Overview & Update

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www.txalzresearch.org

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Fort Worth, Texas
How Does Alzheimer’s Disease Impact Texans?
Public Health Impact of Alzheimer’s Disease
Texas - 2010

Occurrence of AD in Texas

- Prevalence: 340,000 individuals with AD
- Incidence: >30,000 individuals with AD
- Annual Mortality: >4,200 deaths due to AD
- % cognitive impaired in NH (2005): 77%
- US rank in total number of cases: 3rd
- US rank in total number of deaths: 2nd

SOURCE: Alzheimer’s Association Facts and Figures, 2010

Note: There are no formal studies published to date on the occurrence and cost of Alzheimer's disease in Texas. These estimates are extrapolated from studies of the total US population.
Public Health Impact of Alzheimer’s Disease
Texas - 2010

Annual costs to Texas
- Total economic burden $14 billion
- Costs to businesses (coverage, loss of productivity) $7 billion

Caregiver Challenges in Texas
- Number of caregivers >850,000
- Annual hours of unpaid care >950 million
- Annual value of unpaid care $11.2 billion

SOURCE: Alzheimer’s Association Facts and Figures, 2010

Note: There are no formal studies published to date on the occurrence and cost of Alzheimer’s disease in Texas. These estimates are extrapolated from studies of the total US population.
What is the Texas Alzheimer’s Research Consortium?
Current TARC Sites

Established in 1999 by 76th Texas Legislature

2007 Population*
Overall: 23,523,700
60+ YRS: 3,354,600

* From US Census Bureau Projections
Organizational Chart

Texas Council on Alzheimer’s Disease and Related Disorders

External Advisory Committee
(Drs. Petersen, Chair; Yaffe; Galasko; Schellenberg)

Steering Committee
(Drs. Doody, O’Bryant, Fairchild, Adams, Royall)

Council Chair
(Debbie Hanna)

Scientific Subcommittees
- Genetics
- Neuropsychology
- Biomarkers
- Tissue/Data Allocation
- Publications

Scientific Coordinator
(Dr. Robert Barber)

Project Coordinator
(Jim Hinds)

Consortium Public Communications

General Counsel
(James Crowson)

Data Management
(Dr. Joan Reisch)
Texas Alzheimer’s Research Consortium

**Timeline: September 2005 – August 2011**

<table>
<thead>
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<th>Biennium</th>
<th>Sep 05 – Aug 07</th>
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<td>Hispanic and MCI</td>
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<td></td>
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<td>200 new Controls</td>
<td>400 new Hispanic</td>
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<td>Controls; 80 new</td>
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<td>Hispanic AD patients;</td>
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<tr>
<td></td>
<td></td>
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<td>125 MCI patients</td>
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Overview of Current Research

Study Design

- Construct an integrated centralized research database of clinical, neuropsychological, and biological data derived from baseline and annual follow-up examination
Overview of Current Research

Study Design

- Establish a longitudinal cohort of well-characterized individuals with AD, Mild Cognitive Impairment (MCI) and cognitively normal controls

- Enroll significant numbers of Mexican Americans to study how the disease process impacts this underserved ethnic group
Overview of Current Research

Research Objectives:

- Identify potential genetic factors associated with earlier age at onset among patients with AD

- Examine the role of biological and clinical markers for inflammation, cardiovascular disease, cardiovascular risk factors, hyperinsulinemia
Current Research Methods

TARC Research Participants

Recruitment – Completed
- 500 Individuals with Probable AD
- 300 Cognitively normal individuals

Recruitment – Ongoing
- Annual follow up of initial 800 subjects (incl. attrition replacement)
- 125 Individuals with Mild Cognitive Impairment (25 Hispanic)
- 80 Hispanic patients with AD
- 300 Hispanic normal controls
Current Research Methods

TARC Examination procedures

• IRB approved informed consent obtained from all participants
• Standardized examination procedures across all five sites
• Comprehensive clinical, neurological, and neuropsychological evaluation
• Blood drawn for genetic, biomarker, and laboratory analysis and to biobank for future studies
• Complete annual follow-up examination
• Blood collected at annual follow-up examinations for biobank
What Are Some Current and Emerging Themes in Alzheimer’s Disease Research?
Themes in Alzheimer’s Disease Research

- Search for novel genes and biomarkers associated with Alzheimer’s disease

- Identification of modifiable risk factors for Alzheimer’s disease that may lead to preventative strategies

- Search for “at risk” groups who
  - Mild Cognitive Impairment (MCI)
  - At increased risk for developing MCI and AD

- How is Alzheimer’s disease differentially manifest among diverse ethnic/racial groups?

