Alzheimer’s and Dementia Research: An Advanced Discussion

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Theoretical Constructs in Aging/Dementia Research

Alzheimer’s Disease Spectrum

Frontotemporal Lobar Degeneration (FTLD) Spectrum

Lewy Body Disease Spectrum

Alzheimer’s and Dementia Research: An Advanced Discussion

Theoretical Constructs in Normal-MCI-Dementia

Observational/Natural History

Clinical Trials – Symptomatic

Clinical Trials – Disease-Modifying
Normal – MCI – Dementia Continuum

Observational/Natural History Studies

Clinical Trials - Symptomatic
Alzheimer’s and Dementia Research: An Advanced Discussion

Alzheimer’s Disease Spectrum

- Observational/Natural History
- Clinical Trials – Symptomatic
- Clinical Trials – Disease-Modifying

Observational/Natural History Studies

Normal – MCI - AD
Observational/Natural History Studies

https://www.nia.nih.gov/alzheimers/alzheimers-disease-research-centers
### NIA-Funded ADCs

**Primary Aims:**

- Characterize individuals along the normal-MCI-dementia spectrum longitudinally (annually)
- Advance research in clinical, neuropsychological, biofluid, genetic, neuroimaging and neuropathological aspects of neurodegenerative diseases
- Contact: Mayo ADRC 507-284-1324

https://www.nia.nih.gov/alzheimers/alzheimers-disease-research-centers

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### Alzheimer's Disease Neuroimaging Initiative 3 (ADNI3) Protocol (ADNI3)

**Primary Aims:**

- Characterize individuals along the normal-MCI-AD spectrum longitudinally (annually)
- Advance research in clinical, neuropsychological, biofluid, genetic, neuroimaging
- Contact: Mayo ADRC 507-284-1324

http://adni-info.org/
https://clinicaltrials.gov/show/NCT02854033

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### Atypical AD Study

**Molecular and Structural Imaging in Atypical Alzheimer’s Disease: A Longitudinal Study**

**Primary Aims:**

- Characterize individuals with atypical AD
- Clinical, neuropsych, MRI and PET studies
- Contact: Sarah Boland (Mayo ADRC) 507-293-4707

https://clinicaltrials.gov/show/NCT02740634
Late Onset Alzheimer’s Disease (LOAD) Family Study

Primary Aim:

• Identify additional genes involved in the pathophysiology of late onset (>65) Alzheimer’ disease

Closest Sites: Mayo Clinic Rochester, Chicago

Contact: Mayo ADRC 507-284-1324

MCI-AD Clinical Trials

• Effects of Aerobic Exercise for Treating Alzheimer's Disease (FIT-AD)
  https://clinicaltrials.gov/show/NCT01954550

• Intranasal Glulisine in Amnestic Mild Cognitive Impairment and Probable Mild Alzheimer's Disease
  https://clinicaltrials.gov/show/NCT02503501

• 221AD301 Phase 3 Study of Aducanumab (BIIB037) in Early Alzheimer's Disease (ENGAGE)
  https://clinicaltrials.gov/show/NCT02477800

MCI-AD Clinical Trials (cont.)

• A Study of LY3314814 in Participants With Mild Alzheimer's Disease Dementia (DAYBREAK-ALZ)
  https://clinicaltrials.gov/show/NCT02783573

• The Study of Nasal Insulin in the Fight Against Forgetfulness (SNIFF)
  https://clinicaltrials.gov/show/NCT01767909

• Safety and Efficacy of Suvorexant (MK-4305) for the Treatment of Insomnia in Participants With Alzheimer's Disease (MK-4305-061)
  https://clinicaltrials.gov/show/NCT02750306
Disease-Modifying Therapeutic Trials in Prodromal AD

Prodromal AD Clinical Trial
“A4” Study

http://a4study.org/

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Frontotemporal Lobar Degeneration (FTLD) Spectrum

- Observational/Natural History
- Clinical Trials – Symptomatic
- Clinical Trials – Disease-Modifying
FTLD Spectrum Research

Observational/Natural History

- Advancement of Research and Treatment in Frontotemporal Lobar Degeneration (ARTFL)
  https://clinicaltrials.gov/show/NCT02365922
- Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects (LEFFTDS) Study
  https://clinicaltrials.gov/show/NCT02372773
- FTD Disorders Registry
  https://ftdregistry.org/
- Longitudinal Multi-Modality Imaging in Progressive Apraxia of Speech
  https://clinicaltrials.gov/show/NCT01818661

