PET & MRI Imaging in Alzheimer’s Disease

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Positron Emission Tomography (PET) Imaging: How Does It Work?

Annihilation

Detector

GAMMA

Detector

GAMMA
PET Scanner
Types of PET Scans for Alzheimer’s Disease

Amyloid PET
- Florbetapir (Amyvid), Florbetaben (Neuraceq), Flutemetamol (Vizamyl)

Tau PET

Glucose Metabolism PET (Fluorodeoxyglucose, FDG)
Why use PET for Alzheimer’s disease?

Recent research has shown that information provided by amyloid PET scans can lead to changes in medications and/or counseling that are consistent with PET scan findings (presence of absence of Alzheimer’s disease pathology).
What is magnetic resonance imaging?

Magnetic resonance imaging uses a very high magnetic field and computer-generated radio waves to create images of the brain and other organ systems. The high magnetic field causes the protons in your body to align with the magnetic field, and the radio waves perturb the protons, causing them to give off weak signals that are used to make images of the brain or other organs.
MRI Scanner
Some Kinds of Magnetic Resonance Imaging

Structural Magnetic Resonance Imaging

Magnetic Resonance Angiogram

Cerebral Blood Flow

Functional Magnetic Resonance Imaging
MRI and Alzheimer’s Disease

Detection of atrophy associated with Alzheimer’s disease

Rule out structural changes associated with other brain conditions
A proteomic approach to resolve racial differences in Alzheimer’s disease biomarkers

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Alzheimer’s disease

• AD is a neurodegenerative disease characterized by progressive memory loss

• AD is a proteinopathy defined by two neuropathologies in the brain:
  • Amyloid-beta (Aβ) plaques
  • Tau tangles

• Currently no effective therapies (Prince et al, 2015 & Weuve et al, 2014)

• Failure of current treatments has been attributed to initial treatment being administered at too advanced of a stage of AD. (Salloway et al, 2014, Morris et al, 2011, & Sperling et al 2011)
Cerebrospinal fluid can aid in the early detection of AD

Decreases in Aβ and elevations in tau in CSF have high specificity and sensitivity for distinguishing between healthy controls and AD (Henry et al, 2013 & Hansson, 2006)
The impact of race on AD

- Biomarker research is **predominantly** conducted in **Caucasian** populations
- There is an **increased incidence** of AD in African Americans
- The diagnosis of AD in African Americans is often **delayed** and have **reduced rates** of enrollment in clinical trials
- African Americans have **lower levels of tau** compared to Caucasians in CSF (Howell et al., 2017, Morris et al., 2019)
  - Aβ levels are similar between races
  - Tau levels differ between races
Proteins are the “working molecules” of the body. 

Central Dogma

Increased Complexity

DNA
~25,000
genes

mRNA
~100,000
transcripts

Proteins
~1,000,000
Modified Proteins
Proteins are the “working molecules” of the body

Proteins

~1,000,000 Modified Proteins

Discovery Proteomic Biomarker Study in AD CSF

Control
Aβ42 (pg/mL): 554.3
Tau (pg/mL): 41.0
MOCA: 26.7
8 African Americans
(n=20)

AD
Aβ42 (pg/mL): 223.4
Tau (pg/mL): 141.5
MOCA: 13.8
6 African Americans
(n=20)

Mass Spectrometry
Quantification of:
~3,000 proteins

Higginbotham et al., bioRxiv, 2019
Resolving global differences in cerebrospinal fluid proteome using Correlation Network Analysis

Network Analysis is premised on the understanding that proteins respond to biological stimuli as a “system”, changing expression as groups or “modules”.
Defining communities of proteins in CSF using WGCNA resulted in the formation of 21 modules.
The M2 module most strongly correlated to CSF tau levels
Interestingly, this M2 module also exhibited racial specificity
Interestingly, this M2 module also exhibited racial specificity
The M2 module includes **MAPT**, which encodes tau

Top 100 proteins in M2 Blue module
The M2 module was also enriched in proteins involved in biological processes known to be related to tau.
Conclusions & Future Directions

Conclusions
- Communities of proteins in the CSF differ by disease and race.

Provides insight into the underlying biology and pathways that differ by race which allows us to prioritize of race-specific biomarkers

Future Directions
• Replicate this analysis in a larger, racially balanced cohort across brain and CSF
Acknowledgements

PI: Dr. Nicholas Seyfried

Fellow Lab Members:
Dr. Eric Dammer
Dr. Duc Duong
Dr. Lingyan Ping
Dr. Measho Abreha
Dr. Erik Johnson
Dr. Lenora Higginbotham
Dr. Sruti Rayaprolu
Dr. Kathleen Carter
Pritha Bagchi
Luming Yin
Kiaiming Xu
Qi Guo
Sean Kundinger
Sally Zhang
Cheyenne Hurst
Sydney Sunna
Christine Bowen

Me: Erica Modeste

Collaborators:
Dr. Allan Levey (Emory)
Dr. James Lah (Emory)

Funding

Grants from the Accelerating Medicine Partnership AD (U01AG046161-02), the National Institute on Aging (R21AG054206, 5R01AG053960, RF1AG057470, and RF1AG057471), the NINDS Emory Neuroscience Core (P30NS055077), NIA Diversity Supplement (U01AG061357), and the Emory Alzheimer’s Disease Research Center (P50AG025688).
The Importance of Biomarkers & Minority Representation

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Mission: The Global Alzheimer’s Platform (GAP) Foundation is a patient-centric, non-profit organization dedicated to speeding the delivery of innovative therapy to those in need by reducing the time and cost of Alzheimer’s disease (AD) clinical trials.