- Are there subgroups of patients with Alzheimer’s disease that may
  - Express Alzheimer’s disease in a different manner
  - Respond better or worse to particular therapeutics
How is the TARC Working to Advance these Research Themes?
Search for novel genes and biomarkers

- The TARC is collecting large-scale genetic and biomarker information on participants.
- We have a biobank that is updated at each annual evaluation so change in biomarkers can be studied.
- We are planning collaborations with other large-scale studies for combined analysis of pooled data.
- TARC investigators are working to create a blood-test for Alzheimer’s disease.
- TARC investigators have data on novel genetic variations associated with the disease.
Identification of modifiable risk factors that may lead to preventative strategies

- TARC investigators are studying diabetes, hyperinsulinemia, hypertension, among others

- We are investigating inflammation as a potential biological pathway for cardiovascular-induced cognitive decline/dysfunction

- Studying how these factors change over time

- We are now investigating how these factors may be differentially related to disease expression between non-Hispanics and Mexican Americans
Search for “at risk” groups

- The identification of Mild Cognitive Impairment as a prodrome for Alzheimer’s disease was a major advancement to the field
  - TARC investigators have included MCI in the cohort to be followed over time
  - We are searching for novel genetic, biomarker, and clinical factors associated with progression of MCI to AD

- We are following non-AD controls over time to identify factors associated with the development of MCI and AD
Differential risk for Alzheimer’s disease among various ethnic/racial groups

- The TARC recently added a 5th site, the University of Texas Health Sciences Center at San Antonio (UTHSC-SA) specifically for recruitment of Mexican Americans.
  - UTHSC-SA is recruiting from a previously established longitudinal study, the San Antonio Heart Study.
  - These Mexican American elders with and without MCI and AD will be followed over time to determine ethnic-specific risk factors for disease onset and progression.

- TARC investigators and working towards collaborations with other ongoing Texas-based studies enrolling ethnic minorities.
Identification of subgroups of patients with different disease mechanisms

- TARC investigators are searching for subgroups of Alzheimer’s patients that are based on genetic, biomarker, and clinical information.

- We are establishing a Translational Research Core specifically aimed at translating endophenotypes into targeted therapeutic trials.
What Data Has the TARC Collected?
## Number of Subjects by Diagnosis and Visit Number

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<th>Visit Number</th>
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<tr>
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<tr>
<td>AD</td>
<td>685</td>
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<tr>
<td>Control</td>
<td>421</td>
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<tr>
<td>MCI</td>
<td>53</td>
</tr>
<tr>
<td>Total</td>
<td>1160</td>
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Distribution of participants by primary residence at baseline examination

Areas based on first 3 digits of zip code

Note: 15 non-Texas residents (NM: 10; LA: 2; OK: 3)
Genetics

Affymetrix Genome-Wide 6.0 Array
  Nearly 2 million genetic markers
  906,600 genetic polymorphisms
  946,000 copy number variation probes

Completed
  500 Alzheimer’s disease patients
  300 Cognitively normal individuals
Lipid and Diabetes Profile

- Total cholesterol
- Triglycerides
- HDL
- Cholesterol
- LDL
- VLDL
- Homocysteine
- Hemoglobin A1c
- C-peptide
- Lipoprotein-associated phospholipase A2

Completed on

- 300 Alzheimer’s disease patients
- 300 Cognitively normal individuals
Serum Proteins

Human Multi-Analyte Profile Panel

Measures concentrations of 190 blood proteins, including markers of infectious disease, autoimmunity, cardiovascular risk, hormones and growth factors

Completed on

300 Alzheimer’s disease patients
300 Cognitively normal individuals
Publications

Peer-reviewed Manuscripts
4. O’Bryant SE, Grammas P. A Case for the Creation of a Biomarker-Based Algorithm for the Detection of Alzheimer’s Disease. JTPHA 2008;63(3):14-17

Abstracts
Summary

TARC research focus
- novel genetic and biomarker studies
- longitudinal follow-up of subjects
- inclusion of MCI subjects
- inclusion of Hispanic individuals

Multidisciplinary study
- a robust centralized research database of prospectively collected clinical, genetic, and biological data from subjects with sufficient follow-up to address an unlimited number of research questions now and into the future
This unique longitudinal study could not feasibly be conducted at a single institution due to inherent budget, resource, and recruitment constraints and would not be possible without the vision and support of the Texas legislature.