)
- Common goals:
 - Measures of cognitive decline
 - Various biomarkers for transition to MCI & dementia
 - Explore link between $A\beta$ & neurodegeneration & dementia
 - Relationships between biomarkers and AD pathogenesis
 - Share data publically with the scientific community

NiAD

- University of Pittsburgh (Benjamin Handen, PhD, William Klunk, MD, PhD)
- University of Wisconsin, Madison (Brad Christian, PhD)
- University of Cambridge (Shahid Zaman, MD)
- Barrow Neurological Institute (Marwan Sabbagh, MD)

ADDS

- Columbia University (Coordinating Center) (Nicole Schupf)
- University of California-Irvine (Ira Lott)
- Harvard/MGH (Flo Lai, Diana Rosas)
- New York State Institute for Basic Research in Developmental Disabilities (Sharon Krinsky-McHale)

Protocol overview

- Both program entail longitudinal visits over 36-48 months (different design for each study)
- Cognitive testing (wide range of vehicles and issues of utility of testing methods)
- Informant data
- Imaging – structural, amyloid PET (PiB), Tau PET (AV1451)
- Blood and CSF banking (via NCRAD)

Additional aspects

- Proteomics
- Metabolomics
- Image repository
- Central data sharing

Subjects

NiAD

- 180 Adults with Down Syndrome (ages 25+)
- 40 Sibling controls
- To date: 69 DS and 9 controls have baseline data collected so far

ADDS

- 225-300 with DS
- Age 40-85
- Premorbid IQ > 30
- No Dementia/no MCI 40%
- No Dementia with MCI, 35%
- Prevalent Dementia, 25%

Age 40-44: N=15 Age 45-49: N=60
Age 50-59: N=90 **Age 60-69: N=90**
Age 70-79: N=30 **Age 80+: N=15**

Neuropathology

- Could be an important contributor to these studies but...
- Not formally budgeted as part of the overall projects
- BUT nearly all the clinical sites have ADC/ADRC centers!
- How can we help? What is needed? What models would work?

2017 Core Leader Survey

Do you currently include Down syndrome (DS) specimens in your brain bank? If so, roughly how many DS brains are in your brain bank?

- 14 of 29 centers have DS specimens.
- 13 of these centers reported very few banked DS specimens (few, few, 2, 3 over 30 years, 3-4 over 10 years, 3-5, <5, 5-10, ~10, <10, 15, ~28 since 1990).

2017 Core Leader Survey

Have you performed autopsies on persons with Down syndrome in the past 3 years? If so, approximately how many?

- 15 of 29 centers have not performed a Down syndrome autopsy in the past 3 years.
- 11 centers performed one or two DS autopsies.
- The remaining responses were 3, 1/year, and <5.

2017 Core Leader Survey

Do you have capacity to perform autopsies using your standard protocol for research studies at your institution involving DS participants? If so, approximately how many per year?

- Only 4 centers responded negatively (no; not a focus of this ADC; no effort to collect these; no unless funding available as stretched thin already).
- Other 25 centers said “yes” with varying qualifiers.
 - Cost?
 - Low volume
 - Two centers explicitly are willing to have larger engagement to support DS research program

2017 Core Leader Survey

Would you be interested in participating in the implementation of a specialized brain banking protocol (currently under development) designed for postmortem correlation to in vivo imaging studies in participants with DS?

- 15 respondents stated “yes.”
- 10 said maybe depending on
 - specific details, aims, scope of the protocol
 - availability of funding to support these autopsies.
- 2 centers said only if collaboration (vs. just collecting tissue)
- 4 were less clearly interested

2017 Core Leader Survey

If you prefer not to implement the specialized protocol, would you be willing to send DS brains to a central facility via a courier service (at no cost to you) in order to have the specialized protocol performed?

- 13 of 19 responses were Yes
- 2 Yes...if they are provided financial remuneration
- 2 already doing this
- 1 Maybe
- 1 No (technical service and a waste of time).

Interpretation

- At some ABC-DS sites there are opportunities for local collaboration to be explored
- Neuropathology Cores want to be seen as valued collaborators, not as tissue procurers
- Financial pressures on Cores are significant shapers of behavior
- Desire to be able to include DS cases as part of local resource as well as contribute to larger program



What should we do?