What We Do:
• GAP-Net site network: unique network of institution and private sites aligned to a single central IRB and set for rapid start-up
• Enable clinical trials:
  • Site Selection and Accelerated Study Start-Up Services
  • GAP Participant Services (GPS) and Recruitment Assistance
  • Additional Services: site optimization, protocol implementation tools, etc.
• Innovative Initiatives in North America: Medicare Advantage Program, pre-screening tools/processes, Lyft transportation, Citizen Scientist Award, Alliance Communities, etc.
Alzheimer’s disease is the 6th leading cause of death in the United States\(^1\)

More than **5 million** Americans are living with Alzheimer’s, and two-thirds of them are **women**

**1 in 3** seniors dies with Alzheimer’s or another dementia. It kills more than breast cancer and prostate cancer combined\(^1\)

Older Blacks/African Americans and Hispanics/Latinos are disproportionately more likely to have Alzheimer’s or other dementias

- Hispanics/Latinos are about **1.5 times** as likely to have Alzheimer’s as older Caucasians\(^1\)
- African Americans are **twice as likely** to have Alzheimer’s in comparison to older Caucasians\(^1\)

Importance of Early Detection in AD

Researchers believe future treatments will be most effective when **administered early** on in the disease stage.¹

As a result, **early detection** of Alzheimer’s disease will be critical.

A **cognitive assessment** evaluates different areas of brain function like memory, processing speed, and language.¹

Getting a **baseline** assessment is important to set a benchmark of your brain health for a future comparison.

In addition to cognitive assessments, the **recent development of biomarkers** for Alzheimer’s enables even earlier detection of the disease.

A **biomarker** is a measurement of what is happening inside your body, typically shown by laboratory and/or imaging tests²

Biomarkers in Alzheimer’s Disease

- Biomarker tests will help physicians diagnose Alzheimer’s and identify which individuals should receive treatments when they are available. Biomarkers also will be critical for monitoring the effects of treatment.

Minority representation in clinical trials evaluating biomarkers is essential to ensure biomarkers and future Alzheimer’s therapies work in all races and ethnicities.

- Drs. Howell & Garrett of Emory University have recently determined that race matters when looking at cerebrospinal fluid (CSF) – a leading biomarker in Alzheimer’s disease.
- African Americans had lower levels of biomarkers p-tau and AB40, but still had signs of cognitive decline.
- The studies concluded diagnosing AD in African Americans, especially early/prodromal AD, is especially challenging. These differences in biomarkers may lead to an under-diagnosis of Alzheimer’s. \(^1,^2\)

- Researchers believe that biomarkers, in combination with a commonly-used and validated cognitive assessment such as the Mini-Mental State Examination (MMSE), will increase physician efficiency and improve accurate diagnoses of AD. \(^3\)

- The most effective biomarker test or combination of tests may differ depending on where the individual is on the disease continuum and other factors.

\(^1\)Howell et al. Alzheimer’s Research & Therapy. 2017; 9(88)
\(^2\)Garrett et al. JAMA Network Open. 2019; 2(12)
\(^3\)Mattke et al. Diagnosis Assessment & Disease Monitoring. 2020; 12:e12081
What You Can Do Today

The Eight Pillars of Brain Health

* Stay Active
* Eat Well
* Sleep Well
* Exercise Your Brain
* Connect with Friends and Family
* Relax and Reduce Stress
* Control Risk Factors

* GET INVOLVED IN RESEARCH

Learn more at activ8yourbrain.org
THANK YOU!

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COGNITIVE EMPOWERMENT PROGRAM – PHYSICAL ACTIVITY LIVE SESSIONS

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PHYSICAL ACTIVITY SESSIONS

• Full body workout (Aerobic & Resistance training)
  • Balance, Functional Fitness, Dual Tasking
• Modifications to exercises
• Exercise along with trainer
• 45 Minute session – all fitness levels welcome
FUNCTIONAL FITNESS

Maintaining and Improving day-to-day quality of life

Simulate real-life/daily activities
DUAL TASKING EXERCISE

• Working on memory and recall
  • Quick math + Exercise Game

• Examples:
  • Walking while counting backwards from 100 by threes (97, 94, 91…)
  • Balance on one foot while recalling past meals you ate that day/week
  • Many more exercises – get creative!
YOU’RE INVITED

SESSION REGISTRATION: HTTP://BIT.LY/CEPLIVEREG

PHYSICAL ACTIVITY 10 – 10:45AM ON WEDNESDAYS

ALSO OFFERED: YOGA, TAI CHI, COGNITIVE TRAINING
THANK YOU!