DIAN
Dominantly Inherited Alzheimer Network

Data and Tissue Available for Sharing

Access to DIAN data is dependent on review and approval by the DIAN Steering Committee and agreement to compliance with DIAN data sharing policies.

DIAN Clinical Core

General Information about the clinical assessment:

Participants are evaluated in a uniform manner at entry and longitudinally thereafter with instruments to include: the clinical and cognitive batteries that comprise the Uniform Data Set (UDS) (Morris et al., 2006) and additional DIAN-specific testing listed below. Each site has designated a study coordinator who manages the day-to-day conduct of the study, ensures accurate administration of all instruments at the site, and supervises accurate data collection. Sites are responsible for identifying trained clinicians and raters to complete assessments such as the Clinical Dementia Rating (CDR), and the Neuropsychiatric Inventory (NPI), etc. It is the site's responsibility to train interviewers and all other personnel who assess the participant and caregiver. Typically the CDR rater is a trained MD Clinician, but a RN or a PhD can also train and become certified for CDR rating. All clinicians must be blinded to the genetic status of DIAN participants. Clinicians must successfully complete the training modules in order to administer the DIAN assessments.

The clinical assessment, psychometric testing, MRI, PET PIB, FDG PET, and blood and CSF collection may be completed over a few days or in several visits spread over no more than 12 weeks. The exact order of measures is not dictated by the protocol, but it is highly recommended that the clinical assessment be performed first. The rationale is that the clinical assessment could reveal that the participant is unable to complete all of the measures within the protocol prescribed 12-week window. The frequency of the in-person follow-up interval is determined by the current age of the participant (P) in relation to the parent's age at onset (AAO). If cognitive decline is detected at an in-person visit, the in-person visit frequency becomes annual, regardless of the interval between the participant's age and the parental age at onset. If the participant is cognitively normal, the affected parent's AAO is used as the index for the frequency of assessments as stated on the worksheet.

Available Clinical Data:

- Estimated Parental Age at Onset
- Participant Demographics
- Informant Demographics
- Exercise Questionnaire
- Hollingshead Index of Social Position (including participant level of education)
- Clinical Dementia Rating (CDR)
- Geriatric Depression Scale (GDS)
- Functional Assessment Questionnaire (FAQ)
- Neuropsychiatric Inventory-Q (NPI-Q)
- United Parkinson's Disease Rating Scale (UPDRS)-Motor
- Hachinski Ischemic Score/Cerebrovascular Risk Factors
- Clinician Judgment of Symptoms (UDS Form B9)
- Form D1: Clinician Diagnosis – Cognitive Status and Dementia
- Vital Signs
- Neurologic Exam Findings
- Physical Exam Findings

- Clinician Judgment of Symptoms

Psychometrics include:

- CDR Sum of Boxes
- Category fluency for animals and vegetables (Goodglass 1983 a,b)
- Trailmaking A and B (Armitage, 1946)
- Wechsler Adult Intelligence Scale-Revised (Weschler, 1981)
- Word list recall (immediate and delayed) designed specifically for DIAN
- Letter Fluency for F, A, S
- International Personality Item Pool (IPIP)

DIAN Neuropathology Core

Tissue:

- Formalin-fixed, paraffin wax-embedded (FFPE) histological sections of brain only (call for availability)
- Frozen brain tissue (call for available brain areas)

Data:

- Neuropathologic diagnosis: Khatchaturian, CERAD, NIA-Reagan, and NIA-AA neuropathologic diagnostic criteria
- Neuropathologic assessments: Thal beta-amyloid stage; Braak neurofibrillary tangle stage; CERAD neuritic plaque stage; Braak Lewy body stage

DIAN Genetics Core

Tissue:

- **DNA/Cell Lines** – Upon approval from DIAN Steering Committee, DNA/cell lines may be obtained from the National Cell Repository for Alzheimer's Disease (NCRAD). Researchers requesting DNA samples will have two request options: A) pre-made plates that will have a reduced cost structure and are sent out rapidly; or B) customized set of samples that have a higher cost structure and will have a delay in shipment time due to preparation. The DNA for both options is cell line derived DNA and available in 25µg aliquots. There is a fee to obtain tissue from NCRAD.
- **Dermal Fibroblasts** – Dermal fibroblasts have been, and continue to be, collected from a subset of DIAN participants (both mutation carriers and noncarriers). For an up-to-date list of the family mutations represented among banked fibroblast lines (not necessarily mutation carriers), please contact Dr. Alison Goate (goatea@psychiatry.wustl.edu). There is a fee to have fibroblast lines expanded for sharing.
- **Induced Pluripotent Stem Cells (iPSCs)** – Dr. Celeste Karch, with the DIAN Genetics Core, has reprogrammed select fibroblast lines into iPSCs. These iPSC lines are available for sharing through the standard DIAN resource request mechanism, with the stipulation that Dr. Karch be included as a collaborator on proposed research. For an up-to-date list of iPSC lines from DIAN participants, please contact Dr. Goate (goatea@psychiatry.wustl.edu) or Dr. Karch (karchc@psychiatry.wustl.edu).

Data:

- APOE Genotype
- Mutation Status (request must permit adequate de-identification, e.g. more than a few participants)

DIAN Biomarker Core

Tissue:

- Fasted cerebrospinal fluid (CSF)
- Fasted plasma
- Fasted serum

Cross-sectional Data:

- CSF $A\beta_{40}$ (INNOTEST ELISA)
- CSF $A\beta_{1\text{-}42}$ (INNOTEST ELISA)
- CSF $A\beta_{1\text{-}42}$, total tau, ptau181 (AlzBio3)
- Plasma $A\beta_{1\text{-}40}$, $A\beta_{1\text{-}42}$, $A\beta_{x\text{-}40}$, $A\beta_{x\text{-}42}$ AlzBio3 for plasma)
- Assay date
- Kit lot number
- Plate number

Future: CSF VILIP-1 and CSF YKL-40.

DIAN Imaging Core
Available on the Central Neuroimaging Data Archive (CNDA)
And from the Database Management Statistics Core (DMSC)
Data Formats

- **PiB**
  - Full or Partial Scan Download - *CNDA*
  - Regional Distribution Volume Ratios based on Manual Template and FreeSurfer derived Regions of Interest- *DMSC*
- **FDG**
  - Full or Partial Scan Download – *CNDA*
  - Regional Averages of activity to assess relative metabolism based on Manual Template and FreeSurfer derived Regions of Interest **-** *DMSC*
- **MRI**
  - Full or Partial Scan Download for both anatomical and functional MRI – *CNDA*
    - Series Available
    - MPRAGE (Volumetric)
    - Rs-fcMRI (resting state)
    - DTI (Diffusion tensor imaging)
    - ASL (Blood flow)
    - T2* or SWI (for assessment of microbleeds)
    - FLAIR
    - T2
    - Field map
  - Regional volumetric/subcortical volumetric and cortical thickness using FreeSurfer Version 5.2 - *DMSC*

Additional Image Analyses: Investigators can submit proposals for additional data analysis to the DIAN Executive Imaging Committee and DIAN Steering Committee. Once the proposal is approved, investigators may be given access to the DIAN Global Project in the Central Neuroimaging Data Archive (CNDA, primary data repository for DIAN). Requested modalities will be available in the CNDA for specified approved analysis.