ARTFL/LEFFTDS Consortium

ARTFL

Advancing Research & Treatment for Frontotemporal Lobar Degeneration

Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects

LEFFTDS

Both

ARTFL only
ARTFL

• Focus: mainly on sporadic FTD +/- ALS, PPA, CBD and PSP

LEFFTDS

• Focus: familial FTD/PPA +/- ALS with mutation in MAPT, PGRN or C9ORF72

ARTFL/LEFFTDS

Clinical, neuropsych, biofluid (blood +/- CSF), genetic and MRI

FTD

Preparing for Disease-Modifying Therapeutic Trials in FTLD

Normal Subtle FTD or PPA Overt FTD or PPA (+/- ALS)

(ARTFL: also CBD and PSP)
Preparing for Disease-Modifying Therapeutic Trials in FTLD

Questions?

Mayo Alzheimer’s Disease Research Center

see our booth for more information

507-284-1324
FTD Disorders Registry

https://ftdregistry.org/

Multimodal Imaging in FTLD

FDG-PET

bvFTD

PPA – nonfluent/agrammatic

PPA – semantic

PPA – logopenic

Multimodal Imaging in FTLD
tau PET (AV-1451)

Salvatore Spina et al. Neurology 2017;88:758-766
FTLD Spectrum Disorders
Clinical Trials

- Low-Dose Lithium for the Treatment of Behavioral Symptoms in Frontotemporal Dementia (Lithium)
- Impact of Emotional Mimicry and Oxytocin on Frontotemporal Dementia (IEMO)
- tDCS Intervention in Primary Progressive Aphasia

many more being developed

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Lewy Body Disease Spectrum

- Observational/Natural History
- Clinical Trials – Symptomatic
- Clinical Trials – Disease-Modifying

Preparing for Disease-Modifying Therapeutic Trials

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Lewy Body Disease Spectrum Disorders
Observational/Natural History Studies

Primary Aims:
• Evaluate individuals:
  • REM sleep behavior disorder (RBD)
  • Mild cognitive impairment (MCI) + RBD
  • Dementia with Lewy bodies (DLB) + RBD

Goals:
• Study the natural history of changes in cognition, behavior, and biomarkers
• Identify genes involved in the pathophysiology of Lewy body disease
• Prepare for disease-modifying therapeutic trials

Lewy Body Disease Spectrum Disorders
Observational/Natural History Studies
ADC Program – DLB Module

Design:
• Identify and follow individuals with RBD, RBD+MCI and RBD+DLB
• Questionnaires, neuropsychologic assessment, blood samples, MRI scans, PET scans, DaTscans, etc.

Funding: National Institute on Aging, Mangurian Foundation, generous donations from families
**Lewy Body Disease Spectrum Disorders**

Multimodal Imaging

Images courtesy:
Cliff Jack, Jr., MD
Kejal Kantarci, MD
Val Lowe, MD

Walker et al. The Lancet 2015

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**Preparing for Disease-Modifying Therapeutic Trials**

Lewy Body Disease

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**Lewy Body Disease Spectrum Disorders**

Clinical Trials

- Study Evaluating Inteipridine (RVT-101) in Subjects With Dementia With Lewy Bodies: The HEADWAY-DLB Study
  
  [https://clinicaltrials.gov/show/NCT02669433](https://clinicaltrials.gov/show/NCT02669433)

- Study Evaluating Nelotanserin for Treatment of Visual Hallucinations in Subjects With Lewy Body Dementia
  
  [https://clinicaltrials.gov/show/NCT02640729](https://clinicaltrials.gov/show/NCT02640729)

- Study Evaluating Nelotanserin for Treatment of REM Sleep Behavior Disorder in Subjects With Dementia (DLB or PDD)
  
  [https://clinicaltrials.gov/show/NCT02708186](https://clinicaltrials.gov/show/NCT02708186)
Lewy Body Disease Spectrum Disorders Research

Questions?

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see our booth for more information

507-284-1324

Ultimate Goal of Disease-Modifying Interventions

- Good Diet
- Exercise
- Etc.

Normal